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Conferences

(C-01 — C-08)

C-01

New pathophysiological and therapeutical strategies after ischemic stroke: roles of drug transporters, circadian rhythm and fetal microchimerism

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Neuroprotection therapies have made limited progress in recent years. Several compounds shown to be efficacious in animals were tested in humans in cost-expensive trials. Unfortunately, none of these studies were able to demonstrate efficacy under clinical conditions in patients. In order to establish treatments that are of benefit not only in animals but also humans, new strategies and research to understand pathophysiology of stroke are clearly needed, comprising (i) The role of solute carrier OATP1a5 in the brain pharmacotherapy after stroke: By preventing access of drugs to the CNS, the blood-brain barrier hampers developments in brain pharmacotherapy. Strong efforts are currently being made to identify drugs that accumulate more efficaciously in ischemic- brain tissue. We identified a solute carrier transporter OATP1a5, which is expressed in the CNS and playing roles in the accumulation of its substrates and their neuroprotective efficacy; (ii) The role of melatonin and circadian rhythm protein Bmal1 on the pathophysiological changes occurring after ischemic stroke: Circadian rhythm plays an important role in the regulation of almost all physiological conditions as well as pathophysiological processes such as cerebral ischemia. The role of these molecules in the brain neuroprotection will be discussed; and (iii) The role of fetal microchimerism on the brain injury and plasticity after ischemic stroke: Microchimerism is the presence of a very small population of genetically different cells in another person. Fetal microchimerism was described as the transition of stem cells of the fetus to mother during pregnancy. Here, the fetal cell transition from fetus to maternal ischemic brain tissue will be discussed. In this talk, aforementioned studies, pursued at the REMER at the Istanbul Medipol University will be presented.

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Keyword: ischemic stroke, microchimerism, circadian rhythm, OATP1a5

C-02

Neurobiological basis of migraine

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Migraine headaches show typical features of a visceral pain. The pain arises from stimulation of the nociceptive nerves around meningeal vessels and in meninges, not from the brain tissue. These nerves originate from the upper cervical dorsal root ganglia and ophthalmic branch of the trigeminal ganglion. Their central fibers terminate in the trigeminocervical complex in the brain stem. Because the brain does not have a representation in the sensory cortex, the painful signals from brain are reflected over the forehead or back of the head and neck. Fibers ascending from the brain stem to the thalamus and cortex give

branches to the amygdala and hypothalamus, which are associated with mood changes and feeling of sickness seen during migraine. Sensitization of the trigeminocervical nerve endings leads to sensation of the vascular pulsations, causing throbbing headache. Sensitization of brainstem neurons leads to allodynia in the head, especially around the eye. Allodynia emerges in 75% of patients within two hours. Convergence of the pain and visual pathways in the thalamus leads to photophobia. Activation of the trigeminocervical nerve endings releases neuropeptides, such as CGRP, which initiate a sterile neurogenic inflammation in dura. Triptans and CGRP antagonists relieve migraine headache by suppressing the neurogenic inflammation. Propagation of a depolarizing wave along the occipital cortex causes visual aura preceding the migraine headache. Aura activates the meningeal nociceptors generally within 20-60 minutes and induces headache. Neuronal stress caused by massive depolarization triggers neuroinflammatory signaling. This induces synthesis of inflammatory mediators, such as cytokines and prostanoids within astrocytes, which are then released to CSF. Dural neurogenic inflammation amplifies this warning signal from the parenchyma and translates it hours lasting headache. Mutations detected in familial cases are thought to cause aura and headache as a result of uncontrolled glutamatergic transmission. In non-familial cases, insufficient energy supply from the astrocytic processes to glutamatergic synapses may similarly trigger aura and headache. Transcriptional changes induced by migraine triggers such as sleep deprivation, prolonged hunger and psychological stress may provoke synaptic stress by reducing glucose/lactate derived from glycogen and initiate the inflammatory pathway and headache. Migraine attacks may also be triggered by brief hypoperfusion due to vascular factors (e.g. cerebral microembolism or CADASIL).

C-03

Principles of astrogliopathology

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The common and prevailing set of neurological thoughts considers neurones as the primary substrate of pathological progression. This "neurone-centric" concept, however, is changing. It has become universally acknowledged that the homeostasis of the nervous tissue is regulated by a complex fabric of neuroglial cells. Astroglia in particular represent a main element in the maintenance of homeostasis and providing defense to the brain. Consequently, dysfunction of astrocytes underlies many, if not all, neurological, neuropsychiatric and neurodegenerative disorders. Astrogliopathology is manifested by diametrically opposing morpho-functional changes in astrocytes, *i.e.* their hypertrophy along with reactivity or astrodegeneration with atrophy and asthenia. These complex plastic changes underlie pathophysiology of all neurological disorders including genetic (*e.g.* Alexander disease, which is a primary sporadic astrogliopathy), environmentally caused, (*e.g.* heavy metal encephalopathies or hepatic encephalopathies), neurodevelopmental (*e.g.* different forms of autistic spectrum disorder) or neurodegenerative (*e.g.* amyotrophic lateral sclerosis, Alzheimer's and Huntington's diseases).

C-04

Multimodal imaging and intrinsic connectivity networks in neurodegenerative diseases

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During the second half of the 20th century neuroanatomical tracing methods allowed the elucidation and mapping of the anatomical connectivity patterns of non-human primates. Due to extensive genetic homology, parallels were drawn between the primate and human brain, and human cognition was started to be understood as subserved by large-scale neuroanatomical networks that was based on those connectivity patterns. In time, different neurodegenerative processes as progressive disorders of distinct cognitive profiles have become associated with distinct neural networks. However, as human cognition is the unique feature of our species, analogy with the non-human primate brain could be far-fetched. Turn of this century witnessed a major breakthrough in human brain imaging, which allowed the imaging of functional neural networks in living human beings, also called resting state magnetic resonance imaging (rsMRI), the so-called intrinsic connectivity networks (ICNs). These networks were somewhat overlapping with the previously supposed anatomical connectivity patterns, but were not completely identical with them. In due time, evidence started to accumulate suggesting the vulnerabilities of different ICNs to distinct type of neurodegenerative processes. Currently, we are witnessing a paradigm-shift-like change in the area, where more than one-to-one correspondences between disease states and networks, dynamic interplays among ICN's, patterns of connectivity, which can be illustrated with graph theoretical approaches can be taken as signatures of different neuropsychiatric disorders ranging from Alzheimer's disease to schizophrenia. Recently, in our Hulusi Behcet Neuroimaging Lab we have undertaken a number of studies with the aim of contributing to this effort in the international cognitive neuroimaging community. In these studies we focus on rsMRI, but also use a plethora of other imaging methods, including task-related fMRI, diffusion tensor imaging (DTI) for axonal fiber tracking, arterial spin labeling (ASL) MRI for cerebral perfusion and MR Spectroscopy for brain

metabolic changes accompanying neurodegenerative disorders. This talk will report some of the yet to be published preliminary data from our lab in populations ranging from at risk populations to Alzheimer's and Parkinson's cognitive impairment continuum, to learning deficits in spinocerebellar ataxias.

C-05

New generation gene therapies: preclinical and clinical applications in rare neuromuscular disorders

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The development of genome editing technologies has given the chance to researchers to manipulate any genomic sequences precisely. This ability is very useful for creating animal models to study human diseases *in vivo*; for easy creation of isogenic cell lines to study *in vitro* and most importantly for overcoming many disadvantages that the researchers faced during the human classical gene therapy trials. So these are also known as new generation gene therapies. There exist many applications of these novel technologies in preclinical and clinical studies especially for uncurable rare diseases such as metabolic disorders, Duchenne Muscular Dystrophy (DMD), Huntington Disease, etc. The mostly studied neuromuscular disorder in this context is the DMD, manifests as severe muscle weakness that leads to an inability to walk, generally by age 12 and can be fatal, often causing premature death from cardiomyopathy or respiratory failure. Since the gene responsible for DMD, dystrophin, is too large for classical gene therapy trials; genome editing technologies create a chance to correct the mutated gene in the patient instead of adding a normal copy of dystrophin gene for therapy. In near future, as the preclinical studies continue to improve our knowledge about safety and efficacy issues in genome editing therapy strategies, the number of these trials will definitely increase to cover more diseases.

C-06

Cerebral cortex interneuron myelination: fundamental mechanisms and clinical implications

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Schizophrenia is highly heritable, yet its underlying pathophysiology remains largely unknown. The strongest known determinant for developing schizophrenia is family history. Recent genetic and induced pluripotent stem cell (iPSC)-based studies have converged on a model by which neuronal function, and in particular synaptic transmission, is a major pathophysiological mechanism of schizophrenia. However, functional neuronal alterations may arise either by direct cell-type autonomous changes to neurons themselves, or indirectly through a primary pathophysiological influence on other cell types that influence neuronal function. Previous studies have identified well-replicated structural abnormalities of white matter in schizophrenia, including in first-episode and treatment-naive patients. However, the causality of these changes has been difficult to ascertain. Seemingly unrelated abnormalities of parvalbumin (PV) interneurons in schizophrenia postmortem neocortex have also been consistently observed, the leading candidate mechanism for disease-related deficits in gamma oscillations. We have recently combined family-based rare variant genetic discovery with induced pluripotent stem cell (iPSC) modeling which now suggest that oligodendrocyte progenitor cell dysfunction should be considered as a candidate etiological cell type in schizophrenia. Our findings are consistent with the growing body of evidence implicating white matter integrity in schizophrenia neuropathology. Furthermore, recent in-depth characterizations of our group and others have established that fast-spiking PV interneurons in the neocortex and hippocampus have a stereotyped topography of myelination, exhibit a novel form of activity-dependent myelin plasticity, and highly determined by quantifiable biophysical metrics of axonal morphology. Together, these findings raise the intriguing possibility that some forms of schizophrenia might result from neurodevelopmental alterations of PV interneuron myelination.

C-07

Gut-brain axis: impact of peripheral regulators of energy balance on the reward system

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The brain's reward system is engaged in food intake, no matter whether this is driven by energy deficit or by the anticipated pleasure of a palatable meal. Human functional resonance imaging studies have revealed that brain pathways involved in (visual) food reward processing are regulated by dietary, hormonal and potentially other energy metabolic signals. The neural substrates engaged include the ventral striatum and rodent studies have shown that the ventral tegmental area is an important target for adiposity signals (such as leptin and insulin) and gut-derived hormones (such as ghrelin, $PYY_{(3-36)}$ and GLP-1). We have shown that the orexigenic hormone ghrelin engages the mesoaccumbal dopamine pathway involved in incentive salience and that this is important for its effects on food motivated behavior. Ghrelin also alters food choice, food anticipatory and other behaviours in ways that would lead us to question whether it is only a hunger hormone (for which its release and effects might be expected to be limited to a state of

negative energy balance) or whether we should instead be considered an "appetite-stimulating" hormone. Although obesity is associated with reduced sensitivity/resistance to certain circulating hormones, we recently discovered the existence of a novel body weight sensing mechanism that appears to be independent of leptin and other circulating hormones and labelled it the "gravitostat", revealed through loading studies in rodents (*i.e.* implantation of weighted capsules). Loading is effective for reducing body weight in obese animals. The mechanism appears to include a weight sensing mechanism in bone and we are currently exploring the mechanisms, including neural circuits involved.

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C-08

Translating neurodegeneration: modeling, mechanisms and gene-based therapeutics

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This seminar will give an overview and discuss the use of adeno-associated vectors for disease modelling and gene therapy in animal models of human neurodegenerative diseases such as motor neuron diseases (ALS and SMA) and frontotemporal dementia (FTD). In addition, using viral vectors, experimental models of disease including human cells and mouse model we will present and discuss mechanistic pathways and therapy development for ALS/FTD. Steps to translate gene therapy approaches into human clinical trials will be highlighted.

Symposiums

(S-1 — S-9)

Symposium 1

The Role of P2X7, NMDA and Cannabinoid CB1 Receptors in Experimental Epilepsy Models

S1-1

The role of P2X7 receptors in the experimental epilepsy models

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Adenosine triphosphate acts as a fast neurotransmitter through activation of ionotropic P2X7 receptors (P2X7Rs). P2X7Rs subunits form homomeric ATP-gated, calcium permeable cation channels. P2X7Rs have been found in neurons and glia in various regions of the central nervous system, including the cortex, brainstem and cerebellum. The role of P2X7Rs in epileptogenic processes has been widely investigated in different experimental models of epilepsy. Recently, the effect of intracerebroventricular injection of P2X7R agonist BzATP and antagonist A-438079 were studied on the penicillin-induced and absence-like epileptic activity in rats. Intracerebroventricular injection of a P2X7R agonist has been shown to increase the severity of seizures during status epilepticus induced by kainic acid injection, while pre- or post-treatment uses of P2X7R antagonists reduce seizure severity in mice. Intraperitoneal administration of P2X7R antagonist A-438079 has been reported to reduce the number of seizures during hypoxia in mouse pups, though not the number of post-hypoxia seizures, suggesting, the limited function of P2X7Rs. P2X7Rs knockout mice have shown greater susceptibility to pilocarpine-induced status epilepticus. P2X7R agonist BzATP caused an increment in the frequency of penicillin-induced epileptiform activity while antagonist A-438079 reduced it without changing the amplitude. Interestingly, agonist and antagonist of P2X7R did not alter the properties of epileptic activity in WAG/Rij rats in our studies. The studies on experimental epilepsy models suggest the limited function of P2X7Rs in the pathophysiologic mechanism of epilepsy. Several potential mechanisms have been suggested to contribute to the signalling cascades of P2X7Rs, including calcium-dependent manner. Complementary studies are necessary to explore the interaction between P2X7Rs and other systems effective in epilepsy.

S1-2

The role of NMDA receptor in the experimental epilepsy models

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Epilepsy is a chronic neurological disease caused by abnormal and hypersynchronous discharges of cortical neurons. The changing of the balance between GABA and glutamate in favour of glutamate leads to epilepsy. The glutamatergic system has two groups of receptors: metabotropic (mGluR) and ionotropic (iGluR). There are three types of ionotropic glutamate receptors: α-amino-3-hydroxy-5-methyl-4-isoxasolepropionic acid (AMPA) receptor, kainic acid receptor and N-methyl-D-aspartate (NMDA) receptor. NMDA receptors play a role in neurological diseases, including epilepsy. NMDA-mediated glutamatergic transmission was increased in the hyperthermia-induced zebrafish seizure model. Astrocytes modulate neuronal NMDA receptors leading to temporal lobe epilepsy. *Citrus aurantium* increased the latency of PTZ-induced seizures in zebrafish by NMDA and mGluRs. Nitric oxide / NMDA pathway may contribute to the biphasic effects of D-penicillamine on PTZ-induced seizures. Felbamate, reduced glutamate release by blocking presynaptic NMDA receptors in the entorhinal cortex-hippocampus slices. Micro RNA 219 suppressed seizure by modulating the calcium/calmodulin dependent proteinase II / NMDA receptor pathway. Dizocilpine, a non-competitive NMDA receptor antagonist, dose-dependently reduced orphhenadrine-induced generalized convulsive status epilepticus. In our laboratory studies, memantine, an uncompetetive NMDA receptor antagonist, reduced the frequency of penicillin-induced epileptiform activity. In another our study, memantine decreased the number of seizures, duration of seizures and the number of spike-wave activity in absance-like epileptiform-activity of WAG Rij rats. Further studies are needed to elicit the mechanism of NMDA receptor system and also the interaction of NMDA and other pathways in different models of experimental epilepsy.

S1-3

The role of cannabinoid CB1 receptors in the experimental epilepsy models

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The cannabinoid system is one of the key systems in the formation and control of epileptic seizures. Cannabinoid CB1 receptors are found in the brain, especially in the cerebral cortex, hippocampus, basal ganglia and cerebellum, whereas CB2 is abundant in the peripheral tissues and the immune system. CB1 receptors are thought to play a role in many brain pathologies including epilepsy because of their effects on the central nervous system. Herein, we investigated the effects of cannabinoid CB1 receptors on penicillin-induced focal seizures and absence-like seizures in WAG/Rij rats. Several cannabinoid analogs have

been tested in experimental epilepsy models and endocannabinoid system has been shown to play an important role in regulating seizure activity. Stimulation of cannabinoid CB1 receptors suppressed seizure activities in pilocarpine, maximal electroshock, pentylenetetrazole and kainic acid models. In contrast, blocking of CB1 receptors led to an increase in seizures. In addition, epileptic seizure activity increased the secretion of endogenous endocannabinoids. We found that CB1 receptor agonist, ACEA, decreased the spike frequency, wheras CB1 receptor antagonist AM-251 increased the spike frequency in penicillin model of experimental epilepsy. At the same time, ACEA reduced the number and duration of spike wave discharges, while the AM-251 significantly increased both of these parameters in genetic absence epileptic WAG/Rij rats. Cannabinoid CB1 receptors affect many intracellular signaling pathways. Therefore, they interact with many receptors and peptides which involved in epilepsy. We also investigated the interaction of glutamate NMDA receptors, leptin and ghrelin hormones with cannabinoid CB1 receptors. The use of cannabinoids in the treatment of epilepsy was approved by the US Food and Drug Administration (FDA) in 2018. We believe that cannabinoid treatment will become more common with the advanced studies.

Symposium 2

Metaphor at the Intersection Point of Neuroscience and Linguistics

S2-1

To trace the thought in the brain; neuroscience and metaphor studies

Lütfü Hanoğlu

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Metaphor is not only a type of figure of speech, but also a special mental processing system associated with people's thinking, judgment and imagination, and in this sense is an important part of human cognition. The metaphor language is thought to be built together with the neural infrastructure of thought and provides a suitable basis for the investigation of abstract thought. This area has yet to be studied very little, but it offers very important opportunities to explore the relationship between human thought and neural infrastructure and language. For this reason, it is increasingly the subject of neurolinguistics and neuroscience studies. The exploration of metaphors through neuroscience and brain processes provides a special opportunity to understand the human mind, especially the processes we call thinking, and how these functions are revealed in the brain. In recent years, analogy, categorical classification and conceptual mapping theories are the conceptual frameworks proposed to understand the metaphors and the way in which the brain performs this. In this speech; the current neuroscience approaches in this field will be reviewed by taking into account the data we have obtained from the different pathological samples we carry out through the dichotomy of memory and executive functions.

S2-2

Abstract thought disorder in Alzheimer's and frontotemporal dementia: understanding the metaphor language

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Metaphor is not just a type of figurative language, but a cruical part of human cognition, which includes a specific mental mapping system that affects people's thinking, judgment and imagination. Lakoff claims that, in Conceptual Metaphor Theory, metaphoric thinking and metaphorical understanding of a situation arise independent of language. Metaphor language is not only a matter of words, it is a matter of abstract thinking. A crucial idea in the study of metaphor is the conceptual metaphor system for characterizing a domain of thought. With this theorization, the metaphor language is thought to have been built together with the neural structure of thought and provides a suitable basis for studying abstract thought. The disorder of abstract thinking is evaluated on the ability to understand and explain nonliteral language such as idioms, proverbs in clinical and research routine. Although this procedure is not a consensused procedure on the application of dementia, the evaluation of complex language distortions on verbal tasks is considered to be an important diagnostic criterion in diseases such as Alzheimer's, MCI's (Mild Cognitive Impairement) and frontotemporal dementia. The metaphor language is frequently used as novel and conventional types in the ERP studies, which claims that N400, P200, P600 components are important in metaphor comprehension. In this presentation, the differences in the N400, P200 and P600 components in patients with Alzheimer's and frontotemporal dementia behavioral variants to the novel and conventional metaphor language compared to the literal and anormal sentences will be presented. Althought in Alzheimer's disease loss of memory is a main deficit, frontotemporal Dementia disease is characterized by a frontal deterioration. For this reason, it is aimed to observe the differences in response to novel and conventinal metaphor sentences in Alzheimer and frontotemporal dementia disesases.

This study was supported by TÜBİTAK (Project No: 117S470).

S2-3

How cognitive are metaphors? An ERP study

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Studies in the field of cognitive linguistics suggest that metaphors are not only literary, but that everyday language is inherently metaphorical in nature. For example, in the phrase "Dolar yükseldi. *'Dollar has risen.'*", which we often encounter in everyday language, the increase in the value of money is expressed by means of the verb "yükselmek 'rise'" which encodes information about

physical direction, and it is thought that the reason behind is that we have metaphoric coding in the form of "MORE IS UP, LESS IS DOWN" in our mind. The main purpose of this study is to determine how cognitive processing of such linguistic metaphors is performed in healthy subjects who are native Turkish speakers by using the methodology of Event Related Brain Potentials (ERP). For this purpose, 15 participants were presented with four different sentence types: a) literal (Adamın kalemi *düştü*. 'Man's pen fell.'), b) conventional metaphor (Adamın geliri *düştü*. 'Man's income fell.'), c) novel metaphor (Adamın güveni *düştü*. 'Man's confidence fell.') and d) anormal (Adamın teni *düştü*. 'Man's skin fell.'). In order to determine whether the cognitive system is sensitive to different types of metaphors, these conditions are also formed in three different categories of metaphors, namely, direction metaphors, ontological metaphors and structural metaphors. While the participants were reading the sentences silently, the ERP was recorded with the 32 channel EEG system. Sentence Type (literal, conventional, novel, anormal) × Metaphor Type (direction, ontological, structural) × A(nterior) - P(osterior) distribution (front area and back area) × LAT(eralization) (right and left hemispheres) have been used in the statistical analysis. The results of the study revealed that cognitive system is sensitive to different forms of metaphors.

This study was supported by TÜBİTAK (Project No: 117S470).

S2-4

Conceptual metaphor theory: experience and embodiment

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The *mind-body* problem refers to a dichotomy that has been introduced into history of ideas by Cartesian philosophy. The various developments in different fields of cognitive science over the years, however, yielded this dichotomy untenable in the current context. One such recent contribution to cognitive science in recent years comes from cognitive linguistics studies with the introduction of *Conceptual Metaphor Theory*, which asserts that linguistic expressions of experiences via embodiment are fundamental conceptual tools of our understanding. In its broadest definition, a conceptual metaphor refers to understanding of one domain of experience (generally an abstract one) in terms of another (generally a concrete one). Hence, following from this broad definition, a conceptual metaphor simultaneously refers to the process and the product itself. The conceptual metaphors, however, are not confined to particular text types where they are created and used to enhance the local linguistic expression as suggested in traditional studies. On the contrary, they are found in all text types and are pervasive in everyday language as devices for conceptualizations. For example, a quite ordinary expression like *close friend* can hardly taken as a sample of creative use of language for artistic purposes yet conceptualizes a social relationship via a specific measure for distance. In the formation of conceptual metaphors, there occurs a set of complex *mappings* between items of the *source* domain (concrete) and the *target* domain (abstract). In the process of mapping between source and target domain, we find linguistic manifestations of embodiment. For example, in the expression of highly complex emotion experiences with multitude of components, we find frequent use of the conceptual metaphor of *THE BODY IS A CONTAINER FOR EMOTIONS* (e.g. *filled with anger*, *overflow with joy*, *the happiness in her eyes*). The conceptual metaphors, as in the expression of abstract emotion concepts, are also pervasive in the expression of ordinary daily conceptualizations of time, state, causality, and purpose, among others. While the conceptual metaphors are universal tools for human understanding of abstract concepts, they tend to display variations among different cultures only in the degree of emphasis. The body as a container for emotions, for example, is found in all cultures with differences in parts of the body lexemes that goes into the linguistic expression of the conceptual metaphor. Some languages, including Turkish prefers the use of a very generic term inside (*iç*, as in *içim acıdı* 'my inside hurts') some others prefer more specific terms referring to particular body parts which is locus of the experience. This paper will concentrate on conceptual metaphors of emotional experiences and the linguistic means of expressing such states in Turkish.

Symposium 3

Biobanking, Molecular Diagnosis, Biomarkers and Gene Therapy in Neurodegenerative Diseases

S3-1

Genetic components of neurological disorders

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Genetic risk factors that underlie many rare and common neurological disorders remain poorly understood partly because of the multifactorial and/or heterogeneous nature of these complex conditions. Next generation sequencing (NGS) based genetic tests are becoming first trier diagnostic applications for patients with neurogenetic disorders, given the decreasing costs and rapid turnaround of results in NGS applications. This seminar will focus on the collaborative efforts for interpretation of genomic data, implications of this data for patients and also how subsequent research is guided. The importance of biobanking will be underlined within the context of data production, interpretation and storage. Several neurological conditions are used as interpretation models.

S3-2

MicroRNA biomarkers in neurodegenerative diseases

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MicroRNAs (miRNAs) are small, single-stranded noncoding RNAs of 17-25 nt length. They are considered as one of the major post-transcriptional regulators of gene expression in animals, plants, and unicellular eukaryotes. miRNAs participate in silencing the genes upon binding to their mRNA target sequences. miRNA levels are controlled strictly in order to maintain cellular functions. It has been recently understood that deregulation of miRNA expressions is directly linked to the molecular pathology of human genetic diseases. For that reason, regulation of the maturation pathways of miRNAs and changes in their expression levels at certain pathological conditions should be considered as key factors in understanding the molecular mechanisms of the diseases. In conjunction with this, miRNA deregulation patterns can serve as important biomarkers for diagnostic, prognostic, and treatment purposes for most of the genetic diseases. Among them, neurodegenerative diseases take the most attention since they are usually late onset and progressive conditions with overlapping mechanisms, and there is no cure yet. In neurons, miRNAs are ubiquitously expressed and perform important roles in neuronal differentiation, synaptogenesis and neuronal plasticity. There's increasing evidence that miRNAs are deregulated at the very early stages of neurodegeneration, their expression levels change in response to medical treatments and they can be easily detected in the biological fluids. It has also been shown that inhibition of upregulated miRNAs or enhancement of downregulated miRNAs can be used in the treatment of neurodegenerative conditions. These findings make the miRNAs powerful and non-invasive biomarkers in the diagnosis, prognosis and treatment of neurodegenerative disorders.

S3-3

Gene therapy for neurological disorders

Esra Battaloğlu

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Convergence of recent key developments lead to important progress in gene therapy for neurological disorders. The research to shed light to the genes and underlying molecular mechanisms responsible for these diseases is increasing our knowledge and many genes and mutations have been identified for monogenic diseases. These findings reveal new targets for gene therapy approaches. The recently developed genetic tools allow gene replacement for loss of function and gene silencing for gain of function mutations. Besides, Adeno-associated virus (AAV) has been shown to target both central and peripheral nervous systems making it an advantageous vector to deliver the transgene safely and permanently with a single dose. As a result of these advances, the number of clinical trials of gene therapy for neurological disorders are increasing rapidly. Thirty-seven clinical trials for neurological disorders are ongoing and in 20 of those AAV viruses are being used as vectors. Most of these trials are focused on Parkinson, Alzheimer and spinal muscular atrophy but the results of research in animal models for many other rare neurological disorders are highly promising. These findings implicate that the number of trials will increase in near future. The design and production of the transgene, its cloning into a vector and delivery to the patient are the major steps of the gene therapy approach. Use of CRISPR-Cas9 system in transgene design is preferred most since it is now commonly used in molecular genetics laboratories with ease, allows both gene silencing and replacement, and it is safe. Construction of minigenes, micro-RNA mimics, and genes for antibodies are also possible approaches for producing transgenes. These advances in gene therapy unraveled the factors that should be improved. The absence of biomarkers complicates the determination of the pharmaceutical effect of the transgene after delivery. We still need to find the answers for several questions for effective gene therapy such as, at which stage/stages of the disease gene therapy can be used, what should be the dose of AAV/transgene, how long the transgene will be expressed in the target tissue, and which delivery procedure should be preferred.

Symposium 4

Neuroscience-Based Personalized Medicine Treatments

S4-1

Neuromodulation treatments

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Neuromodulation treatments include transcranial magnetic stimulation (TMS), deep TMS (dTMS), transcranial direct current stimulation (TDCS), electroconvulsive therapy (ECT) and deep brain stimulation (DBS). From a historical perspective, the first use of neuromodulation treatment (ECT) dates back to centuries ago. TMS involves applying magnetic pulses to the brain. Currently use of TMS for treatment resistant depression is approved by Food and Drug Administration (FDA). Beyond depression, TMS can be used in several disorders including obsessive compulsive disorder (OCD), bipolar disorder and stroke. dTMS can apply magnetic stimulation to areas inaccessible by the conventional TMS such as insula and anterior cingulate cortex. The use of this method in depression and OCD is also approved by FDA. TDCS means applying direct current directly to the brain. It is most commonly used for depression and cognitive problems. A more recent neuromodulation treatment is DBS, which involves surgical placement of deep electrodes into the brain tissue to alter neuronal activity. Although this method is most commonly used for Parkinson's disease, studies showed efficacy in depression, OCD and addiction. Neuromodulation treatments are can be effective especially for treatment resistant cases. Careful selection of patient, method and indication are factors that would increase the efficacy.

S4-2

Pharmacogenetics applications in neuropsychiatry

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Pharmacogenetics has become one of the most important issues of today and it is a discipline that includes studies to help the physicians to regulate the most appropriate drug and treatment protocol by following the changes caused by both pharmacodynamic and pharmacokinetic data depending on the genetic variations of the individuals (personalized medicine). The levels of expression of proteins such as cytochrome P450 enzymes, drug receptors and drug carriers, which play a role in drug metabolism, are changed by mutations that occur with SNPs, microsatellite repeats, insertion and deletion. 1/1000 part of the human genome has the above-mentioned mutations, and ~10,000 of this ratio is related to pharmacogenetics. Phase I and Phase II enzymes that play a role in neuropsychiatry and how they are effective in treatment with PM, IM, EM and UM characteristics will be discussed.

S4-3

Medical data analysis using deep learning algorithm

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Conventional machine learning algorithms are widely used in the processing and classification of biomedical data in the literature. However, in recent years, it has become a necessity to use a multilayered learning network due to the increase in the resolution and quantity of the data. The concept of deep learning comprises the whole set of applications that separate sub-classes with high performance, especially in the case of the existence of multi-dimensional data and insufficient human-decision making processes. These methods have the ability to examine the inter-departmental interactions of data in depth. Deep learning is superior to conventional machine learning methods since the classification capability of the model is better if the data size gets larger despite a complex patterns exit. In addition, when the data size is expanded, classification performance is clear compared to standart conventional machine learning methods. Electroencephalography (EEG) data can be expressed in high-dimensional, complex and spatial domains. It is precious for analysis using deep learning-based networks as they have the potential to work with large datasets. Deep learning models developed for the analysis of EEG signals are expected to automate many repetitive cognitive tasks. This review article covers the general introduction of deep learning architectures used in the field of biomedical and neuroscience, the applications of these architectures on EEG-based analytical tasks, possible difficulties encountered and possible solutions. As a result of a detailed study, it is underlined that deep learning methods extract complex patterns in the clinical or cognitive data and present a strong method to determine the abstract relationships between different data types. This study also addresses the needs of deep learning-based applications in clinical practice and neuroscientific research and aims to provide researchers with an overview of the deep learning-based analysis methodology of EEG signals and potential challenges in future research.

S4-4

The future of qEEG biomarkers in psychiatry

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Quantitative electroencephalography (qEEG) means converting brain oscillations recorded using electroencephalography to quantitative values. The values obtained via this method can also be used to visualize brain activity as topographic maps. qEEG has been used as a diagnostic aide for more than a quarter century. It is well known that frontal alpha asymmetry is increased in patients with depression. In addition, the use of frontal theta increase as a diagnostic tool in ADHD has been approved by USA Food and Drug Administration (FDA). Besides these disorders, biomarkers for diagnosing bipolar disorder, obsessive compulsive disorder, schizophrenia, Alzheimer's disease were identified. Recently emerging research findings suggest that qEEG can also be used to predict treatment response and resistance beforehand. Such use of qEEG is important from a personalized medicine perspective. In this presentation, I will aim to give a summary of the history and current use of qEEG in psychiatry in addition to providing future directions.

Symposium 5

Computational Physiology of the Basal Ganglia and of their Disorders, Anatomical Considerations and Neurosurgical Implications

S5-1

Computational physiology of the basal ganglia and of their disorders and therapy

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The striatum and the subthalamic nucleus (STN) constitute the input stage of the main axis of the basal ganglia (BG) and together innervate BG downstream structures. The subthalamic nucleus (STN) activity shapes the main features of BG downstream activity, whereas the striatum probably provides the fine details.

This STN driving of BG downstream activity may explain why the STN is such an effective site for deep brain stimulation (DBS) in Parkinson's disease and other BG disorders. Following MPTP intoxication, and the development of Parkinsonism, the STN neurons are engaged in synchronized beta oscillations even during deep sleep. However, these synchronized oscillations are episodic, and STN long (>2 seconds) beta episodes can be detected only after MPTP treatment. Today, DBS systems are manually adjusted every 1-3 months during visits to the doctor's office. Thus, DBS treatment is not optimally adjusted to the patient real life and to the dynamic nature of Parkinson's disease. We suggest that a better treatment of BG disorders would be achieved by personalized closed-loop adaptive DBS that would inactivate the basal ganglia only when they "misbehave", *i.e.*, following detection of STN long beta events.

S5-2

Parkinson's disease and deep brain stimulation (DBS)

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Parkinson's disease is the second most frequent known progressive "synucleinopathy" following Alzheimer's disease and it affects almost 1 % of the population aged over 65 years. The prevalence of Parkinson's disease, which increases twofold for every decade of a person's life, has caused more careful investigation of mortalities and morbidities related, and development of therapeutic options. Following the manifestation of anatomical and especially computational physiology of basal ganglions, assessments has been concentrated on stimulation based reversible methods rather than ablative and irreversible surgical procedures. Deep brain stimulation (DBS) method for Parkinson Disease has been developed as a natural consequence of this course. Patient and target election plays a crucial role in treatment of Parkinson's disease with DBS method. Only true appropriate candidates should be chosen. Detailed neurological examination should be done primarily, and one should be certain that the other potential medical therapies and combinations had been tried. In addition to neurological assessment, candidates' psychiatric and neuropsychological analyses should be done by the related disciplines. Psychiatric and cognitive examination of DBS candidates plays a crucial role in choosing the target nucleus. Both subthalamic nucleus (STN) and globus pallidus Interna (GPi) can often be chosen as the surgical target in treatment of Parkinson's disease with DBS. Targeting each of these nuclei has some advantages and disadvantages on one another. Clinical situations which can be improved, which cannot be provided advantage, and contraindications of DBS Method should be determined with caution, and following the election of the patient, appropriate target should be chosen. Afterwards, the election surgical technique comes into the forefront. Regarding to surgical technique, if the patient undergoes general anesthesia, "interventional MRI" (iMRI) is used and surgical procedure is performed with or without microelectrode-recording system. If the patient is awake, microelectrode-recording system during lead placement can be used. In the future, improvements in implants and leads is predicted to result in enhancement of appropriate stimulus rate, decreases in side-effects, increases in benefits gained, and perhaps better understanding of pathophysiology of Parkinson's disease, and helping the development of new treatment protocols.

S5-3

New insights of the functional anatomy of basal nuclei network

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The basal nuclei (BN) are defined as the feed-forward part of a closed circle connecting all cortical areas sequentially through the BN direct and indirect pathways back to the motor cortex. In the conventional D1/D2 direct/indirect model of the BN, "direct pathway" is a monosynaptic GABAergic inhibitory projection from the striatum to the GPi/SNr, whereas the "indirect pathway" projection is polysynaptic and dis-inhibitory through the GPe and the glutamatergic (excitatory) STN. However, recent basic sciences based and theoretical studies have revealed that the BN connectivity is more complex than the simple connectivity depicted by the D1/D2 direct/indirect model. This explanation is also having shortages in explaining the dynamic patterns of BN activity and Parkinson's disease and ignores the emerging roles of the BN in reinforcement learning and behavioral adaptions to the changing environment. More modern computational models of the BN treat the BN as an actor/ critic reinforcement learning network. The main axis or the actor part puts into action the mapping between states and actions (behavioral policy), and the critic calculates the mismatch between predictions and the actual state (prediction error). The reinforcement actor/critic model of the BN has revolutionized current understanding of physiological mechanisms of model-free (procedural, implicit) learning and may provide insights into certain BN-related disorders such as akinesia and levodopa-induced dyskinesia. General prediction of the next generation of DBS devices will exploit BN actor/critic multi- objective optimization algorithms and will provide even better therapy for human patients.

Symposium 6

A Multidirectional Approach to a Complex Neurodegenerative Disease: Anatomy, Physiology, Genetics and Biochemistry of ALS

S6-1

The complex biology of ALS and G93A rats as models of disease

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ALS is a progressive neurodegenerative disease, characterized by the degeneration of motor neurons in the brain and spinal cord. The upper motor neurons make direct or indirect connections with lower motor neurons, which innervate skeletal muscles and trigger their contraction. Similar to most neurodegenerative diseases, ALS is usually a late-onset disease, starts focally and spreads to the paralysis of almost all skeletal muscles, thus ALS is relentlessly progressive and invariably fatal. Still the variability in disease duration is large, with some patients dying within a year after onset and others surviving for several years. Large differences in ALS survival and AO within the same family suggest the existence of other factors modifying the phenotype. Why some subsets of motor neurons, eg those that innervate the extraocular muscles and the sphincter are spared until late into disease is not understood. ALS is classified into two categories as familial (10 %) and sporadic ALS (90%), fALS and sALS are clinically very similar. Patients who do not have affected relatives are said to have the sporadic form. FALS is caused by mutations in a heterogeneous set of genes. In fact, the increasing number of genetic factors identified in recent years points to a great heterogeneity of ALS at molecular and mechanistic levels. When ALS has its biological onset is unknown. In rodent models of fALS, all overexpression models, abnormalities in excitability, axonal transport and neuronal architecture are present as early as embryonic development. Still, as in humans these animals develop no clinical signs until late in adulthood. Thus, biologically the disease may start early in life and become clinically apparent much later, the reasons for this are unknown. In the framework of this study transgenic G93A rats were used as model systems to investigate disease progression by recording the physical strength and weight loss of the animals and measuring the biochemical parameters at different disease stages. DNA was isolated from rat tails using the DNeasy Blood & Tissue Kit. After measuring the yield of the DNA, PCR was performed using the primers and the protocol supplied by the manufacturer. The 160bp PCR product was visualized on a 2% agarose gel. The ratio of incorporation of the human gene into rats was 128 transgene-positive vs 100 gene-negative in a total of 228 samples genotyped.

S6-2

Comparison of the inhibitory circuitries in healthy people and patients with ALS

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Spinal neurons shape the inputs on the motor neurons and regulate their firing properties. However, in some cases, these neurons may be impaired which results in imbalance of inhibition-excitation homeostasis. In turn, motor neurons may be subjected to extreme calcium influx and degenerated in long-term, referred to as excitotoxicity. Malfunction in the inhibitory neurons may lead excitotoxicity due to reduction in inhibition of the motor neurons, such as in Amyotrophic Lateral Sclerosis (ALS). Despite the efforts in the last decades, the exact mechanism behind ALS development is yet to be discovered. Therefore, we aimed to shed light on excitotoxicity phenomenon by investigating two inhibitory circuits: 1. Cutaneous silent period; 2. Recurrent inhibition by Renshaw cells. To evoke cutaneous silent period, we electrically stimulated the cutaneous receptors in little and ring fingers and investigated the inhibitory silent period on the voluntarily-recruited single motor units of first dorsal interosseus muscle. We showed that cutaneous silent period in the more affected hands by ALS was shorter compared to less affected hands as well as than healthy people. This finding revealed the role of excitotoxicity as it is involved in ALS. Next, we will study the recurrent inhibition towards further understanding of excitotoxicity phenomenon.

