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- *Standard entire book:* Sengul G, Watson C, Tanaka I, Paxinos G. Atlas of the spinal cord of the rat, mouse, marmoset, rhesus and human. San Diego (CA): Academic Press Elsevier; 2013. 360 p.

- *Book with organization as author:* Federative Committee of Anatomical Terminology (FCAT). Terminologia anatomica. Stuttgart: Thieme; 1998. 292 p.

- *Citation to a book on the Internet:* Bergman RA, Afifi AK, Miyauchi R. Illustrated encyclopedia of human anatomic variation. Opus I: muscular system [Internet]. [Revised on March 24, 2015] Available from: http://www.anatomyatlases.org/AnatomicVariants/AnatomyHP.shtml

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- *Standard reference to a contributed chapter:* Potten CS, Wilson JW. Development of epithelial stem cell concepts. In: Lanza R, Gearhart J, Blau H, Melton D, Moore M, Pedersen R, Thomson J, West M, editors. Handbook of stem cell. Vol. 2, Adult and fetal. Amsterdam: Elsevier; 2004. p. 1–11.

- *Contributed section with editors:* Johnson D, Ellis H, Collins P, editors. Pectoral girdle and upper limb. In: Standring S, editor. Gray's anatomy: the anatomical basis of clinical practice. 29th ed. Edinburgh (Scotland): Elsevier Churchill Livingstone; 2005. p. 799–942.

– *Chapter in a book:*

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16th Turkish Neuroscience Congress

20–23 May 2018, Istanbul, Turkey

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Editorial

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Welcome Address of the Congress Presidents

Anatomy 2018;12(Suppl 1):Sv

Dear Neuroscientists,

We welcome you to the 16th National Neuroscience Congress, 20-23 May 2018, at the Istanbul Technical University Ayazağa Campus, hosted by ITU with the support of Brain Research Society (BAD).

This year, in order to underline the recently available and increasingly important technical approaches to the Neurosciences, the National Neuroscience Congress is held at a technical university under the overlying theme "Neuroscience: From Biology to Engineering", featuring breakthrough research that cover the nervous system architecture from the molecular and cellular scale to motor and cognitive systems. This event comprises 8 conferences, 10 symposia with 53 speakers, 4 panels, 9 oral sessions with 54 short talks and 135 poster presentations. The presented research highlights computational neuroscience, neuroimaging and neuroinformatics among other fields of neuroscience.

The congress commemorates two very influential, distinguished scientists who have passed away in the past year: Prof. Dr. Erol Başar and Prof. Dr. Ray Guillery who have contributed immensely to neuroscience and Turkish science in general and will continue to guide future work in this area. Accordingly, we will hold memorial talks on the scientific contributions of these two great scientists, as well as a plenary lecture and a symposium where we will hear the work of scientists who have continued their work.

We hope the 16th National Neuroscience Congress will offer a rich educational and scientific experience as well as a social one for the participants, and wish a productive and enjoyable meeting to all.

Sincerely,

Congress Co-Presidents
Tamer Demiralp *(BAD)*
Arzu Karabay Korkmaz *(ITU)*

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16th Turkish Neuroscience Congress

20–23 May 2018, Istanbul, Turkey

Program Schedule

20 May 2018 Sunday	*21 May 2018 Monday*	*22 May 2018 Tuesday*	*23 May 2018 Wednesday*
09:00–16:00 **Courses**	09:00–11:50 **Scientific Program**	09:00–11:50 **Scientific Program**	09:00–11:50 **Scientific Program**
16:15–18:00 **Opening Ceremony**	11:50–13:00 **Lunch**	11:50–13:00 **Lunch**	11:50–13:00 **Lunch**
18:00–19:00 **Opening Conference**	13:00–19:00 **Scientific Program**	13:00–18:20 **Scientific Program**	13:00–18:20 **Scientific Program**
19:00–21:00 **Reception**		20:00–23:00 **Gala Dinner**	18:20–19:00 **Closing Ceremony**

20 May 2018 Sunday

	09:00–17:00	**Registrations**
	09:00-13:00	**Courses**
	09:00–13:00	**Course 1** Using Compact Organ Electrophoresis System for Clearing Brain Tissue (CLARITY) Esat Adıgüzel, Ayşegül Güngör Aydın
	09:00–13:00	**Course 2** Genome Analysis Using New Generation Sequencing Methods in Neurological Diseases Eda Tahir Turanlı, Sibel Uğur İşeri, İlker Karacan, Burak Turan
	09:00–16:00	**Course 3** Neuroscience from Engineering Perspective: Computational, Mathematical Methods and Neuromorphic Circuits Neslihan Serap Şengör, Yunus Babacan, Melih Yıldırım
	09:00–13:00	**Course 4** Functional Near Infrared Spectroscopy: Technical Fundamentals and Advanced Applications Aykut Eken, Sinem Burcu Erdoğan
	09:00–16:00	**Course 5** Anxiety and Depression Tests in Laboratory Animals Emel Güneş, Hasan Çalışkan, Gözde Karabulut
Hall A		
	16.15–17.00	**Opening Ceremony**
	17:00–18:00	**Talks in Memoriam of Prof. Erol Başar and Prof. Ray Guillery** Sirel Karakaş, Bahar Güntekin, Filiz Onat, Zoltan Molnar
	18:00–19:00	**Opening Conference** New Perspectives in Neurosciences M. Gazi Yaşargil

21 May 2018 Monday

Hall A

09:00–10:30 **Symposium 1: Biomarkers in Brain Disorders**
Moderator: Tolga Esat Özkurt
Metehan Çiçek, Pınar Kurt, Murat Perit Çakir, Tolga Esat Özkurt

Hall B

09:00–10:30 **Symposium 2: Disturbances of Cellular Mechanisms in Glioblastoma**
Moderator: Arzu Karabay Korkmaz
Türker Kılıç, Tuğba Bağcı Önder, Aslı Kumbasar, Arzu Karabay Korkmaz

10:30–11:00 **Coffee Break**

Hall A

11:00–11:50 **Conference**
Chair: Filiz Onat
Cortical Layer with No Known Function / Zoltán Molnár

11.50–13.00 **Lunch**

13:00–14:00 **Poster Communications**
Moderators: Ertan Yurdakoş, Mehmet Aygüneş, Murat Okatan, Mehmet Kocatürk

14:00–15:30 **Oral Presentations**
Behavioral and Cognitive Neuroscience-1
Chairs: Metehan Çiçek, Mehmet Ergen

Hall B

14:00–15:30 **Oral Presentations**
Nervous System Disorders and Their Treatments-1
Chairs: Gülgün Şengül, Esat Adigüzel

Hall C

14:00–15:30 **Oral Presentations**
Neuroimaging and Neuromicroscopy-1
Chair: Hülya Karataş Kurşun

15:30–15:45 **Coffee Break**

Hall A

15:45–17:15 **Symposium 3 *(in memoriam of Erol Başar)*: Brain Oscillations in Neuropsychiatric Diseases**
Chair: Tamer Demiralp
Canan Başar Eroğlu, Bahar Güntekin, Görsev Yener, Ayşegül Özerdem

Hall B

15:45–17:15 **Panel 1 (Turkish Neuropsychiatric Society)**
Charles Bonnet Syndrome: from Perception to Conciousness
Chairs: Betül Yalçiner, Çiğdem Özkara
Saffet Murat Tura, İnci Ayhan, Lütfü Hanoğlu

17:15–17:30 **Coffee Break**

Hall A

17:30–18:20 **Conference**
Chair: Filiz Onat
Advances in Neuroimaging of Neurodegenerative Diseases / Emrah Düzel

18:20–19:00 **Conference**
Chair: Emel Ulupınar
Health Institutes of Turkey: Foundation, Structuring and Research Funding Programs / Bayram Yılmaz

22 May 2018 Tuesday

Hall A		
	09:00–10:30	**Symposium 4: Analysis of Motor Unit with an Electrophysiologic Microscope** **Moderator:** M. Barış Baslo A. Emre Öge, M. Barış Baslo, N. Görkem Şirin, Tuğrul Artuğ, İmran Göker
Hall B		
	09:00–10:30	**Symposium 5: New Approaching Strategies to Pathophysiology and Treatment of Neuronal Injury** **Moderator:** Ertuğrul Kılıç Berrak Çağlayan, Ahmet Burak Çağlayan, Mustafa Çağlar Beker, Taha Keleştemur
Hall C		
	09:00–10:30	**Symposium 6: Dynamics of Brains Intrinsic Connectivity Networks Under Task Conditions** **Moderator:** Tamer Demiralp Ali Bayram, Elif Kurt, Görkem Alban-Top
	10:30–11:00	**Coffee Break**
Hall A		
	11:00–11:50	**Conference** **Chair:** Arzu Karabay Korkmaz Nanomedicines for Nervous System Disorders / Turgay Dalkara
	11.50–13.00	**Lunch**
	13:00–14:00	**Poster Communications** **Moderators:** Gülgün Şengül, Gürkan Öztürk, Emel Ulupinar, Güher Saruhan Direskeneli
	14:00–15:30	**Oral Presentations** Neural Networks and Compuational Neuroscience **Chairs:** Yusuf Ziya İder, Burak Güçlü
Hall B		
	14:00–15:30	**Oral Presentations** Nervous System Disorders and Their Treatments-2 **Chairs:** Mehmet Kaya, Özlem Akman
Hall C		
	14:00–15:30	**Oral Presentations** Behavioral and Cognitive Neuroscience-2 **Chairs:** Görsev Yener, Lütfü Hanoğlu
	15:30–15:45	**Coffee Break**
Hall A		
	15:45–17:15	**Symposium 7: Computational Neuroscience: Contemporary Research Ranging from Extracellular Neural Recordings to Mathematical Models of the Brain** **Moderator:** Murat Okatan Neslihan Serap Şengör, Burak Güçlü, Mehmet Kocatürk, Murat Okatan
Hall B		
	15:45–17:15	**Panel 2: Stress: If It Don't Kill You It Makes You Stronger** **Moderator:** Yağız Üresin Sacit Karamürsel, Hakan Kiziltan, Yağız Üresin
Hall C		
	15:45–17:15	**Panel 3: Molecular Mechanisms of Neurodegeneration** **Moderator:** Erdem Tüzün Erdinç Dursun, Duygu Gezen-Ak, Erdem Tüzün
	17:15–17:30	**Coffee Break**
Hall A		
	17:30–18:20	**Conference** **Chair:** Neslihan Serap Şengör Mathematical Modeling and Deep Learning Techniques in Neuroimaging / Gözde Ünal

23 May 2018 Wednesday

Hall A	
09:00–10:30	**Panel 4: Zebrafish Model for Neural Aging, Cognitive and Perceptual Processes** **Moderator:** Hulusi Kafalıgönül Michelle M. Adams, Hulusi Kafaligönül, Elif Tuğçe Karoğlu, Ayşenur Karaduman
Hall B	
09:00–10:30	**Symposium 8: Genetic and Molecular Bases of Neurological Diseases** **Moderator:** Eda Tahir Turanlı Güher Saruhan Direskeneli, Esra Battaloğlu, Eda Tahir Turanlı
10:30–11:00	**Coffee Break**
Hall A	
11:00–11:50	**Conference** **Chair:** : İ. Hakan Gürvit The Arduous PATH to Understanding Gliomas: Keystones and Perfect Storms / Tarık Tihan
11.50–13.00	**Lunch**
13:00–14:00	**Poster Communications** **Moderators:** Bülent Elibol, Candan Gürses, Haşmet Hanağasi, Ersin Koylu
14:00–15:30	**Oral Presentations** Molecular and Cellular Neuroscience **Chairs:** Aslı Kumbasar, Nazlı Başak
Hall B	
14:00–15:30	**Oral Presentations** Neuroimaging and Neuromicroscopy-2 **Chairs:** Esin Öztürk Işık, Gürkan Öztürk
Hall C	
14:00–15:30	**Oral Presentations** Nervous System Disorders and Their Treatments-3 **Chairs:** Fatma Töre, Ertan Yurdakoş
15:30–15:45	**Coffee Break**
Hall A	
15:45–17:15	**Symposium 9: Antiepileptic Drug Delivery into the Brain Parenchyma with Nanocarriers for Treatment of Refractory Epilepsy** **Moderator:** Mehmet Kaya Candan Gürses, Mehmet Kaya, Serkan Emik, Nurcan Orhan, Canan Uğur Yılmaz
Hall B	
15:45–17:15	**Symposium 10: Neuroimaging Based Biomarker Development for Neurodegenerative Disorders** **Moderator:** İ. Hakan Gürvit İ. Hakan Gürvit, Esin Öztürk IşIk, Başar Bilgiç
17:15–17:30	**Coffee Break**
Hall A	
17:30–18:20	**Conference** **Chair:** : Eda Tahir Turanlı Molecular Genetics of Schizophrenia, Alcohol Dependence and Major Depression / Brien P. Riley
18:20–19:00	**Closing Ceremony**

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Invited Lectures

(IL-01 — IL-02)

IL-01

Prof. Erol Başar and his contributions to neuroscience

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Prof. Erol Başar was born in 1938 in İstanbul. He had his junior and senior high school education in Galatasaray Lycée (1950-1958), where French was the major foreign language. His Bachelor's (1959-1964), and Master of Science (1965) degrees from Munich and Hamburg Universities. He was the student of Karl Werner Heisenberg, the Nobel Awardee in physics, and the Carl Friedrich von Weizsaecker, the famous quantum physicist. It was von Weizsaecker who, as his mentor, advised a long-range plan to the young Başar. The plan was to study the physiology of circulation, and then pass onto the physiology of the brain. In line with this plan, Erol Başar had his Doctor of Philosophy Degree on "Physiology and Biophysics" (1965) on a joint program of the Munich University and the Hamburg University. He studied circulatory autoregulation in Germany. In the USA, where he went with a Postdoctoral Fellowship Program, he recorded and analyzed the evoked potentials (EPs) of the brain. This was between 1968 and 1970 in the Nathan Kline Brain Research Institute (Rockland State Hospital, New York). As a physicist, Başar knew that the oscillations were one of the basic principles of the universe; he thought that they should also apply to the brain. During his years in New York, he deeply ruminated over this subject. He came to the conclusion that the EPs should not be analyzed as amplitude variations over the time axis. They should be decomposed into their the oscillatory components, and should be analyzed on this basis. These studies attracted attention, and Dr. Başar was invited to Hacettepe University by the Rector, who was, at the time, the visionary Prof. Dr. İhsan Doğramacı. Dr. Başar's mission would be to establish the Institute and Biophysics and conduct research on the brain potentials. Dr. Başar now had the chance to extensively study the brain oscillations that compose the evoked potential waveform. At around the 1970s, there were still those who cherished the idea that the brain oscillations are just noise. Dr. Başar could thus publish his papers in technical journals, which were liberal enough to include physiology. His first book "Biological and Physiological Systems Analysis "attracted the attention of mainly a group of scientist who were studying or were aware of the importance of the oscillations in neuroscience, and a large group of ardent students of neuroscience. The book includes the prototypes of his research perspectives, and marks of the explanatory formulations that he developed throughout his lifetime. All this shows how systematically Prof. Başar adhered to the basic roadmap that Prof. von Weizsaecker proposed to him, and how he developed his very unique elaborations around the long-range scientific plan. Throughout his lifetime, Prof. Başar recorded EPs, and event-related potentials (ERPs) of originally cats, and simpler species (e.g. Aplysia), and later of healthy humans and clinical samples using very many experimental paradigms. The time -domain EPs and ERPs were decomposed to oscillatory components in various frequency ranges. Further studies were conducted on the evoked oscillations (EOs), and event-related oscillations (EROs). Such critical issues as the superposition of the oscillations on the time axis, their coherences over the spatial axis, entropy, the effect of prestimulus oscillations on poststimulus ones were extensively studied. Based on the findings of these variegated studies, he formulated principles of brain functioning, the basic one being the following: "Oscillations are the real responses of the brain." The empirical findings and the theoretical formulations appeared in his book, titled "EEG-Brain Dynamics". Soon after he was invited to Germany as Richard Merton Professor. He stayed in Germany between years 1980 and 2000 as the Director of the Physiology Institute, and the Neurophysiology Research Group in the Medical University of Lübeck. Prof. Başar's years in Germany were enriched by such

eminent neuroscientists as T. H. Bullock, L. Deecke, R. Galambos, , H. Haaken, H. Petsche and J. Polich, with whom he was also in close social relationship. He ran his studies in high technology research laboratories that he, himself, designed and developed. His institute was staffed by devoted and capable young scientists, and technical personnel who, under his guidance, were able to develop the software that he used for brain analysis. At this period, Prof. Başar started studying also the cognitive correlates of the oscillations. His research repeatedly demonstrated that the oscillations are selectively distributed in the brain in parallel processing pathways. He started developing the theory that he sometimes called the "Whole Brain Work". Prof. Başar is among the pioneers who conclusively refuted the old saying, according to which the electrical activity of the brain is noise. During his years in Germany, Prof. Başar maintained his relations with Turkey. With his colleagues, namely Prof. Dr. Ahmet Ademoğlu, Prof. Dr. Tamer Demiralp, Prof. Dr. Sirel Karakaş and Prof. Dr. Çiğdem Özesmi, he established the TÜBİTAK Research Group on Brain Dynamics. Prof. Başar acted as the Director of the Brain Dynamics Multidisciplinary Research Center, and continued studying the oscillatory dynamics of the brain from many perspectives. At this period, he also pioneered the development and standardization of a battery of neuropsychological tests to the Turkish culture. Prof. Başar returned to Turkey in 2000 as a director of Dokuz Eylül University Multidisciplinary Research Center. He has founded a very established laboratory and conducted essential studies in this research center between 2000–2006. Prof. Başar published a monograph named "Memory and Brain Dynamics" during this period. In 2006 he moved to Istanbul as a director of İstanbul Kültür University Brain Dynamics Cognition and Complex Systems Research Center, he worked as a director in this research center for ten years. In this period Prof. Başar's work was focused on two different topics. He has analyzed the differentiation of event related oscillations in different brain pathologies and also he has proposed a new theory named "Nebulous Cartesian System." In his new theory, he has described a new approach to the understanding of brain-body-mind integration based on empirical data and concepts from physiology, psychology, physics, and philosophy. He has published a monograph named "Brain-Body-Mind in the Nebulous Cartesian System: A Holistic Approach by Oscillations" to describe his theory. Brain Dynamics Research Center at Istanbul Kültür University was a center of attraction for the researchers from different countries who were studying EEG brain oscillations. Prof. Başar organized several international conferences and workshops during this period as he always did during his scientific career. He has also edited special issues in SCI journals after each workshop or conference. In the last years, Prof. Başar was working in a particular theory which he named as "CLAIR." In this theory, he was proposing a set of diagrams called "CLAIR" diagrams in which it is possible to represent the biomarkers of EEG brain oscillations in different brain pathologies. In his theory, he has indicated that the time has arrived to replace the static "Broadman areas" with dynamical maps for a specific function which will include specific networks of the whole brain. Prof. Başar's empirical findings, his research methodology, and the ensuing theoretical formulations were published in nearly 250 SCI articles, and 19 international books that he wrote. The impact of this work is represented by an H-Factor of 67, and citations that is presently close to 16.000. Prof. Başar's scientific fame is international, and this internationally renowned personage has passed his scientific knowledge and wisdom to a numerous number of neuroscientists: He is the "Doctorvater/ Doktorväter" of many young scientists in Germany and in Turkey; he is the mentor of a selected few; and the colleague of numerous scientists all over the World. Prof. Başar was indeed a very unique scientist. He dedicated all his life to science and to scientific research. He very ingeniously amalgated physiology, psychology, physics and philosophy; he discovered principles of cognitive neuroscience; and has formulated theories on the "Dynamics of Brain Function". All this was interrupted by an untimely departure to the timeless, and has left behind a name that will undoubtedly be inscribed to the history of neuroscience.

IL-02

Ray Guillery as a great mentor and critical eye

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Ray Guillery was a perfect scientist and academician role model for the young generation. As neuroscientists, our scientific interactions with Ray influenced our way of thinking about brain structure and function. His influence helped us develop our scientific rigour and ideas about not only thalamocortical system but also its role in pathophysiological conditions such as epilepsy. 'Finding the right questions' is the most important challenge that reflects the impact of Ray on our lives. He was very generous in sharing his scientific knowledge and had an enormous sense of humor which showed his brilliant, sharp intelligence. Not only for the characterization of scientific activity and complicated interactions within the brain, but also for the interrogation of our existence in the world, aims and future dreams, he provided us with significant vision. We had the privilege to work with him in Oxford and Marmara University and kept in contact until he passed away in 2017. Ray came to Istanbul via connection with John Crabtree in 2004 and thereafter joined in 2006 as a emeritus professor in Marmara University, Medical School. Ray contributed greatly to the development of neuroscience both in Marmara University and the neuroscience society from various parts of Turkey. Ray gave noteworthy and fascinating talks to the members of Brain Research Association, Turkish Neuroscience Congress and at international Turkish scientific meetings as an invited speaker in different parts of Turkey from 2006 to 2010. He impressed us not only with his scientific backround, extensive knowledge and approach to the neuroscience but also with his plain and modest remarks on life.

Conferences

(C-01 — C-08)

C-01

New perspectives in neurosciences

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In 1953, the first microscope suitable for operative surgery, (Opmi 1. Carl Zeiss, Oberkochen, Germany), became available, and finally opened a door for microsurgery, and was welcomed in otology, ophthalmology, vascular surgery, and neurosurgery. Microneurosurgery is not just the combined application of the operating microscope with certain micro-instrumentation. Microneurosurgery means the application of new road maps, designed according to new neuroanatomic, neurophysiologic, and neuropathologic concepts to access and explore lesions. In contrast to every other organ, the human brain has a history. It has developed over hundreds of millions of years; a co-evolution among numerous specific structural regions and distinct functional circuits. Each "Topos" in the brain is linked to the "Chronos", therefore all areas and functions within the brain are directly related to a certain chronologic or phylogenetic-ontogenetic period of development. Examples will be presented in the lecture.

C-02

Cortical layer with no known function

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The lowermost cell layer of the cerebral cortex that contains interstitial white matter cells in humans has great clinical relevance. These neurons express higher proportions of susceptibility genes linked to human cognitive disorders than any other cortical layer and their distribution is known to be altered in schizophrenia and autism (Hoerder-Suabedissen et al., 2013; Bakken et al., 2016). In spite of these clinical links, our current knowledge on the adult layer 6b is limited. These cells are the remnants of the subplate cells that are present in large numbers and play key role in the formation of cortical circuits but a large fraction of them die during postnatal development. The adult population that remains in all mammals to form interstitial white matter cells in human or layer 6b in mouse display unique conserved gene expression and connectivity (Hoerder-Suabedissen et al., 2018). We study their input and output using combined anatomical, genetic and physiological approaches. Selected cortical areas, relevant for sensory perception, arousal and sleep (V1, S1, M1, prefrontal cortex) are studied using chemogenetic and optogenetic methods. Our preliminary data suggest that 6b is not just a developmental remnant cell population in the adult, but a layer that plays a key role in cortical state control, integrating and modulating information processing (Guidi et al., 2016).

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C-03

Advances in neuroimaging of neurodegenerative diseases

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Amyloid and Tau pathology progress along distinct anatomical networks before they overlap in the course of Alzheimer's disease. As a consequence, both pathologies are likely to affect different functional brain networks and related cognitive functions in the early course of AD. Converging evidence from functional imaging studies in humans suggests that posterior cortical networks and functional pathways in the medial temporal lobe support recognition memory as well as mnemonic discrimination. In particular, recent research could reveal the fine-grained architecture of functionally and anatomically separated cortico-hippocampal pathways that distinctly support memory for objects and scenes. I will show how amyloid and tau pathology, measured by CSF and PET, affect functional processing in these pathways and related episodic memory functions in aging and the preclinical AD spectrum.

C-04

Health Institutes of Turkey: foundation, structuring and research funding programs

Bayram Yılmaz

Secretary General, Health Institutes of Turkey, Istanbul, Turkey

Health Institutes of Turkey (TÜSEB) was established in 2015 and functions under the Turkish act # 6569. TUSEB aims at improving science and technology in health sciences in Turkey. There are seven institutes, and a few more institutes are planned to be announced as structural establishment is completed. TÜSEB headquarters are found in İstanbul. Physical structuring is ongoing at Koşuyolu campus. In addition, Aziz Sancar Research Center is in the process of establishment. Recruitment of qualified personnel for departments such as project funding, computing technology and general management is ongoing. Several regulatory documents have been published, and rules and regulations for project funding programs are in the process of preparation. TÜSEB plans to provide most of its research budget for extramural funding (about 80%) and about 20% of the resources will be allocated for intramural research at its institutions. TÜSEB project funding programs are being prepared under three categories: strategic, primary subjects and periodic (researcher-initiated) projects. TÜSEB initiated an award program in 2017 dedicated to Aziz Sancar's name to provide science, incentive and service awards in health sciences. TÜSEB shall contribute to improvement of ecosystem for scientific research in Turkey, promote research in health sciences and technology and provide funding for research projects.

C-05

Nanomedicines for nervous system disorders

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Majority of available pharmaceutical agents cannot efficiently reach the brain parenchyma because of the blood-brain barrier (BBB). For the same limitation, several peptides that have been experimentally shown to be neuroprotective in models of neurological disorders could not be translated to clinic. To overcome this obstacle, we have developed nanocarriers that can transport large as well as small peptides to the brain after systemic administration by incorporating these peptides to brain-targeted nanoparticles (NPs) made of chitosan, a biocompatible polymer. Chitosan NPs were coated with polyethyleneglycol to reduce NP clearance from plasma by reticuloendothelial system. NPs were loaded with peptides and then targeted to brain by conjugating them with antibodies directed against the transferrin receptor-1 on brain microvascular endothelia, Binding of NPs to transferrin receptor-1 readily induced transcytosis of NPs across the BBB. We found that systemic administration of bFGF- or z-DEVD-loaded NPs significantly decreased the infarct volume in mouse stroke models. The neuroprotection was not observed when receptor-mediated transcytosis was inhibited or when NPs were not conjugated with the targeting antibody that enables them to cross the BBB. Targeting NPs to the brain reduced the bFGF dose required for neuroprotection by 300 times. On the other hand, many neuroprotective drugs like adenosine are inefficient on systemic administration because of their rapid clearance from the blood. For this, we have recently shown that NPs formed by conjugating adenosine to the lipid squalene provided a prolonged blood circulation time and, the animals receiving systemic administration of squalenoyl adenosine NPs had a significantly reduced infarct volume after ischemia in a mouse stroke model and an early motor recovery of the hindlimbs in rats subjected to spinal cord injury. Both chitosan and sequalene NPs were safe to administer to rodents. Nanomedicines targeting CNS appear to be promising therapeutics for neuroprotection.

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C-06

Mathematical modeling and deep learning techniques in neuroimaging

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Mathematical modeling has been an important component of data analysis and information extraction in neuroscience. On the other hand, recent overwhelming advances in artificial intelligence is poised to extensively impact the field of neuroscience. Deep learning, which refers to a branch of machine learning techniques that depend on neural networks, is a data-driven approach where computers learn to model and extract information from big data. Touching upon both modeling and deep learning, I will present several interesting solutions to certain data analysis problems in neuroimaging. The first problem I will talk about consists of employing tensors in modeling either higher order mathematical structures in capturing inherent asymmetry in white matter fibers of the brain or tree-like structures such as vascular trees in human brain. This technique demonstrates the asymmetry of underlying fibers at the voxel level for bending, crossing or kissing fibers of the brain white matter using Diffusion MRI data. The second problem is how to organize brain white matter fibers into meaningful anatomical bundles. I will show a novel neighborhood diffusion orientation distribution idea to represent fibers, as well as an artificial neural network based approach to classification of fibers. The third problem I am going to talk about is on neuroimage synthesis for missing modalities using a generative deep learning approach. I will conclude by some computational methods on neuroimaging data and where to go from here.

C-07

The arduous PATH to understanding gliomas: keystones and perfect storms

Tarık Tihan

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Recent advances in molecular, radiological and clinicopathological understanding of gliomas point to some critical phenotypic and genotypic features of these tumors. Since the beginning of the current millennium, we have been able to recognize distinctions between adult and pediatric as well as diffuse and solid glial tumors. Recent WHO classification scheme of 2016 has solidified this understanding and has incorporated genotypic information into what has typically been a phenotypic classification system. In addition, recent advances allowed us to understand the critical genetic aberrations as "keystones" in the development of gliomas, but such keystones have been identified as critical but insufficient for tumorigenesis. In addition to these molecular alterations, additional abnormalities lined in a particular sequence in time and space gives us the end result, which could be interpreted as a collection of otherwise innocuous aberrations culminating in a catastrophic outcome; hence the so-called perfect storm. Our recent progress has focused on understanding these keystones and perfect storms in order to better tailor treatment and prognostication. These efforts have led to the "personalized" orientation of medicine and the realization that biology is far more flexible and fickle than perceived by man.

C-08

Molecular genetics of schizophrenia, alcohol dependence and major depression

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The last decade has seen rapid acceleration in identification of genetic loci contributing risk for human complex traits, including psychiatric disorders like schizophrenia, major depression and alcohol dependence. While studies by individual groups have provided some key results, the vast majority of progress has been made in large consortium meta-analyses of data from many samples. More than 250 independent loci contributing risk for schizophrenia have been identified in samples of >150,000 subjects, compared to 44 loci associated with major depression in samples of >480,000 subjects, and 1 locus associated with alcohol dependence in samples of >52,000 subjects. Four main themes have emerged from this work. 1) Complex traits are highly polygenic with great variation in the complexity of their genetic architecture and widespread pleiotropic effects of associated loci. Successful study designs require very large samples and consideration of key epidemiological differences between traits. 2) Common genetic variation assessed by genomewide association studies, rare genetic variation assessed by sequencing and copy number variation are all implicated in risk, with the largest proportion attributable to common alleles of very small effect size. Identification of these alleles and elucidation of their functional impact is critical to translate these discoveries into clinical action. 3) The identification of specific alleles driving risk in associated loci remains challenging and requires very large sample sizes due to linkage disequilibrium and small effect sizes for common alleles, and due to the high background rate of mutations in the human genome and low individual allele frequency for rare alleles. 4) These signals are enriched in non-coding genomic regions. Identification of non-coding elements in the genome and functional variation within them is critical to elucidate disease mechanisms. Despite these challenges, the pace of discovery is expected to remain high for the next decade.

Symposiums

(S-01 — S-10)

Symposium 1
Biomarkers in Brain Disorders

S1-1

Detection of obsessive compulsive disorder using task-related and resting-state functional connectivity data

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Obsessive Compulsive Disorder (OCD) is a frequent, chronic disorder producing intrusive thoughts which results in repetitive behaviors. It is thought that this psychiatric disorder occurs due to abnormal functional connectivity in certain regions of the brain called Default Mode Network (DMN) mainly. Recently, functional MRI (FMRI) studies were performed in order to compare the differences in brain activity and also functional connectivity between patients with OCD and healthy individuals through different conditions of the brain (Koçak et al., 2011, 2012). The study included 12 right-handed (six male and six female) OCD patients and 12 right-handed healthy volunteers matched for gender and level of education (control group). We used the resting and imagination task conditions for the functional connectivity analysis for the presented work. In the resting condition, subjects were instructed to rest, eyes closed in the scanner and think freely. In the imagination condition, subjects were instructed to imagine previously shown object. A blocked fMRI design was used in the experiment. Each block lasted 25 s (five TRs). Preprocessing of the data was performed using SPM8 software (Wellcome Department of Cognitive Neurology, London, UK) running in a MATLAB 7 environment (Mathworks, Sherborn, Mass., USA) and functional connectivity analysis was performed on the preprocessed data with conn software (http://www.nitrc.org/projects/conn/). The obtained functional connectivity images were used to extract features to discriminate between healthy and OCD groups. We tried to extract a disease signature for OCD that is determining the features for discrimination of OCD patients from healthy individuals based on their task-based and resting-sate functional connectivity data. We found quite promising results revealing high classification accuracy, using the SVM classification method.

Keywords: Obsessive compulsive disorder, functional MRI, functional connectivity, support vector machine (SVM)

S1-2

Electrophysiological biomarkers in Alzheimer's disease and amnestic mild cognitive impairment

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Alzheimer's Disease (AD) is a slow, progressive disorder, in which pathological changes onset years before the initial clinical symptoms. Amnestic Mild Cognitive Impairment (aMCI) is considered as an early form of AD, which is characterized by anterograde episodic memory deficits with annual conversion rate of 10-18%. The pathology of both diseases includes transsynaptic neuron-to-neuron disconnection leading to cognitive impairment. Recent studies suggest that impaired synaptic plasticity, which is the most dominant feature of AD/aMCI, is responsible for altered rhythmicity in neuronal oscillatory network in those patients. Electroencephalography (EEG) is a cost-effective, non-invasive technique with high temporal resolution and is capable to identify "oscillopathies" associated with cognitive dysfunction by means of event-related potentials (ERP) and event-related oscillations (ERO) responses. Growing findings in the field have contributed several EEG/ERP/ERO indices of synaptic neurotransmission to be considered as potential biomarkers. Reduction of power in the alpha and beta bands along with the increase of power in delta and theta bands obtained by the spectral analysis of spontaneous EEG recording is a prominent aspect of AD as well as conversion from MCI to AD. In ERP studies, alterations in N200, P300, MMN components in patients with AD/aMCI are widely reported. Research on event related oscillations underlines the decrease in delta and beta oscillatory responses amplitude and gama band responses delay as an indication of cognitive dysfunction in AD/aMCI patients. Besides, differences in theta phase-locking and coherence findings between patients with AD and healthy elderly is stated. Recent evidence supports the candidacy of EEG/ERP/ERO indices as a promising biomarker.

Keywords: Electroencephalography, biomarker, Alzheimer's disease, amnestic mild cognitive impairment

S1-3

Eye movement patterns in adult autism spectrum disorder

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There is a growing interest towards the nature of autism spectrum disorder (ASD) in adults in the social cognition literature to gain further insights about the nature of language and cognition. Joint attention, which constitutes the basis of any social encounter, is one of the important predictors of language development and social learning. Referring expressions are linguistic resources that speakers use to achieve joint attention by identifying and referring to the objects relevant to the ongoing interaction. Reference production and understanding involve the ability to think of and represent objects, to direct others' attention to relevant objects, and to identify what other speakers are talking about when they use such expressions. People with ASD exhibit difficulties for using such references since their competent use requires an understanding of the partner's cognitive status and what information might be available/accessible from the partner's perspective. Existing studies have produced conflicting characterizations since they tend to use simulated scenarios at the individual level of analysis. New experimental paradigms are needed that include both sides of naturalistic social interaction where eye movements and linguistic structures can be analyzed together. This study aims to address this need by employing a dual eye-tracking paradigm where linguistic structures are analyzed in relation to gaze correlates of joint attention. 21 ASD adults and 21 age/education-matched controls participated in the study. During the experiment, participants interacted through a computerized tangram puzzle. Participants assumed two interchanging roles; the presenter had access to the target shape and the workspace but could not move the tangram pieces, whereas the operator could only see the workspace and had control of the mouse. Our initial findings suggest that controls exhibited significantly higher level of gaze coordination than the ASD group, and there is a significant difference between gaze coordination levels observed for presenters and operators.

Keywords: Adult autism spectrum disorder, dual eye tracking, gaze reurrence analysis, referring expressions

S1-4

High frequency oscillations: a robust biomarker in Parkinson's disease

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Abnormal neural oscillatory activity observed in cortical and subcortical networks is widely recognized as a hallmark of Parkinson's Disease (PD). Subcortical local field potentials are typically collected from patients undergoing operations for deep brain stimulation (DBS). Recently, high frequency oscillations (HFO; > 200 Hz) in the subthalamic nuclei of PD patients have enjoyed growing interest. Özkurt et al. (2011) derived a ratio that takes into account the power of slow (~250 Hz) and fast (~350 Hz) HFO. In PD patients of the akinetic and rigid subtype, this ratio was shown to be consistently and significantly higher while they are on dopaminergic medication. It was also correlated to symptom severity scores. Interestingly, not all patients did exhibit the notorious abnormal beta power levels in the same study. Another study conducted by the same group (Hirschmann et al., 2016) revealed that the HFO ratio consistently increases for durations of Parkinsonian tremor regardless of the dopaminergic condition. Moreover, this measure outperformed previously suggested oscillatory markers of PD, i.e., power in the tremor frequency, beta and low gamma bands. Neurophysiological markers of PD provide useful parameters for adaptive DBS devices apart from medical diagnosis and stimulation target localization. Ongoing studies investigating further the coupling of HFO to other oscillatory activities underline the promising role of HFO as a robust biomarker for PD.

Keywords: Parkinson's disease, deep brain stimulation, neural oscillations, local field potentials

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Symposium 2

Disturbances of Cellular Mechanisms in Glioblastoma

S2-1

Personalized approaches in glioma surgery

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Gliomas make up about 70% of the primary brain tumors seen in adults, with a global incidence rate reported as 6/100,000. The etiological factors responsible for the appearance and development of gliomas is mostly unknown, although it does appear that genetic factors, somatic mutations and various external factors play a role. Gliomas are neoplasms that appear

in the glial cells of the brain and usually progress as malignant. Unfortunately early diagnosis is statistically rare. Therefore, even if surgical and chemotherapy/radiotherapy treatment is successful, it is likely that it will turn into a high grade glioma and result in high mortality. In gliomas, diagnosis is made through radiological tests, with the tumor being radiologically followed-up after surgical or chemotherapy treatment. In the treatment of secondary high grade glioma, taking a marginal approach in the surgery or chemotherapy of the tumor may lead to extending the time in which the tumor reaches the brain. Personalized approaches in treating gliomas have been successful, extending survival and preventing recurrence and metastasis. The personalization strategies available can be divided into three: First; anatomical personalization involves a personalized surgical approach depending on the tumor and where it is located within the central nervous system, and the use of intraoperative MRI can result in a successful resection/removal of the tumor. The second, or physiological personalization, refers to the mapping of the speech center and motor mapping during the excision of the tumor to preserve the patient's functions. Third, biological personalization is determining the mutations carried by the tumor and collecting information about the postoperatively to chemotherapy and radiotherapy, and the selection of suitable medication according to the genotype of the tumor and predicting the prognosis of the tumor. At our Clinic, we utilize all three personalization methods in glioma surgery during treatment and follow-up. Furthermore, liquid biopsy and intraoperative molecular diagnosis methods are used for preoperative planning and the surgical approach along with genetic information on the tumor. This approach has increased our success rates in the treatment of such tumors.

S2-2

Epigenetic changes and therapy resistance in glioblastoma

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Glioblastoma Multiforme (GBM) is the most common and aggressive type of brain tumors with extremely poor prognosis. Current therapeutic approaches include surgical resection of the tumor, radiotherapy and chemotherapy with an agent called Temozolomide (TMZ). Despite the recent refinements in these therapeutic approaches, the mean patient survival remains as low as 14 months after diagnosis. Therefore, there is an unmeet need for developing more effective and novel therapies. A mechanism of therapy resistance is transcriptional dysregulation of cell death and survival-related genes. Changes in the epigenome are stably inherited through cell divisions and are thought to play a role in acquired therapy resistance. Epigenetic modifications occur on chromatin and consist mainly of DNA methylation, histone acetylation and methylation. These modifications regulate gene expression by influencing the packaging of chromatin and accessibility of transcription machinery to specific genes. A number of protein complexes write, read and erase chromatin modifications and the role of these complexes in tumor biology is starting to be heavily investigated. These complexes can be broadly categorized as DNA methyl-transferases (DNMTs), histone acetyltransferases (HATs), histone deacetylases (HDACs), histone methyl-transferases (HMTs) and histone demethylases (HDMs). In order to decipher the relationship between therapy response and epigenetics, we undertake loss-of-function approach and interrogate the roles of chromatin modifying proteins with functional screens. These screens are based on genetic or chemical ablation of protein functions. In the first one, we use shRNA or CRISPR/Cas9-based libraries, in the second one we use chemical probes in order to discover novel molecular mechanisms to overcome therapy resistance. In our studies, we utilize next generation sequencing to profile and map the differences between drug-sensitive and drug-resistant populations of GBM cells. In this talk, we will talk about our current approaches and highlight the roles of our recently identified molecular mechanisms.

Keywords: Glioblastoma, therapy resistance, epigenetics, CRISPR/Cas9, screens

S2-3

Nuclear factor one transcription factors and their roles in brain development and cancer

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During brain development numerous and diverse set of cells, neurons, astrocytes and oligodendrocytes, are generated from a single layer of progenitors; the required gene expression program is executed by variety of transcription factors. Three of these regulatory proteins, NFIA, NFIB and NFIX, are members of the Nuclear Factor One (NFI) transcription factor family. NFIs are expressed in the ventricular zones of the embryonic neocortex, hippocampus and spinal cord as well as postmitotic neurons and glia, cerebellar granule progenitors populating the external granule layer in the hindbrain, regulating neural differentiation, particularly gliogenesis. NFIs are also present in differentiated cells of the adult brain, where their function has not been determined. Interestingly, NFIA and NFIB levels are upregulated in astrocytomas, inversely correlating with the tumor grade while patent survival increases. Moreover, in glioma and medulloblastoma mouse models insertional mutagenesis of NFI genes exacerbates tumor growth. NFI's action as a tumor suppressor in brain cancer is consistent with their role in gliogenesis and cerebellar granule neurogenesis. CDO, an extracellular protein that promotes neurogenesis, is upregulated in NFIA or NFIB null hippocampus and cerebellum. In differentiating human neural progenitor cell culture, CDO expression increases as expression of NFIB, the prominent NFI in this system, decreases. Indeed, NFIs can bind the NFI motifs in the 5kb promoter region of CDO and occupy

two sites in human neural progenitors in vivo. NFIs can also inhibit CDO promoter activation in luciferase promoter assays. Meanwhile, two miRNAs that are abundant in human neural progenitors, miR124 and miR153, can bind the NFIB 3' UTR and repress its expression. Interestingly, in astrocytomas, miR124 expression is also inversely correlated with that of NFIB and increased tumour grade. We are investigating whether targets downstream from NFIB or upstream regulators of NFIB are in fact significant regulators of NFI function in vivo.

Keywords: NFI, transcription, neurogenesis, gliogenesis, astrocytoma

S2-4

The role of cytoskeletal proteins in invasion of glioblastomas

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Gliomas are the largest primordial central nervous system tumors originating from glial cells in the brain parenchyma. Gliomas rarely spread outside the nervous system but grow diffusely in the surrounding brain tissue. Glioblastoma multiforme (GBM) is the most common and malignant type of gliomas and characterized by severe and abnormal vascularization. Although multimodal treatments with surgical intervention, radiotherapy and chemotherapy are avaliable, glioblastomas are still difficult and impossible to treat. Since glioblastomas can become resistant to chemotherapy and radiotherapy, a single glioma cell that survives after removal of the tumor site leads to the recurrence of the tumor. For this reason, the factors involved in the invasion and migration mechanisms of glioblastomas must be elucidated to provide treatment for the disease. The capacity of tumor cells to migrate and invade is attained by the formation of dynamic protrusions that are not found in normal mitotic cells and they are caused by the rearrangement of microtubule and actin cytoskeletal proteins. These protrusions are formed by severing long microtubule polymers present in the cytoplasm into shorter pieces by microtubule-severing proteins. While the expression of Spastin, one of the microtubule-severing proteins, is at basal levels in healthy glial cells, it is highly expressed in glioblastomas. It has been shown that the microtubule severing Spastin protein is localized in the cortex area where the actin involving cell motility and migration is intensively located, rather than being co-localized with microtubules. Spastin is co-localized with Actin in proliferative SH-SY57 neuroblastoma cells as in GBM cells. However, Spastin is co-localized with microtubules in differentiated SH-SY57 neuroblastoma cells. The difference in Spastin localization between proliferative and differentiated neuroblastoma cells may be due to phosphorylation resulting from increased kinase activity in mitosis in the case of proliferation. Possible hosphorylation dependent role of Spastin in metastasis and invasion will be investigated in 217S466 coded TUBITAK project.

Keywords: Glioblastoma multiforme, spastin, cell motility, cell migration

Symposium 3 *(in memoriam of Prof. Erol Başar)*
Brain Oscillations in Neuropsychiatric Diseases

S3-1

Historical perspective for the brain oscillations: EEG oscillations in patients with schizophrenia

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The aim of this study was to investigate event related alpha and theta oscillations during perception of an ambiguous stimulus termed stroboscopic alternative motion (SAM). We recorded EEG during the continuous perception of both, the ambiguous and unambiguous control stimulus. In our study 19 patients and 19 healthy controls were investigated. All patients were recruited as in-patients after clinical stabilization. Time frequency analysis was conducted. For each participant amplitude modulations between perceptual stability and perceptual changes were determined for each single trial for both tasks (ambiguous and unambiguous) and a wide frequency range. Our results presented that the reduced modulation of theta activity in patients might reflect impairment of top- down capacities within the perception-action cycle. During phases of perceptual stability alpha activity of patients is increased when compared to controls and may indicate increased dependency of the patients' perception on bottom-up processes. Higher and lower alpha sub-bands may be affected differentially during ambiguous and unambiguous perception. Recently we extended our results for more patients and analyzed all frequency bands. The results present theta- reduced activity at the frontal and central locations, whereas the gamma activity showed clear topographical shift from parieto-occipital to central locations. We conclude that the alterations in gamma, alpha and theta activities are more apparent in the ambiguous condition. In patients with schizophrenia, the balance of top-down and bottom-up mechanisms of visual perception seem to be disturbed.

Keywords: EEG, brain oscillations, schizophrenia, top-down, bottom up

S3-2

General principles of EEG brain oscillations and their application in Parkinson's disease

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EEG Brain Oscillatory activity in various frequency bands may reflect different aspects of information. EEG activity gives rise to "evoked" or "induced" responses by application of sensory or cognitive stimulations. It is possible to analyze the different sensory and cognitive processes by the help of different methodologies of Event-Related Brain Oscillations. Among these methodologies, digital filtering, evoked/induced power spectrums, phase locking factors and coherence analysis are commonly used. The studies of our group in the last two years focused on the EEG event-related oscillatory dynamics of patients with Parkinson's disease. Our research aimed to show the potential electrophysiological indicators of cognitive decline in Parkinson's disease. In total EEG of 75 patients with Parkinson's disease (PD without cognitive deficits, PD with mild cognitive impairment, PD with dementia) and 25 healthy controls were recorded. Spontaneous EEG and event-related oscillatory responses during visual and auditory oddball paradigms were evaluated. Analysis of data with different methodologies of brain dynamics indicated that cognitive decline in Parkinson's disease is reflected with abnormal EEG dynamics. As the cognitive decline increased, delta responses decreased more. In general phase locking was impaired in PD patients with cognitive decline (both MCI and dementia), theta, alpha and beta phase locking of dementia patients were less than PD patients without cognitive decline and healthy controls. Event-related coherence analysis revealed that not only local circuits but long distance connections were also impaired in PD patients with dementia. PD patients with hallucinations had a different type of dynamics in comparison to PD patients without hallucinations. Analysis of spontaneous EEG revealed that PD patients with hallucinations had increased gamma power and increased gamma coherence over different electrode pairs. The studies performed proved that the methodologies of event-related oscillatory dynamics could successfully present the electrophysiological indicators of cognitive decline in Parkinson's disease.

Acknowledgments: This work (grant number 214S111) was supported by the Turkish National Science and Research Council (TUBITAK).

Keywords: EEG, EEG brain oscillations, Parkinson's disease

S3-3

EEG brain oscillatory responses: healthy aging, mild cognitive impairment and Alzheimer disease

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Alzheimer's disease (AD) as the most common reason of dementia causes a public welfare problem with the increasing rates of aged population. Amnestic type of mild cognitive impairment (aMCI) is considered as a prodromal stage of AD in the majority of cases. There is a great need to develop a biomarker to discriminate the healthy aged people from MCI or AD to administer some interventions for early management. In this presentation we will discuss the EEG-brain oscillatory responses in AD/MCI and healthy controls (HC) that our group has investigated according to Prof. Erol Başar's brain oscillatory dynamics principle. It was shown that over fronto-centro-parietal regions there is a continuum in delta responses across groups of HC, MCI and AD with the highest decrement in AD. Beta responses also decreased as delta in MCI, on the other hand late appearing and increased responses were seen in gamma responses of AD. Simple sensory visual responses yielded increased theta responses over the occipital regions in AD as a possible indication of hyperexcitability over visual cortices. As indicated by coherence values, decreased connectivity was observed in alpha, theta and delta responses in AD. For all groups, the connectivity measures were almost doubled in event-related tasks in comparison to simple sensory stimulation. Magnetic resonance volumetry showed relation between frontal volume and frontal delta responses. Lastly, cholinergic treatment caused increased frontal theta phase locking in AD. All of these findings indicate that EEG brain oscillatory dynamics as described by Erol Başar, can be helpful in understanding brain dynamics, disease progression, and monitorization of treatment effects, as a possible biomarker candidate in AD.

Keywords: Aging, mild cognitive impairment, Alzheimer, EEG, oscillation

S3-4

Brain oscillatory responses in bipolar disorder

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Bipolar disorder is a chronic, severe and often debilitating brain illness which is associated with significant cognitive deficits in a number of domains including executive functions, processing speed, attention, memory and social cognition as well as neuroanatomical abnormalities containing neural circuits that regulate cognitive processing. The course of illness is characterized by episodes of mania and depression and well being states (euthymia) between the episodes. Biomarkers for early diagnosis as well as for predicting treatment response are crutial for improving quality of life and longevity in patients suffering from bipolar disorder. Our group focused on oscillatory brain dynamics in bipolar disorder both in euthymic and manic states of illness, with and without medication. Spontaneous, and event related oscillatory activity in the theta, alpha, beta, and gamma frequency ranges as well as long distance coherence in the gamma frequency were assessed in patients in comparison to healthy controls. In drug free patients, during both mania and euthymia, spontaneous and event related alpha activity, event related theta activity and long distance gamma coherence were significantly reduced as opposed to beta range activity which was significantly increased both in mania and euthymia before treatment. Treatment with mood stabilizers seem to cause alterations in oscillatory responses compared to unmedicated state. The findings will be discussed with regard to the corresponding cognitive functioning for the assessed oscillatory activity in different frequency ranges as well as location of the alterations in the oscillatory activity. A proposal for a constellation of oscillatory biomarkers in bipolar disorder will be brought to the attention of the audience.

Keywords: Bipolar disorders, brain oscillatory responses, cognitive dysfunction

Symposium 4
Analysis of Motor unit with an Electrophysiologic Microscope

S4-1

Motor unit with an electrophysiologic microscope: from outside

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It is possible to analyze the motor units by stimulating their muscles' nerve and recording the activity with surface electrodes (from outside) or by recording the signal with needle electrodes within the muscle during voluntary activation (from inside). From both point of view, the recorded activity reflects the features having structural counterpart. From outside; CMAP is the most simple and reproducible signal among the surface recorded activity yet it gives an overall impression about the condition of the muscle. The denervation – reinnervation cycle can be recognized by higher magnification like F-wave analysis and motor unit number estimation (MUNE). The persistence, amplitude and reproducibility of F-waves give an impression about the number of motor units and their reinnervation status like classical MUNE methods. Besides, a relatively novel method, namely "CMAP scan" gives valuable and reproducible information about the number of functional motor units as well as the constituents of CMAP. In this lecture, it is aimed to introduce routine electrophysiological methods along with the relatively new and advanced ones dealing with the activity of motor unit via recording its activity with surface electrodes. The software and hardware systems which are designed and developed by the authors will also be presented.

Keywords: Motor unit, MUNE, F-waves, CMAP scan.

S4-2

New electrophysiological methods in ALS: our results

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Amyotrophic lateral sclerosis (ALS) is a degenerative disorder affecting upper and lower motor neurons. Electrophysiological assessment is necessary in order to diagnose the disease by showing motor unit loss as an indicator of lower motor neuron (LMN) dysfunction. Brisk tendon reflexes and babinski sign in neurological examination is still the only tool to display upper motor neuron (UMN) dysfunction. There is a need for assessing subclinic UMN dysfunction and for following UMN and LMN loss quantitatively to mantain early diagnosis and endpoint for clinical trials. Electrophysiological tests are good candidates as they are reproducible, objective and easy to access, In this symposium our experiences about new electrophysiological techniques for assessment of UMN and LMN dysfunction in patients with ALS in Istanbul University, Istanbul Faculty of Medicine were discussed. Repeater F-waves presenting as having the same amplitude, latency and shape in F-wave analysis were reported to occur in diseases with LMN loss, such as ALS, poliomyelitis, polyneuropathies and mononeuropathies. Neurophysiological index which is calculated by F-wave frequency, motor distal latency and amplitude correlated with functional scales and motor unit loss. CMAP Scan which is another candidate for assessment of LMN dysfunction can provide information about all functional motor units in a muscle. A stimulus-response curve is recorded by applying high number of stimuli and parameters calculated from this curve reveal peripheral nerve excitability, motor unit loss and instability and reinnervation. Recently, a new MUNE method elicited from CMAP Scan was described and called MScanFit MUNE. MscanFit MUNE was reported to reveal motor unit loss in ALS. To asses UMN dysfunction electrophysiologically, transcranial magnetic stimulation (TMS) techniques were studied in ALS. Motor threshold, cortical silent period and paired stimulation methods showed some promising results however, large variability in results of these conventional TMS methods due to desynchronization, restricts their utility in clinical practice. To overcome this problem, triple stimulation technique was described which is consisted of two TMS and one peripheral electrical stimulation with two collisions and gave better results in assessing UMN dysfunction compared to diffusion tensor imaging.

Keywords: Amyotrophic lateral sclerosis, MUNE, CMAP scan, F-waves, transcranial magnetic stimulation

S4-3

Automated analysis of F-waves

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F-waves are elicited in response to the supramaximal stimulus and they are consisted of the action potentials that are bounce back to muscle after invading anterior horn cell. F-waves' morphology and latency are variable. Morphology of the F-wave for a single motor unit is constant. F-waves with same morphology are known as repeaters. They can be used to estimate the number of motor units (MUNE). Signals are filtered from noise and first 2 ms part (stimulus artifact) is discarded. Maximum amplitude of M-response is determined for each signal. Mean value is calculated

(MGloMax). F-waves are cut from both ends. Maximum (Fmax) and minimum (Fmin) amplitudes are calculated with locations. Signals with peak to peak amplitudes greater than 40µV are approved as F-waves. If a signal does not go down 40µV to the left and right in 3 ms from the Fmax location, it is floored to 0. All signals are aligned according to Fmax. Signal pairs closer than 0.5ms are determined as repeater F-wave candidates. If Fmax difference is lower than 10% and individual power difference is lower than 20% between the candidates, they keep their candidacy. Pairs having correlation coefficient more than 0.9 were also kept. A "similarity coefficient" is calculated relying from amplitude and power difference. If similarity coefficient is lower than 0.6 (determined by authors) than it becomes a repeater F-wave. Same repeater F-waves are combined in the same basket. The mean of peak to peak amplitude (sMUP) for all signals are calculated. MUNE is calculated by dividing the MGloMax with mean sMUP amplitude. The number of F-waves, the number of repeater F-waves and the MUNE value can be seen on monitor. The most similar signal pairs can be plotted with similarity coefficient.

Keywords: Electromyography, F-waves; MUNE, software

S4-4

Motor unit with an electrophysiologic microscope: from inside

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It is possible to analyze the motor units by stimulating their muscles' nerve and recording the activity with surface electrodes (from outside) or by recording the signal with needle electrodes within the muscle during voluntary activation (from inside). From both point of view, the recorded activity reflects the features having structural counterpart. From inside, the duration and amplitude of single muscle-fiber action potential (SFAP) reflect the size of this fiber. The observed increased dispersion among the SFAPs created by moving recording needle from end-plate zone to near tendon unveil the variability in fiber size. It is also possible to record the activity of same motor unit from one end to another by moving the recording needle step by step. Known as "scanning EMG", this method allows us to study the temporal and spatial characteristics of the motor unit action potential throughout motor unit territory. In this lecture, it is aimed to introduce routine electrophysiological methods along with the relatively new and advanced ones dealing with the activity of motor unit via recording its activity with needle electrodes. The software and hardware systems which are designed and developed by the authors will also be presented.

Keywords: Motor unit, single fiber action potential, motor unit action potential, scanning EMG

S4-5

Scanning EMG: basic principles and biological counterparts

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Scanning EMG is an experimental method eliciting the electrophysiological cross-section of motor unit (MU). This method was first introduced by Stålberg and Antoni (1980). In this method, while a concentric needle electrode is moved upwards with 50Ì steps via a stepping motor, motor unit action potential (MUAP) in each step is recorded through the second channel of an EMG system. A Single-Fiber Action Potential (SFAP) belonging to a single muscle fiber of the same MU is recorded by SFEMG electrode via the first channel of the EMG System which is used for triggering as well. The time-locked MUAP with SFAPs and being generated by the same MU are used to build the 3-D electrophysiological maps of the MU territory. These maps present the distribution of time-varying MUAP signals along the MU territory and they reflect the temporal and spatial features of MU. Hence, features such as length of MU cross-section, fractions of MUs, silent areas, polyphasic and complex portions of MUPs, maximum duration and maximum amplitude can be revealed beside those such as amplitude and duration being studied by means of conventional needle EMG. It is possible to investigate the changes in these features in either neurogenic or myopathic disorders through scanning EMG. The changes can be helpful in monitoring the reinnervation process in neurogenic diseases and progressive loss of muscle fibers in myopathic diseases. Thus, Scanning EMG is considered as an experimental method that can have a role in studying the progression of neuromuscular diseases.

Keywords: Scanning EMG, electrophysiological cross-section, motor unit territory, neuromuscular diseases

S4-6

Scanning EMG: signal processing

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The signals that are recorded with EMG instrument consist of 1000 samples. According to contraction level, traces harbor more than one motor unit potential so it is difficult to determine cutting locations for feature extraction by observing only one sweep. To solve this, "activity corridor" is determined by aligning the signals back to back. The scanning EMG signals are filtered by a vertical median filter to discard the other motor units' activity.

Consequently, a wavelet transform based noise reduction is applied. The noise-free signals are summed and autocorrelation function is obtained in order to determine the cutting locations of the signals. The maximum amplitude for each sweep is calculated and the signals having silent areas floored to zero. The alpha trim filter is applied for smoothing. While calculating "spike duration" low amplitude baseline noises were discarded by "windowing process" to reach the local minimums. Following the windowing, second derivative of the signal is calculated to locate the very left and right local minimums. The spike duration is between these two minimums. The signals that are obtained after median filtering are filtered by a high pass filter which has 2 KHz cut off frequency for calculating the number of peaks. After that the signals are smoothed with the alpha trim filter and wavelet transform based noised reduction is applied to the signals. Finally, the second derivative is applied to the signals and the number of peaks is calculated. Maximum amplitude x spike duration and the number of peaks x spike duration features are calculated easily by using the previous features. The sixth feature is the ratio of the power outside the activity corridor to the power inside the activity corridor. The last feature is the number of peaks outside the activity corridor.

Keywords: Scanning EMG; neuromuscular diseases; activity corridor; wavelet transform; autocorrelation function

Symposium 5
New Approaching Strategies to Pathophysiology and Treatment of Neuronal Injury

S5-1

The role of fetal microchimerism on the brain injury and plasticity after focal cerebral ischemia

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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. Although the transition of fetal cells during pregnancy is known in healthy individuals and animals, the role of these transiting fetal microchimeric cells on the injury of the mother is yet to known. In this study, it is aimed to analyze the fetal cell transition from fetus to maternal ischemic brain tissue following brain ischemia of the mother during pregnancy. With the induction of ischemia during the different trimesters of the pregnancy, the number and cellular type of the cells transiting to maternal tissue will be able to be evaluated. In order to demonstrate the fetal cells transition wild type female mice were mated with green fluorescence protein (GFP) expressing male mice and ischemia was induced at different trimester periods of the pregnancy. Because the green fluorescent expressing cells in the maternal tissue following ischemia cannot origin from maternal tissue, these cells were considered as fetal microchimeric cells. During the preliminary work to evaluate fetal cell transition, female pregnant mice were subjected to middle cerebral artery occlusion followed by 72 hour reperfusion and demonstrated the presence of fetal cells in the maternal brain tissue 72 hour after the injury using both flow cytometry and immunofluorescence methods. It is believed that fetal microchimeric cells are able to differentiate and that their presence in the injured tissue can enhance plasticity through the induction of endogenous mechanisms and neurogenesis. Therefore, it is suggested that the results that will be obtained from this project will provide important insights into both stem cell treatment and cellular treatment. In addition, it is believed that in order to develop personalized treatments, promising results that can promote the ex vivo differentiation of fetal cells present in the patient's own blood for use in cellular treatments will be obtained. This study is supported by TUBITAK (217S453).

Keywords: Fetal microchimerism, cerebral ischemia, plasticity

S5-2

Effect of CDNF and MANF factors on survival mechanisms following cerebral ischemia and optic nerve injury

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Neurotrophic factors are known to enhance neuronal survival and differentiation and believed to play important roles in the treatment of neurodegenerative disorders. To this end, it was suggested that Cerebral Dopamine Neurotrophic Factor (CDNF) and Mesencephalic Astrocyte-Derived Neurotrophic Factor (MANF) neurotrophic factors which have different protein structures than the previously identified neurotrophic factors, may exert their effects through different mechanisms than the other known factors. Identification of such mechanisms can contribute to development of new approaches for the treatment of neurodegenerative disorders. Here, we aimed to investigate the restorative effects of CDNF and MANF neurotrophic factors on cellular survival after cerebral ischemia and optic nerve injury. It was demonstrated that CDNF and MANF promoted neuronal survival and reduced the number of apoptotic cells following the induction of ischemia or optic nerve injury in mice. To elucidate the underlying signaling pathways, angiogenesis, neurogenesis and tissue remodeling-related gene expressions were analyzed. Effects of CDNF and MANF on functional recovery were investigated using motor coordination and grip strength evaluations. We demonstrated that both CDNF and MANF enhanced functional recovery and plasticity by promoting axonal projections. In addition, these factors supported neurogenesis and reduced glial scar area. In conclusion, these results are expected to contribute to the development of novel target molecule-based therapies not only for cerebral ischemia and optic nerve injury, but also for several other neurodegenerative disorders. This study was supported by TUBITAK, 1001 ARDEB program (114S402).

Keywords: CDNF, MANF, cerebral ischemia, optic nerve injury

S5-3

The role of circadian rhythm protein Bmal1 on the pathophysiological changes occurring after cerebral ischemia

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Circadian rhythm plays an important role in the regulation of almost all physiological conditions as well as pathophysiological processes such as cerebral ischemia. In this study, we aimed to examine the effects of both circadian rhythm and circadian rhythm regulator protein Bmal1 on the injury mechanisms occurring after cerebral ischemia and in-vitro oxygen glucose deprivation (OGD). 8-12 week-old male Balb/C mice were subjected to 30 min middle cerebral artery occlusion in 6-hour intervals depending on the circadian rhythm (06:00, 12:00, 18:00 and 00:00) followed by 72 hour reperfusion. Impact of biological rhythm on brain injury, edema, neuronal survival and DNA fragmentation as well as intracellular signaling pathways following cerebral ischemia were evaluated using planar surface immunoassay and broad spectrum proteomic analysis. Effects of Bmal1 on cellular survival were investigated using oxygen glucose deprivation method in lentivirus mediated Bmal1 overexpression or Bmal1 silencing via shRNA in N2A cells. In addition, using targeted proteomics (immunoprecipitation combined with mass spectroscopy (IP-MS)) effects of Bmal1 on intracellular signaling pathways were investigated. Ischemic injury area and apoptotic cell death were shown to be lower and neurological scores were better in mice having ischemic injury in the night time when compared with day-time ischemia, depending on the biological clock. It was demonstrated that these effects were specifically through Bmal1, Akt, Erk-1/-2 and mTOR proteins. We have shown that cellular death was decreased in Bmal1 overexpressing cells, while it was increased in Bmal1 knockdown cells. In addition, Bmal1 was shown to affect intracellular signaling pathways especially through DNA binding proteins and chaperone proteins. Results obtained from this study indicated that Bmal1 reduced brain injury especially through the activation of survival kinases in the pathophysiology of cerebral ischemia and increased cellular survival following OGD in vitro. These results may contribute to the determination of pharmacological therapy-oriented novel target molecules.

Keywords: Circadian rhythm, Bmal1, cerebral ischemia, oxygen glucose deprivation

S5-4

The effects of purinergic P2X7 receptors on brain epileptic activity: role of blood circulation, ECE-1 and NMDA receptor activation.

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Epilepsy results from the hypersynchronus discharges of the neuron groups located at the cortical or subcortical regions and generally produces, a recurring clinical chart. P2X receptors are ATP-dependent cation channels and play a role in rapid signal transduction in several regions of the brain. P2X7 subtype of these receptors, has the ability to change its ion selectivity during prolonged ATP exposure. In this study, we studied the effects of P2X7 receptor agonist; BzATP, antagonist; BBG, well-known free radical scavenger; melatonin and melatonin receptor blocker; luzindole on spike frequency, spike amplitude, cerebral blood flow and cell signaling pathways after the induction of epilepsy. We induced epilepsy by penicillin injection into the cortices of the mice and ECoG recordings were taken for 90 minutes. At the end of these experiments, spike frequency and amplitude measurements for changes in the electrical activity, changes in the blood flow and laser speckle analyses were used to determine microcirculation. FITC dextran injection was performed to measure arterial vessel diameters in the cortical area under a 2-photon microscope. P2X7R knock-out animals were used to determine the possible effects of BzATP independent from the P2X7 receptor. Additionally, the activated endothelin converting enzyme (ECE-1) and NMDA receptor NR1 signaling pathways have been investigated in addition to NOS1-3, which can affect blood circulation in the brain. It was found that BzATP increased brain electrical activity, while BBG and melatonin decreased significantly. Also, these findings were parallel to the laser speckle analysis, as well as decreased ECE-1 activity after melatonin administration. These results suggest that the inhibition of P2X7 receptor activity by BBG or melatonin suppresses epileptic activity of the brain and has a positive effect on the regulation of cerebral blood flow. Consequently, in future clinical trials these molecules could be combined with existing therapies when necessary to provide more effective treatment options and to increase the functional recovery of the patients.

Keywords: Epilepsy, P2X7, ECE-1, melatonin, 2-photon

Symposium 6

Dynamics of Brains Intrinsic Connectivity Networks under Task Conditions

S6-1

Dynamics of brain's intrinsic connectivity in functional magnetic resonance imaging

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Brain's intrinsic activity is spontaneous slow fluctuations in the functional magnetic resonance imaging (MRI) signal, which could be measured when there are no external stimuli. The similarity of intrinsic activity between different measurement points or sets of voxels in the brain gives clue about the possible information transfer or connectivity among them. Studies on intrinsic connectivity presented brain regions showing high connectivity during rest and named these regions as resting

state networks (RSN). Major RSNs are the default mode network, sensory-motor network, visual network, salience network, dorsal attention network, frontoparietal network. RSNs can be found using different analyzing approaches, with high reproducibility but they have not completely described concerning their structure, function and interaction among them. Intra- and inter-network connectivity of the RSNs are not stationary in time. Besides, intrinsic connectivity changes of RSNs could be presented based on the given cognitive tasks. According to these statements, data analyzing methods aiming to clarify dynamics of the RSNs will be presented.

Keywords: Functional magnetic resonance imaging, functional connectivity, resting state networks

S6-2

Alteration of brain's intrinsic connectivity during sensory, motor and cognitive activation states

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Aim of this study is to investigate the resting state networks (RSNs) that represent the ongoing brain activity, and to reveal their contribution to brain functions. For this purpose, the modulations of the RSNs will be examined under experimental conditions covering simple sensory stimulation, motor task and cognitive task conditions, since it is known that RSNs also persist in the task conditions. 17 healthy volunteers have participated in the study. fMRI data were recorded during four different tasks with 3T-MRI scanner. Functional connectivity (FC) analyses were performed between regions of interest (ROIs) using CONN-toolbox. In the analyses, 14 ROIs corresponding to DDAs (default mode network-DMN, sensory-motor network-SMN, visual network-VN, salience network-SN, dorsal attention network-DAN and fronto-parietal network-FPN) were used. Correlation values between ROIs were compared between different task blocks and differences showing significance at pFDR-corrected<0.05 were reported. In passive visual condition, increased FC between DMN and FPN nodes and in simple motor condition, reduced FC between DMN and SN nodes compared to fixation condition were found. In Go/NoGo condition, there were increased FC between SN and FPN nodes and decreased FC between SN and VN nodes compared to simple reaction condition. Also, reduced FC was found between DMN and FPN nodes. In addition, negative FC between SN and DMN nodes has disappeared. In 2-back condition of N-back memory task, increased FC between the nodes of SN, DMN and VN and decreased FC among FPN's nodes were found compared to 1-back. In 3-back condition, increased FC was found between DMN and FPN and between VN and FPN nodes and decreased FC was found between DMN's and FPN's own nodes compared to 1-back. Also, reduced FC was found between FPN and DAN nodes. Findings revealed that DDAs modulate their functional connectivities between their own nodes and other networks according to task difficulty.

Keywords: Functional magnetic resonance imaging, functional connectivity, resting state networks

S6-3

Context and novelty-related changes in brain intrinsic connectivity

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Although there are numerous of different explanations of resting state networks RSNs functions that reflect synchronous activity between brain regions in a resting state which is the absence of any experimental task or behavior, it is not yet fully explained what the RSNs functions are. In this study, context and novelty-related changes of intrinsic connectivity of RSNs are examined. Novelty, entrainment, vigilance task registrations and resting state registration records used in this block design study were recorded with 3T-MRG (MRI) scanner. CONN software was used for functional connectivity (FC) analysis. In this analysis, regions of interest (ROI) were selected corresponding to the default mode network (DMN), sensory-motor network (SMN), primer and seconder visual network (VN), salience network (SN), dorsal attention network (DAN), frontoparietal network (FPN), bilateral lateral prefrontal cortex (LPFC) and posterior parietal cortex (PPC) and significant differences were reported at pFDR-corrected <0.05 level. When the condition is difficult context in novelty task, comparing it with easy context condition, at target stimuli FC increases between left FPN and SMN-Superior and SN-RPFC while it decreases between SN-RPFC and primer VN; at new stimuli FC increases between all regions of the SN except the insula and DMN regions; at standard stimuli, FC increases between SN-RPFC and SN-SMG and left DMN-LP. In the random condition of entrainment task, comparing with the regular condition; FC between the SN-RPFC and the primer VN is decreases in the target stimuli; FC decreases between the left insula and the right insula from the SN-fields in the standard stimulus, otherwise FC increases between the right SMN-Lateral and the left seconder VN. When the vigilance task is responded fast, comparing it with the slow responded, FC between the left FPN-LPFC and the left and right SMN-Lateral is decreases while FC increases between the SN-ACC and the left secondary VN. There is also FC increases between SMN-Superior and VN-Dorsal and Ventral. As a result; it is seen that RSNs change FC's both within themselves and between each other according to the context and stimuli presented in con-

text. It is also believed that the changes in FC levels of RSNs modulate the level of vigilance throughout the task.

Keywords: Functional magnetic resonance imaging, functional connectivity, resting state networks, contextual novelty, vigilance

Symposium 7

Computational Neuroscience: Contemporary Research Ranging from Extracellular Neural Recordings to Mathematical Models of the Brain

S7-1

Various tools for understanding the role of the basal ganglia network in cognitive processes: mathematics and computation

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Using mathematics is one way to express the concepts when modelling a phenomenon or a process. This conceptualizing is done in terms of equations, which can even be solved analytically especially, if the equations written are linear and time-invariant. Even though equations written are non-linear and time varying there are methods to analyze such systems, as long as the dimension of the system is small. But for complex systems, where the number of states and parameters used to define the system are too large and the relations can be expressed only with non-linear equations, it is no longer possible to have analytical solutions and analyze the behavior of the system. The phenomena we encounter in neuroscience are complex, thus mathematics is not sufficient by itself and computational tools are needed. Here, models of basal ganglia circuit in two different scales will be introduced. In one scale, the mean behavior of a group of neurons is modeled with a single equation, giving rise to a mass model. In other scale, the different behaviors at single neuron level are considered to build the whole circuit and thus spiking neuron model is obtained. The pros and cons of these models will be discussed, especially to give an idea about how mathematical models are set up and what knowledge we can get from the models and their simulations. In both scales, the role of dopamine in action selection is considered and in the simulation results, one can follow the effect of dopamine. With the spiking neural network model it will be shown that, it is possible to obtain Parkinson's disease (PD) case by modifying the parameter corresponding to dopamine effect and to observe the effect of deep brain stimulation in PD.

Keywords: Computation, mathematics, basal ganglia circuits, Parkinson's disease

S7-2

Information processing in the somatosensory system and neuroprostheses

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Until a short time ago, psychophysical responses measured for tactile inputs applied on the skin were interpreted based on neurophysiological recordings from single neurons. Our initial work focused on understanding the population responses of mechanoreceptive neurons. By recording spikes from the peripheral nerves and computational models, psychophysical predictions have become more accurate. Next, we recorded spikes from rat cortical neurons to study the transformation of tactile information from the periphery to the brain. Experiments with stimuli at varying levels showed that single cortical neurons do not encode intensity well according to Shannon's information theory. Our human data on magnitude scaling and population models suggest that vibrotactile intensity is correlated with the total number of spikes in the cortex. Additionally, we showed that vibrotactile information is suppressed in single cortical neurons by three mechanism with the help of drug microinjection studies. A single neuron is tuned to only low frequencies. Based on this fundamental work, we are designing techniques to implement somatosensory feedback for patients with cortical neuroprostheses. In a recently completed project, we established a psychophysical equivalence between intracortical electrical microstimulation and vibrotactile stimulation on the skin. Consequently, rats could perform behavioral tasks by using artificial tactile sensation. In the real-time application of the technique, mechanical stimuli were presented to a boot worn by the animals. The vibrotactile information captured by artificial sensors were processed by analog and digital electronic circuits, and converted to signals for artificial touch. The signals were applied to the rat brain as weak current pulses through implanted electrodes. Although the results were not as good as natural sensation, the performance was significantly higher than the condition for which the neuroprosthesis was switched off. In other words, the rats could utilize the artificial tactile information during movement and haptic interaction.

Keywords: Sense of touch, population model, cortical neuron, information theory, psychophysics

S7-3

Brain-machine interface decoder adaptation inspired by dopamine dependent plasticity

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Brain-machine interfaces (BMIs) aim to restore lost motor functions by directly communicating with the cortical neurons. BMI decoders predict the intended prosthetic actions from the activity of recorded motor cortex neurons. The firing patterns of the neurons change over time by nature and continuous adaptation is required in the decoder for the changes in the neural activity in order to provide high performance neuroprosthetic control. In our recent study, we proposed a novel decoder which utilizes model neurons as neural information processors and realizes adaptation via simulating dopamine-dependent synaptic plastic-

ity. Real-time simulations realized for a two-target reaching task showed that the decoder is capable of adaptation for changing activities of the motor cortex neurons and realizes perfect target reach accuracy. We stated that it would be possible to implement an autonomously adapting decoder if the signal providing the adaptation in the present decoder can be identified from the changes in the dopamine concentration in the brain of the subject. Our ongoing studies aim to study the performance of the present decoder using animal experiments. To this end, we currently develop a behavioral paradigm for enabling the rats to control a neuroprosthesis through motor cortex neurons. In addition, we develop voltammetric methods in order to record the changes in the dopamine concentration in the brain during neuroprosthetic control. In this presentation, extracellular neural recordings from the rats during neuroprosthetic control via neuronal operant conditioning and the dopamine concentration measurements during Pavlovian conditioned approach task will be evaluated. The usability of these recordings in the present decoder will be discussed. Supported by the Scientific and Technological Research Council of Turkey (TÜBİTAK), Grant No: EEEAG-115E257

Keywords: Neuroprosthetics, adaptation, electrophysiology, voltammetry

S7-4

Information extraction from neural recordings using Truncation Thresholds: a new paradigm

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Extracellular neural recordings are collected from awake behaving subjects through microelectrode arrays that are chronically implanted into the brain. Spike trains of single units are extracted from these recordings via signal processing. In the past 60 years this method has been used in behavioral neurophysiology experiments for investigating how behavioral information is encoded in the activity of individual neurons. These investigations have produced a wealth of information about what types of information are encoded in neuronal activity in various brain regions. At the turn of this century the information thus gathered has reached the level that permitted the development of decoding algorithms. In this way bidirectional information transfer between the nervous system and machines has been possible at high spatio-temporal resolution thanks to neuroprostheses implanted in various neural centers, such as the sensorimotor cortices. How information is to be extracted efficiently from extracellular neural recordings, be it in behavioral neurophysiology experiments or in brain-machine-interfaces (BMI), is an active research topic in computational neuroscience. One of the first steps in this process is the separation of spikes (information) from the background activity (noise) through thresholding of the filtered recording using an amplitude threshold. Truncation Thresholds are a pair of amplitude thresholds designed for achieving this separation in a fully automated and data-driven way. That these thresholds can be computed in a fully automated and data-driven way implies that they have the potential to be used as a standard method in BMI systems consisting of thousands of electrodes. Moreover, the use of Truncation Thresholds is not limited to spike detection; these thresholds find general use in the separation of continuous-valued time series into two parts as signal and noise. For this reason these thresholds can also potentially be applied on neural recordings such as EEG, ERP, fMRI and fNIRS. The software of the algorithm that computes the Truncation Thresholds has been registered under the resource number RRID:SCR_014637 at SciCrunch.org, one of the largest biomedical databases on the internet. This presentation will explain how Truncation Thresholds are computed and illustrate the advantages of using them with respect to competing methods, along with their application on various neural recordings. This work is supported by the Scientific Research Project Fund of Cumhuriyet University under the project number TEKNO-002.

Keywords: Spike detection, EEG, ERP, brain-machine interface

Symposium 8
Genetic and Molecular Bases of Neurological Diseases

S8-1

Genetic susceptibility to myasthenia gravis

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As a prototypic autoimmune disease, myasthenia gravis (MG) has evolved to many subgroups with probable different immunological mechanisms. Genetic susceptibility to MG has been evaluated as one of the autoimmune diseases and many candidate genes are studied. Considering immune mechanisms involved in the disease pathogenesis, genes of the MHC region, related to immune response, have been selected and candidates in class I, class II and class III gen regions are screened in different populations. Main finding of these studies was the association of a MHC haplotype (HLA-A1, B8, DR3) with the group of patients with early-onset disease and with anti-acetylcholine receptor antibodies (EOMG). Furthermore some autoimmune genes such as PTPN22, CTLA4 or some cytokine genes with possible functional roles are investigated. With the technical progress, genome-wide association studies (GWAS) have been applied to MG. In GWAS the disease susceptibility has also been shown to be associated with MHC genes, class I association of EOMG was confirmed and the role of new genes such as TNFAIP3, was detected. The data of other subgroups of the disease has revealed that associations with different loci implicate that different pathophysiological mechanisms in MG. The current concept of the role of these different associations with disease subgroups will be discussed.

Keywords: Myasthenia gravis, genetic, susceptibility

S8-2

Description of novel genes and mutations responsible from hereditary spastic paraparesis

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Hereditary Spastic paraplegia (HSP) is a neurodegenerative disease that is characterized by progressive spasticity and weakness in lower extremities. The inheritance pattern can be autosomal dominant, recessive or X-linked. In the context of this study, 27 families presenting autosomal recessive HSP were investigated to unravel the causative gene. As a preliminary step, genomic DNA of one patient from each family was analyzed by whole exome sequencing (WES). Three families were found to have mutations in SPG11 and each of SPG15, SPG7, CYP7B1, CCT5, SACS and ALS2 genes were mutated in one family. Upon repeated analysis of the WES data for variants in genes responsible for other neurological disorders, three novel genes were identified in three further families, namely, in KIF1C, PLA2G6, and SAMHD1 genes. To identify novel HSP genes in the rest of the families homozygosity mapping was performed either directly using the WES data or whole genome SNP genotyping. The haplotypes were generated by PLINK program and the homozygous regions in affected sib-pairs were used to determine the candidate genes/mutations in the WES data. The variants were investigated by segregation analysis and insilico tools to confirm their involvement in disease pathogenesis and two further novel genes have been identified. Thecandidate genes were investigated in vivo using immortalized lymphocytes from patients and knocked out by CRISPR-Cas9 in HEK cells. The expression pattern of them were analyzed by quantitative RT-PCR, western, and immunochemical approaches. This study have provided further evidence for genetic heterogeneity of HSP, showed importance of genetic analysis for differential diagnosis, and identified five novel genes, one of which is the probable SPG27 locus gene. The results indicated the necessity of primary genetic screening of SPG11 in TCC-AR-HSP and CYP7B1 in pure AR-HSP cases.

Keywords: Hereditary spastic paraplegia, whole exome sequencing, candidate gene identification

S8-3

Genome and proteome biomarkers of multiple sclerosis

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Multiple sclerosis (MS) is a complex inherited disease that occurs in genetically predisposed individuals exposed to environmental risk factors. Although 64–72% of the estimated heritability of the disease is still unknown, most of the approximately 250 known risk variants are identified by genome-size association studies. With the progress of the sequencing technology, candidate pathologic variants can be identified which are specifically responsible for the disease or susceptibility to disease by whole exome and familial linkage analyzes in familial forms of the disease. The disease mechanisms of MS with complex pathophysiology can be elucidated through integration of genomic, transcriptomic and proteomic data, which leads to identification of pathophysiological pathways by bioinformatics analysis, and understanding the biological relevance of this high-throughput data. Using this approach, we identified the most significantly disease-associated pathways by bioinformatic analyses of proteomic and genomic data of the same MS patient group. 9 pathways were detected in both pathway analyses performed for proteomic and genomic data. Among those, complement and coagulation cascade emerged as the most significantly associated pathway (hsa04610, p=6.96E-30). Other pathways that are known to involve in neurological and immunological mechanisms were adherens junctions (hsa04520, p=6.64E-25), pathogenic Escherichia coli infection (hsa05130, p=9.03E-14) and prion diseases (hsa05020, p=5.13E-13).

Keywords: Multiple sclerosis, genetics, neurodegeneration, inflammation, pathway analysis

Symposium 9

Antiepileptic Drug Delivery into the Brain Parenchyma with Nanocarriers for Treatment of Refractory Epilepsy

S9-1

Drug resistant epilepsy, probable causes and solutions

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Epilepsy is a neurological disorder affecting more than seventy million people and seen in every sex, age and race. Patients who have repeated seizures is diagnosed as epilepsy. By definition, seizure which is characterized as paroxysmal transient condition lasting minutes, may manifest as episodic impairment or loss of consciousness, as well as abnormal motor, psychic, autonomic or sensory disturbances. Drug-resistant epilepsy is having more than one seizure a month despite taking either mono or polytherapy of required drugs at appropriate doses. Patients with drug-resistant epilepsy comprise 1/3 of the patient population. In cases where treatment cannot achieve seizure cessation, sudden unexpected death in epilepsy patients (SUDEP) may occur. Although its exact causes remain to be unknown, there have been studies suggesting cardiac, autonomic or respiratory reasons. This risk increases in patients with longer duration of epilepsy. Even the most recent antiepileptic drugs (AEDs) could not provide solution to the problem. Among the most likely probable causes of resistance are pharmokinetic, neuronal network, gene variant, target, intrinsic severity and

transport hypotheses. According to pharmokinetic hypothesis, in peripheral organs such as intestines, kidney and liver, the overexpression of transport leads to a decrease in the serum level of AEDs and thereby their ineffectiveness. In neural network hypothesis, molecular information indicate abnormal growth in the axons. The animal and human studies in both hypotheses are still insufficient. Intrinsic severity hypothesis is based on the elucidation of the relation between pretreatment seizures and resistance with clinical findings. However, there may be cases of drug-resistance without such complex relation. The correlation between gene variant and drug-resistant epielpsy has been reported but the hypothesis needs to be verified with studies on larger population of patients. Another hypothesis is target hypothesis. Although AEDs have various specific targets, they fail to be effective in some cases. There are not enough treatment alternatives either. Data retrieved from P–glycoprotein (P-gp) inhibitors studies will soon be used extensively in treatment. Because sistemic use of P-gp has toxic effects, its efficacy is rendered limited. Stem cell and gene therapies are promising advancements but are still at their initial stages. The role of nanotransporters is to carry drugs, which cannot get across the blood brain barrier, with exogenous compounds to the brain. Once causes of drug resistance is better understood, it will be far more easily resolved.

Keywords: Drug resistant epilepsy, antiepileptic drugs, P-glycoprotein inhibitors.

S9-2

Ways of overcoming the blood-brain barrier in the treatment of drug-resistant epilepsy; nanocarriers

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In recent years, organic and inorganic nanostructures have been used in medical research and studies have begun to give promising results, especially in the treatment of cancer and brain diseases. The use of nanoparticles ranging from 0.5 to 200 nm in size for pharmacological purposes is intended to deliver the drugs or biological materials to the target tissue. Ligands capable of binding to various carrier receptors in the endothelial cell membrane, such as transferrin transport systems, and glucose transporter-1, collaborate with nanocarriers in the transportation of drugs to the brain. About 30% of epileptic patients do not respond to pharmacological treatment with the use of these drugs either alone or in combination. In cases of resistant epilepsy, the blood-brain barrier (BBB) formed by the brain capillary endothelial cells constitutes a major problem in the passage of the above-mentioned antiepileptic drugs from circulation into the brain. The specialized BBB blocks 98% of the blood-borne small molecules and 100% of the large molecules and hence prevents the entry of drugs to the brain at therapeutic doses. For this reason, new technologies and techniques are needed to ensure sufficient passage of such pharmacological agents into the brain tissue. Highly promising animal studies are being carried out using nanocarriers linked to one or more antiepileptic drugs to suppress seizures by achieving effective antiepileptic doses. For the improved diagnosis and treatment of drug-resistant epilepsy, it is necessary to find mechanisms for physiological opening and closure of BBB, to inhibit the efflux pumps on BBB such as p-gp, and to silence the structures causing excessive neuronal excitation. Thus, an important step towards the discovery of new methods will be made possible by supporting the use of nanostructures in the effective treatment of drug-resistant epileptic patients by current findings.

Keywords: Neuronanotechnology, blood-brain barrier, refractory epilepsy

S9-3

The conjugation of antiepileptic drugs to the nanocarriers in treatment of refractory epilepsy

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Gold nanoparticles (GNPs) have extensive potential biomedical applications in drug delivery, gene therapy, photothermal and radiotherapy, biosensing as well as contrast agents for cancer, diagnostic tracers, immobilization of enzymes and cell imaging, which make them excellent candidates for use in delivery applications. Because of their non-toxic, and biocompatible nature, ease of fabrication with core sizes in the range of 1–100 nm and functionalization of their surface with different ligands, which makes them effective in both the active and passive targeting, GNPs are one of the main candidates for drug delivery to the brain. Nowadays, glucose tagged GNPs (Gly-GNP) are very popular subjects of research in drug transport across blood-brain barrier (BBB) since surface modifications of GNPs can be easily performed by conjugation with functional ligands that can readily pass the BBB (e.g., glucose) and with the drug desired to be transported across the BBB. Therefore, the present study is designed to produce Gly-GNP conjugated with lacosamide (LA), an antiepileptic drug, yielding a conjugate size <10 nm to easily cross the BBB, and to evaluate the effects LA-conjugated Gly-GNP (LA-Gly-GNP) in an experimental rat model of epilepsy. 2.5 nm-diameter Gly-GNPs were synthesized by the direct method, which consists in controlling the growth of nascent gold cores by in situ reduction of a gold chloride trihydrate (HAuCl4 ·3H2O) in the presence of three different ligands bearing a thiol end-group. The chemical structure of the Gly-GNPs were confirmed by FTIR, and the particle size measurements were performed by Dynamic Light Scattering (DLS) technique. Finally, the antiepileptic drug, LA was physically conjugated to the Gly-GNPs in order to use in an experimental rat model. The results showed that the synthesized Gly-GNPs were quite successful in crossing BBB, thus they can be used as efficient and selective carriers of therapeutic agents across the BBB.

Keywords: Gold nanoparticles, lacosamide, epilepsy, drug conjugation

S9-4

Are nanocarriers safe? Effects of nanoparticles on oxidant/antioxidant system and inflamation

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The role of nanocarriers in medical treatments has emerged as one of the most interesting research areas recently. Despite of surgical and other treatment modalities, it still remains as clinical problem to treat epileptic cases resistant to antiepileptic agents, that constitute approximately 30% of all epileptic patients. During epileptic seizures, the prolongation of the duration of neuronal excitation causes neuronal damage and the brain becomes quite vulnerable to free radical damage. The increase in oxidative stress leads to depletion of mitochondrial ATP and deterioration of the blood-brain barrier (BBB). Oxidative parameters such as malondialdehyde (MDA) and antioxidant parameters such as glutathione (GSH) are decreased in different regions of the brain in epileptic cases. In the literature it was reported that the antiepileptic drugs such as valproate, carbamazepine and phenytoin reduce plasma GSH levels while increasing MDA levels. Recent studies have shown that epileptic seizures lower the seizure threshold by causing inflammation. In these clinical and experimental studies therapeutic effects of anti-inflammatory agents are tested in inflammation caused by neurons and glial cells. The BBB, release of cyclooxygenase and relevant prostaglandins, classical cytokines and their targets are considered responsible factors for inflammation in epileptic seizures. It is known that the antiepileptic drugs used in the treatment of epilepsy have problems in reaching to the brain tissue in effective doses. Most of the antiepileptic drugs are unable to show their therapeutic effects, since they cannot protect themselves from hydrophobic areas and enzymatic degradation before reaching the target cells, and they are unable to cross some barriers. It is currently possible to modify the structure of proteins, nucleic acids and other small molecules by using technology, thus they can be recognized by the immunological system. Nanoparticles are able to pass through membranes, but the defensive mechanism against to hazardous effects of nanoparticles at cellular levels are not known yet. These nanocarriers that will be used in medical treatment procedures may cross the cell's nuclear membrane and cause genetic damage and mutations. In order to understand nanoparticle toxicity, it is necessary to know cellular responses to the size, shape, chemical structure and surface properties of nanoparticles. It is also necessary to define potential effects of nanoparticles on translocation, degradation and oxidant/antioxidant capacity and inflammation process.

Keywords: Epilepsy, inflammation, nanoparticles, oxidative stress.

S9-5

Epilepsy treatment; from Istanbul University to Uppsala University, from nanocarriers to antibodies

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Despite the emergence of effective methods and approaches in the treatment of resistant epilepsies, especially with the acceleration of the development of nanobiotechnology that leads to the development of many different molecules and the difficulties in exploring the toxicity of each of these molecules still remains a major obstacle to treatment. Gold nanoparticles (GNP) and nanostructures are unique because of their strong drug transport capacities and their ability to pass easily through the blood-brain barrier (BBB). In addition to the acute therapeutic properties of GNP investigated in many pathological conditions particularly associated with neurodegenerative diseases, their therapeutic effects in diseases such as epilepsy and Alzheimer's may be elucidated by long-term results. The rapid development of biotechnology, not only in the field of nanotechnology but also in the immunology and pharmacology, has opened up the possibility of treating neurological diseases with immunotherapy methods. Although successful results have been obtained in immunotherapy methods which include specifically designed antibodies to target BBB proteins and areas/structures that are responsible for disease containing recombinant technology, there has been limited published studies available in this area. Despite a biological drug that targets the protofibrils responsible for Alzheimer's disease and prevents the progression of the disease is developed, this type of development has not emerged yet for resistant epilepsy. The development of an immunotherapy method for resistant epilepsy will not only eliminate the side effects of chemical/non-biological drugs but also will provide the targeted therapy.

Keywords: Resistant epilepsy, gold nanoparticle, biological drug, immunotherapy, BBB

Symposium 10

Neuroimaging Based Biomarker Development for Neurodegenerative Disorders

S10-1

Mental disorder and its imaging in Parkinson's disease

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Parkinson's disease (PD), which was until recently considered a pure motor disorder, it has been understood by the new millennium that the mental (cognitive-emotional-motivational) impairments are the essential components of the disease. Neural networks approach to the sensory-motor and mental functions had

a great impact on this new understanding. Network approach, which had initially been derived with analogy from neuroanatomical studies using axonal tracing methods in non-human primates, was recently made possible to study in living human brain, thanks to the development and increasing sophistication of the imaging of brain's structural connectivity by the diffusion tensor imaging (DTI) and its functional connectivity by the functional connectivity magnetic resonance imaging (fcMRI). Accumulating evidence showed that a progressive mental disorder reaching to dementia severity (malign) was almost inevitable during the entire course of the disease. Dementia is a very early, even a pre-motor phenomenon in some subtypes, such as dementia with Lewy bodies (DLB), a relatively early or mid-stage phenomenon most often in late-onset PD cases and a relatively late or end-stage phenomenon most often in young-onset PD cases. Deciphering which neuropsychological and neuroimaging patterns of mental disorder connote the relatively benign subtype (no-dementia or end-stage dementia) and which connote the relatively malign subtype (early dementia) is important in terms of the management of PD. The neuropsychological correlates of the mental disorder and alteration patterns in the neural networks affected by mental disorder in PD will be reviewed.

Keywords: Parkinson's disease, dementia, structural connectivity

S10-2

Multimodality MR imaging techniques for detecting biomarkers for diagnosis and follow-up of neurodegenerative diseases

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Magnetic resonance (MR) imaging has been commonly used in diagnosis and follow-up of neurodegenerative diseases. Multimodality MR imaging provides chemical, functional and anatomical information of the underlying tissue of interest. MR spectroscopic imaging provides noninvasive information regarding the biochemistry of the tissue. Arterial spin labeling MR imaging is used to acquire cerebral blood flow and arterial blood volume maps without the need of using contrast agents. Resting state functional MR imaging provides brain activation connectivity information during rest. Diffusion MR imaging tracks the water movement along the white matter tracts, providing diffusivity and anisotropy information of water movement. In this talk, information will be shared regarding multimodality MR imaging techniques and biomarkers of especially mild cognitive impairment in Parkinson's disease.

Acknowledgements: Some MR images that will be displayed in this talk were collected as a part of TÜBİTAK 115S219 project.

Keywords: MR spectroscopic imaging, diffusion weighted MRI, arterial spin labelling MRI, resting state functional MRI, Parkinson's disease

S10-3

Intrinsic connectivity networks in the course of neurodegenerative diseases

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The resting-state functional magnetic resonance imaging (fMRI) is a new MRI technique based on detecting spontaneous activity in the cortical and subcortical regions which are spatially different but functionally related in the absence of any task during the acquisition. Resting-state activities detected by fMRI led to definition of new term "intrinsic connectivity networks -ICN" and "Default mode network-DMN" is the first defined ICN. Impaired connectivity of DMN has been shown in the course of Alzheimer's Disease and these abnormalities appear before the symptoms as shown in studies including asymptomatic carriers of autosomal dominant mutations of familial Alzheimer's disease. Another neurodegenerative dementia, the frontotemporal demantia (FTD), is associated with hypoconnectivity of the another ICN so-called "salience network" and hypoconnectivity of this ICN is correlated with the severity of the disease. DMN is usually unimpaired or show hyperconnective pattern in FTD. In Parkinson's disease (PD) which is the second common neurodegenerative disease, there are connectivity changes especially in the sensorimotor network and striatocortical networks. These abnormalities can be shown before the appearance of clinical findings of PD in high-risk individuals carrying the GBA gene mutation. In the symptomatic phase, connectivity changes in the ICNs are associated with clinical signs and cognitive functions. In this talk, focus will be on impairments of ICNs in the presymptomatic stage as well as association of ICNs with clinical and cognitive parameters in the symptomatic stage of neurodegenerative diseases.

Panels

(PS-1 — PS-4)

Panel 1

Charles Bonnet Syndrome: From Perception to Conciousness

PS1-1

Neuron and conciousness

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Neural Correlates of consciousness, a new biological research area, Global Neuronal Workspace, one of the most advanced models in this field, will be discussed and reinterpreted.

Keywords: Consciousness, neural correlates of consciousness, global neuronal workspace

PS1-2

A discussion on the neural correlates of perceptual awareness using Charles Bonnet syndrome as a model

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Charles Bonnet Syndrome (CBS) is a rare neurological condition, where a damage to visual pathway triggers visual hallucinations, with other sensory modalities remaining intact. Hallucinations related to CBS may be as complex as images of people, faces, animals, plants and caricature-like figures, as well as simple percepts such as geometrical shapes, grids and light patterns. Currently, the most widely accepted theory in relation to CBS is the sensory deprivation theory. According to the sensory deprivation theory, loss of visual input to the brain due to an ocular pathology leads to spontaneous neural discharges, changing the excitability in the visual association cortex. How these changes in the neurophysiology are transformed into the perceptual experiences of hallucinations, however, is still an open question yet to be answered. Here, I will present a discussion on the neural correlates of perceptual awareness using hallucinations triggered by different disorders such as schizophrenia or intracranial tumors, as well as Charles Bonnet Syndrome as models.

Keywords: Visual hallucinations, perceptual awareness, phenomenal experience

PS1-3

Charles Bonnet syndrome: an approach to pathophysiology of CBS in the light of clinical, electrophysiologcal and neuroimaging data

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Charles Bonnet syndrome (CBS) defines the emerging complex visual hallucinations in the patients that have severe sight defecit without any sign of cognitive decline. Although, some theories are suggested to explain the pathophyiology of CBS, there is none that can clarify the exact mechanism of VH in CBS. "Releasing Theory" is the commonly accepted as the most promising one, which suggests that CBS is caused by the deafferentation of the visual cortex due to the damage to the visual pathways. On the one hand, this deafferentation causes the depression of the primary visual pathways, on the other hand, it causes especially a hyperexcitability in the visual assosiation fields which is called "Cortical Release Phenomenon". Collerton et al. suggests a common mechanism to series of conditions that causes VH. According to their theory "Perception and Attention Deficit (PAD) Model"; a combination of perception deficit (bottom-up) and the defecit of canalizing attention (top-down) is another way to explain the underlying mechanism. During this speech, the possible underlying neurobiological mechanisms of CBS will be argued in the frame of case reports and our past studies.

Keywords: Charles Bonnet syndrome, electrophisiology, neurophyscometry, functional imaging

Panel 2

Stress: If It Don't Kill You It Makes You Stronger

PS2-1

Stress, learning and learned stress

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In today's world, long-term cognitive stress is more prominent rather than the classical stress that arises from the physical danger that threatens the life of the individual. As a result, stress is generally an expectation or perception of expectation of performance that is more likely than the level that the person is accustomed to and perhaps not possible to achieve. This talk will focus on the structures of nerve cells and neural networks, their working dynamics, and their responses to solved and unresolved situations. It will be argued how learning can affect changes in neural networks, the effect of memory on the responses generated during recurrent and emerging situations. Neural networks and nervous system's general working principles and the positive feedback mechanisms and its results of their control and effects on other systems with repetitive and prolonged stress conditions will be evaluated.

Keywords: Neural networks, stress, learning

PS2-2

Evolutionary stress *vs* human adaptation

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Neoteny had been used as a concept for the first time by Kollman to express the preservation of infantile characteristics in adulthood. Human being, evolved by the deceleration of development of his primate ancestors, has preserved his ancestors' infantile characteristics: technically speaking "neoteny" ("preserving the youth"). Homo sapiens is essentially a neotenic sprecies; a sexually mature but an infantile monkey, he is rather like a chimpanzee who never grows up to adulthood. Neoteny has critical function in human adaptation. Neotenic gains help to improve the learning capacities of human in active interaction with his natural and social environment. Human being is basically a cultural animal who has far reaching learning capacity. He has not evolved to fit a specific environment; he is not strong or swift to act. He has an advatageous brain which has extraordinary cognitive skills. In his evolutionary period, he succeeded to prolong his infantile period to preserve his learning ability and has remained as an eternal child in some respects.

Keywords: Evolution, neoteny, adaptation

PS2-3

Obesity, inflammation, depression

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Shuttle box experiment demonstrated that rats which could not escape from electrical stimulus have developed biological, behavioral changes and learned helplessness resulting in impaired immune and cardiovascular system. In the same experiment when a second rat was placed in the shuttle box these two rats attacked each other and no behavioral or biological harm occurred. This is a very fine example of how the perception and the coping mechanisms of stress, rather than its physical intensity determines its consequences. Publications in the medical literature have shown that after a stimulus is perceived as a stressor two different coping patterns arise: the active pattern -known as "fight or flight" response- or the passive pattern. In case of the active response sympathetic adrenal medullary system is being activated which results in increases in noradrenaline, adrenaline, gonadotropins, testosterone, oxytocin, prolactin, beta-endorphin, renin, fatty acids and glycogenolysis. In case of the passive response pituitary-adrenal cortical system is being activated with increases in adrenocorticotropic hormone (ACTH), cortisol, pepsin and decrease in gonadotropin and testosterone levels. Chronic increases in catecholamines and cortisol lead to an enhanced inflammatory response which may result in insulin resistance, visceral obesity, high levels of triglycerides, low levels of high-density lipoprotein cholesterol (HDL) as well as hypertension. These changes in different parameters are also associated with atherosclerosis and increase cardiovascular morbidity and mortality. Another consequence of psychological stress is sickness behavior which includes lethargy, sleep disturbance, and depression. Stress should be conceived as the adaptive mechanism in response to any demand for change and not as the psychological response of the organism to unusual external stimuli.

Keywords: Stress pathways, inflammatory response, atherosclerosis, obesity, depression.

Panel 3
Molecular Mechanisms of Neurodegeneration

PS3-1

Genetic and biochemical aspects of vitamin D background in Alzheimer's disease

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Alzheimer's disease (AD) is progressive neurodegenerative disorder seen mostly in elderly population. AD researches focused on either neurochemical disruptions, genetic studies, or the pathological hallmarks. Not much has been done to establish a novel perspective that encompasses all three approaches in order to overcome the current barriers in AD research and determine the cause of AD and an ultimate treatment. Recent studies have reported significantly low levels of serum 25(OH)D in individuals suffering from AD, PD, mood disorders and cognitive decline. Within last fifteen years, the genes that are related to vitamin D metabolism and transport and the receptors involved in vitamin D action became a subject to be focused on in the genetic background of AD and neurodegeneration. This speech aims to define how vitamin D perspective encompass all aspects of AD research and contributes to the genetic, molecular and biochemical background of the disease.

Keywords: Alzheimer's disease, Parkinson's disease, vitamin D deficiency, vitamin D receptor (VDR), biomarker

PS3-2

Molecular aspects of vitamin D related mechanisms in amyloid pathology and neurodegeneration

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The disruption of vitamin D pathways via either vitamin D receptor (VDR and Pdia3) by siRNAs, a tool used as post transcriptional gene silencing, regardless of whether it was from the presence of A„ resulted in the induction of voltage sensitive calcium channels A1C, A1D, and iNOS and attenuated NGF. Each of these events known to has the potential to induce Aβ accumu-

lation and neurodegeneration. Based on these results, we suggest that the disruption of vitamin D pathway-related mechanisms may trigger neurodegeneration and/or Aβ production. To answer this question, we focused on the effects of disrupted VDR/Pdia3 pathways and/or 1.25(OH)2D3 treatments on the components of secretase complexes and A, production. Our data indicated that vitamin D and/or its receptors regulate the expression of certain proteins involved in secretases including Presenilin 1, Presenilin 2, NICASTRIN, ADAM10, BACE1, and the APP substrate in either VDR or Pdia3 or double silenced neurons or vitamin D-treated neurons, yet the regulation is time, concentration and receptor dependent. We also demonstrated the induction of intracellular Aβ 1–42 production in VDR or Pdia3 or double silenced neurons. In accordance with these results, 1.25(OH)2D3 treatments attenuated intracellular Aβ 1–42 production and secretion. After these findings we thought that the relation between VDR and amyloid pathogenesis is complex and all of the regulative properties of VDR over the production of A, cannot be explained solely with its transcriptional regulation. Given that we hypothesized that neuronal plasma membrane surface might involve VDR in close proximity with APP and secretase complexes. We determined the localization of VDR on the neuronal plasma membranes. We also demonstrated the co-localization of VDR and APP or ADAM10 or Nicastrin and limited co-localization of VDR and PS1. This presentation will summarize the role of vitamin D and its related mechanisms in neurodegeneration and amyloid pathogenesis.