S6-3

Biochemical and metabolic effects of SOD1 mutation in amyotrophic lateral sclerosis

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Amyotrophic lateral sclerosis (ALS) is a motor neuron disease which causes motor neuron death, and skeletal muscle degeneration. ALS is initiated by the death of nerve cells that regulate muscle movement. About 5% to 15% percent have familial form and others are accepted as sporadic ALS disease. Chemical imbalance (higher than normal concentration of glutamate), disorganized immune response, abnormal forms

of various proteins, smoking, environmental toxin exposure, viruses, metabolic diseases, cancer, neuroinflammation, head trauma, pesticides, accumulation of mercury and other heavy metals, electromagnetic field, electric shock, a higher level of physical fitness and lower body mass index (BMI) than average are risk factors for ALS. Mutations in the Cu, Zn superoxide dismutase (SOD1) is the second most common cause of familial forms of ALS (accounts for 10–20% of familial ALS). More than 150 single point mutations of SOD 1 gene are found to be related to familial ALS. In ALS disease, biochemical pathways and the mechanisms are not completely understood. The aim of our study was to characterize biochemical changes in serum, several organs and tissues, from an enzyme activity, trace element and minerals and oxidative stress point of view in SOD-1 related ALS. We measured various enzyme activities such as alkaline phosphatase, alanine aminotransferase, amylase trace element and mineral levels in serum female and male SOD (G93A) rats. This study will explain variations of various antioxidant enzyme activities and trace element and vitamin levels in female and male SOD (G93A) rats for understanding the ALS disease progression.

S6-4

TRiALS study group - introduction and clinical trials

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TRiALS study group is a multi-centre, international research group focusing mainly on evaluation of motor neuron disorders based on clinical, genetic, and cyto-chemical perspectives, and degenerative processes in in neurons. *TRiALS* group investigators study on ALS patients, animal models, and cell cultures focusing mainly on enlightening of pathogenesis and early diagnosis in motor neuron disease. Considering heterogeneous presentation and heterogeneous progress of the disease, the clinical trials on motor neuron disease patients could be listed as; use of MRI to detect reflection of different involvement patterns on central nervous system, the use of motor unit number estimation techniques, CMAP scanning, and MUNIX to detect early motor neuron degeneration, multi-centre ONWEB-dual ontogenetic trial, evaluation of sensory nerve degeneration in ALS patients and the use of degeneration in sensory nerves for diagnostic purpose, evaluation of frontal lobe dysfunction in ALS patients, evaluation of respiratory dysfunction in ALS patients, cutaneous silent period recordings and evaluation of Renshaw circuit in ALS patients.

Symposium 7

H2020 Project AUTOIGG Showcase: Building an Inovative Medical Device Through Networking

S7-1

Spontaneous electrical activity of developing neurons in the cerebral cortex

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Information about development of the human cerebral cortex (proliferation, migration, and differentiation of neurons) is largely based on postmortem histology. Physiological properties of developing human cortical neurons are difficult to access experimentally and therefore remain largely unexplored. We performed electrical recordings from individual cells in acute brain slices harvested postmortem from the human fetal cerebral cortex (16th– 23th gestational week). Neurons located in the SP exhibited the highest level of cellular differentiation, as judged by their large sodium currents, ability to fire repetitive APs, and presence of cluster of sodium channels in the axon initial segment. Before the human cortex is able to process sensory information, young postmitotic neurons must maintain occasional bursts of action-potential firing to attract and keep synaptic contacts, to drive gene expression, and to transition to mature membrane properties. Before birth, human subplate (SP) neurons are spontaneously active, displaying bursts of electrical activity (plateau depolarizations with action potentials). Using whole-cell recordings in acute cortical slices, we investigated the source of this early activity. The spontaneous depolarizations in human SP neurons at midgestation were not completely eliminated by tetrodotoxin - a drug that blocks action potential firing and network activity - or by antagonists of glutamatergic, GABAergic, or glycinergic synaptic transmission. We then turned our focus away from standard chemical synapses to connexin-based gap junctions and hemichannels. PCR and immunohistochemical analysis identified the presence of three connexin isoforms (C×26, C×32 and C×36) in the human fetal cortex. However, the connexin-positive cells were not found in clusters but, rather, were dispersed in the SP zone. Also, gap junction-permeable dyes did not diffuse to neighboring cells, suggesting that SP neurons were not strongly coupled to other cells at this age. Application of the gap junction and hemichannel inhibitors octanol, flufenamic acid, and carbenoxolone significantly blocked spontaneous activity. The putative hemichannel antagonist lanthanum alone was a potent inhibitor of the spontaneous activity. Together, these data suggest that connexin hemichannels contribute to spontaneous depolarizations in the human fetal cortex during the second trimester of gestation.

S7-2

Automated functional screening of IgGs for diagnostics of neurodegenerative diseases (H2020 AUTOIGG project)

Pavle Andjus

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We will present the scientific background, rationale and state of the art of the project AUTOIGG. The project proposes to organize the exchange of staff of three Academic institutions from Serbia (coordinator), Turkey and Finland, two SMEs from France and Turkey and three TC institutions (two from USA and one from Costa Rica) towards the production of an innovative automated multifunctional device for diagnostics of neurodegenerative diseases. The objectives addressed will be: development of experimental cellular models and procedures with immunoglobulins (IgGs) from patient sera as diagnostic and prognostic technologies related to neurodegenerative diseases (particularly based on studies of amyotrophic lateral sclerosis - ALS); defining mark-up characteristics of the standardized *in vitro* approach for personalized diagnostic protocols; design of a small-scale platform based on automated fluorescence microscopy.

The idea to use ALS IgGs for *in vitro* diagnostics is based on previous experimental results (Andjus et al. J Physiol 1997;504 (Pt 1):103; Milošević et al. Cell Calcium 2013;54:17; Stenovec et al. Acta Physiol (Oxf) 2011;203:457; Milošević et al. Front Immunol. 2017;8:1619). After standardization of *in vitro* procedures, it should offer robust multipurpose processing of single samples on cultured cells in microfluidic setups that can give a complex information based on different cellular signalling responses as recorded by electrophysiology/voltage sensitive

dyes or fluorescent imaging of Ca2+, ROS generation and intracellular vesicle mobility. Using this combination of sensitive readouts, ALS IgGs will thus be tested in order to differentiate mark-ups of disease phase and severity for personalized *in vitro* diagnostics. In order to do this in a robust point-of-care setup an innovative automate microscopy system will be designed.

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S7-3

Computer assisted methods for classification and analysis of neuroglial structures

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Neuroglial cells have several essential roles in the nervous system. Oligodendrocytes myelinate neurons accelerating impulse propagation and supporting neuronal survival. Astrocytes contribute to formation of a privileged environment within the central nervous system (CNS). Dysfunctional neuroglia is observed in several neurodegenerative diseases. For example, demyelination due to immune attack is the culprit of multiple sclerosis (MS). Response of astrocytes to immunoglobulin Gs (IgGs) isolated from amyotrophic lateral sclerosis (ALS) patients differ from their response to IgGs isolated from controls. Our goal is to develop computer software to assist researchers in their analysis of myelin and astrocytes. First, existing and custom machine learning based algorithms were compared in classification of myelin from fluorescent microscopy images. Both our custom convoluted neural network and support vector machine algorithms performed more accurately then other algorithms (over 98% accurate). The methodology will be used for drug screens against demyelinating diseases such as MS. Second, we are evaluating different segmentation strategies to accurately classify astrocytes in time series images. We aim to identify astrocytes and extract calcium (Ca2+) dye intensity variation data over time. IgG from sera of ALS patients induce Ca2+ transients in cultured rat astrocytes. We aim to automate analysis of analysis of Ca2+ intensity variation in order to develop IgG from sera of ALS patient as diagnostic marker of the disease.

Symposium 8

Near Future of Treatment of Neurological Diseases (Symposium of The Turkish Neurological Society)

S8-1

The never-ending fire of stroke: inflammation

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There is a two-way and complex interplay between cerebrovascular diseases and the immune system. The contribution of inflammatory states to stroke pathophysiology, directly or indirectly, is being studied for many years and the details are still not fully revealed. On the other hand, many immunological changes occur both in the brain tissue and systemically in the post-stroke period. The local inflammatory response, in which many inflammatory cells, including the leukocytes migrating from the systemic circulation and local microglia, and the cytokines released from these cells, play a role, accumulates over the hours and days following stroke. Although this response contributes to tissue damage, release of trophic factors at the same time creates an environment suitable for neurogenesis and neuroplasticity. From the perspective of systemic immune response, a severe state of immunodepression is observed following stroke; hypothalamus-pituitary-adrenal system, sympathetic nervous system and vagus nerve play a key role in this response. Observation of local and systemic inflammatory changes in the post-stroke period has led to studies focusing on the treatment of these processes. However, the complexity of the immunological response, the presence of numerous molecules and cellular pathways in this complex process and the possible positive effects of inflammation on the healing process constitute the biggest challenges in these efforts.

S8-2

The role of lipoxygenase inhibitors in ischemic and hemorrhagic stroke

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Stroke is the second leading cause of death and first disability reason in the world. There are two types of stroke: ischemic and hemorrhagic, approximately 85% is ischemic stroke. One patient dies every 4 minutes due to stroke. In addition to the deaths, the economic burden caused by the morbidity constitutes an important part of the health expenditures. For this reason, special attention is paid to the research on stroke therapies. However, the only treatment option approved by the FDA is tPA that has many limitations including the low number of treated patients because of narrow time window, the risk of bleeding and other complications in elderly patients and patients with chronic diseases. Therefore, it is important to invent new options for stroke treatment. 12/15 lipoxygenase (LOX) is known to have a role in the development of atherosclerosis, diabetes, stroke, heart failure, hypertension and brain ischemia-recanalization injury. In experimental ischemia models, 12/15 LOX inhibition has been shown to reduce infarct size and brain edema in the acute period and accelerate the healing process with axonal regeneration and revascularization effects in long-term period. Recent studies showed that 12/15 LOX inhibitors reduce tPA-associated hemorrhage and edema used in ischemia treatment. 12/15 LOX inhibitor was found to limit hemorrhagic transformation in middle cerebral artery occlusion model applied and warfarin treated mice. A study showed elevated cerebrospinal fluid levels of 12-Hydroxieicosatetraenoic Acid,

lipoxygenase metabolic product, in subarachnoid hemorrhage patients and in the experimental model of subarachnoid hemorrhage 12/15 LOX inhibitor has reduced neuronal damage. Literature indicates that 12/15 LOX inhibition plays a role in reducing both cerebral ischemia injury and limiting the hemorrhage complication due to tPA therapy. In addition, 12/15 LOX inhibitor may have a protective role in decreasing neuronal damage caused by hemorrhagic transformation in stroke patients under warfarin treatment or after subarachnoid hemorrhage. These studies bring 12/15 lipoxygenase inhibition as an effective and reliable treatment option in clinic for ischemic, hemorrhagic stroke and hemorrhagic complications.

S8-3

Recent translational approaches to biomarker and neuroimaging in the diagnosis of Alzheimer's disease

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Terminologically, the stages of Alzheimer's disease (AD) are called asymptomatic, presymptomatic, pre-mild cognitive deficit (MCI), MCI, AD. Biomarkers and neuroimaging are important in AD. There is a latent neurodegenerative process that begins years before the diagnosis of dementia. In this process, neuroimaging, blood or CSF changes should be determined for the treatment that will prevent the development of the disease. According to the studies, CSF biomarkers are more sensitive and specific than those in the plasma. The staging of the disease is not only based on clinical terminology, but also according to the biomarkers. Changes in biomarkers may herald potential clinical changes. In addition, the relationship between parenchymal changes and glucose metabolism, when the hippocampal volume begins to decrease, amyloid and tau pathology can be detected by neuroimaging are factors that reveal the character of the disease. MRI and PET used for neuroimaging are important tools for understanding these changes. Studies have shown a low correlation between low levels of amyloid B, increased tau levels in CSF and hippocampal volume. Although amyloid beta and tau PET molecular imaging are recently updated, MR anatomic morphometric measurement (hippocampal volume) is more sensitive in the diagnosis of AH than BOS and PET biomarkers. Combination (hippocampal volume and FDG-PET) determines cognitive destruction better than CSF biomarkers. The advantage of MRI is that it shows cognitive impairment with high accuracy and is noninvasive and cheaper compared to CSF, PET studies. Diffusion Tensor Imaging (DTI) in AD, white matter change, decreased anisotropy and increased diffusion were seen especially in frontal, temporal lobes, cingulum and uncinate fasciculus, corpus callosum, and posterior cingulum. Functional MRI (fMRI) (Functional connections) has identified impaired functional connectivity networks. In addition, 18F-FDG PET Amyloid PET, Tau PET are used in the AD diagnosis. Both amyloid PET and Tau PET have more predictive of progression and pathophysiology. In the light of all these findings, all the markers, pathophysiological changes, and all the correlation analyzes (*i.e.* TNM classification) are included in the classification will provide more targeted diagnostic and treatment strategies in AD.

S8-4

New neuroprotective treatment approaches in Alzheimer's disease in the light of experimental and clinical studies

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The drugs of the treatment of Alzheimer's disease (AD) show action on acetylcholine, glutamate, amyloid plaque load, neurofibrillary tangles and neuroinflammation. In the last year of 2018, approximately 112 agents have been studied in the treatment of AD. The majority of these studies (65%) focused on modifying agents, 31% on neuropsychiatric symptoms suppressor, 4% on the smallest section on agents that improved symptomatic cognition. Anti-amyloid mechanism-based studies are leading among the modifying therapies. Epidemiological studies respond to the reason why so many studies are performed in AD. Until 2050, it is estimated that 7 million 85 aged and above, half of the people of 65 aged and above (51%) will have Alzheimer's disease. Thus, there is an urgent need for disease modifying therapies to prevent or delay the progression of AD. Similarly, studies on the neuropsychiatric symptoms and behavioural disorders of patients with symptomatic stages of AD should be increased. New experimental and clinical approaches have been focused on the protection of people with cognitive impairment but with a potential for Alzheimer's disease in whom CSF or PET has amyloid pathology or has a genetic burden. Phase III studies are ongoing. In addition, many agents have been tested under the heading of phosphorylation of tau, post-translational modification of tau, tau aggregation inhibitors, anti-tau immunotherapy. In addition, biomarkers play an important role in symptomatic and modifying therapy. Clinical and clinical studies of active and passive immunotherapies in AH and PSP are ongoing. New tau and B Amiloid targeted immunotherapy strategies are eagerly followed. In particular, a number of key questions regarding the selection of the immunogen, the tau species to be targeted, the safety and action mechanism, are waiting to be answered. The aim is to increase the number of personal treatments that are comprehensive and responsive to the patient's needs.

Symposium 9

Neuron-glia Interactions in Central Nervous System Development

S9-1

The connection between nervous and immune system in *Drosophila melanogaster*

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Drosophila glia originate from neural stem cells and strictly depend on the expression of a single transcription factor that makes the choice between the glial and the neuronal fates, Glide/Gcm. Glia ensure normal development of the nervous system, including the regulation of stem cell proliferation. They are also required for the function of the nervous system and act as immune cells in a broad range of pathological conditions, such as brain injury and degeneration. The *Drosophila* glia therefore display the combined features of the vertebrate micro- and macroglia, mesoderm-derived immune cells that invade the CNS during development and neuroectodermally derived cells, respectively. Microglia represent the professional scavenger cells of the nervous system, macroglia insulate/protect the axons and control the proliferative state of the CNS. Thus, the complex nervous system of vertebrates requires more cell types, calling for a division of labor occurring during evolution. Interestingly, the *Drosophila* Glide/Gcm transcription factor is also expressed and required in the immune cells of the fly called hemocytes. These are cells that patrol the organism and control the immune response outside the nervous system. Glide/Gcm inhibits the inflammatory response in these cells. This suggests that Glide/Gcm may have a function in immunity in vertebrates. Recent data support this hypothesis.

S9-2

PEA3 proteins in neuroglial circuitry?

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Pea3 subfamily of the ETS transcription factor superfamily has been implicated in metastasis, particularly in HER2/Neu-positive subclass of breast tumors, and was shown to regulate anchorage-independent growth and epithelial-to-mesenchymal transition of prostate cancer cells. Pea3 proteins were also shown to regulate normal development, including FGF-dependent differentiation of retinal cells, and regulate motor neuron circuit selectivity in the spinal cord. Our laboratory has for a long time been working on how such a neural circuit specificity could be generated by Pea3 proteins, and what surface proteins might Pea3 proteins regulate to bring about such a circuit specificity. On the other hand, glial cells, including astrocytes and microglia, are also vital for neural circuitry and have been in the past years shown to be functionally diverse among different brain within compartments, or unique subpopulations of glia that support adult neurogenesis. It is an intriguing question whether this diversity originates during development or acquired later with neuronal activity, and whether glial diversity can be exploited or indeed directed to remedy CNS disorders, and whether Pea3 proteins can be used to that purpose.

S9-3

The role of PEA3 proteins in neurons

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Pea3 proteins are a subfamily of the ETS transcription factor superfamily, consisting of Pea3, Erm and Er81. These proteins, which are expressed in different tissues exhibiting branching, play a role in a variety of events such as the formation of motor neuronal circuits in the nervous system, retinal differentiation, neurite extension. These proteins we have been working for many years in our laboratory soon began to be determined in our group by deciphering neurite extension mechanisms. The purpose of this present study is to understand the mechanisms of neurite extension through Pea3, to identify the genes which are regulated by Pea3. For this, novel target gene expression levels were investigated by microarray analysis and qPCR in Pea3 overexpressed various neural cell lines. The genes were classified by bioinformatic analysis, the pathways associated with neurons (neurotrophin signaling pathway, axon dynamics, etc.) were selected and the relationship between the genes in these pathways was examined and mapped by bioinformatic analysis. Our results showed that the members of Pea3 family regulate the expression of both common and unique genes in neuron-specific pathways at similar and / or different levels. In addition, the interaction mapping was created as a result of the informatics analysis. In order to elucidate which of these identified genes play a role in the selectivity of the motor neuron - sensory neuron circuits in Pea3 - overexpressed cells, studies on the relationship between different Pea3 family members should be conducted in a co-culture system and the role of the Pea3 in circuit formation system as well as neuroglial connectivity should be studied.

Panels

(PS-1 — PS-3)

Panel 1

RASopathies: RAS Pathway and Diseases

PS1-1

RAS pathway and diseases

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RAS is a member of small GTPases that regulate cell growth, proliferation and differentiation. RAS GTPases convey an extracellular signal to its target of effector proteins in cells. RAS cycles between the guanosine diphosphate (GDP)-bound inactive form and the guanosine triphosphate (GTP)-bound active form. The RAS/mitogen-activated protein kinase (MAPK) pathway is an essential signaling pathway that controls cell proliferation, differentiation and survival. Numerous studies have revealed that dysregulation of the RAS/MAPK pathway causes clinically overlapping genetic disorders, termed 'RASopathies' or 'RAS/MAPK syndromes'. Although each RASopathy has a unique phenotype, these syndromes have many overlapping characteristics, including craniofacial dysmorphology, cardiovascular abnormalities, musculoskeletal abnormalities, cutaneous lesions, neurocognitive impairment and increased risk of tumor (for a review of the details of each of these disorders, see Rauen4). These disorders include the following: (a) neurofibromatosis type 1 (NF1) caused by haploinsufficiency of neurofibromin; (b) NF1-like syndrome caused by haploinsufficiency of SPRED1; (c) Noonan syndrome (NS) caused by mutations in PTPN11, SOS1, RAF1, KRAS, BRAF and NRAS; (d) NS with multiple lentigines (NSML) caused by mutations in PTPN11 and RAF1;(e) Costello syndrome caused by activating mutations in HRAS; (f) cardiofaciocutaneous (CFC) syndrome caused by mutations in BRAF, MAP2K1/2 and KRAS; (g) Noonan-like syndrome caused by mutations in SHOC220 or CBL; (h) hereditary gingival fibromatosis caused by a mutation in SOS1; and (i) capillary malformation–arteriovenous malformation caused by haploinsufficiency of RASA1.

PS1-2

Clinical picture in two Ras-opathies: neurofibromatosis Type 1 and tuberous sclerosis

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Neurofibromatosis type 1 (NF1) and Tuberous Sclerosis (TS) are autosomal dominant single gene disorders. Major findings in NF1 pertain to neural tissues and skin, justifying the term "neurocutaneous disorder": pigmented spots, neurofibromas, alterations in brain myelin, optic pathway gliomas are common findings. In addition, macrocephaly, learning disabilities, and epilepsy can accompany NF1. However the term "neurocutaneous" does not cover the skeletal dysplasias, blood vessel stenosis, or short stature encountered in patients, all suggesting the involvement of mesenchymal tissue. Therefore the skin and the central nervous system having the same ectodermal embryologic origin fails to explain all features of NF1. The NF1 gene has a role in the neural crest. Neurofibromin, the product of NF1, interacts with the Ras pathway where mechanistic target of rapamycin (mTOR) functions are indispensable for neural crest development, proliferation, survival, and differentiation. Therefore the term "neural crestopathy" might be more representative of the pathogenesis as the neural crest induces differentiation of the tissues relevant to NF1 in embryonic life. A defective neural crest in NF1 explains the involvement of melanocytes, nerve sheaths, cranial bones and the high incidence of neuroendocrine tumors which all are of neural crest origin. Meningiomas and nerve sheath tumors of NF1 can also be attributed to defective neural crest, but also to the tumor suppressor function of the NF1 gene: tendency for neoplasms in NF1 is the result of the mutant gene being unable to regulate the Ras pathway. Tuberous sclerosis, another disorder affecting the RAS pathway, can be caused by mutations in one of the genes TSC1 and TSC2 whose products, hamartin and tuberin, interact with Ras. Brain, renal and lung neoplasms indicate the oncogenic nature of TS. Mechanistic target of rapamycin complex 1 (mTORC1) is activated in TS-associated tumors. Beside being cancer regulatory, the other major role of the Ras-MAPK and PI3K-AKT-mTOR pathways is in synaptic plasticity and behavior, resulting in cognitive problems and epilepsy. mTORC1 signalling affects neural progenitor cells, resulting in megalencephaly and increased cortical thickness. Experimental work indicates mTOR activation leads to hippocampal epileptogenesis. As in NF1, the main characteristics of TS are neurological and skin findings of which some can be attributed to neural crest defects: abnormal melanocytic distribution in the skin. The pathogenesis of other typical findings of TS: bone cysts, intracranial aneurysms are to be clarified, as are many aspects in the molecular pathogenesis of these multisystemic disorders.

PS1-3

Molecular mechanisms of neurofibromatosis type 1 (NF1) clinical variability

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Neurofibromatosis type 1 (NF1) is the most common neurogenetic disorder worldwide, caused by mutations in the neurofi-

bromatosis type 1 (NF1) gene. NF1 is caused by dominant loss-of-function (LOH) mutations in the NF1 gene, which encodes neurofibromin, a negative regulator of Ras proteins. A 360-amino acid region of the gene product shows homology to the catalytic domain of the mammalian GTPase-activating protein (GAP). This region is referred to as the NF1–GAP-related domain (NF1-GRD) and is encoded by the central part of the NF1 gene. The GAP proteins down-regulate the activity of the Ras oncoprotein by stimulating its intrinsic GTPase activity. Therefore, neurofibromin is part of the Ras-mediated signal transduction mechanism. Several genetic disorders are caused by dysfunction in gene products associated with this pathway, and owing to their common phenotypes, they have been recently classified together and termed as "Rasopathies." Three genes, EVI2A, EVI2B, and OMGP, are embedded within intron 27b of the NF1 gene. However, little is known about the function of these genes. A hallmark of the NF1 gene is its high mutation rate; almost half of all NF1 cases Although NF1 is a single-gene disorder with autosomal-dominant inheritance, its clinical expression is highly variable and unpredictable. NF1 patients have the highest known mutation rate among all human disorders, with no clear genotype–phenotype correlations. Therefore, variations in NF1 mutations may not correlate with the variations in clinical phenotype. Indeed, for the same mutation, some NF1 patients may develop severe clinical symptoms whereas others will develop a mild phenotype. Variations in the mutant NF1 allele itself cannot account for all of the disease variability, indicating a contribution of modifier genes, environmental factors, or their combination. Considering the gene structure and the interaction of neurofibromin protein with cellular components, there are many possible candidate modifier genes. Gaining a deeper understanding of the molecular basis of variable phenotypes may improve the prediction, treatment, and prevention of several NF1-related complications. These new findings will be crucial in providing more accurate genetic counselling. This presentation aims to provide an overview of the potential modifier genes contributing to NF1 clinical variability.

Panel 2
Ion Channels and Current Research Methods

PS2-1
Mechanosensitive ion channels

Nuhan Puralı

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Though the mechanosensation might be the earliest among all the senses, the mechanosensitive ion channels and the related structures, responsible for the conversion of mechanical stimulus into bioelectrical signals (mechanotransduction), has not been determined at scientific certainty yet. As a matter of fact, the evidences for the presence of the mechanosensitive channels largely based on the current recordings in patch clamp experiments only. Presently, no convincing information is available for the genetic and molecular properties of the mechanosensitive ion channels. The lack of information largely stems from the absence of appropriate preparations to perform experiments at cellular level, difficulty in generation and application mechanical stimulus, polymorphic nature of the mechanosensation and short list of specific pharmacologic tools. Recently, some improvements in the area has achieved and it was reported that various ion channels have been reported to be involved in mechanotransduction process. However, relevancy of those are a matter debate at present. For many years we have been working on an ideal mechanosensor organ preparation. Recently, in relation to a project funded by Hacettepe University we have attempted to clone the genes potentially related to the structure of mechanosensitive ion channel or channel complex. By using bioinformatic analysis and conventional cloning methods we have attempted to clone about ten genes which may potential be related mechanosensitive channel complex. We have cloned five of those targets with some success. We are very much excited particularly by one of them which has a substantial sequence similarity to Piezo channel proteins, proposed to be mechanosensitive by many authors. The present presentation is consisted of two parts; in the first part the present knowledge about the mechanosensitive channel (complex) has been discussed and in the second part the early outcomes of the ongoing investigation has been given.

PS2-2
Working mechanism of the ligand gated channel P2X7 purinoceptor

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P2X7 receptor is an ionotropic purinoceptor. ATP, ADP, UTP are the known natural ligands for purinoceptors. ATP is well known for its role in cellular energy metabolism. However it is also secreted from the cells via various mechanisms and acts as a neurotransmitter or an autacoid. ATP acts through binding and activating two main classes of membrane receptors; P2X and P2Y. P2Y receptors are G-protein coupled metabotropic receptors which can be activated by ATP, ADP and UTP. However P2X receptors are activated only by ATP and they are ionotropic receptors. P2X receptors have seven subtypes (P2X1-7). These subtypes have very different activation-inactivation kinetics and agonist selectivity. As P2X receptors are ligand-gated cation channels, they act through mechanisms of membrane depolarisation, Ca+2 influx, or K+ efflux. However P2X receptors, especially the P2X7 receptor significantly differs from other ligand-gated cation channels (such as Nicotinic Acetylcholine receptors, 5HT3 receptor) by its ability to permeabilise the membrane to large molecules and also to directly activate some intracellular signalling pathways, through some unclear mechanism, that does not involve ligand gated ion channel activity. Today P2X7 receptors thought to play a significant and even central role in growth

and metastasis of tumor cells, and also in some important immunological responses such as interleukin processing and release form macrophages. P2X7 receptor shows a very wide distribution among mammalian tissues and organs. Thus it is involved in numerous, yet not well-understood, physiological and pathological processes and its significance in biology is getting clearer every day. This talk is a general view of the mechanisms of action that the P2X7 receptor utilizes.

PS2-3

Investigation of ion channels using molecular modeling methods

Turgut Başţuğ

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Ion channels formed by specific proteins embedded in the cell membrane and provide pathways for fast and controlled flow of ions down the electrochemical gradient. This activity generates action potentials in nerves, muscles and other excitable cells, and forms the basis of all movement and sensation in living beings. While the functional properties of ion channels are well known from physiological studies, lack of structural knowledge has hindered development of theoretical models necessary for understanding and interpretation of these properties. Recent determination of the molecular structures of ion channels (sodium and potassium channels) from x-ray crystallography has finally broken this impasse, starting a new age in the field of channels where study of structure-function relationships will take a central stage. MD simulations are indispensable tools for the investigations of structure and function of biological molecules. We have investigated successes and shortcomings of MD in the channels studies. In this presentation I am going to give an overview of our MD studies on the ion channels.

Panel 3

Central Nervous System Microcirculation in Neurological Diseases

PS3-1

Effects of hypertension and diabetes on brain microcirculation

Yasemin Gürsoy Özdemir

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Dementia became a major healthcare problem, as the mean life span of humans got higher in the last decade. In year 2016, more than 46 million people were diagnosed with dementia worldwide, and the number is expected to triple in 2050. A new meta-analysis shows that 7-13% of dementia in patients above age 60 is associated with type-2 Diabetes or metabolic syndrome. Moreover, people with T2DM have more risk of developing any type of dementia, and they are also 2 times more likely to have Alzheimer's disease at an older age. Approximately 80% of Alzheimer's disease patients have a glucose metabolism disorder. These numbers are expected to rise, as the prevalence of T2DM itself is expected to increase and the lifespan of humans are continually rising every year. The association between hypertension and cognitive decline has been widely researched, and it seems to differ according to age. While midlife hypertension is found to be a relative risk factor of AD and dementia, late onset hypertension had no significant association. In this presentation, data obtained from different animal models of hypertension, type-1 diabetes and metabolic syndrome will be presented. Brain microcirculatory changes are detected through immunoflorescent staining and iDisco method for 3D visualization. Cognitive changes are studied *in vivo* with behavioral experiments.

PS3-2

Dynamic microcirculatory problems in ischemic penumbra

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The cerebral microcirculation is specialized to maintain the continuous high metabolic needs of the brain. Especially in vascular pathologies like ischemic stroke, microcirculation can be affected very differently compared to large vessels, with significant functional consequences. Studying microcirculation experimentally *in vivo* is extremely difficult, due to small size, complexity and dynamic nature of the structures. For such investigations, high-tech equipment should be properly utilized and data should be processed with correct algorithms. Novel tools like *in vivo* multiphoton microscopy (MPM) and optical coherence tomography (OCT) applications, can image microcirculatory structures, flow parameters and even oxygenation with very high spatial and temporal resolution, yielding data to detect previously unrecognized problems and develop solutions. During cerebral ischemia, microcirculation is affected severely and mostly irreversibly. Capillary dysfunction can be initiated with the earliest ischemic changes, because of endothelial or glycocalyx injury, changes in blood cell adhesion or pericyte contractions and these changes may not reverse despite recanalization of the occluded artery. For optimum tissue oxygenation, flow distribution and heterogeneity across the capillary bed are as important as the capillary morphology. OCT and MPM time series performed in the under-risk ischemic brain tissue following reperfusion, can characterize the time-dependent changes in the tissue in very high detail. These applications reveal that, even in capillaries with maintained flow, movement of erythrocytes can temporarily stall individually, and these flow interruptions cumulatively result in a very severe flow heterogeneity for the tissue. Leukocytes trying to traverse through the narrow capillary lumen is a major cause for these stalls, resulting in prominent fluctuations in capillary microoxygenation. The exact subcellular causes and consequences of these described dynamic problems is under ongoing investigation and these data can be expected to help understand

the clinical and imaging phenomena in ischemic stroke patients as well as develop innovative approaches targeting microcirculation.

PS3-3

The role of pericytes in the pathophysiology of multiple sclerosis

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Capillary pericytes are mesenchymal cells which play an important role in blood vessel formation and its integrity and are involved in regulation of capillary diameter and cerebral blood flow. Furthermore, pericytes are involved in immunological responses and repair mechanisms in the central nervous system (CNS) such as glial scar formation, all which indicate that pericytes could be the very main players in the pathophysiology of Multiple sclerosis (MS), a chronic inflammatory demyelinating disease of the CNS. The pathophysiology of MS presents lesion formation especially around blood vessels in the CNS, which is associated with blood?brain barrier (BBB) leakage, infiltration of inflammatory cells, damage to myelin and neurons, and glial scar formation. Although, several studies point possible roles for pericytes in MS pathophysiology, it has not been documented in detail whether pericyte dysfunction triggers the disease or vice versa disease progress leads to pericyte dysfunction. Pericytes lack a single specific marker due to their ability to change their phenotype in response to different milieu, they are usually identified by a combination of surface markers and their anatomical location. Depending on their location and circumstances, pericytes may act as stem cells, (myo-) fibroblasts, microglia and other yet unclassified phenotypes which make them rather difficult to track down. In MS disease progression, noteworthy findings are the presence of increased pericyte numbers at lesion sites, the decreased pericyte coverage on endothelial sites and the appearance of different pericyte phenotypes. This presentation aims to provide a brief overview on the role of pericytes in MS in order to improve our understanding of molecular and cellular changes in vascular MS pathophysiology.

Oral Presentations

(O-01 — O-51)

O-01

Molecular motor mechanism of contraction in central nervous system pericytes

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Objective: Pericytes, the microvascular mural cells, are present in high density in central nervous system. Although pericytes are considered to be contractile, the molecular motor mechanisms and proteins involved are not well characterized *in vivo*. Thus, the elucidation of pericyte contractile machinery along the arteriovenous axis in central nervous system may provide deeper insight to microvascular blood flow regulation *in vivo*.

Methods: Pericyte contraction was induced in the retinas of male and female *Swiss albino* mice weighing 25–35 g by intravitreal injection of noradrenaline. Whole-mount retina preparations were fixed with methanol and fluorescently labeled for globular (G) and filamentous (F) actin or alpha-smooth muscle actin (α-SMA) and smooth muscle myosin heavy chain (Myh11). α-SMA knockdown was performed by intravitreal injection of siRNA against Acta2 gene's transcript. Signal quantification and colocalization evaluation was performed on the imaged acquired with confocal microscope.

Results: Myh11 labeling was positive in both pericyte soma and processes and exhibited tight overlap with α-SMA labeling (n=6). Myh11 expression was evident in all types of microvascular pericytes, regardless of the fixation method used (n=4), α-SMA expression level, retinal vascular order or layer. α-SMA knockdown with RNA interference disrupted microvascular contraction and α-SMA protein levels but not Myh11 expression (n=2). F-actin to G-actin signal ratio was 2.05±0.43 fold higher in contracted segments compared to noncontracted ones (n=4), supporting the involvement of F-actin in contraction, which is further supported by the linearized pattern of F-actin signal.

Conclusion: Adult mouse retinal microvascular pericytes are contractile and express Myh11, the smooth muscle specific myosin isoform in addition to α-SMA. Both proteins are tightly coupled. Contractile stimuli promote F-actin polymerization. These data suggest that pericytes *in vivo* contract with similar mechanisms to smooth muscle cells although they harbor thinner fiber bundles.

This study has been approved by Hacettepe University Animal Experimentations Local Ethics Board with the decision number 2018/02-18.

Keywords: pericyte, microvasculature, actin, myosin, contraction

O-02

The effect of coating materials on morphology and function of the cells in two and three-dimensional primary neuronal cultures

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Objective: Although primary neuronal cultures are frequently used in experiments to understand the basis of neurological diseases and to test the therapeutic effects, the effect different coating materials on cultured neuronal cells has not been studied extensively. The aim of this study is to investigate and compare the effects of two different coating materials on primary neurons in terms of cellular growth parameters, cellular morphology and functional characteristics. Poly-D-lysine (PDL) ve Matrigel® were used to construct two and three dimensional cultures.

Methods: Primary mixed cortical neurons from E15 mouse (Balb/C) embryos were seeded onto culture plates coated with PDL or Matrigel®. 4–14 days after, cells were fixed by 4% paraformaldehyde for fluoresence/confocal/superresolution (Leica dmi8/SP8/STED) microscopy and by 2.5% glutaraldehyde for scanning electron microscopy. Cell were stained with GFAP, beta III tubulin, MAP2, Neu N, Nav 1.2 ve Nav 1.6. The images were analysed by Image J. At the end of 14-days, cells were tested by "patch klamp" to evaluate neuonal firing. In primary neurons, adult and newborn brains qPCR and Western blot were used to analyse expression of neuronal sodium and potassium channels quantitatively and semi-quantitatively.

Results: Primary neurons seeded on Matrigel® have depicted cells that grow in clusters and interact through tight, linear extensions like axons. On neurons seeded on PDL were found

to be located singly, interact through short, curling extensions. Neuronal markers as Neu-N and sodium channel markers were increased in Matrigel® group compared to PDL group. Neuronal growth on different coatings showed significant alterations in neuronal firing threshold, with 80<Iinj>120 pA on PDL matrix and 2<Iinj>160 pA on Matrigel® matrix.

Conclusion: Due to the findings in morphological and functional developments, and neuronal firing threshold levels, seeding primary neurons on Matrigel® was found to be more effective in construction of a three dimensional culture model that can mimic the adult neuronal cells.

Keywords: neuron, culture, matrigel, PDL

O-03

Investigation of myelin membrane expansion dynamics of the central nervous system

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Objective: Function of the myelin membrane is to accelerate impulse propagation and support metabolism and health of an axon that may extend a long distance off the neuronal body. In the central nervous system specialized glia cells -oligodendrocytes- wrap the axons. An oligodendrocyte has to generate a striking amount of membrane as it can wrap up to 30–40 internodes, which are myelinated regions between nodes of Ranvier. During the expansion of the oligodendrocyte membrane towards the nodes of Ranvier large amounts of lipid and protein are trafficked to the cell membrane. Thus, defects in the cellular vesicular transport may result in myelin disorders such as "Pelizaeus–Merzbacher" disease (PMD). Cellular transport and the resulting membrane expansion processes were studied in detail at the ultrastructural level mainly by immunocytochemistry and electron microscopy, yet their dynamics are poorly understood during myelination. In order to fill the gap in our understanding, we aim to monitor lipid and protein transport to the cellular membrane in real-time.

Methods: Using oligodendrocytes derived from stem cells, the cargo vesicles, lipids and lipid rafts in oligodendrocytes were monitored in real-time during myelin formation using fluorescent dyes and fluorescent proteins. Monitored oligodendrocytes were categorized according to their maturation status.

Results: Our early results revealed that membrane lipids and cargo vesicles carrying different proteins followed different transportation patterns and integrated to the membrane at different locations.

Conclusion: Higher temporal and spatial resolution observations are needed to reach a more detailed description of molecular physiology of myelination. Increased knowledge on myelination will not only result in a better understanding of the basic biology of the oligodendrocytes but will also improve our understanding of the myelination disorders such as PMD.

This project was supported by TUBITAK with the project number:116S506.

Keywords: myelin, oligodendrocyte, pelizaeus–merzbacher disease, embryonic stem cell, live imaging

O-04

Effect of paracetamol in proliferation of glioblastoma cell line: the role of apoptosis and COX-2, IRS1 and Cyclin B expressions

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Objective: Glioblastoma is the most common central nervous system tumor. Paracetamol has been found to have anti-cancer effects in many studies and these effects have been suggested to be performed by different mechanisms due to the inhibition of the weak cyclooxygenase enzyme. In this study, we aimed to investigate the relationship between paracetamol and COX-2, IRS1, cyclin B expression levels, cell proliferation and apoptosis in glioblastoma cell line.

Methods: A172 glioblastoma cells line were used in the study. Cells were treated at different concentrations of paracetamol and Phosphate Buffer Saline (PBS) as a vehicle for 24, 48 and 72 hours. Cell viability was detected by MTT. Bax, procaspase 3, COX-2, Cyclin B and IRS1 expressions were detected by Western Blotting. Data were evaluated using Microsoft Excel and SPSS programs.

Results: 0.5 mg/ml paracetamol treatment for 24, 48 and 72 hours led to decrease in 14%, 31%, 37% of viability of cells respectively. We also observed that the level of cell death increased depending on dose and duration of paracetamol incubation. Expression of COX-2, cyclin B, IRS1 levels decreased 36%, 52%, 6% respectively after treatment of 0.5 mg/ml paracetamol. While paracetamol concentration increased, expression of COX-2, cyclin B, IRS1 gradually decreased compare to the other concentrations (1 mg/ml, 43%, 58%, 25% respectively). On the other hand, treatment of 0.5 mg/ml and 1 mg/ml paracetamol significantly induce the expression of procaspase 3 and Bax proteins compare to control group (40%, 21% and 18%, 17% respectively).

Conclusion: The results of our study show that paracetamol has antitumoral effects on glioblastoma cells and this activity was induced by different signaling pathways such as COX enzyme, apoptosis cascade, intracellular signaling pathways and IRS.

Keywords: paracetamol, glioblastoma, COX-2, IRS, cyclin b, apoptosis

O-05

Investigation of high frequency oscillations in BDNF heterozygous mouse hippocampus and entorhinal cortex

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Objective: High frequency oscillations (HFO) in the central nervous system result from a combination of potential fluctuations in the neuronal membrane and changes during synaptic transmissions. Brain-induced neurotropic factor (BDNF) is involved in neuronal function and adaptive responses in the central nervous system. Its effects on neuron excitability and on synaptic transitions are well defined. The aim of our study was to investigate the effects of physiological chronic BDNF deficiency on HFO and to show whether BDNF has an effect on HFOs.

Methods: This study was approved by Karadeniz Teknik University local animals ethics committee. In the study, BDNF heterozygous mice were used. 350–400 micrometer thick slices were cut from the brain tissues of 30–35 days old mice. Electrophysiological field potentials were recorded from transverse slices of the entorhinal cortex-hippocampus. Artificially synchronized discharges were induced in the slices by 4 Aminopyridine application. Recordings containing short lasting (<3 s.) discharges were filtered by applying appropriate digital filters and ripple and fast ripple fluctuations were determined. The ratio of the event that include an HFO to the all events were calculated. Ratios were statistically compared by using t-test between wild type and heterozygous mice.

Results: The ratio of synchronous events including HFO in heterozygous mice was significantly less in the entorhinal cortex ($p<0.05$) and in the hippocampus CA1 region ($p<0.05$) than in the wild type mice of the same age and gender.

Conclusion: Our present data shows that similar to EEG bands, chronically reduced concentrations of BDNF resulted in reduced high frequency fluctuations. As a result, our data revealed that BDNF contributes to the synchronicity of HFOs.

Keywords: BDNF, brain slice, mice, ripple, high frequency oscillations

O-06

Effects of 7,8-dihydroxyflavone, a tyrosine kinase-B receptor agonist, on epileptiform activity in mice brain slices

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Objective: 7,8-dihydroxyflavone (DHF), TrkB receptor agonist, has BDNF like properties and showed beneficial effects in many experimental models. It has been shown that acute activation of the TrkB receptor suppressed GABAergic inhibition and increased neuronal excitability. These changes are similar to the cellular causes of epileptiform activity. The aim of this study was to investigate the effect of acute DHF application on normal and epileptiform activity in slices.

Methods: This study was approved by Karadeniz Teknik University local ethics committee. Entorhinal cortex-hippocampus (EC-CA1) slices obtained from 30–35 days old mice were used (n=10). Extracellular field potentials were recorded from EC and CA1 regions. In epileptiform activity, induced by 4-Aminopyridine (4AP), ictal and interictal activities were observed. The effects of DHF on these two activities were evaluated by examining the records before and after administration of DHF. Frequency and duration of ictal and interictal events were compared statistically with paired t-test.

Results: Dihydroxyflavone alone did not induce any epileptiform or abnormal activity in the entorhinal cortex and hipocampus slices. However, DHF increased the frequency of 4-AP induced ictal and interictal events ($p<0.005$). It was also observed that the duration of ictal events was prolonged after the administration of DHF to the slices ($p<0.05$). Finally, DHF caused ictogenesis in some EC and CA1 slices in which ictal activity was not observed by inducing ictal discharges.

Conclusion: In the central nervous system, TrkB pathway might be an ideal target for new drugs and treatment strategies as this pathway is able to change neuronal functions over a long period of time. The beneficial effects of DHF have been shown in many experimental studies. However, it has been shown in this study that acute modulation of the TrkB pathway has an enhancing effect on the activity of the neural circuits, and this effect of DHF must be considered in future treatment approaches.

Keywords: 7,8-dihydroxyflavon, BDNF, entorhinal cortex, epileptiform activity, tyrosin kinase-B

O-07

Investigating GABAergic control of the dentate gyrus in the reversal of long-term potentiation

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Objective: γ-aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the adult brain. Altered GABAergic function has been related with impaired long-term potentiation (LTP) observed in Alzheimer's disease. However, whether GABAergic alterations lead to impairment of weakening of synapses is largely understudied. We investigated the contribution of GABA function to the reversal of LTP in the dentate gyrus (DG), the gateway for information input to the hippocampus, a critical brain region involved in learning and memory.

Methods: A total of 30 adult Wistar rats were enrolled in the study. After a 15-minute baseline recording, LTP which was

induced by application of high-frequency stimulation (HFS) protocol was reversed by low-frequency stimulation applied within the first 5 min following LTP induction. Infusions of saline, picrotoxin (50 µmol) or bicuculline (20 µmol) were made for 1 hour starting from the application of HFS, using Hamilton pump. The ratio of 5-min averages of the excitatory postsynaptic potential (EPSP) slopes and population spike (PS) amplitudes before and after LFS were used as a measure of the magnitude of LTP reversal.This study was approved by Erciyes University Ethics Committee.

Results: The input-output curves of the infusion groups were comparable to each other, as shown by the non significant interaction observed between stimulus intensity and infused drug. The one-way ANOVA indicated that the groups varied significantly on their depotentiation magnitudes for fEPSP slope ($F_{2,23}=5.93$; $P=0.009$) and PS amplitude ($F_{2,23}=4.29$; $P=0.027$). Post-hoc Tukey's test confirmed that bicuculline inhibited reversal of EPSP-LTP ($P=0.007$), also picrotoxin that of PS-LTP ($p=0.026$) when compared to saline infusion.

Conclusion: The present study provides evidence for a role of the GABAergic transmission in the reversal of LTP, suggesting that neurodegeneration of GABAergic hippocampal neurons could result in deficits in hippocampus-mediated learning.

This study was supported by Erciyes University Research Found (TTU-2018-8240).

Keywords: GABA, plasticity, dentate gyrus, reversal of LTP

O-08

Effect of γ-aminobutyric acid receptors inhibition on the low-frequency primed long term potentiation

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Objective: γ-aminobutyric acid (GABA) is the major inhibitory neurotransmitter that conveys its inhibitory effect through GABA-A receptors. Metaplasticity refers to activity-dependent changes in neural functions that modulate subsequent synaptic plasticity such as long-term potentiation (LTP). Much research on metaplasticity has been focused on glutamatergic excitatory synaptic system in the hippocampus, whereas the inhibitory GABAergic synaptic system has received less attention. Herein, we investigated low-frequency stimulation (LFS) - primed LTP at dentate gyrus synapses in the presence or absence of GABAA receptor antagonists.

Methods: The study was carried out with the decision of Erciyes University Animal Experiments Local Ethics Committee dated 14.02.2018 and numbered 18/022. A total of 30 adult Wistar rats were enrolled in the study. After a 15-minute baseline recording, a LFS was applied to prime the LTP by application of high- frequency stimulation (HFS) protocol. Infusions of saline, picrotoxin (50 µmol) or bicuculline (20 µmol) were made for 1 hour starting from the application of HFS, using Hamilton pump. The 5-min averages of the excitatory postsynaptic potential (EPSP) slopes and population spike (PS) amplitudes 60 min after HFS were used as a measure of the metaplastic LTP reversal.

Results: The input-output curves of the infusion groups were comparable to each other, as shown by the non significant interaction observed between stimulus intensity and infused drug. It was found that 1-Hz priming prevented subsequent LTP induction at dentate gyrus synapses when GABAA receptors are functional. However, a primed LTP accompanied with increased PS-LTP was observed in the presence of bicuculline ($p<0.05$) or picrotoxin ($p<0.05$) with respect to saline infusion.

Conclusion: The present study provides evidence for a role of the GABAergic transmission in metaplastic control of LTP, suggesting that neurodegeneration of GABAergic hippocampal neurons could result in deficits in hippocampus-mediated learning.

This study was supported by Erciyes University Research Found (TTU-2018-8240).

Keywords: metaplasticity, dentate gyrus, GABA, hippocampus

O-09

Evaluation of clock drawing test in patients with schizophrenia

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Objective: The aim of this study was to compare the clock drawing test performance of schizophrenic patients and healthy control group in terms of gender, age and education.

Methods: 50 patients diagnosed with schizophrenia and age gender and education matched 50 healthy volunteers included the study.The participants were evaluated by the Mini-Mental Test (MMT) for the educated people and then the ones who had 24 points or more from the MMT were evaluated by the Clock drawing test (CDT) performances. The symptom severity of patients with schizophrenia was evaluated by Positive and Negative Syndrome Scale (PANSS) and Brief Psychiatric Rating Scale (BPRS).

Results: In the study, there was no significant difference between groups in terms of age and education level which was evaluated with MMT ($p=0.898$) ($p=0.129$). Performance of patient group on CDT was found to be significantly lower than the control group ($p<0.001$). No significant difference was found between anticholinergic drug users and nonusers in terms of CDT performance ($p=0.690$). A significant negative correlation was founded between CDT and PANSS points ($p<0.05$). Significant negative correlation was found between MMT and PANSS score ($p<0.05$). Pperformance of schizophrenic patients' on CDT was founded lower than the control group. Also, these lower performances were founded parallel with overall disorder's severity. When we compared performances of anticholinergic drug users and non-users, there was no

significant difference. CDT is not only sensitive to cognitive deficits but it is also sensitive to changes in visual-analytic functions. Impairment in many aspects of neurocognitive functions including semantic memory, attention and executive functions, can be revealed by this test. According to findings of by brain imaging neuroanatomical differences was founded in schizophrenia patients comparing to healthy controls.

Conclusion: Decreased performance of schizophrenic patients on CDT can be explained with neuroanatomical differences.

Keywords: clock drawing test, cognitive neuropsychology, schizophrenia

O-10

Flashbulb memories in Alzheimer's disease

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Objective: Alzheimer's disease is a neurodegenerative disorder characterised by a progressive memory loss. However, it is not clear whether flashbulb memories, a subgroup of autobiographical memories with an emotional component, are influenced to the same extent in Alzheimer's disease. The aim of this study was to test the integrity of flashbulb memories in Alzheimer's disease.

Methods: A total of 29 Turkish patients diagnosed with probable early-stage Alzheimer's disease (AD) according to the NINCDS-ADRDA criteria participated in the study. Participants verbal memory performance was measured by using Öktem-Verbal Memort Processes Test (SBST). Participants' recollections about 15th July coup attempt were evaluated to test their flashbulb memories. Patients were firstly tested in July 2016 following the attempt. The same participants were retested 6 months later the attempt, in February 2017. A total of 18 college students were recruited to the study as a control group only for FBM assessment.

Results: As expected, the immediate memory score ($M=3.1\pm 1.58$; $t(28)=-6.90$, $p<0.01$), the total learning score ($M=62.07\pm 20.697$; $t(28)=-11.644$, $p<0.01$),and the total delayed memory score ($M=10.82\pm3.23$; $t(28)=-2.95$, $p<0.01$) of patients on SBST were below the normal range of age-matched Turkish population. However, no significant difference was found between flashbulb memory performance of Alzheimer's disease group and control group either in the first assessment ($t(45)=-1.264$, $p=>.05$) or second assesment $t(45)=0.692$, $p=>.05$).

Conclusion: The most robust finding of the study was the preserved FBM scores in AD group while they had a noticable deficit in verbal memory encoding. In conclusion, our study supports the notion that flashbulb memories can have a special neural network and suggests that flashbulb memories are preserved in early stage Alzheimer's disease.

Keywords: Alzheimer's disease, dementia, flashbulb memory, emotional memory

O-11

Cognitive decline is reflected with aberrant EEG theta and alpha responses in patients with Parkinson's disesase dementia and dementia with lewy body disease

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Objective: Parkinson's disease dementia (PDD) and dementia with Lewy bodies (DLB) have similar pathophysiology. The clinical symptoms of these two disease are different. Investigation of EEG event-related responses in PDD and DLB is significant to understand the mechanisms underlying the pathophysiology. The aim of the present study was to investigate the event-related theta and alpha responses during a visual cognitive task in patients with PDD and DLB.

Methods: 15 PDD patients (70.2±6.48), 12 DLB patients (72.2±9.69) and gender, education, aged-matched 15 healthy controls (67.8±6.69) were included in the study. There were no significant difference for the Mini Mental State Examination score between two dementia groups. EEG was recorded from 32 channels during visual oddball paradigm. Phase-locking analysis and power spectrum analysis were performed with EEGLAB toolbox for theta (4–7 Hz) and two different alpha (8–10 Hz and 10–13 Hz) frequency bands for all groups. Repeated measures of ANOVA was used for statistical analysis ($p<0.05$).

Results: Group difference was significant for theta power and theta phase locking ($p<0.05$). Healthy controls had enhanced theta power and theta phase locking with increasing cognitive loading. Healthy controls had higher theta power and theta phase locking than both PDD and DLB patients. PDD patients had the worst theta power in comparison to other groups in the occipital locations whereas DLB patients had the worst theta phase locking in comparison to other groups in the frontal locations. Group difference was significant for upper alpha power (10–13 Hz) ($p<0.05$). PDD patients had the highest upper alpha power whereas healthy controls had the lowest upper alpha power in the occipital locations.

Conclusion: Dementia is reflected with decreased theta responses in patients with PDD and DLB and increased upper alpha responses in PDD patients. This aberrant responses could be candidate of biomarkers for dementia in PDD and DLB patients.

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Keywords: alpha, EEG, Lewy body, dementia, Parkinson's disease, theta response

O-12

Decreased visual sensory evoked oscillations in Parkinson's disease mild cognitive impairment

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Objective: Amnestic mild cognitive impairment (aMCI) is considered as a prodromal stage of Alzheimer's disease.The presence of cognitive impairment in Parkinson's disease (PD) is named as PD-Mild cognitive impairment (PD-MCI).Our earlier reports showed lower event-related theta power in response to cognitive tasks in both aMCI and PD-MCI.The present study investigated sensory-evoked-oscillations (SEO) in aMCI, PD-MCI and healthy controls (HC) with time-frequency-analysis and compared event-related-spectral-perturbation (ERSP) and inter-trial phase locking (ITC) values in two MCI conditions.

Methods: The study included 30 aMCI, 30 PD-MCI and age-education-gender-matched 30 HC. For SEO, a light with 10 cd/cm^2 luminance was used as stimuli. Morlet wavelet transform was applied to EEG data in the range of 1–30 Hz. Frontal (F3, Fz, F4), central (C3 ,Cz, C4), parietal (P3, Pz, P4), occipital (O1,Oz,O2) ERSP and ITC values of groups were compared in delta (1–3.5 Hz, 0–600 ms), theta (4–7 Hz, 0–600 ms), alpha (8–13 Hz, 0–500 ms) and beta (15–30 Hz, 0–400 ms) frequency bands. This study approved by DEU ethics committee (Approval ID:2018/09-08).

Results: Main GROUP [F2,87=4.948; p=0.009] and GROUPxLOCATION interaction effects were found on theta ERSP; PD-MCI had lower values in frontal, central, parietal locations than HC (p<0.031) and in occipital location than aMCI (p=0.031). Main GROUP effect [F2,87=9.844; p<0.001] on alpha ERSP was found;PD-MCI had lower values compared with HC and aMCI (all, p=0.001). In theta ITC, a main GROUP effect [F2,87=9.844; p<0.001] was found; showing lower ITC values in PD-MCI compared with HC and aMCI (all, p<0.019).Main GROUP [F2,87=18.544; p<0.001] and GROUPxLOCATION [F6,261=2.664; p=0.030] interaction effects were found on alpha ITC,indicating lower values in PD-MCI than HC and aMCI on all electrodes (all, p<0.031).There were main GROUP [F2,87= 8.744; p<0.001] and GROUPxLATERALITY [F4,174=2.543; p=0.045] interaction effects on beta ITC; showing PD-MCI had lower values than HC and aMCI on all electrodes (for all, p<0.050).

Conclusion: PD-MCI displayed lower visual-SEO responses in theta and alpha frequency ranges than both HC and aMCI. These findings indicate that the visual-sensory system is distinctively impaired in PD-MCI, which could be a result of peripheral (i.e., retinal) dopaminergic loss and/or affected visual cortical areas.

Keywords: event-related-spectral-perturbation, inter-trial phase locking, Parkinson's disease, amnestic, MCI, oscillation

O-13

Research for the relationship between Lyme disease and the activity of CXCL-13 in cerebrospinal fluid (CSF) of multiple sclerosis patients

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Objective: Multiple sclerosis (MS) is an autoimmune disease characterized by chronic inflammation, demyelination and neuronal damage. The diagnostic criteria of MS are based on clinical and paraclinic evaluations that emphasize the need to demonstrate lesions in different central nervous systems. There are similar clinical and MRI findings such as SLE, APS, Behçet's Disease, Sjögren's syndrome, isolated CNS vasculitis, infectious causes such as rheumatologic and neurosarcoidosis, neuroinsulitis, syphilis in MS differential diagnosis. The fact that the immune mechanism of these two diseases is similar to each other is a neurological disease and in some cases makes the diagnosis difficult. In particular, the fact that Lyme disease can mimic many diseases and sometimes show common symptoms may cause certain problems. Lymeneuroborrel based on the detection of a partially intrathecal Borreliaburgdorferi specific antibody. Lymeneuroborreliosis (LNB) laboratory diagnosis is based on the detection of a partially intrathecal Borreliaburgdorferi specific antibody. Measurement of the concentration of chemokine CXCL13 in CSF is presented as a novel and promising diagnostic tool to complement antibody-based diagnostic methods of LNB. In this study; The aim of this study was to investigate anti-Borrelia IgG and IgM and CXCL-13 for the control of Lyme disease in CSF samples of patients with MS who were admitted to Neurology Clinic.

Methods: CSF samples of MS patients were included in this study(n=28). In the Diagnosis of Neuroborreliosis, Borrelia

antibodies should be investigated not only in serum samples but also in CSF samples.

Results: The results of our study were evaluated; The high incidence of CXCL-13 in CSF samples of MS patients with positive Borrelia ELISA tests once again proved that CXCL13 is still the best marker / biomarker for LNB.

Conclusion: In the diagnosis of neuroborreliosis, Borrelia antibodies should be investigated not only in serum samples but also in CSF samples.

Keywords: CXCL-13, Lyme disease, multiple sclerosis

O-14

The relationship between CSF oligoclonal band positivity and IgG index and visual evoked potential measurements in patients with multiple sclerosis

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Objective: Multiple sclerosis is a chronic inflammatory and neurodegenerative disease. It progresses with progressive neurological dysfunction. Diagnosis is supported with laboratory methods and is based on history and clinical findings. In this disease, cerebrospinal fluid IgG increase and IgG oligoclonal band positivity may be seen. 30% of the initial symptoms of the disease are related to the visual nerve. With visual evoked potential, visual pathways are evaluated from the retina to the occipital cortex. In this study, the relationship between cerebrospinal fluid (CSF) findings and visual evoked potential was investigated in patients with multiple sclerosis.

Methods: This study included 186 people aged 16–78 years who were admitted to Ondokuz Mayıs University Neurology Polyclinic and were diagnosed with multiple sclerosis. SPSS v.22 package program was used for statistical analysis.

Results: The mean age of the patients was 45.6±11.9 and 68.3% (n=127) were female patients. In 176 patients with CSF examination, 77.8% had oligoclonal band positivity. The visual evoked potential result was found to be pathological in 63.5% of these patients with oligoclonal band positivity and this was not statistically significant (p>0.05) (p=0.945). Of the 121 patients with IgG index, the visual evoked potential was found to be pathological in 70.2% of the patients with IgG index positive (p>0.05) (p=0.287). In both of the 113 patients who underwent both oligoclonal band test and IgG index measurements, 50 were pathological in two tests.

Conclusion: According to the results of this study, visual evoked potential abnormality was not statistically significant in oligoclonal band test and / or positive IgG index. There is a need for studies investigating the relationship between evoked potential abnormality and CSF findings in which there are more MS patients with different clinical forms and different disability.

Keywords: multiple sclerosis, visual evoked potential, oligoclonal band, IgG index

O-15

Cognitive processing of relative clauses in a Turkish population: an ERP investigation

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Objective: Psycholinguistic studies on the processing of relative clauses (RCs) revealed that Subject Relative Clauses (SRCs) and Object Relative Clauses (ORC) display an asymmetry as the latter are more difficult to syntactically process. The present study investigates Turkish RCs by using the ERP methodology to address the issue of asymmetry and some remaining problems from the previous studies.

Methods: 32 healthy subjects participated in this study. Each subject was visually presented a total of 240 sentences, where 120 of those sentences had SRCs in them (60 with subject function, and 60 with object function), and the other 120 sentences had ORCs (60 with subject function, and 60 with object function). Following factors are used in the statistical analysis: Grammatical Function (GF) (subject, object) × Clause Type (SRC, ORC) × A(nterior) P(osterior) distribution (frontal, parietal) × LAT(eralization) (left, right).

Results: A P200 component was formed in the first time window. GF, $F(1.31)=4.032$, $p<.05$, and Clause Types, $F(1.31)=10.849$, $p<.01$, show that there is significant difference. In the second time window, a LAN component was observed, and a significant difference of $F(1.31)=5.589$, $p<.05$ manifested itself in the interaction between Clause Type $F(1.31)=5.283$, $p<.05$, and GF x Clause Type. In the last time window, a difference $F(1.31)=4.530$, $p<.05$ was observed in the interaction between GF and Clause Type, and a late LAN component was present.

Conclusion: This study shows in line with the previous psycholinguistic studies that ORCs are more difficult to process than SRCs in a Turkish population, and that the difficulty in processing is prominent in the head noun region of RCs. It further revealed that the processing of RCs is sensitive to the GF of an RC, but with a certain type of asymmetry.

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Keywords: event related brain potentials, LAN, language processing, P200, relative clauses

O-16

The effect of transcranial direct current stimulation on static and dynamic balance in healthy volunteers

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Objective: Postural control, motor adaptation and motor learning are being investigated in terms of rehabilitation and performance enhancement. Transcranial direct current stimulation (tDCS) studies showed positive results especially in patients and older adults. We aimed to investigate the effect of anodal stimulation of cerebellum in healthy young on dynamic-static balance tests which are not used before for evaluation. Besides, the effect of impulsivity, attention and reaction time (RT) were also investigated to consider the use of tDCS for performance enhancement in the future.

Methods: This study was apporved by İstinye University Clinical Ethics Committee (#12). Eleven young healthy volunteers participated in the study. Two different cerebellar tDCS applications were performed with 1-week interval (anodal tDCS-sham tDCS). The duration of tDCS was 20 minutes (anode-vermis, cathode-right shoulder). Y-balance test, flamingo balance test and continuous performance test (CPT) were applied to the volunteers before and after each tDCS. Participants and researchers who conducted balance tests were blind to tDCS applications. Balance test scores and number of errors, ommissions and RT were compared between anodal and sham tDCS applications.

Results: There was no significant difference between anodal and sham tDCS in terms of Y-balance test, Flamingo balance test scores and the number of errors and ommissions in CPT (p=0.9, p=0.7, p=0.6, p=0.5 respectively). There was a significant delay in reaction time in anodal stimulation compared to sham stimulation (p=0.02).

Conclusion: The positive effect of tDCS on postural control in patients and old adults in previous studies was not elicited in the tests we used in healthy young. On the other hand, although the number of errors did not increase, the delay in reaction time is not a desired effect for performance enhancement. As a result of the study, there was no evidence to support the use of cerebellar tDCS to improve balance performance in healthy young individuals.

Keywords: balance, neuromodulation, cerebellar transcranial direct current stimulation

O-17

Effects of the menstrual cycle phases on working memory

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Objective: Hormonal fluctuations starting from adolescence and occurring throughout their lives cause many physiological changes in women. Studies showed that emotional and cognitive processing have been altered by the menstrual cycle in women. The aim of this study was to investigate the effects of follicular and luteal phases on short-term memory.

Methods: Thirty-two regularly cycling women with mean age 24.2±6 (range: 18–38) participated in this study. Thirteen of the participants were follicular and 19 were in luteal phase groups. All participants were right handed, determinate with Edinburg Oldfield Handedness Inventory (87.2±12.9). Presentation of stimuli to the participant was performed using the Sternberg paradigm. This paradigm is a widely used method in the study of visual and auditory short-term memory/working memory. The application of the paradigm and the presentation of stimuli were performed with E-prime software. Event related potential (ERP) analyzes obtained from EEG records were performed with Acqknowledge data-acquisition system. The data obtained from the behavioral measurements were evaluated by Mann-Whitney U test. The ERP peaks were evaluated by independent sample t-test.

Results: In the Sternberg paradigm, control, 3 and 6 conditional memory sets were used. As the conditions become complex the reaction time per-item and the error rate increased in both phases (p<0.001).There were no significant differences in reaction time and error rates between the two groups (p>0.05). It was observed that P100 latency in matched correct trials was shortened and the amplitudes were increased in the follicular phase compared luteal phase (p<0.05). There was no significant difference in other ERP peaks.

Conclusion: P100 is the first step of detection of external stimulus showing that the sources of attention were used more effectively in the follicular phase. However, there was no difference in short-term memory between the phases.

Keywords: EEG, ERP, menstrual, P100, Sternberg

O-18

Modulation of hypothalamic hunger circuits by a catecholaminergic pathway in TH-cre transgenic mice

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Objective: Energy balance is controlled by central circuits monitoring peripheral signals. Arcuate nucleus of hypothalamus (ARC) and nucleus of solitary track in the brain stem (NTS) are two critical brain regions, which receive energy associated signals, and regulate food seeking and consumption.

ARC is widely known to increase or decrease food intake, whereas NTS is involved in suppressing food consumption through vagal satiety signals. Furthermore, agouti-related peptide (AgRP) and proopiomelanocortin (POMC) neurons located in the ARC are the major neuron populations for appetite and metabolism. Signals modulating the activity of AgRP and POMC neurons are still not well understood. In this study, we investigated the interaction of ARC and NTS regions, and their effects on feeding behavior.

Methods: In stereotaxic frame, we intracranially delivered rAAV2/1-EF1a-FLEX-hChR2(H134R)-eYFP, rAAV-EF1a-DIO-hM4D(Gi)-mCherry and rAAV2/1-CAG-FLEX-tdTomato viruses to the NTS regions of TH-cre mice (15 mice for each group). Chemogenetic and optogenetic modulations were applied on the projections of the NTSTH neurons in the ARC and their effects on animal behavior were analyzed. Electrophysiological recordings were performed by using patch clamp techniques to isolate synaptic currents of stimulated TH axons from ARCAgRP and ARCPOMC neurons.

Results: Here, we observed intense projections of NTSTH neurons to the ARC, which, when stimulated, gave rise to a robust increase in appetite via bi-directional controlling of AgRP and POMC-expressing neurons. Optogenetic and chemogenetic analyses showed that norepinephrine (NE) signals originating from the NTSTH terminals in the ARC are crucial for stimulation of appetite ($p<0.001$). NTSTH fibers innervate the paraventricular hypothalamic nucleus (PVH) as well, which inhibit MC4R-expressing neurons and increase food intake. Additionally, we showed that inhibition of PVHMC4R neurons is, in part, mediated by NE-dependent release potentiation from ARCAgRP PVH terminals (→PVH terminals ($p<0.05$).

Conclusion: Consequently, an orexigenic effect was strongly observed on feeding at the first time when NTSTH axons in the Arc were stimulated.

Keywords: catecholamine, electrophysiology, hypothalamus, optogenetics, tyrosine hydroxylase

O-19

Effects of fasting and re-feeding on neuronal activation

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Objective: Expression of c-fos is commonly used as an indirect marker of neuronal activity. Various factors such as light, odor, nutrition and stress, increase c-fos immunoreactivity in various brain regions. In present study, we investigated the effect of different food deprivation periods and re-feeding on c-fos expression.

Methods: Male Balb/C mice (27–30 g), were divided into fed (control) and 1, 3-, 6-, 12-, 24- and 48-hour fasted groups (n=8) after weighing. At the end of the fasting period, half of the animals were re-weighed and allowed to eat for 30 minutes. The brains were quickly removed and c-fos expression in the arcuate nucleus was examined in paraffin-embedded tissue sections immunohistochemically.

Results: After fasting for 1-, 48-hours, animals lost 2.5–18.9% of the initial body weights. Food deprivation for 6-hours ($p<0.05$), 12-, 24- and 48- hours ($p<0.001$) caused significant weight loss. Fasting for 12-hours decreased the number of c-fos positive cells ($p<0.05$), compared to the control group. c-fos expression was higher in re-feeded mice after 1-, 6-hours ($p<0.05$), 3- and 12-hours fasting ($p<0.005$) compared to food deprived mice.

Conclusion: In accordance with recent literature, food deprivation for 6- and 24-hours did not affect the number of c-fos positive cells in arcuate nucleus. However, c-fos expression decreased significantly in mice fasted for 12-hour and deprived of food from 08:00. Neuronal activity increased in re-feeded animals after 1-, 3-, 6- and 12-hour fasting. We determined that fasting does not effect c-fos expression, except for 12-hour fasting period, and re-feeding increases c-fos expression in the arcuate nucleus.

Keywords: c-fos, hunger, mouse, neuronal activation

O-20

Role of MCH neurons on reward and appetite regulation in Pmch-cre transgenic mice

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Objective: The brain drives great enthusiasm towards palatable nutrients. Craving and consuming palatable foods with high fat or sugar content often overcome homeostatic feeding. Even though certain brain regions are known to control physiological fed and fasted states along with hedonic and homeostatic feeding, neural populations that regulate hedonic feeding through predominating physiological needs remain unidentified. Earlier genetic studies have implicated a role for melanin concentrating hormone (MCH) neurons of lateral hypothalamic area (LHA) in food reward. In this study, we aimed to use acute neuronal activity manipulation tools to functionally characterize MCH neurons in terms of appetite and reward.

Methods: We used a combination of optogenetic and chemogenetic approaches in Pmch-cre transgenic mice to acutely stimulate or inhibit MCH neuronal activity, while probing food intake, locomotor activity, anxiety-like behaviors, glucose homeostasis and reward. We also investigated rewarding capacity of MCH neuronal stimulation alone by optogenetic

activation. For this purpose, we conducted nose poke assay, lever press assay and real time place preference assay to assess reward value of MCH neurons.

Results: MCH neuron activity is neither required nor sufficient for short-term control of appetite for chow food unless stimulation is temporally paired with consummatory period. While MCH neuronal activity does not affect short-term locomotor activity, its inhibition improves glucose tolerance and has mildly anxiolytic effect. Finally using two different operant tasks we show that activation of MCH neurons alone is sufficient to induce reward.

Conclusion: Collectively, these experiments confirm diverse behavioral and physiological functions of MCH neurons and suggest a direct role in reward function. Our results support a role for MCH neurons in reinforcement of ongoing consumption, rather than directly increasing the motivation to eat.

Keywords: MCH, appetite, reward, optogenetics, chemogenetics

O-21

Establishment of an animal model that causes proteinopathic changes in neurons by virus-mediated gene transfer method

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Objective: In neurons, trans-acting RNA-binding proteins regulate splicing, polyadenylation, stability and transport at axons and dendrites. Their misregulation or functional disruption due to mutations or sequestration into nuclear or cytoplasmic inclusions have been linked to pathogenesis of several neuropsychiatric and neurodegenerative disorders. In this study, we aimed to create an animal model by using virus-mediated gene transfer to induce proteinopathic changes in neurons.

Methods: Adeno-Associated Virus (AAV) serotype-9 is used to design construction of a casette encoding TarDNA binding protein-43 (TDP43) expression. The control plasmid is comprised sequences for replication and structural proteins, green fluorescent protein (GFP), polyadenylation signal driven by cytomegalovirus (CMV) promoter between two inverted terminal repeats, while the transgene plasmid is additionally included wild-type TDP43 sequences. Systemic delivery of viruses to rats (n=3 for each age) were done throughout diverse injection sites at different ages. Facial and tail veins were used in neonatal (postnatal day 3) and adult (postnatal day 80) animals, respectively. Phenotypic changes were followed by walking pattern and rota-rod tests.

Results: In neonatal animals, motor deficits observed two weeks after injections. Hindpaw withdrawal reflex was disturbed in all CMV-TDP43-GFP-injected animals. Due to the excessive weight loss, muscle weakness and respiratory problems animals were perfused on postnatal day 15. Adult animals survived without a major motor deficit. Their motor performances were examined with regular intervals by rota-rod test between P80-P350. No significant difference was found between CMV-TDP43-GFP and CMV-GFP-injected animals.

Conclusion: Discoveries of new AAV vectors crossing blood-brain barrier have made gene transfer possible to adult animals by intravascular injections. However, timing of injection significantly influences the biodistribution of AAV. Neonatal injections result in widespread expression in the central nervous system, but transduction is quite limited in adult animals. Therefore, manufacturing improvements are still necessary for translational gene therapy paradigms.

Supported by Eskişehir Osmangazi University Scientific Research Projects Commission.

Keywords: AAV, viral vector, gene transfer, TDP43, rota-rod

O-22

Effects of BDNF deficiency and endoplasmic reticulum stress on GABAergic system

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Objective: The aim of this study was to investigate how the inhibitory neurons expressing the different Ca2+-binding proteins of the GABAergic system will be affected with changes in Ca2+ homeostasis in BDNF deficiency and endoplasmic reticulum stress (ERS).

Methods: Wild-type (WT) and BDNF heterozygous (BDNF+/-) male mice were used in 4 groups (n=7-8); WT, BDNF(+/-), WT+Tm, BDNF(+/-)+Tm. Group 3 and 4 were treated with a single dose of tunicamycin (Tm) (0.5 mg/kg, intraperitoneal) to form ERS. On the 3rd day of Tm injection, animals were sacrificed, blood and brain tissues were taken. In serum samples BDNF, in tissue homogenates GRP78, Caspase-12, Parvalbumin, Calretinin, Calbindin, GAD65 and GAD67 levels were investigated by ELISA. One-way ANOVA and Tukey tests were used for statistical evaluation.

Results: Serum BDNF levels were significantly lower in BDNF(+/-) and BDNF(+/-)+Tm groups, than in WT and WT+Tm groups. GRP78 level did not show any significant difference between the groups. Caspase-12 level was similar in WT and BDNF(+/-) groups, however Tm injection significantly increased Caspase-12 level. Parvalbumin, calretinin and calbindin levels in basal conditions were higher in BDNF(+/-) group, but this difference was not statistically significant. On the other hand, Calbindin level decreased significantly with ERS. GAD65 and GAD67 levels were similar in WT and BDNF(+/-) groups. However, GAD65 level was significantly decreased during ERS in WT and BDNF(+/-) groups.

Conclusion: It is known that parvalbumin-positive neurons express GAD67, Calbindin and Calretinin-positive neurons express GAD65. Our findings suggesting a significant decrease in Calbindin and GAD65 isoform of glutamic acid decarboxylase enzyme levels during ERS indicate that the sensitivity of varied intermediate neurons in GABAergic system to ERS may be different. However, endogenous BDNF deficiency did not affect the ERS sensitivity of these intermediate neurons.

Keywords: BDNF, endoplasmic reticulum stress, calcium homeostasis, GABA

O-23

The role of T-type calcium ion channel in the effect of P2X7 receptors on the absence-like epileptic activity in WAG/Rij rats

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Objective: Absence epilepsy is a non-convulsive type of epilepsy seen in childhood. ATP-sensitive P2X7 receptors are non-selective cation channels in the nervous system. P2X7 receptor activation is known to increase intracellular calcium and lead to increased T-type calcium channel activation. In this study, we investigated the effect of NNC 55-0396 on the epileptic activity on WAG/Rij rats, a genetic model of absence epilepsy in humans, and its interaction with P2X7 receptor agonist BzATP and antagonist A-438079.

Methods: 6-8 months aged, 21 male WAG/Rij rats were used. Tripolar electrodes were placed on the animal's skulls. Basal electrocorticography recordings were taken, then 30 µg (i.k.) NNC 55-0396 was injected and 20 µg (i.c.v.) A-438079, 100 µg (i.c.v.) BzATP were injected ten minutes apart and ECoG recordings were continued. The obtained data were evaluated using the Kruskal Wallis and Mann Withney U test in SPSS 15.0. The study was carried out with permission of OMU Animal Experiments Local Ethics Committee 2015/56.

Results: NNC 55-0396, BzATP-NNC 55-0396 and A-438079-NNC 55-0396 compared with basal records significantly decreased the number of clusters, duration and number of spikes from the 20th minute ($p<0.01$) but no significant changes in the amplitudes. There was no statistically significant difference between NNC 55-0396 and BzATP+NNC 55-0396 and A-438079 + NNC 55-0396.

Conclusion: In the present study, T-type calcium blocker NNC 55-0396 had an anticonvulsive effect. BzATP and A-438079 did not alter the effect of NNC 55-0396. Further studies are needed to elucidate the effect of P2X7 receptors on abscess epilepsy in WAG/Rij rats.

This work was supported by OMU BAP (PYO.TIP.1905.15.002).

Keywords: absence, epilepsy, calcium, P2X7, WAG/Rij

O-24

Interaction between caffeine and cannabinoid CB1 receptors in penicillin-induced epileptiform activity

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Objective: Caffeine, a psychoactive substance found in many beverages, acts by antagonizing the adenosine receptors. It has been known that, caffeine has proconvulsant effects in epilepsy. The possible interaction between adenosine receptors and cannabinoid receptors, except epilepsy, is available in the literature. In this study, we aimed to investigate the interaction between caffeine and CB1 receptors in penicillin-induced epileptiform activity.

Methods: Male Wistar rats weighing 205–225 g (n=36) were randomly divided into 6 groups. Animals were fixed to the stereotaxic apparatus after urethane anesthesia and bipolar electrodes were placed over the cortex for electrophysiological recordings. 500 IU penicillin-G potassium was injected intracortically. Caffeine (10 mg/kg; i.p.), CB1 receptor agonist ACEA (7.5 µg; i.c.v.), CB1 receptor antagonist AM251 (0.25 µg; i.c.v.) and combinations of these drugs were administered 30 minutes after the penicillin injection. The experiment was terminated 180 minutes after the first drug injection and ECoG activities were analyzed. One-way analysis of variance (ANOVA) and Tukey–Kramer post hoc tests were performed for multiple comparisons.

Results: Intraperitoneally administered caffeine significantly increased the spike frequency from 20 minutes after injection ($p<0.05$). Administration of AM251 together with caffeine, also increased the spike frequency, however this increase was not significant compared to caffeine group ($p>0.05$). When ACEA was applied with caffeine, anticonvulsant activity was observed such as ACEA group ($p<0.05$). No significant difference was determined between any groups about spike amplitudes ($p>0.05$).

Conclusion: Non-selectively adenosine receptor inhibitor caffeine increased penicillin-induced epileptiform activity. Reversing the effect of caffeine by the administration of the CB1 receptor agonist, and the fact that the CB1 receptor antagonist did not enhance the proconvulsant effect of caffeine suggests a possible interaction between caffeine and CB1 receptors.

Keywords: rat, epilepsy, penicillin, caffeine, cannabinoid CB1 receptor

O-25

Effects of basal forebrain stimulation on the distribution of nicotinic acetylcholine receptors with α4/α7 subunits in the somatosensory and motor cortex of rat brain

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Objective: In this study, we specifically investigated the effects of basal forebrain (BF) stimulation (activating the cholinergic system) on the receptor distributions in different layers of rat primary somatosensory cortex (barrel field and hind limb areas in SI) and motor cortex (agranular field) to understand the cholinergic circuitry.