Keywords: Neurodegeneration, vitamin D deficiency, VDR, Pdia3, amyloid beta

PS3-3

The role of antibodies in neurodegeneration

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A group of antibodies participates in the physiopathology of disorders characterized with neurodegeneration. In progressive stages of multiple sclerosis, detection of meningeal B cell follicles and their association with cortical atrophy, deterioration of cognitive parameters, enhancement of disability and intrathecal antibody production have suggested that antibody-dependent mechanisms may culminate in neurodegeneration. In this context, neurofilament, neurofascin and contactin antibodies have been shown to induce neurodegenerative processes in animal models. Among these antibodies, contactin antibodies dissociate axon and myelin of the nerve thus exposing ion channels, increase the energy demand of neurons during nerve conduction and subsequently cause mitochondrial dysfunction. In the animal model of neuro-Behçet's disease, another inflammatory central nervous system disease frequently encountered in our country, serum IgGs have been shown to deteriorate motor functions and induce neuronal apoptosis. Otoimmune encephalitis is a usually acute-onset, monophasic and generally reversible inflammatory disease characterized with neurological symptoms generated by antibodies directed against neuronal membrane proteins. Nevertheless, some of the autoimmune encephalitis patients may develop permanent neuronal loss, hippocampal sclerosis and cognitive-affective disorders. Autoimmune encephalitis antibodies LGI1 and IgLON5 have recently been reported to induce neuronal death. NMDA receptor and voltage gated K channel antibodies have been detected in chronic cyptogenic epilepsy patients with hippocampal sclerosis and mononuclear cellular infiltration has been shown in resected medial temporal lobe specimens of these patients. Moreover, expression of target ion channels has been demonstrated to be reduced in brain samples of these patients and ion channel expression levels have been shown to be correlated with the intensity of cellular loss and cellular infiltration. In conclusion, antibodies have been recently recognized to generate neurodegenerative processes using several different mechanisms. Identification of precise mechanisms underlying these processes may culminate in development of novel methods that can be used in management and treatment of neurodegenerative diseases.

Keywords: Neurodegeneration, antibody, apoptosis, multiple sclerosis, autoimmunity

Panel 4

Zebrafish model for Neural Aging, Cognitive and Perceptual Processes

PS4-1

Zebrafish – a model organism to study neurobiology underlying brain aging

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Recently, the zebrafish has become a popular model to study biological changes in the aging brain and use potential interventions to alter their course due to the large amount of molecular tools to use in this organism. Similar to other mammals, zebrafish exhibit advanced behavioral properties like spatial memory and social behaviors (Lieschke et al., 2007; Kishi et al., 2009), as well as an integrated nervous system, proposed to contain homologous brain structures to those found in humans, like the hippocampus (Wulliman et al., 1996; Friedrich et al., 2010, Ganz et al., 2015). Moreover, like humans, zebrafish exhibit age-related declines in hippocampal-dependent spatial memory (Yu et al., 2006). Evidence suggests that neuronal (Rapp and Gallagher, 1996) and significant synapse loss (Poe et al., 2001; Shi et al., 2007; Newton et al., 2008) in the hippocampus is not occurring, and therefore, does not contribute to potential cognitive changes with aging. Rather subtle cellular and synaptic alterations appear to underlie cognitive declines. However, only a few studies have focused on the neurobiological consequences of aging in the zebrafish brain. In this presentation, I will review what is known about the neurobiological consequences of brain aging in the

human hippocampus and then I will relate these findings to what is known about some of the neurobiological changes in the rodent. Finally, I will turn to the research that we have done in understanding the neurobiological changes in the zebrafish brain and the use of a potential decelerated aging model in which the acetylcholine levels are overexpressed. Taken together, these data expand our knowledge of normal aging in zebrafish, as well as further establish this model as an appropriate one for examining human brain aging.

Support: This was supported by an Installation Grant from the European Molecular Biology Organization and TUBITAK (215S701).

Keywords: Cellular senescence, synapses, gene expression, microarray, synaptic proteins

PS4-2

Zebrafish as a model for perceptual and cognitive performance

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Zebrafish have a rich repertoire of behaviors which depend on perceptual and cognitive processes (Meshalkina et al., 2017). As in other vertebrates, zebrafish have basic sensory systems and pathways for low-level sensory processing. For example, the basic components and pathways of zebrafish visual system and the processing hierarchy are similar to those commonly found in other species (Bilotta and Saszik, 2001). Visual acuity and contrast sensitivity function have been found to be qualitatively similar to those of humans (Tappeiner et al., 2012). More importantly, it has been observed that zebrafish experience motion adaptations and illusions which are even thought to be seen only by humans (e.g., Gori et al., 2014). Accumulating evidence also indicates that zebrafish can be a promising model of cognitive functioning. They have both simple and relatively complex forms of learning, and also display good performance on cognitive tasks that mostly rely on short-term and long-term memory (Blaser and Vira, 2014; Gerlai, 2016). In this talk, I will first review previous and recent behavioral studies on perceptual and cognitive performance of zebrafish. I will also discuss how similar behavioral studies combined with molecular testing can provide novel information on the functional links between perception and key synaptic targets. At the last part, I will present our recent research efforts along this direction. Using our initial measurements on motion perception, I will provide specific examples on the advantages of such approach for neural aging studies.

Support: This work was supported by The Scientific and Technological Research Council of Turkey (TUBITAK Project Number: 215S701).

Keywords: Perception, cognition, behavior, neural aging

PS4-3

Cholinergic modulations of synaptic protein levels in male and female aged zebrafish

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No significant neuronal or synaptic loss is observed during normal-aging, yet subtle molecular changes in synapses and hypofunction in cholinergic system are observed. The aim of this study was to investigate age-related changes in synaptic integrity of the mutant cholinergic system zebrafish line (ache sb55/+) which is characterized with higher levels of acetylcholine due to low levels of the acetylcholinesterase (Behra et al., 2002). Another focus was to determine if sexually dimorphic patterns and region-specific vulnerabilities in age-related changes exist in this model. For the analysis of whole-brain, 6 wildtype (WT) and 6 ache sb55/+ (ache) male and female zebrafish (30 mo.) were used. Another set of 8 young (8-10 mo.) and 8 old (21-35 mo.) WT and ache male and female zebrafish were used for micro-dissection to isolate optic-tectum (TeO). Proteins were isolated and samples were subjected to Western blot analysis. Post-synaptic density-95 (PSD95); gephyrin (GEP); synaptophysin (SYP) and gamma-Aminobutyric acid-alpha-1(GABRA1) were analyzed as markers of pre-post and excitatory-inhibitory synaptic integrity. Whole-brain analyses revealed significant increases in GEP ($F(1.8)=13.890$, $p=0.006$) and SYP ($F(1.8)=38.419$, $p<0.0005$) levels of ache compared to WT, and more interestingly increases in SYP was significantly driven by ache females ($F(1.8)=29.401$, $p=0.001$). Region-specific analyses of the TeO, indicated an opposite pattern in GEP expression, with age-related decreases observed in both WT and ache ($F(1.24)=26.778$, $p<.0005$), but similarly this decrease was prominent in old ache females ($F(1.24)=5.317$, $p=.030$). Taken together, our findings support the notion that manipulations of cholinergic system may alter the course of synaptic proteins changes during normal-aging and interestingly the patterns are gender-dependent. These neurobiological changes may underlie differences in synaptic communication, and hence may alter neural processing in the aging brain.

Support: This work is supported by an EMBO Installation Grant and TUBITAK (215S701).

Keywords: Acetylcholine, aging, synaptic-proteins, gender, acetylcholinesterase

PS4-4

A systematic investigation of motion direction discrimination in aged zebrafish

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Older adults deteriorate in different aspects of vision such as motion perception (Owsley, 2011). Zebrafish have gained popularity as a model to study aging (Arslan-Ergul et al., 2013), and it has been suggested that they have similar motion systems as in humans because they detect first-order and second-¬order motions (Orger et al., 2000). Using this animal model, we assessed contrast and spatial frequency dependency of first- and second-order motion direction discrimination of young (7–10 months) and old (24–40 months) wild-type zebrafish by examining their optomotor responses (OMR). The first-order motion stimuli were drifting sine-wave gratings with varying contrasts (1–75%) and spatial frequencies (0.01–0.8 c/deg). The second-order motion stimuli consisted of flicker-frequency-modulated random dots and the flicker-frequency was defined by a drifting square-wave with the same spatial frequencies as those of the first-order motion. The normalized OMR to these motion types was computed. The results showed a significant main effect of contrast ($F(5.135)= 2.44$, $p<0.05$) in OMR to first-order motion. No significant effects of age or spatial frequency were found for either type of motion, $ps > 0.05$. Follow-up planned tests revealed that spatial frequency ($F(5.70)= 2.72$, $p=0.047$) and contrast ($F(5.70)= 4.663$, $p=0.001$) significantly affected OMR of young zebrafish to first-order motion. However, for the old group spatial frequency and contrast were not significant, $ps>0.05$. Our findings suggest that contrast alters the discrimination of first-order motion direction. Specifically in young adults, both spatial frequency and contrast characteristics of the first-order motion change the perception of motion direction while older adults' performance is not affected by these properties. These results are in line with the view that processing of visual features deteriorates throughout aging.

Support: This work was supported by The Scientific and Technological Research Council of Turkey (TUBITAK Project Number: 215S701).

Keywords: Motion perception, aging, zebrafish

Oral Presentations

(O-01 — O-54)

O-01

Investigation of brain white matter fractional anisotropy in children with and without dyscalculia

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Objective: The aim of this study is to investigate the structural connectivity in children with mathematical-learning-disability (dyscalculia) and normally-developing-peers.

Methods: Firstly, we tested 1944 third-grade students (7-9,5 years) in elementary schools with Mathematics and Arithmetic-Performance tests, and Raven Progressive Matrices test for fluid intelligence. Regarding screening results, children with normal-intelligence were assigned to dyscalculia (lowest 25th-percentile) and typically developing (between 35th-75th-percentiles) groups. Secondly, determined children were tested two-years later with mathematics-tests and Weschler Intelligence Scale for Children, and evaluated by child-psychiatrists. After co-morbidities were eliminated, dyscalculia and typically developing groups were precisely identified. Then, we invited children for MRI-scan and required them to practice in mock-scanner before real MRI-scanning. Lastly, we acquired DTI (Diffusion-Tensor-Imaging) data via Siemens 3Tesla-scanner using 16-channel-head-coil. Images were sampled along 60-different-encoding-directions. There were 70-images in total, and b-value for the first 10-images was 0s/mm2 and b=700s/mm^2 for other 60-images for each of 60-directions. The thicknes of transversal-slices (74slices) was 1.55mm and paralell to Anterior-to-Posterior-plane. TR:9.506s, TE:85ms, FOV:198mm, voxel size 1.5×1.5×1.6 mm. Duration was about 11 min for each child and children watched cartoons which they wanted during scanning. We obtained 11 dyscalculics' and 16 control children' usable data.

Results: We used FSL-software for DTI analyses. Initially, head movements and eddy-currents were corrected, and then fractional-anisotropy (FA) maps of participants were created. After that, TBSS (Tract-Based-Spatial-Statistics) analysis was performed on FA maps to investigate groups' whole-brain voxel-wise comparisons with TFCE (Threshold-free-cluster-enhancement) method (Smith et al., 2006)*. In Controls>Dyscalculics contrast, FA values for some particular white matter connections such that left-inferior fronto-occipital fasciculus, left-right anterior-thalamic-radiations and left cortico-spinal tract were significantly higher in typically developing children than dyscalculics ($p<.05$, FWE-corrected). In Dyscalculics>Controls contrast, FA values in dyscalculics were not significantly different from controls ($p>.05$, FWE-corrected).

Conclusion: The findings suggest that low white matter integrity and/or structural connectivity especially in left brain areas might be related to mathematical-learning-disability in children. This study was supported by The-Scientific-and-Technological-Research-Council-of-Turkey under the-project-code-214S069.
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Keywords: Dyscalculia (mathematical learning disability), magnetic resonance imaging, diffusion tensor imaging, brain imaging, connectivity

O-02

Neural mechanisms of number sense in typically developing children and children with dyscalculia

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Objective: Dyscalculia is a learning disability affecting the acquisition of arithmetical skills in children with normal intelligence and age-appropriate education. Neural basis of dyscalculia is still unclear. In this study, number processing in children with dyscalculia and typically developing children were examined via functional magnetic resonance imaging (fMRI).

Methods: Firstly, we tested 1944 third-grade students (7–9.5 years) in elementary schools with Mathematics-and-Arithmetic-Performance-Tests, and Raven-Progressive-Matrices-Test for intelligence. Secondly, children with low and normal mathematical performance was determined and tested two years later with mathematics tests, Weschler-Intelligence-Scale-for-Children, and evaluated by child-psychiatrist. After co-morbidities were eliminated, dyscalculia (n=12, mean age:11.25) and control (n=15, mean age:11.26) groups were identified. Participants were asked to perform a numerosity comparison paradigm while undergoing fMRI. Paradigm consists of two types of number condition and two difficulty levels. Imaging data was analyzed with repeated-measures ANOVA with group (dyscalculia/control), number (symbol/dot) and difficulty (0.5/0.7 ratio) as factors via MATLAB toolbox SPM12. Voxels presenting $p<0.001$ and

belonging to clusters of at least 100 voxels were considered activated.

Results: The main effect of number showed bilateral intraparietal sulcus (IPS), dorsolateral prefrontal cortex (DLPFC), supplementary motor area and occipitotemporal cortex activations. The main effect of difficulty activated bilateral insular cortex (IC), anterior cingulate cortex (AIC), IPS and right DLPFC. For the main effect of group orbitofrontal cortex was activated. There was no significant interaction effect.

Conclusion: The frontoparietal network activation during number task is compatible with literature. IC and AIC activation were related to task difficulty in the previous reports. Higher frontal activity in dyscalculia group could be related to the requirement of more cognitive control, which might be the result of a deficiency of parietal brain regions related number sense mechanisms. This study was supported by TUBITAK under the project code 214S069.

Keywords: Dyscalculia, fMRI, frontoparietal network, number sense

O-03

Correlations between resting-state brain oscillations and behavior under time constraints

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Objective: Human neuronal oscillations exhibit long-range temporal correlations (LRTCs) that are closely related with behavioral outcome measures. In the Libet task, subjects perform a single abrupt movement, spontaneously, at a time of their own choosing. They then report the time of their conscious intention to act (W-time) using a rotating clock dial. In this study, we hypothesized that, with its close relationship with behavior, LRTCs could explain the inter-subject variability in response time (RT) and W-time.

Methods: We recorded magnetoencephalogram (MEG) and electroencephalogram (EEG) data from 19 subjects. Subjects were doing a self-initiated movement task and reporting their W-time in five different time limit conditions (2, 3, 5, 8 s and Inf) using a rotating clock dial. There were 40 trials per condition. Subjects also had a 5 min. resting-state recording. In order to estimate the LRTCs, we used detrended fluctuation analysis. Then we calculated a Spearman correlation between the behavioral outcome measures and the scaling exponents (·) of neuronal LRTCs in the resting state data.

Results: We found negative correlations between · of resting-state LRTCs in the delta band and median RT when the time limit was 5 s (p=0.0024), 8 s (p=0.0108) or Inf (p=0.0111). We also found a negative correlation in the low-alpha (p=0.0054) band between · of resting-state LRTCs and std of W-time in the infinity condition. These results were found only in EEG channels.

Conclusion: The results show that people who respond earlier have higher scaling coefficients of LRTCs in their resting-state delta oscillations if they are not tightly limited by time. Moreover, people who report their W-time more precisely have higher scaling coefficients of LRTCs in their resting-state low-alpha oscillations if they are not limited by time constraints. The study has been funded by the ERC Horizon 2020 Starting Grant: ACTINIT.

Keywords: Electroencephalogram, long-range temporal correlations, magnetoencephalogram, response time, self-initiated movement

O-04

The role of theta oscillations in the lexical-semantic processing in Turkish: theta-phase locking

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Objective: The aim of this study is to investigate the role of event related theta oscillations (ERO) in the lexical-semantic processing in Turkish.

Methods: The study sample consisted of 31 healthy, native Turkish speakers, aged between 18–30. Each subject fulfilled a lexical decision task, which was comprised of 240 trials. Two words which the first one was prime and the second one was target, were presented successively to participants for semantic priming and participants were asked to decide whether the target was a real word or not. One hundred twenty of target words were real Turkish words which half were semantically related with prime, half were unrelated and 120 target words were pseudo-words in the paradigm. The EEG was recorded according to the international 10–20 system. EEG signal was segmented into epochs of 3 sec and time locked EEG trials were decomposed by wavelet transform into theta (4-6 Hz) frequency range. Theta inter-trial coherence (ITC) values which were were normalized with respect to the pre-stimulus window from -250-150 msec were analyzed, within the time window 350-500 ms by using repeated measure of ANOVA, within group factors CONDITION (related, unrelated, pseudo-word) X LATERALIZATION (left, midline, right) X REGION OF INTEREST (frontal, central, parietal, occipital).

Results: Theta ITC values revealed a significant difference between conditions [F(2.60)=6.658 p=0.002]. Post-hoc test indi-

cated that theta ITC values were higher for pseudo-words and semantically unrelated targets than semantically related ones. In statistical analysis, there were interaction effects for REGION OF INTEREST [F(1.583, 47.493)=12.382 p=0.000] and LATERALIZATION [F(1.532, 45.950)=3.668 p=0.044]. The highest ITC values were measured from occipital regions and right side.

Conclusion: Theta ERO phase locking is sensitive to semantic priming effect. This research has been supported by Ankara University Scientific Research Projects Coordination Unit. Project Number:16L02000001

Keywords: Event related theta oscillations, inter-trial phase coherence, lexical decision, lexical-semantic processing, priming effect

O-05

Emotion modelling based on multivariate adaptive orthogonal signal decomposition

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Objective: Empirical Mode Decomposition (EMD) provides an adaptive signal processing tool and its multivariate extension is useful to model multi-channel signals. Recently, EMD and multivariate EMD (MEMD) have successfully been applied to solve different signal processing problems. Electroencephalographic (EEG) signals are often employed in order to understand the emotion recognition concepts for human-machine interaction. In this paper, an emotion recognition model is presented via EEG signal decomposing by utilizing MEMD. The Intrinsic Mode Functions (IMFs) extracted from MEMD algorithm are quasi-orthogonal. Hence the Gram-Schmidt Orthogonalization method is applied to the extracted IMFs. The quantity of orthogonal components detects the quantity of modes which is used in the second step of the proposed method where Empirical Wavelet transform is used to measure different dynamical features of the IMFs. Our aim is to evaluate the emotional states according to the selected frontal lobe electrode on the calculated features.

Methods: Multivariate Empirical Mode Decomposition, Empirical Wavelet Transform, Gram-Schmidt Orthogonalization, Complex Tree Classifier

Results: The emotional states are classified as high-low arousal, valence and dominance with 72.2%, 67.2%, and 70.3 % classification performance respectively.

Conclusion: For the selected frontal lobe(Fp2) electrode, the most successful result belongs to high-low arousal classification performance.

Keywords: Emotion recognition, multivariate empirical mode decomposition, empirical wavelet transform, gram-schmidt orthogonalization

O-06

The effects of the working memory capacity on transcranial direct current stimulation benefit

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Objective: Transcranial Direct Current Stimulation (tDCS) is a neurostimulation technique that has been used for improving the working memory (WM) performance. Recently, the use of this technique has increased and many studies have been investigating the most effective use for improving cognition and relieving psychiatric symptoms. While conventional tDCS creates a broader excitement or inhibition through the cortex, a more recently developed high-definition (HD) tDCS can provide more locality. As a result, this technique has been advertised as a more effective way to deliver neurostimulation. Previously, we showed that the beneficial effects of tDCS depend on group differences such as working memory capacity (WMC). In the current study, we aim to investigate such effects both conventional tDCS and HD-tDCS.

Methods: We measured the WMC of 48 young adults and divided them into high and low capacity groups by the median scores. We conducted 2 WM experiments that are each testing half of these participants, and compared tDCS, HD-tDCS and control stimulation performances. We analyzed the accuracy and response times of the WM tasks. We placed the anode electrode on either right (Experiment 1) or left (Experiment 2) posterior parietal cortex and the cathode electrode on the contralateral cheek. The stimulation was given at 2 mA and for 20 minutes.

Results: 2-way ANOVA with factors of stimulation (tDCS x HD-tDCS x control) and WMC (high x low) results yielded not significant main effects in both experiments. However, the interaction was significant (p=.025) in Experiment 1, while it reached borderline significance (p=.07) in Experiment 2. The response time results did not support the interaction effects.

Conclusion: These results extend our previous results on how the effects of tDCS are influenced by group differences to HD-tDCS. Such differential accounts of group differences should be noted for the effective use of neurostimulation techniques.

Keywords: Electrical stimulation, working memory, attention, group differences

O-07

Decrease in mesocortical dopaminergic neurons and fibers is associated with ADHD

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Objective: Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized with attention

deficit, locomotor hyperactivity and impulsivity. Although no single hypothesis is accepted in the etiology of ADHD, research suggests that all symptoms in ADHD are resulted from the dysfunction of different synaptic circuits in the prefrontal cortex. Based on the hypothesis that this dysfunction is due to the reduction of dopaminergic neurons and fibers, this study aims to investigate whether there is a decrease in neuron and fiber density of the dopaminergic mesocortical pathway.

Methods: Five SHR juvenile male rats as animal models of ADHD and three WKY juvenile male rats as control were used in this study. TH immunohistochemistry was used to identify dopaminergic neurons in VTA and dopaminergic fibers in mPFC, dopamine beta hydroxylase (DBH) immunohistochemistry was used to identify noradrenergic fibers. Quantification of density of TH-immunolabeled (TH-positive) DAergic fibers was performed and percentage of TH (+) Daergic fibers in the PrL subregion of mPFC was evaluated. We also quantified the TH (+) DAergic neurons density in the VTA. Data were analyzed with independent sample t test and Mann Whitney U test.

Results: We observed statistically significant decreasing TH (+) neurons in the VTA rats (p=0.04) and TH (+) fibers in the mPFC (p=0.02) of the SHRs compared to the WKY. There was no significant difference in the percentage of TH positive dopaminergic fibers in mPFC between WKY and SHR (p=0.7).

Conclusion: There was a decrease in mesocortical dopaminergic neurons and fibers in juvenile SHRs used as an animal model of ADHD. We observed that the percentage of TH (+) dopaminergic fibers in mPFC did not change. These findings indicate that noradrenergic fibers as well as dopaminergic fibers decrease in ADHD.This study was supported by TUBITAK (2214/A) international doctoral research fellowship programme.

Keywords: Attention-deficit/hyperactivity disorders, mesocortical pathway, dopamine, prefrontal cortex, ventral tegmental area

O-08

Differentiation of NSC-34 cell line on graphene oxide sheets

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Objective: Consiedered as one of the most attractive nanomaterial s, the biomedical applications of graphene and graphene oxide to the nervous system is an ideal breakthrough model, because neural cells are electro-active. NSC-34 is a hybrid cell line, produced by fusion of motor neuron enriched, embryonic mouse spinal cord cells with mouse neuroblastoma cells.The aim of this work was to investigate the differentiation of NSC-34 cells on graphene oxide sheets using PCR analysis.

Methods: NSC-34 cells were grown in DMEM high glucose containing 10% fetal bovine serum. Graphene oxide powder was coated onto glass slides as a thin film. NSC-34 cells were cultured on graphene oxide sheets. Cultivated cells on polystyrene were used as the control group. The cells were differentiated in DMEM F12 containing 1% fetal bovine serum and we investigated the mechanism of the differentiation with different markers using PCR analysis. We also performed Hb9 immunostaining.

Results: According to PCR results, NSC-34 cells were better differentiated on GO films compared to polystyrene coated slides. Hb9 immunostaining and PCR analysis also indicated more neurite formation on GO films.

Conclusion: GO can be a potential nanomaterial that can be used for neuronal differentiation.

Keywords: Differentiation, graphene oxide, NSC-34 cell line, PCR

O-09

FTIR imaging of spinal cord injury treated with levetiracetam and magnetic field

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Objective: Different approaches have been proposed for the treatment of spinal cord injury (SCI). However, only methylprednizolone is routinely used in clinics. Recent reports indicated that usage of antiepileptics and magnetic field separately promotes neuroregenerative activities and thus were introduced into the treatment arsenal against neurological disorders. This study extends the current efforts and aims to investigate whether combination of magnetic field and levetiracetam therapy would benefit the recovery from SCI.

Methods: Adult Wistar rats were subjected to laminectomy (L) and contusion-type SCI at T10 level. The rats were then treated with levetiracetam (LEV, 100mg/kg/day) and magnetic field (MF, 50 Hz, 1 mT, 30 min/day) separately or in combination (LEV&MF) for 21 days. Functional behavior was assessed using BBB scoring. Spinal cord sections were analyzed using Fourier transform infrared (FTIR) imaging to evaluate the structural alterations in white (WM) and grey matters (GM). The results were compared with those of methlyprednizolone administration (a single standard dose, 30mg/kg).

Results: SCI initially produced functional deficits in all rats. The applied treatments in general improved the recovery, but prominently by methylprednizolone. SCI decreased the amount of phosphate and ester containing lipids, especially in WM. Injury also increased the unsaturation and unsaturated/saturated ratio (unsaturation index) of lipids, suggesting an increase in the end products of lipid peroxidation. LEV&MF elevated the ester containing lipids in WM, and also decreased the unsaturation and increased the ethyl group amounts in lipids, demonstrating the power of treatment in prevention of lipid peroxidation. In these regards, however, methylprednizolone did not produce consistent performance.

Conclusion: The combined strategy of levetiracetam treatment in the presence of magnetic field appears to be effective in restoring the SCI-induced functional loss and alterations in the spinal cord lipid structure. This study was funded by Scientific Research Council of Adnan Menderes University (TPF-17041).

Keywords: Spinal cord injury, methylprednizolone, levetiracetam, low frequency magnetic field, FTIR imaging

O-10

Investigation of the neuroprotective effect of mildronate in the rat model of traumatic brain injury

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Objective: Oxidative stress following traumatic brain injury (TBI) leads to further deterioration of brain damage. Mildronate, known for its vasodilator and anticonvulsant effects, has been shown to be useful in a variety of experimental models and ischemic diseases. In this study, it was aimed to investigate possible antioxidant and neuroprotective effects of mildronate in a rat TBI model.

Methods: Under ketamine anesthesia, TBI (n=20) was induced by dropping a metal weight (300 g) from a height of 70 cm on the skull of male Wistar albino rats. Half of the rats was treated intraperitoneally with vehicle, while the other half was treated with mildronate (100 mg/kg) immediately after TBI. Control group (n=8) was not exposed to any trauma. Twenty-four hours after TBI, transcardial paraformaldehyde perfusion was performed and brain injury was graded histopathologically following hematoxylin-eosin staining. Activities of myeloperoxidase (MPO) -marker of neutrophil infiltration-, apoptosis-marker caspase-3, antioxidant superoxide dismutase (SOD) and catalase (CAT), and levels of luminol- and lucigenin-enhanced chemiluminescence (CL) were measured in brain tissues. The data were evaluated by one-way ANOVA.

Results: In the mildronate-treated group, the damage in the cerebral cortex that has occurred due to TBI was lighter compared to that of the vehicle-treated TBI group. Antioxidant SOD activity, which was found to be decreased in the brain tissues of the vehicle-treated TBI group ($p<0.01$), was increased in the group that has received mildronate treatment ($p<0.05$). Higher levels of CL, increased MPO and caspase-3 activities ($p<0.01$-0.001) in the vehicle-treated TBI group were found to be suppressed in the mildronate-treated group ($p<0.05$–0.001).

Conclusion: Suppression of oxidative damage and apoptosis in brain tissues of rats in mildronate-treated TBI group, and alleviation of brain damage by stimulating antioxidant systems suggest that mildronate should be further evaluated for its possible therapeutic effect in traumatic brain injury.

Keywords: Antiapoptotic effect, diffuse brain injury, mildronate, neuroprotection

O-11

Metfomin decreases degeneration of dopaminergic neurons induced by rotenone

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Objective: Parkinson's disease (PD) is a common neurodegenerative disorder characterized by motor symptoms including tremor, rigidity and bradykinesia. Aggregation of misfolded alpha-synuclein oligomers in Lewy bodies is a patognomonic finding for PD. Therefore, prevention of abnormal handling of alpha-synuclein is suggested as the most effective disease modifying approach for PD. Accumulating evidence suggests that the risk of PD is higher in patients with type 2 diabetes those using metformin. In this study, we investigated the effect of metformin administration on the expression of tyrosine hydroxilase and alpha-synuclein in substantia nigra, by using in a presymptomatic in vivo model of PD induced by rotenone.

Methods: In vivo studies were performed using 8–10 weeks male C57BL/6 mice. Animals were divided into four different groups consisting of (i) vehicle, dimethylsulfoxide:glyceryl trioctanoate, 1:50 (v/v), 0.1 ml/kg/day; (2) metformin, 300 mg/kg/day; (3) rotenone, 2.5 mg/kg/day; (4) metformin and rotenone (300 mg/kg/day, 2.5 mg/kg/day, respectively). Mice were intraperitoneally injected with for 10 days. After drug treatment, behavioral tests (locomotor activity and rotarod) were performed. Tyrosine hydroxylase and alpha-synuclein expression in substantia nigrae were measured by immunohistochemical analysis.

Results: Performances on rotarod (10 rpm, $p=0.079$; 20 rpm, $p=0.515$; 30 rpm, $p=0.944$) and locomotor activity tests (ambulatory, $p=0.647$; vertical, $p=0.151$; horizontal, $p=0.708$; total distance, $p=0.721$; total locomotor activity, $p=0.674$) were not significantly different between the groups. The immunoreactivity for tyrosine hydroxylase decreased by rotenone treatment, while it remains unchanged by vehicle, metformin and, rotenone-metformin treatments. In addition, alpha-synuclein expressions was increased by rotenone group compared to vehicle, metformin and, rotenone-metformin groups.

Conclusion: The results of the present study indicated that metformin may have protective effects on dopaminergic neurons in rotenone-induced presymptomatic model of PD. The underlying mechanism of neuroprotective effect may be associated with the alpha-synuclein related pathways.

Keywords: Parkinson, rotenone, metformin

O-12

Investigating the neuroprotective effects of nicotinamide adenine dinucleotide precursors

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Objective: Nicotinamide adenine dinucleotide (NAD) is a dinucleotide metabolite which serves as a rate-limiting co-substrate for the sirtuin enzymes, NAD+-dependent protein lysine deacetylases in all living cells. In addition to nicotinamide (NAM), nicotinic acid (NA), and nicotinamide mononucleotide (NMN), nicotinamide riboside (NR) which is a pyridine-nucleoside form of vitamin B3 also acts as a precursor of NAD+. Supporting data have been accumulated to indicate the important roles of NAD+ and its precursors in protecting cells against oxidative and chemical stress and preventing cell degeneration.

Methods: In our study, we wanted to compare NAD+ precursors in terms of their capacity to increase intracellular NAD+ levels, to protect neurons against oxidative stress and to prevent the formation of intracellular abnormal protein aggragates. We cultured SHSY neuroblastoma and other cell lines used as a model to study neuronal cells, exposed them to oxidative stress by the treatment with 6-OHDA and formed intracellular protein aggregates by the treatment with beta amyloid peptides.

Results: It was observed that providing cells with non-toxic doses of NAM, NA and NMN 2 hours prior to or together with 6-OHDA treatment led to increase in cell survival against oxidative stress at the end of 24 hour-period.

Conclusion: In addition to protective effects of NAD+ precursors tested against oxidative stress, toxic effect of NAM itself in high doses was observed most likely due to inhibition of sirtuin activity. We plan to study the effects of NAD+ precursors on intracellular NAD+ levels and the molecular mechanisms underlying their protection of cells against oxidative stress. We will test whether these precursors can prevent the formation of intracellular abnormal protein aggregates. We will include to our study the most interesting of all the NAD+ precursors, Nicotinamide riboside, which has been widely studied in neurodegenerative disease models and can be a potential and valuable tool to fight against these diseases.

Keywords: NAD+, nicotinamide, neuroprotection, oxidative stress

O-13

Morphological changes of LV pyramidal neurons of primary motor cortex in Parkinson model rats

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Objective: Parkinson's disease (PD) is second most common progressive neurodegenerative disease. PD is characterised with the difficulty of executing the movements, called akinesia, which is related with exaggerated beta oscillatory activity seen in basal ganglia and the primary motor cortex (M1). The Layer V (LV) pyramidal neurons constitute a large proportion of M1, they are also main output neurons to the subthalamic nucleus and the spinal cord. Previous studies have shown that PD causes a number of morphological changes, such as reducing the number of dendritic spines in the medium spiny neurons of the striatum. In our study, we investigated morphologic changes in pyramidal neurons in LV, where pathological electrical activity in M1 was observed in PD model rats.

Methods: Unilateral 6-hydroxydopamine lesioned rat model is a useful tool for investigating akinesia in PD. In this study, the LV pyramidal neurons of M1 were evaluated morphologically among three groups [sham, PD-right hemisphere (PD-RH) and PD-left/lesioned hemisphere (PD-LH), (15 neurons from 5 animal for each group)] using Neurolucida 360 (v2018).

Results: We found that both the apical and basal dendritic volumes of the pyramidal neurons of PD-LH were significantly increased. On the other hand, the density of mushroom spines (according to the length of dendrite) were significantly reduced in the apical dendrite of PD-LH and in the basal dendrites of PD-RH and PD-LH.

Conclusion: These results showed that the dopaminergic depletion resulted in some morphological changes in M1 output pyramidal neurons. The role of these morphological changes on pathological beta activity in PD is a new question as a result of our study. This study was supported by Marmara University Scientific Research and Research Projects Committee (Project No: SAG-C-DRP-080415-0102).

Keywords: M1, neurolucida, Parkinson, pyramidal neuron

O-14

In-vivo imaging of cerebral extracellular potassium changes in mice by a novel fluorescent dye

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Objective: Microdialysis or ion-selective microelectrodes are commonly used to investigate the extracellular potassium changes in in-vivo systems. Nevertheless, there are limitations in the application of these methods, such that the measurements can be acquired from only a single point.More practical methods are needed for experiments in small laboratory animals. In this study, Asante Potassium Green(APG-4), a recently synthesized fluorescent dye was used to show extracellular potassium changes in the mouse barrel cortex.

Methods: First,the potassium sensitivity of APG-4 and its selectivity over sodium have been assessed in-vitro.Then a closed cranial window was prepared after craniotomy over the barrel cortex of Swiss albino mice under anesthesia.To boost the extracellular potassium level, ouabain (0.1mM),a Na-K ATPase

inhibitor, was applied epidurally and incubated for 30 minutes. After washing out ouabain, the cranial window was incubated with APG-4(250 uM) for 30 minutes. Contralateral whiskers were stimulated with aid of a motorized brush at 10hz for 5min after excess APG-4 was washed out. Potassium changes during stimulation were followed in-vivo under a stereomicroscope with a fluorescent attachment.The change in extracellular potassium levels in ouabain-applied and whisker-stimulated animals was compared with the control animals subjected to whisker stimulation only.

Results: In-vitro experiments showed that APG-4 fluorescence linearly rises with increasing potassium concentrations and is not affected by sodium concentration in the medium. Hence,APG-4 was considered to be a reliable probe for measuring extracellular potassium changes in vivo. Extracellular potassium signal increased by 3.8±0.9% (n=3) over the barrel cortex within 5 min in 10Hz-whisker-stimulated group during stimulation. In ouabain-treated and whisker-stimulated group,the extracellular potassium signal increase reached to 8.8±0.3% (n=3). The means were significantly different (p=0.05).

Conclusion: In this preliminary study,we showed that APG-4 is a relatively easy-to-use and reliable fluorescent probe for in-vivo experiments. Extracellular potassium changes resulting from neuronal activation in live experimental animals can be detected by APG-4 in both physiological and pathological states. This study was supported by TÜBİTAK(ID:113S211).

Keywords: Potassium imaging, physiological stimulation, ouabain

O-15

Determination of paracingulate sulcus length in healthy individuals according to age and gender

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Objective: Paracingulate sulcus (PCS) has gained importance as recent studies discovered the association between decreased PCS length and increased risk of hallucination in schizophrenic patients and disruption of reality monitoring in otherwise, healthy individuals. The interhemispheric variations of the PCS has been inconsistently reported in the literature. Our aim is to demonstrate the hemispheric differences of PCS length in otherwise, healthy subjects based on age and gender.

Methods: We retrospectively evaluated 3T brain MR images of 48 patients (26 F, 22 M) between the ages of 20–40. The studies were selected from structurally normal brain MRIs performed for various indications other than schizophrenia. PCS length was manually measured in both hemispheres. PCS lengths greater than 40 mm were classified as distinct, those between 20 and 40 mm were classified as present, and those shorter than 20 mm were classified as absent. Hemispheric asymmetry was tested with McNemar-Bowker and group comparisons with One-Way ANOVA.

Results: There was no statistically significant difference between right and left hemispheres, when the PCS lengths were grouped as prominent, present and absent (p=0.719). No statistically significant difference was detected between right and left hemispheres, when the PCS lengths were grouped as absent or present, which represented both prominent and present groups (p=0.701). The results comparing the PCS lengths did not differ significantly by sex, both for right (p=0.389) and left (p=0.335). There were no significant differences in terms of mean age between the groups according to the PCS lengths both hemispheres.

Conclusion: The current literature reports the association of PCS with hallucinations in schizophrenia. Our findings showed that PCS length in healthy individuals does not change with gender and age. The lack of statistical difference in PCS length in healthy individuals suggests that PCS shortening in pathological conditions is a reliable finding.

Keywords: Paracingulate sulcus, paracingulate sulcus length, hemispheric asymmetry

O-16

The effect of FreeSurfer troubleshootings on neuroanatomical measurements

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Objective: FreeSurfer is a tool which used to measure the functional, connectional, and structural properties of the brain. In FreeSurfer's website, it is stated there are five types of anatomical errors need to be corrected before they can be analyzed. These troubleshootings contain to remove the dura mater contained in the gray matter, to fix the mixed white and gray matter, to fix the topological defect in the white matter, fix if the skull strip process is failure, that the white and gray matter are completely and correctly separated by adding control points to the zones defined as gray matter by the program. The main purpose of this study is to determine whether there is a difference between cortical thickness, volume, and surface area variables in the parcels made according to the Destrieux atlas before and after the troubleshooting were made. Also the second purpose of the study is to determine whether total white and gray matter volume, total mean cortical thickness and segmentation volume change before and after troubleshooting.

Methods: For this purpose, the anatomical data of 20 healthy individuals (10 female, age mean: 37.55) were corrected for errors using FreeSurfer program and paired-sample t-test it is made.

Results: As a result of the analyzes made, it was found that various parcels showed significant differences in cortical thickness, volume and surface area after troubleshooting (p<.05). It was also appeared that the total segmentation volume (p<.05) and total white matter volume increased after troubleshooting (p <.001). There was no significant difference in total gray matter and mean cortical thickness (p>.05).

Conclusion: It is thought that troubleshooting are needed for cleaner anatomical data due to discover differences. Especially in studies which the total white matter volume will be use as a variable, it is predicted that troubleshooting will be extremely important.

Keywords: Freesurfer troubleshooting, brain volume, cortical thickness, surface area, white mater volume

O-17

Sensorimotor integration in motor sequence learning

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Objective: Motor skill learning has been investigated with various sequence learning (MSL) paradigms in the literature. This fMRI study investigated changes in activation of regions engaged in visuomotor sequence learning in relation to sensorimotor integration.

Methods: Fourteen healthy right-handed participants (6 females, age: 26.9±6.2) performed an MSL task during fMRI. On the first day, they completed two runs consisting of training and test and then a re-test session on the fifth day. They trained daily for three days between these sessions. Data were collected with 3T Philips Achieva MRI scanner. Preprocessing and GLM analysis were performed with SPM8. Activation changes were compared with paired-samples t-tests between training and test runs of the first day and between the test runs of the fifth and first days. Results with cluster forming threshold p<0.005, cluster level FWE corrected p<0.05 are reported. Mean error rate and response time were compared between training and test runs of the first day and between the test runs of the first and fifth day with paired samples t-test.

Results: Activations of the left cerebellum, inferior parietal lobule, middle temporal, occipital and postcentral gyri decreased on the test compared to the training runs of the first day. Further decline was found on the fifth day compared to test of the first day in right cerebellum, occipital, temporal, postcentral, precentral gyri, Brodmann 6, bilateral superior and inferior parietal lobules and precunei. Accuracy and response time improved on the first day in test compared to the training run (p<0.01) and further on the fifth compared to the first day (p<0.05).

Conclusion: Our findings reveal decreased activation in a network that includes dorsal attention, sensorimotor and cerebellar areas due to visuomotor learning and support the notion of neural sharpening in skill learning. The present work was supported by the Research Fund of Istanbul University. Project No: 42362

Keywords: Sensorimotor integration, motor sequence learning, functional magnetic resonance imaging

O-18

The effect of stimulant use on resting state networks connectivity in adult ADHD

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Objective: In this experiment, the acute effects of methylphenidate on adult attention deficit and hyperactivity disorder (ADHD) and the difference of healthy adults are examined by the connectivity changes on resting state functional connectivity networks using functional MRI (fMRI). The underlying mechanisms of ADHD and the relationship with the pscho-stimulant drug use must be clarified for understanding the disorder.

Methods: The experiment conducted with ADHD diagnosed (N=24) and healthy comparison (N=23) subjects. ADHD group underwent fMRI after 24 hours of washout and one hour after taking the medication. Image pre-processing was performed using SPM12 software in MATLAB platform. ROI-to-ROI connectivity analyze was performed using the pre-defined network template in Conn: Functional Connectivity Toolbox. The cerebrospinal fluid, white matter and motion parameters are regressed-out from the analyze. The Band-pass filter was set (0.01–0.1 Hz) in denoising step. In the first-level analyze the correlation values of 19 components from Default-Mode Network (DMN), Salience Network (SN), Dorsal Attention Network (DAN) and Fronto-Parietal Network (FPN) was calculated. In the second-level analyzes, analyze-level-correction was applied to calculate the connectivity differences.

Results: Unmedicated ADHD group has significantly greater connectivity values compared to the control group. There was a significant difference between the lateral prefrontal cortex(PFC) component of FPN and SN, p<0.05. There was a significant difference between posterior cingulate cortex component of DMN and bilateral lateral PFC of FPN, p<0.05. Unmedicated ADHD group has significantly greater connectivity values compared to medicated group. In addition, there was not any significant difference between the medicated group and control group.

Conclusion: Taken together, the existing literature states that the negative correlation between DMN and FPN improves the behavioral performance. Results showed that there is an increase in connectivity between these networks for unmedicated ADHD group. Furthermore, the connectivity between these networks is disappeared in the medicated-unmedicated comparisons. These results may show that stimulant drugs may improve the behavioral performance by modulating the connection between these networks.

Keywords: Attention deficit and hyperactivity disorder, connectivity, resting state networks, fMRI

O-19

Graph analyses of the neural structures during multiple-cue probability learning task

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Objective: Learning is a dynamic process which is affected by attention, emotional state, environment and social factors. Reward and emotion adjust the value of the information to be learned, skill or behavior for the organism. Studies showed significant functional activation changes in striatum and nucleus accumbens activations during processing information with reward and amygdala, prefrontal and orbitofrontal cortex during emotional information processing. Findings of the combined effect of emotion and reward on information processing are limited. The aim of this study is to investigate the connections between different neural structures,are activated in response to the interaction between the reward system and different emotional facial expressions, during probability learning process.

Methods: 45-healthy controls are included in this study. Following psychiatric assessment is performed and structural, functional MRI is obtained with 3T-MRI scanner. For functional images,participants have been asked to make selections by learning the characteristic of the different hints presented after certain facial expressions in each trial.The connectivity between the active brain regions has been examined by graph theory according to the effect of emotion in the probabilistic learning process of healthy volunteers with creating fMRI task. Correct answer count,wrong answer count, reaction time and reward amount were recorded as behavioral data during task. They were compared with ANOVA. Preprocessing for fMRIs were analyzed by using Matlab-SPM12. Network structures for each emotion were formed by time series. The formed graph was analyzed with BRAPH.

Results: There has not been found statistically significant difference between the emotions in participants' behavioral data. But, with graph analysis, participants use different networks according to different emotions during the probabilistic learning task.

Conclusion: Considering the influence of emotions on cognitive functions, different emotions network with different brain regions during learning. The absence of behavioral difference overlaps with the hypothesis of this paper. Emotions-specific network patterns have not reflected on behaviors but resulting in different connections in brain networks.

Keywords: Functional magnetic resonance imaging, graph theory, probability learning

O-20

A connectomic atlas of the inferior longitudinal fasciculus

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Objective: The Inferior Longitudinal Fasciculus (ILF) is one of the major white matter tract bundles connecting key cortical areas of the cerebrum. The location, functional connectivity, and structural connectivity of the cortical regions giving rise to the ILF have previously been described. Using these data we demonstrate the extent and anatomical boundaries of the ILF.

Methods: We built an anatomic model of the ILF based on the parcellation scheme previously published under the Human Connectome Project. Through Diffusion Spectrum Imaging, we demonstrate the tractography of this fasciculus arising from its relevant cortical regions, and show a tract map summarizing those regions with white matter connections specific to the ILF.

Results: The ILF extends from the ventral and lateral temporal cortices to parts of the occipital lobe. Seven parcellations of the temporal lobe and one from the posterior parietal lobe demonstrate structural connectivity in the distribution of the ILF. Most demonstrate fiber tracts via the ILF to early visual areas, V1–V4.

Conclusion: The literature describes several critical functions to the ILF including visual processing, object recognition, reading disturbance, emotional processing, facial recognition, ventral semantic processing, visual hallucinations, and arithmetic. Precisely what cortical information is integrated and transfered from the occipital lobe to areas of the temporal and parietal lobes remains poorly understood. Our connection model of the ILF is one step forward towards elucidating these processes. We show the anatomic connections of the ILF and define the cortical regions from which the ILF arises. Future studies will refine this model for clinical application.

Keywords: Inferior longitudinal fasciculus, parcellation, tractography, white matter

O-21

The dependence of first spike latency on the potassium and sodium conductances

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Objective: First spike latency (FSL) is a fast and efficient temporal coding mechanism found in auditory, visual, and somatosensory neural systems. In this work the dependence of FSL on the potassium and sodium conductances in a neuron is investigated.

Methods: Hodgkin Huxley neuron model is studied. Stimulus current has the constant value of 4 μA/cm^2 and is applied 100 ms after the simulation start so that transients die out in the meantime. In the original model the conductivities of the voltage gated potassium and sodium channels have fixed values gK=36 mS/cm2 and gNa=120 mS/cm^2. In this work, they are varied between 0–70 mS/cm2 for potassium, 0–400 mS/cm^2 for sodium. The delay between the on time of the stimulus and the first upward crossing of the membrane voltage exceeding 20 mV threshold is found for each conductivity value.

Results: There are three different kind of neuron behavior depending on the conductivity values. Membrane voltage may oscillate before the stimulus current is applied or membrane voltage settles down to its equilibrium value or a spike is generated after the stimulus current is applied. Four different regions are separated by three critical lines in the gK-gNa plane. First spiking times have greatest values at the critical line gK=0.43, gNa=0.71 and become smaller as the sodium conductivity increases for a specific potassium conductivity. Exception occurs i.e. FSL time increases for a few points in the conductivity plane where FSL exits in the otherwise oscillating region. Maximum first spiking time has the value 8.653 ms and occurs when gK=36 mS/cm^2 and gNa=79 mS/cm^2.

Conclusion: Stimulus current is applied in the Hodgkin Huxley model and stable, oscillatory, spike generating regions and FSL times are obtained by varying conductivity values of potassium and sodium ions.

Keywords: First spike latency, potassium conductance, sodium conductance, Hodgkin Huxley model

O-22

Chemical processes in memory formation: from mathematical model to simulation

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Objective: Being one of widely accepted approaches to explicate memory formation, long-term potentiation (LTP for short) is a mechanism that addresses the chemical processes behind memory formation and learning. Yet, the notion of how these chemical processes govern memory remained unclear to date. This is partly because of lack of a suitable environment wherein parameters affecting these chemical processes can be tested. Undoubtedly, the expression of chemical processes with mathematic will certainly sort out working principle of the brain, whilst simultaneously expounding the events on cellular level. With this paradigm, we fabricated a computational model based upon the mathematical model of Ca^{2+}/Calmodulin-dependent protein kinase (CaMKII), which possesses paramount significance for memory formation.

Methods: By the help of a set of differential equations, which biochemical processes of LTP are predicated with, we prepared a code in MATLAB to construct a model for dynamic systems. Upon comparing the results of simulations with those reported in the literature, we fine-tuned mathematical model.

Results: Based on dynamics of Ca^{2+}, changes in the position and the number of the stable equilibrium points of the dynamic system are investigated. By achieving this goal, we managed to express the dynamic systems of LTP in mathematical language. Also, simulation environment allowed us to elucidate the effects of parameters that are decisive over LTP.

Conclusion: The changes in the chemical process are interpreted upon altering the parameters of mathematical model, in conjunction with the simulation environment. It has been shown that; (i) understanding of CaMKII system, which is the key component of LTP, and thus, to learning and memory formation, is very much possible with this environment, and (ii) mathematical model, and the simulations derived from this model could be of great advantage to examine CaMKII system on LTP.

Keywords: LTP, Ca^{2+}, Ca^{2+}/calmodulin-dependent protein kinase II, dynamic system

O-23

Experimental and model-based investigation of period doubling phenomenon in human SSVEP responses

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Objective: Periodically flashing light stimuli generate nonlinear responses in the brain. In Steady State Visual Evoked Potentials (SSVEP), EEG responses are observed at the stimulus frequency, its harmonics, and subharmonics. The accuracy of the predictions (e.g. photosensitive seizure) of mathematical models, which attempt to explain the mechanisms behind such responses, increases by verifying them under different experimental paradigms. Objective of this study is model-based analysis of the mechanisms of period doubling (PD, subharmonic generation) in SSVEP experiments.

Methods: Seven subjects were presented full visual field flickering white light (bright LEDs in a VR headset) in 15–42Hz range. EEG was recorded at 2 kSps in 6 occipital channels (O1, Oz, O2,

P3, Pz, and P4). A parameter-sweep was conducted on Robinson's Corticothalamic Model (RCM) to identify the PD-related sub-blocks and parameters. RCM was implemented in C and 1 million parameter sets could be swept in 15 minutes. Analyses of RCM and other models with nonlinear feedback theory methods were done in Simulink.

Results: Statistics were obtained regarding repeatability of PD which could occur in all stimulation frequencies and EEG channels. Parameters were swept with high precision as PD in RCM may vanish with small changes in parameter values. The source of PD in RCM, which contains 3 nonlinear sub-blocks, 3 feedback loops and 17 parameters, is identified to be the intrathalamic feedback loop that has 2 nonlinear sub-blocks and 9 parameters. Harmonic balance and oscillation theory are used to explain the theory behind PD generation in the intrathalamic loop. A nonlinear block modulated by the stimulus seems to be the crucial element for PD generation.

Conclusion: The potential source of PD, observed both in experiments and RCM, is identified through parameter-sweep and nonlinear analysis. The results uncover the potential to relate physiological parameters with PD phenomenon. This work is supported by TUBITAK under Grant 116E153.

Keywords: SSVEP, EEG, subharmonic, corticothalamic model, period doubling

O-24

Effect of code duration on c-VEP based speller BCI

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Objective: It has been argued that shorter code durations and hence more frequent code presentations in a Code Modulated Visual Evoked Potential (c-VEP) based speller-BCI (Brain Computer Interface) may increase the ITR (Information Transfer Rate) of the system, decrease the visual fatigue and the training time of the system. In this study, effects of code duration and repetition rate on c-VEP based speller-BCI are investigated experimentally, and furthermore, widely-used Robinson's Corticothalamic Model (RCM) is used for simulating the salient behaviors which are observed in experiments.

Methods: A 6x6 speller-BCI is designed using a 240Hz monitor. Six subjects participated in experiments where the refresh rate of the monitor is set to 60Hz (E1), 120Hz (E2) or 240Hz (E3) to vary the code duration and the code repetition rate. Targets (symbols) are modulated by the time-shifted versions of a binary-pseudorandom-sequence. Canonical correlation analysis is used for target identification. RCM is simulated in MATLAB Simulink.

Results: Average ITR and accuracy values are 134.9 bits/min and 95.8% for E1, 128.6 bits/min and 93.3% for E2, and 101.1 bits/min and 79.2% for E3 respectively. Increasing refresh rate drastically shortens the time required for training from 212 seconds to 53 seconds. Also, 5 subjects stated that E3 was more comfortable. Cross-correlations between the EEG signal for a target letter and the 36 templates are similar in the experiments and the simulations, for all refresh rates. In both cases, although the highest correlation coefficient corresponds to the target letter's template, correlations become periodic w.r.t. shift of the template as the refresh rate is increased.

Conclusion: ITR values and accuracy rates decrease with increasing refresh rate, while visual fatigue and training time decrease. It is shown, for the first time that RCM can explain some of the experimental observations in a c-VEP experiment.

This work is supported by TUBITAK under grant 116E153.

Keywords: EEG, code-modulated visual evoked potential, c-VEP, corticothalamic model, refresh rate

O-25

Selective synaptic effects of the basal forebrain GABAergic projections on hippocampal circuitry

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Objective: Basal forebrain septo-hippocampal GABAergic projections, which are required for the emergence of hippocampal theta oscillation, are known to be important for spatial navigation and several forms of memory encoded by cortico-hippocampal circuits. However, specific postsynaptic targets of these GABAergic neurons, which form synapses exclusively with interneurons in their target limbic regions, are yet to be discovered. This study aims to investigate the electrophysiological and morphological properties of basal forebrain medial septal GABAergic cells targeting cortico-hippocampal circuits together with their postsynaptic targets in a comprehensive manner.

Methods: Septal cells, which were estimated to be GABAergic based on their electrophysiological properties, were extracellularly recorded together with hippocampal EEG recordings in anaesthetized Sprague-Dawley rats; and the correlation between septal action potentials and hippocampal oscillations were determined. The axonal distributions of juxtacellularly labelled single GABAergic neurons were recorded, and their postsynaptic target cell types were characterized by immunohistochemistry.

Results: We discovered that each neurobiotin-labeled septo-hippocampal GABAergic cell was phase-locked to the hippocampal theta oscillation and selectively innervated a specific subregion of the hippocampus or a parahippocampal or subicular cortical area. More importantly, we showed that basal forebrain GABAergic cells can very selectively target only a specific type of GABAergic interneuron in their target hippocampal regions.

Conclusion: This study revealed that the fast-acting disinhibitory effect of basal forebrain GABAergic cells on hippocampal pyramidal neurons is carried out by various complementary neurons that are differentially activated to selectively inhibit diverse types of interneuron. Hence, it is likely that the investi-

gated septal cells carry out distinct functions in hippocampal computations/processes such as spatial navigation. In the light of these findings, it is theorized that the synaptic selectivity of GABAergic septo-hippocampal projections is shared by other basal forebrain-limbic system projections (e.g. GABAergic ventral pallidum/substantia innominata cells that innervate basolateral amygdala), likewise contributing to distinct cognitive processes in these regions.

Keywords: Basal forebrain, electrophysiology, GABAergic, hippocampus, interneuron

O-26

Investigation of epileptogenesis in the post-prolonged febrile seizure process

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Objective: In this study, it was aimed to investigate the time-dependent genomic RNA profiling of hippocampal tissues induced by febrile seizures (FS) and the epilopterogenesis process with subsequent bioinformatics approaches. Epileptogenesis is the process of developing epilepsy over normal brain differentiation in a period of time and is characterized by spontaneous seizures that develop after the initial seizure and after the seizure-free latent period. Extended febrile seizures are one of the most common causes of limbic system epilepsies at the end of epileptogenesis process.

Methods: A total of 120 Sprague-Dawley rats were used in the study, consisting of 40 control and 60 FS groups divided into 12 time groups for 120 days after FS, and febrile seizure induction was performed with a vertical hot air flow model on postnatal day 10. The rats were disrupted during the possible epileptogenesis process and hippocampal material was collected. Expression profiling for a total of 28.407 transcripts was performed using Affymetrix RatGeneST2.0 microarray chip with RNA isolated from hippocampus tissues.

Results: Klotho (Kl) and Transthyretin (Ttr) genes showed significant differences in FN-induced animals when the expression data set was time-dependent and multidimensional analyzed. In this context, it has been concluded that these genes are potential biomarkers for the epileptogenesis process. However, the hippocampal expression of the calcium receptor-associated olfactory receptor genes in the cell differed in animals that had febrile seizures.

Conclusion: Kl and Ttr genes were found to be important roles in latent period after febrile seizure and they were selected as candidates for meta-analysis studies. However, the difference in olfactory receptor gene expression has led to the interpretation that long-term accumulation of intracellular calcium in the epileptogenesis process may be regulated by these genes. Findings are very important in terms of understanding the nature of epilepsy and febrile seizures. This study was supported by the project numbered 214S222 of TUBITAK.

Keywords: Febrile seizures, epilepsy, bioinformatics, microarray, expression

O-27

Effects of erythropoietin on memory and nitric oxide synthase types in epileptic seizures

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Objective: Nitric oxide, an important mediator in learning/memory and pathogenesis of epilepsy, is formed by nitric oxide synthase (NOS) in neuronal cells in many areas of the brain, primarily the hippocampus. It is has been shown that erythropoietin (EPO) has neuroprotective and antiepileptic effects. The aims of the study is that to investigate the EPO pre-treatment on learning/memory and NOS species in pentilenetetrazole (PTZ)-induced generalized seizure model.

Methods: Wistar albino adult male forty rats were divided into four groups: Control-saline; PTZ-single dose 60 mg/kg; EPO-3000 IU/kg; EPO+PTZ- EPO pretreatment 24 hours before PTZ administration. After PTZ injection, latency and severity of seizures were observed; 24 hours after the seizures, the passive avoidance test was performed for learning period. One hour after learning, short-term memory was tested and long-term memory was tested after 24 hours. The levels of neuronal NOS (nNOS), endothelial NOS (eNOS), inducible NOS (iNOS) levels in the serum, hippocampus and frontal cortex specimens of animals and expressions of NOS species in hippocampus tissues were examined.

Results: EPO pretreatment before PTZ administration elongated the seizure latency ($p<0.05$), decreased seizure severity ($p<0.01$). Short-term memory deteriorated with PTZ ($p<0.05$). EPO administration alone reduced nNOS levels in serum ($p<0.001$), frontal cortex ($p<0.05$), hippocampus ($p<0.001$). Hipocampus nNOS level and expression increased in EPO+PTZ group compared to PTZ group ($p<0.001$). eNOS ($p<0.01$) and iNOS ($p<0.05$) levels of hippocampus decreased in PTZ group; EPO pretreatment before PTZ application improved nNOS level.

Conclusion: EPO pre-treatment has a neuroprotective effect by improving seizure behaviors and correcting short-term memory. This effect may be partially active with eNOS and iNOS, predominantly with nNOS in hippocampus and frontal cortex. The effect of EPO on NO in the normal state and after epilepsy may vary depending on regions of brain. This work was supported by Scientific Research Project Coordination Unit of Istanbul University (21796).

Keywords: Erythropoietin, nitric oxide, seizure, hippocampus, memory

O-28

Effects of methyl-beta-cyclodextrin on blood-brain barrier in acute hypertension animal model

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Objective: The present study was intended to examine the effects of methyl-beta-cyclodextrin (M,CD), a cyclic oligosaccharide, on blood-brain barrier (BBB) permeability in angiotensin (ANG) II-induced acute hypertension in rats.

Methods: The experimental groups were designed as control, M,CD, ANG-II, and M,CD+ANG-II. BBB permeability was evaluated using Evans blue (EB) and horseradish peroxidase (HRP) tracers. At five minutes after M,CD administration (5 mg/kg; i.v.), acute hypertension was induced by ANG-II (60 µg/kg; i.v.), and arterial blood pressure measurements were taken.

Results: ANG-II caused a significant increase in arterial blood pressure when compared with baseline values ($p<0.01$). The content of EB dye in the left and right cerebral cortex and left hippocampus regions of animals significantly increased in ANG-II, M,CD, and M,CD+ANG-II groups when compared with controls ($p<0.05$). We also studied the caveolin-1, and tight junction proteins, claudin-3 and -5 using immunofluorescent methods. The immunostaining intensity of caveolin-1 was observed a slight increase in the treated groups. Claudin-3 immunostaining intensity remained unchanged in all groups, while the claudin-5 was observed a slight decrease in the treated groups. Ultrastructurally, frequent vesicles which did not contain HRP reaction products were observed in endothelial cells of venules and veins in the cerebral cortex and hippocampus regions of brains of animals in ANG-II, and M,CD+ANG-II groups. The endothelial cells of capillary bed in these areas are full of HRP reaction products.

Conclusion: Our results revealed that M,CD did not provide overall protective effects on the BBB integrity in acute hypertensive conditions and even led to BBB disruption in intact animals.

Keywords: Acute hypertension, methyl-,-cyclodextrin, blood-brain barrier, horseradish peroxidase, electron microscopy

O-29

The effects of catalase on the distrupted BBB integrity by hyperosmolar mannitol infusion in rats

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Objective: In this study, we investigated whether catalase exerts protection against blood-brain barrier (BBB) disruption induced by hyperosmolar mannitol (25%) in rats.

Methods: Following intravenous catalase-PEG (2.500 IU/0.2 mL) pretreatment, mannitol (0.25 ml/kg/sec) was infused into the right external carotid artery. BBB integrity was assessed using Evans blue (EB) and horseradish peroxidase (HRP) tracers.

Results: In ipsilateral brain regions, mannitol-induced increase of EB content was significantly alleviated by catalase ($p<0.01$). While immunoreactivity for claudin-3 tight junction (TJ) protein was decreased in all brain regions by mannitol with differences being significant in hippocampus ($p<0.01$), higher immunostaining intensity was achieved by catalase with significant differences in cortex ($p<0.05$). The significantly decreased claudin-5 immunoreactivity of mannitol-treated animals was significantly increased by catalase ($p<0.01$). GFAP immunoreactivity showed no widespread alteration by mannitol whereas ipsilateral brain regions of catalase-pretreated animals had significantly higher immunostaining intensity than animals in sham and mannitol groups ($p<0.05$). Ultrastructurally, HRP reaction-products were significantly increased by mannitol in the endothelium and basement membranes of capillaries and parenchymal areas in all brain regions predominantly the ipsilateral side ($p<0.01$). In these regions, TJs between endothelial cells were mostly open and swelling and edema of the astrocytic end-feet were observed. The frequency of HRP reaction-products in the endothelium and perivascular parenchyma of catalase-pretreated animals was similar to that of sham animals.

Conclusion: Our results suggest that catalase may be effective in protecting BBB integrity against hyperosmolar BBB injury through its activity on paracellular and transcellular pathways that are functional in the regulation of barrier function of brain microvessels. The present work was supported by the Research Fund of Istanbul University. Project No. 55840

Keywords: Blood-brain barrier, evans-blue, HRP, mannitol, PEG-catalase

O-30

The effects of growth hormone on motor findings and neuronal morphology in Parkinson model rats

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Objective: Parkinson Disease is a neurodegenerative disease, characterized by the degeneration of dopaminergic neurons in Substantia nigra (SN). Growth hormone (GH) is a hormone that plays a role in the development of important functions in the control of brain development. There are studies showing that BH administration may be associated with recovery of neuronal functions after brain injury. Dendritic spines increases the surface area and causes the communication between all stimulating cells in the brain.There is a connection between the structural properties and functions of dendritic spines. This study aims to investigate the effect of GH therapy on motor function and neuronal morphology for 3 months.

Methods: Sprague Dawley rats; Treatment group (PD+GH) (n=6) and Sham (PD+Saline) (n=6) were injected with 4 µl 6-OHDA solution (Bregma AP: -2.1 mM, Lat: 2.0 mm and VL: -7.8 mm) stereotaxically. Following the injection GH and saline (0.15 mg/kg/day, s.c.) is administered daily. Rotation preferences and lesion grade are evaluated according to the rotation test. Golgi (FD Rapid Kit) and Tyrosine hydroxylase (TH) staining procedures are applied to sections of the striatum and substantia nigra (40 µm). Golgi staining was evaluated using Neurolucida 360(v2018).

Results: According the results of the rotation, the number of rotations in BH treatment group was significantly decreased (p=0.0112). No significant difference was observed between the groups in SN and striatum in TH staining. Thin type dendritic spine density is significantly increased in the treatment group, which indicates restoration of neuron morphology.

Conclusion: Long term GH administration has been shown to have positive effects on motor function and neuronal morphology. This study was supported by Marmara University Scientific Researches and Projects Committee (SAG-K-070617-0339).

Keywords: Parkinson disease, growth hormone, dendritic spine

O-31

Spontaneous EEG and neuropsychological test results in early-onset vs late-onset Alzheimer's disease

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Objective: Alzheimer's Disease (AD) is a neurodegenerative disorder, often seen over the age of 65, characterized by impaired daily functioning and cognitive functions such as memory, attention and executive functions. Early-onset AD (EOAD) seen before 65 is less common than late-onset AD (LOAD) and consists of 1-6% of all cases. In the present study, spontaneous EEG band power and neuropsychological test scores of EOAD, LOAD and healthy control (HC) groups.

Methods: Eighteen EOAD patients, 18 LOAD patients and age-, education- and gender-matched 18 young HC and 18 old HC were included. Participants underwent a detailed neuropsychological assessment and 4 minutes eyes-closed spontaneous EEG recordings. EEG was segmented into 2-seconds epochs and Fast Fourier Transform was applied. Delta (0.5–3.9 Hz), theta (3.9–7.8 Hz), alpha (7.8–12.6 Hz), beta (12.6–30 Hz), alpha1 (7.8–10.3 Hz), alpha2 (10.3–12.6), beta1 (12.6–20 Hz) and beta2 (20–30 Hz) power values (µVÇ) were measured from F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, Oz and O2 electrode locations.

Results: Repeated measures of ANOVA showed main GROUP effects on delta [F(3,68)=6.444; p=.001] and theta [F(3.68)=6.839; p<.001] power. Patients with EOAD had higher delta power than LOAD in all electrode locations (all; p<.028) and higher theta power at Fz and Cz locations (p=.026, p=.027, respectively). There were significant differences in delta, theta, alpha, alpha1 and alpha2 power between EOAD and young HC; and in theta, alpha and alpha1 power between LOAD and old HC. Neuropsychological test scores were negatively correlated with delta and theta power and positively correlated with alpha and beta power.

Conclusion: In the present study, both EOAD and LOAD groups differed electrophysiologically from healthy subjects, with more prominent and widespread changes in EOAD compared with LOAD. These findings can be related to the early involvement of cortical areas in EOAD, whereas limbic areas in LOAD patients.

Keywords: Alzheimer's disease, early-onset AD, EEG, late-onset AD, oscillations

O-32

Event-related delta oscillations in Parkinson's disease with and without cognitive impairment

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Objective: Mild cognitive impairment in Parkinson's disease (PD-MCI) has been considered to be a risk factor for PD dementia. Delta event-related oscillations (EROs) are recognized to be particularly useful in investigating cognitive impairments. Our group's earlier work demonstrated reduced delta

ERO responses in patients with Alzheimer's disease, amnestic MCI and cognitively normal PD. In the present study, we investigated whether these changes in delta EROs differ between cognitively normal PD (PD-CN) and PD-MCI patients when compared to healthy controls.

Methods: Nineteen PD-CN patients, 19 PD-MCI patients and 19 age-, gender- and education-matched healthy controls were participated in the study. A comprehensive neuropsychological test battery was applied to all participants. PD-MCI was classified with the diagnostic criteria of the Movement Disorder Society Task Force. EEG was recorded according to the 10-20 system using a classical visual oddball paradigm. The maximum peak-to-peak amplitudes of the delta (0.5–3.5 Hz) target EROs on F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, Oz and O2 locations were measured.

Results: Repeated measures of ANOVA revealed a main GROUP effect on peak-to-peak amplitude values of delta EROs [$F(2,54)=10.644$; $p<0.001$]. Compared to healthy controls, PD-CN showed decreased delta ERO responses at all frontal locations, while PD-MCI had delta ERO reductions over all frontal, central and parietal electrode locations. PD-MCI patients had also significantly lower delta ERO responses than those of PD-CN patients over centro-parietal electrode locations.

Conclusion: Disease-related cognitive changes were reflected as delta ERO reductions over frontal regions in PD-CN, spread to centro-parietal regions along with cognitive decline at the stage of PD-MCI. This finding further suggests that delta ERO reductions may be used as a sensitive parameter to indicate preclinical cognitive changes in PD.

Keywords: Delta, EEG, event-related oscillations, mild cognitive impairment, Parkinson's disease

O-33

Event-related potential responses to emotional facial expressions in Alzheimer's disease: N170 and VPP

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Objective: Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive and social impairment. Behavioral studies showed that AD patients have difficulties in recognizing and interpreting emotional facial expressions. In this study, event-related potential (ERP) responses to emotional facial expressions during a passive viewing task were examined in AD relative to healthy controls (HC).

Methods: The study included 20 individuals with AD and 22 age, gender and education matched HC. EEG was recorded while participants passively viewed blocks of emotional facial expressions (i.e., happy, fear, angry, sad, and neutral). Peak amplitude values of ERP N170 from parieto-occipital electrode locations and Vertex Positive Potential (VPP) from fronto-central midline locations were measured.

Results: A main GROUP effect were found on N170 amplitudes [$F(1.40)=5.648$; $p=.022$], indicating lower N170 amplitudes in AD than HC in all conditions (all; $p<.043$). Moreover, there was a main CONDITION effect [$F(4.160)=3.090$; $p=.043$]. N170 amplitudes in response to happy faces were higher than feared, sad, and neutral (all; $p<.001$). There was no main GROUP effect on VPP amplitudes; however, there was an interaction effect for GROUPxCONDITION [$F(4.160)=5.604$; $p=.001$]. AD patients had larger VPP amplitudes than HC in response to feared ($p=.013$) and neutral ($p=.009$) faces.

Conclusion: To our knowledge, this is the first study to compare N170 and VPP responses in AD and HC using a passive viewing task. While N170 and VPP have been used interchangeably; our findings suggest that they are differentially influenced by dementia, likewise emotional facial expressions. Participants showed larger N170 amplitudes in response to happy faces, which may refer to an age-related positivity effect. Besides, AD patients showed higher VPP amplitudes to neutral and feared faces, which may indicate an impairment in early perceptual processing and connectivity dysfunction between the posterior facial processing areas and the prefrontal regions in mild dementia. This study was supported by TUBA-GEBIP.

Keywords: Alzheimer's disease, emotional facial expressions, Event-related potentials, N170, VPP

O-34

Fronto-cerebellar tDCS regulates prefrontal hemodynamic response pattern in multiple sclerosis

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Objective: Multiple sclerosis (MS) is characterized by demyelinating central nervous system plaques and deterioration of functions of the regions which the plaques are formed. Pattern of activation in the prefrontal cortex (PFC) of individuals with MS differs from the healthy population during cognitively challenging tasks. In this study, we aimed to investigate the prefrontal hemodynamic response in MS and tDCS effects on cognitive dysfunction which is a common symptom for relapsing-remitting multiple sclerosis (RRMS).

Methods: 8 RRMS patients with impaired neuropsychometric test performance are included in the study. Ten sessions of tDCS were administered. The anode electrode was placed over the left dorsolateral prefrontal cortex (DLPFC) and the cathode electrode over the right hemisphere of the cerebellum. Electric current intensity was set to 2 mA. for 20 minutes per session. The

efficacy of tDCS is assessed by using fNIRS, before the first and after the last sessions. During fNIRS registration, patients are required to perform a computerized color-word Stroop task.

Results: fNIRS analyzes before the first session showed that the left PFC is mainly activated during difficult cognitive tasks in RRMS patients. Also a decreased activation intensity was observed in the right DLPFC. After the stimulation period, the activation area was seen to change between hemispheres and showed a significant increase in the right prefrontal region. Moreover, increased oxyhemoglobin concentration was observed in all regions of PFC (p=0.012 for DLPFC, p=0.022 for orbitofrontal cortex, p=0.008 for medial prefrontal cortex).

Conclusion: An impaired prefrontal activation and hemodynamic response pattern, which is may be due to abnormal hemispheric connections and decreased regional activation intensity, have been demonstrated by fNIRS method in MS patients. Also we found that tDCS can reverse these abnormalities into as seen in healthy population (demonstrated by earlier fMRI studies) and be an alternative treatment approach. Studies with higher number of subjects are necessary.

Keywords: fNIRS, hemodynamic response, multiple sclerosis, prefrontal cortex, tDCS

O-35

Testing the facial feedback hypothesis in facial transplant patients

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Objective: According to Facial Feedback Hypothesis (Adelmann&Zajong, 1989;McIntosh,1996), facial movements have also influence on emotions in addition to visual and contextual cues. Mimicking facial expressions occurs very quickly, automatically and specific to the emotion (Dimberg, Thunberg &Elmehed, 2000).This feedback from muscles to brain leads same kind of emotion to be experienced by the receiver, therefore contributes to understanding the emotions of conveying person. Oberman, Winkielman, Ramachandran (2007) indicated that blocking facial mimicry in healthy individuals can selectively impair recognition of emotional expressions. Thus, we aimed to test recognition of emotional expressions in face transplant patients who have difficulties in mimicking.

Methods: Two face transplant patients and a control group were participated. Data collection on the patients who are going to be operated or transplanted is continuing. The patients were tested in two tasks in order to measure recognition of facial expressions of emotions. Task1: Seven different emotional expressions on different faces were presented on computer screen and the participants were asked to evaluate the presented expression correctly as soon as possible. The correct response rate (CRR) and reaction time were recorded. Task2: "Reading the Mind in the Eyes Test"(RMIET) which was developed by Baron-Cohen (1999–2001)- measuring social cognition and mind reading abilities in adults- was applied.

Results: The CRR of the face transplant patients were lower than the CRR of the healthy control. The scores changed in respect to the expression ($p<.05$). The CRR for happiness (100%) and surprise (90%) were high, but it was lower for fear (%10) and disgust (%30). Happiness could be recognized fast (2781.50 ms), however, fear (5640.80 ms), sadness (5585.20 ms) and disgust (4091.86 ms) were recognized slowly. The maximum score of RMIET is 32. The scores of Patient1 and Patient2 are 12 and 13. Their scores were low comparing to their matched sample.

Conclusion: The facial structure and facial feedback seem to be critical in recognizing emotional expressions on other faces.

Keywords: Facial expressions of emotions, face transplantation, facial feedback hypothesis

O-36

Investigation of protective effects of long term L-carnitine treatment on presbyacusis

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Objective: Presbyacusis is a bilateral and sensorineural hearing loss seen in elderly which occurs as a result of degeneration in the cochlea and central auditory pathways. Although the mechanisms of the initiation of presbyacusis is not fully understood, it is claimed that free oxygen radicals produced because of noise exposure, ototoxic agent use, and immune system changes may cause irreversible damage to mitochondrial and nuclear DNA structure and degeneration of the cell by activating apoptotic pathways. In our study, it was aimed to investigate the effects of L-carnitine, an antioxidant agent, on presbyacusis.

Methods: In our study, 10 months-old 40 Wistar rats were divided into two groups. One milliliter of distilled water was administered to control rats and 50 mg/kg L-carnitine to rats of L-carnitine treatment group by intragastric gavage once a day for 7 months. At the end of 17 months, all groups underwent auditory brainstem response testing at 8 kHz and 16 kHz frequencies after administration of intraperitoneal urethane anesthesia in the silent room and cochlear caspase-3 levels were examined. T Test analysis was performed in comparing variables between groups.

Results: L-carnitine treatment significantly reduced I, II, III and IV latencies and threshold levels in 8 kHz, 60 dB and 16 kHz, 70 dB compared with the control group. Interpeak latencies were not significantly different between groups. Caspase-3 expressions in cochlear sections were also decreased in the L-carnitine treatment group compared to the control group.

Conclusion: L-carnitine administration had positive effects on hearing tests and cochleas-3 levels and hence may be an alternative for the prevention of presbyacusis. Our project was supported by the Coordination Unit of Scientific Research Projects of Akdeniz University (project no: TSA-2017-2621).

Keywords: L-Carnitine, auditory brainstem response, presbyacusis

O-37

Sex-related differences on a valproic-acid-induced neurodevelopmental disorder model

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Objective: The effect of sex on the symptoms of a rodent autism-spectrum-disorder-like symptomatic model was investigated.

Methods: In the experimental group, two pregnant rats were injected with 400 mg/kg valproic acid (VPA) at E12 and two pregnant rats with saline solution. Pups were seperated at P21 and monitored for 90 days. VPA group contained 9 female and 13 male pups, the control group contained 4 female and 4 male pups. The olfactory discrimination (OD) task was applied on P 22, social recognition (SR) and social preference (SP) tasks on P 25, and prepulse inhibition test (PPI) on P35, P60 and P90. The differences among the groups were assessed by one-way ANOVA and post-hoc Tukey-Kramer test.

Results: Without grouping for sex, PPI for 86 dB prepulse at P30 ($p=0.016$), average PPI at P60 ($p=0.035$), performances in SR ($p<0.0001$) and SP ($p=0.0003$) were lower for VPA group. No sex-related difference was found in the control group. PPI for 86 dB prepulse at P30 ($p=0.0238$) and for 74 dB ($p=0.0258$) and 78 dB ($p=0.04$) at P60, average PPI at P60 ($p=0.037$), performances in SR ($p=0.0011$) and SP ($p=0.02$) were lower for female VPA group compared to mixed control. Male VPA group exhibited lower performance only in SR ($p<0.0001$) and SP ($p=0.0008$). For 3 male and 5 female pups with developmental malformations, performances in OD ($p=0.0132$) and SR ($p<0.0001$); PPI for 78 dB prepulse ($p=0.03$) and average PPI ($p=0.02$) at P60, PPI for 78 dB prepulse ($p=0.018$) at P90 were lower compared to control group. When compared to VPA group without malformations, their performance in SR ($p=0.0002$) and PPI for 78 dB prepulse at P90 ($p=0.0047$) were lower.

Conclusion: Results suggest a sex-related difference in the existence and severity of the symptoms in our model. Follow-up study with increased number of subjects is in progress.

Keywords: Neurodevelopment, valproic acid, autism

O-38

Differentiation of SH-SY5Y cells to neuroblastoma and their neurophysiological responses

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Objective: SH-SY5Y cells are obtained from the bone marrow tumor of a 4-year old patient, and can be differentiated to neuron with the addition of different chemicals; e.g., retinoic acid (RA), cholesterol, estradiol, brain drived neurotrophik faktor (BDNF), phorbol ester. SH-SY5Y cells are used to generate neurodegenerative disease models. Chemicals causing the differentiation of SH-SY5Y cells to neuron, their concentrations, electrophysiological properties are not well defined yet. To determine the optimum differentiation conditions and electrophysiological properties of SH-SY5Y cells to neurons by using patch clamp technique. Also, to study the intracellular calcium dynamics by fluorescence imaging.

Methods: SH-SY5Ycells were incubated in DMEM/F12, %5FBS. Differentiation to neuron induced by RA (10 µM) and BDNF (50 ng/mL) and neuronal morphology was observed. Currents were recorded from undifferentiated and differentiated cells. Results were obtained from 22 neuroblastoma cells.

Results: During differentiation potassium current is dominant in SH-SY5Y neuroblastoma cell line. Comparison between I-V diagrams of the RA and BDNF groups show the mean activation threshold of the BDNF group is less than the RA group but it doesn't imply a significant difference ($p<0.1$ two-sample t-test). With BDNF, the inward current increased significantly (320 pA vs 1406 pA, $p<0.0063$, two sample t-test), the increase in outward current was not significant ($p<0.8$, two sample t-test). Derivatives of current profiles (dI/dt) and current slopes showed significant difference in two groups ($p<0.01$, two-sample t-test) implying increase in BDNF group.

Conclusion: During the firing of an action potential, ion channels open stochastically. Increased inward current with BDNF points increased number of sodium channels open, the outward current remains the same in two groups, implying that open potassium channels remained same. The slope increase of both currents with BDNFapplication indicates that channels open faster and for longer period of time. This research supported by Boğaziçi University Research Projects (BAP project no:17XP5).

Keywords: SH-SY5Y, neuroblastoma, patch clamp recording, sodium and potassium currents

O-39

The role of sigma-1 receptor on neurite outgrowth in primary hippocampal neurons

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Objective: Neurite outgrowth, the first and fundamental step in axonal and dendritic development in neurones, is an essential process for nervous system development, its plasticity and formation of synaptic connections. Inducing neurite outgrowth and increasing neuronal survival are important strategies to treat neurodegenerative diseases. Sigma-1 receptor (Sig-1R) is

a molecular chaperone which is located mitochondria-related endoplasmic reticulum membrane. Sig-1R plays a vital role in several cellular processes, for example neurite outgrowth, neuronal plasticity, Ca+2 transport from ER to mitochondria, neuroprotection. The aim of this study is to investigate the possible effects of cutamesin (SA4503), a selective Sig-1R agonist, in neurite outgrowth and to search the interaction between Sig-1R and inositol 1,4,5-trisphosphate receptor (IP3-R).

Methods: Primary hippocampal neuron culture, isolated from neonatal BalbC (n=20) mice, was used as an in vitro model. The presence of Sig-1R in hippocampal neurons was investigated by immnunocytochemistry in confocal microscopy and by western blotting of total protein extracts from hippocampal cell culture. Cells were seeded in petri dishes and cutamesin was applied in most effective dose (10 μM) determined previously. NE100 (10 μM), Sig-1R antagonist, and Xestospongin C (1 μM), an IP3-R antagonist, were added to cell culture before cutamesin application. Neurites were labeled in confocal microscopy by using beta III tubulin antibody. The percentage of neurite containing neurons was calculated from microscopy images and data were statistically evaluated by one-way ANOVA test.

Results: Cutamesin increased neurite outgrowth in primary hippocampal neurons significantly ($p<0.001$). On the other hand, applications of NE100 and Xestospongin C decreased the cutamesin induced neurite outgrowth significantly ($p<0.001$).

Conclusion: Our findings showed for the first time in primary hippocampal neurons that cutamesin elevates neurite outgrowth, whereas inhibition of IP3-R decreases it. We concluded that Sig-1R has a positive effect on neurite outgrowth and this effect is mediated by regulating Ca+2 transport between ER and mitochondria.

Keywords: Sigma-1 receptor, neurite outgrowth, hippocampal neurons, cutamesine

O-40

Identification of a novel gene in Brown-Vialetto-Van Laere syndrome

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Objective: Brown-Vialetto-Van Laere syndrome (BVVLS) is a rare ALS-like childhood neurodegenerative disorder, which causes severe morbidity and mortality. Mutations in the genes encoding riboflavin transporters, SLC52A2 and SLC52A3 are known to cause this syndrome and the only therapeutic approach is high dose riboflavin therapy. In a family with four affected siblings, BVVL was diagnosed based on typical clinical and laboratory findings, however, genetic testing did not reveal any mutations in the riboflavin transporter genes. In this study, we aimed to identify a novel BVVLS-associated gene and additionally investigate the molecular mechanisms related to disease pathognesis.

Methods: We performed whole exome sequencing to identify candidate disease-related genes. We obtained skin biopsy samples from patients and one healthy sibling to generate fibroblast cultures for molecular studies and to generate IPSC lines. We used PCR, Sanger sequencing, qPCR, nucleofection, integration free IPSC reprogramminning, immunofluorescence, karyotype analysis, and teratoma formation assay for functional studies on patient-derived cells and various cell lines.

Results: Whole exome sequencing revealed two candidate genes. One of these genes belonged to the family of kinesin motor proteins and the other one was a transcriptional factor. Neither of these genes have been reported as a disease-causing gene before. After further genetic and molecular studies, the gene encoding for the motor protein remained as the only candidate disease-related gene. This protein is known to be involved in the vesicular transport of proteins, but has no known association with riboflavin metabolism. Additionally, IPSCs from affected individuals and their healthy sibling were generated successfully and characterized for further studies.

Conclusion: Our results indicate that the mutation in the gene that encodes a motor protein belonging to the kinesin family is the cause of BVVL syndrome in this family. Additionally, our preliminary results show that this protein may be involved in the vesicular transport of riboflavin transporters.

Keywords: BVVL, ALS, iPSC, disease, modelling

O-41

Investigation of the cytokine profile of opticospinal multiple sclerosis

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Objective: Opticospinal multiple sclerosis (OSMS) patients are known to exhibit different clinical features than conventional multiple sclerosis (MS) and neuromyelitis optica spectrum disease (NMOSD) patients. Our aim was to find out whether OSMS patients have a distinctive serum cytokine profile.

Methods: Sera levels of IL-6, IFN-y, IL-17, TNF-α, GM-CSF, IL-2, IL-4, IL-8 and IL-10 were measured by Luminex. Sera of 20 conventional MS (CMS),14 OSMS,23 NMOSD patients and 21 healthy controls were collected. Patients were in remission and not under treatment with immunomodulating reagents. OSMS but not CMS patients satisfied Kira's 2003 criteria. All patients had a history of at least one spinal cord and one optic nerve attack. Serum aquaporin-4 (Aqp-4) and myelin oligodendrocyte glycoprotein (MOG) antibody levels were determined with cell-based assays. Neuropsychological test battery was

employed to OSMS patients. In the tests p<0.05 was considered statistically significant.

Results: Age, onset of disease,duration of illness,total number of attacks and annual episodes of MS, NMO and OSMS cases included in this study were compared by ANOVA,gender characteristics by chi-square test and EDSS and progression index were compared with Kruskal-Wallis test.There was no statistically significant difference between the study groups in these parameters. Aqp-4 antibody was only detected in NMOSD patients, whereas MOG antibody was not detected in any of the participants. OSMS and CMS patients had significantly increased IL-6, IL-17 and TNF-α and reduced IL-8 and IL-10 levels than NMOSD patients and healthy controls (p<0.001). Serum IL-6 levels,memory and executive test scores were correlated with progression indices of OSMS patients.

Conclusion: Serum cytokine profile of OSMS patients is distinct from NMOSD patients but identical to CMS patients,suggesting that OSMS is a clinical variant of MS and cytokine measurements can be utilized for diagnostic discrimination of OSMS and NMOSD. IL-6 might be involved in pathogenesis and cognitive dysfunction of OSMS patients.

Keywords: OSMS, CMS, NMOSD, cytokines

O-42

Role of NF-kappa B p65 in meningeal inflammation triggered by cortical spreading depression

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Objective: Migraine is a common disorder. Migraine pathophysiology needs deeper understanding in order to develop more effective drugs. Cortical spreading depression (CSD) is the neurophysiological correlate of migraine aura. The idea that "CSD-triggered migraine pain emerges as a result of parenchymal and subsequent meningeal sterile inflammatory response" is generally accepted. Among the members of the nuclear factor kappa B (NF-kappa B) transcription factor family, p65 is an inflammatory mediator that has been shown to be activated in different systems and under different pathological conditions. This study investigates the role of NF-kappa B p65 in relation to the persistence of CSD-induced parenchymal as well as meningeal inflammation

Methods: A single CSD was induced by pinprick in Swiss Albino mice. Activation of NF-kappa B p65 in S100B (+) astrocytes and meningeal cells after CSD was investigated by assessing its nuclear translocation using immunofluorescent labeling. Brain and dura mater sections were assessed for the study.

Results: Activation of NF-kappa B p65 was found to be persisting in the brain parenchyma when assessed immediately and 1, 2, 3, 4, 5 hours after CSD. Activation was observed in 25% of all parenchymal cells at the aforementioned time points, which corresponded to 64% in S100B (+) astrocytes. NF-kappa B p65 activation (nuclear translocation) was also detected in meningeal cells after CSD.

Conclusion: In conclusion, NF-kappa B p65 is immediately activated in the brain parenchyma by CSD and this activation lasts at least five hours. At the same time, p65 is also translocated to nucleus in dural cells suggesting that it has a role in meningeal inflammation after CSD. This study is supported by Hacettepe University Scientific Research Projects Coordination Unit (project number: TSA-2017-14418).

Keywords: Cortical spreading depression, migraine, neuroinflammation

O-43

The relationship between resting state connectivity and episodic memory in Alzheimer's disease

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Objective: This study aimed at identifying the extent to which resting state connectivity relates to episodic memory performance within different stages of Alzheimer's disease.

Methods: 78 participants were enrolled in the study. Each participant was assigned to one of the three groups: subjective cognitive impairment (SCI, n=31), mild cognitive impairment of the amnestic type (aMCI, n=31), and early-stage Alzheimer's dementia (AD, n=16). Episodic memory performance was assessed via Free and Cued Selective Reminding Test (FCSRT). Resting state networks were obtained by using independent component analysis (ICA) in Group-ICA fMRI Toolbox. ICs corresponding to RSNs including default mode (DMN), dorsal attention (DAN), executive control (ECN), and salience (SN) networks were evaluated by computing network expression scores of each participant.

Results: The results of Spearman correlational analyses indicated that ECN connectivity was significantly correlated with total recall (rs=.453) and cue index scores (rs=.425) of FCSRT within SCI group (p<.05). ECN connectivity was also significantly correlated with both total recall (rs=.361) and cue index scores (rs=.461) in the aMCI group (p <.05). In this group, DAN connectivity was also positively correlated with FCSRT cue index score; rs =.389, p<.05). As for the AD group, on the other hand, DMN connectivity was strongly related to FCSRT free recall (rs=.543, p<.05), total recall (rs=.514, p<.05), and delayed total recall (rs=.664, p<.01).

Conclusion: Significant correlations were obtained between resting state functional connectivity measures and episodic memory performance within different stages of the Alzheimer's continuum. Specifically, episodic memory performance was related to ECN connectivity within SCI and aMCI groups whereas it was correlated with DMN connectivity within the AD group. This study is supported by Turkish Scientific and Technological Research Council (TUBITAK) Project #114E053 and Turkish Ministry of Development Project #2010K120330.

Keywords: Alzheimer's disease, functional connectivity, episodic memory

O-44

Structural and functional alterations related with cognitive impairment in Parkinson's disease

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Objective: Parkinson's disease-mild cognitive impairment (PD-MCI) has a higher risk of developing PD dementia (PDD) and a reliable biomarker for the diagnosis of PD-MCI has not developed yet. In this study, in order to develop discriminative neurobiological parameters for PD-MCI, functional and structural differences among PD-MCI, cognitively normal PD (CN-PD) and healthy controls (HC) were investigated using resting-state functional MRI (rs-fMRI) and diffusion tensor imaging (DTI) modalities.

Methods: 60 PD (27 PH-CN, 33 PD-MCI) patients and 17 HC were included in this study. MR imaging was performed on 3T Phillips MRI scanner. Resting state networks (RSN) were obtained by using independent component analysis (ICA) in Group-ICA fMRI Toolbox. Expression scores specific for each subject were fed into logistic regression to obtain RSNs discriminating three groups from each other. ROI based approach was used for analysis of DTI data and fractional anisotropy (FA) values of each subject were compared with one-way ANOVA.

Results: Logistic regression analysis yielded maximum separation of between PD-MCI and PD-CN groups with default mode network (DMN) – posterior cingulate component with an overall accuracy of 63,3% (χ^2=6.945, df=1, p=0.008). Sensorymotor and visual network provided maximum separation between PD-MCI and HC groups with an overall accuracy of 80% (χ^2=9.514, df=2, p=0.009). FA values differed among three groups in the superior longitudinal fasciculus (SLF) (p=0.028) and SLF-temporal part (p=0.026) and FA values in these ROIs significantly decreased in PD-MCI compared to HC.

Conclusion: In previous studies, lower connectivity in DMN and decreased FA values in SLF have been demonstrated in patients with PDD. In this regard, our similar results in PD-MCI may be an indicator for cognitive decline in PD. Additionally, lower connectivity in visual network could be associated with visuospatial impairment in PD-MCI. Supported by TUBITAK #115S219 and IU-BAP #21336.

Keywords: Parkinson's disease, mild cognitive impairment, fMRI, diffusion tensor imaging

O-45

MRI based classification of mild cognitive impairment in Parkinson's disease using machine learning

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Objective: The aim of this study was to classify Parkinson's disease mild cognitive impairment (PD-MCI), cognitively normal Parkinson's disease (PD-CN) and healthy control (HC) groups based on multimodal magnetic resonance imaging (MRI) using machine learning methods.

Methods: 33 PD-MCI, 27 PD-CN and 17 HC participated in this study. The participants were diagnosed by neurologists according to the neuropsychological test and physical examination results. MRI data was obtained at a 3T Philips clinical MR system using a 32-channel head coil. Mean cerebral blood flow (CBF), arterial blood volume (aBV) and bolus arrival time (BAT) maps obtained from arterial spin labeling MRI (ASL-MRI), fractional anisotropy (FA) and mean diffusivity (MD) maps obtained from diffusion tensor imaging (DTI), and metabolite peak ratios obtained from proton MR spectroscopic imaging (1H-MRSI) at various brain regions were used as features. Various machine learning methods were employed with appropriate hyperparameters. In addition, feature selection algorithms and dimension reduction techniques such as principal component analysis (PCA) and non-negative matrix factorization (NNMF) were assessed. Features having high correlation with each other were eliminated.

Results: Removing highly correlated features increased the model performance. The subset of features selected by the randomized logistic regression and leave one out cross-validation (RLR-LOOCV) method contained 10% of all features from all the MRI modalities. The classification accuracies were 77% for

PD-MCI versus HC, 80% for PD-MCI versus PD-CN, and 71% for PD-CN versus HC.

Conclusion: Machine learning based on multimodal MRI might be helpful in early diagnosis of PD-MCI. Future studies aim to improve the classification of PD-MCI in a larger patient cohort. This study has been supported by TÜBİTAK #115S219 and Ministry of Development #2010K120330.

Keywords: Machine learning, Multimodal MRI, Parkinson's disease

O-46

Assessment of cerebral perfusion in mild cognitive impairment in Parkinson's disease using ASL-MRI

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Objective: In this study, cerebral blood flow (CBF), arterial blood volume (aBV) and bolus arrival time (BAT) maps of Parkinson's disease patients with mild cognitive impairment (PD-MCI) or normal cognition (PD-CN) and healthy controls (HC) were calculated using arterial spin labeling MRI (ASL-MRI) technique, and the aim was to define biomarkers, based on perfusion, that might indicate cognitive impairment.

Methods: Twenty-nine PD-MCI, twenty-four PD-CN and sixteen HC were scanned on a 3 Tesla clinical MR system (Philips Medical Systems, Best, The Netherlands). ASL-MR images were acquired by using STAR labeling with Look Locker sequence at eight different inversion times (TIs) (TR/TE=250 ms/16ms, number of acquisitions=30). A program was written in MATLAB (The Mathworks Inc., Natick, MA) for calculating the CBF, aBV and BAT maps. Then, mean CBF, aBV and BAT values were estimated in several different brain regions of Montreal Neurological Institute (MNI) structural, and Harvard-Oxford cortical and subcortical structural atlases. A Kruskal-Wallis test followed by Dunn's post-hoc test including multiple comparison correction, was applied for comparing the perfusion values between PD-MCI, PD-CN and HC.

Results: We observed lower mean CBF in thalamus (p= 0.005) and insular cortex (p=0.014) in PD-MCI than HC. PD-MCI had lower aBV in cuneal cortex (p=0.016) than HC. There was a trend for decreased perfusion in cingulate gyrus (p=0.025) and left hippocampus (p=0.026) in PD-CN patients in comparison to HC, and in cuneal cortex (p=0.026), occipital pole (p=0.023), and precuneus (p=0.045) in PD-MCI with respect to HC. Also, we observed a trend for lower aBV in lingual gyrus (p=0.026) and left hippocampus (p=0.040) in PD-MCI than HC.

Conclusion: ASL-MRI technique might be useful for defining biomarkers for detecting cognitive decline in Parkinson's disease at an early phase and following-up the disease. This study was supported by TÜBİTAK project #115S219 and the Ministry of Development project #2010K120330.

Keywords: Arterial spin labeling, Parkinson's disease, cerebral blood flow, arterial blood volume, bolus arrival time

O-47

Motor and non-motor symptoms in AAV-mediated alpha-synuclein overexpression model of PD in rats

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Objective: Our aim is to develop a Parkinson's disease (PD) model, which express motor and non-motor symptoms together for studying etiology and/or treatment of the disease by AAV-mediated alpha-synuclein overexpression in substantia nigra (SN) and dentate gyrus (DG) bilaterally at the same time.

Methods: Female SD rats (200-250g) were used. AAV-carrying a-syn (n=11), GFP (n=11) or saline (n=8) were injected bilaterally SN and DG. Further 7 animal used as a naive controls. All animals were tested for memory, spatial learning, anxiety, anhedonia, motor coordination and locomotion by novel object recognition (NOR), Morris water maze (MWM), elevated plus maze, sucrose preference, rotarod and locomotor activity tests respectively, 16-18 weeks following injection. Phosphorylated alpha-synuclein (p-a-syn) and synaptophysin expression levels was shown by immunohistochemistry. Neuronal loss in SN (TH+cells) and hippocampus CA2 area (NeuN+cells) were evaluated with stereological quantification.

Results: Compared to naive controls, a-syn group spent 28% less time with novel object in NOR test, had difficulties in spatial learning in MWM and spent 40% more time to find the platform in probe test ($p<0.05$). A-syn group could stay on the rod 41% less than naive controls in rotarod test. In apomorphine-induced increase in mobility in locomotor activity test was the highest in a-syn group ($p<0.05$ a-syn vs GFP, SF and naive controls). P-a-syn overexpression was seen in both SN and hippocampus especially in CA2 area. Stereological count of TH-positive neurons in SN showed %43 loss ($p<0.05$) and there was a tendency to lose NeuN-positive neuros in CA2 area in the a-syn compared to naive controls.

Conclusion: Bilateral a-syn overexpression in SN and DG could be a good model to study motor and non-motor symptoms; this may be useful to understand underlying mechanisms of PD and try possible treatments. Supported by Hacettepe University SRPCU (ID:5291). Alpha-synuclein and GFP viral vectors were kindly obtained from M.J.Fox Foundation.

Keywords: Parkinson's disease, alpha-synuclein, streology, hippocampus, non-motor symptoms

O-48

A preliminary description of the command-and-control axis

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Objective: There is a body of evidence that supports the idea of a coordinated interplay between three large-scale cerebral networks, the default mode network (DMN), the control network (CTRL), and the salience network (SN). Interactions between these networks have been linked with the process of transitioning from internal to external mental states.

Methods: Using meta-analytic software provided by BrainMap, we generated anatomic likelihood estimates (ALEs) of the DMN, SN, and CTRL networks. ALEs were displayed using Mango. Pre-constructed Region of Interests(ROIs) corresponding to the 180 cerebral parcellations published under the Human Connectome Project were used to identify the parcellations comprising each network. DSI-based fiber tracking was performed to establish the connectivity between parcellations of each network.

Results: The DMN includes parcellations that localize to the posterior and anterior cingulate cortex and inferior parietal lobule. The CTRL network localizes to the dorsolateral prefrontal cortex and lateral parietal lobe. The SN localizes to the middle cingulate cortex and anterior insula. The SN also connects to SCEF, a parcellation in the supplementary motor area.

Conclusion: The DMN is a well-known resting-state network that is anti-correlated with the CTRL network. The SN has been described as the switch between these two networks. The SN's connection to SCEF may explain how the brain prepares for proposed activity during such transfers. We propose models of three critical brain networks that play a role in the transition from internal to external mental states. Future studies will refine these models of the command-and-control axis for clinical application.

Keywords: ALE, control, default mode network, salience, tractography

O-49

Effects of cervical sympathectomy and mast cell degranulation on the levels of CGRP and SP in rats

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Objective: Migraine is multifactorial disabling neurovascular disease. Neurogenic inflammation is substantially responsible for migraine that has no yet effective treatment. Calcitonin gene-related peptide(CGRP) and substance-P(SP) released as a result of activation of trigeminovascular system and dural mast cell mediators lead to neurogenic inflammation. There are few studies showing that balance of autonomic nervous system can shift towards the sympathetic or parasympatical dominance in migraine patients. We aimed to investigate effects of cervical sympathectomy and systemic mast cell degranulation on CGRP and SP levels in structures including the generation and conduction sites of migraine pain.

Methods: 21 wistar male rats (200–250 g) were divided into 3 groups (n=7). Left superior cervical sympathetic (LSCSG) ganglions of rats in sympathectomy group were surgically excised. LSCSGs of rats in C-48/80 and Control groups were surgically reached but not excised. After 5 days of surgical operations, C-48/80 group intraperitoneally received compound-48/80 (2 mg/kg) but other groups received saline(0.2 ml). CGRP and SP contents of dura mater, brainstem and brain tissues were measured using enzyme-immunoassays. Data were analyzed with one-way ANOVA using SPSS_22.0 software.

Results: Compound-48/80 increased SP levels in brainstem, dura mater and brain, and it also increased CGRP levels in trigeminal ganglion and brainstem, compared to control ($p<0.05$). While sympathectomy decreased CGRP levels in both cerebral hemispheres(more on the side of the operation), it increased SP levels ($p<0.05$), but it didn't change SP or CGRP levels in the other tissues, compared to control.

Conclusion: Our results shows that mast cells contribute migraine pathophysiology. Although it was seen that balance between sympathetic and parasympathetic systems shifts towards sympathetic hypofunction in migraine, sympathectomy operation didn't change levels of SP and CGRP. Effect of sympathectomy on the levels of neuropeptides in the brain tissue is associated to central sensitization, however clinical investigations are also required due to results of experimental studies on this topic are different.

Keywords: CGRP, mast cell, migraine, sympathectomy, SP

O-50

The investigation of effect of macrophages on neural cells of the central nervous system

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Objective: Macrophages have a dual effect on multiple sclerosis (MS) they promote remyelination via secreted factors and they phagocytose myelin causing demyelination. Thus, signaling pathways regulating macrophage physiology are investigated as therapeutic targets. Among those pathways, dopamine and adenosine signaling pathways, drew attention due to positive results in animal models. Additionally, the two pathways were shown to act synergistically in in vitro experiments.

Therefore, synergistic modulation of dopamine and adenosine pathways in macrophages may be a key target for MS therapy. Goal of this study is to investigate the effect of modulation of dopamine and adenosine pathways on myelin damage and remyelination using macrophage oligodendrocyte co-cultures.

Methods: First, co-cultures were established with inactivated and lipopolysaccharide (LPS)-activated macrophages isolated from adult mice peritoneum and oligodendrocytes differentiated from the cortex of newborn mice. 48-hour old co-cultures were treated with single, double and triple combinations of dopamine signaling pathway agonist (Quinpirole), adenosine signaling pathway agonist (Istradefylline) and antagonist (CGS21680). Then, co-cultures were fixed and analyzed using immunocytochemistry. Macrophages were labeled with CD11b, oligodendrocytes with SOX10 and mature oligodendrocytes with Myelin Basic Protein (MBP) and quantified by cell counting.

Results: In co-cultures with inactivated and LPS-activated macrophages, an increase in the number of mature oligodendrocytes was observed while the total number of oligodendrocytes did not change. However, a triple combination of agonists and antagonist treatment reduced number of mature oligodendrocytes in the LPS-activated macrophage-oligodendrocyte co-cultures.

Conclusion: Inactive and LPS-activated macrophages increased the number of mature oligodendrocytes under co-culture conditions. Therefore, macrophages have a positive effect on oligodendrocytes when not activated by MS cues or to a similar extend and LPS treatment alone is not enough to simulate MS like conditions. Observed positive effect can be inhibited by modulating dopamine and adenosine signaling pathways. We thank TUBITAK for their support.

Keywords: Multiple sclerosis, macrophages, oligodendrocytes, dopamine, adenosine

O-51

Development of IDH mutation detection system intended for diagnosis and prognosis of glial tumors

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Objective: Molecular diagnosis of glial tumors, identification of molecular subclasses, have vital importance upon prediction of prognosis and treatment in terms of estimating the rate of success. 70% of grade-II and grade-III tumors and small sub-group of glioblastoma patients show IDH mutations. Intraoperative detection of mutations is crucial in the matter of determining the surgical limitations as well as increasing the success rate of the operation. Our study aims to provide an easy, economical, rapid and ultrasensitive mutation detection system to diagnose specific mutations during surgical operation.