Methods: Fourteen anaesthesized Wistar albino rats were used (control n=5, ipsilateral n=5, contralateral n=4). BF was electrically stimulated in either hemisphere (240 trials of 50 current pulses of 50 μA at 100 Hz). Coronal sections (thickness: 50 μm) were studied by a standard immunofluorescence protocol. Nicotinic acetylcholine receptors, α4 and α7 subunits, were localized by polyclonal antibodies. For immunofluorescence imaging, a secondary antibody conjugated to Alexa Fluor 594 was used. Statistical analyses were performed by repeated measures ANOVA on two dependent variables: number of labeled receptor complexes (N) and number of receptor complexes normalized by layer thickness (D).

Results: Three-way ANOVA showed significant main effects of cortical layer and area on N and D both for subtypes including α4 and α7 (all p values <0.01). Moreover, there was a significant main effect of BF stimulation on N and D for the subtype including only α7 (p=0.003 and p=0.008, respectively). Post-hoc tests showed that the control (no stimulation) group is significantly different from the ipsilateral (same hemisphere as stimulation site) and the contralateral groups, but there was no difference between ipsilateral and contralateral groups. Additionally, there was a strong cortical layer × area interaction.

Conclusion: The electrical activation of massive cholinergic input to sensorimotor cortex changes nicotinic receptor distribution of the subtype α7, but not as much for the subtype α4. These results are consistent with the literature regarding the involvement of α7 in attentional processes. Due to lower binding affinity for α7, both synaptic and extrasynaptic sites may be required for modulating attentional signals.

Keywords: nicotinic acetylcholine receptors, basal forebrain, cholinergic system, somatosensory cortex

O-26

Prilocaine induced epileptiform activity and cardiac toxicity is alleviated by thymoquinone treatment

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Objective: The aim of this study was to investigate whether thymoquinone (TQ) could alleviate prilocaine-induced (PRL) central nervous system, cardiovascular toxicity in anaesthetized rats.

Methods: With the approval of the Local Ethics Committee of the Animal Experiments of Akdeniz University; Rats were randomized to following groups: Control, PRL, TQ, PRL+TQ treated. Rats were anesthetized intraperitoneally. Fronto-occipital EEG and ECG electrodes were placed and the trachea was intubated. Mechanical ventilation was initiated with a tidal volume of 10 mg/kg and a rate of 50–55 breaths/min. Right femoral artery was cannulated for continuous blood pressure measurements and blood-gas sampling while the left femoral artery was cannulated for PRL infusion (8 mg/kg/min).TQ was given by gavage (15 mg/kg per day) for 3 days prior to drug administration. Arterial blood sample for blood gas analysis was drawn before drug infusion, during drug infusion and after cardiac arrest. Markers of myocardial injury, oxygen/nitrogen species generation, total antioxidant capacity were assayed by standard kits. AQP4, NFκBp65, p50 subunit in brain tissue were evaluated by immunohistochemically.

Results: Blood pH,partial oxygen pressure was significantly decreased after PRL infusion.The decrease in blood pH was alleviated in the PRL+TQ group.PRL produced seizure activity on EEG at significantly lower doses compared to PRL+TQ rats. Cardiac arrhythmia, asystole on ECG occured at significantly lower doses in the PRL. PRL caused as significant increase in serum myoglobin, CK-MB levels. PRL+TQ treatment attenuated levels of myocardial injury.PRL caused increased ROS/RNS formation and decreased TAC in the heart, brain tissues.TQ increased heart, brain TAC and decreased ROS/RNS formation in PRL groups. AQP4, p50, p65 expressions were increased in cerebellar, cerebral cortex, choroid plexus in PRL treated rats. PRL+TQ decreased the expression of AQP4, p50, p65 in brain tissue ($p<0.05$). One-way Anova test was used for statistical significance between groups.

Conclusion: The data shows that TQ is a protective agent against prilocaine-induced CNS and cardiovascular toxicity.TQ could ameliorate CNS and cardiac toxicity induced by high dose PRL treatment.

Keywords: epilepsy, cardiotoxicity, thymoquinone, prilocaine, AQP4, EEG

O-27

Common flavonoids in a single seizure: behavioral and cognitive aspects

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Objective: Flavonoids are suggested to have anticonvulsive properties, and to improve behavioral disturbances. Despite enormous amount of research, behavioral and cognitive consequences of a single seizure and flavonoids' effects on behavior and cognition still need to be elucidated.

Methods: We investigated two common flavonoids, sophoretin (quercetin) and rutoside (rutin), in a single GABA-related seizure in mice. Except for the controls (n=10), a single dose of picrotoxin (3 mg/kg) was injected to provoke seizure following 21-day-long vehicle (n=10), sophoretin (n=10, 50 mg/kg/day) or rutoside (n=10, 50 mg/kg/day) treatments. All animals were introduced to behavioral (forced swim, open-field, hot plate) and cognitive (novel object recognition, Morris' water maze) tests. The study has been approved by the local ethics committee (#2018/9-11). One-way ANOVA was used for parametric data whereas Kruskal-Wallis test for non-parametric data.

Results: Both sophoretin and rutoside reduced the seizure onset and stage ($p<0.05$). A single seizure did not result in any behavioral disturbances ($p>0.05$); however, both flavonoids displayed an antidepressant-like effect ($p<0.05$). Cognitive performances of the animals were affected by neither seizure nor treatments ($p>0.05$).

Conclusion: Unlike epilepsies, in which paroxysmal convulsions are prominent, a single GABA-related seizure does not initiate behavioral or cognitive impairments. Moreover, sophoretin and rutoside are able to relieve the seizure severity without deteriorating behavior and cognition.

Keywords: seizure, GABA, sophoretin, rutoside, cognition, behavior

O-28

L-DOPA treatment increases the striatal secretogranin II and alpha-synuclein mRNA expression in MPTP-treated marmosets

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Objective: Aggregated alpha-synuclein is found in Lewy bodies of idiopathic Parkinson's disease. Although its role is not fully understood, the main function of alpha-synuclein would appear to be the control of neurotransmitter release. Similarly, the function of secretogranin II (SgII) in basal ganglia is unknown but is thought to be involved in the modulation of endoproteolytic processes, vesicle formation and neurogenic inflammation. In the present study, we report on the effect of MPTP treatment of the common marmoset and subsequent chronic administration of L-DOPA, bromocriptine and ropinirole in relation to produce dyskinesia by measuring alpha-synuclein and SgII mRNA expression in the striatum by in situ hybridisation.

Methods: Animals were divided in 4 groups and received either placebo (10% sucrose), bromocriptine (0.5 mg/kg), L-DOPA plus carbidopa (12.5 mg/kg+12.5 mg/kg) or ropinirole (0.3 mg/kg) once daily for 4 weeks orally. All drug treatments produced an equivalent increase in motor activity and reversal of motor disability. Further four animals were used as naive controls. In situ hybridisation histochemistry were performed on the sections with probes for human SgII and alpha-synuclein (Home Office Licence PPL 70/03563).

Results: L-DOPA rapidly induced marked dyskinesia whereas bromocriptine or ropinirole induced only mild dyskinesia. MPTP-treatment had no effect on α-synuclein or SgII mRNA expression in either the caudate nucleus or putamen. Bromocriptine also had no effect on levels of alpha-synuclein or SgII mRNA expression. Ropinirole tended to elevate the levels of alpha-synuclein but not SgII mRNA in the caudate nucleus and putamen. However, L-DOPA administration markedly elevated alpha-synuclein and SgII mRNA expression in both the caudate nucleus ($p<0.05$) and putamen ($p<0.05$).

Conclusion: L-DOPA administration may cause synaptic dysfunction in striatum. Hence the increase in alpha-synuclein or SgII mRNA levels induced by L-DOPA may explain the motor complications occurring on long-term treatment of Parkinson's disease. Supported by Parkinson's Disease Society UK and National Parkinson's Foundation USA.

Keywords: Parkinson's disease, dyskinesia, L-DOPA, marmoset

O-29

The neuroprotective effects of ursodeoxycholic acid (UDCA) on experimental Parkinson model in rats

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Objective: Parkinson's disease (PD) is a chronic neurodegenerative disorder mainly characterized by progressive dopaminergic neuron death. Growing evidence verifies that neurodegeneration in PD likely involves inflammation, apoptosis and oxidative stress. Ursodeoxycholic acid (UDCA) is an endogenous bile acid that has been used in the treatment of liver diseases. Several anti-apoptotic, anti-oxidant and anti-inflammatory mechanisms have been advocated for UDCA. UDCA has been shown to have neuroprotective effects in Alzheimer's-Huntington's disease. In the present study, we investigated the antioxidant, neuroprotective and anti-inflammatory effects of UDCA in an experimental neurodegenerative PD model induced by rotenone in rats.

Methods: Eighteen adult Sprague-Dawley rats were infused with rotenone (3 µg/µl in DMSO) or vehicle (1 µl DMSO) into the left substantia nigra pars compacta (SNc) under stereotaxic surgery. This study was approved by the Institutional Animal Care and Ethical Committee of Ege University. PD model was assessed by rotational test ten days after drug infusion. The valid PD rats were randomly distributed into two groups; Group 1 (n=6) and Group 2 (n=6) were adminis-tered saline (1 ml/kg/day, oral gavage) and UDCA (250 mg/kg/day by oral gavage) through 28 days, respectively. The effects of UDCA treatment were evaluated by behavioral (rotation-score), biochemical [oxidant/antioxidant status-(by Elisa)] and immunohistochemical (tyrosine hydroxylase (TH)) parameters. Statistical analyses were performed using two-way ANOVA and two-tailed independent t-test.

Results: Rotations in PD rats were significantly suppressed by UDCA ($p<0.05$). The rats in which PD was induced by rotenone showed increased MDA and decreased TH levels. On the other hand, UDCA treatment resulted in markedly decreased MDA and increased TH levels ($p<0.05$). UDCA treatment in group 2 resulted in improvement of striatal neurodegeneration and a significant increase in immunohistochemical TH positive neurons ($p<0.05$).

Conclusion: Results of the present study demonstrate the neuroprotective, anti-inflammatory and antioxidant effects of UDCA in a rotenone-induced neurodegenerative animal model.

Keywords: ursodeoxycholic acid, UDCA, rotenone, Parkinson's disease, oxidative stress

O-30

Investigation of the neuroprotective effect of humanin in an *in vitro* Parkinson's disease model

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Objective: Humanin (HN), a peptide with 24 amino acids, has been studied in many neurodegenerative diseases including Alzheimer's disease after its discovery. The aim of this study was to investigate whether HN has a neuroprotective effect in an *in vitro* Parkinson's disease model induced by 6-hydroxydopamine (6-OHDA).

Methods: The neuroprotective effect of HN against 6-OHDA neurotoxicity was investigated through mitochondrial dysfunction, apoptosis and cytotoxicity parameters in SH-SY5Y human neuroblastoma cells. Different concentrations of 6-OHDA (1600–100 µM) and humanin (20–0.3125 µM) were applied on cells. The neuroprotective effect of humanin was investigated using MTT, LDH and caspase-3 assays. Statistical analysis was performed using GraphPad Prism 8 program. The differences between the groups were evaluated with one-way ANOVA statistics.

Results: The IC50 dose was calculated as 233.7 µM. HN did not have a proliferative effect when administered alone. However, 24 h pretreatment by 10 µM and 20 µM HN showed a neuroprotective and proliferative effect against 6-OHDA neurotoxicity.

Conclusion: Neuroprotective effect of HN against 6-OHDA neurotoxicity was shown in this study. HN can therefore be further studied in other *in vitro* and *in vivo* animal Parkinson's disease models to further investigate if it can be used for the treatment of Parkinson's disease.

Keywords: apoptosis, cytotoxicity, humanin, neuroprotective effect, mitochondrial dysfunction, Parkinson's disease

O-31

Identification of drug targets for Parkinson's disease through the integration of transcriptome data into genome-scale metabolic networks

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Objective: By integrating genomic-scale metabolic networks with gene expression information, it is aimed to elucidate the molecular mechanisms of the disease and to identify candidate drug targets.

Methods: In this study, the brain-specific metabolic model, iBrain606, was used to estimate metabolic changes in Parkinson's disease. We use transcriptome datasets from Parkinson's disease patients, obtained from NCBI Gene Expression Omnibus. iBrain606 and the transcriptome data were used as input to a bioinformatic algorithm, which enables the prediction of metabolic reaction rates for healthy and disease cases. This computational approach was used to determine candidate drug targets, the genes whose deletions will bring the activity of metabolism closer to the the healthy case.

Results: Simulation results show a decrease in glucose and oxygen uptake rates, a significant increase in lactate secretion, a decrease in ATP production and a significantly low activity for the Krebs cycle rates. Additional simulations to bring the diseased state to healthy state enabled the identification of novel drug targets.

Conclusion: Using the molecular crowding constraint with the integration of transcriptome data into the genome-scale metabolic network is a successful approach to understanding the mechanism of Parkinson's disease, finding new drug targets and candidates.

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Keywords: Parkinson's disease, genome-scale metabolic networks, constraint-based metabolic modelling, transcriptome data, molecular crowding

O-32

Effect of different types of calorie restriction on circulation miRNAs

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Objective: Beneficial effects of calorie restriction (CR) have been shown in variety of pathophysiological conditions such as neurological diseases, cardiovascular diseases, ageing and cancer. The aim of the present study was to test and compare the miRNA profile in whole blood due to different types of CR methods; chronic calorie restriction (CCR) and intermittent calorie restriction (ICR). In addition pathway analysis was performed.

Methods: MMTV-TGF-α female transgenic mice were enrolled in different dietary groups; ad libitum (AL, have access food all the time, control, n=3), CCR (15% of CR application compared to AL, n=3) or ICR (one week 60% CR application following three weeks AL feeding in cyclic manner, n=3) groups starting at 10 until 82 weeks of mouse age. Blood samples were collected at weeks 10, 49/50 and 81/82 of mouse age and total of 3.195 miRNAs were analysed (Affymetrix microarray, ebayes ANOVA). Then, Gene ontology (GO) analysis in neurogenesis signalling pathways was performed. Animal studies were approved by Yeditepe University Animal Research Ethical Committee.

Results: Compared to AL group, 11 miRNAs were differentially expressed in CCR, 39 miRNAs were differentially expressed in ICR-R and 11 miRNAs were differentially expressed in ICR-RF at week 49/50. GO analysis revealed that neural tube development, generation of neurons and positive regulation of neuron differentiation term was enriched. Compared to AL group, 6 miRNAs were differentially expressed in CCR at week 81/82. Compared to AL group, 26 miRNAs were differentially expressed in ICR-R at week 81/82. Synaptic membrane term was enriched in this comparison. Compared to AL group, 33 miRNAs were differentially expressed in ICR-RF at week 81/82. Axonal transport term was enriched.

Conclusion: As results, due to different types of calorie restriction, miRNAs detected in whole blood belong to different functions were enriched such as generation of neurons, positive regulation of neuron differentiation, synaptic membrane and axonal transport term.

Keywords: calorie restriction, intermittent calorie restriction, microRNA, neurogenesis

O-33

The effect of different fat containing diet exposure in maternal-maturation periods on oily taste perception and fat preference in male Sprague-Dawley offspring rats

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Objective: The aim of this study was to investigate the possible effect of exposure to the different concentration of dietary lipids during gestation, lactation and maturation periods on oily taste perception and fat preference in male Sprague-Dawley offspring's.

Methods: Pregnant Sprague-Dawley rats were randomly divided into three main groups as standard fat diet (SFD), high fat diet (HFD), and low fat diet (LFD) during maternal periods (gestation and lactation). Next 120 days; the male offspring obtained from three main groups were fed with SFD, HFD, and LFD during the maturation period. 84 male-offspring rats in nine different groups were used for this study. Long and short-term fat preference of offspring were measured by two bottle preference test and lick-o-meter algorithm respectively. Statistical analyses were performed by Kruskal Wallis and Mann-Whitney U tests. $p<0.05$ was considered as statistically significant.

Results: According to the data from 48 hours two bottle preference test, maternal/SFD-fed offspring's more preferred the solution containing 2% rapeseed oil when the animals exposed to LFD during the maturation period ($p<0.05$). Maternal/HFD-fed and maturation/HFD-exposed offspring's more preferred 2% rapeseed oil solution compared to STD and LFD offspring in maternal period ($p<0.05$). Similarly, it was determined that maternal/HFD-fed and maturation/LFD-fed offspring's more preferred the 2% rapeseed oil solution compared to maternal/LFD-fed offspring's ($p<0,05$). The result of the fatty taste preference test which is performed by lick-o-meter was maternal/SFD-fed and maturation/LFD-exposed offspring's licking percentage of 1% oleic acid decreased when compared to maturation/HFD-fed offspring's ($p<0.05$).

Conclusion: The exposed fat during maternal and maturation periods affects oily taste perception and fat preference in male Sprague-Dawley offspring rats.

Experimental protocol of project supported by TUBITAK was approved by Yeditepe University Local Ethical Committee (2017/575).

Keywords: maternal nutrition, two bottle preference, lickometer, taste perception

O-34

The effect of selenium on learning and memory and Tau relationship in young rats

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Objective: Recent studies have focused on antioxidant theory in the pathogenesis of dementia diseases. Selenium (Se) is an important trace element found in the structure of antioxidant selenoproteins. Investigation of selenium effect in dementia diseases may be involved in the elucidation of the molecular pathways of these diseases.This report describes the effect of selenium on learning, memory and tau relationship.

Methods: The experiments were carried out on 2 months-old adult male Wistar rats.The rats were divided into 3 groups; fed with standard chow (C group, n=7), Se deficient diet (Se-

group, 0.007ppm Na2SeO3, n=7) and Se-supplemented diet (S+group, 10ppm Na2SeO3, n=7). After these diets were applied to experimental animals for 21 days, experiments were started. Hippocampus dependent spatial learning was measured using the water maze. Hippocampal Se levels were measured in rats by using inductively coupled plasma mass spectrometry (ICP-MS). Phosphorylated and total tau levels were measured in whole hippocampus by Western blot.

Results: Selenium deficiency showed significant effect ($p<0.05$) on EL (Escape Latency) and DM (Distance movement). Both parameters support that selenium deficiency impairs learning. However, Se deficient group had lower swimming speed than control group ($p=0.002$) and Se supplemented ($p=0.027$) group. Parameters such as EL and DM that can be affected by swimming speed. The mean distance to platform values which not affected by swimming speed showed that Se deficient rats have impaired learning performance. The duration of being in the target quadrant of groups was not statistically significant (probe). Se supplementation did not show effect on learning and memory. Se supplementation resulted in an increase in Se levels of blood and hippocampus tissues and an increase in the ratio of p231Tau-to-Tau in the hippocampus.

Conclusion: This study showed that insufficient Se levels impaired motor function and spatial learning but there were no adverse effects on memory functions in rats. Changes in phosphorylated tau/tau ratio suggest that selenium is involved in antioxidant mechanisms to prevent neuronal degeneration

Keywords: hippocampus, learning, selenium, Tau

O-35

The role of glutamate in the neurotoxicity due to exposed to sulfite in the prenatal and/or postnatal period in rats

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Objective: One of the most widely used food additives is sulfite. It is known that consumption of sulfite over the daily safe level can also lead to toxic effects. It has been demonstrated that sulfite cause to impair the learning and spatial memory by inducing damage to the pyramidal neurons in the hippocampal tissue in rats. In this study, the impacts of sulfite neurotoxicity on glutamate pathway were examined in prenatal and postnatal period.

Methods: Experimental groups were separated as; control(C), prenatal(PR), postnatal(PS), prenatal and postnatal(PR+PS). C group were administered standard tap water. Other groups were given 100 mg/kg/day sodiummetabisulfite in drinking water in prenatal, postnatal and both prenatal and postnatal periods. Plasma S-sulfonate level was examined. In the hippocampi of rats Glutamate and glutamine levels were analysed by mass spectrometry and NMDA/AMPA receptor proteins, CaMKII, PKA, CREB protein levels were evaluated by Western-Blotting method. Statistical analyzes were performed by One-Way ANOVA test.

Results: In the Morris water maze test, it was seen that the PS and PR+PS groups increased escape latencies compared to the control ($p<0.05$). Plasma S-sulfonate levels were increased in the PS and PR+PS groups levels compared to the control group ($p<0.01$). According to the control, glutamate and glutamine concentrations in PR and PR+PS groups ($p<0.05$), AMPA receptor subtypes in PS and PR+PS groups, NMDA receptor subtypes PR, PS and PR+PS was observed to decrease in groups ($p<0.01$). Likewise, CaMKII and PKA protein levels decreased in PS and PR+PS groups. Lastly, it was observed that CREB protein level decreased in PS group compared to the C group ($p<0.001$).

Conclusion: It has been shown that sulfite exposure during prenatal and/or postnatal period may have negative effects on learning, glutamate and glutamate receptors.

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Keywords: sulfite, learning, glutamate

O-36

The investigation of analgesic efficacy of Gasser ganglion radiofrequency thermocoagulation therapy in trigeminal neuralgia

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Objective: Trigeminal neuralgia (TN) is a neuropathic pain syndrome, characterized by paroxysmal electric shock-like pain confined to the distribution of one or more divisions of the trigeminal nerve. Anticonvulsants, especially carbamazepine, are still the gold standard in their treatment. Surgery or minimally invasive procedures may be performed when medical therapy is insufficient. In this study, percutaneous radiofrequency thermocoagulation (PRFT) treatment in gasser ganglion applied in TN was evaluated in terms of analgesic effect, complications and patient satisfaction.

Methods: Fifty-three patients (29 female, 24 male) with TN who underwent PRFT to the gasser ganglion were evaluated after the approval of the Clinical Ethics Committee of Firat University. The study was started with 53 patients, but could be completed with only 40 patients. The pain duration, the involved side and branch, the drug dose used and the preoperative pain score (VAS) were recorded. Patient satisfaction was evaluated according to Odom's criteria and VAS scores at 1st, 3rd, 6th and 12th months after the procedure.

Results: The mean age of the evaluated patients was 60.5/year and the mean duration of pain was 65/month. The preoperative VAS score of the patients was 6.7. In the 40 follow-up patients, VAS score was 1.8 at the first month, 2.05 at the 3rd month, 2.9 at the 6th month and 3.1 at the 12th month, and the patients were found to be painless at 10.8 months. According to Odom's criteria, patient satisfaction was excellent-good in 44% and weak in 4 patients. Although none of the patients developed any serious complications, hypoesthesia was reported in 3 patients.

Conclusion: Trigeminal neuralgia affects the quality of life of patients. Although the basic treatment is anticonvulsants, minimally invasive procedures, especially gasser ganglion PRFT, are used as an effective and safe option in cases where medical treatment is insufficient and the results of this study support this.

Keywords: trigeminal neuralgia, gasser ganglion, radiofrequency thermocoagulation, analgesia

O-37

A new approach in treatment of peripheral nerve injury: electro-acupuncture stimulation

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Objective: Peripheral nerve injuries, caused by traumas or acute compression, results in the loss of motor and/or sensory function. Development of methods to expedite nerve regeneration is important to enhance patient well-being. Melatonin, having free radical cleansing and antioxidant properties, was shown to reduce the injury in nervous tissue. Electro-acupuncture is a complementary medicine method, combining classical acupuncture with modern electrotherapy. The aim of this study is to determine and compare the therapeutic effects of electro-acupuncture and melatonin supplementation on sciatic nerve injury.

Methods: Adult Wistar rats were divided into four groups, namely control, nerve injury, 5 mg/kg melatonin administration after nerve injury, electro-acupuncture after nerve injury. Unilateral nerve injury was induced by the placement of an aneurism clamp onto sciatic nerve for 1 minute. After nerve injury, treatments were applied once every 5 days throughout 4 weeks. Electro-acupuncture was applied onto the acupuncture points at the top and base of the injured region (GB30, GB34). 70 Hz frequency electric current was applied to the acupuncture points by a stainless steel acupuncture needle for 15 minutes. Sciatic functional index (SFI) was measured weekly and at the end of the treatment, nerve conduction velocities (NCV) and distal latencies were evaluated and results were compared statistically by one-way ANOVA.

Results: The results demonstrated that sciatic nerve injury resulted in a significant decrease ($p<0.05$) in NCVs. Electro-acupuncture led to a significant increase ($p<0.05$) in the NCVs in comparison to nerve injury group. However, melatonin supplementation, which was used as a positive control, resulted in only a slight increase in NCVs. SFI results showed that sciatic functions recovered much faster in both treatment groups in comparison to nerve injury group. However, no significant difference was observed in between the treatment groups.

Conclusion: Electro-acupuncture is a promising complementary medicine method in peripheral nerve injuries and warrants further investigations.

Keywords: sciatic nerve injury, electro-acupuncture, melatonin, sciatic functional index, nerve conduction velocity

O-38

Multiple intracranial meningioma

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Objective: Meningiomas are the most common intracranial tumors in adults, originating from the membranes of the brain and spinal cord. According to the World Health Organization (WHO) classification; meningothelial, fibroblastic, transitional (Grade 1), chordoid, clear cell, atypical (Grade 2), papillary, rhabdoic and anaplastic (Grade 3) subtypes are available and most often subtypes are grade 1. Multiple ıntracranial menengiomas are very rare tumors without neurofibromatosis Type 2. In this report,a case with primary multiple intracranial meningioma will be discussed.

Methods: Meningiomas comprise 24–30% of primary intracranial tumors. It is often seen in middle and old aged adults but also could be seen in children. Meningiomas originate from arachnoid cap cells.In etiology; ionizing radiation, hormonal factors, obesity, genetic predisposition are involved. Most common sites as intracranial are cerebral convexities, falx and parasagittal areas. They are often solitary tumors,but can also be multifocal. Terminologically, multiple intracranial meningiomas are present at two or more meningiomas in different localizations. The development of multiple meningioma is known, especially in the background of NF Type 2. Although the development of multiple meningioma without NF Type 2 is not very common,it has been reported in the literature.

Results: A 68-year-old male patient was admitted to our clinic with complaints of diminished in smell perception for 2 months and tremor in the hands for 15 days.The head MRI revealed multiple intracranial masses compatible with meningioma; a 23×30 mm in the anterior clinoid in the frontal, 25 mm in the left parietal, 40×52 mm in the right occipital, and 25 mm in the right temporal lobes. Surgery was planned for the occipital meningioma, a large lesion causing mass effect.

Conclusion: Multiple intracranial meningiomas are very rare lesions without NF type 2. There is no difference in solitary meningiomas with regards to histopathological subtypes and treatment approaches. However, in cases with multiple meningioma,each of the meningiomas may be in various grades and

malignancies. The main treatment of meningiomas is surgical total excision. Surgery must be arranged, based on patient-dependent factors such as age, performance scale, morbidity; treatment-dependent factors such as degree of symptoms and surgical success.

Keywords: meningioma, multiple meningioma, neurofibromatosis

O-39

The evaluation of screw entry points and angles with 3-dimensional reconstruction method to guide the transpedicular screwing technique

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Objective: The aim of this study was to determine the distances to the reference points of the screw entry points, screw insertion angles to transverse and sagittal planes and the maximum screw length that can be used from C2 to C7 in the Turkish society according to gender, age groups, and the vertebra.

Methods: The images of patients who underwent CT (Computed Tomography) for various reasons in Gazi University, Faculty of Medicine, Department of Radiology were evaluated retrospectively. The study involved 100 patients (41 males, 59 females) aged 18–79 years (mean 43 years). CT image examinations were reviewed retrospectively. CT images were transferred to OSIRIX software in DICOM format. With the 3D Volume Rendering feature of the OSIRIX software, two-dimensional images were converted into three-dimensional images. Density settings were made so that bone tissue could be best observed. Pedicle axis length (PAU), pedicle transverse angle (PTA), pedicle sagittal angle (PSA), distance of the entry point to the lateral notch (LNU) and distance of the entry point to the inferior articular process (PAIU) from C2 to C7 has been measured bilaterally.

Results: LNUL and IAPUL in C2, LNUR, IAPUR and PAIUL in C3, PAIUR and PAIUL in C4, PAIUR in C5 measurement was statistically significant between males and females ($p<0.005$). Measurements of C6 and C7 did not show any statistically significant difference between males and females ($p>0.05$). LNUR and LNUL in C2, LNUL in C3 was increasing; PAIUR in C2; PSAL in C3; PTAL parameters in C7 was decreasing with age ($p<0.005$). In females, the intersection was most seen in C3 (36.58%) and no intersection was seen in C2 and C7. In males, the most intersection was seen in C4 (25.37%).

Conclusion: The results obtained from this study, may help surgeons to determine the appropriate screw selection and surgical method for the application of Transpedıcular Screwing Technique.

Keywords: anatomy, cervical vertebrae, cervical pedicle screw, 3D reconstruction

O-40

Healing effect of *Hericium erinaceus* in experimental peripheral neuropathy model

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Objective: Cisplatin is one of the most effective anticancer drugs used in the treatment of various solid tumors. However, cisplatin-induced peripheral neuropathy (CIPN) is the most common and dose-limiting side effect of cisplatin. In clinic, it is aimed to increase the survival rate and increase the quality of life of cancer patients receiving chemotherapy. Lion's mane (*Hericium erinaceus*) mushroom (HE) is an edible and medical fungus. It has been reported that HE exhibits anti-cancer and neuroprotective activities. The current study was aimed to explore the regenerative effect of HE on a peripheral neuropathy model in BALB/c mice.

Methods: In the present study, the experimental CIPN model was created using cisplatin in BALB/c mice. For treatment of the CIPN, the hot aqueous extract of HE was prepared and applied to the animals intraperitoneally. Its therapeutic effects on peripheral nerves were investigated by body weight changes' analysis, electromyographic (EMG) measurements, and immunohistochemistry technics using confocal laser scanning microscopy.

Results: HE treatment significantly prevented cisplatin-induced weight loss ($p<0.05$). In EMG measurements, although there is no significant difference among the groups, HE treatment showed a trend in functional recovery by increasing compound muscle action potential (CMAP) amplitude and accelerating latency period. Immunohistochemical findings exhibited that HE treatment initiates regeneration of myelin and axon significantly in animals with CIPN ($p<0.05$).

Conclusion: HE exhibited therapeutic effects on a mouse model of peripheral neuropathy. HE may be an efficient and safe therapeutic agent to be used in peripheral neuropathy. Therefore, our study warrants further detailed investigation of HE as a potential therapeutic agent.

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Keywords: cisplatin, peripheral neuropathy, *Hericium erinaceus*, therapeutic effect

O-41

Neuroprotective effect of curcumin in diabetic neuropathy: an FTIR imaging study

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Objective: Diabetic neuropathy is one of the most common complications of diabetes. The only treatment strategy of diabetic neuropathy is the control of blood sugar, but its prevention will improve patient well-being. The aim of this study was to determine the possible neuroprotective effects of curcumin, a potent antioxidant, on sciatic nerves in an experimental diabetic rat model.

Methods: Diabetes was induced by a single 50 mg/kg dose of streptozotocine (STZ) injection in adult Wistar rats. After the induction of diabetes, the rats were administered with gliclazide (10 mg/kg), low-dose (60 mg/kg) and high-dose curcumin (200 mg/kg) by oral gavage daily for 5 weeks. The control group only received solvent administration. 12 µm thick sciatic nerve sections obtained by a cryotome were placed onto BaF_2 windows and analyzed by Fourier transform infrared (FTIR) imaging.

Results: Diabetes led to an increase in lipid/protein ratio and carbonyl amount in lipids in sciatic nerves. Curcumin application, especially in the low-dose, was observed to be effective in preventing these alterations. Diabetes-induced increase in the unsaturated lipid content and unsaturation index was not observed in curcumin administration, especially in the low-dose, revealing that curcumin administration reduces lipid peroxidation end products. In addition, diabetes-induced increase in lipid acyl chain length was restored upon curcumin application. There was no change in the amount of phosphate-containing lipids together with an increase in ester-containing lipids and lipids without phosphate in diabetes. Curcumin administration resulted in a higher content of phosphate-containing lipids and a decreased content of ester-containing lipids, especially in the high-dose.

Conclusion: Diabetes results in neurodegeneration by causing alterations in the structure of sciatic nerve macromolecules. Curcumin is a substance that has a promising neuroprotective effect in the prevention of diabetic neuropathy.

This study was funded by Scientific Research Council of Adnan Menderes University (TPF-17039).

Keywords: curcumin, diabetes, diabetic neuropathy, FTIR imaging

O-42

Protective effects of sesamol against secondary injury in the rat model of traumatic brain injury

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Objective: Traumatic brain injury (TBI) has high mortality and morbidity rates. Oxidative stress, apoptosis, inflammation, and ischemia cause tissue damage after TBI. Sesamol is a powerful antioxidant, antiapoptotic, and neuroprotective substance. The aim of this study was to investigate possible antioxidant, antiapoptotic effects of sesamol in a rat TBI model.

Methods: A total of 32 male rats were used and divided into four groups as control, trauma, vehicle and sesamol groups. Trauma, vehicle, and sesamol groups were subjected to closed-head contusive weight-drop injuries, and either vehicle (saline) or sesamol (100 mg/kg) was administered intraperitoneally immediately after trauma. At the 24th hour after trauma induction, brain samples were removed and the activities of glutathione peroxidase (GSH-Px), malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), nitric oxide (NO), nitric oxide synthase (NOS), xanthine oxidase (XO) and caspase-3 were measured and histomorphological evaluation was performed by electron and light microscopy in the cerebral cortex.

Results: In the trauma and vehicle groups, TBI-induced decrease in GSH-Px, SOD, and CAT activity were reversed with sesamol treatment. Increased MDA, and XO activities in the trauma, and vehicle groups were suppressed in the sesamol group. Higher levels of NO in the trauma and vehicle groups were decreased in the sesamol group which is reverse for NOS. Increased caspase-3 activity in the trauma, and vehicle group were suppressed in the sesamol group. In histopathological examination, the damage in the cerebral cortex induced by TBI was lighter in the sesamol group.

Conclusion: The results of this study revealed for the first time that sesamol, via its antioxidant, and antiapoptotic activities, exhibits neuroprotective effects againts TBI.

Keywords: sesamol, antioxidant, brain

O-43

Effects of the endocrine disrupting chemicals on the trace element and mineral levels in the brain

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Objective: Humans are exposed to the various dangerous chemicals via industrial products including cosmetics, food wrappings, personal care products, medical tubes, plastic bottles, toys etc daily basis. Di(2-Ethylhexyl) (DEHP) is the most commonly used plasticizer in the industry and belongs to the endocrine disrupting chemicals family. Daily human exposure to the DEHP is 3–30 µg/kg and occurs via inhalation, diet and/or dermal absorption. There is an increasing concern against DEHP and its metabolites since their adverse health effects on human and wildlife.

Methods: 24 prepubertal male Wistar albino rats were randomly divided into four groups based on the DEHP administration as 0, 100, 200, 400 mg/kg/day. DEHP administration was performed by oral gavage daily. Glucose-6-phosphate dehydrogenase (G6PD), 6-phosphogluconate dehydrogenase (6PGD), glutathione reductase (GR) and glutathione S-transferase (GST) enzyme activities were measured by spectrophotometer. Trace element (Ag, Al, As, Ba, Be, Cd, Co, Cr, Cs, Cu, Fe, Ga, Li, Mn, Ni, Pb, Rb, Se, Sr, Ti, U, V, Zn) and mineral levels (Ca, K, Mg, Na) were evaluated in the brain samples of DEHP-administered rats via ICP-MS.

Results: Sodium (Na), magnesium (Mg), potassium (K), manganese (Mn), rubidium (Rb) and iron (Fe) levels significantly increased in 400 mg/kg/day DEHP treated groups compared to the control in rat brain tissue samples ($p \leq 0.0001$). Zinc (Zn) and strontium (Sr) levels significantly elevated 1.5 times more in 200 mg/kg/day DEHP treated groups compared to the control ($p \leq 0.0001$). On the other hand, Cu levels significantly decreased in 200 mg/kg/day group compared to the 100 and 400 mg/kg/day treated groups in brain samples ($p \leq 0.0001$). This increase was 1.5 times less in 200 mg/kg/day group compared to others.

Conclusion: Our data have revealed that, DEHP can disrupt trace element and mineral concentrations, therefore long-term exposure to the DEHP may cause biochemical or physiological impairment in the brain.

Keywords: DEHP, brain, anti-oxidant metabolism, trace elements, minerals

O-44

A computational model for investigating the role of nitric oxide due to activation of glia cells during long term potentiation

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Objective: Cognitive processes, motor actions all emerge due to communication of neurons. The role of glia cells on the communication between neurons has been neglected till recently. Now, there is increasing number of work focusing on glia cells, especially on their role in learning and memory formation. Recently, some mathematical models have been proposed to model the role of glia cells on long term potentiation. In these work, though the role of nitric oxide has been mentioned, its effect has not been included to the models. Here, the effect of nitric oxide on the calcium channels will be modelled based on Hodgkin-Huxley neuron model.

Methods: The most detailed neuron model, considering the physiological properties of a neuron model is Hodgkin-Huxley model, but it includes only the sodium, potassium channels in detail and the effect of others are included as leak current. To observe the effect of nitric oxide, the model should include terms for calcium channels. To this respect, three different types of calcium related ion channel models are included to Hodgkin-Huxley model and then the diffusion of nitric oxide is expressed with a differential equation. Then, the dynamical properties of the whole process has been modelled with a set of differential equations and the simulation results based on this model is obtained in Python, using the libraries of BRIAN2 simulator.

Results: Simulation results revealed that calcium uptake is enhanced as a response to diffusion of nitric oxide and consequently, the behaviour of the neuron membrane potential is altered. Especially, the frequency of spike train is increased with nitric oxide concentration at constant stimulating current value.

Conclusion: The simulation results are in agreement with experimental results carried out in hippocampus and it clearly reveals that the spike frequency is increased with the amount of nitric oxide concentration.

Keywords: computational neuroscience, glia, learning, LTP

O-45

The GG4 (GXXXG) motif difference between TRPA1 and TRPM7 ion channels

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Objective: TRPA1 and TRPM7 ion channels are known to interact with some ligands but detailed information on these interactions are not known. The importance of motifs including GXXXG (GG4) motif on the protein-protein interactions were recently shown. The aim of this study was to investigate the differences between human TRPA1 and TRPM7 in terms of GG4 motifs using bioinformatical methods.

Methods: The information of TRPA1 and TRPM7 ion channel sequences were obtained using Uniprot web servers, information were processed using Bash commands of GNU/Linux operating system and Clustal omega (ver. 1.2.4) was used for investigating the similarities of these ion channels. The distribution of amino acids were shown using R programming language.

Results: Presence of similar GG4 motifs were observed on these ion channels. Only TRPA1 was observed to possess tyrosine-containing GG4 motif on the other hand only TRPM7 had a similarity of GG4 motif of ACH10, a subunit of the nicotinic receptor. MXXXM (MM4) motif was observed only on TRPM7 but not on TRPA1 ion channel structure.

Conclusion: GG4 motif is important on protein-protein interactions. The presence of similar GG4 motifs on TRPA1 and TRPM7 ion channels may also be the sites for ligand interactions but the importance of tyrosine-containing GG4 motif which was observed only on TRPA1 is not known. The similarity of GG4 motifs between TRPM7 and ACH10, a subunit of nicotinic receptor is another differences between these two ion channels. Possible involvement of the TRPM7 ion channel on nicotinic activities are suggested in the present study which requires further investigations.

Keywords: TRPA1, TRPM7, GG4 motif, bioinformatics

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Simulation of morphologically and biophysically realistic single nerve cells using user-friendly software

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Objective: The aim of this study is to present the capabilities of user-friendly software which is developed for simulating neuronal dynamics of morphologically and biophysically realistic single cells.