Methods: From the various mutation detection techniques, Amplification Refractory Mutation System (ARMS) PCR method was selected and optimized. The most important feature that makes our study unique is establishing the PCR reaction by primers having 3 base mismatch to achieve 100% accuracy, sensitivity and specificity. 230 tumor sample with different grades were analyzed. R132H mutation of IDH1 was analyzed in those tumor samples by our mutation detection system followed by sanger sequencing of IDH1/2 gene mutations. Results were evaluated by immunohistochemical (IHC) analysis of IDH1 and ATRX proteins. In order to test our sensitivity, minimum DNA amount for our detection system was determined by using cloning and mutagenesis techniques to create a plasmid DNA containing different types of mutations as well as the wild type IDH sequence.

Results: Our detection system is 92.93% coherent with Sanger sequencing results. The remaining 7.07% was resulted R132H positive with our detection system, however sanger sequencing seems to be insufficient for detecting these mutations. As a result of comparison between ARMS PCR and IHC, it has been seen that ARMS method is superior to IHC in terms of mutation detection success.

Conclusion: Intraoperative ARMS-PCR based mutation detection system allowed to analyze IDH mutations less than 67 minutes with a rapid and ultrasensitive protocol without the need of sanger sequencing.

Keywords: Glial tumors, IDH mutations, intraoperative diagnosis, ARMS PCR

O-52

Therapeutic evaluation of minocycline and clodronate in chronic pain model

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Objective: Pain is defined as a sensory, emotional, or unpleasant feeling related to the experience acquired over time. Neuropathy occurs due to damage to the nerve fibers. The neural degeneration that develops in neuropathic pathophysiology is accompanied by pain. In this study, we aimed to demonstrate the protective and therapeutic effects of minocycline and clodronate on developing degeneration by preventing nerve feeding in the developed neuropathy model.

Methods: Rats (Wistar/mature male) produced by KSU Experimental Research and Application Center were used in the

study. The mononeuropathy model was performed by ligating the healthy sciatic nerve. Rats were anesthetized by intraperitoneal administration of ketamine (80 mg/kg), Xylazine (2.5 mg/kg), followed by a sciatic nerve with a 1 cm incision along the median line, 1 mm intervals lightly ligated from 4 sites and incision 4.0 was closed using silk suture. In the sham group, the sciatic nerve was removed and closed. The sensory functions of the rats in the mononeuropathic pain model were evaluated by using the thermal plantar test (for hyperalgesia), the dynamic plantar aesthesiometer (for allodynia) and the anti-hypernociceptive effect of minocycline and clodronate by neurobiophysics.

Results: In chronic pain groups developed with neuropathy, hyperalgesia and allodynia responses appeared, whereas in the minocycline treated group there were significant anti nociceptive effects depending on the time. Minocycline suppressed the effects of hypernocceptive emergence, but no effect of clodronate was observed in this direction. The minocycline induced significant anti-nociceptive and anti-hypernocceptive effects.

Conclusion: When the findings were examined, the healing effect of clodronate on the effects of hyperalgesia and alloidin on neuropathy was not significantly affected, while minocycline had antihyperalgesic and alloidini reducing effects. These results suggest that minocycline reduces microglial cell reactivation in neuropathies, indicating protective and therapeutic potential of minocycline.

Keywords: Pain models, minocycline, clodronate

O-53

Allosteric modulation of adenosine A2A receptors induces slow-wave sleep in mice

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Objective: Insomnia is one of the most common sleep problems with an estimated prevalence of 10% to 15% in the general population. Although adenosine A2A receptor (A2AR) agonists strongly induce sleep, their cardiovascular effects preclude their use in treating sleep disorders. Enhancing endogenous A2AR signaling, however, may be an alternative strategy for treating insomnia, because adenosine levels in the brain accumulate during wakefulness.

Methods: We established A2AR-expressing Chinese hamster ovary cells to measure cAMP produced upon A2AR activation by using a fluorescence resonance energy transfer immunoassay. Subsequently, we screened several thousand small-molecule compounds for allosteric effects at A2AR in the cell-culture bioassay.

Results: We identified a positive allosteric modulator for A2AR, termed A2AR PAM-1. When we examined the sleep-inducing activity of A2AR PAM-1 by monitoring the electroencephalogram, we found that the intraperitoneal (IP) administration of A2AR PAM-1 dose dependently (30–75 mg/kg) increased the total amount of slow wave sleep (SWS). In addition, the SWS-inducing effect of A2AR PAM-1 was suppressed by A2AR antagonist ZM241385 (15 mg/kg, IP) and abolished in A2AR knockout mice. In contrast to A2AR agonist CGS 21680, blood pressure measured by using an electrosphygmomanometer and heart rate monitored by using telemetry transmitters were not affected after IP administration of A2AR PAM-1.

Conclusion: Small molecules like the A2AR allosteric modulator A2AR PAM-1 may help people with sleep problems to fall asleep.

Keywords: Adenosine A2A receptor, allosteric modulator, slow-wave-sleep, cardiovascular effects

O-54

Relationship between retinal abnormalities and confounding factors in patients with bipolar disorder

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Objective: Prior optical coherence tomography (OCT) studies of bipolar disorder (BD) have identified changes of retinal layers. However, findings have varied across reports, and most studies have had serious methodological limitations. Therefore, we determined whether: (1) retinal changes occurs independently of metabolic parameters such as age,gender and BMI; (2) OCT indices are related to sleep disturbances in patients with BD.

Methods: Fourthy patients with BD and fourthy,age/gender/BMI matched,healthy controls (HC) were recruited in this study. Spectral domain OCT generated data on retinal nerve fibre layer (RNFL), macula, and ganglion cell-inner plexiform layer (GCL-IPL) thickness. All subjects also completed measures of subjective sleep.

Results: GCL has been found thinner in patient with BD than HC. When BMI, age, sex, and increased sleep disturbances were added to the general linear model as a confounding factor, the significant difference between the groups was not still significant. In addition, sleep disturbances and retinal parameters were highly correlated in both patient and control groups.

Conclusion: Past reports of retinal changes may be artefacts of the metabolic state that is over-represented in bipolar disorder. However, retinal abnormalities may hold promise as biomarkers with determining confounder factors in bipolar disorder.

Keywords: Bipolar disorder, retina, SD-OCT, biological rhythm

Poster Presentations

(P-001 — P-113)

P-001

Brain connectivity during picture sequencing task: an fNIRS study

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Objective: Investigation of the Prefrontal Cortex (PFC) connectivity during Picture sequencing task via fNIRS imaging.

Methods: Autistic patients suffer from lack of empathy and planning which can be attributed to an impairment of the connectivity patterns in the PFC. This study investigated the brain dynamics of 4 adults (30±8 years old, 2 males) via a 16 channels fNIRS system (ARGES Cerebro, Hemosoft, Ankara) during a Picture sequencing task. Three scenarios were presented (mechanical, behavioral, intentional) printed on cardboards. Participants were asked to sort these cards according to a scenario that they had to figure out. HbO and Hb data from 16 channels were analyzed with partial correlation analysis to compute functional connectivity matrices. Global efficiency values were then computed from the %10 strongest correlation values.

Results: Behavioral results did not show any significant performance differences among scenarios (M=2, B=1.8±0.2, I=1.7±0.3, p=0.188), while a significant difference was observed between mechanical and intentional scenarios (p=0.0398). Since no statistical difference was observed between the GE values of HbO and Hb (GEHbO=0.107±0.021, GEHb=0.105±0.025, p=0.75) the GE values were consolidated for three different types of scenarios. GE values for intentional scenarios (GEB=0.123±0.029) was higher than resting GE (GER=0.094± 0.009) and mechanical scenario (GEM=0.101±0.018) ı (p=0.0084, p=0.0068) but not with behavioral GE (GEB=0.108±0.021).

Conclusion: As expected, GE values were higher during tasks than resting periods. Several studies confirmed that functional connectivity increases during tasks that require attention. We investigated the connectivity during Picture sequencing and showed that fNIRS can reliably predict the connectivity demand of the brain during empathy demanding tasks.

Keywords: fNIRS, functional connectivity, global efficiency, picture sequencing

P-002

Neuroimaging in sepsis induced brain dysfunction: association with clinical and laboratory findings

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Objective: Incidence and patterns of brain lesions of sepsis-induced brain dysfunction (SIBD) have been well-defined. Our objective was to provide findings from brain magnetic resonance imaging (MRI) and voxel-based morphometry (VBM) of the brain in patients showing neurological alterations due to sepsis and relate it to the inflammatory and disease severity markers of SIBD.

Methods: In this prospective observational study, 93 SIBD patients (45 men, 48 women; 50.6±12.7 year-old) were enrolled. Patients underwent a neurological examination and brain MRI. Several severity-of-disease scoring systems were used for evaluation of patient outcome. Serum levels of a panel of mediators [IL-1 β, IL-6, IL-8, IL-10, IL-12, IL-17, IFN-γ, TNF-α, complement factor Bb, C4d, C5a, iC3b, amyloid-b peptides, total tau, phosphorylated tau (p-tau), S100b, neuron-specific enolase] were measured by ELISA. Voxel-based morphometry (VBM) was employed to available patients for assessment of neuronal loss pattern in SIBD.

Results: MRI of SIBD patients were normal (n=27, 29%) or showed brain lesions (n=51, 54.9%) or brain atrophy (n=15, 16.1%). VBM analysis showed neuronal loss in the insula, cingulate cortex, frontal lobe, precuneus, and thalamus. Patients with abnormal MRI findings had worse APACHE II, SOFA, GOSE scores, increased prevalence of delirium and mortality. Presence of MRI lesions was associated with reduced C5a and iC3b levels and brain atrophy was associated with increased p-tau levels. Multivariate regression analysis identified an association between reduced IL-12 level and occurrence of coma.

Conclusion: Neuronal loss predominantly occurs in limbic and visceral pain perception regions of SIBD patients. Complement breakdown products, IL-12, and p-tau stand out as adverse neuroimaging and neurological outcome markers for SIBD. This work was supported by Scientific Research Projects Coordination Unit of Istanbul University. Project number 35165 and 46960.

Keywords: Brain dysfunction, C5a, neuroimaging, p-tau, sepsis

P-003

fNIRS analysis of brain function during stroop task

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Objective: Quantitative determination of functional-connectivity of prefrontal cortex from fNIRS data during Stroop Task.

Methods: In this study, 15 adult subjects (20±2 years, 10 males) without neuropsychiatric disease performed Stroop task. Attention, response-control and working-memory evaluated with 16-channel fNIRS system (ARGES Cerebro, Hemosoft, Ankara). For each person a functional-correlation matrix system is created by partial-correlation analysis using the HbO-data collected from fNIRS.In this matrix, the strongest %10 correlation coefficient and the global efficiency (GE) value (one of the graph theory theorem) is calculated.

Results: Subject data divided into two groups according to the GE values taken in the beginning: (Rest1), test (Test) post-test (Rest2) durations.It was taken into consideration that the GE value before test was larger or smaller than at the test time.For the first group: GEHbO (Rest1)=0.139±0.019, GEHbO (Test)= 0.104±0.0085 and GEHbO (Rest2) = 0.1236±0.0187; for the 2nd group: GEHbO (Rest)=0.1051±0.0099, GEHbO (Test)= 0.1348± 0.0233 and GEHbO (Rest2)=0.134±0.023.Mean score of the groups for task was over 40: first group score was 37±2.8 and duration was 32±5 seconds; second group score was 37±2.5 and duration was 30±6 seconds.One-sided t-test shows, the GE values (p(Rest1&Test)=0.0056, p(Rest1&Rest2)=0.0735 and p(Test& Rest2) =0.0695) were significantly different. Similarly, the GE values in second group (p(Rest1&Test)=0.0016, p(Rest1&Rest2)= 0.003 and p(Test&Rest2)=0.532), were significantly different.

Conclusion: When the first group (GEHbO (Rest1) > GEHbO (Test)) and second group (GEHbO (Rest1) <GEHbO (Test)) compared; while the GEHbO (Rest1) was higher, a decrease in score and an increase in test duration was observed, while the GEHbO (Test) was higher, an increase in the score but a decrease in test duration observed.However, subjects who had higher GE during the pre-test spent more time with less accuracy. Based on these data, GE indicates 'focusing, increases in inhibition ability. The functional-connectivity seems to be more efficient in the test-focused brain.

Keywords: fNIRS, functional connectivity, global efficiency, stroop

P-004

Investigation of neurogenesis in kindled Wistar albino rats

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Objective: The most common type of epilepsy affecting about 50 million people worldwide is temporal lobe epilepsy (TLE). Chemical and electrical kindling methods in animals can be used to form the TLE model. In this study, it was aimed to investigate neurogenesis by immunofluorescence methods in the hippocampus of adult Wistar rats, which were applied chemical kindling.

Methods: Adult male Wistar albino rats weighing 250-300 gr were injected PTZ (35 mg/kg) subcutaneously every other day to produce chemical kindling (Wistar kindling 7th day group n=6; 14th day group n=6). Sham-operated control groups were injected physiological saline solution subcutaneously (Wistar sham-operated 7th day group n=6; 14th day group n=6). Animals having grade 5 seizures five times were considered to be kindled. Intracardiac perfusion was performed under deep anesthesia on the 7th and 14th days after the last grade 5 seizure. Then, the animals were decapitated and brain tissues were removed and incubated at 4°C overnight within the same fixative. The tissues were frozen at -80ºC and 5 µm sections were obtained with a cryomicrotome. Immunofluorescence methods were used to show doublecortin (DCX) positive newly formed neurons and glial fibrillary acidic protein (GFAP) positive cells. Sections were then examined under fluorescence microscope.

Results: DCX positive cells were observed in the subgranular zone of gyrus dentatus in the control and kindling groups. An increase in GFAP positive cells in the kindling groups, compared to the control groups, was observed.

Conclusion: The findings of the present study indicate the existence of neurogenesis in the control and kindled adult Wistar rats. The increase in GFAP positive cells in the kindling groups suggests astrogliosis.

Keywords: Doublecortin, hippocampus, kindling, neurogenesis

P-005

Examination of Alzheimer's disease with voxel-based morphometry analysis

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Objective: Alzheimer's is a neurodegenerative disease which has been rapidly increasing with the elderly population in the world. While the structural character of Alzheimer's disease was being investigated, in addition to their cognitive impairments, the patients have also been found to have some changes in their brain anatomy as a result of their autopsy. The aim of the study is to investigate the issue loss caused by Alzheimer's disease via structural MR images. Voxel-based morphometry (VBM) analysis was chosen the most suitable method for this purpose. Additionally, by incorporating a common neuropsychological test called Mini Mental State Examination (MMSE) scores into the study, a linear relationship between the test and the volumetric change of grey matter and/or white matter were examined.

Methods: Structural T1 weighted MR images of 46 patients who were diagnosed with second grade, mild-moderate Alzheimer's disease according to the criteria set by the

NINCDS and ADRDA together with 23 healthy subjects are available in the MIRIAD (Minimal Interval Resonance Imaging in Alzheimer's Disease Dataset) database. Statistical parameters were estimated using VBM on the SPM platform, based on a general linear model for each voxel in all 69 MR images. The analyses were repeated to check if there is a relation between the tissue loss and the factors as MMSE, age and gender by adding them to the model.

Results: Anatomical differences were found between Alzheimer's patients and healthy individuals due to the tissue loss in the regions of the right and left; thalamus, caudate, hippocampus, hippocampal gyrus. Additionally, there have been a increase in the right and left lateral ventricles, CSF, and cerebral white matter.

Conclusion: Understanding Alzheimer's disease goes through the identification of distinctive regions in the brain anatomy. Tissue loss caused by Alzheimer's disease can be studied by VBM analysis.

Keywords: Alzheimer's disease, voxel-based morphometry, atrophy, volume change

P-006

QEEG analysis of epileptic EEG signals

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Objective: Epileptogenic Zones (EZ) detection using noninvasive EEG neuroimaging is aimed in this paper. Quantitative EEG (QEEG) analysis is used for artifact reduction, processing and source localization of recorded epileptic signals. Results are compared with others reported in the literature to better understand the importance of QEEG analysis in the context of epilepsy.

Methods: EEG recordings of 5 patients from a dataset recorded in 10-20 system using 19 electrodes and sampled at 250 Hz are analyzed. Dataset includes pre-surgical EEG recordings and 4 out of 5 patients real MRI images. Patients' names are coded using 6 digits for privacy. Data is obtained from Zwoli*f*ski P. et al. (2010) by email. The ethics committee approval procedure was conducted at the Warsaw Memorial Children's Hospital. Seizure initial times in EEG recordings are marked carefully by an expert neurologist. Epochs 300 ms before and 500 ms after marked seizures are generated from the dataset. Artifact reduction, sub-bands analysis and source localization are performed on epochs. The Brainstorm software from The Biomedical Imaging Group of USC at LA is used for the analysis.

Results: Brain maps are obtained after QEEG analysis. MRI scalp maps are analyzed by expert neurologist. Since EEG artifacts effect source localization considerably they are reduced before running both distributed and dipolar methods. EZs provided by source localization algorithms almost overlap with identified EZs. They show active regions while epileptic seizure begins. Expert neurologist compared visually findings with postoperative MRI or defined EZ areas. Localization errors are obtained visually.

Conclusion: Considering the findings QEEG analysis helps us to understand complex brain signals better. Brain maps by inverse algorithms indicate promising results compared with ECoG findings obtained before. Noninvasively detection of EZs by neuroimaging methods developed in the last four decades help clinical and brain research. The co-operation between physicians and engineers have improved understanding of complex brain signals.

Keywords: Epilepsy, epileptogenic zone (EZ), quantitative electroencephalogram (QEEG)

P-007

Investigation of the effect of tDCS on resting state network connectivity in MTLE

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Objective: The purpose of this preliminary study is to examine the effect of tDCS on resting state network connectivity in patients diagnosed with mesial temporal lobe epilepsy (mTLE) in order to develop a new method to inhibit epileptic seizures.

Methods: The present study analyzed the resting state functional MRI data from a homogenous group of mTLE patients with left hippocampal sclerosis using seed-based correlations. Nine drug-resistant unoperated patients with left mTLE (mean age 36.8±9.95) participated in this study. Resting fMRI scans were acquired before and after 2 mA cathodal tDCS lasting 20 min over the temporal region (T3) while anode electrode was placed over supraorbital region. Pre- and post-tDCS resting state fMRI data were recorded with 3T MRI scanner and SPM8 was used for data preprocessing. Functional connectivity analyses were conducted with the CONN-fMRI toolbox and 62 seeds were selected. The corrected results with significant cluster level of $p < 0.05$ FDR have been calculated.

Results: Increased functional connectivity following cathodal tDCS was apparent between left supramarginal gyrus (anterior

division) and right posterior cerebellum (pFDR=0.03), left fronto-parietal network and left posterior cerebellum (pFDR=0.03). While an increased correlation was also observed between left insula and left inferior frontal operculum (pFDR=0.005), there was decreased correlation between left temporal fusiform cortex and left inferior frontal gyrus (pFDR=0.03).

Conclusion: Increased connectivity between cerebellum and the fronto-parietal network after tDCS may indicate a positive finding to control the seizures. Increased connectivity between the left insula and left inferior frontal operculum may also be important in controlling seizures by providing a feedback mechanism. Furthermore, increased connectivity between the left anterior supramarginal gyrus and right posterior cerebellum could be speculated to have a positive value on cognitive functions. On the other hand decreased connectivity between the left temporal fusiform cortex and left inferior occipital gyrus may be evaluated in regard to clinical symptoms.

Keywords: Resting-state connectivity, left mesial temporal lobe epilepsy, transcranial direct current stimulation

P-008

Role of electron microscopy in sural nerve biopsies: case report

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Objective: Nerve biopsies are very valuable in the diagnosis of peripheral neuropathies as well as in many other diseases but there are some disadvantages. The most common one is an invasive procedure may cause sensory loss. In this study, we investigated the results of light and electron microscopy of sural nerve biopsy taken from an 81-year-old female patient who applied to Gulhane clinic with pre-diagnosis of vasculitis and investigated the importance of electron microscopy in diagnosis.

Methods: One half of the sural nerve biopsy taken from the patient was stained with hematoxylin-eosin followed by routine paraffin procedure in the pathology laboratory. The other half of the biopsy was applied a routine EM follow-up procedure in the histology laboratory and semi-thin sections from the material were stained with Toluidine Blue and examined under light microscope. Thin sections were examined and evaluated with LEO 906E transmission electron microscope (TEM).

Results: In light microscopy, we found normal peripheral nerve bundles and there's no clue for vasculitis. Myelinated and unmyelinated axons were identified as damaged in semi-thin sections. Examination of thin sections in EM; degenaration of myelin sheaths, thickening of basal laminae of the vessels in the perineural region and endoneurium attracted attention. The axoplasm of many axons was seen as damaged. The presence of these neuropathologic changes has been interpreted as a change due to a secondary disease.

Conclusion: The electron microscopic evaluation is important for showing the presence of neuropathologic findings that can not be observed with light microscopy in routine paraffin sections. We supported the report of pathology in order to exclude the diagnosis of vasculitis. The duty of physicians is to be able to provide good balance of benefits and harms of the methods used, to use the right method in the right place, and to take into consideration the harm to the patient.

Keywords: Peripheral neuropathy, sural nerve biopsy, transmission electron microscope

P-009

ANN-based classification of fNIRS data recorded during motor imagery

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Objective: Use of Artificial Neural Network (ANN) classifier on fNIRS data to determine which hand is being imagined during a motor imagery task.

Methods: 4 adults (20+2 years old, 1 female) were recruited. HbO data recorded from the forehead via a 16 channels fNIRS system were analyzed while the subjects performed a motor execution followed by a motor imagery task of opening (20 seconds) and closing the four fingers (20 seconds) simultaneously for both hands. To accurately classify the data, a feed-forward Artificial Neural Network with supervised learning was used. The network was trained by the motor imagery/motor execution/rest classes as outputs and the HbO dataset as the inputs.

Results: Accuracy of the ANN classifier was tested for Rest data (R), motor execution (ME) and motor imagery (MI). An accuracy of 61.96%±6.42% was achieved using only a single channel of the fNIRS. An accuracy of 87.03%±3.78% using the two outer left and right channels (1–2, 13–14) and an accuracy of 94.45% ±0.69% using the four outer left and right channels (1–4, 11–14) were computed. Using all 14 channels, an accuracy of 97.86%± 0.34% was obtained.

Conclusion: The accuracy achieved through the usage of a single channel is expectedly low. Interestingly, using only the first two left and two right channels provide an impressive improvement in accuracy and reaches a value of 87.03% in accuracy. Using eight channels increases the result to 94.45% in accuracy. These findings demonstrate that a good classifier for motor execution and imagery should use bilateral measurements. The extreme similarity in accuracies of the 8 and 14 channel datasets also shows that the usage of eight channels can be an optimal number in the measurements of prediction of intent in the prefrontal cortex in further research.

Keywords: fNIRS, motor imagery, brain computer interface, artificial neural networks

P-010

A new approach to myasthenia gravis: functional near-infrared spectroscopy

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Objective: Myasthenia gravis (MG) is an autoimmune disease with fluctuating muscle weakness and impairment of neuromuscular transmission caused by antibodies to nicotinic acetylcholine receptor (AchR). Early detection of MG may increase early intervention chances. In this study, we aimed to investigate changes in oxyhemoglobin (HbO) and deoxyhemoglobin (HbR) concentrations in unilateral biceps muscles during resting state and exercise via functional near infrared spectroscopy (fNIRS) in MG patients and healthy controls.

Methods: Five patients who were diagnosed with MG at the Department of Neurology, Istanbul Medipol University and five healthy controls were recruited. Experiment protocol with the NirStim program was recorded with 3 sources and 3 dedectors on a muscle band.

Results: This study focused on whether there was a difference in HbO and HbR concentration changes in the biceps muscle between MG patients and healthy controls.

Conclusion: It will be discussed whether fNIRS can be used to diagnose MG disease.

Keywords: Functional near infrared spectroscopy, myasthenia gravis, neuroimaging

P-011

Cerebellar contribution to implicit associative learning: a seed-based functional connectivity study

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Objective: This study, aiming to investigate the cerebellar role on non-motor implicit associative learning (IAL), is based on seed-based connectivity analysis on functional magnetic resonance imaging (fMRI) data obtained from patients with spinocereballar ataxia (SCA) and healthy controls (HC) during Triplet Learning Task (TLT). In the experiment, implicit learning is occurred when the associations between predictive cue and target are acquired with practice.

Methods: 15 SCA patients (8 females) and age-sex-education matched healthy subjects performed TLT in 3T MRI scanner. The experiment consisting 6 blocks was repeated twice. Seed-to-voxel connectivity analysis was performed with chosen seeds (striatal, thalamic, hippocampal, cerebellar structures and networks) using the CONN toolbox. The results surviving height threshold uncorrected $p<0.001$ and cluster-level FWE-correction ($p<0.005$) were presented.

Results: SCA group did not improved in task performance with practise. Compared to SCA, IAL was found related with increased functional connectivity in HC between (1) putamen and middle temporal, supramarginal, angular gyri, (2) right serebellum lobule IV-V and left fusiform, inferior temporal, lateral occipital, hippocampal, parahippocampal areas, (3) left cerebellum-X and left orbitofrontal, right lateral occipital areas, (4) vermis-VI and right supramarginal, angular gyri, partly superior parietal lobule (SPL), (5) vermis-VIII and primer visual areas, (6) right superior temporal gyrus and right putamen, pallidum, and decreased connectivity between (1) superior sensorimotor network and postcentral gyrus, SPL, (2) dorsal attention network and central opercular, insular cortices.

Conclusion: IAL was associated with increased connectivities of putamen with ventral (what) and dorsal (where) pathways, cerebellum with the structures that have critical role on visual long-term memory in contralateral cerebral cortex, and superior temporal gyrus with right putamen and pallidum. Our results indicate that cerebellar interaction with ventral systems mediating long-term visual memory formation and reward-based associative learning as well as occipitotemporo-neostriatal projections supporting stimulus-response association formation play important role on IAL. Supported by TÜBİTAK project # 115S437.

Keywords: Non-motor implicit associative learning, implicit memory, cerebellum, spinocerebellar ataxia, seed based functional connectivity

P-012

Assessment of head movements using AFNI and ReHo in fMRI images

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Objective: The aim of this preliminary study is to detect head movements and to identify the affected brain regions using Analysis of Functional NeuroImages (AFNI) software and ReHo (Regional Homogeneity) analysis.

Methods: This preliminary study is done to understand the effects of head movements in fMRI (functional Magnetic Resonance Imaging) studies.Total 12 fMRI shots were examined which are gathered from two groups of six volunteers aged between 9–16 years. Moco group which has head movements reduced to 0.3 mm by eliminating head movement artefacts and not moco group which has head movements at the range of 1mm-2 mm without motion correction were created. Resting-State fMRI scans were performed in 1.5 Tesla Siemens MR, at Erciyes University Hospital Pediatric Radiology Department. With AFNI,pre-processing steps which are time-shifting, alignment, volume-registration, blurring and finally filtering were performed. Using the 3dReHo command in AFNI, Kendall's fit coefficient was calculated and ReHo analysis was performed. A single sample t-test ($p<0.05$) was used to statistically evaluate the results and to determine activation regions with distinctive values. In order to determine the meaningful cluster threshold AFNI 3dClustSim command is used to determine the cluster threshold which can be considered significant (thr>50) distinctive values.

Results: The highest activation in the Moco group was observed in BA19, BA7 and BA32 respectively in the ReHO result. In the Notmoco group, BA39, R-Thalamus and BA7 were the most activated regions. When two groups were combined and analyzed as a single group, result shows a tendency in favor of moving data and the highest activation was observed in BA39, R-Talamus and BA7 respectively.

Conclusion: This preliminary study reveals the importance of correcting the head movement artifacts by investigation the changes in the activated regions due to head motion. This project was approved by Erciyes University Ethics Committee for Clinical Investigations (Decision No.2015/27) and supported by Tübitak (Project No: 215E356).

Keywords: fMRI, resting state, regional homogenity (ReHo), AFNI

P-013

Effects of early anesthesia exposure on human brain development: a machine learning approach

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Objective: Functional connectivity is an emerging field of medicine which helps to analyze the spatiotemporal relations of hemodynamics between different regions of the brain. In this part of the study, we aimed to come up with a robust classifier that is able to distinguish the resting state fMRIs of test subjects, who were exposed to anesthesia in their early age, from those of control subjects using popular methods in machine learning.

Methods: We used the confidential dataset obtained by the preprint study "Effects of Early Anesthesia Exposure on Human Brain Development Using Multimodal Neuroimaging" which has 24 sessions of fMRI data half of which are from the exposed group. We employed partial correlation to convert times series into the functional connectivity matrices since it has been reported to be a useful metric to analyze functional connectivity on resting-state fMRI data (Zhen et. al 2007). After constructing the correlation matrices of patient and control subjects, we have performed advanced machine learning methods such as the random forest and gradient boosting classifiers and support vector machine using parameter optimization, feature selection, and cross-validation techniques.

Results: We obtained 61.6% mean test accuracy using SVM classifier kernel=RBF, C=0.001, gamma=0.001 which is the highest among other machine learning methods Random forest: 0.55 ± 0.16, Gradient Boosting: 0.48 ± 0.18. Feature selection algorithms have reduced feature size from 741 to 115. However mean accuracies for most classifiers have decreased by 10% SVM: 0.508, Random Forest: 0.426, Gradient Boosting: 0.482

Conclusion: It is concluded that the feature space extracted from these subjects has exceeded the capability of available sample size, as more data was required for classifiers in order to yield a better test accuracy. All in all, SVM classifier with given parameters has given the best result among 3 different classifiers with a test accuracy of 0.616.

Keywords: Anesthetic neurotoxicity, machine learning, classification, functional connectivity, fMRI

P-014

Statistical parametric mapping of hand movements using block design in ffMRI

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Objective: One of the purposes of this research is to demonstrate that a mapping result in accordance with the current literature has been achieved using a standard procedure and then to make an improvement by recovering the statistical parametric mapping made by the standard procedure with the bootstrap technique where the β parameters are more accurately estimated.

Methods: Data were collected using a Siemens Magnetom 7T (Minnesota, USA) system. The block design consists of 10 data sets with a 12 seconds rest as 12 seconds task and the slice thickness is 1.5 mm. The motor task in the experiment consisted of pressing the button with the left or right hand and a left-facing arrow for left-handed movement and a right-facing arrowed visual for right-handed movement. In this experiment TR=2.7 s. For the analysis of the data in this study, the General Linear Model (GLM) was used for statistical parametric mapping. $Yi = \beta 0 + \beta i\, Xi + \varepsilon i$ Motion correction, smooting, etc. corrections are selected as FWE 0.05, DOF 12 according to the instruction manual of the SPM (program).

Results: In both hemispheres, the signal change associated with hand movement, especially in the motor cortex, was taken into

account and t test were used to identify significantly activated regions. Data analysis and parameter estimates were made and active brain regions were marked for p<0.05.

Conclusion: The SPM mapping found in this experiment was obtained in such a way that the activations would be on the left side of the motor cortex for the right hand and on the right side for the left hand, as appropriate to the current literature. The bootstrap technique has not been implemented yet and will be used in the second part of this exercise.

Keywords: Functional magnetic resonance imaging (fMRI), statistical parametric mapping (SPM), hand movement task

P-015

Comparing performance of AI techniques based wavelet transforms for detection of epileptic seizures

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Objective: This study presents an efficient procedure that provides an accurate classification of Electroencephalogram (EEG) signals for detection of epileptic seizures.

Methods: Essentially, this procedure hybridizes various artificial intelligence techniques with the discrete wavelet transforms (DWT) and the feature selection methods. In analysis, the performance of artificial neural networks (ANNs), support vector machines (SVMs), regression trees (RT) and Naive Bayes Classifiers (NBCs) is compared with each other on a benchmark data set. This data set consists of five sets (A–E), each containing 100 single channel EEG signals. A and B has EEG recordings of five healthy volunteers with eyes open and closed, respectively. Sets C, D, and E are recorded intracranially from five patients selected from EEG archive of presurgical diagnosis in different brain regions. To ensure the efficient classification performance, the automated multi-resolution signal processing technique splits EEG signals into the detailed partitions with different bandwidths, and then decomposes them into detail and approximation coefficients using DWT. By means of the feature selection methods, the dimension of feature matrix is reduced into the significant components where they are used as the inputs in the estimation procedures.

Results: According to the analysis results, the proposed procedure gives the accuracy rates close to one hundred percent with lower mean square error and information criteria (Akaike and Bayes information criteria) and lower dimensional features.

Conclusion: This procedure not only allows making an efficient analysis of EEG signals for detection of epilepsy, but also provides the best model configurations in the context of reliability and complexity. Besides, this procedure can be easily adapted to another epilepsy data set.

Keywords: EEG signal processing, epileptic seizures, discrete wavelet transform, artificial intelligent techniques, feature selection methods

P-016

Dealing AI problems with natural intelligence: a spiking neural network for pattern representation

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Objective: Those who work on intelligent systems aim to acquire the hardware and tools that can solve problems with artificial intelligence. In this study, spiking neural networks, especially for pattern representation applications are created based on information obtained by the neuroscience studies of the learning rules and neural network structures.

Methods: The proposed structure is a simple model of cortex and models the representation of sensory inputs of different stimuli coming from the visual field. First, the stimuli were transformed into 10-dimensional vectors by the singular value decomposition and the analysis of the principal components, so that the stimuli coming from the retina into the V1 area were represented by these vectors. The cortex region for the visual association is modeled by taking into account the nerve cells producing the spikes and the connections between them. The weights of the connections between the cells in the cortex were updated according to the Hebbian rule to build the representation of different stimuli. Thus, the neural networks model and dynamic connections between cells are defined and the connection dynamics are modeled using protocols developed for the adaptation of synaptic connections. The simulation environment is prepared on BRIAN library written in the Python programming language.

Results: It has been observed that, during the simulation certain neurons have started to fire over time in response to the patterns belonging to the same class in the model, by repetition of stimuli. For each pattern, the firing of the same group resulted in the representation of the different patterns with different neuron groups.

Conclusion: A model is proposed that has a dynamic connection inspired by of the structure in the cortex and self-regulated pattern representation. The proposed model can be used in artificial intelligence applications since it is a simple structure suitable for realizing on hardware such as FPGA.

Keywords: Hebbian rule, computational neuroscience, spiking neural networks, spike time dependent plasticity rule

P-017

Effect of transcranial sinusoidal direct current stimulation on hand grip exercise and fatigue index

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Objective: Handgrip force is an important indicator of body's general health and plays a crucial role in many daily and sportive activities. The aim of this study was to investigate the effects of 10 Hz frequency modulated transcranial sinusiodal direct current stimulation (ts-DCS) on handgrip exercise performance.

Methods: Twenty-four healthy young volunteers without neuromuscular disorders or drug use, participated in this study. In order to measure the handgrip exercise performance, maximal intermittent grip endurance (MIGE) protocol was used. First day, baseline handgrip force values of participants were measured from two minutes of MIGE. Second day, electrical or sham stimulation was applied to participants for 20 minutes. During last two minutes of this stimulation final handgrip force values of participants were measured with the same MIGE protocol.The stimulation parameters were defined as 0.35 mA sinusoidal amplitude and 1.70 mA offset. Frequency modulation was set at 10 Hz. Maximal force and mean force values of participants were recorded during the MIGE protocol. Participants' fatigue index results were calculated by using their force values.

Results: Statistical analyses revealed significant differences between maximal force values (p=0.026) and mean force values (p=0.013) of 10 Hz ts-DCS and sham groups of left primary motor cortex stimulation. 10 Hz ts-DCS compared to sham condition did not show any significant effect on fatigue index values.

Conclusion: 10 Hz ts-DCS had a positive effect on maximal force values and mean forces values. In the literature, it is already shown that alpha synchronization is correlated with successful motor performance. We propose that 10 Hz ts-DCS may cause alpha synchronization and enhance neural efficiency of cerebral cortex.

Keywords: Alpha waves, motor cortex, transcranial electrical stimulation

P-018

Therapeutic effect of adhesive capsulitis proprioceptive neuromuscular facilitation techniques

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Objective: Proprioceptive Neuromuscular Facilitation (PNF) techniques have been performed to examine the effectiveness of treatment in patients with adhesive capsulitis.

Methods: 40 cases participating in the study were randomly divided into two groups. Patients in the control group (n = 20) were treated with conventional physical therapy with hot pack, ultrasound and home programs, and patients in the study group (n=20) with conventional physical therapy and additionally, physical therapyconsisting of PNF patterns for 15 sessions. Visual Analogue Scale was used for pain assessment. Observational posture analysis was used to evaluate postural disorders. Range of motion measurements were made with goniometer. Lateral Scapula Slip Test used for evaluation of scapular position. Functional performance of patients was assessed with Shoulder Pain and Disability Index (SPADI).

Results: As a result of the study, it was seen that pain in activity group decreased significantly and joint range of motion increased in both groups ($p<0.05$). The increase in flexion and abduction range of motion was greater in the PNF group ($p<0.05$), but there was no difference between the groups in the internal and external rotation range of motion. There was no significant change in the control group ($p>0.05$) while a decrease in night pain was detected in PNF group ($p<0.05$). The scapular position did not change in both groups after treatment ($p>0.05$). SPADI scores were significantly decreased in both groups ($p<0.05$).

Conclusion: In patients with adhesive capsulitis, PNF applications have significant effects on night pain, shoulder flexion and abduction range of motion parameters. Better results may be obtained by adding PNF applications to the adhesive capsulitis treatment program.

Keywords: Neuromuscular, the facilitation, treatment

P-019

The determinative effect of semantic content and color on attention response

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Objective: Our cognitive responses depend on different features of the stimuli such as saliency, physical properties and semantic content. In this study we tried to understand the effect of semantic content (threat or neutral) and color, on our attentional response in terms of response time (RT) and accuracy.

Methods: 49 participants between the ages 18-30 joined a computer-based attention task in which they were shown threat words and their neutral counterparts, either gray or in color, in a random order (and in the same frequency) at the centre of the screen and asked to respond to these words. Threatening and neutral words were previously nominated the strongest among candidate words by 300 participants.

Results: We first compared response to threatening and neutral words to understand the effect of semantic content on our attentional performance. The number of correct responses was significantly higher for neutral words ($p<.001$), although no difference was observed for RTs ($p<.301$). We then included color in our analysis and found that RTs were significantly slower when the threatening words were presented in blue or red ($p<.001$; $p<.001$), while no difference was observed for the accuracy of the answers ($p<.802$; $p<.471$). In case of neutral words, however, color had no effect on the response. We next focused on the color specific effect by comparing the stimuli in blue and red, and found no difference in the response for either threat (RT: $p<.152$; accurracy: $p<.490$) or neutral words (RT: $p<.181$; accuracy: $p<.431$).

Conclusion: Our results uncovered the differential effect of semantic and physical properties on the accuracy and timing of attentional performance and the interdependent influence of semantic and physical properties on attentional performance. We also found that our motor responses by left and right hands are significantly different in a simple response task, but this difference is diminished in more complex tasks.

Keywords: Attention, response accuracy, response time, threat

P-020

Investigation of the modulation in motor evoked potentials recorded from tibialis anterior muscles

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Objective: In understanding the motor control mechanism, the use of motor evoked potentials (MEP) in identifying central and spinal lesions is a fundamental method of investigation. In this study, the response changes in the excitability of lower leg muscles using the transcranial magnetic stimulation (TMS) were investigated in tibialis anterior (TA) as well as its antagonistic muscles during relaxed (R), dorsiflexion (DF) and plantarflexion (PF) positions. Bipedal walking mechanism has been studied.

Methods: TMS stimulation was performed on the scalp at an average stimulator output of 90%. The MEP amplitude and latency of TA muscle were recorded using a TMS (Magstim 200) round coil. MEP responses were taken at 10 kHz sampling frequency with an EMG device (Nihon Kohden Neuropack) trigerred by the TMS device. 36 (15 female, 21 male) healthy volunteers with no pathological symptoms were included in the study. Superficial EMG electrodes were used in 30 subject and needle EMG electrodes were used in 6 subject.

Results: Average age of 36 subjects was 21.52±2.68, height average was 174.11±11.43 cm and average weight 70.72±17.01 kg. In 30 healthy volunteers using surface electrodes; TA-R MUP; latency: 29.8 ms, amplitude: 4.5 mV. TA-DF MUP; latency: 27.5 ms, amplitude 8.4 mV. TA-PF MUP; latency: 30.4 ms, amplitude: 5.3 mV. In 6 healthy volunteers using needle electrodes; TA-R MUP latency, 31.7 ms. TA-DF MUP 29.0 ms. TA-PF MUP was found to be 32.0 ms.

Conclusion: In view of the findings, in the motor excitability study, the latency of the TA muscle during F and DF movements changed significantly (p=0.004). Latency was prolonged with target muscle stretch, and when the target muscle contraction was about 20% MVC. It has been found that the cortex is more effectively excitable when it contracts the T.A. This study is supported by TUBITAK 1919B011700467.

Keywords: TMS, MEP, tibialis anterior, excitability

P-021

A new system for the measurement of sensory reactions on the central nervous system

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Objective: To obtain information from central nervous system, a system to stimulate the mechanoreceptors on tip of finger including all softwares was designed and tests using the system have been started

Methods: When central nervous system has any problem, Somatic Area I-II responds to the receptors' pulses differently. In this respect, it is possible to identify some of central nervous diseases, if somatosensory that are placed on tip of finger is stimulated and responses of subjects are recorded and analyzed. Tests are conducted on healthy and diseased subjects in experimental group we identified. Aim of test is to isolate diagnosed patients from healthy subjects. To demonstrate this, we designed a new system to stimulate receptors on tip of fingers. System mechanical design made with autoCAD and CATIA, the system was manufactured precisely on laser cutting machines. Stepping motors and drivers used for movement. To gain linear motion to stepper motors, mod1 sized metal creamier and castpoliamid pinion were used and they were manufactured on lathe machines. Embedded board controller designed using PIC18F46K22, programmed in MicroC and circuit diagram was designed using ARES/ISIS. Type of test and its parameters can be identified by test creators easily. However, current system CM4 should be reprogrammed by producer because test parameters and types are embedded in to the CM4 system. During test, machine stimulate mechanoreceptors that are placed on tip of fingers according to test protocol and asks questions to subjects. Questions are "which started first", "which touched more" and "Whichever pushed upward". Subjects' answers are recorded to be evaluated by help of a software developed using DotNet C# and SQL Express 2014.

Results: Test phases still continue at KOU School of Medicine and Istanbul Faculty of Medicine Department of Geriatrics. Results will be analysed after collecting enough data.

Conclusion: Results will be analysed and going to be shared in end.

Keywords: Neural measurment, central nervuous activities measurement, cortaical metrics, embedded

P-022

Validity and reliability of sensory sensitivity scale

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Objective: There are differences in sensory sensitivity among general population. Abnormal sensory sensitivities coexist with psychiatric/neurologic disorders such as schizophrenia, bipolar disorder, autism spectrum disorder. Turkish literature is lacking a sensory scale which can evaluate sensitivity on modalities separately. The purpose of this study is to develop a scale that evaluates non-social visual, auditory and somatosensory sensitivity.

Methods: Two studies were completed with different populations. Visual-Auditory Sensitivity Scales were developed in Study-1; Somatosensory Sensitivity Scale was developed in Study-2. In pilot stage, 16 visual, 20 auditory, 34 somatosensory sensitivity questions and self-evaluation questions for each modality were generated. Pilot studies conducted with 405 healthy participants for study-1 and 294 healthy participants for study-2. Data were examined with exploratory factor analysis, items with low factor load (<0.40) were eliminated. In second stage, visual and auditory sensitivity scales (12 items on each) were applied to 429, somatosensory sensitivity scale (19 items) was applied to 636 healthy participants. Factor structures were examined via confirmatory factor analysis. Cronbach's Alpha coefficients were computed. Participants were divided into two groups as low-high autistic traits by Autism-Quotient scores. External-validity was examined with the Autism Quotient and self-evaluation scores.

Results: Cronbach's alpha coefficients were 0.86, 0.79 and 0.78 for visual, auditory and somatosensory sensitivity scale, respectively. Model-fit measures were CFI=0.973, TLI=0.965, RMSEA= 0.075 for visual; CFI=0.943, TLI=0.927, RMSEA=0.074 for auditory; CFI=0.955, TLI=0.946, RMSEA=0.048 for somatosensory scale. Visual and auditory scales showed one-factor structure; somatosensory scale items showed three, representing touch, pain and itch. Visual, auditory and sensory sensitivity scores were significantly higher in high autistic trait group (p=0.010, p<0.001, p=0.002, respectively).

Conclusion: A Sensory Sensitivity Scale was developed in this study which can effectively evaluate sensitivity on visual, auditory and somatosensory stimuli. Participants with high autistic scores showed significantly higher sensory sensitivity in accordance with previous studies.

Keywords: Sensory sensitivity, scale development, autistic traits

P-023

Sorting spikes from S1 cortex for prediction of behavioral events in neuroprostheses

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Objective: Operational performance of cortical neuroprostheses depends on the decoding algorithms running on spikes recorded from somatosensory and motor cortices. We are conducting a project which involves predicting psychophysical responses of rats based on sensorimotor cortical activity and which will provide tactile feedback directly to the brain. This preliminary work establishes the protocol for real-time spike sorting for the project.

Methods: 29 extracellular recordings from S1 cortices of 4 Wistar rats were collected under anesthesia using single carbon-fiber electrodes (diameter: ~7 µm). Vibrotactile stimulus (amplitude: 100 µm, duration: 0.5 s) was applied for three frequencies (5, 40, and 250 Hz) on the glabrous skin of the rat hindpaws after receptive field mapping. Extracellular action potentials were amplified (×1000) and band-pass filtered (200 Hz – 10 kHz). They were further processed by TDT RZ5D processor with DSPs. Candidate action potentials for sorting were selected by thresholding (6×noise rms level) the raw data. Action potential snippets were represented according to the first three (largest variance) principles components (PCs). K-means algorithm was used for clustering in the PC space (cluster count: 3, outlier STD: 2). Resulting cluster was identified as single unit if within cluster SNR>3 and refractoriness was observed; otherwise, it was used as multi-neuron unit.

Results: Spikes from 29 recordings were sorted into 61 multi-neuron units and 4 single units. Consistent with previous studies, excitation-inhibition bouts were observed for several multi-neuron units in their respective peristimulus time histograms and interspike interval histograms. The results support our previous conceptual model with longer-latency inhibition after 100 ms.

Conclusion: Understanding the cortical activity generated by vibrotactile stimulation of the skin is important for designing better decoding algorithms and finding the correct somatosensory feedback signals used in neuroprostheses. The longer-latency inhibition effect observed in this study may be utilized in such devices to shape repetitive intracortical stimulation for more natural sensation.

Keywords: Neuroprosthetics, decoding, spike sorting, excitatory inhibitory bout

P-024

Limb preference, fine motor performance and preference of turning direction in adults and children

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Objective: The aim was to investigate the relationships between hand-foot preferences (HP and FP), hand-foot tapping rates and preference of turning direction (PTD) in adults and children.

Methods: Data from 4 studies between 2001–2011 years were analysed. Participants were 115 adults, 17–22 years old (59 man-38 right-handers, 56 woman–38 right-handers); and 80 children, 7–13 years old (42 boys–39 right-handers, 38 girls–34 right-handers). HP and FP were evaluated with Handedness Questionnaire

(13 items) and Footedness test (9 items). A mouse was used for tapping test. Foot (FTR) and hand tapping (HTR) rates were calculated as the number of taps/sec. The participants were asked to turn to a sound coming from one of the 4 loudspeakers which were placed on the walls of a room. The percentage of left turning direction to the 40 sounds coming from behind was computed as PTD. In children PTD data were collected from 27 participants without FP and FTRs datas.

Results: Right-left HTRs and left FTR were higher in right-handed men than women in adults. Right-left HTRs and right FTR were higher in nonright-handed men than women. No gender difference was observed in PTD. In the entire group, PTD was higher in right-handers than nonright-handers. Positive correlations were found between left HTR and HP in both men and women. With adults, there were negative correlations between PTD and left-right HTRs. Right-left HTRs were higher in right-handed boys than girls. No gender difference was observed in PTD. There were no correlations between PTD and HP-HTRs in the entire group. HP, FP, HTRs and FTRs were higher in right-handed adults than children. The PTD was not different between the two groups.

Conclusion: HP and HTRs affect the PTD. Gender differences in motor speeds begin from childhood. The relation between limb preference and fine motor performance is evident in nondominant limbs.

Keywords: Handedness, foot preference, hand tapping task, foot tapping task, turning direction preference

P-025

Event-related potentials in the deese-Roediger-McDermott paradigm - A case study

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Objective: The mechanism of DRM paradigm was investigated using both behavioural tasks and electroencephalography (EEG) (Duzel et al., 1997). A false memory experiment was designed to investigate behavioural task differences between true and false memory with respect to the remember/know responses. Unlike Duzel et al. (1997), the current study has an additional component to measure recognition confidence on a continuous scale, as the aim of the study was to provide further evidence related to false memory and to investigate the level of confidence in false-target item responses.

Methods: One subject participated in the study. This experiment consists of two phases as study and recognition. In the study phase, semantically related words were presented. Some semantically associated words were not presented, whereas they were served as false target items in the recognition phase. The subject was asked to decide for each word whether these words were present or absent on the study phase (old/new response) and whether they remember or know (R/K judgment) that it was decided for every old response. Subsequently, a continuous confidence scale was used to measure subject confidence. While subject made old/new responses, ERPs were recorded.

Results: The false targets were judged "old" at nearly the same level as true targets. The false targets were recognized as "remember" in almost identical proportions with true targets. The subject was highly confident that false targets had been shown in the study phase. Old/new effect was explained with ERP effects. FN400 component was associated with familiarity of words, (new>old) whereas parietal effect was related to recollection (old>new). For the late frontal effect, old items were more positive than new.

Conclusion: The proportion of false targets was found almost at the same level as true targets. The different ERPs were obtained due to underlying neural changes between true targets and false targets.

Keywords: False memory, ERPs, false recognition

P-026

The effects of sulfite exposure on learning and memory in prenatal and postnatal periods

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Objective: Sulfite compounds is one of the most widely used food additives due to its antimicrobial and antioxidant properties. It has been shown that sulfite causes damage to pyramidal neurons in the hippocampal tissue and disrupts learning and spatial memory in rats. In our study we aimed to investigate whether sulfite exposure in the prenatal and postnatal period has any effects on learning, spatial memory and locomotor activity.

Methods: In our study, 20 Wistar rats in each group control (C), prenatal (PR), postnatal (PS) and prenatal+postnatal (PR+PS) groups were formed. While the rats of C group were given normal drinking water during prenatal and postnatal period, the PR group during pregnancy, the PS group after birth and PR+PS group during both pregnancy and postpartum were given sodium metabisulfite at 100 mg/kg/day in their drinking water. Rats were taken to Morris WaterMaze (MWM) experiments for spatial memory starting on the 55th postnatal day and for 6 days, and open field test (OF) was used to measure locomotor activity on the 55th postnatal day. Statistical analysis was assessed by One Way ANOVA.

Results: In the PR+PS group there was a significant decrease in the total distance and mean velocity in the OF test compared to the other groups ($p<0.05$). Similar results were seen in the mean velocity of the MWM test.In the MWM test, there was a decrease in the PS group compared to the other groups in the

total distance taken on the target dial ($p<0.05$). The time spent on the target dial in the MWM test was observed to decrease in the PR+PS group compared to the other groups ($p<0.05$).

Conclusion: It has been shown that sulfite exposure during prenatal and postnatal periods has adverse effects on learning, memory and locomotor activity. Our project was supported by TÜBİTAK (project no: 116S382).

Keywords: Sulfite, spatial memory, Open Field test, Morris Water Maze Test

P-027

The impact of biotin deficiency on spatial memory in rats

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Objective: Nutrition in the prenatal and postnatal period plays an important role in the development of motor, cognitive, social and emotional functions. Vitamin deficiency has been shown to play a role in diseases such as depression, anxiety, memory loss, dementia. Biotin known as B7 and H vitamins, is involved in protein, carbohydrate and fat metabolism and deficiency leads to central nervous system symptoms such as depression, hallucination, and lethargy. The aim of this study is to investigate the effects of prenatal and postnatal biotin deficiency on spatial memory in rats.

Methods: 40 Wistar rats were divided into 4 groups: control group fed with normal diet (C), prenatal biotin deficiency (PreN), postnatal biotin deficiency (PostN) and the biotin deficieny in both prenatal and postnatal periods (PreN+PostN) group. On the 40th day of postnatal period, rats were taken to Y maze and object localization tests (OLT) to evaluate spatial memory. In the OLT, the time passed and the number of taps around the displaced object, and in the Y maze, the time spent in the novel arm were evaluated. Statistical analysis was done by ANOVA test, Tukey test was used in multiple comparisons.