Methods: As our previous studies show, we have developed a versatile educational software. In this study, we have extended the software with additional attributes in order to make it suitable for scientific purposes. This extension grants multiple types of current clamps, voltage clamps and synaptic inputs. As an example we have chosen a morphologically and biophysically realistic mouse brain cell which is resident in layer 4 of primary visual area. This cell's morphological details were reconstructed and biophysical parameters were fitted according to experimental studies by Allen Institute. By using these, we re-establish the experiment on our extended software and tested it with the same inputs such as long square, short square, ramp current clamps.

Results: Under 34 °C temperature conditions, the nerve cell responded 21 spikes/sec to 217 pA long square current. To ramp current clamp experiment with 35 sec duration to 800 pA, the cell responded first spike on 7460 ms and its rate was 61.57 spikes/sec. In short square experiment, the minimum current amplitude for firing the cell was 570 pA. According to result, the simulation showed significant match with experiments.

Conclusion: This study shows that software is suitable not only for educational but also scientific purposes. Any user can use this to investigate the neuronal dynamics of various cells. As it is a versatile interface, users do not have to be experts in coding. This software is expected to help wide range of people from students to scientists.

Keywords: computational neuroscience,modelling, neuron, software

O-47

Development of accurate brain computer interface using cortical source space

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Objective: This study aimed at classification accuracy of recorded electrode EEG signals related to motor imagery movement of right hand and right foot in comparison with cortical activations of the same signals. Cortical activations are obtained using EEG source imaging which transforms electrode recordings to cortical sources. Accurate control of Brain Computer Interface (BCI) based hand and foot prosthesis is aimed in this paper using both computed cortical and electrode level.

Methods: Motor imagery data recorded by 118-channel EEG from 5 healthy subject BCI-Competition-III-Dataset- IVa is is used in this work. Subjects are asked to imagine right hand or right foot tasks shown on screen. Brainstorm software and ICBM152 head model is preferred to compute cortical signals. Common Spatial Patterns (CSP) features are classified by Support Vector Machine (SVM) is used for classification.

Results: Raw electrode data and computed cortical sources corresponding to motor imagery (sensorimotor) areas marked by a physiologist are used in this study. Total 6 areas located in both left and right lobes include primary foot somatosensory area (S1F), primary hand somatosensory area (S1H) and somatosensory association cortex (SAC). Computed sources inside these sensorimotor areas yield 100%, 98.21%, 100%, 100% and 98.81% accuracy for 5 volunteers respectively whereas raw sensor data achieved 100%, 92.86%, 99.49%, 87.95% and 64.29% accuracy.

Conclusion: Even though BCI is a technology that could help people especially with motor disability, limited signal classification accuracy and ease of use as well as lack of standards and regulations impair its widespread use. Two-class motor imagery movement EEG dataset is classified to compare accuracy with classification using both raw EEG and computed cortical sources which improved classification considerably. Using cortical sources in sensorimotor areas improved accuracy even if training data set size is limited as in 5th volunteer.

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Keywords: EEG, brain computer ınterface, motor ımagery, cortical sources

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On the human vomeronasal organ: a preliminary study of radiology and bioinformatics

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Objective: Vomeronasal organ (VNO) is a neuropethelial structure, bilaterally located in antero-inferior region of nasal septum, with projections to olfactory bulbus, in vertebrates. Being regarded as part of accessory olfactory system, its role in the formation of social and sexual behavior in animal is evident,

whereas in humans its anatomical existence and physiological function(s) are controversial. This study aims to detect rate of existence and review possible functions of VNO, thought to be mostly atrophic in adult human.

Methods: Since radiological studies in the literature show that VNO structure has pit or ductus shape uni/bi-laterally on the nasal septum; vomeronasal pit/ductus was investigated on temporal bone high resolution computed tomography (HRCT) images taken at Karadeniz Technical University Medical Faculty within the last one year. Bioinformatics analysis, tissues expressed in human for VN1R (1–5) genes (provide synthesis of VNO receptors in vertebrates) were detected from Bgee database. Intracellular functions of synthesized proteins were analyzed in FFPred application, predictive protein interactions were investigated in String database.

Results: Among the total of 288 HRCT images, VNO pits were detected in 14.2%(40/282), [men:16.7%(28/168), women: 10.5% (12/114)]. Bioinformatics analysis revealed VN1R1 expression in many brain regions including adenohypophysis, prefrontal cortex, nucleus accumbens, hypothalamus; VN1R2 expressions in testes, ovary, brain; VN1R3 expressions in testes and vagina; VN1R4 in only testes; VN1R5 in prefrontal cortex and hypothalamus. A functional interactions was predicted among VN1R1 with OR7D4, OMP, CNGA2; RHO/rhodopsin protein; RTP1-2; ZNF772-773. VN1R2 and VN1R4 receptors have also predictive interactions with AVPR2 (vasopressin-2 receptor), OMP, RHO, RTP2 proteins.

Conclusion: The incidence of VNO pits in this cross-sectional study was lower than reported in literature(>25%). According to the bioinformatics analysis,the concentration of VNO related genes in especially reproductive organs and their predictive interactions with olfactory receptors and rhodopsin, suggests that this structure is likely to be functional in human but for a more conclusive statement further multidisciplinary studies are needed.

Keywords: vomeronasal organ, neuroepithelium, chemoreception, computed tomography, bioinformatics

O-49

Connections and drainage of meningeal lymphatic system: a new target to study pathogenesis of neurodegenerative diseases

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Objective: Drainage system of brain is crucial to remove cerebrospinal fluid, and waste substances and neurotoxic solutes in brain interstitial fluid. Recently, meningeal lymphatic drainage system of brain has been discovered. But drainage networks and mechanisms of this system to extracerebral structures haven't yet been well known. We aimed to investigate connections and drainage of meningeal lymphatic system by injecting evans-blue (EB) into cisterna magna (CM) in rodents.

Methods: In experiments were used six male Wistar rats weighing 250–300 g and mice weighing 24–28 g. 60 µl EB (2%) was injected by Hamilton-needle into CM of rats for 30 min. In another series, 10 µl EB was injected by an automatic micropump into CM of mice for 10 minutes. After 2 hours, qualitative and quantitative evaluation of superficial and deep cervical lymph nodes, brain, duramater, cerebellum and eyes were performed in terms of accumulation of EB in the tissues. EB concentrations in the tissues were spectrophotometrically quantified using an elisa plate-reader. Data were analyzed with one-way ANOVA.

Results: By tracing EB accumulation, we found that there are drainage networks from meningeal lymphatic vessels to the superficial and deep cervical lymph nodes, eyes, cerebral arteries and cerebellum, but not brain and duramater tissue, in both rats and mice. However EB concentration in deep cervical lymph nodes was higher than that in superficial cervical lymph nodes ($p<0.05$), and moreover EB concentration in cerebellum was higher than that in both cervical lymph nodes and eyes ($p<0.05$) in both rats and mice.

Conclusion: Our findings suggest that neurotoxic solutes and metabolic end-products in interstitial fluid of brain are removed to mostly deep cervical lymph nodes. Obstruction or disfunction of this system may play a role in pathogenesis of neuroimmune and neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and migraine. Meningeal lymphatic vessels may be crucial targets to study these diseases' pathophysiology.

This study was supported by TUBITAK-2219 and Virtanen-Institute.

Keywords: cervical lymph nodes, lymphatic clearance, meningeal lymphatics, neurodegenerative diseases

O-50

The effect of intravitreal mesenchymal stem cell and tamoxifen applications on intraocular pressure and VEP in diabetic rats

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Objective: To evaluate the effects of tamoxifen and intravitreal bone-marrow mesenchymal stem cell(MSC) on intraocular pressure(IOP) and visual evoked potential(VEP) in diabetic rats.

Methods: 2–3 monthly 64 Spraque-Dawley rats (150–250 g) were used. 8 groups were generated randomly and applications were performed for 25 days. All groups physical and some physiological characteristics were determined. Diabetic rat model was generated with a single dose of streptozotosin (60 mg/kg). Tamoxifen was administered (10 mg/kg) until the end of the

study. All groups IOP was monitored by portable tonometer and measurements were performed on the first, tenth and twentieth days. MSC applications (4 µl/1×10^6) were injected to the right eye twice 48 hours apart and left eye was used as control. Data were evaluated using statistical methods in computer environment and significance level was taken as 0.05.

Results: According to the control data, the Tamoxifen group's body weight decreased whereas there was a significant increase between groups body weights, especially in the diabetes. Fasting blood sugar levels were significantly decreased in the MSC and Tamoxifen group when compared to the control group. Significant increases in body temperature levels were observed in the groups MSC-Diabetes and Tamoxifen. Statistically significant decreases were observed in stem cell groups IOP. The oxygen saturation levels in diabetes, MSC and Tamoxifen groups compared with the control group data, were statistically significant. Latency and amplitude levels from the VEP data at 24 Hz were statistically significant in the diabetes compared with control group.

Conclusion: Increase in VEP amplitude of factors causing retinal degeneration such as diabetes and tamoxifen, increased body temperature in diabetes, MSC and tamoxifen groups; variable findings in IOP, it was thought to occur under the influence of GABAergic and dopaminergic systems in addition to the sympathetic system response.

The study was supported by the Scientific Research Projects Unit of Erciyes University with 7751 project code.

Keywords: mesenchymal stem cell, intravitreal enjection, intraocular pressure,diabet, streptozotocin

O-51

Role of cytokines in the antidepressant-like effect of dipyrone using chronic unpredictable mild stress model

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Objective: Two-way relationship of pain and depression is likely to occur due to cytokines, given their role in pain and depression mechanisms. In this study, we aimed to investigate the role of cytokines in the antidepressant-like effect of dipyrone, a powerful analgesic, in chronic unpredictable mild stress model (CUMS).

Methods: Male rats weighing 20–25 g were divided into control, stress and stress+dipyrone groups. CUMS model was used to induce depression. Mice were subjected to a variety of mild stressors several times a day for 6 weeks. Dipyrone (8 mg/g, ip) was administered to CUMS-exposed mice, each day beginning from the 2nd week. Splash, rota-rod (RR) and forced swimming (FST) tests were performed at the 7th week as behavioural tests. Coat state score (CSS) and weights of animals were recorded. Lastly, blood samples taken from mice were examined in proinflammatory IL1β, IL6, IL17, IFN and TNF-α, antiinflammatory IL-10, M-CSF, G-CSF levels. Results were analyzed using one way ANOVA followed by the Bonferonni post hoc test. This study is supported by Çukurova University Research Foundation (Project # TSA-2016-5856).

Results: No weight change was observed in UCMS-exposed mice. Significant physical changes were observed in CSS. RR latency decreased (64.4±16.7, 115±5 sec, respectively, $p<0.05$), immobility time enhanced in FST test (194.6±10.9, 124.3±25.7 sec, $p<0.05$). The number of grooming decreased in the splash test (181.5±19.25, 122.6±12.86 sec, $p<0.05$). Dipyrone reversed the latency time and immobility time to normal values and augmented the number of grooming. The levels of proinflammatory cytokines were increased ($p<0.05$) while antiinflammatory cytokine levels were unchanged in stressed mice. Proinflammatory cytokynes levels decreased to normal value ($p<0.05$) while antiinflammatory cytokines levels remained same in dipyrone applied group.

Conclusion: Results show that dipyrone has an antidepressant-like effect on CUMS model, and it shows antidepressant-like effect by decreasing proinflammatory cytokines levels which increase with stress.

Keywords: dipyrone, antidepressant-like effect, chronic unpredictable stress, cytokines, mice

Poster Presentations

(P-01 — P-68)

P-01

Effects of chronic brain-induced neurotrophic factor (BDNF) deficiency on sensory motor performance

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Objective: Brain-Induced Neurotrophic Factor (BDNF) plays a major role in the structural and functional development of the central nervous system. BDNF heterozygous mouse showed low performance in tests such as hippocampal learning and fear learning. However, it isn't known how reduced BDNF concentrations affect cortical functions. The aim of this study is to evaluate sensory motor behavior test performance of BDNF heterozygous mice associated with cortex.

Methods: Mice were obtained from Karadeniz Technical University (KTU) Surgical Research Center. An average of 20–25 g male C57BL/6 strain BDNF heterozygous (+/-) and normal (+/+) mice were used in the experiments. The study was approved by the local animal ethics committee of KTU. For the experiments, two groups (n=8) were formed: Group I: 8 wild-type mice: BDNF homozygous (+/+); Group II: 8 heterozygous mice: BDNF heterozygous (+/-) Three different behavioral tests were performed to test cortical sensory-motor functions. 1. Cylender test, 2. Hang wire test, 3. Adhesive removal test. Video images of behavioral experiments were recorded. Scoring and analysis were confirmed by the offline evaluation of recordings. Statistical analysis were made by Student'ss t-test.

Results: BDNF heterozygous mice were found to have lower performance than wild type mice in all behavior tests. This decrease was found to be statistically significant in cylinder test ($p < 0.05$), and in adhesive removal tests ($p < 0.05$).

Conclusion: It is known that BDNF is necessary for normal synaptic function, and plays a role in normal developmental and cognitive processes by affecting neuroplasticity. The applied tests evaluate the functions related to the sensory motor cortex, such as postural coordination, muscle strength, responding to touch stimuli. According to our results, it was observed that BDNF deficiency in cortex could cause dysfunctions. Our findings imply that, for normal cortical development and functions the concentration of BDNF is important.

Keywords: BDNF, sensory motor behavior tests, cortex, mouse

P-02

Effects of experimental diabetes on cerebellar oxidative stress and motor function

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Objective: Diabetes mellitus (DM) is a chronic disease with high mortality and morbidity risks. It is well established that diabetes-related alteration of the central nervous system increases the risk of neurobehavioral disturbances and locomotor disruption. Cerebellum plays a fundamental role in coordination of movements and performing of the motor functions in the body. Complex pathophysiological mechanisms such as oxidative stress have been shown to play a role in neuronal cell damage associated with diabetes mellitus.The possible harmful effects of experimental diabetes on the cerebellum are not understood well. The aim of this study was to investigate the effects of experimentally induced diabetes on cerebellum.

Methods: In our study, 24 male Wistar Albino rats weighing 300–350 g were randomly divided into two groups. 1) Normoglycemic group 2) Diabetic group. Streptozotocin (STZ) was administered intraperitoneally as a single dose (60 mg/kg) to induce DM. After 3 days of STZ administration, fasting blood glucose level >250 mg/kg was accepted as diabetes. The beam walking test was applied to assess motor coordination in animals before the experiment was terminated. Malondialdehyde (MDA) levels as a lipid peroxidation marker and glutathione (GSH) levels as an antioxidant indicator were measured by collecting cerebellum tissues from the sacrificed rats.

Results: The time to complete the platform was lower in the diabetes group compared to the normoglycemic group in the beam walking test ($p < 0.05$). MDA levels were significantly higher in the diabetes group than in the control group in the cerebellum ($p < 0.05$). Although cerebellum GSH levels were low in the diabetes group, there was no significant difference between the two groups.

Conclusion: This study showed that diabetes distrupts motor function by raising oxidative stress in cerebellum.

Keywords: diabetes mellitus, cerebellum, oxidative stress, streptozotosin

P-03

Toll-like receptor-4 expression in glial cells in mouse model of cuprizone-induced demyelination

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Objective: Multiple sclerosis (MS) is a T-cell mediated autoimmune central nervous system (CNS) disease. Although the etiopathogenetic factors of multiple sclerosis remain unclear, autoimmune mechanisms that associated with genetic predisposition and environmental triggers are suspected. Toll-like receptors (TLRs) mediate immune response to autologous components. It has been shown that microglia are the highest TLR4 expressing cell in the CNS. Several studies have shown that certain TLRs are over-expressed in MS. However, to our knowledge, the expression of TLR4 in cuprizone-induced demyelination has not been demonstrated previously. In the light of the information mentioned above, we aimed to evaluate the expression of TLR4 in glial cells in a mouse model of cuprizone-induced demyelination.

Methods: In this study, we used the cuprizone model in mice to investigate the expression of TLR4. Forty male C57BL/6 type mice were used. Four groups were designed as demyelination/control and remyelination/control. 0,2% cuprizone was used to induce demyelination. TLR4 expressions in glial cells were evaluated with immunohistochemistry.

Results: We show a significantly increased expression of TLR4 in the glial cells of the demyelination group. The expression of TLR4 was significantly higher in the demyelination group than the remyelination group. Besides, TLR4 expression in demyelinated mice glial cells was higher than the control groups.

Conclusion: We showed that TLR4 expressions were significantly higher in demyelinated mice. High expressions of TLR4 may indicate that it could be one of the underlying mechanisms of immune activation in MS. We believe that histopathological and molecular studies are necessary to obtain further information on the background of the disease.

Keywords: multiple sclerosis, toll-like receptors, cuprizone, inflammation, TLR4

P-04

Assessment of imagery ability in obstetric brachial plexus palsy

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Objective: Obstetric brachial plexus palsy (OBBP) is the paralysis of the ipsilateral upper extremity after a brachial plexus injury that occurs during labor. Imagery is determined as a new rehabilitation tool in neurological and orthopaedic treatments. The aim of this study was to investigate motor and kinesthetic imagery ability in children with OBPP.

Methods: The study was approved by Medipol University Institute of Health Sciences Non-interventional Clinical Research Ethics Committee with 159 decision no and 10840098-604.01.01-E.10507 approval number. 20 children with OBPP (8–18 years old; 12 female and 8 male) and 20 healthy subjects (8–18 years; 10 female and 10 male) who were chosen similarly in the way of age and gender according to the OBPP group were assessed. The right extremities of the 13 children and the left extremities of the 7 children with OBPP were affected. Of the 20 children with OBPP, 11 were in Type 1 group, 4 were in Type 2a group, 2 were in Type 2b group and 3 were in Type 3 group according to Narakas Classification System. Imagery ability was assessed with Movement Imagery Questionnaire-3 (MIQ-3) and Kinesthetic and Visual Imagery Questionnaire (KVIQ).

Results: When compared with the control group, it was found that the imagery ability in children with OBPP was weaker ($p<0,05$). Among the groups, there were found significant differences between Movement Imagery Questionnaire internal imagery, external imagery and kinesthetic imagery subscores.

Conclusion: It was concluded that in order to poor imagery ability in children with OBPP, it is crucial to assess the imagery ability and to add the imagery practice to the rehabilitation program.

Keywords: obstetric brachial plexus palsy, imagery, motor imagery, kinesthetic imagery

P-05

A longitudinal investigation of event related EEG brain oscillations in patients with Parkinson's disease

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Objective: Parkinson's disease (PD) is characterized by the presence of nonmotor deficits such as cognitive abnormalities that especially occurs with increasing disease duration. There is well known fact that event-related theta and alpha responses are asso-

ciated with cognitive abilities. The present study aims to longitudinally investigate changes in event-related response in PD patients.

Methods: Eight PD patients (disease duration 1.5–15 years, education 14±5 years, age 67±9, levodopa-equivalent dose 361± 177 mg) and matched 8 healthy controls (HC) were included in the study. Neuropsychological measures (Mini-Mental State Examination test, verbal memory processes, visual memory, verbal fluency and, visuospatial tests), were applied to participants. EEG was recorded with 32 channel-DC system. During the EEG recording visual oddball paradigm was used as a cognitive task. EEG recordings and neuropsychological assessments were performed twice for PD patients, approximately one year after their baseline measurements. Seven locations (frontal, central, parietal-1, parietal-2, temporal, temporoparietal, occipital) were chosen. Event-related theta (4–7 Hz) and alpha (8–13 Hz) phase-locking (ITC) and power (ERSP) were analyzed in EEGLAB. Repeated measures of ANOVA and Kruskal-Wallis were used as the statistical analysis.

Results: Between-subjects effects were found statistically significant ($p=0.01$) for Theta ERSP. There was a gradual decrease from HC to PD follow-up. Between-subjects effects were found statistically significant ($p=0.02$) for Alpha ITC. Accordingly, the HC had the highest phase locking and PD follow-up was higher than PD baseline. There was no statistically significant difference in Teta ITC and Alfa ERSP. Neuropsychological assessments scores were not statistically different between PD baseline and PD follow-up ($p>0.05$).

Conclusion: This preliminary study showed that the event-related theta power of patients with PD decreased over time. However, neuropsychological measurements did not differ in patients longitudinally. The increase in the PD follow-up for alpha ITC could be interpreted as a compensatory mechanism of the decrease in theta ERSP.

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Keywords: alpha, EEG, event-related oscillations, Parkinson's disease, theta

P-06

Investigation of mental fatigue and attentional control abilities in obstructive sleep apnea (OSA) patients

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Objective: Obstructive sleep apnea (OSA) is the most common respiratory disorder in sleep. It is known that patients with OSA suffer from mental fatigue and attention control difficulties during the day. In this study EEG signals are recorded during both resting state and selective attention tasks. Aim of this study is investigating the variation of EEG signals in terms of Apnea Hypopnea Index (AHI) during both tasks.

Methods: Ten voluntary OSA patients contributed to this study. Permissions is obtained from the Human Research Ethics Committee of TOBB ETU. Subjects, following their wake up, to measure their mental fatigue and attentional control level participated in 3 minutes eyes-closed resting state and 13 minutes Simon-Flanker tasks respectively. During both tasks EEG signals are recorded from Fp1, Fp2, F1, F2, P3, P4, C3, C4, O1, O2 according to the 10–20 electrode placement system. Baseline noise is filtered by implementing 5th order 61 sample Savitzky-Golay filter. The amplitudes of EEG signal subbands, cross rate of these amplitude values and relative power of the subbands are used as features for signal analysis. Mixed-ANOVA statistical method is used in this study.

Results: Firstly patients split into 2 groups in terms of their AHI (AHI>15). There are meaningful differences noted in EEG subbands relative power values, between electrodes and lateraziation variables, also in ElectrodesxAHI>15, LateraziationxElectrodesxAHI>15 interactions ($p<0.05$).

Conclusion: For patients AHI<15, there is not significant difference in their relative Alpha power between both tasks. Subjects in this group operated attentional control task easily. We conclude that this group wake up less tired. This result matches with the previous findings in literature that conducted on control group. Additionally, there is negative correlation between relative Theta band power and relative Alpha band power ascending trend. Analysis of EEG subband signals for cognitive task is more beneficial than other techniques, because each band is related with special cognitive ablities.

Keywords: attentional control, EEG, Epworth, mental fatigue, obstructive sleep apnea

P-07

How do we place man and woman in our minds? Investigating masculinity and feminity representations by SNARC

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Objective: According to the Mental Number Line hypothesis, representations of numerical magnitudes tend to be mapped on a left-to-right oriented line. This prediction has been supported by the SNARC Effect, a tendency to respond faster to small numbers with left and big numbers with right key. The effect might also be generalized to non-numerical magnitudes. However, there is little work showing the spatial properties of mental representations of some psychological characteristic such as gender on the masculinity-feminity dimension. Therefore, we aimed to investigate the role of space on visual and conceptual representations of gender by a SNARC-like procedure.

Methods: Seventy-nine right-handed students, aged between 18–24, served as participants. A set of 180 words with semantically varied by the levels of masculinity and feminity, and a set of male and female facial pictures obtained from the Boğaziçi University Facial Database with different feminity and masculinity scores, were used. Stimuli were presented randomly at the center of a computer screen and the participants were asked to determine each of them as male or female by pressing the keys either on the left or right. Assignments of keys and conditions were counterbalanced across trials and participants.

Results: A significant interaction between gender and masculinity-femininity of pictures was observed (F(1.70)=104.68, p=.000). Reactions given to feminine-female faces were faster than masculine-female faces, and reactions given to masculine-male faces were faster than feminine-male faces. This effect did not differ by the response side. The reaction time measures did not differ by feminity or masculinity of the words. The reactions for the neutral words were significantly slower than the other word conditions (F(2.138)=214.05, p=.000). Reactions were faster to high masculinity male pictures and to high femininity female pictures.

Conclusion: These findings provide support for the schema-related information processing approach, suggesting that gender representation occurs at extreme levels of their representative features.

Keywords: masculinity, feminity, mental representation, non-numerical magnitude, SNARC

P-08

Investigation of visual and auditory memory processes in young healthy adults with the methodology of EEG event related oscillations

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Objective: The present study aims to investigate the different dynamic properties of visual and auditory memory processes in the human brain. The brain dynamic responses of healthy adults were investigated with the EEG event related theta and alpha responses.

Methods: The study included 8 young-adults (18–24 years) with no neurological or psychiatric disorders. Two separate memory paradigms (visual and auditory) have been applied to individuals. 20-channel EEG was recorded with Ag/AgCl electrodes. In the visual stimulus paradigm, 15 different images from the Boston Naming Test (BNT) were shown. In the auditory stimulus paradigm, the subject listened the audio reading of 15 objects. Participant asked to name all the objects that they kept in mind after each recording session. The data was segmented by stimuli, artifacts was rejected with using ındependent component analysis. The data was analyzed in the ranges 4–7 Hz, 8–13 Hz and 0–400 ms with event-related spectral perturbation and inter-trial coherence in EEGLAB program.

Results: The interaction of the paradigms and the regions was significantly different (p=0.049), in the ERSPs of the theta. The theta power at the all regions without the central channels was increased at the visual task (Occipital is the highest). No significant difference was found in the ERSPs of the alpha frequency band. In the ITCs, a significant difference was found in the paradigms (p=0.01) and the regions (p=0.004). Phase locking of trails was high in frontal-central areas and during the visual task.

Conclusion: According to these findings, we can conclude that visual memory processes may be differentiated from auditory memory processes by increased theta power and increased alpha phase locking. Increased theta power in visual paradigm could also be related more increased working memory processes in visual system than in auditory system.

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Keywords: EEG, event related oscillation, memory, theta

P-09

Investigation of EEG event-related theta responses to the processing of dynamic facial expressions

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Objective: Facial expressions recognition has a crucial role in the maintenance of social life. While in this field of research the utilization of photographs as stimuli is a widely accepted approach, it is perhaps insufficient for elucidating the exact neural mechanisms underlying facial expression recognition. The purpose of this study is to analyse via EEG-Brain Oscillations approach the perception and recognition of dynamic facial expressions, which we expect would provide an improved representation of the real-life mechanisms used in these processes.

Methods: 15 healthy young-adults constituted our sample population. 12 videos showing three facial expressions (joyful, fearful, neutral) were chosen from Amsterdam Dynamic Facial Expression Set as stimuli. Seven locations (frontal, central, temporal, temporaparietal, parietal-1, parietal-2, occipital) were chosen for EEG analysis. Analyses were done through two different time Windows (0–400 ms, 1000–1400 ms). Event-related theta (4–7 Hz) responses were analysed via the Inter-Trial Coherence and Event-related Spectral Perturbation methods. Repeated measures ANOVA was used for statistical analysis.

Results: Statistical analyses showed that time was significant for theta power (p=0.03) and theta phase-locking (p=0.001). Accordingly, the theta power and phase-locking occuring within the first time window are higher than that within the second. Time*facial expression comparison was also found to be statistically significant both for theta power (p=0.008) and theta phase-locking (p=0.011). While the responses within the first time window remained unchanged between different facial expressions, in the second time window, the highest phase-locking occured for fearful, and the lowest for neutral expressions; the highest theta power occured for joyful, and the lowest for neutral expressions.

Conclusion: The results indicate that the theta responses given in the first time window represent a rather physiological response to visual perception that is independent of the precise facial expression, and that the processing and differentiation of facial expression occurs within the second time window.

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Keywords: EEG, emotion, event-related oscillations, facial expression, theta

P-10

Successful working memory encoding is represented with increased EEG theta responses in children

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Objective: Brain Dynamics methodologies present essential results on the understanding of cognitive functions. There are very few studies on the dynamic responses of the brain during visual and auditory memory processes in children. The present study aims to investigate the differences between auditory and visual memory processes in children by EEG Brain Dynamics methodologies.

Methods: Ten children between the ages of 6–7 years were included in the study. EEG of children during visual and auditory memory paradigms was recorded from 18 channels with BrainAmp 32-Channel DC System (500 Hz sampling rate; 0.01–250 Hz band limits). WISC-IV IQ test was also applied to all children. Fifteen objects that are compatible for the age of children were selected from the Boston Naming Test for both visual and auditory paradigm. The children asked to memorize all objects that they see or hear in two separate sessions and they were asked to name all the objects that they could remember at the end of the recordings. Event related theta (4–7 Hz), alpha (8–13 Hz) power and phase locking were analyzed.

Results: The mean number of objects that the children could remember was 7.8±1.8 for the visual and it was 6.6±2.6 for the auditory paradigm. Most significant results were found for theta phase locking, the children had increased frontal theta phase locking during remembered objects in comparison to forgotten objects (p=0.011). Furthermore, visual memory paradigm elicited higher theta and alpha responses in comparison to auditory memory paradigm.

Conclusion: The present study showed that frontal theta response is an important indicator of remembered objects in working memory processes in children. It is already known that frontal theta response has a role in cognitive processes. This study further showed frontal theta response also has an essential role in the working memory processes in children.

Istanbul Medipol University Ethical report no:E34153

Keywords: alpha, children, EEG oscillations, memory, theta

P-11

Hippocampal changes in male rat brain prenatally exposed to radiofrequency electromagnetic field

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

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

Results: First generation male rats;There were statistical significantly difference between the control group and exposure groups in pERK level ($p<0.05$).But there were not statistical significantly difference between the control group and exposure groups in ERK, p38 and p-P38 levels. Second generation male rats;p-ERK and p-P38 MAPK levels were statistical significantly decreased in the 2nd group compared to the control group ($p<0.05$). Total protein levels were not statistical significantly difference between the control group and exposure groups ($p>0.05$).

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

This work was supported by ERUBAP of Turkey Project number:TCD-2017-7275.

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

P-12

Effects of chronic irisin administration on body weight and reproductive organ weights in rats

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Objective: It is stated that irisin, an exercise hormone, can be anti-obesity effects cause to decreasing of body weight and fat mass by increasing energy consumption. The mechanism of this effect of exogenous irisin treatment on rats is not known exactly. The aim of the present study was to determine the effects of chronic exogenous irisin treatment on body weights and reproductive organ weights in female and male rats in pubertal period.

Methods: In this study, totally 48 female and male Sprague-Dawley rats, 21 days old and 35±2 g weight, were divided into control and irisin groups (n=12). The animals started to receive daily intraperitoneally irisin (100 ng/kg) from postnatal day 21 for the about 10 weeks. The control groups received only saline. During the experiment, body weights of all animals were measured weekly. The total weights of the ovaries, uterus, testes, epididymides and ventral prostate were calculated for 100 g body weight at the end of the experiment.

Results: When compared to control group, irisin significantly increased the body weight of female rats ($p<0.05$ for weeks 1 and 2, $p<0.001$ for weeks 3–7 and $p<0.01$ for weeks 8 and 9), but no difference in the male rats. Irisin did not affect the weights of the ovaries, uterus, testes and epididymides and also significantly decreased the ventral prostate ($p<0.05$).

Conclusion: In this study, exogenous irisin treatment only cause an increase in body weight of female rats suggests that irisin may have shown this effect by means of a different mechanism in female rats.

This study was supported by TUBITAK-118S519.

Keywords: irisin, body weight, reproductive tissues, rat

P-13

Vanilla odor improves cognitive functions

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Objective: History of aromatherapy using various odor dates back to 5000s. Recently, it has been argued that odor has many effects such as antidepressant, stimulation, increased memory, correction of cognitive impairment. This situation is alsovery popular among the public. It is widely believed that vanilla odor is effective in learning. Şeker and Özerdem, in their study on the effects of odor activity, showed that vanilla scent caused wave changes in EEG. However, there is nostudy onthe effect of vanilla scent on cognitive functions. In this study, we aimed to investigate the possible effect of vanilla odor cognitive functions.

Methods: The study included healthy male right handed volunteers, non- color blindness, aged between 18–22 years (n=20). In the study, simple visual reaction time (VRT), complex VRT, simple recognition VRT and complex recognition VRT tests were applied to evaluate possible cognitive effects of vanilla odor. Tests were repeated in 3different days inthe normal room atmosphere, in the room with vanilla odor and onion odor. Using odors; While the effect of vanilla odor oncognitive functions was examined, the

odor of onion was used as bad odor in order to exclude whether the smell had anoverall effect. In order to make odor density as standard, 1ml of vanilla oil was dripped into 2 sponges of 5x5x2 cm size and the test room was kept closed for 30 minutes. For the smell of onion, 2 onion slices were used which were prepared in 5×5×2 cm dimensions.

Results: Median (IQR) duration ofthe complex VRT testwas 325.77(162.97) ms in the normal room atmosphere and 309.57(34.64) ms in the test in the presence of vanilla scent ($p<0.05$). In the complex recognition VRT tests, the mean±standard deviation was 580.14±134.94 ms in the normal room atmosphere test 495.50±96.55ms in the vanilla odor environment test ($p<0.001$). No statistically significant difference was found between the othertests.

Conclusion: The results of the study showed that vanilla odor accelerated complex VRT and complex recognitionVRT times and had a positive effect oncognitive functions. For this reason, it can be useful touse vanilla odor in libraries, work rooms and workplaces.

Keywords: cognitive function, reaction time, vanilla odor

P-14

An ERP analysis of time-based and event-based prospective memory task

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Objective: Prospective memory is the remembering to do intended action after a certain period of time. Prospective memory task is classified as evet-based when retrieval the intended event with an external cue (use drug after meals) and time-based when retrieval in particular moment (closure of the oven at 6 o'clock). The aim of this study is evaluate the brain activities associated with time and event-related prospective memory tasks.

Methods: Participant: 5 healthy patients (18–30 years) participated in the experiment. Experimental Design: In order to evaluate prospective memory, participants were asked to attend ongoing task, event-based and time-based prospective memory. The task was prepared using Task E-prime (2.0). EEG Recordings: EEGs recorded from 32 leads (Fp1, Fp2, F7, F3, Fz, F8, FT7, FC3, FCz, FC4, FT8, T7, C3, Cz, C4, T8, TP7, CP3, CPz, CP4, TP8, P7, P3, Pz, P4, P8, O1, Oz, O2, EOGH, EOGV) The recordings were performed (low cut off (Hz), 0.1 Hz; high cut off (Hz), 96 Hz; sample rates, 1000 Hz). Impedance of all electrodes was checked below 10 kilo ohm.

Results: All datasets processed by BrainVision Analyzer 2 (Brainproduct, Munich, Germany, 2.0.4 Version) in 256 Hz sample rates. N300 amplitude and latency differencies will be evaluated for event-based and time-based prospective memory conditions.

Conclusion: The results of the study will be discussed according to current literature.

Keywords: prospective memory, EEG, time-based, event-based

P-15

Metformin ameliorates depressive and anxiety like behavior by reducing oxidative stress in ovariectomized female rats

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Objective: The decrease in estrogen level during periods of postmenopausal periods is associated with the incidence of depression. Ovariectomy (OVX) produces depressive-like behaviors in rats. Metformin,which is widely used to treat Type 2 diabetes has potent antihyperglycaemic activity. Recent studies have shown that metformin has various beneficial effects in the brain such as anti-inflammatory and neuroprotective effects. Oxidative stress in the brain areas such as prefrontal cortex (PFC) and hippocampus is a major contributor to the pathophysiology of depression in OVX rats. In this study, we examined the therapeutic potential of metformin in depressive and anxiety like behavior as well as oxidative stress in PFC and hippocampus of ovariectomized female rats.

Methods: Four groups, 8 rats per group, were designed: control, metformin-treated control, OVX control, and metformin-treated OVX group. Rats were treated with metformin (25 mg/kg, perorally) for 2 weeks. Status of oxidative stress in brain was assessed by the measurements of the tissue malondialdehyde (MDA), ascorbic acid and reduced glutathione (GSH) contents. Depressive and anxiety like behaviour were evaluated by forced swimming test (FST) and open field test, respectively. Statistically analyses were performed by Kruskal Wallis and Bonferroni test.

Results: Metformin exerted antidepressant like effects on OVX rats, which were characterized by decreased immobility time in the FST. In OVX animals, latency time increased and ambulatory activity decreased in open field test. Metformin treatment improved OVX-induced depression and anxiety-like behaviors compared to OVX control group. OVX resulted in an increase in MDA level and decrease ascorbic acid level in PFC and hippocampus. Metformin treatment was effective to reduce MDA level in PFC.

Conclusion: Our results showed that metformin has a potential new use in the treatment of neuropsychiatric complications in women in postmenopausal period.

Keywords: metformin, anxiety, depressive like behaviour, oxidative stress

P-16

Effects of high frequency rTMS on treatment of eating and appetite changes in behavioral variant of frontotemporal dementia

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Objective: Behavioral variant of frontotemporal dementia (bvFTD) is characterized by progressive behavioral abnormalities, personality changes, impaired social behavior, and impaired executive functions. In addition to these features, since the first diagnostic criteria of bvFTD were proposed by Neary in 1998, eating abnormalities and overeating are one of the main symptoms in diagnosis. It is known that eating changes in bvFTD patients are associated with orbito-frontal-striatal cycle. This system can be indirectly induced by rTMS due to its cortical projections in the dorsolateral prefrontal cortex (DLPFC). In this report, we present the results of high frequency rTMS treatment on DLPFC in a bvFTD patient who has overeating and weight complaints.

Methods: The patient who was followed up with the diagnosis of bvFTD was admitted to dementia outpatient clinic of Istanbul Medipol University due to loss of feeling of satiety and weight gain as well as complaints of memory loss, inertness and speech. For treatment, patient underwent 10 sessions of high frequency rTMS with 75 pulses and 50 seconds breaks for each train and totally 3000 stimuli/day over the left dorsolateral prefrontal cortex. Before and after neuromodulation, Appetite and Eating Habits Questionnaire that Ikeda et al. developed for use in patients with FTD is applied To measure appetite and eating habits.

Results: As a result a decrease was observed especially in the category of appetite changes. And also, amelioration was noticed in the food selection, eating habits and oral behaviors categories of the questionnaire.

Conclusion: Our report was the first to show that rTMS, a neuromodulation technique, has efficiantly improved the symptoms of eating and appetite changes in bvFTD. The results of this study suggest that high-frequency rTMS on the left DLPFC can be used as an alternative treatment for the treatment of eating changes in patients with bvFTD.

Keywords: bvFTD, rTMS, appetite and eating changes

P-17

The relation between cognitive, mood and motor symptoms with amnestic mild cognitive disorder subtypes in Parkinson's disease

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Objective: Parkinson's disease mild cognitive ımpairment (PD-MCI) is an intermediate stage between normal ageing and dementia and the cognitive decline of the patients is different from their healthy peers,however, it is expressed as the situation that does not significantly affect the functionality. The recent studies show that there are different subtypes with different clinical features and prognoses of the disease.The main aim of this study is to determine the possible subtypes of PD in order to investigate the relationship between Parkinson MCI amnestic subtypes in cognitive, mood and motor symptoms.

Methods: A total of 24 PD-MCI amnestic patients, 8 females and 16 males, were included in the study which was carried out at Medipol University Hospital and approved by the ethics committee numbered 10840098-51.Informed consent was obtained from all patients.Inclusion criteria were;the diagnosis of Parkinson disease and clinical dementia rating scale (CDR)a nd the cut off score should be 0.5(MCI's diagnostic cut off score) and memory affected. An extensive neuropsychological test battery applied to all patients which includes 5 cognitive domains; attention,executive functions, memory, visuospatial abilities, and language. In addition, mood and motor symptoms were evaluated as well.

Results: The results of the neuropsychometric evaluation of the 24 patients with PD-MCI in the amnestic subtypes showed that 12 of them had only memory deterioration (amnestic-single domain); the rest of the 12 patients had deterioration in both memory and other cognitive functions (amnestic-multiple domain). There was no significant difference between the two groups in terms of mood and motor behaviour.For the cognitive functions, only visuospatial functions were found to be significantly impaired in the amnestic-multiple domain group compared to the amnestic-single domain group.

Conclusion: Our findings suggest that MCI subtypes (amnestic-multiple-domains/amnestic-single domain)in the PD-MCI group do not show a distinctive phenotype in terms of motor and behavioral symptoms of PD. In the amnestic-multiple domain MCI group, the dominant disorder other than memory was found to be visual spatial functions.

Keywords: parkinson disease, mild cognitive impairment, amnestic, mood, motor symptoms

P-18

Investigation of hippocampus field potentials in rats with starch based sugar

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Objective: Studies in which experimental animals were fed with fructose for a long time showed that insulin resistance occurred and this was associated with poor performance in hippocampus dependent learning. In this study, the effect of high-fructose corn syrup consumption (HFCS) on the synaptic plas-

ticity forms which underlies learning and memory processes were investigated.

Methods: The study was performed on sixty (100±15 g; 20/group) 21-day old male Wistar Albino rats obtained from Erciyes University Experimental Animal Research Center. On the 21st day, the male rats leaving their mothers are fed with unrestricted standard rat chow and tap water, HFCS solution (8%; 0.24 Kcal/mL) or sucrose solution (10%, 0.4 Kcal/mL) for at least 21 days. The field potentials were recorded from the right dentate gyrus with stimulation of the right medial perforant path. Long-term potentiation (LTP) and long-term depression (LTD) were induced by high and low frequency stimulation (HFS and LFS), respectively.

Results: The input/output curves of the study groups did not differ ($p>0.05$). After 1 hour of induction, LTD was 92±8% and 90±5% of the pre-LFS value in the control and sucrose groups, while LTP was 121±4% and 119±5%, respectively. There was no statistical significance between these groups ($p>0.05$). In the group fed with HFCS, the LFS and HFS did not induce LTP or LTD responses. In control and sucrose groups, it was found that the induced UDB was accompanied by spike potentiation (154±8% and 128±15%, respectively) and this potentiation was not observed in the HFCS group ($p<0.01$).

Conclusion: These findings suggest that high fructose-containing diets may disrupt the balance between two forms of synaptic plasticity and thus adversely affect learning processes.

Keywords: high fructose, corn syrup, long-term potentiation, long-term depression, hippocampus

P-19

Effects of excessive sugar consumption on social recognition behavior of rats exposed to prolonged stress

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Objective: As a result of non-tolerable toxic stress caused by negative life experiences, the first symptoms causing impairment in functionality of an individual are seen in social field. we aim to investigate the alterations in the social recognition and memory tests in excessive sugar consumed animals exposed to single prolonged stress.

Methods: Adult female rats (n=15) were divided into two groups and 10% corn syrup was added to the diet of the experimental group for 10 days, while only water and standard pellets were given to the controls. At the end of the diet, single prolonged stress protocol (2 hours immobilization, 20 minutes forced swim and ether until anesthesia) was applied to the animals. Animals were kept under control conditions for 7 days. Animals were conditioned with high-intensity sound and light to create contextual fear condition and subjected to social recognition and elevated plus maze tests.

Results: In training stage of the social recognition test, no significant difference was observed in time spent in the rooms between control and experimental groups. Although, in recognition phase of the test, number of sniffing stranger rat and object was significantly different ($p<0.01$) in animals, there was no significant difference between experimental and control groups. Similarly, no significant difference was observed in control (3.51±1.2) and experimental group (7.25±2.1) in social preference test when the number of sniffing familiar or stranger rat were compared. There was no significant difference between experimental and control group in the time spent in the closed arms of the elevated plus maze.

Conclusion: Social recognition behavior of experimental animals exposed to prolonged stress is negatively affected, regardless of excessive sugar consumption. In excessive sugar consuming group no difference in elevated plus maze test scores demonstrates that level of stress tolerance of experimental animals can be evaluated by social recognition test, independently of anxiety levels.

Keywords: single prolonged stress, social recognition, social preference, corn syrup

P-20

The effect of agomelatin on pain threshold and neurogenesis in depressed male rats

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Objective: It is known that depression reduces the pain threshold and neurogenesis. New drugs for the treatment of depression and secondary effects of depression continue to be produced. Despite these drugs, depression is still an important health problem. The aim of this study was to show the effect of agomelatine on neurogenesis and pain threshold in depressive rats.

Methods: 40 male Wistar albino rats (10–12 weeks old) were used in the study. Rats were divided into four groups as control (CONT), control-agomelatine (KONT-AGO), depression (DEP), depression-agomeletin (DEP-AGO) groups. Depression model was developed based on the method developed by Porsolt and saline applied to this group for 15 days. DEP-AGO group was administered agomelatin (1 mg/kg) with gavage for 15 days after the depression model was developed. CONT-AGO was applied agomelatin (1 mg/kg) for 15 days without ZST. Sucrose preference test was applied to all groups. The pain thresholds were measured with hot plate and tail flick methods of all groups. Sections from the hippocampus region of the brain were taken and neurogenesis was demonstrated by evaluating doublecortin

(DCX) immunoreactivity intensity. Statistical comparisons between groups were evaluated by one-way ANOVA followed post-hoc LSD test.

Results: When the sucrose preference, pain threshold (avoidance times) and DCX immunoreactivity were evaluated, it was found that DEP group rats decreased significantly compared that in CONT and CONT-AGO group ($p<0.05$). In addition, when the same parameters were evaluated, it was found that DEP-AGO group rats increased significantly compared to DEP group ($p<0.05$). No significant difference was found between the CONT, CONT-AGO and DEP-AGO groups ($p>0.05$).

Conclusion: Study findings support that depression decreases pain threshold and neurogenesis and that melatonin analog agomelatine, which is used as antidepressant, normalizes these effects of depression.

This study was supported by Erciyes University Scientific Research Projects Unit under TTU-2016-6430 project.

Keywords: depression, forced swimming test, sucrose preference test, pain threshold, neurogenesis, agomelatin

P-21

Investigation of the effect of kisspeptin neurons in the arcuate nucleus on the spatial learning and memory in Alzheimer's disease by pharmacogenetic methods

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Objective: The effects of chronic activation or inhibition of kisspeptin neurons on spatial learning/memory are investigated in female kiss-cre transgenic Alzheimer's disease (AD) model mice.

Methods: Female kiss-cre transgenic mice were used. AD model was induced by bilateral intrahippocampal infusion of amyloid-β to kiss-cre mice. hM3D receptor (for activation) or hM4D receptor (for inhibition) genes were injected intracranially into the hypothalamus by using adeno associated virus (AAV) for pharmacogenetic (chronic) manipulation of kisspeptin neurons. Clozopine-N-Oxide (CNO) was intraperitoneally given to the animals for one month to chronically activate or inhibit kisspeptin neurons. Spatial learning and memory performance of all animals was evaluated by Morris Water Maze test (MWM). Injection coordinates and the presence of amyloid-β were shown using a confocal microscope with immunofluorescent staining. Experimental protocol was approved Yeditepe University Animal Ethics Committee.

Results: Chronic manipulation of kisspeptin neurons in AD mice showed a trend towards decreasing of learning performance in the activation group and a trend towards increased cognitive parameters in the inhibition group. There was no statistically significant difference between groups (One-Way ANOVA).

Conclusion: The chronic kisspeptin stimulation group has been associated with decreased cognitive performance in AD model mice. It was thought that kisspeptin had no direct effect on spatial learning, and had an indirect effect. This study was supported by TÜBİTAK (Project # 115S327)

Keywords: Alzheimer disease, arcuate nucleus, cognitive functions, kisspeptin neurons, pharmacogenetics

P-22

Time depending effect of hippocampal infusion of ERK inhibitor on the long-term depression (LTD) in dentate gyrus

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Objective: It is generally assumed that high frequency activity induces long-term potentiation (LTP) and prolonged, low frequency activity long-term depression (LTD). The MAPK/ERK pathway has been shown to be required for essentially all forms of LTP, but some previous studies had reported that the cascade transduces signals from the synapse to the nucleus during LTD. A new form of synaptic plasticity which is induced by low frequency stimulation (LFS) exhibits more potentiation in spike amplitude than the LTP of synaptic transmission (E-S potentiation). Here, we further characterize the role of ERK in this LFS-induced potentiation in the DG of intact, urethane-anesthetized preparations.

Methods: The experiments were carried out on 2–3 months old adult male Wistar Albino rats. Animals were divided to 3 groups (n=8/group). After a 15-minute baseline recording, LTD was induced by application of a LFS protocol (900 stimuli at 1 Hz) and measured as 5-min average of two components of field potential (EPSP spike) 60-min after its induction. Infusions of ERK inhibitor (PD98059) were made for 15 minutes or 60 min starting from the application of LFS. Saline infused rats were used as control. LTD magnitude was compared using one-way ANOVA test.

Results: We found that ERK inhibition has no effect on the LTD of synaptic component, while LFS-induced E-S potentiation was significantly enhanced by 15-min ERK inhibition (234±16% of baseline; $p<0.01$), but decreased 60-min ERK inhibition (105±16% of baseline; $p<0.05$) when compared with saline infusion (153±8% of baseline).

Conclusion: Our findings indicate that activation of the ERK cascade does not contribute critically to the persistence of LTD and that its short-term inhibition appears to promote spike potentiation, probably due to reducing threshold for neuronal discharge. This study was supported by Erciyes University Research Found (TDK-2016-6628, TSA-2018-7748).

Keywords: ERK, plasticity, dentate gyrus, hippocampus

P-23

Effect of methylene blue on tau phosphorylation during long-term potentiation

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Objective: Long-term potentiation (LTP) in hippocampal neurons is associated with an increase in several kinase-mediated in AMPA receptor membrane expression, of which some have tau-kinase activity. Promising results have emerged from animal researches testing Methylene blue (MB) as a potential neuroprotector in learning deficits and a potential therapeutic for Alzheimer disease (AD). Despite these reports, no investigation of MB in synaptic plasticity has been published, and thus its mechanism of action in relation to LTP-associated phosphorylation of tau phosphorylation yet remains unknown.

Methods: 16 (2–3 months old, n:8/group) adult male rats were divided into 2 groups. After a 15-minute baseline recording, LTP was induced by application of high- frequency stimulation (HFS) protocol. Infusions of saline or MB were made for 1 hour starting from the application of HFS. The averages of the excitatory post-synaptic potential (EPSP) slopes and population spike (PS) amplitudes, between 55 to 60 minutes,were used as a measure of the LTP magnitude. Total and phosphorylated tau levels were measured in LTP-induced hippocampus in the presence and absence MB (50 µM, 0.33 µL/min, 20 uL) 1 hour after induction of LTP. This study was approved by Erciyes University Ethics Committee (decision no:18/139).

Results: LTP was impaired in MB-infused rats, as indicated by significantly lower magnitudes for fEPSP slope and PA amplitude ($p<0.001$) in these rats. The hippocampus exhibiting impaired LTP as a result of MB infusion showed comparable total tau expression with that of saline infused rats. In general, the density of the phosphorylated form of threonine 231 epitope of tau was lower in the LTP-induced hippocampus, whereas that of the serine 416 epitope was higher in MB infusion than in saline infusion.

Conclusion: The data presented here support the use of MB for the treatment of AD and offer a possible mechanism of action because thr231 is one of the most important phosphorylation site in AD.

This study was supported by Erciyes University Research Found (TYL-2018-8661).

Keywords: Alzheimer disease, hippocampus, methylene blue, long-term potentiation

P-24

Dose-dependent effect of thyroid hormone on tau phosphorylation associated with reversal of long-term potentiation

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Objective: Dysfunctions in thyroid like hypo- and hyperthyroidism causes a high risk for the dementia development. It has been shown that high tau CSF levels were associated reversal of long-term potentiation (LTP)-like cortical plasticity and faster clinical progression in Alzheimer's disease patients. Therefore, we investigated whether the intra-hippocampal infusion of different doses from T4 will affect tau protein phosphorylation during reversal of LTP.

Methods: Twenty-four (2–3 months old, n=6/group) adult male rats were divided into 4 groups. After a 15-minute baseline recording, LTP which was induced by application of high- frequency stimulation protocol were then reversed by a low- frequency stimulation protocol (900 stimuli at 1 Hz). Infusions of saline, T4 (100 pM) or T4 (100 nM) of were made for 1 hour starting from the application of HFS. One of the groups was stimulated with 0.33 Hz during the experiment and the changes in the amount of protein in the samples obtained from infusion groups were evaluated according to this group. This study was approved by Erciyes University Ethics Committee (Decision no:17/044).

Results: The results of the Kruskal-Wallis test revealed that total levels of Tau protein differ among group ($p=0.017$). Analysis of the ratio of phosphorylated-to-total tau protein showed that the fraction of phosphorylated tau at Thr231 was constitutively similar in all rats irrespective of their group ($p>0.05$), while there are significant differences at Ser416 ($p=0.005$). Mann–Whitney U tests confirmed that increased pSer416 tau-to-t-tau ratio in the saline infusion group was inhibited by T4 at the dose of 100 pM ($p=0.016$) but not at the dose of 100 nM ($p>0.05$).

Conclusion: These observations may suggest that weakening of potentiated synapses is associated with an obvious tau phosphorylation at Ser416 epitope maybe decreased by administration low concentration of T4.

This study was supported by Erciyes University Research Found (TDK-2016-6628, TSA-2018-7748).

Keywords: hippocampus, protein tau, thyroid hormones, reversal of lTP

P-25

Inhibitory action of (+)-terpinen-4-ol on inflammation

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Objective: Terpinen-4-ol is an oxygenated monoterpene found in nature and also obtained by synthesis which has (+) and (-) isomers. As a natural substance found in many plants, this compound was shown to act on nervous sytem and suggested to play role on the ethnopharmacological uses of various plant extracts including antiinflammatory activities. The aim of this study was to investigate the effect of (+)-terpinen-4-ol on chronical inflammation.

Methods: Adult albino rats of either sex were used in the study which were approved by the local animal ethical committee of

Anadolu University. Sterilized and dried cotton pellets were implanted under the skin of the scapular region of animals under the propofol anesthesia. Three different doses of (+)-terpinen-4-ol (10, 50 and 100 mg/kg, i.p.) diluted in dimethylsulfoxide was applied once a day for a week. Indomethacine as used a standard antiinflammatory agent. Data obtained by weighing the dried the cotton pellets at the end of experiments were evaluated using one way variance analysis and post hoc Tukey HSD test for multiple comparison and results were considered as significant where p value was <0.05.

Results: (+)-Terpinen-4-ol was observed to exert antiinflammatory activity in a dose-depent manner.

Conclusion: In the present study, (+)-terpinen-4-ol was shown to act as an antiinflammatory compound on the *in vivo* chronical inflammation. To the best of our knowledge *in vivo* antiinflammatory actions of (+)-terpinen-4-ol was shown for the first time. Due to its lipophilic nature and ethnopharmacological use of extracts containing this compound, (+)-terpinen-4-ol is suggested as a new antiinflammatory drug acting on tissues including nervous system which requires further investigations.

Keywords: montoterpene, terpinen-4-ol, inflammation

P-26

Inhibition of long-term potentiation by low frequency stimulation in the perforant pathway – dentate gyrus synapses

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Objective: Long-term potentiation (LTP) and depression can be considered in terms of the relationship of stimulation frequency and resultant change in synaptic plasticity. Low-frequency stimulation (LFS) given before induction of LTP inhibits LTP without affecting either basal synaptic strength or the early phase of LTP. This anterograde inhibitory effect of LFS is persistent and is blocked by inhibitors of phosphatases. Herein, we investigated the effect of LFS on subsequent LTP magnitude using four different stimulus frequencies.

Methods: The study used four groups of adult Wistar rats. The effect of different stimulation patterns (0.5-Hz, 1-Hz, 2-Hz and 5-Hz, n=8/ group) designed to induce long-lasting depression of the perforant pathway inputs to the dentate gyrus on subsequently induced LTP was investigated. All paradigms consisted of 900 pulses. LTP was induced by a strong tetanisation protocol and measured as 5-min average of excitatory-postsynaptic potential (EPSP) and population spike (PS) 5 min and 60 min after its induction. LTP magnitude was compared using one-way ANOVA test.

Results: The input-output curves of the groups were comparable to each other, as shown by the non-significant interaction observed between stimulus intensity and frequency. We found that 0.5-Hz, but not 5-Hz, stimulation inhibited for 60 min the subsequent induction of fEPSP-LTP by a normally efficient LTP-inducing protocol. There was significant difference in PS-LTP between two groups at two measurement intervals ($p<0.001$) and positive correlations between LTP magnitudes and frequencies.

Conclusion: These data indicate that certain patterns of LFS can activate different intracellular molecular cascades, and that long-lasting activation of phosphatases by prior LFS can suppress the subsequent expression of LTP. We suggest that this form of metaplasticity may influence information storage by modulating the capacity of synapses to express LTP after repeated bouts of activity.

This study was supported by Erciyes University Research Found (TYL-2018-8215, TYL-2018-8210).

Keywords: hippocampus, priming stimulation, long-term potentiation, metaplasticity, rats

P-27

The metaplastic properties of the dentate granule cells alter in adult onset hypothyroidism by decreasing Akt phosphorylation

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Objective: In the present study, we examined whether stimulation known to induce LTD has modulating effects on LTP induction at the dentate gyrus synapses, where first relay of the hippocampus is, and whether thyroid hormones (THs) play a role in LTD and subsequent LTP modulation. We also investigated the differences in activation of two main MAPKs and Akt between control and hypothyroid rats in the hippocampus which was dissected out from the brain at least 95 min after priming onset.

Methods: To this end, *in vivo* electrophysiological recordings were performed from the dentate gyrus of control and 6-n-propyl-2-thiouracil (PTU)-treated animals, during which we employed two different types of low-frequency stimulation (1 Hz and 5 Hz) of the perforant pathway prior to tetanic stimulation to induce LTP. Activation of extracellular signal-regulated protein kinases 1/2, c-Jun N-terminal kinase, and Akt was measured in the hippocampus which was dissected out from the brain at least 95 min after priming onset.

Results: The LTD elicited by 5 Hz stimulation negatively impacts the LTP induced by subsequent tetanic stimulation in hypothyroid animals; manifest by a more rapid diminution in the fEPSP slope and population spike amplitude. This phenomenon was accompanied by lower phosphorylated levels of Akt in surgically resected hippocampi of hypothyroid rats compared to those of euthyroid rats. Metaplastic response and the expression of mentioned proteins were not different in 1 Hz primed hippocampus between two groups.

Conclusion: These observations might suggest, by asserting that, decreased PI3K/Akt signaling may be involved in the compromised metaplastic regulation of LTP seen with hypothyroidism, which may account for the learning difficulties/cognitive impairments associated with this condition.

This study was supported by The Research Foundation of Erciyes University of Turkey (TSA-2018-7748).

Keywords: thyroid hormones, plasticity, dentate gyrus, hippocampus, protein kinase

P-28

Drug-induced alterations in thyroid hormone concentrations are potentially associated with deficits in metaplasticity and Akt phosphorylation

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Objective: Thyroid hormone (TH) deficiency leads to changes in long-term potentiation (LTP) and behavioral deficits in adulthood ages. The ability to induce LTP, however, is governed by the prior history of activity. This process called metaplasticity is associated with a transient increase in several kinases such as Akt kinase. The aim was to determine the consequences of dysthyroidism on metaplasticity in the dentate gyrus, a thyroid hormone receptor-rich region of the brain.

Methods: Alterations in TH levels were produced by administering 6-n-propyl-2-thiouracil (drinking water, %0.5) or L-thyroxine (ip, 400 µg/kg) to young adult rats for 3 weeks starting at postnatal day 40. Field potentials composing of a field excitatory-postsynaptic potential (fEPSP) and a population-spike (PS) were recorded from granule cell layer of dentate gyrus in response to stimulation of perforant pathway (PP) under urethane anesthesia. Low-frequency stimulation protocols, at 5Hz for 180 sec, preceding a high-frequency stimulation protocol (HFS:100Hz, 4 times, 5 min intervals) was used to investigate the metaplasticity of LTP. Phosphorylated and total-Akt levels were measured in whole hippocampus at least 95 min after priming onset by Western blot.

Results: We found that a priming stimulation at 5Hz for 3 sec negatively impacts the LTP induced by subsequent tetanic stimulation in hypothyroid animals; manifest by a more rapid diminution in fEPSP slope and PS amplitude. This phenomenon was accompanied by lower phosphorylated levels of Akt in surgically removed hippocampi of hypothyroid rats compared to those of euthyroid rats. Metaplastic LTP could be induced in hyperthyroid rats, but expression of Akt was not different in these animals.

Conclusion: These observations might suggest, by asserting that, decreased PI3K/Akt signaling may be involved in the compromised metaplastic regulation of LTP seen with hypothyroidism, which may account for the learning difficulties/cognitive impairments associated with this condition.

This study was supported by Erciyes University Research Found (TDK-2017-7696).

Keywords: thyroid hormones, plasticity, dentate gyrus, hippocampus, protein kinase

P-29

The role of 5-hydroxytryptamine receptor-1 (5-HT1) on pentylenetetrazole-induced chronic epilepsy in rats

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Objective: Recent neurophysiological studies have showed that 5-hydroxytryptamine Receptor-1 (5-HT1) can have an anti-epileptic effect. The aim of this study was to investigate the effects of 5 HT1 receptors in the pentylenetetrazole induced chronic epilepsy model.

Methods: In our study, 24 (240–260 g) male Wistar Albino rats were used. 35 mg/kg pentylenetetrazole (PTZ) was administered intraperitoneally to animals on every Monday, Wednesday and Friday up to 15 injections. After each injection, the animals were observed for thirty minutes and the seizure stages were determined according to the Racine scale. The animals that had three sequential five stage seizures three times were accepted kindled. Than electrodes were placed these animals' skulls under sterotaxy to receive EEG recordings. Animals grouped as saline (1 ml/kg saline; n=8), 5-HT1 agonist (8-OH-DPAT; 0.3 mg/kg; n=8) and 5-HT1 antagonist (WAY-100135; 1 mg/kg; n=8). After thirty minutes administration of drugs, 35 mg/kg ptz was given to induce seizures. EEG and video recordings of animals were taken simultaneously for thirty minutes. In the evaluation of the video and EEG recordings, the seizure stages of animals, the first myoclonic jerk time (FMJ), the number of spike wave discharge per minute (SWD) and the percentage of spike wave discharge time (% SWDs) were calculated.

Results: 5HT1 agonist and antagonist did not change the seizure stage compared to the saline group ($p>0.05$). The 5HT1 agonist increased FMJ compared to the saline group ($p<0.05$). However, the 5HT1 antagonist decreased FMJ, but this was not statistically significant compared to the saline group ($p>0.05$). In addition, 5HT1 agonist decreased SWD and %SWDs compared to saline group ($p<0.05$). However, 5HT1 antagonist increased SWD and %SWDs, but this was not significant compared to saline group ($p>0.05$).

Conclusion: We think that 5HT1 receptor has anti-epileptic properties in chronic epilepsy, but advanced molecular studies are needed to elucidate mechanisms.

Keywords: epilepsy, pentylenetetrazole, 5-hydroxytryptamine receptor-1, rat

P-30

Effects of agomelatine on food intake and body weight in the rats

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Objective: The hypothalamus plays a key role in regulation of energy homeostasis where many hormones involved in this regulation. Agomelatine is a novel antidepressant which behaves as a melatonergic (MT1/MT2) receptor agonist and serotonergic (5-HT2C) receptor antagonist. The antidepressant properties of agomelatine have been demonstrated in both animal models and clinical studies. Over the past decade, a great deal of research has focused on the importance of cognitive processes in the control of energy intake/expenditure and change of body weight. The study was designed to evaluate effects of agomelatine on food intake and body weight in the rats.

Methods: In this study 40 male *Wistar-Albino* rats were used. Rats were divided into four groups (n=10). Experimental groups received two different doses of agomelatine (20 and 40 mg/kg) via orally. Solvent (10% hydroxy methyl cellulose) was also orally administered into sham group for seven days. No application was performed to the control group. Rats were housed in individual cage during the experimental period and food consumptions and body weights of the animals were daily recorded.

Results: At the end of the study, both concentrations of the agomelatine caused to significantly decreases in food consumption and body weight of rats ($p<0.05$).

Conclusion: The results of the study revealed that agomelatine suppresses appetite. This results also provides evidences that agomelatine can play important roles on regulation of feeding behavior and control of energy metabolism in hypothalamus.

Keywords: agomelatine, food intake, body weight, obesity

P-31

Simulation of biological networks

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Objective: This study aims to create a network structure between multiple biological nerve cell models and perform the simulation operations of this network structure in a flexible way with the help of a user friendly interface.

Methods: In this study, the simulated cell models were downloaded via Allen Institute site where the actual nerve cells were scanned in three dimensions and the morphology data obtained were shared as open source. Morphological data were obtained with the help of NEURON software to establish synaptic connections between nerve cells. Hodgkin & Huxley model was used in the nerve cells in the network structure. The simulation of the most recently created network model is based on NEURON-based interface with a flexible structure.

Results: The experimental studies were performed by using the synaptic connections between the nerve cell models made by Allen Institute. In this simulation study, the action potential was generated on the externally induced source cell and the effects on the target cell were investigated. The parameters of the synaptic connections were changed by means of the designed interface software and the effects of the source cell on the target cell were examined graphically. In addition, the effects of the signal locations on the neural network model, the number of synapse connections and the synapse connection points on the target cell were examined graphically.

Conclusion: In the study, the simulation of the neural network models is performed with the help of interface designed. The parameters in the network model were changed much more easily and the effects of these parameters on the target cell could be obtained quickly. In this study, interface is designed to simulate the neural network models. It is thought that the designed interface will be further developed and published as open source. So, simulation processes can be made much easier and faster.

Keywords: interface, nerve cell model, network model, NEURON, simulation

P-32

Analysis of frequency current relation with respect to parameter values in spiking neural networks

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Objective: The aim of computational neuroscience is to understand the formation of cognitive processes, neurological and neuropsychiatric diseases by focusing on the effects of physiological and chemical processes. Models based on spiking neural network are one mean to fulfil this ambition. An important physiological phenomenon that must be considered in spiking neural network models is the relation between the stimulus and the frequency of the spikes generated by the model. This phenomenon is a measure of the biophysical integrality of the computational model. In this study, how the parameter changes in the neuron models affect the relationship between the stimulus current and spike frequencies of the neurons (fI) will be investigated.

Methods: The value of the parameters in the dynamic equations of the proposed models determines the behavior of the neurons. The modification of the parameters may be required for modeling different types of neurons, and it is also important in obtaining different behavior of the same neuron type. Here,

a model is presented to show how the parameter values in the neuron models effects the relationship between the stimulus current and spike frequencies of the neurons (fI). For this spiking neural network composed of Izhikevich model is considered. The simulation environment is prepared on BRIAN library based on Python.

Results: The simulation results show that the slope of the fI curves of the neurons remained constant and the frequency of the spiking neurons changed over a band depending on the range of the parameter value.

Conclusion: To model a neural structure with the spiking neural networks, a computational model is considered and the effect of the parameter values of the dynamic equations is analyzed. It is shown that the interval of the chosen parameter values is reflected in fI relationships. This study can be versatile especially in evaluating the models for nucleus accumbens.

Keywords: spiking neural networks, frequency-excitation current relationship, computational neuroscience

P-33

Comparative analysis of mouse and human metabolisms in Parkinson's disease at genome-scale

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Objective: Constructing a list of all reactions in the metabolism of the cell of interest was proven to be very useful to model metabolic behaviors and pathway activities of organisms. These reactions together are referred as metabolic network. Such a metabolic network model was previously constructed in brain-specific manner for neuron and astrocyte metabolism in human. However, experimental and clinical studies are mostly carried out on model organisms. Mus Musculus (mouse), is one of the most commonly used model organism for human diseases. Also numerous transcriptome data of mouse are available in public databases such as Gene Expression Omnibus (GEO). This study aims to construct the first brain-specific metabolic network model of mouse at genome-scale for investigating the quality of animal models of PD to predict the effect of the disease on metabolism at the transcriptional level.

Methods: Brain-specific mouse metabolic network model was constructed by a homology based approach. The existing model of human was used as a template. The final model includes 871 reactions distributed over 107 pathways. The genes responsible for each reaction was also included in the model, and there are 585 genes in the model. After construction, reaction rates were predicted by computational methods to identify the effect of Parkinson's Disease on metabolism. Different algorithms were used to integrate the gene expression data into metabolic network model.

Results: The affected reactions and pathways of mouse and human metabolism in PD were identified by comparing the reaction rates of control and disease groups.

Conclusion: Through this model, changes of the mouse brain metabolism in PD can be predicted in a computational way. Also using human and mouse versions of the brain-specific metabolic models together in a comparative way can serve as a new approach to develop interpretation of preclinical studies in mouse for human.

Keywords: Parkinson's disease, mouse, metabolic model, genome-scale, transcriptional level

P-34

The relationship between clinical and demographic characteristics and suicidal ideation in patients with multiple sclerosis

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Objective: Study was planned to investigate the link between suicidal thinking and clinical and demographic characteristics in patients with multiple sclerosis.

Methods: The investigation was carried out in Samsun OMU Research Hospital. The participants of the study was composed of 179 MS patients who were registered in neurology polyclinic. The personal data form that developed by the researcher reviewing the literature on this subject, Beck Depression Inventory, Suicidal Idea Scale, Life Satisfaction Scale, Visual Similarness Scale for Fatigue, Stress Tendency Scale and EDSS (Expanded Disability Status Scale) scores. The analysis of the data in this study was evaluated with IBM SPSS.22 package program. In the evaluation of the data; Descriptive statistics, T-test, Mann-Whitney U test, Kruskal-Wallis H test were used. The relationship between the suicidal ideation scale and the other measurements was evaluated by correlation analysis.

Results: The mean age of the patients was 41.3±11.44. Of these,%68.2 were female and %31.8 were male.It is known that %38 of the patients have primary, %33 have high school education, %23.5 have undergraduate education and %5.6 do not have education. Patients strong positive correlation has been observed between EDSS score and suicidal ideation ($r=0,244$; $p<0.05$). And also, a significant positive correlation has been noticed between suicidal ideation and depression scores ($r=0.772$; $p<0.05$). A high positive correlation has been determined between suicidal ideation and fatigue scores ($r=0.377$; $p<0.05$). A positive difference has appeared between suicidal ideation and tendency to stress ($r=0.421$; $p<0.05$). There was a negative correlation between suicidal ideation and life satisfaction scale scores ($r=-0.607$; $p<0.05$).

Conclusion: Depression and fatigue contribute to suicidal thoughts in patients with MS. At the same time, decreasing quality of life and increasing susceptibility to stress influence suicidal ideation. In the light of the outcomes of the investigation, a better understanding of this effect will enable the improvement of more strategic treatments for MS patients.

Keywords: depression, fatigue, life quality, multiple sclerosis, stress, suicide ideation

P-35

The effect of clinical findings on relatives' burden of patient care for multiple sclerosis

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Objective: This study was conducted to measure the care burden of circle of patients with multiple sclerosis and to determine the effects of clinical and demographic findings on maintenance load. The mobility loss due to the disease affects the individual's daily living activities (DLA) highly, and at the same time reduces the ability to perform independently and makes the dependence on others compulsory. As the disease progresses, the self-care capacity of the individual decreases and the need for the assistance of the family members relatively boosts.

Methods: This descriptive study was carried out in the Polyclinic of Neurology Department of Ondokuz Mayıs University Research Hospital between 01.08.2018 and 07.11.2018. The sample size was calculated as 100 in the calculations using the purposive sampling method. The data were evaluated by the questionnaire, Beck Depression Inventory, Stress coping style scale, Pier Tiredness Scale and Zarit Care Burden Scale presented by researchers.

Results: Most of the participants were males, spouses/partners and primary school graduates. It was determined that the maintenance burden increased with age. The burden of relatives of newly diagnosed patients is found to be low and the rise of care load was observed when the duration of dis-balance extends and EDSS rates increase. The mean score of the participants relating Zarit Care Burden Scale was 29.3±1.68 (2-75). The relationship between clinical findings and care burden was examined.

Conclusion: There is a real possibility relating to relationship between the clinical characteristics of the patients and the caregiver burden in MS patients and the importance of this disease can be seen as a problem nowadays. Determining the care load of caregivers in MS and providing support in this regard will reduce the burden of caregivers who support the patient and will positively affect the quality of life of patients.

Keywords: caregivers, maintenance load, multiple sclerosis

P-36

Effects of COX and 5-LOX pathways on penicillin induced experimental epileptiform activity

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Objective: Recent studies have shown that inflammation, cyclooxygenase (COX) and lipoxygenase (5-LOX) pathways, may be associated with epileptogenesis. However, there are conflicting results in the literature. The aim of this study is to investigate the effect of COX and 5-LOX pathways on experimental epilepsy models.

Methods: In this study, a total of 24 Wistar albino rats were divided into four groups as Penicillin, DMSO, Penicillin + Esculetin and Penicillin + Licofelone. After the animals were given to the urethan for anesthesia, 3 holes were drilled into the determined coordinates for screw electrode connection and penicillin injection to the skulls. Epileptiform activity was initiated by intracortical injection of penicillin (500 IU, 2.5 µl). Licofelone (20 mg/kg) and Esculetin (20 mg/kg) were administered intraperitoneally 30 minutes after stable epileptiform activity.

Results: The mean spike frequency in the penicillin group was 28.86 sp/min. The mean spike frequency values of the 5-LOX inhibitor, Esculetin 20 mg/kg was 37, 29.61, 27.05, 24.62 and 16.9 sp/min in the 30th, 60th, 90th, 120th and 180th minutes, respectively and gradually decreased ($p<0.05$). In the group of Licofelone 20 mg/kg, dual inhibitor, the mean spike frequency values were determined as 47.05, 39.28, 33.74, 24.72 and 21.28 sp/min in 30th, 60th, 90th, 120th and 180th minutes, respectively ($p <0.05$).

Conclusion: Both the Esculetin and the Licofelone group had anticonvulsant activity compared to the control group in the acute experimental model. On the other hand, this report constitutes the acute part of our project. After the experiments of the chronic groups completed, the comparison and interpretation of the results will be healthier.

Keywords: penicillin-induced epilepsy, Esculetin, Licofelone

P-37

Extracellular ATP induces nociceptive firing and mast cell-mediated oxidative stress in dura mater

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Objective: Emerging data suggest that oxidative stress is involved in pathophysiology of migraine. Mast cell degranulation (MCD) in dura mater activates pain pathway in migraine. Mast cells contain high concentration of ATP, a nociceptive neurotransmitter, and express ATP receptors. There is no study directly addressing relationships among ATP, dural mast cells and oxidative stress. We investigated the effects MCD agent compound-48/80 and ATP on meningeal nerve activity and oxidative stress in dura mater.

Methods: 5 weeks-old Wistar rats (n=6) were used in the experiments. Under isoflurane anesthesia, rats were decapitated. Dura mater were removed while attached to skull and were exposed to compound-48/80 (10 µg/ml) for 10 min or ATP (1

mmol) for 30 min ex-vivo. Oxidative stress was evaluated by measuring levels of protein carbonyls, ORAC and lipid peroxidation in tissue and ORAC levels in medium-fluid. H2DCFDA imaging is also performed for ex vivo reactive oxygen species (ROS) measurements. Mast cells were stained with toluidine-blue and evaluated for degranulation. Nociceptive firing in trigeminal nerve was recorded using suction electrode technique. Data were analyzed with one-way ANOVA or t-test.

Results: Both compound-48/80 and ATP induced MCD ($p<0.01$) and nociceptive firing in trigeminal nerve terminals ($p<0.05$), respectively. Compound-48/80-induced MCD increased levels of ORAC and protein carbonyls in dura mater ($p<0.01$). ATP increased ORAC levels in medium-fluid ($p<0.05$). Neither compound-48/80 nor ATP evoked lipid peroxidation in dura mater possibly due to exposure time. Ex-vivo ROS analysis by H2DCFDA imaging showed increased oxidative stress in compound-48/80 exposed dura mater.

Conclusion: MCD induces oxidative stress by increasing ROS, and also nociceptive firing in dura mater. ATP contributes pathogenesis of migraine by inducing MCD and local ROS in dura mater as well as nociceptive firing in dural nerve terminals.

Keywords: dura mater, mast cells, ATP, oxidative stress, nociceptive firing, migraine

P-38

Behavioral and histopathological validation of ketamine-induced schizophrenia

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Objective: Schizophrenia is a one of the most devastating and complex psychiatric disorder. Due to this complexity, its difficult to find adequate animal models. It has been known that D-amphetamine, phencyclidine, ketamine can induce strong psychotic effects both in human and rodents. In this study, we aimed to validate the behavioral and histopathological alterations in the subchronic ketamine-induced rat schizophrenia.

Methods: We administered a sub-anesthetic dose of ketamine (25 mg/kg, i.p.) daily for eight consecutive days to adult male Wistar rats (n=8). The animals in the ketamine group received acute intraperitoneal injections of either chlorpromazine (1 mg/kg) or saline on test days. On the 7th and 8th days, the behavioral tests were evaluated. Behaviors related to the positive (locomotor activity), negative (social interaction) and cognitive (novel object recognition) symptoms were assessed. The tyrosine hydroxylase (TH) staining was implemented to observe dopaminergic neurons in the striatum.

Results: The results of locomotor activity test demonstrated that admistiration of ketamine significantly increased the total distance traveled (3626±350.6 vs 2176±169.8, $p<0.01$) and the percentage of stereotypic behavior (11.07±0.917 vs 7.14±0.63, $p<0.05$), as compared to saline controls. Also acute chlorpromazine injection decreased the hyperlocomotion (2381±220.4 vs 3626±350.6, $p<0.05$) and stereotypy (7.769±0.49 vs 11.07±0.91, $p<0.05$) as compare to ketamine-induced group. As compared to saline control, ketamine significantly decreased social interaction time (331±24.7 vs 171.1±22.2, $p<0.0001$) and chlorpromazine did not reversed this social deficit. Also ketamine impaired the object recognition (0.457±0.02 vs 0.677±0.03, $p<0.002$) as compared to sal controls and chlorpromazine did not reversed the deficit. Histopathological evaluation showed that the density of TH immunoreactivity in the ketamine-administered rats was increased in the striatum compared to controls ($p<0.001$).

Conclusion: The results of this study imply that subchronic administration of ketamine can induce schizophrenia-like alterations in rats and therefore this animal model may be beneficial in the research of schizophrenia.

Keywords: schizophrenia, ketamine, behavioral test, tyrosine hydroxylase

P-39

Regenerative effect of *Lignosus rhinocerus* on a mouse model of peripheral neuropathy

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Objective: Currently, there is no pharmacological agent to prevent or treat cisplatin-induced peripheral neuropathy. Medicinal mushroom have been recommended as natural remedies to increase the survival of patients in cancer treatment. This study aimed to investigate the regenerative effect of *Lignosus rhinocerotis (L. rhinocerotis)* on mouse model of peripheral neuropathy.

Methods: A cold water extract of L. *rhinoceros* was prepared. BALB/c mice were divided into three groups as control (n=12), cisplatin (n=12) and cisplatin + *L. rhinocerotis* (n=12). Cisplatin and cisplatin + *L. rhinocerotis* groups were treated with cisplatin (2.4 mg/kg/day, total dose 24 mg/kg) to create a peripheral neuropathy model. The control group received same volume of saline. *L. rhinocerotis* extract was given intraperitoneally to the cisplatin + *L. rhinocerotis* group to treat peripheral neuropathy. To determine regenerative effects, it was measured body weight, peripheral nerve sensory function using thermal hyperalgesia and compound muscle action potential (CMAP) with electromyography (EMG) device.

Results: Cisplatin caused significant loss of weight and sensory function in the experimental groups when compared to the control group ($p<0.05$). The sensory response rate of L. rhinocerotis-treated peripheral neuropathy animals to thermal

hyperalgesia were significantly increased compared to the cisplatin group ($p<0.05$). In the electromyographic examination of the sciatic nerve and the gastrocnemius muscle, BKAP findings of the animals treated with *L. rhinocerotis* were significantly higher than the cisplatin group ($p<0.05$). However, there was no statistically significant difference concerning sensory function and CMAP findings between the control group and cisplatin + *L. rhinocerotis* group.