Results: Both the time and number of taps around the displaced object in the OLT and, the time spent in the novel arm in the Y maze were reduced in the biotin deficiency groups compared to the control group.

Conclusion: Sufficient and balanced nutrition is requiredin the growth and development period. Biotin deficiency has been found to have negative effects on spatial memory during periods of rapid growth and development. This study revealed the importance of biotin feeding on the development and physiology of the central nervous system.

Keywords: Biotin deficiency, spatial memory, object localization test, Y maze

P-028

Effects of food restriction and ketamine on atropine and food induced convulsions in fasted animals

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Objective: Fasted rats and mice treated with an antimuscarinic develop convulsions after food intake. Dopaminergic hyperactivity and changes in [3H] glutamate binding sites seem to be the possible underlying mechanisms. In this study investigated whether food restriction-induced dopaminergic hypersensitivity or the glutamatergic N-methyl-D-aspartate (NMDA) receptor antagonist ketamine given alone or with antiepileptics could affect these convulsions.

Methods: Rats were divided into individually housed fed-ad libitum and food-restricted and group-housed fed-ad libitum groups. All animals were deprived of food for 24 h after 10 days of food restriction. They were observed in the new environment and afterwards for convulsions after being treated with saline or 2.4 mg/kg atropine and given food. Mice deprived of food for 24 h were given saline, ketamine (5–10 mg/kg), sodium valproate (250 mg/kg) or carbamazepine (24 mg/kg) in combination with saline or ketamine (5 mg/kg). Convulsions were evaluated in mice treated with saline or 2.4 mg/kg atropine and given food.

Results: There was no change in weight loss, grooming duration and number of rearings among the rats. Convulsions occurred in group-housed (78%), food-restricted (89%) and fed-ad libitum (44%) animals. The incidence of convulsions was found significantly higher in the group-housed and food-restricted animals. In mice, the incidence of convulsions was significantly higher in all groups except the valproate (50%) and valproate + ketamine (37%) groups.

Conclusion: Behavioral data for hypersensitivity in dopaminergic receptors could not be obtained, but re-feeding induced dopamine release in food-restricted animals might augment convulsions due to possible increased susceptibility. Ketamine did not prevent the convulsions or potentiate the anticonvulsant effect of carbamazepine. Using different food restriction method and other NMDA antagonists or different doses of ketamine, further studies may better clarify the roles of dopamine and glutamate in convulsions.

Keywords: Fasting, atropine, ketamine, convulsion, food restriction

P-029

IAPS animal pictures' mean valance and arousal values for a group of university students

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Objective: IAPS pictures have been used in so many studies to inflict emotions to the participants. The researchers published these pictures' mean values for valance, arousal and dominance. However emotional experience is affected by so many factors such as gender, cultural differences etc. So it is important for the affect researchers to know the effects of the pictures on their sample. In this study it is aimed to share valance and arousal mean values of animal pictures in IAPS for a small group of Turkish university students with interested researchers.

Methods: Fourty-two pictures were evaluted by 32 healthy university students with the age range 19–32 for their valance (between -4 and 4) and arousal levels (between 1-none to 9 very strong).

Results: Mean age of the participants were 22.9 (Sd=2.77) and 56.3% (n=21) of them were females. Twenty-one people has been attending undergraduate education and the rest are graduate students. 68.8% (n=22) have been studing medicine. The least negative valance mean score was -2.51 (Sd=1.51) and the highest was 3.46 (Sd=1.04). The least mean for arousal was 4.08 (Sd=2.45) and the highest was 6.93 (Sd=2.07). For only one picture gender created significant mean differences in valance (t(30)=-3.01, p=.005). Women evaluated this picture more negatively than men. Gender has no effect on arousal levels (p>.05).

Conclusion: Each pictures' codes, mean valance and arousal levels will be presented. Interested researchers may use these to design their studies on emotion. They can classify the pictures positively-laden, negatively-laden and neutral according to their mean values. Study may be repeated in a more representative sample to contribute the realm much more.

Keywords: Emotion, cultural difference, affective neuroscience

P-030

Decreased delta and theta EEG event-related oscillations and coherence in Alzheimer's disease

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Objective: Alzheimer's Disease (AD) is the most common neurodegenerative disease characterized by cognitive impairment in the elderly population. In the present study, the event-related oscillations (ERO) and event-related coherences (ERC) in delta and theta frequency bands were examined in patients with AD in comparison to healthy controls (HC).

Methods: Twenty-six patients with AD and 26 age-, gender- and education-matched HC were included. EEG was recorded using a classical oddball paradigm. Delta (0.5–3.5 Hz) and theta (4–7 Hz) ERO and delta (0.977–2.930 Hz) and theta (3.906–6.836 Hz) ERC values were measured.

Results: There was a main GROUP effect for delta ERC [(F1,50)=32.194; p<.001]. Delta ERC values were significantly lower for AD than HC in F3–P3, F4–P4, F3–O1, F4–O2, C3–O1, F3–T7, F4–T8, F3–TP7 and F4–TP8 electrode pairs (all; p<.022). Moreover, there was a main GROUP effect on delta ERO [(F1.50)=21.598; p<.001], indicating lower delta responses in AD patients than HC in all frontal, central and parietal locations (all; p<.003). There was also a main GROUP effect for theta ERC [(F1.50)=9.958; p=.003], demonstrating lower theta ERC in AD than HC in F3–P3, F3–O1, F4–O2, F4–T8, F3–TP7 and F4–TP8 electrode pairs (all; p<.035). There was no main GROUP effect for theta ERO.

Conclusion: In the present study, we have shown that intrahemispheric connectivity was reduced in AD patients in delta and theta bands compared with HC. However, in line with the previous literature, delta and theta oscillatory responses were differentially affected by dementia, as decreased delta but not theta oscillatory responses were found in AD. It is thought that theta activity is generated in the midline prefrontal areas of the cortex generate in the mental arithmetic process. Previous studies showed that delta oscillatory responses are generated in neocortex and related to attention and immediate memory. Our results emphasize connectivity dysfunction in prefrontal areas and neocortex in AD.

Keywords: Alzheimer's disease, delta, event-related coherence, event-related oscillations, theta

P-031

The value of pre-/post LP neuropsychometric evaluation in NPH patients with degenerative dementia

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Objective: Normal pressured cerebrospinal fluid (CSF) and enlarged ventricles. NPH has a clinical triad of gait disturbance, urinary incontinence and cognitive decline. Lumboperitoneal or ventriculoatrial shunt operation performed as the common method of treatment. However, since the patient profile is at an advanced age, possible vascular problems and degenerative dementia are added to the complications of the surgery. So, it is difficult to decide whether to apply the shunt operation, or the risks originated from the operation is too great to consider. Histopathologic biopsy studies suggest that concurrent Alzheimer's dementia is also present in some patients with NPH. Although this shows a temporary relief in the clinic of patients who have received NPH diagnosis and then undergo shunt operation, the presence of underlying neurodegenerative changes are associated with long-term outcomes. Neuropsychometric evaluation performed before and after voiding lumbar puncture (VLP) in patients may help to illustrate the complexity of the situation. This study was designed to investigate the neuropsychometric and behavioral features underlying forgetfulness, gait disturbance, and urinary incontinence complaints. The purpose of cur-

rent study is to examine the pre and post VLP data of the NPH patients who were admitted to the dementia Polyclinic of Medipol University Hospital.

Methods: Neuropsychometric evaluation was performed on five axes: attention and executive functions, memory, visual-spatial functions, language and mood.

Results: Six patients -2 women and 4 men- with normal pressure hydrocephalus were diagnosed. Prior to lumbar puncture low performance in propulsive (executive) functions of the patients was monitored in spite of self-reported dementia complaints. Results indicated that moderate progress occurred after LP, mainly, moderate progress has been made, mainly on executive functions. Findings suggest that combination of neuropsychometric assessment and VLP is a useful tool to distinguish between degenerative process and NPH-related processes.

Conclusion: Results of the study will be discussed in the light of literature.

Keywords: Normal pressure hydrocephalus, lumbar puncture, neuropsychometric evaluation

P-032

Simultaneus cognitive therapy with TMS in brain injury patient: Effect on EEG and cognitive functions

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Objective: Traumatic brain injury (TBI) is the deterioration of normal brain functions due to external factors. After the TBI occurs, depending on the injury's extension and location, some of the cognitive abilities might show deterioration for example attention, memory, and executive functioning. Cognitive rehabilitation intervention has important duties when it comes to improving the deteriorated cognitive abilities as well as increasing the patient performance while affecting their psychosocial circumstances. Repetitive Transcranial Magnetic Stimulation (rTMS), a non-invasive brain stimulation technique, is usefull to treat cognitive impairments by affecting neuroplasticity of individuals with traumatic brain injury (TBI). In this study, the main goal is to determine whether rTMS used to treat patient with TBI enhance his cognitive functions. In order to evaluate results we will assess pre and post cognitive rehabilitation's and rTMS's results with neuropsychological evaluation and EEG recordings.

Methods: One TBI patient, who was followed up at the Medipol University Dementia Policlinic in Istanbul, was taken to work. Before and after the online application of cognitive rehabilitation and rTMS to the patient; neuropsychometric evaluation and EEG recording were performed. A detailed neuropsychometric battery including attention, verbal and nonverbal memory, executive functions, and visual perception functions was applied for neuropsychometric evaluation. EEG recording was performed by applying spontaneous EEG and audiovisual oddball paradigms.

Results: Neuropsychometric evaluation and EEG data before and after treatment will be compared.

Conclusion: Results of this study will be discussed with literature.

Keywords: Traumatic brain injury, cognitive rehabilitation, TMS, neuropsychometric evaluation, EEG

P-033

Examination of the effect of PreSMA on voluntary actions by TMS in Parkinson freezing model

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Objective: The Presupplementary Motor Area (pre-SMA) is an interface between the prefrontal and motor systems. The area has strong connection to prefrontal cortex and basal ganglia which provides functional integration of information from the motor, cognitive, and limbic cycles. Pre-SMA is effective in the selection of the suitable motor plan for both external stimulus and internal motivation. The freezing phenomenon arises from the information processing conflict leading to inability to move while the subject want to. Attacks have a complex pathophysiology involving motor, cognitive and limbic deficits. The basis of the pathophysiology is that the motor plan information can not be given from Pre-SMA to the basal ganglia or that more than one plan is given at the same time. The aim of our study is to investigate the possible effect of Pre-SMA on mainly freezing phenomenology and motor, cognitive and behavioral symptoms of voluntary actions.

Methods: 9 Parkinson's patients with freezing phenomenon were admitted in our study. Motor symptoms, cognitive functions and behavioral findings were assessed with various tests before treatment. Ten sessions of 5 Hz repetitive TMS is applied to the left pre-SMA of the patients. Tests are repeated a week after the last session.

Results: After the stimulation, it was found that the symptoms of frozen attacks and motor problems, cognitive skills, behavioral symptoms and non-motor symptoms showed statistically significant improvement.

Conclusion: Our findings support the idea that Pre-SMA has a central role in motor control of voluntary actions by acting in motor, cognitive and limbic cycles.

Keywords: Presupplementer area, voluntary action, Parkinson's disease, freezing attacks, transcranial magnetic stimulation

P-034

The effect of temporal, spatial and semantic properties of visual stimuli on the working memory

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Objective: The study aims to understand how processing different visual stimuli affect visual attention and working memory performance, based on their properties such as duration, location in the visual field (VF) and the semantic content.

Methods: The subjects (age mean±STD=20.30±2.29) were exposed to different words both threat inducing and neutral. Threat words and their neutral counterparts with similar length and letters were nominated as the strongest by a group of 300 participants of different gender and age. The words were integrated in a computer based attention task, and presented from different VF with an exposure time of 1s or 1ms. At the end of the task, the subjects were asked to report the words. The results were analysed in SPSS.

Results: The results showed that threat words were better remembered compared to their neutral counterparts ($p<.001$) in different visual fields except when presented at the lower VF and for 1 ms ($p<.609$). Threat words lowered the reaction time significantly more in the attention task in 1s exposure compared to 1ms, irrespective of their VF ($p<.007$). Spatial comparisons showed that if the threat words were presented from the upper VF, the effect on reaction time is significantly bigger and the number of threat words remembered was higher (memory score: $p<.009$; attentional performance: $p<.044$).

Conclusion: Our results indicate that different visual fields have different temporal and semantic sensitivity. Also for the semantic property to induce a difference in attention and memory, a certain presentation time is required, which indicates the minimal critical time for the perception of threat.

Keywords: attention, visual stimuli processing, working memory

P-035

The color, location and time specific effects of distractor stimuli on the selective attention

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Objective: In our daily lives we attend to very different stimuli in our environment and yet we have the ability to selectively attend to some. In this study we tried to understand the effect of secondary distractor stimulus on the selective attentional performance and how it is influenced by the physical properties of the stimuli.

Methods: 90 participants (age Mean±STD=19.26±1.95) joined a computer-based visual attention task in which they were asked to attend and respond to a simple visual stimulus appearing from different locations, while they are interrupted by a secondary stimulus of different color, location and for different times. The task was written in JAVA programming language and the analysis was made by SPSS.

Results: A secondary stimulus presented during a primary attention task had differential effects, based on its color and location. Red stimulus was shown to decrease the response time upon a primary stimulus specifically in the location it was presented ($p<.003$) (without any significant change in the accuracy of the response ($p<.154$)). We saw a similar effect for a secondary blue stimulus, but it took a longer time to exert its effect compared to red (response time: $p<.043$; accuracy: $p<.784$). In addition to the color, these effects of distractors significantly varried upon its location in the visual area as well as its duration. Some of the visual areas were more sensitive to the distractors compared to others and the increased duration of each distractor enhances its effect (1s vs. 1 ms exposure, $\triangle$ response times: 175.19 ms vs.156.52 ms).

Conclusion: The results indicate that a secondary stimulus exerts its effect on attentional response to a primary stimulus, based on where it is presented and for how long. It also has differential effects when presented in different colors, which supports that our visual attention system has differential sensitivity for stimulus of different physical properties.

Keywords: color, distractor, selective attention, visual field

P-036

Effects of mood induction on feeling of knowing judgment under face-name recognition task

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Objective: Feeling of knowing (FOK) is a metacognitive judgment that enables people to predict whether they will remember a specific piece of information which they currently failed to remember. Research shows that mood has an effect on cognitive processes, such as language and memory. However, there are limited number of studies examining the effect of mood on FOK judgments, and in these studies, mood manipulation was done through experimental stimuli. The aim of this study is to examine the effect of mood induction on FOK judgments as well as the change of these in relation to personality traits under the face-name recognition (FNR) task.

Methods: 39 undergraduate students (28 females) aged between 19 and 24 (M=20.39) participated in the study. Participants were selected through Big-Five Personality Inventory, and grouped as people high in neuroticism (n=18) or extroversion (n=21) score. Positive and negative images selected from Geneva Affective Picture Database, and neutral object icons were used for the mood induction. After the mood induction, participants' FOK judgments and reaction times were measured under FNR task composed of neutral faces. The classical learning-judgment of learning-recognition-FOK judgment-recognition paradigm was used for FNR task.

Results: Results of 2×3 MANOVA for 2 (Extroversion, Neuroticism) × 3 (Positive, Neutral, Negative mood inductions) factorial design showed that, for correctly recognized faces and FOK judgments, extroverted participants indicated higher ratings under positive mood condition, but neurotic participants did under neutral mood condition. Additionally, participants needed longer time while making confidence judgments under negative mood condition.

Conclusion: The interaction of personality traits and mood induction has an effect on FOK judgments. As suggested by literature, mood induction had significant effect on memory and FOK judgments but our results also indicated that this effect was affected from individuals' personality traits.

Keywords: Face-name recognition, feeling of knowing, mood, personality

P-037

Potential effects to fetal exposure of DS on brain morphology and behavior in young rats

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Objective: Diclofenac sodium (DS) is potent cyclooxygenase inhibitor. 2nd trimester of gestation DS crosses the human placenta. In the adult brain, DS was reported to inhibit the proliferation and differentiation of neural stem cells. This study aimed to investigate the effects of the gestational DS administration on the performance of both male and female Wistar rats pups in a variety of behavioral tasks.

Methods: The DS, in a dose of 1 mg/kg/day was applied to the drug-treated group of pregnant dams beginning from the 5th day after mating for a period of 15 days during pregnancy. Physiological serum at 1 ml dose was s.c injected to the control group. Total number of rats are 6 female and 6 male young wistar rats. Visual Placing Test is used to assess visual discrimination in rats mode known as a sensorimotor test. Walking Initiation, Turning on İnclined Screen, Wire Hanging, Clasping The Limbs, Climbing The Vertical screen, Swimming Skills Tests are used to assess motor skills. Morris Water Maze (MWM) and Radial Arm Maze (RMZ) tests are used to evaluate for learning and memory performance. Stereological Method is used to assess the cell counting in rats model.

Results: The results showed more worse results in DS group in sensorimotor tests, respectively (p=0.029, and p=0.079, female and male). Working memory showed more impairment in DS female group (p=0.022), no difference in DS male group. Dentate gyrus and cerebellum purkinje cells showed significant decrease in DS group in sterological cell count method.

Conclusion: It is suggested that i.u. exposure to DS may induce neuro-developmental retardation in animals models. The comparison was calculated by using Carnegie Stage Comparison model. The symptoms such as hyperactivity and a decline in learning capacity and especially working memory, observed in rats exposed to DS during the2nd and the 3rd trimester.

Keywords: diclofenac sodium,behaviour,pregnancy, teratogenicity

P-038

tDCS effects on hemodynamic response to emotional stroop task in non-depressive MS patients

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Objective: Mood disorders and cognitive impairment are common in MS patients. tDCS has been used for such neuropsychiatric disorders. We aimed to investigate the prefrontal cortex of MS patients during an emotional and cognitive task by using fNIRS. Also we aimed to see tDCS effects on the emotional Stroop performance.

Methods: Among MS patients assessed with Beck Depression Inventory (BDI), 9 patients without depression were included in the study. Patients are seated in front of a computer and performed an emotional Stroop task. The stimuli was made with photographs of 8 happy and sad people selected from Ekman's faces. The words that express the emotion of the face was placed in the middle of the photograph for congruent stimuli, and the opposite was made for incongruent stimuli. Patients are asked to press "1" for congruent and "2" for incongruent situations. During the test, prefrontal hemodynamic activation was recorded by fNIRS. After the test, 10 sessions of tDCS stimulation were applied to the left dorsolateral prefrontal cortex (+) and right hemisphere of cerebellum (-). Emotional Stroop test was repeated after the tDCS period.

Results: Before the tDCS stimulation, prefrontal activation of MS patients was found decreased for all situations, especially in medial prefrontal region. After the stimulation period, fNIRS analysis showed an increased hemodynamic activation in all prefrontal regions that is associated with emotional stimuli (p=0,012 for orbitofrontal cortex, p=0.048 for medial prefrontal cortex). There wasn't any significant difference in reaction time and error rate before and after tDCS. Also a decrease was observed in the BDI scores but it was not found statistically significant.

Conclusion: In the future studies with higher number of subjects, although there is not any sign of depression, decreased prefrontal activation to emotional stimuli may be shown as a

biomarker for MS, and tDCS may be an alternative treatment approach.

Keywords: Emotional stroop, fNIRS, multiple sclerosis, prefrontal cortex, tDCS

P-039

Computerized cognitive rehabilitation improves executive functions in benign multiple sclerosis

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Objective: Although benign multiple sclerosis (B-MS) patients display preserved somatic neurological functions, they may nevertheless develop cognitive dysfunction. Our aim was to explore the impact of computerized cognitive rehabilitation (CCR) on cognitive functions of B-MS patients.

Methods: Age-gender matched 21 B-MS (EDSS|≤3.0 at 10 years of disease duration), 22 conventional MS (C-MS, EDSS>3.0 at 10 years) and 38 healthy individuals were recruited. CCR was administered to 10 B-MS patients and a panel of neuropsychological tests were employed to B-MS patients with (n=10) and without (n=11) CCR at baseline and at 6 months. Participants were evaluated by Rao's BRB-N (Brief Repeatable Battery of Neuropsychological Tests) before and after (month 6) intervention. Beck Depression Inventory was administered to evaluate mood. CCR was based on a mental exercise software containing attention, memory, reasoning, visual and verbal task modules. Patients supervised with program's institutional interface every week and were assessed by a psychologist every month. Cases' age, duration of illness, age at onset, EDSS, progression index, total number of attacks and annual number of attacks and neuropsychological and cognitive tests were investigated by Pearson test. $p<0.05$ was considered statistically significant.

Results: Both B-MS and C-MS patients showed significantly impaired selective reminding, spatial recall, symbol digit modalities (SDM), controlled oral word association (COWAT) and paced auditory serial addition (PASAT) tests. Stroop, 9-hole peg and timed 25-foot walk test results of B-MS patients were comparable to healthy controls. B-MS patients with CCR showed significantly improved SDM, COWAT and Stroop test results than those without CCR. CCR also had a moderate positive effect on selective reminding and spatial recall tests, albeit without attaining statistical significance.

Conclusion: Several cognitive domains including memory and executive functions are impaired in B-MS patients. Also, CCR has an ameliorating impact particularly on executive functions of B-MS patients.

Keywords: B-MS, cognitive rehabilitation, executive functions

P-040

Investigation of antioxidant enzymes of hyperthyroided rat's hippocampus

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Objective: The hippocampus is one of brain regions that plays an important role in cognitive functions such as learning and memory. Hyperthyroidism disrupts the balance between antioxidants and oxidants in tissues, resulting in cognitive dysfunctions. On the other hand, aging plays an important role in the disbalance of oxidant system, formation of long-term potentiation and consolidation of learning and memory. This study was aimed to investigate oxidant and antioxidant levels in hippocampus of hyperthyroid rats, depending on aging.

Methods: Young (2-months) and old (12-months) male Wistar albino rats were used in this study. The rats were divided into 4 groups (n=6 for each group) as young (control, hyperthyroid) and old (control, hyperthyroid). To create hyperthyroidism, rats were given L-thyroxine (0.3 mg/kg/day) intraperitoneal for 21 days. Control group rats were given an equal volume of saline. Plasma free T3 (fT3), free T4 (fT4) and hippocampal Nitric oxide (NO), Nitric oxide synthase (NOS), catalase (CAT) and malondialdehyde (MDA) levels were measured using a commercial ELISA Kit.

Results: A decrease in age-related CAT levels ($p<0.001$) and an increase in MDA levels ($p<0.001$) were not affected by thyroid status while NOS activity, which was not affected by age, was significantly higher in old hyperthyroid rats compared to young hyperthyroid rats ($p<0.001$). There were no significant effect of age and thyroid status on NO levels.

Conclusion: Our results showed that the oxidative stress which is strengthened in the hippocampus of elderly person is not affected by the increase of thyroid hormone level. Along with that, because the changes at NOS levels which is considered as indicator of glutamate toxicity are not supported by the changes in NO levels, further studies are needed. This study was supported by Erciyes University Scientific Research Projects Unit under TCD 2016-6262 project.

Keywords: Hyperthyroidism, learning, memory, nitric oxide

P-041

Developing a Wistar rat model of Parkinsonism induced by chronic valproate administration

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Objective: Valproate is a well-recognized therapeutic choice in the management of epilepsies and manic episodes of bipolar dis-

orders and has been associated with Parkinson-like symptoms, especially tremor, when used for long-term. Despite being reported as often resolved upon drug discontinuance, the symptoms might be permanent. This study aimed to determine whether a five-day administration of valproate resulted in the development of a Parkinsonism model in Wistar rats.

Methods: Twice daily valproate 400 mg/kg were intraperitoneally injected to adult male Wistar rats (n=6) for five days. Locomotor, stepping, paw reaching, cylinder, and tremulous jaw movement tests were applied three days before the injection and at the end of the last valproate administration. Tremor data scoring is as follows: 0: no tremor, I: intermittent tremor, affecting only head and neck,II: intermittent tremor, affecting whole body, III: continuous tremor affecting whole body, tail, IV: continuous tremor

Results: Tremulous jaw movement stage II and I occurred in 60% and 40% of rats, respectively; while no rats developed stage III or IV tremor upon 5-day course of valproate. There were significant reduction in total distance (%53.8 $p<0.05$), vertical and horizontal movements and in ambulatory time (%77.2, $p<0.05$; %48.64, $p<0.05$ and %52,3, $p<0.05$ respectively) compared to baseline in the locomotor activity test. While the number of stepping at the right side was significantly lower compared to the baseline ($p<0.05$). Cylinder test scores at minutes 0–2 significantly decreased in the right side by %93.4 and in the left side by %90,5 at the end of the study ($p<0.05$).

Conclusion: The findings of the locomotor and cylinder tests imply that a five-day administration of valproate might elicit the development of a rat Parkinsonism model which appears to be substantially consistent with those in the literature. Our study, with dose and time modifications, can provide source for new researches.

Keywords: Valproate, drug-induced parkinsonism, tremor, locomotor test, stepping adjusting

P-042

Evaluation of selenium supplement effect on impaired long term potentiation responses of hypothyroid old rats

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Objective: Hypothyroidism has adverse effects on synaptic plasticity in the brain. The DiO2 is an important factor in adapting the changes in thyroid hormone levels in Central Nervous System. Selenium increases this enzyme activity, which is involved in the conversion of T4 to T3 hormone in the brain. Thus, in this study, it is aimed to investigate the effect of selenium supplimentation on decreased long-term potentiation (LTP) responses in hypothyroidism.

Methods: It was used 2-month-old male Wistar albino rats. The rats were divided into 4 groups as control (C, n=9), hypothyroid [6-n-propyl thiouracil (Ptu), n=9], hypothyroid+ sodium selenite group (Sena, n=7) and hypotiroid+seleno-L-methionine (Semet, n=7). For the hypothyroid group, Ptu (1 mg/kg/day), Sena group was supplemented with sodium selenite (0.5 mg/kg/day)+Ptu (1 mg/kg/day) while seleno-L-methionine (0.7 mg/kg/day)+Ptu (1 mg/kg/day) was given to the Semet group for 21 days with gavage. LTP responses were recorded from hippocampus. The hippocampus was induced by high-frequency stimulation (with a frequency of 100 Hz in 1 sec, 4 times in 5 'intervals) to induce LTP.

Results: LTP responses were assessed based on population spike (PS) amplitude and excitatory postsynaptic potential (EPSP) slopes. One-way ANOVA test results showed that the PS amplitudes for Ptu group was significantly lower than that in control group ($p=0.011$), but no significant difference was found in that on Sena and Semet groups ($p>0.05$). There was no statistical significance between the groups when evaluated EPSP slopes.

Conclusion: According to results, hypothyroidism reduces LTP responses. Selenium improves this decline. The results of this study is suggested that the hypothyroidism, rather than its effect on synaptic connections, may disrupt LTD via the post-synaptic mechanism. So selenium supplements may affect learning and memory disorders by affecting thyroid hormone levels in hypothyroid patients. This study was supported by Erciyes University Scientific Research Projects Unit under the Project of 2016-6732.

Keywords: Hippocampus, hypothyroidism, long-term potentiation, selenium

P-043

Instruction effect on feeling-of-knowing paradigm

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Objective: In traditional feeling-of-knowing (FOK) procedure, judgements are made on only unrecalled items and correctness of this methodological perspective has been a controversial matter in the literature (Eakin ve Hertzog, 2012; Koriat, 1993; Schwartz ve ark., 2015; Souchay ve Isingrini, 2012). According to Koriat (1993) making FOK judgments (FOKs) for only unrecalled items decreases confidence and also inhibits making FOKs based on correct recall. Moreover, Irak and Ozgor (2014) demonstrated that presenting unrecalled items provides an explicit feedback about selection and importance of the participants' incorrect answers. To provide more data for this methodological issue participants were exposed to make FOKs for all items or incorrect items only under episodic and semantic memory tasks separately.

Methods: 184 participants (97 females) aged 18 to 26 (M= 21.40) participated in this study. FOKs under episodic (40 word pairs) and semantic memory (30 general information questions) tasks were used by applying the classical recall-judgment-recog-

nition procedure. 2 (type of the task: semantic and episodic memory) ×2 (type of FOK instruction: only unrecalled and all items) factorial design was conducted.

Results: Participants' calibration scores (equation that evaluates FOK accuracy, lower score means higher accuracy) indicated a significant difference for both episodic [F (2.147)=12.95, p<.01] and semantic memory [F (2.181)=9.18, p<.01] tasks. FOKs made on all items demonstrated higher accuracy than FOKs made on only unrecalled items for both memory type.

Conclusion: It was found that the method used to measure FOKs has an effect on the consistency of FOKs. These findings support that measuring FOKs by using all items has a better resolution compared to using only unrecalled items (Schwartz et al., 2015). Results can be considered as an explanation to the inconsistent findings based on methodological issues in the literature. In this sense, it is suggested that using all items to measure FOKs provides better resolution for further researches.

Keywords: Metacognition, feeling-of-knowing, semantic memory, episodic memory

P-044

Emotion-inflicting animal pictures' effects on Iowa Gambling Task performance: an fMRI study

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Objective: It is limbic structures that step in fast and bias decisions under uncertainty rather than high cortical structures that are responsible for evaluating the choices rationally. It is aimed to test the idea above by modifying the IGT to affect limbic structures.

Methods: Thirty-two right handed and healthy medical faculty students, of which %62.5 (n=20) was male, participated into the study. Two groups were created and their members were equalized in their mean age, gender and class distribution. In cued group there were negative emotion inflicting animal pictures on cards A and B and positive ones on cards C and D. Neutral group saw neutral pictures. After structural imaging they played modified IGT during fMRI. Preprocessed data was investigated for activation and connectivity patterns.

Results: The groups were equal in their alexithymia, state anxiety, decision-making styles, impulsivity, and reward/punishment sensitivity scores. Cued group preferred advantageous cards more often than neutral one. Within groups there were so many clusters that decrease their activation. Only one cluster increased activity towards the end of the task in neutral group. In cued group one cluster (all left, sup., inf., mid. and med. frontal cortex, dor. ACC and partially ven. ACC, SMA, pre and paracentral gyri) decreased its activity in comparison to neutral group. It was determined that this region increased its connectivity towards the end of the task in two clusters: ant. ACC right para-cingulate gyrus., right sup. motor cortex; precuneus cortex and post. cingulate. Posterior DMN, left fronto-parietal network, language network and cerebellar network increased their activation towards the end of the game in neutral group.

Conclusion: As indicated in somatic marker hypothesis, the participants benefited from emotional cues. Although they were not told about the function of the pictures, cues seem helped limbic system to improve the performance.

Keywords: Somatic marker hypothesis, emotion, decision-making, modified IGT

P-045

Measurement of dopamine concentration in the rat striatum using chronically implanted microsensors

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Objective: Fast-scan cyclic voltammetry (FSCV) technique enables in vivo measurement of dopamine concentration during behavior. In this study, our aim was to detect the phasic changes in the dopamine concentration in the rat ventromedial striatum (VMS) using chronically implanted microsensors and FSCV technique during delivery of unexpected primary rewards and reward predictive stimuli.

Methods: One male Sprague Dawley rat was chronically implanted with a carbon fiber microsensor in the left ventromedial striatum (AP: +1.5 mm, ML: 2.1 mm, DV: 6.4 mm). After recovery from the surgery, the rat was enclosed in a behavioral cage and trained on a Pavlovian conditioned approach task. In the task, a light cue presented for 3 seconds and immediately followed by delivery of 0.2 ml of 13% sucrose solution was the predictor of rewards. After the training for Pavlovian conditioned approach task, voltammetric signals in response to presentation of unexpected primary rewards (unconditioned stimuli) and reward predictive stimuli (cue light) were recorded using an in-house built system.

Results: Based on 5 recording sessions in which unexpected rewards were presented and 5 recording sessions in which predictive stimuli were presented, the phasic increase in the dopamine concentration was measured as 50.5±13.1 nM and 40.2±13.9 nM, respectively.

Conclusion: Our results based on the recordings from one rat indicate that phasic increases in dopamine concentration in the VMS in response to delivery of unexpected rewards and reward predictive stimuli can be detected using chronically implanted carbon fiber microsensors. Our research was approved by

Istanbul Medipol University Ethics Committee on Animal Research.

Keywords: Voltammetry, dopamine, reward

P-046

Virtual super market with mild cognitive impairment

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Objective: In this study, it was aimed to evaluate the cognitive impairments that occur in Amnestic Mild Cognitive Impairment (aMCI) patients by using both neuropsychological testing and Virtual Super Market Application (VSM)

Methods: 19 aMCI-Single Domain (mean age: 68.7), 18 aMCI-Multiple Domain (mean age: 72.1) and 57 gender, education and age matched healthy controls (mean age: 66.4) were participated in this study. A detailed neuropsychological test battery, Mini Mental State Exam (MMSE) and Virtual Super Market (VSM) was applied to all participants.

Results: There was a significant difference in neuropsychological test scores between aMCI with patients and healthy controls. aMCI-Multiple Domain (aMCI-MD) patients performed lower in SSU variables than aMCI-Single Domain (aMCI-SD) and healthy controls. Possible diagnosis of aMCI-SD/MD was determined with detailed neuropsychological tests.

Conclusion: There was a significant difference in neuropsychological test scores between aMCI with patients and healthy controls. aMCI patients completed the VSM longer than controls. The VSM test was found to discriminate between the aMCI and healthy controls with a correct classification rate (CCR) of 80.9%, sensitivity 79.1% and specificity 85.1%. MMSE found to discriminate between the aMCI and controls with a CCR 77.2%, sensitivity 75% and specificity 85%. We found to dicriminate between subgroups aMCI with a CCR 73 % in VSM and 81% in MMSE.

Conclusion: . The VSM test was found to discriminate between the aMCI and healthy controls with a correct classification rate of 80.9%.However our rates were lower for accuracy in distinguishing aMCI from controls than the original study using VSM in the literature with the correct classification rate of 87.30%. This difference could be related to be less subjects in that study population than our study population.A more practical and screening tool can be used to discirimante between aMCI and control in the VSM than more the MMSE.

Keywords: Mild cognitive impairment, neuropsychological assessment, virtual super market

P-047

Sulbutiamine HCL alters locomotor activity in *Eisenia fetida*

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Objective: Sulbutiamine HCl (SUL) is a synthetic compound. which composed of two thiamine (vitamin B1) molecules bound together by a sulfur group. Sulfur group provide lipophilic feature. SUL can cross swiftly the blood –brain barrier. SUL is prescribed freuqently for for the treatment of asthenia and chronic fatigue. The aim of this study is to evaluate the effect of sulbutiamine on the anxiety like behaviours and locomotor activity in *Eisenia fetida*.

Methods: 24 *Eisenia fetida* (1 years old, dimension approximately 9 cm. and n=8) were used in the present study. Worms were left for adaptation for 4 weeks. The subjects were maintained under 12 h light/12 h dark cycle at a temperature of 23–25 °C and damp (50–70%) controlled room. Each worm was removed from its home and placed into an exposure chamber containing test compound or saline for 30 minute. Saline, Sulbutiamine 200 mg/kg and 300 mg/kg were administered respectively in experiment group. After 30 min, each worm was placed in to experiment chamber (modified light dark box test) and recorded via camera 10 min. Light zone time, dark time zone, light/dark zone entrance number, locomotor activity, dark zone entrance latency and velocity were analyzed. IBM SPSS Statistics 23.0 was used for statistical analysis.

Results: Light zone time, dark zone time, light/dark zone entrance number and dark zone entrance latency were no difference between the groups. Locomotor activity and velocity were increased signifacntly 200 and 300 mg/kg SUL groups compere to controls ($p<0.01$).

Conclusion: Our Data showed that SUL is not anti-anxiety property. On the other hand SUL demonsrated a psychomotor stimulant like. For this reason SUL must be prescribed heedfully.

Keywords: Anxiety and locomotor activity, *Eisenia fetida*, sulbutiamine HCL

P-048

Effect of exercise on behavioral parameters in rats treated with dizocilpine

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Objective: Schizophrenia is a chronic psychiatric illness that affects about 1% of the whole population and is not fully known. It is characterized by impairments in mental functions, emotions and behavior. Dizocilpine (MK-801) causes adverse effects on the developing brain and is used in animal models of schizophrenia. Many studies have shown positive effects of physical exercise on brain functions. In this study, it was aimed to inves-

tigate whether the possible negative changes in the behavioral parameters in the adult rats with the application of MK-801 changed with exercise training.

Methods: For this purpose, Wistar female 8-week-old rats were given 0.5 mg / kg MK-801 i.p. (n=10). In the control group, the same amount of SF injection was given to the exercise group (n=10 male). The exercise group was training 15 min daily swimming exercise for 10 days and then 0.5 mg/kg MK-801was given i.p. (n=10). After the application of MK-801, on the 6th day, the behavior parameters in the open field aparatus and the pain threshold on the hot plate on the 7th day were evaluated. The mean values of the three groups were compared with the ANOVA test.

Results: The decreasing locomotor activity and rearing (discovery behavior) with MK-801 application were significantly increased with exercise ($p<0.05$),There was no differences in pain threshold between groups ($p>0.05$).

Conclusion: The results suggest that the effect of MK-801 on the central nervous system is limited in female adult rats. Exercise has removed the negative effects of the MK-801. This study was supported by Erciyes University Scientific Research Projects Unit TYL-2017-7249 project.

Keywords: Exercise, MK-801, open field, locomotor activity, pain threshold

P-049

Gelsemium elegans showed anxiolytic effect in *Eisenia fetida*

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Objective: Anxiety and depression are the most frequently diagnosed mental disorders. Different drugs and supplements were prescribed for this disorders. Our aims were to investigate Gelsemium elegans anxiolytic effect on *Eisenia fetida*. It contains 98% pure koumidine from Gelsemium elegans alkoids used in the study. This is the first study of koumidine anxiolytic action.

Methods: 24 *Eisenia fetida* (1 years old, dimension approximately 9 cm. and n= 8) were used in the present study. Worms were left for adaptation for 4 weeks. The subjects were maintained under 12 h light/12 h dark cycle at a temperature of 23–25 °C and damp (50–70%) controlled room. Each worm was removed from its home and placed into an exposure chamber containing test compound or saline for 30 minute. Saline, Gelsemium alkoids 2 mg/kg and 10 mg/kg were administered respectively in experiment groups. After 30 min, each worm was placed in to experiment chamber (modified light dark box test) and recorded via camera 10 min. Light zone time, dark time zone, light/dark zone entrance number, locomotor activity, dark zone entrance latency and velocity were analyzed. IBM SPSS Statistics 23.0 was conducted for statistical analysis.The data were evaluated by analysis of variance (ANOVA) followed by Student's t-test and Neuman–Keuls post hoc test.

Results: Light zone time, dark zone time, light/dark zone entrance number and dark zone entrance latency were increased significantly in 10 mg/kg Gelsemium group compare to control ($p<0.05$). Locomotor activity and velocity were no difference 2 and 10 mg/kg Gelsemium alkoids groups compere to controls.

Conclusion: Our Data showed that Gelsemium was anti-anxiety property and decrease anxiety like behaviour. On the other hand Gelsemium did not demonstrate psychomotor stimulant like effect. Gelsemium alkaloids will be conducted as the treatment anxiety disorders in the future.

Keywords: Anxiety and locomotor activity, *Eisenia fetida*, gelsemium elegans

P-050

Investigating CPAP treatment efficacy using event-related potentials in severe OSAS patients

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Objective: Obstructive sleep apnea syndrome (OSAS), is a sleep disorder characterized by complete or partial obstructions of the upper airway and decrease in oxygen saturation. Many studies reported cognitive impairment in OSAS and the cause of these changes were associated with sleep fragmentation and/or hypoxia which leads to neuronal loss in time. Continuous positive airway pressure (CPAP), is the most common treatment modality used in patients with severe OSAS and the effect of CPAP on cognitive functions is not fully understood. Present study aims to investigate cognitive changes in OSAS by comparing neuropsychological test scores and event-related potentials (ERP) before and after six-month treatment with CPAP.

Methods: 23 severe OSAS patients and age, gender and education matched 23 healthy volunteers underwent an EEG recording and a detailed neuropsychological assessment. Follow-up assessments were repeated after six-month treatment with CPAP. Mean visual P300 amplitudes were measured from Fz, Cz and Pz electrode sites. Baseline neuropsychological test scores and mean P300 amplitudes of groups were compared using independent sample t-test. The baseline and follow-up scores of OSAS group were analyzed with paired sample t-test.

Results: Baseline mean P300 amplitudes of OSAS patients were decreased in the Fz, Cz and Pz electrode sites compared to healthy controls. Neuropsychological test scores did not differ between groups. The mean P300 amplitudes and neuropsychological test scores of OSAS patients did not show any significant increase after CPAP treatment.

Conclusion: The lack of any improvement in neuropsychological test scores and electrophysiological measurements of OSAS patients after CPAP treatment are thought to be related to including only severe OSAS patients with long disease duration

in the study. The investigation of CPAP treatment in less severe patients is aimed in further studies. This study implies the importance of early diagnosis and treatment in OSAS.

Keywords: OSAS, P300, event-related potentials, neuropsychological assessment, CPAP

P-051

Effect of fermented pollen on behavior and pain threshold in depressed male rats

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Objective: Depression is a mental illness that is seen in a significant part of the population. In this study, it was aimed to investigate whether there is a positive effect of fermented pollen on the deteriorated behavior parameters of depression.

Methods: For this purpose, twelve months (n=40 male) Wistar albino rats in the study; control (n=10), depression (n=10), perga (n=10) and depression + perga (n=10) The Porsol Forced Swimming Test has been applied to create depression. Perga and depression + pergene group for 15 days, 250 mg / kg Fermente Polen i.g. while for control and depression group, the same amount of distilled water was given as i.g. On the 9th day, the open area behavior test and the 15th day hot plate test were applied.

Results: Compared to the control group, the number of lines in the open area group significantly decreased in the depression group ($p<0.05$), significantly increased in the parasympathetic group ($p<0.05$) and significantly increased in the depression + parade group ($p<0.05$). Behavior in the open field area center and behavior of reappearance (rearing) were significantly changed ($p<0.05$), similar to the change in peripherial line crossing. The duration of response in the hot plate system in which the pain threshold was assessed was shortened in the depression group according to the control group, prolonged in the perception group, and extended in the depression group ($p<0.05$).

Conclusion: In these findings, it can be said that perga reduces the adverse effects of depression and increases the pain threshold. The result is that pergan has antidepressant properties and can be used in at least part of the depression cases. This study was supported by Erciyes University Scientific Research Projects Unit TYL2017-7532 project.

Keywords: Depression, fermented pollen (perga), open field, hot plate, male rat

P-052

The effects of acute exhaustion exercise on anxiety, panic and hedonic behavior in depressed rats

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Objective: Major depressive disorder (MDD) is a widespread, recurrent and aetiologically complex mental illness; About 3–5% of the world's population suffers from MDD, but the aetiology and pathophysiological mechanisms of depression are not fully defined. There are many health benefits of exercise. The effect of exhaustion exercises on depression is unknown. The purpose of this study is to investigate the effect of exhaustion exercise on behavior, fear responses and hedonic behavior in depressed rats.

Methods: Thirty Wistar albino male rats aged 8 weeks were used in the study.The rats were divided into three groups as randomly as control, depression, depression and acute exhaustion exercise groups.. A depression model was constructed based on the method developed by Porsolt. The depressed rats were administered acute swimming exercise. The locomotor activity and discovery behaviors in the open field area, anxiety and panic behavior (time spent in closed and open arms, escape latent) in the elevated T-maze test, and hedonic behavior as the preference of sucrose were evaluated.

Results: There was no significant difference between the groups except for the increase in the number of crossing lines in the depression-induced rats in the open area ($p>0.05$). In the elevated T-maze, the duration of stay in the closed arm and escape latent decreased in the depressed rats, while the exhaustion exercise extended the duration of stay in the closed mode ($p<0.05$). Water consumption with sucrose was found to be 72%, 47 %, 64% in control, depressive and post-depression exercise groups, respectively ($p<0.05$).

Conclusion: The data show that one-time acute exercise increases panic behavior, but reduces the anxiety and antihedronic behavior in depressed male rats. As a result, it can be said that the antidepressant effect of exercise depends on the duration and severity of exercise. This study was supported by the Erciyes University BAP unit (TOA-2015-5368)

Keywords: exhaustion exercise, depression, anxiety, panic behavior, hedonic behavior.

P-053

Investigation of behavior, anhedonia and spatial learning in rats treated with dizocilpine

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Objective: Schizophrenia is a chronic, common disorder characterized by cognitive, emotional, and other functional disorders affecting 1% of the world's population, often associated with hallucinations or delusions. The high costs for countries and the fact that the aetiology is still not fully understood has led schizophrenia to turn to animal models. The use of dizocilpine (MK-801) to create a model of schizophrenia in experimental animals is preferred because of its easy access and low cost. MK-801 is generally reported to have adverse effects on the developing brain. In this study, it was aimed to investigate whether MK-801

has effects on behavior, emotion and spatial learning in 10–12 month old male Wistar albino rats.

Methods: The rats received 0.5 mg / kg MK-801 i.p. (n=10). In the control group, the same amount of saline was injected (n=10). After five days of application of MK-801 or saline, open field behavior test, Y maze test and anhedonia test were performed on days 6–7, 8 and 9, respectively. The data were analyzed statistically by independent t-test.

Results: The number of line crossing in the open system was significantly increased in the MK-801 group compared to the control group ($p<0.05$), according to the number of rearing, groming and centering. Anhedoni was assessed by sucrose preference test, spatial learning by y-maze test, and there was no significant difference between the groups in both ($p>0.05$).

Conclusion: The result was that MK-801 caused only anxiety in the developed brain of adult rats without decreasing depression and cognitive functions. This study was supported by Erciyes University Scientific Research Projects Unit TYL-2017-7333 project.

Keywords: MK-801, openField, Y-maze, anhedonia, rat

P-054

Investigation the effect of starch-based sugar on spatial learning performance in rats

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Objective: To determine whether there is a difference in hippocampal-dependent learning in rats fed with different fructose contents from corn and sugar beet starch.

Methods: It was used 48 postnatal (21-day) old male Wistar Albino rats were divided into 3 groups. Corn syrup (Carbohydrate ratio: 11%, n=16) for HFSC group; Sugar beet (Carbohydrate ratio: 11%, n=16) for the SB group and a standard rat diet (oral route for 21 days) was given to the Control group (n=16).All rats were tested with (a specific and highly sensitive test) the reverse learning paradigm in the Morris water tank, to assess hippocampus-dependent learning, respectively. 4 consecutive days for the original location of the hidden platform to be learned; were tested 4 times a day and the probe was tested 24 hours after the last attempt. On the sixth day, the platform was relocated and rats were given 3 consecutive days to learn the 2nd place; were tested 4 times a day. All experiments were recorded using the Noldus video monitoring and analysis system to evaluate rats,s behavior.

Results: When the performance was evaluated as the average distance from the platform, the HFSC group was found to make significantly longer distant than that in the SB group. It was determined that the SB group spent significantly more time on the target than that in the HFSC group. The control and HFSC groups were considered to be significantly at the border because it was thought that the daily feeding periods of experimental animals were short (21 days) and also the animals were exposed to stress because they came from other city.

Conclusion: HFSC adverse effects on memory functions have been observed in the presence of insignificant impairment in learning.

Keywords: Hipocampus, rat, high fructose corn syrup, beet sugar

P-055

Interhemispheric transfer between poor and good readers in healthy adults: an EEG study

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Objective: It is proposed that there is a transmission problem from right to the left hemisphere in dyslexia. One of the symptoms of dyslexia is poor reading, which is also a common problem in healthy population. The aim of this study was to investigate if there is a similar transfer problem in healthy poor readers.

Methods: Participants were selected from university students (n=309) based on the results of a reading test. The good (n=9, 8 females) and poor (n=6, 3 females) readers were included in the EEG study. The sixty pseudowords were derived from inanimate object names. The participants were asked to read silently pseudowords presented 50 ms from the right or left visual fields in 5 sets (5×60). The latencies of the P100 in response to pseudowords at parietal and occipital leads of the directly stimulated hemispheres were evaluated as retinocortical transmission time (RCTT). The latency differences between indirectly and directly stimulated hemispheres were calculated for interhemispheric transfer time (IHTT).

Results: Poor readers were completed reading test slower ($p=0.001$). There was no RCTT difference between groups. The RCTT to the left and right parietal regions were shorter than occipital sites in the whole group ($p=0.096$, $p=0.005$, respectively). In good readers, IHTT from right to the left was faster than left to the right, the difference was not significant. This asymmetry was not observed in poor readers.

Conclusion: Slower reading speed of poor readers showed that the grouping was correct. The fast RCTT to the parietal sites might be associated with directly transmission from pulvinar to the parietal cortex. It has been reported that IHTT from right to left is rapid in healthy individuals and this asymmetry disappears in dyslexia. The findings of this study were consistent with the literature. This work was supported by the Scientific Research Projects Coordination of Ankara University (No:18L0230001).

Keywords: Dyslexia, EEG, interhemispheric transfer time, reading, lateralization

P-056

Inhibitory effect of exercise on gastric ulcer-induced anxiety in rats: role of endogenous oxytocin

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Objective: Oxytocin, synthesized in hypothalamic paraventricular nucleus, is a neuropeptide with anti-inflammatory and anti-stress actions. Regular exercise is known to reduce stress and exert protection on gastrointestinal system. The aim was to investigate role of endogenous oxytocin in potential inhibitory effects of exercise on gastric ulcer-induced anxiety response.

Methods: Wistar albino rats (n=56) were randomly divided as exercise (6-week, 30min/day, 5days/week swimming) and sedentary groups. At the end of sixth week, acetic acid (80%; ulcer) or saline (control) was applied on gastric serosa under anesthesia. Starting by 5th week of exercise and on postsurgical 3 days, half of rats were injected intraperitoneally with oxytocin antagonist atosiban (0.1mg/kg/day), while others were injected with saline. To determine anxiety levels, rats underwent a hole-board test on postsurgical 3rd day and decapitated next day. Plasma cortisol levels were measured by ELISA. Gastric damage was assessed in hematoxylin & eosin-stained stomachs. Statistical analyses were made using ANOVA and Student's t-test.

Results: Severe surface and glandular epithelium damage was evident in sedentary ulcer groups, while epithelium damage was moderate in pre-exercised rats. Cortisol level of saline-treated sedentary-ulcer group was elevated as compared to control groups ($p<0.05$). When compared with sedentary rats, cortisol levels were depressed in ulcer-induced rats treated with atosiban or that have exercised before ulcer-induction ($p<0.001$). Indicating increased anxiety, head-dipping numbers in saline-treated sedentary-ulcer group were decreased compared to control groups ($p<0.05$). In parallel, immobilization time and rearing number of sedentary-ulcer group were also decreased without any statistical significance. In saline-treated ulcer groups that have exercised, rearing and head-dipping numbers were increased ($p<0.05$), suggesting depressed anxiety, while elevated anxiety level was not altered in atosiban-treated ulcer group.

Conclusion: Gastric ulcer-induced elevation in anxiety level was not observed in regularly pre-exercised rats and this anxiolytic effect of exercise could be mediated by an oxytocin-mediated mechanism.

Keywords: Ulcer, atosiban, exercise, anxiety

P-057

Effect of lateral parietal cortex TMS stimulation on memory functions in Alzheimer's patients

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Objective: In the treatment of Alzheimer's disease, transcranial magnetic stimulation (TMS) is usually performed with the aim of dorso lateral prefrontal cortex (DLPFC) and the patient's behavioral characteristics and executive functioning are observed to improve. However, this method does not benefit the hippocampal/temporal effect, which is the basic disorder of Alzheimer's disease, namely memory disorders. A different TMS protocol could not be developed in patients with this disorder, and no significant improvement in amnesic syndrome could be achieved. With functional magnetic resonance imaging (fMRI) in recent years it has become possible to detect changes in brain connectivity that occur in neurodegenerative diseases such as Alzheimer, as well as to observe changes in brain connectivity after treatment. We also aim to stimulate the lateral parietal cortex TMS stimulation and indirectly stimulate the hippocampal area, thus improving the memory functions of Alzheimer's patients, as previously described by Wang et al. (2014).