Conclusion: *L. rhinocerotis* elicited regenerative effects in mice with peripheral neuropathy. This mushroom species may contain bioactive substances that are effective in the prevention and treatment of peripheral neuropathy. *L. rhinocerotis* should be further investigated as a potential therapeutic agent.

Keywords: cisplatin, peripheral neuropathy, *Lignosus rhinocerotis*, regeneration

P-40

Investigation of neuron protective and anticancer effects of pyrogallol: *in vitro* experiment

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Objective: Neuroblastoma is the most common solid tumor of the childhood and responsible for approximately %15 of cancer related deaths in children. Oxidative stress plays an important role in the pathogenesis of cancer by affecting different stages of cancer formation. Phenolic compounds with antioxidant properties are important to develop new therapeutic strategies for cancer. The aim of this study was to investigate the effects of pyrogallol on neuroblastoma (SH-SY5Y) cell line and primary cortical neuron cells.

Methods: SH-SY5Y neuroblastoma and primary cortical neuron cells were grown in the appropriate cell culture mediums. Cells were exposed to pyrogallol at different concentrations (20, 40, 80, 200 µM) for 24 hours. The cell viability was determined by using MTT method and GSH levels were assessed to be the indicator of oxidative effect. The statistical analysis was done by one-way analysis of variance (ANOVA) and Tukey's HSD test.

Results: According to MTT analysis results, 200 µM pyrogallol group in cortical neuron culture was found to have reduced cell viability compared to control group ($p<0.05$), however it was determined that the decreases in 20, 40 and 80 pyrogallol groups were not statistically significant compared to the control group. In SH-SY5Y cell line, pyrogallol (20–200 µM) significantly decreased cell viability compared to the control group ($p<0.001$). GSH levels showed compatibility with MTT results in both neuron cells and cancer cell line.

Conclusion: It has been determined that pyrogallol, which has antioxidant chracteristics, has protective effect on primary neurons, but causes inhibition in SH-SY5Y cancer cell line. However, further studies are needed to clarify the anticancer and neuron protective effects of pyrogallol.

Keywords: pyrogallol, SH-SY5Y, neuron, MTT, GSH

P-41

Investigation of neuron protective and anticancer effects of guaiacol glycerol: *in vitro* experiment

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Objective: Guaiacol glycerol (GG) is a commonly used drug in cases of cold and allergy. At the same time, GG decreases cell migration in a dose-dependent manner and induces apoptosis in breast cancer cells. The aim of this study was to investigate the possible effects of GG on neuron and SH-SY5Y (neuroblastoma) cell lines.

Methods: Primary cortical neuron and neuroblastoma (SH-SY5Y) cells were grown in appropriate culture media. Cells were allowed to incubate for 24 hours with GG at concentrations of 5, 10, 20 and 40 µM. Cell viability was determined by MTT method after incubation. Oxidative effect was defined by measuring GSH levels.

Results: According to MTT results, GG decreased cell viability compared to the control group concentration-dependent manner in the cortical cell culture after 24 hours incubation ($p<0.001$). In neuroblastoma cell line, 5 and 10 µM concentration of GG increased the cell viability near to the control level, but 20 and 40 µM concentration of GG decreased the cell viability significantly compared to the control group ($p<0.001$). GSH level decreased in the cortical cell culture, but 5 and 10 µM GG concentration increased GSH level in neuroblastoma cell line.

Conclusion: This study showed the cytotoxicity of GG in neuron cells. In addition, The inhibition of cancer cells treated with GG was a dose-dependent manner. However, the observed toxicity of GG needs to be confirmed in additional studies.

Keywords: guaiacol glycerol, neuron, cancer, apoptosis

P-42

Neuroprotective effects of CurcuEmulsomes on Leishmania-infected astrocytes

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Objective: Leishmanias is a neglected tropical diseases caused by protozoan parasites of the genus Leishmania that affect numerous species including humans, and is endemic in over 98 countries year, including Turkey and its subcontinental region. Although curcumin has been shown to have anti-leishmanial activities, they have some drawbacks including low aqueous solubility and toxicity. Addressing these limitations, the delivery of CurcuEmulsomes into the astrocytes was achived by encapsulating the active molecule in a lipid-based nanocarrier system, so-called CurcuEmulsome. For the scope of the study, we focused on anti-Leishmanial effects of curcuemulsomes on Leishmania infantum parasites and infected astrocytes where non-infected astrocytes testify the safety of the designed formulation.

Methods: Curcuemulsomes were synthesized by thin film hydration method as described before. The formulations were characterized using Zetasizer for their particle size distribution (dynamic light scattering) and zeta potential characteristics (Phase Analysis Light Scattering). The shape and the integrity were analyzed under Scanning Electron Microscopy. Encapsulation rates were quantified through absorbance analysis at 430 nm. Cytotoxicity of CurcuEmulsomes on Leishmania parasites were examined by Alamar Blue cell viability assay. Cell viability of Leishmania-infected astrocytes were investigated using flow cytometer.

Results: CurcuEmulsomes were found to be effective against both Leishmania parasites and Leishmania-infected astrocytes. The viability studies demonstrated the prolonged therapeutic effect which was comparable to free curcumin as assessed by cell viability studies. As the cell culture studies investigated, emulsomes have lower the half maximal inhibitory concentration (IC50) values against Leishmania parasites than that of free form of the compounds.

Conclusion: CurcuEmulsomes were found to be effective against Leishmania parasites and Leishmania-infected astrocytes on *in vitro* model and highlights the potential of the system as a new approach for antileishmania therapy. When curcumin were used as emulsome formulations, it was more efficient against Leishmania-infected astrocytes resulted from the effects of enhanced bioavailability of the CurcuEmulsomes.

This study was suppored by TÜBİTAK (Project Nr.115C022).

Keywords: Leishmania, astrocyte, Leishmaniasis, Curcumin, Emulsome

P-43

Relationship between carpal tunnel syndrome and vitamin B12

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Objective: Carpal tunnel syndrome (CTS) is one of the most common health problems characterized by pain and paresthesia in the distribution regions of the median nerve, caused by excessive pressure on the median nerve passing through the tunnel formed by the carpal bones in the wrist and helping the movement of the fingers. The aim of this study is to investigate the relationship between vitamin B12 deficiency and carpal tunnel syndrome.

Methods: The patient group consisted of 4 male and 36 female, who were applied to Ondokuz Mayıs University Faculty of Medicine Neurology Clinic between December 2013 and March 2018 and have the diagnosis of CTS with clinical and electrophysiological tests confirmed and were measured vitamin B12 values. The control group consisted of 1 male and 19 female people and were measured vitamin B12 values but were not diagnosed with CTS. Vitamin B12 values of 40 patients, who have a diagnosis of CTS clinical and electrophysiological tests confirmed, and 20 people, who have not diagnosis with CTS, were analysed.IBM SPSS Statistics V21 statistical analysis program was used for statistical analysis.

Results: The mean of vitamin B12 values of the patient group was 339.28±212.652 and the mean of vitamin B12 values of the control group was 318.15±97.942. In the statistical analysis, it was found that vitamin B12 values did not have normal distribution and that age values had normal distribution. No significant difference was found in the vitamin B12 values between the control group and the patient group.

Conclusion: In the study, no statistically significant difference was found between vitamin B12 values of the patient group and the control group. The results of this study show that there was no significant relationship between CTS and vitamin B12 deficiency.

Keywords: carpal tunnel syndrome, entrapment neuropathy, median nerve, vitamin B12

P-44

The effect of negative emotions on functional activity of human visual cortex

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Objective: Human visual perception is affected by emotions. It has been shown that the activity of visual cortex may be facilitated by the visual stimuli with emotional content. The aim of this study is to investigate the effect of negative emotions on the receptive fields of visual cortex.

Methods: Population Receptive Field (pRF) estimation method is to define the region of visual field to which the each unit on cortex respond and the size of this region by correlating the visual stimulus and the fMRI data collected from visual cortex. pRF protocol was applied by using three conditions: (1) images triggering fear, (2) their scrambled versions, and (3) emotionally neutral images. All the images were selected from the Nencki Affective Picture Set and grouped depending on the Basic Emotion Ratings. Those images were masked by expanding ring with clockwise rotating wedge or by contracting ring with counter-clockwise rotating wedge. The pRF estimations were compared across conditions with repeated measures ANOVA and post-hoc analyses for one participant.

Results: We found that scrambled images were less successful to map visual area via pRF estimation method than neutral images and images with emotional content. The images with emotional content and their scrambled versions resulted in significantly ($p<0.001$) smaller estimation of pRF size than neutral images. It has been found that the reliability of emotional condition is significantly ($p<0.001$) better than that of neutral condition. There is no significant difference ($p=0.085$ ve $p=0.615$, respectively) between emotional and scrambled conditions in terms of pRF sizes and reliability.

Conclusion: As a conclusion, the images with emotional content resulted in decreased pRF sizes in visual cortex. These results show that negative emotions enhance the activity of visual cortex through decreasing receptive field sizes since the decreased receptive field size has been related to the enhancement in the acuity of visual perception.

Keywords: population receptive field, functional MRI, Images with emotional content

P-45

Effects of vinpocetine treatment on theta activity in rats

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Objective: Although vinpocetine, a neuroprotective antioxidant, is used in treatment of cognitive impairments; the therapeutic mechanisms of vinpocetine have not been fully elucidated. Cognitive functions can be assessed by measuring the electrical activity of the brain, so EEG data helps us to understand cognitive functions. In present study, we investigate the effect of vinpocetine on EEG findings in rats.

Methods: Male Wistar albino rats were placed in stereotaxic instrument under thiopental anesthesia, after that cortical (frontal, parietal, occipital) and hippocampal electrodes were implanted bilaterally. One week after the operation, basal EEG recordings were taken for 10 minutes from all animals. Then, rats were divided into control and experimental groups. The control group was treated with saline and the experimental group treated with vinpocetine (5 mg/kg/day, i.p.) for 15 days, and EEG recordings were taken again. After the EEG recordings were divided into 2-second epochs, the artifacts from the EEG signal were removed. The EEG findings for each channel were compared with Student's t-test. $p<0.05$ was considered statistically significant.

Results: There was no change in the amplitude of theta frequency band in the control group. Vinpocetine treatment for 15 days, caused a statistically significant increase in the amplitude of theta frequency band in left frontal, left occipital and right hippocampal areas.

Conclusion: The increased activity in theta frequency is associated with cognitive processes such as attention and alertness. Although there was no change in the control group, the amplitude of theta frequency band was increased after vinpocetine treatment for 15 days. Therefore, it is suggested that vinpocetine treatment may be useful for increasing of alertness and attention.

Keywords: vinpocetine, rat, EEG, theta

P-46

Effects of intracerebroventricular infusion of salusin-beta on rat testis: a morphological approach

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Objective: Salusins are recently discovered two peptides consisting of 28 and 20 amino acids (salusin-alpha and salusin-beta, respectively). The hypothalamus is a center that has undertaken important roles in the control of reproduction, and it is known that many peptides, especially GnRH, play active roles in control of reproduction in this center. It has been reported that salusin-like immunoreactivity was detected in the rat hypothalamo-neurohypophyseal tract using immunohistochemistry techniques. We previously reported that the intracerebroventricular (icv) infusion of salusin-beta decreased serum LH, FSH and testosterone in rats. This study was designed to determine effects of icv infusion of salusin-beta on testes.

Methods: In the study, 40 *Wistar-Albino* male rats were randomly divided into four different groups such as control, sham and low and high doses of salusin-beta (n=10). Animals were intracerebroventriculary infused with either 2 and 20 nmol doses of salusin-beta or sham (receiving artificial cerebrospinal fluid) via osmotic mini pumps. After seven days, the animals were decapitated and testes were surgically removed and testis morphologies were examined.

Results: As a result of histological examinations, seminiferous tubules in all groups consisted of germinal epithelium with normal histological appearance extending from the basal lamina to the lumen. Mean tubule diameter and germinal epithelial

thickness were decreased in salusin-beta treated groups ($p<0.05$).

Conclusion: Our results show that salusin-beta may change reproduction behavior by affecting testicular process.

This study was supported İnönü University BAP (Project number: TSG-2017-952).

Keywords: salusin-beta, testis histology, reproduction, seminiferous tubules, rat

P-47

The changes in leukocyte formula of peripheral blood in rats exposed to decimeter microwaves

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Objective: The reaction of blood cells in organism exposed to microwaves is of great interest both in terms of elucidation of the mechanisms of non-ionizing radiation action to a living organism, and from a purely medical point of view. This study was conducted to identify changes in the leukocyte formula of peripheral blood at the total body chronic exposure to decimeter microwave radiation.

Methods: Studies were conducted on white Wistar rats weighing 250–300 g contained in normal vivarium conditions. The animals were divided into experimental and control groups of 10 animals in each. The experimental group of animals was exposed to 460 MHz radiation from the physiotherapy apparatus daily for 20 min to 28 days at a direct power flux density of 30 μW/cm2. Leukocyte formula was determined by the method of Putintseva et al. (2008). The level of significance of differences in the experimental and control groups was assessed by Student's t-test.

Results: The study of the leukocyte formula showed the following results: in the blood of the control group, lymphocytes are up to 83%, neutrophils are not more than 15%. Exposure to microwaves leads to a significant and pronounced decrease in the percentage of lymphocytes and increase in the percentage of neutrophils; for 28 days exposition, the relative content of lymphocytes drops to 78% ($p<0.05$), and the relative content of neutrophils increases to 20% ($p<0.05$). It should be noted that in the initial stage of exposure in the percentage of neutrophils there was some tendency to decrease.

Conclusion: Chronic exposure of organism to non-ionizing radiation in the microwave range leads to changes in blood leucoformula, lowering percentage ratio of lymphocytes and neutrophils in the peripheral blood with an increase in immature forms, myelocytes and metamyelocytes. Observed moderate lymphopenia and neutrophilocytosis indicate that microwave radiation is a potential stress factor for living organisms.

Keywords: rat, microwave radiation, blood, leukocyte formula

P-48

Investigation of cellular mechanisms of Ser9Leu proopiomelanocortin (POMC) mutation in neuronal cells

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Objective: POMC is secreted from neurons in arcuate nucleus of hypothalamus and plays a role in body weight. Many mutations in the POMC gene have been found to cause obesity. In the mutation analysis of obese Italian children, Ser9Leu mutation was identified. Ser9Leu mutation is located on the signal peptide of protein which is involved in the translocation and plays an active role in the intracellular trafficking of the protein. Therefore, it was hypothesized that Ser9Leu POMC will cause problems in intracellular translocation since it is on the signal peptide. In this study, cellular mechanisms of Ser9Leu POMC mutation were investigated.

Methods: To investigate the cellular mechanisms, POMC wild type (WT) and Ser9Leu POMC plasmids were generated by molecular biology methods. Cell culture experiments were performed to transfect the plasmids into mouse neuroblastoma (N2a) cells and secretion experiments were performed. For secretion experiments, basal (B) media were collected every 30 minutes to to examine the level of secreted protein. Cells were then exposed to stimulation (S) for 30 minutes. Since B and S samples contain many waste materials, they were concentrated by precipitation with 100% TCA to remove them. Then, samples were analyzed by Western blot using anti-ACTH antibody.

Results: As a result of the Western blot, 35 kDa bands were observed in N2a cells transfected with WT POMC. This band shows the presence of unprocessed, inactive form of POMC. After stimulation, the amount of this POMC form decreased. The same results were also seen in cells transfected with Ser9Leu POMC.

Conclusion: We could only detect the inactive form of POMC with this antibody. In future studies, we expect to see smaller forms using the antibody that displays all forms of POMC. In this way, the effect of mutation on the secretion and processing of the protein will be better understood.

Keywords: neuroblastoma cells, obesity, proopiomelanocortin, Western blot

P-49

Effects of phenobarbital used in pregnant rats on motor behavior of pups

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Objective: Uncontrolled convulsive seizures during pregnancy have negative effects on the development of offspring. The aim of this study was to investigate the changes in motor behavior

of the pups exposed to phenobarbital in the prenatal period after completion of the nervous system development.

Methods: The gestational age was determined with the presence of sperm in vaginal smears taken after mating adult Spraque-Dawley rats. Experimental groups received phenobarbital (20 mg/kg), while the control groups received saline by oral gavage between embryonic day 14–21. Pups were obtained from three different mothers were grouped according to their gender to minimize the litter effect. Offspring (n=7, from both groups and gender) were subjected to rota-rod, elevated plus maze, spontaneous locomotor activity, open field and skill-required grip tests from the postnatal day 40.

Results: In activitymeter and open field tests, the number of movements and the total distance traveled during the test were significantly decreased in females treated with phenobarbital. In the rota-rod test, a significant decrease was found in the motor skills of males treated with phenobarbital. On the other hand, in phenobarbital treated groups, when skill-required grip test performances of the pups were compared according to gender, it was found that the male pups performed better than the females. No significant difference was observed in other tests.

Conclusion: Uncontrolled convulsive seizures during pregnancy have as negative effects on the development of offspring as the least antiepileptic agents. However, according to the data obtained from our study, it is recommended that more reliable antiepileptic agents should be preferred during pregnancy by considering long-term behavior and motor dysfunction caused by phenobarbital exposure in offspring.

This study was supported by ESOGU scientific research projects commission (Grant no: 2017-1602).

Keywords: phenobarbital, anticonvulsant, motor skill, rota-rod, activitymeter

P-50

The effect of gender on the activity of miRNA and transcription factors in Parkinson's disease

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Objective: It is known that there is a significant difference in the incidence of Parkinson's disease (PD) by gender, which is one of the important neurodegenerative diseases. Taking into account this gender difference, the aim of our study is the detection of disease related active transcription factors (TFs) and miRNAs through the analysis of the disease related transcriptome by Protein-Protein Interaction (PPI) based approaches. Another goal is the identification of drug candidates for PD through this bioinformatic analysis.

Methods: Data was collected from online transcriptome databases for this study. It contained BA9 (in the prefrontal cortex) (5 female controls, 6 female PD and 10 male controls, 8 male PD), putamen (5 female controls, 6 female PD and 15 male controls, 9 male PD), substantia nigra (5 female controls, 5 female PD and 13 male controls, 6 male PD) regions microarray data from PD tissue samples. The PPI network contained 501,141 interactions between 19,339 proteins. Omic data were analyzed by using various statistical analysis tools and it was integrated to PPI network via bioinformatics methods.

Results: Groups that were significantly affected by the disease and interacting with each other at the same time were detected in different regions of brain by taking into account gender difference. Neurodegenerative disease related drugs interacting with the proteins in these groups were determined as drug target candidates. In addition, the determined disease and gender-specific molecular subnetworks were combined with the regulation information in the form of TF and miRNA interactions.

Conclusion: In this study, the effect of gender on different brain regions in Parkinson's disease was determined through PPI and regulation analysis. Based on these results, new drug target candidates were described for PD.

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Keywords: genome-scale data, protein-protein interaction, Parkinson's disease, drug target, miRNA, transcription factor

P-51

The effects of peripheral macrophages on microglia inflammasomes pathway after LPS stimulation in cell culture

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Objective: There is a bidirectional crosstalk between resident microglia and bone marrow derived macrophages (BMDM) in central nervous system inflammation. BMDM infiltrating the brain after injury suppress proinflammatory cytokines produced by resident microglia. BMDM regulate microglia-mediated inflammation and form a natural control mechanism against the detrimental effects of excessive inflammation after injury. In this preliminary study, the relationship between microglial inflammasomes pathway and the antiinflammatory effects of BMDM after LPS stimulation, was evaluated.

Methods: Primary microglia and BMDM have been isolated from the brains and long bones of adult C57BL/6 mice, respectively (n=3). Cells were stimulated for 4 hours with LPS and then incubated for 20 hours in serum-free medium. Inflammasomes pathway genes were evaluated using the commercial kit for RT qPCR. Gene expressions were calculated as "CT values" and their up- or downregulations have been evaluated as fold changes.

Results: LPS stimulation increased IL-1, IL-6 and TNF-α gene expression and this increase was suppressed in accordance with the literature after coculture with BMDM. The inhibitory effect of BMDM on NLRP3 and IL-18 expression was not significant ($p>0.05$). Microglia and BMDM coculture caused significant changes in expression of Tab 1 and 2, FADD and cathepsin B genes ($p<0.05$).

Conclusion: The suppressive effect of BMDM on the microgial production of IL-1 after LPS stimulation is regulated in the signal 1 process of the canonical inflammasomes pathway. This regulation takes place at Tab and FADD steps. The expression of Tab genes, which are known to act by modifying intracellular p38MAPK localization, is negatively correlated with proinflammatory cytokines, and is associated with FADD expression. This result suggests that these genes may have a driving effect on microglia polarization rather than cell survival in inflammation. We are planning to continue our study by increasing the n number to reach a statistical significance of our preliminary data.

Keywords: microglia, bone marrow derived macrophage, inflammation, inflammasomes, Tab, FADD

P-52

Investigation of protective effect of *Aloe barbadensis miller* water extract against glufosinate poisoning in neuron culture

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Objective: Although the aloe vera family has protective effects on the neuron, the protective effect of the neurons on *Aloe barbadensis miller* is not known yet. Glufosinate is structurally similar to glutamate and is a herbicide that blocks glutamine synthetase. In our study, it is aimed to investigate the protective effects of *Aloe barbadensis miller* on the glufosinate toxicity model of cortex neuron culture by isolating the aqueous extract of the plant.

Methods: Neuron cortex cells were obtained from Atatürk University Medical Pharmacology Department. *Aloe Barbadensis* plant extract was obtained from Nurbal, Istanbul. The plant aqueous extract was used at 100, 200, 400 microgram (µgr) doses, and glufosinate at 50, 100, 200 and 400 mM doses. Thirteen groups were administered to the neuron cortex cells and read at a wavelength of 570 nm after 24 hours of treatment. MTT results were analyzed by one way ANOVA method in SPSS, IBM 21.00 program.

Results: In our control group, the vitality was defined as 100% and the other groups were rated accordingly. *Aloe Barbadensis* decreased glufosinate toxicity due to dose increase. When the gro were evaluated in itself, it was observed that the glufosinat dose increased and the viability decreased. *Aloe Barbadensis* applied to the glufosinate 400 mM dose with the highest viability of 82% was seen in 400 µgr ($p<0.001$).

Conclusion: PC12 cells are well known as models in neuron cell studies and undergo proliferation or differentiation when treated with different factors such as growth factors or extracellular matrix. Catherine F. Bouthet et al. have also studied the comparative effects of Aloe substances extracted from *Aloe barbadensis miller* on proliferation in human embryonic lung cells (HEL) and cultured PC12 cells. Our results are consistent with this study. According to our study, barbadensis dose increases and protective effect increases.

Keywords: *Aloe barbadensis miller*, glufosinate, MTT, neuroprotective, cortex neuron

P-53

Computational prediction of changes in metabolic reaction rates for Alzheimer's disease in the context of different brain regions

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Objective: Alzheimer's disease (AD) is a type of dementia that causes impairment in memory, reasoning and thinking. Incidence and progression of AD are correlated with metabolic dysfunction. Our aim is to predict changes in the rates of metabolic reactions computationally for hippocampus, entorhinal cortex, superior frontal gyrus, medial temporal gyrus and primary visual cortex. The computational approach integrates measured rates with the changes in gene expression levels of AD patients.

Methods: A basic metabolic network model that includes 71 reactions of central carbon metabolism was used to estimate metabolic reaction rates for five different regions of healthy brain by using a computational approach that combines steady state balancing around metabolites with optimization. Metabolic rates of AD patients were then predicted based on the same model by using the gene expression profiles of AD patients retrieved from a public transcriptome database (Gene Expression Omnibus).

Results: Metabolic reaction rates of healthy subjects and AD patients were predicted, and compared with each other to understand metabolic dysfunction in the five different brain regions. Reaction rates for healthy brain were found to be similar to literature, there are some differences among various regions, though. Comparison of reaction rates of AD patients demonstrate that hippocampus and entorhinal cortex are the most affected and primary visual cortex is the least affected region. Glucose and oxygen uptake rates are predicted to be significantly decreased in the mostly affected regions. Moreover, predicted decrease in ATP production rate and

increase in the GABA shunt activity in AD patients are found to be in accordance with literature.

Conclusion: Mapping gene expression profiles on the metabolic model computationally gave us crucial perspective about changes in the metabolic pathways of different brain regions in AD. A comprehensive brain specific metabolic network model and different mapping algorithms are going to be performed to obtain more reliable results.

Keywords: Alzheimer's disease, metabolic dysfunction, brain regions, computational approach, transcriptome data.

P-54

Investigation of the effects of walnut leaf essential oil on cortex neuron and LN405 cancer cell line: an *in vitro* study

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Objective: Walnut leaves are considered as a source of health care compounds. The aim of my study is to investigate the effects of glutamate toxicity model on cortex neuron and LN405 cell cultures using different doses of walnut leaf essential oil (CYEO).

Methods: Neuronal cells were obtained from medical pharmacology department of Ataturk University, Erzurum, Turkey. Walnut leaves were subjected to hydrogenation for 3 hours using Clevenger type equipment. The resulting fat was used at doses of 10–1, 10–2, 10–3, 10–4 and 10–5 concentrations and glutamate at 10–5 mM. Seven experimental groups were examined by MTT with cytotoxicity after 24 hours of treatment in neuron and LN-405 cells. Results SPSS was analyzed by one way ANOVA method in IBM 21.00 program.

Results: Vitality was defined as 100% in the control groups and the other groups were rated accordingly. Glutamate in the cortex showed 10–5 mM 62% viability. CYEO showed that the viability did not increase in a dose-dependent manner and the highest vitality rate was found in CYEO 10–4 concentrations. In LN-405 cancer cells, glutamate has a vitality rate of 10-5 mM 77%. In CYEO, the highest mortality rate was observed in CYEO 10–2 and 10–4 concentrations.

Conclusion: Rather MA and β-pinene and α-pinene were found in CYEO. Eraldo J, in his studies revealed pinenes have anticancer and neuron protective effects. These studies support our work.

Keywords: walnut leaf essential oil, MTT, neuron, LN-405

P-55

Investigation of effects of walnut leaf water extract on cortex neuron and LN405 cancer line: *in vitro* assay

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Objective: The walnut tree leaves and seeds are used in medicine and cosmetics industry, cores and shells. The aim of my study was to investigate the effects of glutamate toxicity model on cortex neuron and LN405 cell cultures using different doses of walnut leaf water extract (CYSE).

Methods: Neuron cultures, was obtained from the department of medical Pharmacology, Ataturk University, Erzurum, Turkey. Walnut leaves were softened with distilled water for 8 hours/3 days at 30–35 °C. The aqueous extract was filtered, freeze-dried. CYSE was used at doses of 1, 25, 50, 75, 100 and 125 micrograms (µg) and glutamate at 10–5 mM. Eight experimental groups were administered to neuron and LN405 cells. The cytotoxicity was examined after 24 hours of treatment. MTT results were analyzed by one way ANOVA method in SPSS, IBM 21.00 program.

Results: The vitality ratio of the control groups was defined as 100%. Glutamate in cortex neurons showed a minimum viability rate of 10–5 mM 62%. In CYSE, the highest viability rate of CYSE was found to be 25 µgr. In LN405 cancer cells, glutamate has a vitality rate of 10–5 mM 97%. The highest mortality rate was 67%, and CYSE was 25 µgr and there was a significant difference between the control group.

Conclusion: Pereira et al. (2007) investigated the antioxidant activities of leaf extracts of walnut leaf and found strong antioxidant capacity. The antioxidant activity in our study increased the viability of neurons while cancer cells were killed.

Keywords: glutamate, cortex neuron, LN405, walnut leaf, MTT

P-56

Analysis of cognitive impairment and memory disorders based on cellular networks using transcriptome data

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Objective: Memory and cognitive disorders are physical factors affecting the quality of life. There are transcriptome studies in the literature to study these disorders, obtained from the related brain regions of mice and rats. The affected genes were analyzed in these studies to identify underlying molecular mechanisms. Although these studies provide a rich set of data

in literature, they are limited in terms of elucidating mechanisms because the data are not mapped on molecular interaction networks. Our study analyzes the transcriptome data related to memory and cognitive disorders together with protein interaction networks for the first time, contributing to the elucidation of molecular mechanisms behind such disorders.

Methods: In order to map transcriptome data on protein interaction networks, two algorithms mentioned in the literature about their high performance (BioNet and KeyPathwayMiner) are used comparatively. These algorithms aim to find smaller, meaningful and functional groups within the global interaction network. Rat transcriptom data were downloaded from the literature, which compared various age groups, examining factors such as stress, maternal separation, and attempting to elucidate mechanism behind learning (Gene Expression Omnibus Database). As the interaction of the rat protein obtained from the databases in the literature is limited (3704 proteins-7304 interactions), the interaction data was expanded in this study. Assuming that the mouse homolog proteins have same interactions in rat, these interactions were added to the rat interactome (9500 proteins-37043 interactions).

Results: Both algorithms were able to identify significant molecular interaction groups that could explain cognitive impairment and memory disorders. By functional analysis of the groups, we identified proteins related to memory, cognition, learning, aging and plasticity.

Conclusion: By screening the network containing thousands of interactions specific to the organism with the help of transcriptom data, proteins involved in the processes such as myelination, cytokine, intercellular signaling, and circadian rhythm have been identified by bioinformatics approach.

Keywords: bioinformatics, transcriptome data, protein interaction network, memory, learning mechanism

P-57

Effects of chronic nicotine treatment on MC3R and MC4R mRNA expression in the rat brain

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Objective: Alpha-melanocyte stimulating hormone (α-MSH) is one of the pro-opiomelanocortin-derived neuropeptides. α-MSH binds and shows its effects via melanocortin 3 (MC3R) and melanocortin 4 (MC4R) receptors on target cells in the brain. α-MSH and its receptors have been shown to play important roles in natural and drug-induced reward and reinforcement. However, the role of α-MSH and its receptors and their regulation during nicotine reward are not known. The present study investigated the regulation of melanocortin 3 (MC3R) and melanocortin 4 receptors (MC4R) in the hypothalamus and mesocorticolimbic system during nicotine exposure.

Methods: Rats were injected subcutaneously for 5 days with nicotine (0.2, 0.4 or 0.6 mg/kg/day, free base) and were decapitated one hour after a challenge dose on the sixth day. mRNA levels of MC3R in the ventral tegmental area (VTA) and MC4R in the medial prefrontal cortex (mPFC), nucleus accumbens (NAc), dorsal striatum, amygdala, lateral hypothalamic area and VTA were measured by quantitative real-time PCR.

Results: The analysis of PCR data with one-way ANOVA and post-hoc Tukey tests showed that treatment with 0.6 mg/kg/day nicotine upregulated MC4R mRNA in the mPFC ($p=0.029$). Additionally, all three nicotine doses increased MC3R mRNA expression in the VTA [0.2 mg/kg ($p=0.002$), 0.4 mg/kg ($p=0.023$), 0.6 mg/kg ($p=0.001$)].

Conclusion: It is well-known that the nicotine treatment regimen used in this study enhances dopamine release in the mesocorticolimbic system. Previous studies showed that melanocortin receptor activation in the VTA activates dopaminergic neurons. Therefore, the increase in MC3R and MC4R expression in the mesocorticolimbic system following nicotine administration suggests that nicotine may enhance melanocortin signaling in the mesocorticolimbic system and this alteration may be an important mechanism mediating nicotine reward.

This work was supported by Ege University, Scientific Research Projects Commission (Research Fund Grant 16-SBE-007).

Keywords: nicotine, POMC, melanocortin receptor, mesocorticolimbic system

P-58

The effects of nicotine administration on the MCH and MCHR1 expression in the rat brain

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Objective: Melanin concentrating hormone (MCH) and its receptor MCHR1 show intense expression in the mesocorticolimbic pathway, which is referred to as the reward system. It has been suggested that MCH signaling may play a role in the rewarding effects of addictive agents such as alcohol, cocaine, amphetamine, methamphetamine as well as natural substances such as sucrose and food. The aim of our study is to investigate the regulation of MCH and MCHR1 mRNA in anatomic structures which compose the mesocorticolimbic system during the emergence of rewarding effect of nicotine.

Methods: Adult male rats were subcutaneously injected with three different doses of nicotine (0.2, 0.4, 0.6 mg/kg, free base)

for six days; decapitation was performed one hour after the last injection. MCH mRNA expression in the lateral hypothalamic area and MCHR1 mRNA expression in the amygdala, medial prefrontal cortex, nucleus accumbens, dorsal striatum, lateral hypothalamic area, medial hypothalamic area and ventral tegmental area were analyzed by using quantitative real-time PCR method.

Results: Statistical analysis of quantitative real-time PCR data using one-way ANOVA test showed that none of the nicotine doses altered MCH and MCHR1 mRNA expression in the brain regions studied.

Conclusion: Nicotine treatment did not change MCH and MCHR1 transcription in the hypothalamus and mesocorticolimbic system. This result suggests that MCH signaling is not regulated during nicotine reward. However, in this study, we evaluated only MCH and MCHR1 mRNA expression and not the peptide expression. Nicotine may regulate MCH and MCHR1 expression at posttranscriptional, translational or posttranslational levels.

This work was supported by Ege University, Scientific Research Projects Commission (Research Fund Grants 16-SBE-006 and 16-BAUM-003).

Keywords: nicotine, MCH, MCHR1, mesocorticolimbic system

P-59

Nicotine administration effects on pro-opiomelanocortin (POMC) and μ opioid receptor (MOR) mRNA expressions in the rat brain

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Objective: Pro-opiomelanocortin (POMC) is one of the peptide precursors of the endogenous opioidergic system. POMC-derived peptides have roles in processes such as stress response, eating behavior and drug abuse. β-endorphin (β-END), a neuropeptide synthesized from POMC mRNA, plays a key role in addiction. The activity of mesocorticolimbic system leads to the feeling of reward, which is responsible for the development of addiction. The aim of this study was to investigate the regulation of POMC and β-endorphin-binding μ-opioid receptor (MOR) mRNAs in the anatomical structures that constitute the mesocorticolimbic system during nicotine reward.

Methods: One of three doses of nicotine (0.2, 0.4, 0.6 mg/kg, free base) was injected into the rats for five days. Rats were decapitated one hour after the last injection on the sixth day of treatment. POMC mRNA expression in the medial hypothalamic area and MOR mRNA expression in the medial prefrontal cortex, nucleus accumbens, dorsal striatum, amygdala, lateral hypothalamic area and ventral tegmental area were evaluated by quantitative real-time PCR method.

Results: The analysis of PCR data with one-way ANOVA and post-hoc Tukey tests showed that POMC mRNA levels in the hypothalamus were upregulated in rats treated with 0.6 mg/kg nicotine ($p=0.022$). However, none of the nicotine doses altered MOR mRNA levels in the mesocorticolimbic system and associated limbic structures.

Conclusion: Nicotine treatment increased POMC transcription in the arcuate nucleus of medial hypothalamic area. This result indicates that β-endorphin synthesis and release may be elevated in the projection areas of POMC neurons. Therefore, although nicotine did not change MOR transcription, POMC signaling in the mesocorticolimbic system may be enhanced via increased β-endorphin synthesis. We suggest that this alteration may play an important role in nicotine reward.

This work was supported by Ege University, Scientific Research Projects Commission (Research Fund Grant 16-TIP-078 and 15-BAUM-003).

Keywords: nicotine, POMC, MOR, mesocorticolimbic system

P-60

Designing a viral vector that targets to cause damage in motor neurons

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Objective: Utilization of viral vectors for gene therapy has increased rapidly in recent years. For successful treatment, construction of viral expression cassettes should be designed to meet the characteristics of each disease. Therefore, selection and optimization of the target tissue-specific expression elements are critical. The aim of this study was to create a viral vector inducing the expression of a protein shown to cause damage specifically in motor neurons.

Methods: Adeno-associated virus (AAV) vector was used for high-efficient expression of target gene encoding TAR-DNA binding protein (TDP-43), shown to cause damage in neurons. To provide target tissue specificity, different promoters were used; one ubiquitious promoter for all neurons (CMV), the other one (UCHL1) was unique to the cortical motor neurons. Suitable transcriptional regulatory elements were selected to insert 4–5 kb size region between the two inverted terminal repeats (ITR) including post-transcriptional regulatory element, termination sequences of the transcription and sequences required to increase the exportation of mRNA from nucleus to cytoplasm.

Results: The primers of the target gene and elements obtained from source plasmids were designed and added in the expression cassette. The green fluorescent protein (GFP) gene was selected as a marker to monitor transduction efficiency. Sequence analyses confirmed whether there was any mutation or frame shift on the elements in the cassette. After the entire cassette was formed, positive transformants were selected by the colony PCR method and prepared for packaging into the AAV capsid.

Conclusion: Viral vector-mediated gene expression is a new and powerful tool for preclinical studies and a very promising tool for gene therapy. In order to develop successful therapies, the dose of vectors as well as the injection site and timing of administration play important roles in the effectiveness of the method.

This study is supported by TÜBİTAK (Grant No:116S408).

Keywords: AAV, viral vector design, gene therapy, TDP-43

P-61

Effects of lidocaine and articaine on nociceptive calcium signaling in rat trigeminal ganglion cells

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Objective: In this study calcium signaling in sensory neurons was used as a pain marker. And the effects of articaine and lidocaine, which are widely used as local anesthetic in the mouth, on intracellular calcium ([Ca2+]i) signaling in cultured trigeminal ganglion (TG) neurons, cells which are responsible for the primary pain sensation in the orofacial region, was investigated and by this way the anesthetic effects of the selected local anesthetics were compared.

Methods: TG neurons were isolated from 1–2 day Wistar rats and primer culture was prepared by enzymatic treatment. TG neurons were loaded with Ca2+ -sensitive fluorescent dye fura-2 (1 µM) by incubation at 5% CO2, at 37°C for 60 minutes. TG cells were stimulated at 340 nm and 380 nm wavelengths respectively and emissions were recorded at 510 nm and the ratio of 340/380 nm was used as [Ca2+]i indicator. Cells were stimulated with capsaicin (1 µM) or by non-specific membrane depolarization achieved by use of high extracellular K+ (30 mM) and the effects on lidocaine and articaine [Ca2+]i responses were examined.

Results: Stimulation with KCl (30 mM) resulted in a significant increase in basal [Ca2+]i level; and subsequent application of lidocaine (0.1, 0.3 and 0.5 mM) significantly attenuated [Ca2+]i levels. This inhibitory effect did not recover at 5 minutes after washing. While the fluorescence ratio was 0.89 ± 0.06 in basal conditions, this rate was increased to 1.55±0.43 following KCl (30 mM) stimulation and 0.1 mM lidocaine application significantly decreased this ratio to 1.04±0.08 ($p<0.05$). No significant recovery was obtained in this inhibition at 5 minutes following washing (1.05±0.05). Lidocaine also suppressed capsaicin-induced [Ca2+]i levels. Articaine (5 mM) significantly attenuated the increase in both capsaicin and KCl-induced [Ca2+]i response. While basal ratio was 1.07±0.04, this value was increased to 1.21±0.02 following stimulation with capsaicin (1 µM); and application of 5 mM articaine significantly reduced this increase to 0.97±0.03 ($p <0.05$).

Conclusion: The findings of this study indicated that both of the tested local anesthetics blocks pain-related calcium signals in TG neurons that carrying pain signals in orofacial region; considering the efficacy at the tested dose levels lidocaine is more effective.

Keywords: local anesthetics, calcium signaling, trigeminal ganglion

P-62

The endocrine disruptor butylparaben induces brain tissue damage via impairment of the anti-oxidant enyzme metabolism

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Objective: Synthetic chemicals like endocrine disruptors affect both human and wildlife. Parabens belong to the endocrine disrupting chemicals (EDCs) family which leads to the impairment of the hormone metabolism. They are used more than 50 years in the industrial products including personal care products such as cosmetics, deodorants, toiletries, face creams, pharmaceuticals, children products and also used in the food and beverage processing as antimicrobial and anti-fungal preservatives. Some parts of butylparaben can not be metabolized and accumulates in the body that may lead to the disease formation, however impact of butylparaben on the anti-oxidant enzyme metabolism of the brain has not been studied before.