Methods: We determined the resting state of the Alzheimer's patient by performing a seed-based analysis on the fMRI and establishing a point in the left hippocampus region (Wang et al. 2014). We used a neuronavigator that transforms the MR data into 3D brain image to achieve the coordinated TMS excitation obtained. 10 sessions of TMS treatment were performed. Each seansta has 1640 magnetic pulses. The pulse frequency is 20 Hz. The duration of application is 20 minutes in total, and the duration of each period with 40 pulses is 2 seconds.

Results: For the evaluation; Neuropsychometric battery was applied before and after TMS and resting state MR images were taken. Thus, memory functions and changes in hippocampus-cortex connectivity can be analyzed.

Conclusion: Improvement of cognitive function in our study is aimed to create an alternative method to treatment protocols in Alzheimer's disease.

Keywords: Alzheimer's treatment, TMS, lateral parietal cortex

P-058

The effect of liposaccharide-induced preterm delivery on behavior and learning

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Objective: The aim of our study was to investigate the effect of LPS (ip) on the behaviors, learning, memory, sensory and spatial

memory of the offsprings on their young adulthood, which had been exposed to both intra-uterin inflammation and preterm birth by generating intra-uterine inflammation on pregnant rats on the 15th and 16th days of pregnancy.

Methods: The Wistar Albino rats were divided into three groups;The naïve group which was not exposed to any treatment, the group whichSF injections administered ip on days 15 and 16 of gestation and the group which liposaccharide injections administered on days 15 and 16 of gestation. The effects of locomotor activity test, passive avoidance test, and Morris' water maze test on behavior, learning, memory, sensory and spatial memory were examined at postnatal day 45 after the completion of the breastfeeding period.

Results: All results obtained from the experimental groups were shown as±std error. On the second day of the passive avoidance test of all experimental groups, the time of dark compartment pass was found to be 152.6±36.38 in Group 1.1 73.2±33.39 in Group 2 and 54.40±14.09 in Group 3. There was statistically significant decrease in the time of dark compartment transition between Group 1 and 3, between Group 2 and Group 3 ($p<0.05$). The Morris water maze test of all experimental groups was found to be 35.79±3.091 in the Naïve group, 31.44±3.710 in the SF group, and 19.31±3.530 in the LPS group.There was statistically significant reduction between groups1 and 3, between Group 2 and Group 3 ($p<0.05$).

Conclusion: Passive avoidance test and Morris's water labyrinth test performances of the young adulth rats which had pre-term birth induced with LPS exposure showed learning and memory impairment without disturbing the locomotor activity.Exposure to the intrauterine inflammation triggered during pregnancy permanently changes the neurotransmitter balance in the central nervous system by impairing normal brain development processes, suggesting that learning and memory are disturbed in young adulthood.

Keywords: LPS, inflammation, behaviour and learning, Wistar

P-059

The effect of low-calorie diet applied in adolescence on neurogenesis in right and left hippocampus

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Objective: The hippocampus, which plays an important role in the spatial memory, is one of the regions where neuron production (neurogenesis) occurs in the brain throughout life. Hippocampus is known to have anatomical and functional asymmetry. There is a positive correlation between hippocampal asymmetry and improved cognitive function. In our previous study, we showed that the low-calorie diet (LCD) we applied during the adolescence period improves spatial memory in adulthood, in this study we investigated asymmetry in terms of neurogenesis in hippocampus and evaluated the relation with spinal memory.

Methods: 28 day old Sprague-Dawley female rats were divided into 4 groups: SD4 control (fed with standard diet (SD) for 4 weeks), LCD4 (fed with 15% low calorie diet for 4 weeks), SD8 control (fed with SD for 8 weeks), LCD4 + SD4 (fed with 15% LCD for 4 weeks and fed with SD for the next 4 weeks). At the end of the experiment, after the spatial memory test with the Morris water tank, the rats were decapitated and the brains removed and the hippocampus separated. Proliferative cells stained with PCNA immunohistochemically were counted in right and left hippocampus dentate gyrus.

Results: In each group, including the control groups, the right hippocampus had more proliferating cells than the left hippocampus. However, the difference was statistically significant in the LCD4+SD4 group compared to the SD8-control group ($p<0.001$). Spatial memory performance in this group was also significantly increased compared to the SD8-control group ($p<0.001$).

Conclusion: Our findings showed that LCD applied in adolescence increased hippocampal asymmetry in terms of neurogenesis and strengthened spatial memory even when when switched to normal feeding in adulthood. These specific results highlight the importance of neurogenesis in the functional asymmetry of the hippocampus and the contribution of hippocampal neurogenesis in the formation of spatial memory.

Keywords: Hippocampal lateralization, neurogenesis, spatial memory

P-060

Metacognitive processes in superagers

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Objective: Superagers are individuals who are above 60 years old and have similar cognitive abilities along with episodic memory performances with individuals who are 20 or 30 years younger. Superagers age better than their peer groups in terms of cognitive performances. Superagers' metacognitive performances were assessed by the application of episodic Feeling of Knowing (eFOK) monitoring task along with their cognitive abilities (episodic memory, attention, executive function). eFOK is age sensitive and as individual ages their metacognitive ability diminishes. The aim of the study was to find a relationship between metacognitive accuracy results and being a Superager.

Methods: 45 participants were recruited for the study; 15 Superagers (60 years old and older) and two control group; 15 healthy young adults (18–35 year olds) and 15 elderly control group (age-matched to our Superager participants). Basic neuropsychological assessments applied to health elderly adults in order to find Superagers. For metacognitive assessment, 40 cue-target word pairs were used in the eFOK task.

Results: There was no significant difference between Superagers (M =.72, SD =.09) and young control group (M=.75, SD=.08) on episodic memory task (max t=3.87, min p=.01). The group differences on eFOK gamma resolutions assessed by one-way ANOVA. The results of the study indicated that Superagers' eFOK judgments (M =.60, SD=.34) were more accurate and significantly higher compared to both the elderly (M=.28, SD=.29) and young control groups (M=.18, SD=.34), F (2,42)=33.78, p <.01.

Conclusion: The ageing process corrupts the metacognitive abilities because monitoring ability requires some cognitive sources which have already been proven to deteriorate with age. However, Superagers showed that they also have intact metacognitive abilities along with their cognitive abilities. In addition, eFOK performances of Superagers were even higher than young control group.

Keywords: Superagers, metacognition, neuropsychology, feeling of knowing

P-061

Behavior and tissue insulin levels in monosodium glutamate-treated rats

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Objective: (L)-Glutamate is known to stimulate insulin secretion in vitro, from isolated rat pancreas by acting on receptors of the AMPA subtype, and in vivo in normal rats and in a rat model of type 2 diabetes, with glucose tolerance improvement. Monosodium glutamate (MSG) is used as a flavor enhancer in many processed foods. In many countries there are no limitations on the amount of MSG intake which is questioned due to its toxic effects on human health. The present study was designed to investigate the in vivo effects of monosodium glutamate (MSG) on behavior paramethers and brain-liver insulin levels in rats.

Methods: Monosodium glutamate was given (with gastric gavage) only one day in a week for 12 weeks at 8-weeks-old male rats (n=10). The control group rats (n=10) received saline at same time and period. After the exposure period, animals were subjected to behavioral tests on open field area. The locomotor activity and discovery behavior of the rats were assessed by the number of crossing lines and rear respectively. The brain and liver insulin levels were analyzed by ELISA method. The data were analyzed statistically by independent t-test.

Results: The number of line crossings and the discovery behaviors increased in MSG-treated rats compared to the control rats in the open-field area. These changes are not statistically significant. (p>0.05). The changes in the number of grooming and the defecation were not statistically significant (p>0.05). There was no significant difference in the brain and liver insulin levels of MSG-treated and control groups rats (p>0.05).

Conclusion: This protocol did not make a significant difference in behavioral parameters and insulin tissue level in MSG-treated rats. This study was supported by Erciyes University Scientific Research Projects Unit TYL-2016-6478) project.

Keywords: Behavior, male, insulin, MSG, rat

P-062

Depressive mood and memory bias: is breathing exercise effective?

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Objective: The main goal of this study was to investigate the effect of breathing exercises on depressive mood and autobiographical memory characteristics. Moreover, the current study was aimed to extend the depression treatment literature with the understanding of the relationship between mood and memory characteristics.

Methods: This study was conducted with 90 women in total, among which 45 participants were in the control group and 45 participants were in the experimental group. Firstly, Depression, Anxiety, and Stress Scale (DASS) was applied to determine in which group the participants would be included. Participants in experimental group were randomly separated into three conditions (negative, positive or neutral instruction). Autobiographical Memory Characteristics Scale and DASS were applied as pretest and posttest. The effects of breathing exercises on depressive mood (moderate or severe) and the characteristics of the autobiographical memory were examined. The breathing exercise procedures prepared by Ministry of Education, General Directorate of Special Education and Guidance Services (2015) were carried out as intervention.

Results: The results indicated that pre-depression scores of the breathing exercises of depressive participants (M=22.91, SD=4.70) significantly higher than post-test scores (M=17.31, SD=8.62) (p<.05). As expected, depressive participants remember negative autobiographical memories (M=3.73, SD=4.21) faster than intervention (M=5.50, SD=7.50) (p<.05). After breathing exercises, depressive participants were able to recall positive memories more quickly than (M=2.12, SD=1.39) before intervention (M=3.20, SD=1.82) (p<.05).

Conclusion: Research findings have shown that breathing exercises can be accepted as an easy self-help technique for both improving mood and memory characteristics (i.e. the details and the integrity of the memories).

Keywords: Depressive mood, autobiographical memory, breathing exercises

P-063

Attentional bias in exercise dependence

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Objective: Exercise dependence is a condition that physical activity becomes an excessive and compulsive behavior having cognitive, behavioral and physical symptoms. In literature, there are many studies found attentional bias in many dependencies such as alcohol, cigarette, gambling. This study aims to measure attentional bias in exercise dependence.

Methods: 48 male participants were grouped in three based on Exercise Dependence Scale; risk for exercise dependence, nondependent-symptomatic and nondependent-asymptomatic. Participants who are doing fitness in gyms were included. Computerized addiction-stroop task is used to measure attentional bias. A pilot study was conducted to determine fitness related words used in the task. Words were blocked and appearing randomly. Participants were informed about the task and asked them to press the appropriate button as fast and accurate as possible according to the word's color and ignore the world itself. Participants' reaction times and errors were recorded. Participants received Social Physique Anxiety Scale and participants who have high social physique anxiety were excluded from the analysis.

Results: Analysis were conducted with 43 participants. Two separate 3 (group) × 2 (word type; fitness, neutral) mixed ANOVA was conducted both for reaction time and errors. There was no significant interaction between group and word type both for reaction time (p=.350) and errors (p=.831). There is a significant main effect of word type on reaction time (.002). Participants respond slower to fitness related words (M=843ms, SD=141) than neutral words (M=814ms, SD=137).

Conclusion: As different from expected, there is no significant reaction time and error difference on fitness related words among risk for dependence group compared to other groups. However, all participants have significantly longer reaction times to fitness related words compared to neutral words. There is no attentional bias found in exercise dependents compared to other groups. However results indicated that all men have an attentional bias towards fitness related words.

Keywords: Addiction stroop, attentional bias, exercise dependence

P-064

Event related potential (ERP) based wavelet analysis for emotion classification

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Objective: The aim of this study is to discover features to be used in Event Related Potential (ERP) based classifiers for emotion detection.

Methods: 12 healthy subjects with mean age of 27.4 (±2.96) were included in the study. 280 pleasant and 280 unpleasant pictures with positive or negative emotional valence were presented as standard stimuli in two separate sessions, and a neutral stimulus was presented randomly as a target stimulus. Each picture was displayed in the monitor for one second and inter-stimulus interval was two seconds. Pictures were selected from the IAPS dataset with different mean valence levels (7.13/2.96), but equal mean arousal levels for the two sessions (4.99/5.02). EEG data were recorded from 32 channels with a sample rate of 250 Hz. Artifacts were removed by raw data inspection and by ICA method. ERP segments were extracted from EEG data, beginning at the time of stimuli with a length of 1000 ms. Using bior3.7 wavelet function, coefficients belonging to delta (0–4 Hz), theta (4–8 Hz), alpha (8–16 Hz) and beta (16–32 Hz) frequency bands for each ERP segments for each trial of each subject were calculated. Mean of wavelet coefficients in four bands belonging to N100, N200 and P300 ERP's were selected as features during classification. k-NN, LDA and SVM methods were used to discriminate pleasant and unpleasant recordings. The same procedure was applied by selecting energy of wavelet coefficients as feature set.

Results: Classifying for each subject independently, the grand average of classification accuracy, sensitivity and specificity values were obtained as %81.7, %81.9 and %81.5, respectively.

Conclusion: The most successful classification results were obtained with SVM by using the energy of the wavelet coefficients belonging to N200 to P300 interval of the ERP in beta band.

Keywords: EEG, BCI, ERP, classification

P-065

Lateralized ear temperature increase in response to a visual processing experiment

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Objective: It is showed that there is a correlation between the temperature change recorded from tympanic membrane (TMT) and the ongoing activity of the ipsilateral hemisphere and TMT can produce lateralized responses to hemisphere specific stimulation. It is reported that visual processing experiments cause a lateralized response in brain, especially in right hemisphere. In the present study, whether a visual stimuli, consists of puzzle pieces, can produce a lateralized effect on brain or not was investigated by means of TMT measurements.

Methods: 10 postgraduate students were participated in the study. 30 puzzle pieces with different shapes were rendered on a

computer screen and simultaneous TMT recordings were made from both ears throughout the experiment. While 20 of these puzzle pieces are empty, remaining 10 pieces have a black dot withinside and labeled as the target pieces. Target and non-target puzzle pieces are in a randomized order with 20 seconds apart. Each stimulus was rendered on a screen for 500 miliseconds (ms), with a fixation point of 300 ms before the stimulus in order to draw the subjects' attention to the screen and 500 ms white noise mask after the stimulus in order to remove the after image effect on the screen. Before the experiment subjects were told to pay attention to pieces on the screen, coun the number of target pieces and state that number at the end of experiment.

Results: At the onset of the experiment there is no statistcially significant difference between left and right TMT (p=0.2454). However, temperature increase of right ear during the experiment exceeds the that of left ear, 0.336 °C and 0.231 °C, respectively. Furthermore, difference between left TMT increase and right TMT increase throughout the experiment is statistically significant (p=0.0412).

Conclusion: Findings show that a visual stimuli can produce lateralized effects on TMT.

Keywords: Visual process, lateralization, tympanic membrane temperature

P-066

Caffeine administration causes permanent changes in membran lipids of cortical neurons in rat

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Objective: Caffeine is a methylxanthine commonly used in neonatal medicine either acutely or chronically for the suppression of apneic episodes in premature infants. Both clinical and experimental evidence on long-term consequences of chronic caffeine administration are scarce. Wistar Albino Glaxo/Rijswijk (WAG/Rij) rats are a well- established animal model for genetic absence epilepsy. Our previous study revealed that neonatal caffeine administration from postnatal day 7 to postnatal day 11 decreased seizure frequency in WAG/Rij rats.

Methods: We investigated the effects of neonatal caffeine administration on structure and content of membrane components of the neurons in the prefrontal cortex using Fourier transform infrared (FT-IR) spectroscopy. Caffeine (10 mg/kg and 20 mg/kg, i.p.) or saline was injected from the postnatal day 7 to postnatal day 11. The structure and content of the neuron membranes of the prefrontal cortex were investigated in these animals at postnatal day 180. The animals were sacrificed for FT-IR spectroscopic study, and the brains were quickly dissected.

Results: A decline in content of lipids in prefrontal cortical neuron membranes of caffeine- injected rats was observed when compared to saline- injected rats. This was obtained from the ratio of CH3 asym/lipid, CH2 asym/lipid, CO/lipid, and olefinic CH/lipid.

Conclusion: Our findings have shown that neonatal administration of caffeine may affect the molecular organization of membran lipids of prefrontal cortex cells and this effect persists into adulthood. FT-IR spectroscopy may offer promising attempt to identify long term structural alterations in brain tissue membranes.

Keywords: Caffeine, FT-IR, rat

P-067

Distribution of type, location and Incidence of wormian bones: a neurodegeneration indicator?

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Objective: The squamous part of the occipital bone is sometimes divided by one or more longitudinal or transverse sutures. These lead to various types of wormian bones. Knowing the anatomy of Wormian types plays a role in the differential diagnosis of congenital diseases especially CNS disorders. The purpose of this study is to identify the differences in the frequency, types and localization of wormian bones in adult dry skulls and to investigate the differential diagnosis of CNS disorders.

Methods: 102 human adult dry skulls 72 (%71) male and 30 (%29) female were examined in the anatomy laboratory of university of Akdeniz. All the skulls were macroscopically observed for the incidence, types, and localization of the wormian bones. And also the widht, height and distance from mastoid process were measured by digital calliper.

Results: Wormian bones were determined in 32 (22 male, 69%; 10 female, 31%) dry skulls. They were observed on the left: 21; 42% (3 female, 14%; 18 male, 86%), on the right: 21; 42% (15 male, 71%; 6 female, 29%), central: 8 (16%). The bone types was generally observed in bilateral. More than one wormian bone was observed in the same skull: 5 (62%) left, 2 (25%) right, 1 (1.3%) center. The most common site was lambdoid suture; 17 (53%), secondly occipitomastoid suture; 7 (22%), and the least sagittal suture;1.5%. The average width and height of the wormian bones were measured as 16.01 mm (16.07 in women, 15.37 in men) and 15.64 mm (12.31 mm in women and 17.15 mm in men).

Conclusion: Wormian bones were frequently seen in the lambdoid suture and lambda. The frequency, localization, width and height of wormian bones significantly changed by gender. The knowledge of types, localization and incidence of wormian bones are important for early diagnosis and treatment of various neurodegenerative diseases.

Keywords: Wormian bones, neuroanthropology, lambdoid suture, lambda

P-068

Stereotaxic intracerebral injection difficulties in juvenile rats

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Objective: It is inevitable to use stereotaxic methods for injection of intracerebral tracers or, viruses in certain regions of the brain in rodent studies. Thus, it is necessary to know the stereotaxic coordinates well. However, that preparing atlases, which display stereotaxic coordinates, according to adult animals can be challenging for researchers working on newborn or juvenile animals. In this study, it was aimed to determine the stereotaxic coordinates of the ventral tegmental area in juvenile rats.

Methods: 20 juvenile Sprague Dawley rats were used in the study. The rat under general anesthesia was placed in a stereotaxic instrument fitted for juvenile rats in advance. The lambda and the bregma were revealed by conducting skin incision. Possible stereotaxic coordinates of VTA in juvenile rats were calculated by considering atlas VTA stereotaxic coordinates prepared according to an adult rat (AP: -5.3, ML: +0.8, DV: -8.3 mm) and the distance between the lambda and bregma. Stain injection was performed on the calculated coordinates. The injection area was checked at the end of each try by taking sections of the brain tissue.

Results: As a result, trials in the juvenile rats showed that 0.5 mm lateral of the midsagittal suture was sufficient to reach the mediolateral (ML) coordinate of the VTA. However, the correct coordinates for anteroposterior (AP) and dorsoventral (DV) were not reached.

Conclusion: 20 juvenile rats underwent intracerebral injection according to the calculations and the accuracy of the injection site were assessed morphologically. The stereotaxic coordinates of VTA in the juvenile rats could not be reached accurately. As a result, literature information is not sufficient to perform stereotaxic surgery in juvenile rats. Therefore, there is a necessity to develop stereotaxic atlas for juvenile rats.

Keywords: Rodent, stereotaxic surgery, intracerebral injection, ventral tegmental area

P-069

Investigation of miRNAs targeting NFIX transcription factor during neural differentiation

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Objective: The central nervous system (CNS) comprises three major cell types which arise from neural stem cells (NSCs): neurons, astrocytes and oligodendrocytes. Whether cells will undergo self-renewal, maintenance and commitment to a particular fate is determined by interactions between transcription factors and their target genes. Nuclear factor I (NFI) transcription factor family, NFIA, NFIB, NFIC and NFIX, regulates important developmental processes such as neurogenesis and gliogenesis in different regions of embryonic CNS as well as stem cell maintenance in adults. Expansion of ventricular zones in Nfix null mice indicates disruption of progenitor cell proliferation and differentiation. Interestingly, Nfix is induced in cultured NSCs that are quiescent. Furthermore, Nfix is required in NSCs of the adult hippocampus for quiescence. To date, miRHCC1, miR1290, miR1914* and miR1915 which suppress NFIX has been shown to be associated with cancer cell proliferation and invasion. Here, to elucidate mechanisms that regulate NFIX function, we focus on microRNAs in human NSCs.

Methods: NFIX and miRNA expression in differentiating neural progenitors was analyzed by qRT-PCR and microarray analysis respectively. microRNA binding sites in the NFIX 3'UTR were identified using TargetScan and miRanda (microRNA.org) tools. The 2000 bp NFIX 3'UTR region that includes miRNA binding sites was amplified from human genomic DNA in two fragments and subcloned into pmiRGLO Dual-luciferase reporter vector.

Results: NFIX was downregulated by 67% upon differentiation. We selected miR92b, miR124 and miR363 which are predicted to bind the NFIX 3'UTR and are highly expressed in neural progenitor cells for further study.

Conclusion: Interaction between selected microRNAs and NFIX 3'UTR will be analyzed with luciferase supression assay and specificity of these interactions will be tested by mutagenesis. These data will elucidate molecular mechanisms that regulate NFIX expression in human neural progenitor cells.

Support: ITU BAP (TGA-2017-40844) and TUBITAK KBAG (115Z524).

Keywords: Neural differentiation, NFIX, miRNA

P-070

Effects of prenatal and postnatal conditions on motor skills and cerebellar morphology of rats

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Objective: Vermis, one of the first phylogenetically evolved parts of the cerebellum, is associated with balance and motor coordination. The development of macro- and microneurons is completed in two different periods: Embryonic (E) and postnatal (P). In this study, comparison of changes in motor behavior and cerebellar morphology of rats raised in diverse environmental conditions was aimed.

Methods: Male Spraque-Dawley rats were divided into three groups (n=8) as control, stress and enriched environment conditions. Dams of the stress group are exposed to repeated unpre-

dictable stress paradigm (immobilization, food restriction, forced swim, change of day/night cycle, cold or crowded housing) from E14th until birthday. Their offspring were separated from mothers between P1–P25 and socially isolated between P25–P45. Enrichment group is housed in large cages with different objects between E14–P45. All animals were subjected to modified grip and rota-rod test on P27–29 and P42–44. Morphometric counts were done on cerebellar vermis sections.

Results: While there was no significant difference between the groups in the repeated measures in the modified grip test, only a significant increase was observed between the early and late stage measurements of the animals grown in the enriched environment. In the rota-rod test, no significant difference was observed among groups. The number of Purkinje cells per unit length was significantly higher in the enriched group than in the control group ($p<0.05$). The ratio of the granular/molecular layer volume (GL/ML) was significantly lower in the animals raised in the enriched environment than those of controls.

Conclusion: During cerebellar development, Purkinje neurons proliferate in the prenatal period, while granular cells continue to develop in the postnatal period and establish synaptic connections with mossy fibers from the periphery. Reduction in GL/ML ratio in animals raised in enriched environment might be due to increase in the neuronal density of Purkinje cells.

Keywords: Cerebellum, enriched environment, grip test, morphometry, stress

P-071

Suppression of the neural differentiation regulator transcription factor NFIB by CRISPR/Cas9 system

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Objective: The central nervous system arises from a group of neural stem cells that first generate neurons and then glia, and then migrate from the ventricular zones where they are generated and finally undergo terminal differentiation. Three members of the Nuclear Factor I transcription family, Nfia, Nfib and Nfix are involved in regulation of these processes in different brain regions. Specificially, Nfib controls both neurogenesis and gliogenesis in the neocortex and spinal cord by suppressing genes associated with stem cell renewal such as Sox9 and Ezh2. In the cerebellum, Nfib regulates terminal differentiation of cerebellar granule cells by promoting the expression of extracellular molecules such as Ephrin B1, N-cadherin, Tag1, and Wnt7a. In order to explore NFIB's mechanisms of action in differentiating human neural stem cells, we set out to render NFIB non-functional using CRISPR/Cas9 gene editing.

Methods: In order to render NFIB non-functional in human neural progenitor cells, the gRNA design tool developed by Ran et al. (2013) was used to create mutations in the 2nd exon of the gene, and initially 2 target sequences with high cleavage efficiency and specificity were selected. Guide sequence oligos were cloned to a plasmid containing Cas9 and sgRNA scaffold (pSpCas9(BB)-2A-Puro), and subsequently were verified by DNA sequencing. HEK293T cells were transfected with these constructs and subjected to selection with puromycin.

Results: To determine the rate of mutagenesis, target regions were first amplified by Polymerase Chain Reaction from genomic DNA of 5 individual clones isolated from cell populations transfected with gRNA1 and 15 clones isolated from cell populations transfected with gRNA2 and subsequently assayed by T7 Endonuclease cleavage.

Conclusion: The tested gRNAs will be used for genome editing of human neural cells to further explore NFIB's role in regulation of gene expression and neural differentiation. This study was supported by ITU BAP (TYL-2017-40603) and TÜBİTAK KBAG (115Z524).

Keywords: Neural differentiation, NFIB, CRISPR

P-072

Generation of novel tools to study IroC gene function of IroC target

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Objective: The olfactory system depends on the proper gene expression of olfactory receptor (OR) genes in olfactory receptor neurons (ORN) and the proper transfer of olfactory signals to the brain. ORNs have to make two important choices. They have to choose to express one gene from the large repertoire of OR genes and send their axons to a special destination in the brain. Our studies focus on the elucidation of the role of the Iroquois complex (IroC) family, a family of transcription factor genes consisting of three conserved genes called araucan (ara), caupolican (caup) and mirror (mirr) in the differentiation of odorant receptor neurons.

Methods: To elucidate the function of the IroC genes, we tried to generate mutants for all three genes using the CRISPR/Cas technology. In addition, to examine localization of each gene we aimed to add fluorescence proteins to each gene locus using the CRISPR/Cas. The obtained mutants were examined using RNASequencing to identify differentially expressed genes. The identified genes were confirmed by qRT-PCR. Verification by in situ hybridization is underway. Furthermore, the effects of iroC genes on the differentiation of cells are followed by the lineage-tracing experiments.

Results: In this study we showed that the IroC genes are expressed in ORNs. While the maxillary palp iroC is expressed in the pb2 subset of the ORNs, expression in the adult antenna appears to be more dispersed. In order to identify the iroC target genes, we first used RNASeq analysis using triple mutant fly antennae and maxillary palps and identified the differentially

expressed genes. We show that 11 OR genes and 23 transcription factors are differentially expressed. qRT-PCR experiments confirmed that expression of the OR genes is decreased.

Conclusion: Our results confirm that iroC genes play a role in OR gene regulation. However, further experiments will show if this regulation is direct or indirect.

Keywords: Neural diversity, IroC, CRISPR/Cas, RNASeq

P-073

GluK2-NETO2 signalling regulates dendritic spine morphology in developing hippocampus

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Objective: To study the role of kainate receptor signaling in developing brain (hippocampus) Kainate receptors (KARs) are a subtype of ionotropic glutamate receptors, composed of five different subunits (GluK1-5) in tetrameric assemblies. They are highly expressed during early brain development to modulate synaptic transmission, network excitability and synaptogenesis. In particular, recent evidence highlights a robust increase in axonal filopodia by overexpression GluK1-GluK5 while shRNA-mediated knockdown of GluK2/5 reduces the density of filopodia, suggesting a role for KARs in structural plasticity of synaptic contacts. NETO2 is an auxiliary subunit of KARs which modulates their functional properties. In this study, we showed that absence of NETO2 significantly reduced the proportion of dendritic spines in cultured hippocampal neurons, and it was rescued by the overexpression of GluK2. We also studied the effect of NETO2 on the actin dynamics using live-cell imaging. Indeed, the absence of NETO2 had a significant effect on actin dynamics by increasing the stability of F-actin filaments in dendritic spines of hippocampal cultures. In conclusion, our results demonstrate that GluK2-NETO2 signalling developmentally regulates dendritic spine formation and its stability.

Methods: Primary neuronal culture of hippocampus; Lentiviral-mediated knock down and overexpression; In vitro live cell imaging (FRAP, fluorescence recovery afte photobleach); Confocal imaging; Data analysis (qualitative and quantitative comparison of dednritic spines using NeuronStudio).

Results: In this study, we showed that absence of NETO2 significantly reduced the proportion of dendritic spines in cultured hippocampal neurons, and it was rescued by the overexpression of GluK2. We also studied the effect of NETO2 on the actin dynamics using live-cell imaging. Indeed, the absence of NETO2 had a significant effect on actin dynamics by increasing the stability of F-actin filaments in dendritic spines of hippocampal cultures.

Conclusion: Our results demonstrate that GluK2-NETO2 signalling developmentally regulates dendritic spine formation and its stability.

Keywords: Kainate receptor, dendritic spine, developing hippocampus

P-074

Evalution of selenium supplementation on long term depression responses of hyperthyroid old rats

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Objective: In addition to the well-documented functions of Se as an antioxidant, it plays a role in the regulation of the thyroid hormone metabolism and immune function, and in the maintenance of brain function. Long-term depression (LTD) is a persistent, activity-dependent decrease in synaptic plasticity. In the present study we investigated whether selenium supplementation has a similar effect with hyperthyroidism-induced LTD changes.

Methods: 12-month-old male Wistar albino rats were divided into 3 groups (n=6/group) as control, hyperthyroid and selenium group (Se). Hyperthyroidism was induced by administering ip L-Tyroxin (0.3 mg/kg/day) for 1 month. From 8th months, Se treated group was received sodium selenite (0.5 mg/kg/day) in drinking water for 4 months. LTD was induced by a low frequency (1 Hz, 15min) stimulation protocol, and recorded from dentate gyrus granule cells of the hippocampus.

Results: A one-way ANOVA failed to show significant group effect for EPSP slope, but for PS amplitude, a significant effect of group was found (p=0.026). Post hoc LSD test showed that hyperthyroidism-induced potentiation of PS amplitude was not observed in Se and control groups.

Conclusion: The present results show that LFS is not able to LTD in the dentate gyrus in aging rats, but rather induces a form of long-term potentiation (LTP), which is characterized by an increase in PS amplitude exclusively, in hyperthyroid rats. This enhanced LTP may underline memory impairments observed in elderly person with hyperthyroidism. This study was supported by Erciyes University Scientific Research Projects Unit under TCD-2016-6262 project.

Keywords: Hyperthyroidism, selenium, long-term depression

P-075

Investigation of metaplasticity responses in hypothyroided rats

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Objective: Metaplasticity,a higher-level form of synaptic plasticity, is expressed as plasticity of synaptic plasticity. Metaplasticity,

is a process that plays an important role in preserving the balance between long-term potentiation (LTP) and long-term depression (LTD), and there is no study in literature on the change in metaplasticity responses in hypothyroidism. In this study, it was aimed to show the changes in thyroid hormone levels and in metaplastic responses.

Methods: It was used 2-month-old male Wistar albino rats. The rats were divided into 2 groups (n=10 for each group) as control,hypothyroid. Hypothyroidism was induced by administration of 6-n-propylthiouracil (1 mg/kg/day) with drink-water for 21 days.Metaplasticity responses were recorded from hippocampus of rats anesthetized with urethane.To induce metaplasticity, perforant pathway was stimulated with priming stimulation (5Hz; 180sec) followed by high frequency stimulation (HFS: 100Hz, 4 times, 5 min intervals) and changes in field potentials (Population Spike-PS, Excitatory Post-Synaptic Potential-EPSP) occurring in dentate gyrus granule cell layer were recorded.Serum free T4 (fT4) levels of rats were measured using a commercial ELISA kit.

Results: Statistical comparison with independent sample t-test;plasma fT4 levels of hypothyroid group were significantly lower than control group ($p<0.001$). Metaplasticity responses were evaluated for PS amplitude and EPSP slopes. For PS amplitude; There was no significant difference between groups during induction period ($p=0.136$), but during maintenances periode, metaplasticity responses were significantly decreased in hypothyroid group compared to control group ($p=0.005$). Metaplasticity responses were significantly reduced in the hypothyroid group compared to that in control group during induction ($p=0.039$) and maintenances periode ($p=0.003$) for EPSP slope.

Conclusion: Study findings indicate that priming stimulation protocol induces metaplastic amplification in the control group, but the hypothyroid state suppresses this amplification. This result is similar to the findings in the literature that hypothyroidism does not suppress LTP. Hypothyroidism is thought to be responsible for the changes in the functioning of intracellular signaling pathways, which in normal the responsability of thyroid hormones, during suppressing hippocampal metaplastic amplification. This study was supported by Erciyes University Scientific Research Projects Unit under TDK-2017-7696 project.

Keywords: Metaplasticity, hypothyrodisim, synaptic plasticity

P-076

Measure of the container officers' daily MET, sleep duration and efficiency via metabolic holter

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Objective: This study was conducted to determine energy consumption,sleep durations and sleep efficiency in the work environment of 2nd and 3rd officers on container vessels.

Methods: A body tracking monitor which is a multi-sensor wearable technology product was used. It is an armband that provides information about energy consumption, lying and sleeping periods and (MET) metabolic severity of physical activities (BSA: Bodymedia Sensewear Armband Pro3).The study was carried out on the container vessels running between Turkish, Mediterranean and Black Sea ports. A total of 127 daily records were obtained from 8 healthy male volunteers (mean age 25.8, mean BMI 23.8 kg/m^2) with BSA. Bodymedia SenseWearPro 6.1 software algorithms were used in the evaluation of data.

Results: The 2nd officers were responsible for shifts from 00.00–04.00/12.00–16.00 or 00.00–06.00/12.00–18.00, while the 3rd officers from 08.00–12.00/20.00-00.00 or 06.00–12.00/18.00–00.00. 2nd officers' average energy consumption was 3.114 kcal/day (SD±570), daily MET value was 1.6 (SD±0.2). That was 3.523 kcal (SD±762) and 2.0 (SD±0.3) for the 3rd officers'. The average energy consumption of all was 3.320 kcal/day (SD±702); daily MET was 1.8 (SD±0.3); lying time was 7.2 hours/day (SD±2.0); sleeping time was 4.7 hours/day (SD±1.4); sleep efficiency was 66.1% (SD±14.2). A difference was not found between the 2nd and 3rd officers' average lying, sleeping times and efficiency. However, there was a correlation of -0.55 between MET and sleep duration in the 3rd officers,and this value was -0.25 in the 2nd officers.

Conclusion: The watchkeeping officers on container vessels in shortsea shipping, are not able to sleep in sufficient efficiency and time.The officers consume more energy and sleep less.This is seen as dangerous for workers and their environment in a ship atmosphere with various risks. It does not coincide with the aims of international resting arrangements for seafarers. In the 3rd officers with higher MET, higher corelation between sleep efficiency and MET suggest that neuroscience needs more studies on the effects of physical energy consumption on the brain.

Keywords: Watchkeeping officers, sleep, sleep efficiency, energy consumption, MET

P-077

Investigation of the effect of physical activity level on sleep quality among physicians

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Objective: To investigate the effect of physical activity levels on sleep quality (SQ) of physicians by subjective (questionnaire) and objective (metabolic holter) methods.

Methods: In this study, twenty male volunteer physicians, aged between 25–35 years were recruited. Metabolic parameters (total energy expenditure, active energy consumption, average MET

"metabolic equivalent: kcal/(kg.m)", physical activity duration, number of daily steps) and SQ parameters (sleep duration, sleep efficiency) were obtained with a wearable metabolic holter device (BodyMedia Sensewear-Armband 'SWA', monitored for 23 hours). In addition, SQ was assessed subjectively with the Pittsburgh Sleep Quality Index (PSQI), prepared as an online questionnaire. The data were analyzed using standard descriptive statistics (mean±standard deviation) and correlation analysis.

Results: Considering all participants (n=20), mean total energy expenditure of physicians was 2697.85±307.82 kcal, mean active energy expenditure was 514.05±370.68 kcal, mean daily average-MET was 1.47±0.19, mean physical activity duration over 3 MET was 94.55±64.77 minutes, mean number of daily steps was 6757.05±2295.02; the mean duration of sleep was 368.20±75.11 minutes, mean sleep efficiency was %77.55±11.27 according to the data obtained by SWA, and mean global sleep quality score measured by PSQI was 7.10±3.48. Since all data showed normal distribution, Pearson correlation analysis was performed: When the metabolic and physical activity levels were compared with SQ data, there were no significant correlations. (r-value varied between -0.133 and 0.308, and p-value varied between 0.186 and 0.951)

Conclusion: When both SWA and PSQI data are taken into consideration, it can be expressed that participants generally have low metabolic equivalent and mild deterioration in SQ (healthy individuals: sleep activity ≥ 85%, global PSQI score ≤5 in SWA monitoring). In this study conducted among physicians, there was no significant relationship between physical activity measures and SQ parameters.

Keywords: Physical activity level, metabolic equivalent (MET), sleep quality.

P-078

Antinociceptive mechanisms of action of endocannabinoid system on migraine in migraine rat model

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Objective: Trigeminovascular system and dural mast cell activation are principally responsible for migraine pathophysiology. Recently, it was reported that pain impulses from A- and C-fibres which innervate dura mater and convey nociception from dura mater are inhibited via cannabinoid receptor-1 (CB1). But, the mechanisms of antinociceptive effects of endocannabinoid system remain yet unclear. We investigated effects of methanandamide (mAEA) and cannabinoid receptors on calcitonin gene-related peptide (CGRP) and substance-P (SP) levels, and dural mast cell in glyceryltrinitrate (GTN)-induced migraine model in rats.

Methods: Fifty-six male wistar rats (8–10 weeks) were divided into eight groups (n=7). Groups intraperitoneally received saline (0.2 ml), vehicle (0.1% ethanol), GTN (10 mg/kg), mAEA (20 mg/kg), mAEA+GTN, L-Name (NOS inhibitor ,50 mg/kg)+ GTN, Rimonabant (CB1 antagonist, 2 mg/kg)+mAEA+GTN, Capsazepine (TRPV1 antagonist ,10 mg/kg)+mAEA+ GTN, respectively. Rats were sacrificed after two hours. CGRP and SP contents of plasma, trigeminal ganglia, brainstem and brain tissue were measured using enzyme-immunoassays. Dural mast cells were viewed by toluidine-blue staining. Data were analyzed with one-way ANOVA-and posthoc Tukey test.

Results: GTN increased levels of CGRP and SP in plasma, TG neurons, brainstem and brain tissue ($p<0.001$). However while mAEA prevented the increases in plasma and TG neurons ($p<0.05$) it could not prevent increases in brainstem and brain tissue. While Rimonabant reversed effects of mAEA on plasma and TG neurons ($p<0.05$), Capsazepine had no influence. L-Name inhibited effects of GTN($p<0.01$), but had no effects on cannabinoid mechanisms. GTN increased number and degranulation of dural mast cells ($p<0.05$), mAEA and L-Name inhibited the increases, respectively ($p<0.05$), but neither Rimonabant nor Capsazepine reversed the effect of mAEA.

Conclusion: Endocannabinoid system modulates levels of CGRP and SP in plasma and TG neurons via CB1 receptors, not TRPV1, and also number and degranulation of mast cells in dura mater through an unknown mechanism. Development of non-addictive CB1 agonists or drugs that delay degradation of endogenous anandamide may be an effective choice in the treatment of migraine. Study was supported by AIBU Scientific-Research-Fund[Grant-number:2016.08.02.1095].

Keywords: Cannabinoid receptors, CGRP, methanandamide, migraine, SP.

P-079

Design of a novel polyamidoamide-based nanomedicine for treatment of neuro-inflammation

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Objective: A novel PAMAM (Polyamidoamide)-based drug delivery system for the anti-inflammatory small molecule N-acetyl cysteine (NAC) as a brain targeting nano-vehicle with a sustained and slow drug release profile is presented.

Methods: PAMAM dendrimers have recently been utilized as promising biomaterials for intrinsically targeting the brain in CNS-related disorders with no effective therapies, such as cere-

bral palsy (CP) and ischemia. Previous studies have established their ability to penetrate the blood-brain barrier (BBB) and diffuse freely within the brain parenchyma, which are the primary challenges. In addition, PAMAM dendrimers have been shown to selectively localize to activated microglia and astrocytes in regions of neuroinflammation, allowing for efficient delivery of potent therapeutics to sites of injury. This design enables NAC molecules conjugated to the periphery of PAMAM dendrimers with ester and disulfide linkers to release in a step-wise manner by responding to different enviromental conditions.

Results: PAMAM (4th and 6th generations) with hydroxyl groups at the periphery were successfully decorated with NAC drug molecules via both ester and disulfide linkages. Based on generation of PAMAM utilized and the feed ratio of NAC, resultant nano-sized conjugates vary for their drug payloads, still possessing neutral surface charges and high water solubility. Moreover, cellular internalization studies were conducted with a fluorescently labelled version of the conjugate to confirm non-toxicity and time-dependent cellular uptake by activated microglia.

Conclusion: Sustained release of NAC molecules results in improved anti-inflammatory and anti-oxidative efficacies, demonstrating that D-(NAC-NAC) is a very promising drug loaded nanoparticle for prolonged treatment of CNS-related disorders.

Acknowledgment: This study was funded by NIBIB R01EB 018306 project and TUBITAK 2219 post-doctoral scholarship.

Keywords: Neuro-inflammation, nanomedicine, drug delivery, brain targeting

P-080

The effect of acetaminophen toxicity on hippocampal and prefrontal cortex IGF-1 and MMP2 levels

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Objective: The aim of this study was to investigate the effects of different doses of acetaminophen on prefrontal cortex and hippocampal IGF-1 (insulin-like growht factor-1) and MMP2 (matrix metallopeptidase-2) levels, these are important for tissue integrity and health.

Methods: Animals: Twenty-eight outbred male Sprague Dawley rats. All rats were divided into four groups: Control group (n=7), 100 mg/kg acetaminophen group (n=7), 200 mg/kg acetaminophen group (n=7), 400 mg/kg acetaminophen group (n=7). Biochemical analysis: The tissue homogenates were analyzed by enzyme immunoassay for IGF-1 with assay sensitivity <5 pg/mL and detection range 62.5–4000 pg/mL, MMP2 with assay sensitivity <10 pg/mL and detection range 156–10000 pg/mL. Protein analysis performed manufacturers description of BCA protein Assay kit. Histological investigation: Brain tissue samples were removed and were fixed in 10 % formaldehyde solution for 24–48 hours at room temperature. After fixation, the samples were washed overnight with tap water, dehydrated through a graded series of ethanol, cleared in xylene and further processed and embedded in paraffin. Five µm thick sections were cut using a microtome and stained with haematoxylin and eosin (H&E) and examined under a light microscope. Statistical evaluation: All statistical procedures were performed by SPSS software for Windows, Version 11.0.

Results: Only 400 mg/kg dose of acetaminophen decreased IGF-1 levels in the hippocampus, whereas prefrontal cortex IGF-1 levels did not change. MMP2 levels decreased in hippocampus significantly in 400 mg/kg group. In prefrontal cortex, MMP-2 level decreased in only 400 mg/kg group with compared to 100 mg/kg group. Histologic organisational changes were observed in only hippocampus in the 400 mg/kg acetaminophen group when compared to controls. Prefrontal cortex's histological morphology was found normal.

Conclusion: To our knowledge, this is the first study, which investigated effect of dose depending effects of acetaminophen on prefrontal cortex and hippocampal IGF-1 and MMP2 levels, which are related with tissue integrity and health.

Keywords: Acetaminophen, IGF-1, MMP2, hippocampus, prefrontal cortex

P-081

Effects of overfeeding and caloric restriction on body mass index in zebrafish

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Objective: Brain aging is a natural and multifactorial process related to both intrinsic and extrinsic factors. Caloric-restriction, which is an extrinsic factor, is the only non-genetic intervention to affect the lifespan and health span of an organism. In contrast, obesity is associated with several metabolic and cardiovascular diseases and even premature mortality. Since zebrafish age gradually like humans and share similar organs and tissues, as well as energy and lipid metabolism, it is an appropriate model to investigate the interaction between diet and brain aging. In this study, we aim to investigate the effects of overfeeding and caloric-restriction on the aging process using several markers in the zebrafish brain.

Methods: Zebrafish were maintained and raised in standard conditions. Young (9 months old) male and female wild-type animals were divided into an over-feeding (OF), ad libitum (AL) and a caloric-restriction (CR) group. The feeding regimen lasted for 12 weeks at which time their weights and lengths were measured. Whole brain tissues were isolated from 39 animals and RNAs were extracted for further qPCR (quantitative PCR) experiments. A two-way-ANOVA was applied.

Results: At the end of the 12 weeks, the weight and length of the animals were recorded and used for the calculation of body-mass index (BMI) (g/cm^2). According to the analysis, significant main effects of diet [F (2.41)=71.74, p<0.0005] and gender (F (1.41)=24.77, p<0.0005), along with a significant gender by diet interaction [F (2.41)=18,29, p<0,0005] on BMI were revealed. Consistent with our expectations, the OF group had a larger BMI than AL and CR, which was less than AL. Interestingly, this pattern was driven mainly by females.

Conclusion: Our results demonstrate gender-specific vulnerabilities to dietary manipulations. Ongoing experiments are focusing on the analysis of expression levels of genes related to brain aging in the context of OF and CR. This work was supported by an EMBO Installation Grant. 1-Equal contributions.

Keywords: Overfeeding, caloric-restriction, brain, zebrafish, aging

P-082

Identification of protein interaction network-based drug target candidates for Parkinson's disease

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Objective: The primary objective of this study is to investigate protein interactions that are associated with Parkinson's disease (PD) through Protein-Protein Interaction (PPI) based approaches, with the overall goal of identifying candidate drug targets for PD.

Methods: The transcriptome data used in this study was downloaded from online databases. The data included tissue samples from prefrontal cortex (BA9) by RNA-Seq and proteomic analysis. Transcriptomic data were collected from 29 Parkinson patients, and proteomic data from 12 Parkinson patients. The PPI network used was obtained from the BioGrid database, which included 16.499 proteins and 247.720 interactions. In this study, omics data and PPI network were integrated using various statistical analysis tools and bioinformatic approaches in R language.

Results: Proteins that were significantly affected from the disease and interact with each other were identified. The proteins that are in the identified groups were further checked for their interactions with known drug targets for neurodegenerative diseases. Those proteins were determined as candidate drug targets.

Conclusion: This study made it possible to compare the analyses made using microarray-based transcriptomic data with the results of RNA-Seq method, the next-generation sequencing method. In addition, the results of transcriptomics and proteomic data were compared with each other, and the effects of intracellular post-transcriptional modifications on the PPI network were identified. The computational approach enabled the identification of potential new drug targets for PD. This research was financially supported by TUBITAK (Grant Number: 315S302) and by TÜBA-GEBİP (2015).

Keywords: Genome-scale data, protein-protein interaction, Parkinson's disease, drug target

P-083

Effects of short-term caloric restriction and rapamycin on brain aging in zebrafish *(Danio rerio)*

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Objective: Understanding the mechanisms that underlie brain aging will provide insight into potential therapeutic targets. The only nongenetic intervention that reliably increases life- and healthspan is caloric restriction (CR). CR and its mimetic, rapamycin, act on the Mammalian Target of Rapamycin (mTOR) in the nutrient signaling pathway. In this project, we investigated how various short-term durations of CR affect key-synaptic-proteins and transcripts of genes involved in mTOR pathway in zebrafish brain, and whether rapamycin mimics CR's effects.

Methods: Wild type 53 young (9–11 months) and 53 old (27–33 months) zebrafish, maintained in standard conditions, were used to determine the brain response to CR and rapamycin. There were ad libitum (AL)-fed animals receiving no drug treatment, AL-fed animals with rapamycin treatment, and animals calorically-restricted with an every-other-day feeding approach. 4, 6 and 8 weeks of CR and rapamycin treatment were applied. Following euthanization, body weight and length were measured, brains were used for gene and protein expression analysis, and bodies were preserved for measuring cortisol to investigate whether these interventions cause stress.

Results: Our results demonstrated significant changes in body weight as expected (30% reduction in CR, 30% and 35%

increase in AL and Rapamycin groups respectively, p<0.01). Body length showed no significant difference across groups, and initial analysis on cortisol levels showed no effect of age, treatment/diet, duration on stress. Ongoing analysis of synaptic proteins and genes involved in mTOR pathway indicates alterations in response to CR and rapamycin compared to control group.

Conclusion: CR caused significant weight loss in zebrafish, while rapamycin-treated animals gained weight as expected and both CR and Rapamycin did not affect growth as measured by body length. Preliminary data suggest both CR and rapamycin affect genes of interest and expression levels of key-synaptic-proteins in an expected manner. This research is supported by TUBITAK-1001 program (Project no: 214S236). 1-Equal contribution.

Keywords: Aging, brain, caloric restriction, rapamycin

P-084

Effect of selenium on deiodinase activity in the hippocampus of hypothyroid rats

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Objective: Thyroid hormones are essential for the development of the fetal, postnatal nervous system and the continuation of adult brain functions. In this study, the relationship between learning and memory function disorders and deiodinase enzyme activity in hypothyroidism and the effect of selenium supplementation on this relationship were investigated

Methods: Experiments were performed on 2-month-old adult male Wistar rats. Rats are divided into 4 groups, control (C, n=7), hypothyroid (Ptu, 1 mg/kg/day, n=8), hypothyroid+sodium selenite (Sena, 0.5 mg/kg/day, n=8) and hypothyroid+ seleno-L-methionine (Semet, 0.7 mg/kg/day, n=5). Hypothyroidism was induced in rats by gavage with 6-n-propyl thiouracil (Ptu) for 21 days. Rats were sacrificed under anesthesia to remove their hippocampus. Hippocampal DIO2 and DIO3 protein levels were measured by the western blot method. Plasma free T3 (fT3) and T4 (fT4) levels were measured using a commercial ELISA kit.

Results: Plasma fT4 levels of rats were significantly lower in the Ptu (p=0.009), Sena (p=0.037) and Semet (p=0.05) groups than the control group. Plasma fT3 levels of the rats were significantly lower in the Ptu group than the control group (p=0.032). DIO2 protein levels in Ptu group were significantly higher than the control group. There were no significant difference between Sena, Semet and control group DIO2 levels. The Ptu group DIO3 levels were lower than the control group (p<0.001). Sena and Semet groups did not show any significant difference than the control group.

Conclusion: These findings suggest that selenium enhances the activity of DIO1, which catalyzes the conversion of T4 and T3. The increase in DIO2 enzyme activity in the Ptu group seems to be relieved from the suppressive effect of the thyroid hormone in hypothyroid state. DIO 2 enzyme activities were close to control values in Se supplemented groups. The decrease in the level of the DIO3 enzyme in the Ptu group can be explained by the direct action of the T3 hormone on the DIO3 gene transcription.

Keywords: Hypothyroid, selenium, deiodinase, hippocampus

P-085

Age-related changes on levels of Smurf2 expression in wild-type and knock-down zebrafish brains

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Objective: SMAD-specific E3 ubiquitin-protein-ligase 2 (Smurf2) is a conserved gene across humans, mice, and zebrafish, whose protein is a ligase in the TGF-β signaling pathway. Due to the E3 ubiquitin ligase activity, it is known that Smurf2 has roles in multiple signaling pathways but there are no studies about changes in the protein levels of Smurf2 during brain aging. Previous studies showed that Smurf2 protein levels increase with aging in several tissues and we had found that Smurf2 gene expression increases in the old zebrafish brain. The first aim of this study is to investigate whether Smurf2 protein levels are altered in the aging brain. The second aim is to examine Smurf2 protein levels in a knockdown model.

Methods: Zebrafish were maintained and raised in the standard conditions. Whole brain tissues were isolated from 6, 12, 18, 24, and 30 month-old, male and female zebrafish brains (AB/wild-type). For the second aim, Casper animals were used for cerebroventricular microinjections (CVMI) and whole brain tissues were isolated at 1, 4, 12 hours (hpi) and 1, 2, 3, 4 days post injection (dpi). Proteins from brain tissues were extracted and Western Blot analysis was used to determine differences in Smurf2 expression. Minimally three individual brain lysates in each age group and time-point were loaded in duplicates in every gel. An ANOVA analysis was applied (p<0.05).

Results: Initial results demonstrated that Smurf2 protein levels are not altered with aging (p=0.313) nor gender (p=0.959). However, we expected to observe increased protein levels of Smurf2 in aged brains. Preliminary CVMI experiments demonstrated that the best knockdown efficiency is at 1 dpi (42% decreases) and changes in aging-related markers will be examined in ongoing experiments at 1 dpi.

Conclusion: Taken together, these data suggest there may be post-transcriptional or even post-translational modifications in Smurf2 expression during aging. This work was supported by an EMBO Installation Grant.

Keywords: Aging, zebrafish, brain, knock-down, Smurf2

P-086

Effect of selenium supplementation on impaired learning, memory and neurogenesis by hypothyroidism

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Objective: Neurogenesis is the process of formation of new neurons from neural stem cells and progenitor cells. In our study, how these neurons affected by hypothyroidism and different forms of selenium was investigated with ki-67 immunohistochemical staining method.

Methods: Experiments were carried out on 2 month adult male Wistar Albino rats. Rats are divided into 4 groups,control (C, n=16), hypothyroid [Ptu (1 mg/kg/day), n=16], hypothyroid+ sodium selenite [Sena (0.5 mg/kg/day),n=16] and hypothyroid+ seleno-L-methionine [Semet (0.7 mg/kg/day), n=16]. Hypothyroidisim was induced in rats by gavage with 6-n-Propylthiouracil (Ptu) for 21 days. Spatial learning and memory performance were assessed using the Morris Water Maze (MWM, n=16). Neurogenesis was examined by Ki-67 immunohistochemical staining.

Results: The mean distance to platform values of MVM initial learning were found to be significant with the Day and Trial variables of the Group factor ($p<0.001$). On the 5th day when the memory performance of the groups was evaluated, the Ptu group spent significantly less time on the target quadant than the other groups ($p=0.013$). The mean distance to platform values on the days of reverse learning, Day-Group interaction were found to be significant ($p<0.001$). All hypothyroid groups swam further away to platform than the control group. The number of Ki-67 positive cells in the hippocampal sections of the control and experimental groups of rats decreased significantly in the Ptu ($p=0.002$) and Sena ($p=0.011$) groups compared to the control group.

Conclusion: Adult-onset hypothyroidism has impaired learning performance in the Morris Water Tank Test where initial and reverse learning is performed. Se supplementation did not show any effect on this impairment. On probe day when spatial memory was assessed, the deterioration of memory due to hypothyroidism was corrected with Se supplementation. Hypothyroidism decreased number of progenitor cells in subgranular layer of dentate gyrus. Although Se supplementation (Sena group) increased the number of progenitor cells, this increase was not statistically significant.

Keywords: Hypothroid, neurogenesis, selenium, learning-memory

P-087

The effect of molecular crowding on Parkinson's disease by using a genome-scale metabolic network

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Objective: In this study, genome-scale transcriptome data derived from Parkinson's disease patients are analyzed using bioinformatics methods to estimate significantly changed cellular pathways.

Methods: A brain-specific genome-scale metabolic network model previously developed by our group, called iMS570, is used in the analysis. It is the most comprehensive metabolic network model in the literature. Here, we improved iMS570 by fully compartmenting all the reactions as cytosolic or mitochondrial based on the location of the catalyzing enzymes. The updated network included 799 reactions, a considerable improvement compared to the original model that included 630 reactions. The new metabolic network is called iBrain799. Since the aggregation of the alpha-synuclein protein in Parkinson's disease is a well-known phenomenon, the effect of molecular crowding on the functioning of metabolism was investigated in this study using iBrain799 and disease-specific transcriptome data. A computational approach which allows the prediction of reaction rates, called Flux Balance Analysis, was used for this purpose.

Results: As a result of simulations, it was observed that the activity of energy metabolism decreased as the molecular crowding due to protein accumulation increased.

Conclusion: The results reveal the effect of molecular crowding on Parkinson's disease as a function of the increase in the level of alpha-synuclein. This result is reasonable because if molecular crowding increases, then it becomes difficult for the enzyme to reach the substrates. For this reason, the rate of metabolism decreases. Low metabolism is a common phenomenon in neurodegenerative diseases, as in Parkinson's disease. When considered from this point of view, the use of the molecular crowding constraint in simulations gives realistic results. This research was financially supported by TUBITAK (Grant Number: 315S302) and TÜBA-GEBİP (2015).

Keywords: Metabolic network models, molecular crowding, Parkinson's disease, transcriptome data

P-088

Effect of hexagonal boron nitrides and boric acid on mouse hippocampal cells

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Objective: It is a challenge to treat neurological diseases both due to poor understanding of their molecular basis and difficulty in delivery of therapeutic drugs. As a novel nanomaterial, hexagonal boron nitrides (hBNs), can be used as both a carrier and a therapeutic agent through its degradation products. the effect of hBNs and their possible degradation product, boric acid (BA), on Embryonic Mouse Hippocampal Cell Line (mHippoE-14) is investigated.

Methods: WST-8 assay was performed for the cytotoxicity assessment using a concentration range of 10–1000 µg/mL for both hBNs and BA. hBNs suspension and BA solution were prepared in DMEM. Cell cycle, ROS generation and apoptosis-vs-necrosis analyses were performed with Guava Flow Cytometer (Millipore) after PI, DCFDA and Annexin staining, respectively. The concentrations of 10, 50 and 100 µg/mL of hBNs and BA were selected for all experiments. DNA damage was assessed from Confocal Microscopy images after DAPI staining. All experiments were performed for 1st and 3rd days.

Results: Cytotoxicity assessment of hBNs and BA in the range of 10–1000 µg/mL indicates that hBNs are less toxic than BA. A dose dependent cytotoxicity of both was observed. It is clear that HBNs have no influence on cell cycle while BA has a dose dependent effect causing arrest at G2-M phase. Increased ROS production was observed with increased dose and time for BA while no significant effect was observed with hBNs except 100-µg/mL.

Conclusion: Study clearly indicates that low concentrations of hBNs have almost no cytotoxicity on cells while BA shows dose and time dependent cytotoxicity. Cytotoxicity of BA at increased dose and time indicates that the therapeutic effect of hBNs is not possibly through BA, which is thought to be as hBNs' degradation product. An in-depth study is necessary to understand the mechanisms of behind therapeutic effect of hBNs as reported in the literature especially in cancer treatment.

Keywords: Neuron, cytotoxicity, hexagonal boron nitride, boric acid

P-089

Histopathological and hippocampal changes in the brain of rat pups exposed to electromagnetic fields

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Objective: The aim of the study was to investigate the prenatal effects of 2450 MHz radiofrequency-electromagnetic field (RF-EMF) exposure on development of brain tissue in rat fetus and on histopathological changes in female rats and on hippocampal levels of protein kinases including ERK/ MAPK and p38/38 in male rats.

Methods: 12 Wistar Albino female rats (150–250 g) and 4 Wistar Albino male rats (250–350 g) 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 EMF. 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. Exposing time was 12 hours for 30 days. At the end of 30 days all groups were fertilized. Brain of all fetus and all female rats were took 10% formaldehyde for histopathological evaluation. The hippocampal levels of selected kinases of all male rats were measured using Western Blotting technique.

Results: There were statistical significant difference between the control group and exposure groups in pERK level ($p<0.05$).But there were not statistical significant difference between the control group and exposure groups in ERK, p38 and p-P38 levels.The histological appearance of the brain tissue of the control groups was normal. Females and fetuses exposed to EMF had irregular cortex-cellular placement and vascular dilatation in the 1st and 2nd groups compared to the control.

Conclusion: Western blot analysis confirmed that the expression of pERK was significantly increased after EMF exposed in exposure rats, and thus can activated the ERK pathway which affected the function of learning and memory in rats. EMF can causes damage to both the fetus and the adult brain.

Acknowledgments:This work was supported by the Erciyes University-The Scientific Research Projects of Turkey (ERUBAP); Project number: TCD-2017-7275.

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

P-090

Possible therapeutic roles of diet-regulated transcription factor Dp1 expression in aging

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Objective: This study was conducted to search for a reliable therapeutic approach for reversing neurobiological changes during healthy brain aging. Here the effects and potential mimics of dietary restriction (DR) were studied to alleviate the neurobiological hallmarks of brain aging.

Methods: We examined gene expression differences following a 4-week DR using microarray analysis in the brains of 6 aged

male zebrafish, which revealed 526 differentially-expressed genes. Of those, 23 were selected and validated using qPCR in 12 aged fish in order to test Ad-libitum (AL)-fed vs 1-2-4-10 weeks of DR. Finally, we continued with 4 genes related to cell cycle regulation; TFDP1 (downregulated with DR), and CCNB2, CHEK2 and WEE2 (upregulated with DR). To mimic the DR effect, we used morpholino oligos (MO) for TFDP1 to prevent translation, and for the others we gave their in vitro transcribed mRNAs aiming to observe the effect of diet on downstream genes and aging markers. The injections were performed for both embryos and adults. Following TFDP1 MO injections, the downstream targets of TFDP1, i.e. CCNA2, CCNE1, CDK1, MYCA, RRM1, TP53, TYMS, were examined further by measuring their relative expression changes with regard to their Actin controls using q-PCR.

Results: None of the 7 downstream gene expression levels differed significantly in adult animals following TFDP1 MO administrations at 3dpi. However, following the embryo injections, results demonstrated that for genes CDK, TP53 and TYMS there were significant changes in the expression levels as compared to their negative controls. Experiments for mRNA injections are currently being performed.

Conclusion: Downregulating TFDP1 significantly affected genes CDK, TP53 and TYMS, which suggests these genes may act through a protective mechanism against brain aging that will be investigated further in accelerated and decelerated brain aging models. This work was supported by EMBO Installation Grant to Michelle Adams.

Keywords: Zebrafish, brain, aging, dietary restriction

P-091

Action potential comparison in ACD and conventional CA1 and CA3 pyramidal neuron models

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Objective: Studies in recent years showed the existence of a different structure in the pyramidal cells of hippocampal CA1 and CA3 areas in addition to the ones in prefrontal cortex. In significant amount of the pyramidal cells (50% in CA1, 30% in CA3 hippocampal pyramidal neurons), the axon stems from the basal dendrite connected to the soma instead of the conventional axon-soma-dendrite formation. Neither the reason behind this differentiation nor the circumstances under which this phenomenon occurs is discovered. In this study, CA1 and CA3 pyramidal neurons with axon carrying dendrites and with regular neurites are modeled for understanding the purposes of this differentiation in the phenomena.

Methods: The CA1 pyramidal neurons with axon carrying dendrites, CA1 pyramidal neurons with conventional structure, CA3 pyramidal neurons with axon carrying dendrites and CA3 pyramidal neurons with conventional structure are modeled with NEURON simulation program. Action potential characteristics, propagation velocities and propagation trends are examined in detail with MATLAB program.

Results: After the simulation, examination and comparison of the simulated acd-CA1, nonacd-CA1, acd-CA3 and nonacd-CA3 pyramidal neurons are completed and it is observed clearly that in the CA1 and CA3 pyramidal neurons with axon carrying dendrites, action potentials are created and propagated faster, while attenuation of the action potential from axon initial segment to axon terminal is decreased.

Conclusion: The functional properties of pyramidal neurons are observed by simulating single cell neurons. In order to gain more insight about the clustering and soma-dendrite formation in specific areas of CA1 and CA3 pyramidal cells in hippocampal region, network modeling simulations by using NEURON program is being studied.

Keywords: Axon carrying dendrite, pyramidal neuron, CA1, CA3

P-092

Endoplasmic reticulum stress in the pathology of Kufor Rakeb syndrome

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Objective: Kufor Rakeb syndrome is a rare neurodegenerative disorder characterized by spasticity, dementia and supranuclear gaze palsy. Due to overlapping symptoms of Hereditary Spastic Paraplegia, Ataxia and Parkinson, the clinical diagnosis of the disease is very difficult without genetic analysis. Although the disease-causing ATP13A2 mutation is thought to trigger neural cell death through ER stress, underlying molecular mechanism has not been elucidated. In this study, it was aimed to investigate the effecst of de novo mutations of ATP13A gene in the disease pathology in a family associated with Kufor Rakeb syndrome based on the mutations.

Methods: From DNA samples of siblings, who were prediagnosed as Ataxia, and of healty parents, whole exome sequencing (WES) was performed to detect mutations responsible for the disease. Identified mutations were confirmed by Sanger sequencing from genomic DNA of carrier/healthy parents, carrier/healthy sister and patients. The truncated protein caused by mutations in ATP13A2 gene was examined by Western Blot. Moreover, immunocytochemistry analysis was performed to examine intracellular localization of the protein. The effects of ATP13A2 mutations on ER stress were examined by Western Blot.

Results: By WES analysis de novo pathologic variants were identified in 15th exon of ATP13A2 gene. According to bioin-

formatical analyzes, mutations cause premature stop codon in ATP13A2 gene that lead to truncated protein form by losing its transmembrane domains, and this finding was confirmed by Western Blot. In immunocytochemistry analysis, the mutant ATP13A2 protein form was observed to be concentrated around the endoplasmic reticulum. Western blot analysis revealed that Grp78 and PDI levels remained unchanged while GAPDH level increased in patient cells.

Conclusion: The de novo mutations in ATP13A2 gene causing the truncated form of the protein lead to the accumulation of the protein in the endoplasmic reticulum and cause increased GAPDH expression in order to maintain iron homeostasis. This study is supported by İTÜ-BAP(TGA-2017-40943).

Keywords: Kufor Rakeb syndrome, ATP13A2, ER stress

P-093

The role of uutophagy in autistic mouse model

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Objective: Autism is a subgroup of autism spectrum disorders (ASD), classified as a heterogeneous neurodevelopmental disorder occurring within the first three years of life. Autistic brain studies showed that hippocampus have abnormal volume and shape. Autophagy includes the disintegration of major cytosolic components in the lysosome. The link between autophagy and neuropsychiatric diseases is being investigated. LC3 is the major predictor of cellular autophagy. Beclin protein is thought to be an autophagic marker with ongoing studies. Cc2d1a is one of the new candidate genes for autism and acts as a transcription factor in the central nervous system. We investigated the role of neuronal autophagy in the hippocampal tissues of autistic Cc2d1a knock-out mice at the expression levels of LC3 and Beclin proteins.

Methods: In our study, Cc2d1a knock-out and normal Balb-C mice were compared and followed for three generations. Five male and female mice from each group were subjected to open field behavior test at two months of age and then hippocampal tissues were removed by euthanasia with cervical dislocation. Expression levels of Beclin and LC3 proteins were determined by Western Blot analysis.

Results: LC3 expression significantly increased in female mouse hippocampus when compared to controls, while significant reductions were observed in LC3 expression in male mice. Beclin expression were significantly reduced in males and females compared to controls.

Conclusion: Autophagy-inadequacy was observed in male mice when excessive autophagy was observed in female mice in the view of LC3 protein, the main indicator of autophagy. Since Cc2d1a is a new candidate gene for autism, this study provides evidence that CC2D1A acts as a novel biological pathway in autophagy. We suggest that autism is caused by both autophagy-inadequacy and excessive-autophagy. In terms of genders, we suggest that autophagy is regulated differently than normal individuals. This study was supported by Erciyes University Scientific Researches Unit (TYL-2016- 6347).

Keywords: Autism, autophagy, hippocampus, Cc2d1a gene

P-094

Investigation of adenosine dependent neuroplasticity in ventilatory acclimatization to hypoxia

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Objective: Intermittent hypoxia elicits long-term facilitation (LTF) known as a persistent augmentation of respiratory motor output and ventilatory acclimatization to hypoxia (VAH) occurs during sustained hypoxia (SH) due to augmentation of hypoxic ventilatory response that both mechanisms cause ventilatory neural plasticity. The pathways leading to LTF activated by serotonin (Gq) and adenosine (Gs) dependent. We tested the hypothesis that adenozin 2A receptor activation play a main role in constitution of VAH.

Methods: In our study, 5 test groups were used. The normoxic control group (N=3) was housed in a normal room environment and daily SF (1 mg/kg) was administered.The sustained hypoxia group was exposed to 10% O2 in normobaric room for one week. MSX-3 (1 mg/kg, N=3), ketanserin (1 mg/kg, N=3) and CGS21680 (100 µg/kg, N=3) once daily throughout hypoxia and normoxia.VI, fR and Vt measurements were performed with whole body plethysmography. Spinal cord and brainstem tissues was collected perfused rats and 30 µ transverse sections were taken. Quantitative determination of 5-HT2A and A2A receptors was performed by immunofluorescence staining and $p<0.05$ significance level was accepted.

Results: Chronic hypoxia (CH) increases ventilation in normoxia and hypoxia vs. control. Gs pathway block with systemic MSX-3 during or after CH did not significantly change the effects of CH. VI and fR tended to increase with Gs block after CH ($p<0.05$, 0.01 or 0.001 vs. control, Bonferroni after 2-way ANOVA, n=3). Gq pathway block with systemic ketanserin during or after CH did not significantly change the effects of CH ($p<0.05$, vs. control, Bonferroni after 2-way ANOVA, n=3). A2 Aagonist (CGS21680, 100 µg/Kgi.p.) before CH had no significant effect on ventilation in awake rats but tended to increase VT.

Conclusion: Gs and Gq signaling do not interact during or after VAH like they do in LTF after intermittent hypoxia. Evidence for Gs and Gq dependent plasticity is less robust in awake unrestrained vs. anesthetized or sleeping state rat preparations.

Keywords: Adenosine, hypoxia, neuroplasticity, serotonine

P-095

Effects of enriched environment on miR-132 levels in different brain tissues

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Objective: Various studies show that physically and socially enriched environment conditions have positive effects on memory and learning. It is known that the volume and density levels of dendritic spines also change depending on these functions. In this study rats were housed in enriched environment conditions in various time intervals, and aimed to observe changes in the levels of miR-132, a microRNA that controls the dynamic structure of the dendritic spines, in different brain areas.

Methods: Adult female Sprague-Dawley rats (n=21) are divided into 3 groups: control group (n=7), 7 days enriched environment group (n=7) and 14 days enriched environment group (n=7). The control group was housed in standard rat cages while others were in specially designed enriched environment cages for 7 or 14 days. The levels of miR-132 in the left frontal lobe and hippocampus were determined by Real-Time PCR and statistical differences were calculated using one-way ANOVA test.

Results: Compared to control group, the values of miR-132 in the frontal lobe and hippocampus were elevated in animals housed in enriched environment for 7 and 14 days. Statistically significant results were obtained from day 14 data.

Conclusion: These results show that miR-132 values in the frontal lobe and hippocampus may be affected by enriched environment conditions. Previous studies show that dendritic spine volume increase in the same rate with miR-132 level. Therefore, animals kept in enriched environment conditions for 14 days in this study also may have increased synaptic density in the frontal lobe and hippocampus which positively effects cognitive functions. Further studies needed to support our data. This study was supported by Eskişehir Osmangazi University Scientific Research Project Committee with project support number 201611003.

Keywords: Enriched environment, miR-132, frontal lobe, hippocampus, qPCR

P-096

Investigation of the expressions of POGZ and PTEN genes targeted by microRNAs in autism

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Objective: Autism Spectrum Disorder (ASD); it is a group of neuropsychiatric diseases that start in childhood, lasting lifelong and have no effective treatment yet. Autism is a common subtype of ASD. It has repetitive behaviors, lack of social interaction and communication. The prevalence of autism is increasing day by day. The etiology of autism, which is extremely complex with its genetic background and clinical features, is not yet known. Genetic and environmental factors have been shown to play a basic role in the development of the disease. MicroRNAs (miRNAs) are regulators of gene expression in transcriptional and post-transcriptional levels. Abnormalities in the translational control of multiple miRNA targets directed by each miRNA may lead to phenotype differences observed in ASDs. The aim of this study is to determine the expression of the genes POGZ and PTEN that are targeted to miRNAs and shown as candidate genes in autism.

Methods: RNA was isolated from 50 patients with ASD and 50 healthy controls by Trizol method. The obtained RNAs were converted into cDNA and the expression of the genes (POGZ and PTEN) which were targeted by miRNAs (miR-3613-3p, miR-19a-3p) and shown as a candidate gene in autism were determined by Real-Time PCR method.

Results: The POGZ gene was found to be more exaggerated in patients than in controls, and expression of this gene was found to be significant in males (p=0.0002). PTEN gene expression was found to be less in patients than controls and statistically insignificant (p=0.7513).

Conclusion: As a result, we recommend that investigate the number of other possible candidate genes, which may be the target of miRNAs in a larger number of patients, and compare the results with different clinical manifestations. This study was supported by Erciyes University Scientific Research Projects Coordination Unit (TYL-2017-5789).

Keywords: Autism, autism spectrum disorder, miRNA, POGZ, PTEN

P-097

Differences of GG4 motifs for the mu- and delta-opioid receptors

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Objective: G-Protein-Coupled-Receptors (GPCR) have roles on various physiological functions and important role on the actions of medicines. GPCR bind to their ligands and also have many interactions with the cellular structures like Gproteins, beta-arrestins, ion channels and enzymes. The role of GG4 motifs was recently reported for the interactions of GPCR and these macromolecules. Opioid receptors are known to have effects on analgesia, dependence and smooth muscle contractions. In addition to the similar actoins of delta- and mu-opioid

receptors, there are some differences as well. Similarites in terms of GG4 motifs of the delta- and mu-opioid receptors are investigated with the hypothesis of the presence of similarity of GG4 motifs.

Methods: The information for the structures of delta- and mu-opioid receptors for human, rat and mouse were downloaded from Unirot web servers, extracted and processed using GNU/Linux operating system and Linux bash commands. Data were plotted using R language.

Results: The presence of GG4 motifs on delta-opioid receptors was observed, being one GG4 motifs for human and mouse but 2 GG4 motifs for the rat delta-opioid receptor. On the other hand there was no GG4 motif for mu-opioid receptors.

Conclusion: Mu- and delta-opioid receptors are known to exert remarkeble opioid actions including analgesia, but differences were also reported. These receptors show heteromerization by their interaction and also heteromerize by TRP channels and other receptors. GG4 motifs are reported to have important role on the protein-protein interctions and heterodimerization. Presence of GG4 motif only on delta- but not on mu-opioid receptor was shown in this study for the first time and and this is an important factor for the functional differences which may be observed in the future studies.

Keywords: Bioinformatics, GG4 motif, opioid receptor

P-098

Bioinformatical investigation of human rat and mouse TRPV1 ion channels

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Objective: The role of TRP ion channels on the influx of sodium and calcium ions which have at least 27 members are shown in humans. The main actions of TRP channels are on inflammation and analgesia. Mice and rats are used as experimental animals in analgesic and anti-inflammatory investigations which their results are applied for humans. The hypothesis of this study was the presence of GG4 (GxxxG) motif on the TRPV1 and have species specific variation which was investigated using bioinformatical methods.

Methods: The information for the structure of TRPV1 ion channels were downloaded from Unirot web servers, extracted and processed using GNU/Linux operating system and ClustalW programme.

Results: TRPV1 ion channels of human rat and mouse were found to differ in terms of GG4 motifs. Presence of 2 GG4 motifs for the human TRPV1, whereas 3 GG4 motifs for rat and mouse TRPV1 ion channels were shown in this study.

Conclusion: In order to investigate the actions of drugs, in addition to in vitro and in vivo methods, in silico methods are also used. In the present study, differences in the GG4 motifs of human rat and mouse were found using bioinformatical methods. The role and importance of GG4 motif was previously reported for the protein-protein interactions. Since the difference between the number of GG4 motifs of human and rodent TRPV1 ion channels were shown by the present study, it was concluded that results of investigations obtained from mice and rats where TRPV1 ion channel is involed such as pain and inflammation, may be more or less different for humans.

Keywords: Bioinformatics, GG4 motif, TRPV1 ion channel

P-099

The effect of mesenchymal stem cell on the damage of fetal nerve system caused by valproate usage

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Objective: Valproic acid, widely used in the treatment of epilepsy, causes various congenital malformations including fetal neural tube defects when used in pregnancy and neuronal damage to the central nervous system. It was aimed to demonstrate the efficacy of bone marrow-derived mesenchymal stem cells (Bm-MSC) on the central nervous system damage induced by the use of VPA in pregnancy.

Methods: A total of 24 Wistar albino female rats were divided into three groups: Control (n=8), VPA (n=8) and VPA+MSC (n = 8). Rats in the VPA and VPA+MSC groups were injected with 400 mg / 4 ml of VPA on day 9 of their pregnancy. The rats in the VPA+MSC group were also given MSC on the 9th day of their pregnancy and also in the tail vein. All rats in all groups were sacrificed on day 21 of their pregnancy. Brain and spinal cord of fetuses were taken. Brain and spinal cord tissues were analyzed by Hematoxylin&Eosin, Toluidine blue staining with histochemical methods and immunohistochemical methods with S100-beta primer antibody.

Results: In all groups, brain tissue was examined at the level of the bulbus olfactorus. In the VPA group, mesenchymal tissue was observed and no nerve tissue was found. In the VPA+MSC group proliferation and few neurons were found in mesenchymal tissue cells. In the VPA group, deformation in the general structure of the spinal cord, decrease in neuron density, and increase in the number of degenerated neurons were detected. In the VPA+MSC group, it was found that the general structure of the spinal cord tissue showed very close histological appearance to the control group and degenerative appearance decreased significantly.

Conclusion: Bone marrow-derived mesenchymal stem cell treatment has shown that VPA used during pregnancy

reduces/prevents damage to the fetal central nervous system.The statistical significance in Control, VPA and VPA+MSC groupings were; p<0.05, p<0.01, p<0.001.

Keywords: Epilepsy, valproic acid, fetus, central nervous system, bone marrow derived mesenchymal stem cells

P-100

An investigation on alteration of intracellular pH by sibutramine via confocal imaging

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Objective: With high prevalance among obese patients, binge-eating disorder is a health problem with no radical treatment, in this context effective treatments must be developed. Sibutramine, an antiobesity drug with serotonin/norepinephrine reuptake inhibiton activity, has been shown to be efficacious in depression, which is a comorbidity to the syndrome, and weight loss in obese patients with binge-eating disorder. However, sibutramine has been banned due to its cardiovascular toxicity. Comprehension of the mechanisms underlying cardiotoxicity of sibutramine will provide preclinical data to develop new agents with similar efficacy and a safer cardiovascular side effect profile. In this study it is aimed to investigate the effects of sibutramine on intracellular pH of rat cardiomyocytes.

Methods: Cardiomyocytes were isolated from hearts of Wistar rats by digestion with collagenase and obtaining Ca^{2+} tolerance by exposing to Ca^{2+} in a graded manner. Effects of 10^{-5} and 10^{-6}M sibutramine HCl incubation for 1 hour on intracellular pH regulations in cardiomyoctes were investigated by florescence based method. Cells were loaded with 10µmol/L pH sensitive SNARF-2AM dye for 20 minutes. The pH dye was excited by 514 nm with argon laser (leica TCS SP5) and fluorescence emission was detected at 580 and 690 nm. Intracellular pH was estimated from the ratio of emission intensities at these 2 wavelengths. Unpaired t test was used for statistical analysis.

Results: Intracellular pH in control group was 0.512±0.006 (n=78). Sibutramine loading sinificantly increased intracellular pH values to 0.543±0.015 (n=29, p<0.05) for 10^{-6}M and to 0.597±0.017 (n=45, p<0.0001) for 10^{-5}M.

Conclusion: Variations in intracellular pH level has been proposed to involve in impaired cellular functions in cardiomyocytes, leading physiological changes such as altered contractility. Sibutramine derivatives can be evaluated in drug development studies for the treatment of binge-eating disorder and by particularly examining the effect on cardiomyocyte intracellular pH, studies may focus on derivatives which have safer cardiotoxicological profile concerning this mechanism.

Keywords: Confocal microscopy, sibutramine, SNARF-2-AM

P-101

Identification of multiple sclerosis-related pathways by integration of genomic and proteomic data

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Objective: Multiple sclerosis (MS) is a heterogeneous disease of the central nervous system with complex inheritance pattern and pathophysiology; thus, understanding the underlying mechanisms require combinatorial approaches using different types of molecular data. Here, we aimed to explore MS-related pathways in a Turkish cohort by combining genomic and proteomic data of the same patient group.

Methods: Cerebrospinal fluid proteome data were previously obtained through 2D-gel electrophoresis and mass spectrophotometry using 179 MS patients and 42 non-MS controls, revealing 151 differentially expressed proteins in MS and in different clinical MS subtypes. Among the study group, 11 unrelated MS patients and 60 independent healthy controls were subjected to single nucleotide polymorphism (SNP) genotyping (Illumina, 300K), and genome-wide associations were assessed. Pathway enrichment analyses of differentially expressed proteins and MS-associated SNPs were conducted using the functional enrichment tool PANOGA. The resulting enriched pathways were merged, and clustering was performed to establish representative pathways.

Results: Thirty-three representative pathways were found with p-values ranging from 6.96E-30 to 1.04E-11. Among those, nine pathways were detected in both analyses; complement and coagulation cascade being the most significantly associated pathway (hsa04610, p=6.96E-30). Others known to be involved in nervous and immune systems included adherens junctions (hsa04520, 6.64E-25), pathogenic Escherichia coli infection (hsa05130, 9.03E-14), and prion diseases (hsa05020, P=5.13E-13).

Conclusion: We identified possibly altered pathways in a limited Turkish MS cohort, confirming some previously implicated mechanisms and highlighting a number of others. The methodology we used seems to be beneficial for reducing false negative and positive results of genome-wide SNP associations by integrating genomic and proteomic data of the same patient group; therefore, translating the findings into a biological context more efficiently than the conventional methods.

Keywords: Bioinformatics, disease pathways, genomics, multiple sclerosis, proteomics

P-102

Development of imidazolone based small molecule as chemotherapeutic agent for cell cycle inhibition

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Objective: Small molecule structured agents provide important and controllable approaches for treatment of central nervous system tumors. Their capability to easily penetrate to CNS, provide preferred therapy approach to CNS tumors. Study aims to demonstrate potential of imidazolone based small molecule in chemotherapy which led cancer cells to undergo apoptosis by stopping them in cell division.

Methods: Cytotoxic effect of different structured agents, were analyzed at different concentrations. 19D's "cell cycle arrest" potential were proven at different concentrations to show characteristic of drug which specifically arrest cells. Flow cytometric analysis of cell cycle with propidium iodide was performed to six different cell lines; HUVEC, MCF-7, HCT, HEK, RFL6 and U87-MG. DNA histograms of each cell lines were figured at below and above active concentration of 19D molecule for 24 and 48-hour treatments. Alternations of cellular and nuclear morphologies were visualized via hematoxylin-eosin staining and DAPI immunofluorescence imaging. Cell proliferation indexes and viabilities of agent induced cells were analyzed with MTT assay.

Results: Flow cytometric results show that agent cause G2+M arrest in all cell lines and results no further progress in cell division. Immunohistochemical and immunofluorescence staining shows that nuclear disintegration morphologies; agent cause multi lobed nucleus and multi-nucleus formations. MTT assay also provide important finding; agent activate possible apoptosis pathway in a manner of cells' division time. This finding suggest that, fast dividing cells get arrested earlier and stop their division, on the other hand slow dividing cells were arrested afterwards.

Conclusion: There are many G2+M arrest causing agents currently using in chemotherapy. Their action mechanism is achieved through specifically stopping proliferation of frequently dividing cells. In this study, a new imidazolone based agent is found which specifically arrest cells and have great potential in chemotherapy. For further studies, we aim to find out specifically which molecules play role to cause this significant phenomenon in cells.

Keywords: Chemotherapeutic, cell cycle inhibitor, brain tumors

P-103

The antiepileptic effect of exenatide in penicillin induced epilepsy model in rats

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Objective: Epilepsy, resulting in hyperexcitability and hypersynchronization of neurons in the brain is a neurological condition characterized by spontaneous recurrent seizures. Exenatide is a glucagon-like peptide -1 receptor agonist. The aim of this study is to investigate the effect of exenatide on epileptiform activity induced by penicillin.

Methods: Thirty two male Wistar Albino male rats, divided into 4 groups, were used in the study. Intracortical penicillin injection was applied to create epileptic seizure. Only penicillin G (500 IU) was administered to the animals in the control group. Exenatide was administered at doses of 50, 100,200 µg/kg intraperitoneally 30 minutes before the penicillin injection to determine the effective dose of exenatide. Electrocorticography recordings taken for three hours were recorded online with the PowerLab data acquisition system. Comparisons between groups were made using the Post Hoc Bonferroni test.

Results: The 50 and 100 µg/kg doses of exenatide did not cause a significant difference in spike frequency over 180 minutes compared to the control group ($p>0.05$). In the 200 Ìg/kg exenatide group, a significant decrease in spike frequency was observed starting from the 10th minute; spike frequency decreased significantly between 10–20, 60–120 and 140–150 minutes after penicillin injection ($p<0.05$). The mean spike frequency of epileptiform activity in rats given 200 µg/kg exenatide was 55.23±8.55 spikes/min between 10–20 minutes and 136.57±15.60 spikes/min in the control group rats.

Conclusion: The electrophysiological findings obtained in this study indicates that exenatide has anticonvulsant effect in the experimental acute epilepsy model induced by intracortical penicillin injection. This study was supported by project from Ondokuz Mayıs University (PYO.TIP.1904.17.009).

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

P-104

Antioxidant and neuroprotective effects of dexpanthenol in traumatic brain injury-induced rats

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Objective: Traumatic brain injury (TBI) is associated with high mortality and morbidity. Trauma-induced primary damage is followed by apoptosis, lipid peroxidation and oxidative stress that lead to secondary damage, causing exacerbation of TBI. In various inflammation models, dexpanthenol was shown to protect tissues against oxidative damage. It was aimed to investigate possible antioxidant and neuroprotective effects of dexpanthenol in TBI model.

Methods: Wistar albino male rats were randomly assigned to control (n = 8), TBI+dexpanthenol (500 mg/kg; n = 10) and TBI+vehicle (n = 10) groups. TBI was performed under anesthesia (ketamine+xylazine) by dropping a 300 g weight from 70-cm height on the skull of rats, which were injected intraperitoneally with vehicle or dexpanthenol immediately after trauma. At 24th h of trauma, rats were decapitated. Malondialdehyde (MDA) -indicative of lipid peroxidation-, myeloperoxidase (MPO) -marker of neutrophil infiltration-, apoptosis-marker caspase-3, antioxidant superoxide dismutase (SOD) levels and catalase (CAT) activities and levels of luminol- and lucigenin-mediated chemiluminescence (CL), -indicating presence of reactive oxygen species- were measured in brain tissues. Following transcardiac parafolmadehyde perfusion, histopathological damage was graded on hematoxylin-eosin-stained brain tissues. The data was evaluated by one-way ANOVA.

Results: In the vehicle-treated TBI group, MPO level, caspase-3 activity and luminol-lucigenin CL levels were elevated ($p<0.05$-0.001), while in the dexpanthenol-treated TBI group these increases were suppressed ($p<0.05$-$0,001$) and MDA levels were decreased ($p<0.05$). Decreased SOD and CAT activities ($p<0.01$) in the vehicle-treated TBI group were increased above control levels in the dexpanthenol-treated TBI group ($p<0.05$-0.001). Neuronal damage observed microscopically in the cortices of TBI was relatively less in the dexpanthenol-treated group.

Conclusion: Dexpanthenol reduced oxidative damage, suppressed apoptosis by stimulating antioxidant systems and thereby alleviated brain damage caused by TBI. Further experimental and clinical investigations are needed to confirm that dexpanthenol can be administered in the early stages of TBI.

Keywords: Diffuse brain injury, neuroprotection, provitamin B5

P-105

An animal model for interaction between epilepsy and Parkinson's disease

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Objective: Although there is clinical evidence showing an interaction between epilepsy and Parkinson's disease, the mechanism underlying this interaction has not yet been identified. The 6-hydroxydopamine (6-OHDA) injections to the medial forebrain bundle provide a highly useful model of Parkinson's disease leading to a complete lesion of the nigrostriatal pathway.The interaction between epilepsy and Parkinson's disease was investigated in 6-OHDA injected genetic absence epilepsy rats from Strasbourg (GAERS) that is a well-defined animal model of absence epilepsy.

Methods: In the experiments, 3-4 months old male Wistar rats and GAERS were used. Parkinson´s disease was modelled by the administration of 6-OHDA into the medial forebrain bundle of rats. Wistar-Parkinson and GAERS-Parkinson groups received a unilateral 6-OHDA injection (8 µg) to the right medial forebrain bundle. In Wistar-control and GAERS-control groups, cannula was inserted to the medial forebrain bundle region without any injection. At 21st day after injection, apomorphine induced rotational behavior test was made. After behavioral test, animals were deeply anesthetized and perfused.The brains were sectioned in the coronal plane. The sections were treated with mouse anti-TH antibody and were analyzed with a computer based programme. The results were expressed as "mean± S.E.M."

Results: The optical densities of the TH-immunoreactive fibers in the striatum were measured. TH-immunoreactivity in the striatum was decreased ipsilaterally in Wistar-Parkinson and GAERS-Parkinson groups significantly ($p<0.005$). In the rotation behavior test, no rotation was observed in control groups. Wistar-Parkinson animals displayed 5.7+1.1 full body turns/ min rotational asymmetry in apomorphine induced rotation test (over 30 min), whereas in the GAERS-Parkinson group, it was 8.4+2.9 full body turns/ min. The differences in rotational asymmetry between groups was not significance.

Conclusion: The administration of 6-OHDA into the medial forebrain bundle causes the degeneration of nigrostriatal dopamine system in both Wistar and GAERS. This model is a useful tool to investigate the interaction between epilepsy and Parkinson disease.

Keywords: Epilepsy, GAERS, Parkinson's disease, 6-OHDA

P-106

Effect of lacosamide on absence seizure development in genetic absence epilepsy rat model

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Objective: Absence epilepsy is characterized by generalized non-convulsive seizures starting in childhood or early adolescence. Genetic Absence Epilepsy Rats from Strasbourg (GAERS) is one of the rats model of absence epilepsy. In GAERS immature spike-and-wave discharges (SWDs) first appear in most of the animals at around the 30th postnatal (PN30) day. The number of GAERS with SWDs increases grad-

ually with age until at 4 months all of the animals show a mature pattern of SWD. Lacosamide (LCM) is an antiepileptic drug effective on generalized seizures. LCM acts by selectively affecting the slow inactivation of voltage-gated sodium channels. In this study, we aimed to investigate the effect of LCM absence seizures on developmental process.

Methods: In our study, GAERS male rats were administered chronically 10 mg/kg/day LCM or equivalent volume of saline (SF) until PN60 for 40 days starting from PN20. Animals were implanted with cortical screw electrodes by stereotaxic surgery under ketamine/xylazine anesthesia for EEG recording at PN 53 days. Following surgery, the rats allowed to recover for 1 week. EEG recording was taken from animals in PN60 days. The effect of LCM on absence seizures over total duration, number and mean duration was analyzed.

Results: As a result of the EEG analyzes, it was observed that the total number and duration of SWDs in LCM-treated GAERS rats was significantly lower than SF in the same conditions. However, there was no difference between the two groups over the mean SWD duration.

Conclusion: Preliminary results of our study suggest that LCM administered at a dose of 10 mg/kg/day may be effective on the development of absence seizures in GAERS rats. We are still working on how long this activity lasts after the latest administration.

Keywords: Absence epilepsy, lacosamide, GAERS, spike-and-wave discharges, sodium channel

P-107

Selenium supplementation recovered sciatic nerve function in menopause and nerve injury in menopause

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Objective: Menopause, which is linked with some disorders such as depression, headache, neuropathy and Alzheimer's disease, affects the central nervous system by altering the antioxidant-free radical balance. This study was addressed to investigate the effects of menopause and peripheral nerve injury in menopause on the functions of sciatic nerve and to elucidate the role of low and high dose selenium treatment on the recovery of these effects.

Methods: Wistar-albino female rats were divided into seven groups as control, ovariectomized (OVX), low dose (1 µmol/kg) selenium treated OVX, high dose (5 µmol/ kg) selenium treated OVX, sciatic nerve injury+OVX, low dose selenium treated nerve injury+OVX, high dose selenium treated nerve injury+OVX. After ovariectomy, rats were maintained for 5 months for the development of long-term menopause model. Afterwards, sciatic nerves were injured, low or high dose selenium was administered for 5 weeks. Sciatic functional index (SFI) was measured after ovariectomy at regular intervals throughout the study. At the end of the experiments, sciatic nerve conduction velocities (NCVs), serum estradiol and tissue TBARS levels together with tissue catalase activity were determined.

Results: Ovariectomy-induced menopause resulted in the decrease of NCVs ($p<0.001$) and variations in SFI values revealing neurodegeneration. Moreover, sciatic nerve injury in menopause have enhanced the effects of menopause on NCVs and SFI values. Selenium treatment, especially at low dose, led to an increase in NCVs and a recovery of menopause-induced alterations in functions of sciatic nerves monitored by SFI. Moreover, selenium treatment resulted in an increase in serum estradiol levels in ovariectomized rats.

Conclusion: Menopause leads to neurodegeneration in peripheral nervous system. Selenium is an important trace element which can be beneficial in the prevention of menopause-induced neurodegeneration and in the treatment of nerve injuries in menopause. This study was funded by Scientific Research Council of Adnan Menderes University (TPF-15030).

Keywords: Menopause, sciatic nerve injury, nerve conduction velocity, sciatic functional index, selenium

P-108

Whole exome sequencing for candidate gene search in patients with Clippers syndrome

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Objective: Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (Clippers) has been reported recently as a rare inflammatory central nervous system (CNS) disorder. We describe a 20 year old female who has mild speech difficulty, dizziness and gait ataxia with characteristic lesions of cerebellum and pons on magnetic resonance imaging. Her sister, who developed a similar neurologic disease, died at 24 years due to infectious complications. To our knowledge, this is the first familial form of Clippers syndrome in the literature. We also analyzed a patient from a distinct family with similar characteristic symptoms of Clippers. In this study, we analyzed and compared exome data of the two patients to reveal candidate genes for Clippers.

Methods: Exome sequencing was performed for the two patients and candidate variants were selected according to allele

frequencies (MAF<0.001), homozygosity, and phenotypical relevance.

Results: The strongest candidate variant was p.Thr199Met (rs201490782) in LGALS9B gene which was detected in the first patient with family history. Additionally, IFFO2, RNPEPL1, XKR5, LRRC10B, GRK2, UBE2O were selected as other candidate genes due to relevance with disease phenotype. After, we evaluated five possible variants on the MTRF1, TNFRSF18 (rs371599555), TMEM191C, H3F3C (rs150875482), EGFL6 (rs200143589) genes from the second patient. Substantially, novel variant c.806C>T, p.Ser269Phe in MTRF1 gene was predicted as pathogenic and possibly damaging to protein function. Positions of these candidate variants are highly conserved in different species.

Conclusion: Here we report the first exome sequencing data for patients with Clippers in order to identify candidate genes. Our preliminary results suggest that those variants may be risk factors for neuroinflammation associated with Clippers phenotype. All susceptible variants will be validated with Sanger sequencing for our further analysis.

Keywords: Clippers, whole exome sequencing, candidate variants

P-109

Comparison of surgical treatment options in neuroma-in- continuity treatment in rats

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Objective: Peripheral nerve damage can result in a variety of injuries and may result in physical and socioeconomic impediment that affect life. Current treatment options include neuroma in-continuity (NIC) treatment. In our study, we aimed to evaluate the efficiency of primary restoration versus repair with vein graft on nerve regeneration in NIC treatment by using functional tests and to investigate whether it can be used safely in peripheral nerve surgery treatment.

Methods: In Sprague-Dawley adult male rats, crush injury model was used to create nerve damage and rats were divided into two groups; primer repair group (n=5): group treated with NIC on 21st day after right leg sciatic nerve injury; repair via vein graft group (n=5): the group that vein graft admitted to the remaining free nerve endings by removing the neuroma on 21st day following sciatic nerve injury. During the week 12, walking measurements were repeated three times in both groups to obtain sciatic function index (SFI). On day 90, the rats were sacrificed and the healing rate was calculated in each animal using both legs of the gastrocnemius muscle. The results data were analyzed using the Mann Whitney-U test.

Results: Macroscopically, there was no significant difference between groups in gastrocnemius morphological values. In the right leg gastrocnemius muscles, minimal atrophic appearance was found in all experimental groups. SFI values were significantly different in the primary repair group compared to the vein graft group ($p<0.05$).

Conclusion: Vein graft is thought to be an alternative method that can be applied in the treatment of NIC cases because of its low cost, easily applicable and allowing repair without tension at the nerve endings.

Keywords: Neuroma-in-continuity (NIC), nerve damage, vein graft, nerve repair

P-110

Analysis of movement disorder-related genes following knockdowns of ano10, wdr81 and vldlr

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Objective: Neural disruption of motor coordination upon congenital lesions or degeneration in the cerebellum results in a particular movement disorder called cerebellar ataxia. The main focus of this study was to examine how three genes (ano10, wdr81, vldlr) contributing to multiple varieties of cerebellar ataxias influence one another and other genes associated with this disorder.

Methods: Three male and three female wild type adult zebrafish organs and forty embryos from 1 hour post fertilization (hpf)-120 hpf stages were used for qPCR. Forty embryos from the 6–72 hpf stages were processed for whole-mount in situ hybridization (WMISH). In the functional knockdown study, twenty embryos from 24–72 hpf stages were processed for qPCR.

Results: All three causative genes were expressed relatively higher at the 1, 2, 5 hpf stages as compared to later periods, and significantly higher in brain, eye and gonads ($p<0.05$); between males and females ano10 and wdr81 showed significantly different expression levels in eye, gill, liver and gonads, whereas vldlr differed significantly in swim bladder and gonads ($p<0.05$). Secondly, expression pattern comparison of three genes of interest using WMISH during early developmental points showed co-expression in diencephalon, midbrain and cerebellum. Thirdly, clustergram analysis depicted how targeted and other cerebellar ataxia-associated genes interact with each other.

Lastly, single morpholino injections of three targeted genes of interest indicated significant compensatory effects in the expression levels. Particularly, ano10 knockdown resulted in not only wdr81 and vldlrupregulation but also increase in the expression of other disease-related genes including ttbk2b, grid2 and atxn1a ($p<0.05$).

Conclusion: Ultimately, this study examining the consequences of functional knockdowns of targeted genes will aid in the discovery of potential therapeutic interventions against the onset of cerebellar ataxia. The ano10 work was supported by E-Rare–TUBITAK (113S001) and wdr81 and vldlr work by TUBITAK 1001 (111S199) projects. Ethic protocols with numbers 2016/05 and 2016/22 were used.

Keywords: Zebrafish, cerebellar ataxia, morpholino, clustergram analysis.

P-111

Effects of ghrelin on gastrointestinal dysfunction in a Parkinson's disease rat model

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Objective: Gastrointestinal disorders are common in Parkinson's disease (PD) patients. In this study, we aimed to investigate effects of ghrelin, with known antiinflammatory properties, on gastrointestinal motility and myenteric plexus vasoactive intestinal peptide (VIP) and neuronal nitric oxide synthase (nNOS) immunohistochemistry in 6-hydroxydopamine (6-OHDA)-induced PD model in rats.

Methods: Wistar albino rats were divided into 4 groups: Sham-operated -control-, 6-OHDA, Ghrelin-Ghr- and 6-OHDA+Ghr groups (n=12 in all groups). 6-OHDA infusion was performed stereotaxically. Rats in Ghr/6-OHDA+Ghr groups were administered ghrelin (10 ng/kg, s.c.) for 4 weeks. Apomorphine-induced rotational behavior, fecal excretion and weights of rats were evaluated at the end of the experiment. Rats were decapitated and gastric motility was examined. Brain, stomach, and colon tissues were collected after paraformaldehyde (4%) perfusion. TH immunohistochemistry was applied on brain sections and Hematoxylin-Eosin staining and VIP/nNOS immunohistochemistry were applied on stomach and colon sections. Data were analyzed by one-way ANOVA.

Results: In the 6-OHDA group, reduced TH immunoreactivity in the striatum and delayed gastric emptying compared to controls ($p<0.001$, $p<0.05$) were increased ($p<0.001$, $p<0.01$) and apomorphine-induced rotations were decreased ($p<0.001$) with ghrelin administration. Decreased weight of animals in the 6-OHDA group compared to controls ($p<0.001$) was increased with ghrelin administration ($p<0.05$). Increased VIP-immunoreactivity and decreased nNOS immunoreactivity was observed in the 6-OHDA group compared to the controls in the myenteric plexus of colon ($p<0.05$). Parallel with fecal output findings, nNOS immunoreactivity in the 6-OHDA+Ghr group rats was increased compared to 6-OHDA group ($p<0.05$). Increased antral myenteric plexus VIP immunoreactivity ($p<0.05$) and decreased nNOS immunoreactivity in the 6-OHDA group compared to controls was reversed with ghrelin administration ($p<0.05$).

Conclusion: Ghrelin is found to have beneficial effects on decreased gastrointestinal motility observed in 6-OHDA-induced rats. These effects are related with gastrointestinal neurochemical plasticity. This study was supported by Marmara University Scientific Research Projects Commission (BABKO). SAG-CYLP-131216-0539.

Keywords: Parkinson's disease, ghrelin, 6-OHDA, VIP, nNOS

P-112

The effect of ethosuximide on seizure development in genetic absence epilepsy rat model

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Objective: Ethosuximide (ESX) is an antiepileptic drug that acts on T-type calcium channels, which is preferred for the symptomatic treatment of absence seizures. Chronic treatment with ESX has been reported to have disease modifying- antiepileptogenic effect on absence seizures in the WAG/Rij rat model of genetic absence epilepsy. In this study, we aimed to investigate the effect of chronic ESX application on the development of spike-and-slow-wave discharges (SWDs) between the postnatal 20th (PN20) and 60th (PN60) days in genetically absence epilepsy rats from Strasbourg (GAERS), which is another rat model of genetic absence epilepsy.

Methods: In our study, GAERS male rats were treated with ESX at the dose of 25mg/kg/day or serum physiologic (SP) at the same volume for 40 days chronically starting from PN20 to PN60. On the PN53, cortical screw electrodes were placed in animals with stereotaxic surgery under ketamine/xylazine anesthesia for EEG recording. After 1 week of recovery period, the effect of ESX on total duration, number and average duration of absence seizures were analyzed between PN60-62 days for 3 days by EEG recordings for 1 hour and 40 min per day.

Results: As a result of the EEG analysis, it was observed that the total duration of SWDs in GAERS that were treated with ESX at the dose of 25 mg/kg/day was significantly lower than that of the SP group.

Conclusion: The results of our study put forth that the chronic application of ESX may have antiepileptogenic effects on the

development of absence seizures in GAERS rats; but our experiments on how long this antiepileptogenic effect lasts after the latest applicationare still going on.

Keywords: Absence epilepsy, ethosuximide (ESX), T-type calcium channels, GAERS

P-113

3D cell cultures and neural stem cells

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Objective: In two-dimensional (2D) cell cultures, cells are forced to adhere to a flat, hard surface different from mechanical environment. The absence of extracellular matrix support influences the behavior, function, growth and morphology of cells. In vitro 3D cell culture models are intended to fill this gap between standard 2D cell culture and in vivo environment. Grafen oxide (GO) has unique surface characteristics and provides specific topographic, chemical and electrical microenvironment for neural cells, and promotes cell differentiation. Conductivity affects the behavior of electrically active neural cells. Based on their mentioned properties, we aimed to develop a 3D cell culture system with GO.

Methods: The mixture prepared with 2% chitosan and 10mg / ml GO dust was ultrasonicated and then placed in a polystyrene culture vessel with 1mL in each well. After freezing at -80 ° C, this mixture was lyophilized and sterilized with ethylene oxide. NSC-34 cells were cultured in 10% FBS and DMEM-high glucose. The cells seeded onto the foam were differentiated in DMEM-F12 and 1% FBS containing medium. On days 4, 6 and 8 of differentiation, cell morphology was examined by scanning electron microscopy (SEM).

Results: According to SEM images, the scaffolds are able to mimic the 3D microenvironment. These characteristics of scaffolds for this 3D cell culture model has the potential to be easily further developed and improved in order to use different cell lines with different tissue engineering techniques.

Conclusion: 3D cultures can be used in neural tissue engineering and prosthetics, in testing neurotherapeutics and in disease modeling, and 3D tissue scaffolds are needed for future clinical applications.

Keywords: Graphene oxide foam, neural stem cells, 3D cell culture, scaffolds

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Table of Contents

Volume **12** / Supplement **1** / May **2018**

Editorial

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Abstracts

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