Methods: Male Wistar albino rats were randomly divided into four groups and butyl paraben was administered at 200, 400, 800 mg/kg/day for 14 days by daily oral gavage. Afterwards, 6-phosphate dehydrogenase (G6PD), 6-phosphogluconate dehydrogenase (6-PGD), glutathione reductase (GR), glutathione peroxidase (GPx) and glutathione-s-transferase (GST) enzyme activities were evaluated in the brain and histopathological changes were examined.

Results: G6PD, 6-PGD, GR, GST and GPx activities significantly increased in the 400 and 800 mg/kg/day butylparaben-treated groups compared to the control in the brain samples ($p\leq0.0001$). All enzyme activities showed peak at the 400 mg/kg/day dose groups, however, all anti-oxidant enzyme activities decreased in the 800 mg/kg/day butylparaben-treated groups compared to the 400 mg/kg/day group ($p\leq0.0001$). Furthermore GR and G6PD activities significantly elevated in

200 mg/kg/day butylparaben-treated group compared to the control (p≤0.0001). In the brain parietal cortex, we observed many of hyperchromatic cells, especially in the high dose butylparaben-treated group.

Conclusion: Butylparaben treatment can impair oxidative stress metabolism and causes tissue damage in brain. Our results supports the degenerative role of butylparaben on cellular reducing equivalent homeostasis. Butylparaben may not be as safe as initially thought, and this chemical has adverse effects on the cellular homeostasis and causes tissue damage in the brain.

Keywords: butylparaben, brain, anti-oxidant metabolism, histopathalogical changes

P-63

Investigation of the protective effects of *Aloe barbadensis miller* plant juicy extract on glutamate toxicity

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Objective: Although it is known that the aloe vera family has protective effects on the neuron, it has not been studied on the neuron protective effect of *Aloe barbadensis miller* plant.In this study, it is aimed to investigate protective effects of *Aloe barbadensis miller* plant on glutamate toxicity model formed in cortex neuron culture by isolating the water extract.

Methods: Neuron cortex cells were obtained from medical pharmacology department of atatürk university medical faculty. *Aloe barbadensis miller* plant extract was obtained from Nurbal, Istanbul. The plant juicy extract was used at doses of 25, 50, 100, 200, 400, 800 and 1600 micrograms (µg), and glutamate at 10-5 mM. The adjusted doses were applied to the neuron cortex cells and read at a wavelength of 570 nm after 24 hours of treatment. 3-(4.5-dimethylthiazol-2-yl)-2.5-diphenyltetrazolium bromide (MTT) results were analyzed by one way ANOVA method in SPSS, IBM 21.00 program.

Results: In our control group, the vitality was defined as 100% and the other groups were rated accordingly. Glutamate 10–5 mM group showed the least viability rate with 59% (p<0.001). In aloe barbadensis, it was observed that the viability did not increase with dose and the highest vitality rate was between 100 and 400 µg (93%–89%). When compared with our control group, the lowest vitality rate was observed in 25µg (61%) (p<0.001).

Conclusion: We observed that *Aloe vera barbadensis* protects neurons against glutamate toxicity at doses of 100 and 400 µgr.

Keywords: *Aloe barbadensis miller*, glutamate, MTT, neuroprotective, cortex neuron

P-64

Responses to TLR4 increase triggers inflammatory pathways in a mouse model of Parkinson's disease

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Objective: Parkinson's disease (PD) is a common progressive neurodegenerative disease characterized by loss of dopaminergic neurons. Microglial activation leads to neuroinflammation which is an important part of the pathogenesis of PD. 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) is the most commonly used toxin to induce a model of PD. It has been shown that the accumulation of alpha-synuclein (α-synuclein) induced by the toxins caused death in dopaminergic neurons. Previous studies mentioned that α-synuclein accumulation might activate toll-like receptor 4 (TLR4) in the toxin-induced PD model and this pathway may trigger NF-kB mediated cytokines. Based on this hypothesis, we aimed to evaluate the expressions of tyrosine hydroxylase (TH), TLR4 and NF-kB p65 (RelA) in dopaminergic neurons of SNpc in a mouse model of PD.

Methods: In our study MPTP was used to induce PD model in 3-month-old male C57BL/6 mice. The animals were sacrificed, and brain tissues were removed. In the brain tissues, immunohistochemical and immunofluorescent markings were performed with TH, TLR4 and NF-kB p65 (RelA) antibodies.

Results: In the SNpc TH expression was significantly reduced due to the decreased number of dopaminergic neurons. In PH groups TLR4 expression was observed also in dopaminergic neurons of SNpc, besides microglia.The presence of p65 expression in the same neurons was remarkable.

Conclusion: Our results suggest that the increase in TLR4 expression induced the microglial activity in experimental PD model and activated NF-kB pathway and make a contribution to dopaminergic neuron loss.

Keywords: Parkinson's disease, MPTP, p65, TLR4, NF-kB

P-65

SOX2 and NANOG expressions in glioblastoma multiforme

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Objective: Glioblastoma multiforme (GBM) is the most common malignant brain tumor in the human central nervous system. There is compelling evidence that brain tumors, particularly GBM, harbor a population of cancer stem cells (CSCs). These

CSCs can undergo self-renewal, initiate tumors and they are resistant to therapy. It has been shown that CSCs within GBM characterized by the expression of the CSC markers such as SOX2 and NANOG. Previous studies have suggested that the overexpression or gene amplification of SOX2 and NANOG are putatively contributing to cellular invasion in tumors of neural and neural crest origin, including glioma. Even though little is known about the molecular mechanisms involved in GBM pathogenesis, the discovery of CSC has shown that the presence of CSC is correlated with the aggressiveness of gliomas. We hypothesized to identify SOX2 and NANOG as CSC markers in GBM. Therefore, we aimed to evaluate the SOX2 and NANOG expressions immunohistologically in GBM and normal brain tissues.

Methods: With the approval of Akdeniz University Medical Faculty Clinical Research Ethics Committee; GBM samples were obtained from two (n=2) newly diagnosed patients who had not received GBM treatment previously and underwent resection at the Akdeniz University. For comparison, brain tissues of two patients who underwent partial brain resection due to trauma were used. Tissues immunohistochemically stained for the SOX2, NANOG.

Results: Our study was demonstrated that the expression patterns of SOX2, NANOG proteins were clearly identified in tumor cells in GBM compared with normal brain tissues.

Conclusion: Overexpression of SOX2 and NANOG correlates with the tumor progression in GBM. However, it is still not clear whether SOX2 and NANOG are critical for GBM prognosis. Our study was performed in a small number of patients for research but future studies are required for the examination of CSC specific markers in GBM tissues.

Keywords: GBM, SOX2, NANOG, immunohistochemistry

P-66

Investigation of neurotoxicity, neuropotectivity and neuroregenerative efficacy of *Ginkgo biloba* extract *in vitro*

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Objective: Products of *Ginkgo biloba* (Gb) have been used for many years in a lot of countries especially in China as a traditional medicine for treatment of various conditions such as memory and concentration problems, depression, anxiety, dizziness and tinnitus due to the effects of many components such as kaempherol, ishorhamnetin, quercetin, ginkgolides and bilobalides. However, studies on the determination of neuroprotective and neuroregenerative effects of Gb extract at cellular level are quite limited. Therefore, the aim of this study is *in vitro* examination of neuroprotective and neuroregenerative effects of Gb extract on glioblastoma (U87) cells and neuroblastoma (SHSY-5Y) cells which are used as cell model in the treatment of diseases such as Alzheimer and Parkinson's due to their similarity to dopaminergic neurons.

Methods: While U87 and SHSY-5Y cells were used for the investigation of neuroprotective and neuroregenerative effects of Gb extract, it's toxic effect was investigated on the mouse fibroblast cells (L929). Cells were cultured in DMEM F12 containing 10% FBS and 0.5% Pen-Strep. XTT test was performed for measuring cell viability and changes in the cell nucleus were observed by DAPI staining. Afterwards, Scratch Assay was applied to examine the regenerative effect of Gb extract on the cells.

Results: According to the results, it was observed that Gb liquid extract did not show any toxic effect on the cell lines. In addition, it was observed that the extract increased the viability of SHSY-5Y and U87 cell lines and showed neuroprotective effect at concentrations up to 50 mg/mL.

Conclusion: In this study, the effective concentrations and neuroprotective and neuroregenerative effects of Gb extract on the cell lines were demonstrated in *in vitro*. According to the results, different formulations based on the Gb extract can be developed in the future. Special thanks to the IMMUNAT company for supplying the active substance.

Keywords: *Ginkgo biloba*, neuroprotective, neuroregenerative, neurotoxicity, scratch assay, XTT

P-67

New fixation method in anatomy: polymerization

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Objective: The cadaver is the preserved body of a person who has completely lost its vital functions, in order to be examined in education and research. Today, cadavers and the tissues obtained from cadavers are used frequently for anatomy education in medicine. The purpose of cadaver fixation is to cleanse it from the infectious agents, to preserve the natural features of the structures with minimum degradation. To prevent putrefaction and proliferation of bacteria and fungus as an infectious agent are imported. The most commonly used agent for cadaver fixation is formaldehyde (80–90%). However, the alternative methods has been the matter of the researches because of the formaldehyde vapour has unpleasant smell and harmful effect on the health of the users. In this study, it is aimed to prepare the rat organ specimens with "polymerization method" which can be used as an alternative method to formaldehyde fixation.

Methods: Transcardiac perfusion was performed with monomer mixture solution prepared specifically for adult male rat which was anesthetized with ketamine/xylazine. Following the perfusion liver, pancreas, heart and brain to be prepared as specimens were removed and incubated overnight in the same solution at 4°C. Then, oxygen was completely removed from the specimens container and temperature was increased. After approximately four hours, the formation of polymerization in the tissues was completed and the organ specimens were ready for long term use.

Results: Compared to the conventional fixation method, the greatest advantage of the polymerization technique is that it elim-

inates the formaldehyde evaporation exposure of the trainers and students during each use of organ specimens. Body parts or organ specimens prepared with this new technique are education materials that are non-hazardous for students to use, dry, odorless and durable enough to withstand repeated uses. In addition, the tissues prepared by this technique are transparent and suitable for examination with new generation microscopes. The disadvantage of this technique is that the chemicals used for polymerization are more costly than formaldehyde and stratified dissection may be difficult due to the polymer structure of the obtained tissue.

Conclusion: Polymerization fixation is quite useful for cross-sectional anatomy as it allows slicing without deformation.

Keywords: fixation, cadaver, polymerization

P-68

Brain Awareness Week activities of neuroscience Society of Turkey – 2019

Gülgün Şengül

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Objective: The Brain Awareness Week (BAW) was celebrated in Turkey March 11–17, 2019, parallel o the global campaign to let people know about the progress in brain research as well as diagnosis, treatment and prevention of disorders of the brain, such as Alzheimer's, Parkinson's, stroke, schizophrenia and depression. This presentation gives a resume of the 2010 BAW activities organized by Neuroscience Society of Turkey (NST) in different cities of Turkey.

Methods: NST with a grant support from Society for Neuroscience (SfN) given to SfN Turkey Chapter performed a large number of events throughout Turkey in 10 cities with a high number of collaborators.The BAW team was as follows: Necip Kutlu in Manisa, Ferhan Esen in Eskişehir, Ahmet Ayar in Trabzon, İlker M. Kafa in Bursa, Mahmud Mustafa Özkut in Yozgat, Piraye Kervancıoğlu and Mustafa Orhan in Gaziantep, Işıl Aksan Kurnaz and Meral Yüksel in Istanbul, Hilmi Uysal in Antalya, Leyla Şahin in Mersin, and Gülgün Şengül, Burcu Balkan, Ayşegül Keser and Vedat Evren in Izmir.

Results: We performed a high variety of activities including public conferences, school conferences, nursery school activities, visits to house for the elderly, activities in shopping malls, neuroanatomy laboratory tours to high school students, movie evenings, television and radio programs. We estimate we have reached a total of two thousand people in person, and many more with radio and television programs, and newspaper articles.

Conclusion: NST and SfN Turkey Chapter aims to cover more activities in many more cities every coming year and also increase public outreach by media to have an impact on understanding the brain and brain research in our community.

Grant support: BAW 2019 Turkey activities were supported by Society for Neuroscience (SfN).

Keywords: Brain Awareness Week, activity, Turkey

History of Neuroscience Corner Posters

(HC-01 — HC-19)

HC-01

M. Gazi Yaşargil: Man of the century (1950-1999)

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Prof. Mahmut Gazi Yasargil was born in Lice, Diyarbakır, Turkey in 1925. He started to medicine education in Friedrich Schiller University of Jena. Because of the World War-II, he continued his education in University of Basel, Sweden. He worked with Prof. Krayenbühl in Department of Neurosurgery on cerebral angiography. In 1953, he discovered orbital venography and superior sagittal sinus thrombosis. He took 3D photos of brain and modelled venous and arterial vessels of brain. In 1957, he published first book about vertebral and basilar arteries. In 1957, he went to USA to learn stereotaxic surgery from Prof. Mundiger and Prof. Hassler. In 1958 and 1965, he published books about "aneurysm and arteriovenous malformation" and "cerebral angiography". He learned microsurgery techniques on animals in USA. After returning to Sweden, he done first brain by-pass surgery in 1967 and organized microneurosurgery courses. In 1971, he invented his own microscopy, still widely used in micro-brain surgery. Leyla retractor, Yasargil aneurysm clips, scissors, aspirator and forceps were made with his own design. In 1974, tumors originated from ear nerve, in 1976, skull base meningioma were operated successfully by him. He made a breakthrough in epilepsy surgery without excluding a whole lobe. He wrote his most popular book series microneurosurgery between 1984–1996. In 1993, he retired in Zurich. In the following 20 years he worked actively in USA in Little Rock-Arkansas. Laboratory and Education Center established in the name of Prof. Yaşargil and his wife. He came back to Turkey in 2013 to Yeditepe University.

Keywords: Gazi Yaşargil, history, neuroscience, neurosurgery

HC-02

The first trepanation technique in Turkey and Dr. Cemil Topuzlu

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Trepanation is the operation performed on the skull of a living person or a dead person, adhering to a specific technique for a projected purpose. Trepanation history dates back to prehistoric times. However, ritual, magical and therapeutic aspects of the human brain is the oldest type of brain surgeries. Cemil Topuzlu was the first person who used the trepanation in Turkey. He (1866–1958) collected his observations in his book "Mémoires et Observation Médicales", published in 1905 in French. Trepanation is presented in chapter 8 of this book. In the conclusion part of his description he says: "The knowledge based on the localization of motor centers in human, has great importance for treatment. Thanks to the localization information is based on knowledge of the trepanation the first surgery was performed in Turkey in February 24, 1892". This case was presented by Cemil Topuzlu at the International Medical Congress in 1894 in Lyon. As a result, the technique of trepanation had used primarily in Turkey by Dr. Topuzlu and then was started to use all neuroscience world.

Keywords: Cemil Topuzlu, trepanation, operation

HC-03

Mazhar Osman: a distinguished scientist who sheded light on the history and future of neuropsychiatry in Turkey

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In the Ottoman era the mentally ill persons were traditionally kept in small asylums incorporated in religious complexes. The practice of modern psychiatry started at the Neurology and Psychiatry Service in the Military Medical School, in Istanbul, in 1896. During the truce period (1918–22), with the initiation of Mazhar Osman, "Reşadiye Barracks" in Bakırköy, abandoned and dilapidated after the French soldiers, were turned into a new, modern mental hospital. After the establishment of the Republic of Turkey, they were assigned to the institution in 1924. The hospital was opened in 1927 with the name "Mental and Neurological Illness Hospital" and Mazhar Osman was appointed as the head physician. The hospital was a twenty-minute walk distance from the train station and there was no other public transportation. Thus, a large pine forest was planned. In 1934 the new, twenty-first pavilion, and in 1935 the polyclinic was built. The central building and dining hall were opened in 1938. Following the university reform in 1933, psychiatry and neurology clinics of the Istanbul University

were located in Bakırköy Mental Hospital. During this period, numerous workshops were organized for treatment and rehabilitation purposes. Mental Health Festivals, called as "Mad Festival", was held every year in June. Bakırköy Mental Hospital has continually transformed in parallel to changing medical standards and is still a major education and research hospital dedicated to psychiatry, neurology and neurosurgery. It is now called "Bakırköy Ord. Prof. Dr. Mazhar Osman Mental Health and Neurology Training and Research Hospital" after him.

Keywords: Mazhar Osman, history, neuroscience, Bakırköy mental hospital

HC-04

Avicenna: contribution to the historical development of neuroscience

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Ibn-i Sina, the famous Turkish Islamic philosopher and physician, known as "Avicenna" in the West, was born in 980 in Afshana, Bukhara. His father, Abdullah bin Sina, was a high-ranking official in Bukhara. He learned mathematics, law, logic, philosophy and medicine at a very young age and at the age of 16 became a famous physician. Avicenna has about 276 books. The "El-Kanun fi't-Tıb" (Law of medicine) was taught as a textbook (it has 14-volume) in the East and West for 600 years. The work is often referred to as one of the most famous works in the history of medicine. The first book of this encyclopedic work, which contains five books, provides detailed information about anatomy and preventive medicine, the second book is simple drugs, the third book is pathology, the fourth book is treated with drugs and surgical methods and the fifth book contains detailed information about various pharmaceutical preparations. As Avicenna stated in El-Kanun fi't-Tıb, there are different methods of spinal dislocation. Also Avicenna had studies on special diseases in the field of neuropsychiatry and neurology as epilepsy, stroke, dizziness, spasm, tremors, meningitis, amnesia and dementia, head traumas, traumas, hysteria and conversion disorder, love disease, insomnia, paranoia, hydrocephalus and sciatica. Many scientists applied Avicenna's scientific method in their work. His legacy inspired modern colleagues in the field of neuroscience. Avicenna made great advances in the field of neuroscience. This is why modern neurology, neuroscience and neurosurgery owe its present phase to Avicenna's work and experience.

Keywords: Avicenna, Ibn-i Sina, history, neuroscience, law of medicine

HC-05

Development of neuropsychiatry in Turkey

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Neuropsychiatry Association, taking its first steps in 1914, was founded by the neuropsychiatrics, who came together with the call of Avni Mahmud, under the name of "Society for Psychiatry and Neurology" (Tababet-i Akliye and Asabiye Cemiyeti). Avni Mahmud was the head physician of "Toptaşı Asylum" (1873–1927) which is the first mental hospital in late Ottoman period. In his opening speech, he emphasized the fact that medical fields in the Europe has many specialities and there is an urgent necessity for improvement of medicine in Turkey as well. Members who were agree on Avni Mahmud's speeches established a community including both psychiatry and neurology. Thus they took the first steps to establish an association representing the "neuropsychiatry". Although community's founders were medical doctors, neurosurgeons and neuropsychologists also participated to the meetings and gave input to the development of neuropsychiatry. In 1918, the association was officially named as "Ottoman Tababet-i Akliye and Asabiye Cemiyeti" and Mazhar Osman was appointed to the presidency. Some physicians had been sent to Germany from Turkey to study psychiatry and neurology with German psychiatrist Emil Kraepelin in the 1920s and 1930s. One of these physicians was Raşit Tahsin Tuğsavul who is a well-known psychiatrist. When he returned to the country, he was very dominant about electrodiagnostic and electrotherapy. At that time, courses on neurology and psychiatry, carried out under the title of "asabiye", as a part of the internal medicine courses. Raşit Tahsin suggested that psychiatry should be a separate course in medical faculties.

Keywords: Neuropsychiatry, Toptaşı, asylum, history, Raşit Tahsin

HC-06

Connecting the past and the present: historical background of neuroscience development in Anatolia

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Historical development of neurological sciences in Anatolia started in Antic ages. First physicians had emerged during Hittite civilization and some neurological terms such as depression, aphasia, blindness, and deafness were first used by them. A skull of a person who underwent craniotomy in this period and survival of the individuals after trepanation suggest that advanced surgical techniques similar to today's approaches were used in the Urartu Age. Galen of Pergamum named

many structures of the nervous system and classified cranial nerves. Both Anatolian Seljuks and Ottomans used Islamic medical doctrines derived basically from Greco-Roman and Islamic scientists. The first organized hospitals in the world was built during this period. Ottoman medicine remained at the limits of Muslim medicine until the 19th century and "Royal College of Medicine" was founded in 1939. Mazhar Osman (1884–1955), neuropsychiatrist completed his training with Kreaplin (the founder of organic psychiatry), published the first Turkish neuroscience journal. After foundation of Turkey by Mustafa Kemal Atatürk in 1923, many scientists were sent abroad for training. When they returned, scientific studies in neuroscience have started to contribute to the literature in Istanbul (1950s), Ankara (1965) and Ege (1967) Universities. Professor Muhittin Erer built first experimental animal breeding facility and ''Experimental Research Institute" on 12.01.1945. The "Institute of Neurological Sciences and Psychiatry" was established in 1982 at Hacettepe University, to promote integrative research in basic and clinical neurosciences. Finally, "Neuroscience Society of Turkey (TÜBAS)" was founded by Professor Nuran Hariri in 1991.

Keywords: neuroscience, history, Anatolia, Nuran Hariri, Muhittin Erer

HC-07

Who is Şerefeddin Sabuncuoğlu?

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When considering the history of surgery along with medicine, one can argue that they started, evolved and changed in a similar way and at a similar rate the human civilisation did. In the ancient world, the Romans as well as the Greeks were ahead of the game in medicine thanks to names like Hippocrates and Galen who lead the way. It wasn't until the 1400s that medical books in Turkish were written in Anatolia which constitute the main sources of reference to those interested in the history of medicine in the region. A prime example to the books of this time is "*Cerrahiyetü'l-Haniyye*" by Şerefeddin Sabuncuoğlu, a Turkish physician of the time. Born in 1385, Sabuncuoğlu started his medical training in the hospital of Amasya (also a medical school) at the age of 17. After 14 years of service in this institution he worked in various other Anatolian cities like Kastamonu, Gerede and Bolu. At the age of 83, he published his most influential work, *Cerrahiyetü'l-Haniyye*, which deals with fields including orthopedics and traumatology, thoracic surgery, general surgery, pediatric surgery, and neurosurger. Sabuncuoğlu was special in a lot of ways. He was a good clinician, writer, illustrator and a good teacher.

Keywords: Sabuncuoğlu, physician, Anatolian

HC-08

The overview history of neurosurgery in Republic of Turkey

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Modern history of Neurosurgery started in Turkey in 20th century. Dr. Cemil Topuzlu (1868–1958) is the pioneer of modern surgery in Turkey. Dr. Mim Kemal Öke (1884–1955) wrote the first neurosurgery book ''Dimağ ve Cümcüme Afetleri ve Tedavileri" in 1924. Dr. Mazhar Osman (1884–1955) who is a neuropsychiatrist and the founder of modern neuroscience in Turkey, studied on organic reasons of neuropsychiatric diseases and reported them for surgeons. Dr. Abdulkadir Cahit Tuner (1892–1980) became the first neurosurgeon in 1923. The first university which has neurosurgery specialization programme was Istanbul University in 1933. The Ministry of Health organized an examination to certify the physicians as neurosurgery specialists in 1947. Dr. Cemil Şerif Baydur (1894–1967) wrote the first Turkish book of neurosurgery "Nöroşirurji Bahisler". Dr. Cafer Tayyar Kankat (1898–1955) published the first Turkish neurosurgery journal "Modern Cerrahi ve Nöroşirürji Mecmuası" (1936–1947) which is one of the earliest neurosurgery journals in the world. Dr. Hami Dilek (1898–1969) is the founder of the first clinic with neurosurgery specialization program in 1949. Psychosurgical applications were firstly carried out in the early 1950s. The first psychosurgery was performed by Dr. Ertuğrul Saltuk in 1950. After the discovery of the drug named chlorpromazine, these operations were gradually terminated at that times. In 1960s, Dr. Gazi Yaşargil who developed microsurgical technique in neurosurgery became one of the most important scientists in the history and present of Turkish Neuroscience. Dr. Yaşargil was honored as "Man of the Century 1950–2000" in "Neurosurgery at the Congress of Neurological Surgeons Annual Meeting".

Keywords: neurosurgery, history, Gazi Yaşargil, Hami Dilek, Cemil Şerif Baydur

HC-09

Alhazen (Al-Hasan Ibn Al-Haytham): a pioneering neuroscientist in the study of optics and vision

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Alhazen was born during a creative period known as the golden age of Muslim civilization. He began his education in Basra and then went to Baghdad. Alhazen recognized the importance of experiments and observations in science for the first time.He played a pivotal role in the history of optics. His most famous work is seven-volume treatise on optics "Kitab al-Manazir

(Book of Optics)" written between 1011–1021. İn his book, he carefully examined the extromission theories of his predecessors and systematically demolished each of them. According to his new "intromission theory", an object emits rays of light from every point on its surface which then travel in all directions, thereby allowing some light into a viewer's eyes. So, vision is accomplished by rays coming from external objects and entering the visual organ. Alhazan had used a camera obscure in his extensive optical experiments and compared it to the eye. Therefore, he realized that if the light rays orthogonal to the curved surface of the crystalline lens continued, they would project an inverted image on the back of the eye. Alhazen wrote other treatises, including "Treatise on Light". He investigated the properties of luminance, rainbow, eclipses, twilight, and moonlight. He stressed the idea that point-to-point representation of the visual world into the brain had to be maintained and conveyed to the ultimum sensus in the anterior part of the brain. Indeed, this idea forms one of the bases of modern visual physiology.

Keywords: Ibn Al-Haytham, Alhazen, optic, vision, intromission

HC-10

History of neuroscience and neurosurgery in Anatolia before the foundation of the Turkish Republic

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Anatolia is the asian part of the contemporary Republic of Turkey. This area hosted different civilizations throughout the history. There is evidence of practice of trepanation in Anatolia especially in the bronze and iron ages. Trepanation was used for patients suffering from headaches and epilepsy. In the Urartu age, we can see one of the most important examples of craniotomy. The technique they used is quite close to today's technique that follows these steps; drilling several holes and connecting them by using a chisel. There are also reports of the use of cauterization as a treatment of hydrocephalus, epilepsy, sciatica and back pain. In the Seljuks Empire there is not enough evidence of surgical procedures, but Gevher Nesibe Hospital is one of the first organized hospitals of the world. It also had a psychiatry department. In the Ottoman Empire, Serafeddin Sabuncuoglu wrote many medical treatises such as a colored surgery atlas named Cerrahiyetu'l Haniye. It has depictions for neurosurgical applications including cauterization. Cemil Topuzlu (1866–1958) applied surgical procedures about cranio cerebral trauma and peripheral nerve injuries and presented a case of brain abscess in 1894. There weren't neurosurgeons in the Ottoman Empire but the procedures applied by general surgeons. Mim Kemal Oke (1884–1955) is one of them and wrote the first Turkish brain surgery textbook, Dimag ve Cumcume Afetleri. Mazhar Osman (1884–1955) was a neuropsychiatrist who tried to discover organic causes of neuropsychiatric problems and wrote more than 25 neurosurgical articles and published the first Turkish neuroscience journal, Emraz-ı Akliye ve Asabiye Musamereleri.

Keywords: neurosurgery, neuroscience, history, Cemil Topuzlu, Anatolia, Mim Kemal Oke

HC-11

History of psychiatric care and music therapy in Anatolia

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Music has been used not only for entertainment but also treatment purposes throughout the history. Today, music therapy is an established health profession that addresses therapeutic relationship to physical, emotional, cognitive, and social needs of individuals. Even though, the earliest known reference to music therapy appeared in 1789, in Anatolia music therapy was used systematically in hospitals throughout the country as early as 13th century. All hospitals were built in a manner that can provide the necessary acoustics for the music therapy, while spreading the sound of water from the pool that is located in the middle of the courtyard. Their common architectural structure contains a rectangular plan and a wide courtyard. Travelers' accounts from this era show that doctors in these asylums have chosen therapeutic tune for their patients according to their hearth beat and the time of the day. They also indicate that a group of musicians who plays nay, violin, dulcimer, lute would visit patients three times a week. Even though we can come across many of these medical centers throughout Anatolia, Kayseri Gevher Nesibe Medical School (1206), Great Mosque and Hospital of Divriği (1228–1229), Amasya Hospital (1308), Edirne Bayezid II. Hospital (1488) were the main ones that are intact today. Considering their contribution throughout history, one can notice that these hospitals did not only help to patients, but also became effective examples of today's modern psychiatric care centers. In addition, they had a leading role in improving music therapy techniques.

Keywords: Gevher Nesibe, music therapy, history, Anatolia, psychiatric care

HC-12

Abulcasis: neurosurgical contribution to history

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Al-Zahrawi (Latinised as Abulcasis) was an Arab Muslim physician and surgeon who lived Al-Andalus (936–1013 A.D). He published 30-volume medical encyclopedia, the Kitab al-Tasrif liman Ajaza an al-Talif (translated as "The book enabling him who

cannot cope with the compilation") which was taught as a textbook in many universities of Europe. Numerous surgical instruments were firstly introduced in Al-Tasrif such as scalpels, retractors, curettes, pincers, specula, and also instruments for techniques of cauterization and ligature. Instruments related to neurosurgery were defined for diagnosis and treatment of head injuries and skull fractures, spinal injuries and dislocations, hydrocephalus and subdural effusions, and headache. Al-tasrif was first to describe a surgical procedure for the ligation of the temporal artery in migraine. Especially, Albucasis highlighted the need for comprehensive knowledge about the anatomy of brain, skull, and spinal cord on which any operation was to be performed. He defined the ping-pong type of fracture in children and also described the situation of patient who have a spinal injury. In addition, he described the shape of incision to discharge the fluid based on location in between skin and bone or bone and meninges. Albucasis mentioned in Al-Tasrif that paralysis, epilepsies, tremors, and numbness were treated with cauterization on various places of the patient's shaved head. In short, Al-Zahrawi has made numerous important contributions to the field of medicine, especially surgery. His emphasis on anatomy of the skull and brain in relation to the neurosurgical operations of that period inspired many neuroscientists afterwards.

Keywords: neuroscience, history, Anatolia, Nuran Hariri, Muhittin Erer

HC-13

The history of neuroscience in Anatolia and Turkey

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Anatolia, known as Asia-Minor, is one of the most important geo-political areas of the world, from which many civilizations emerged. The first sign of neurosurgical intervention in Anatolia discovered so far is the cranium from the Neolithic Age with a large craniectomy in the left posterior frontal region. It seems a sharp chisel-like object was used to produce the hole. Şerefeddinin Sabuncuoğlu (1385–1470 Ottoman Empire) is one of the most famous surgeons in Anatolia. He is the writer of the first medical textbook with colorful illustrations. Sabuncuoğlu explained migraine headaches, epilepsy, hematomas and fluid collections in the head and treatment of these. Despite the opposing Islamic instructors, Bedbaht Emir Çelebi supported the anatomical dissections on the human body, which he declared crucial in understanding and treating the illnesses. After the foundation of the Republic of Turkey (1923), Hulusi Behçet was a Turkish scientist born in Istanbul. He discovered a new disease, which was named after him in 1937 as "Behçet's Disease". Doubtlessly the most important figure in the history and present of Turkish Neuroscience is "The man of the Century", M. Gazi Yaşargil. Throughout the history of Turkey, in the field of neuroscience many valuable world-renowned scientists have grown.

Keywords: Anatolia, history, neuroscience, scientist

HC-14

Trace Hulusi Behçet's history of medicine

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Hulusi Behçet (1889–1948) is a Turkish dermatologist and scientist. He is the first Turkish physician to receive a professor title in Turkey in 1933. In 1937, he became the first scientist to describe a disease with blood vessel inflammation (vasculitis) which is now referred with his own name (Behçet's disease). His researches which were quite remarkable, were also the pioneer of multidisciplinary studies. His experimental researches for the etiology of the pemphigus, an autoimmune disease, were exemplary. He also studied Cutaneous Leishmaniasis between 1914–1943 and described a nail sign which is cited in the current literature as Behçet's nail sign (the 'Tin-Tack' sign of Hulusi Behçet). Behçet's disease is a chronic and multisystem disease characterized by oral aphthous and genital ulcers, iridocyclitis in the eye, skin, joint, vascular and nerve involvement. Nervous system involvement which increases mortality and morbidity of Behçet's disease is known as Neuro-Behçet syndrome and it is a vital clinical finding that develops 1 to 7 years after the onset. This syndrome has both motor and sensory components. Neuro-Behçet syndrome has two different types, parenchymal and non-parenchymal. In parenchymal type, hemispheres, brain stem, pyramidal tract and spinal cord lesions are observed in non-parenchimal involvement, dural sinus thrombosis, arterial occlusion and aneurysm occur. Prof. Dr. Hulusi Behçet has a well gained reputation both nationally and internationally for his multidisciplinary approach.

Keywords: Hulusi Behçet, Behçet's disease, Neuro-Behçet syndrome

HC-15

History of Turkish neuroscience meetings (USK), in memory of our esteemed plenary lecturer: Yücel Kanpolat

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The first "National Neuroscience Meeting (USK)" was held in Eskişehir, on March 16–20, 2002, with contribution of more

than 350 neuroscientists across from Turkey. Since then, it has been organizing to enhance and explore the research areas in neuroscience and establish collaborations among young and old neuroscientists. As one of the keynote speakers, Professor Yücel Kanpolat gave special lectures in several opening ceremonies of the USK, about lives and disciplines of famous scientists, including Marie Curie, Louis Pasteur, Ramon Cajal, Leonardo da Vinci and Michelangelo. He graduated from Ankara University Medical School in 1965. He won the WHO's "Best Public Health Service Unit Award". He was the president of the "Neurosurgical Society" twice (in 1990–1991 and 1995–1996), and received the "Paxton International Professorship" from Oregon Health Sciences University in 2006. He was elected and appointed as the president of the "Turkish Academy of Sciences" (TÜBA) following his retirement. He also was elected as a member of the "European Academy of Sciences and Arts" where he was a member of up to 30 Nobelian scholars. Kanpolat's main areas of interest were trigeminal neuralgia and pain surgery. "Kanpolat Kit" is a world-renowned design. He was the first surgeon, successfully performed the surgery, known as "chronic atypical facial pain". He developed a special electrode system and practiced "CT-guided stereotactic pain surgery" for the first time worldwide in 1986 and trained more than 100 neurosurgeons from Turkey and abroad throughout his career.

Keywords: Yücel Kanpolat, history, neuroscience, neurosurgery

HC-16

Milestones of neural sciences in Turkey

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Observing undergone trepanation skulls found in the Neolithic period in Turkey, they show us how neuroscience is an ancient science in Anatolia. Herophilus of Chalcedon from the Ancient Age dissected human cadavers for the first time in history and used the term "neuron" for the first time. In the 2nd century, Galen of Pergamon identified many neurological conditions such as the origin of voluntary movement, hemiplegia, spinal cord trauma, delirium, dementia, coma, lethargy, etc. Sabuncuoglu Serefeddin in Amasya prepared the first detailed and illustrated surgical atlas in the history of Turkish medicine in the 15th century. When Sakir Pasha who is assistant of Claude Bernard, founder of modern physiology, returned to Turkey; he has started to give lessons in neurophysiology, established the first experimental physiology laboratory, in the 19th century. In the early 20th century, Mazhar Osman worked with renowned neuroscientists of those times, such as, Emil Kraepelin and Walther Spielmeyer; and oriented neuroscience students to various European cities from Turkey. In the middle of the 20th century, Gazi Yaşargil, a successful neurosurgeon, was the pioneer of microneurosurgery and was selected "the Man of the Century" by the American Neurosurgery Association. Considering the prehistoric times to the present, Anatolian territories seem to continue to grow powerful minds in the field of neuroscience.

Keywords: trepanation, Chalcedon, history, neuroscience, Pergamon

HC-17

A rising phoenix: Dr. Aysima Altınok

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For many years women have been playing an active role in medicine, yet they are rarely specialized in neurosurgery. The number of women taking up the surgical specialties is very low. In spite of this, Aysima Altınok became the first Turkish female neurosurgeon. Dr. Altınok was born in Erzincan in 1929. There was a major earthquake in Erzincan in 1939 which was a turning point for the Altınok family who had lost everything. After this tragic event, they moved to Istanbul. Altınok whose home was burnt to ashes in Erzincan, reborn from ashes like a phoenix in Istanbul. She enrolled in Istanbul University, School of Medicine, she noticed that nothing was completely known about the brain functions. Thus, she decided to become a neurosurgeon in the phase II. After graduation, she started working as a neurosurgeon assistant at Haydarpaşa Numune Hospital in 1956. Haydarpasa Numune was the only hospital providing neurosurgical education in Turkey. In 1959, she completed her education and she became a neurosurgeon. In this manner, Dr. Altınok went down in history as the first female brain surgeon in Turkey. Finally, she was appointed to Bakırköy Emrazi and Akliye Hospital and she retired after 33 years. Thus, the entry of women into neurosurgery in Turkey was earlier than most of the other countries. Dr. Altınok was a pioneer for women dreaming of becoming a brain surgeon in Turkey. Like the phoenix's association with immortality, Dr. Altınok's contribution to the literature will be a guide for female neurosurgeons.

Keywords: Aysima Altınok, neurosurgeon, phoenix, neurosurgery, immortality

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Rufus of Ephesus – the precious historical insight into neuroscience

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Ephesus is a World Heritage City, located in Izmir, was home to many civilizations as a center for philosophy and medicine. Rufus was an eminent physician from Ephesus. A bridge between Hippocrates and Galen, Rufus (80–150 AD) was one of the four excellent physicians for the Byzantines and highly cited. He studied anatomy, physiology, pathology, psychiatry, medical botany, nephrology and a wide range of medical and surgical illnesses. He observed an important correlation between pulse and heart systole. Rufus described the optic chiasm for the first time, as well as the differences between motor and sensory nerves. His observations on the anatomy of eye and lens was very detailed. His famous book of "On Melancoly", in addition to the four humors theory described the hypochondriac type of melancholy and its origins that may be attributed to the autonomic nervous system in our current understanding. Development of anatomical terminology was affected majorly by his anatomy manual *(Elementary Treatise of Anatomy)* and Rufus' lexion *(Onomastikon)*. His pioneering work presented anatomical nomenclature according to a systematic discription via using relevant terminology. He demonstrated the internal workings of human organs without human dissection by using comparative anatomy of the monkey and pig. The significant source for anatomy is 'Onomastikon' was comprised neuroanatomy terminology mostly. With his descriptions of meninges of encephali, medulla spinalis, choroid plexus, motor and sensory neurons, difference between medulla ossium (bone marrow) and medulla spinalis, nervus vagus, optic chiasm, foramen magnum, varicous (telencephalon) and parencephal (cerebellum), Rufus of Ephesus was definitely ahead of his time.

Keywords: Ephesus, Rufus, neuroanatomy, neuroscience

HC-19

Herophilos: the great anatomist and neuroscientist of antiquity

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Herophilos was born around 335 B.C in Chalcedon known as Kadıköy in Istanbul, Turkey. He was known as 'The Father of Anatomy'. He examined the body of animals and human comparatively. He disssected the human body and seperated brain from cerebellum. He described the brain as the seat of the intelligence. He distinguished the nerves according to their functions: 'movement (motor)' and 'sensory', and described at least six cranial nerves and the lower brainstem and spinal cord. He also identified and described several brain structures. Some of the anatomical terms which he used are still used, such as the internal surface of the occipital bone known as the Herophilos' press (torcular Herophili). His work on neuroanatomy in his age is astounding.

Keywords: antiquity, Herophilos, neuroanatomy

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