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M. Mustafa Aldur, MD-PhD
Department of Anatomy
Hacettepe University
Faculty of Medicine
06100 Ankara-Turkey
e-Mail: mustafa@aldur.net
Phone: +90 312 305 24 66
Fax: +90 312 478 52 00

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Neurologist

1969
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2006



S. Murat Rezaki, MD
Assoc. Professor of Psychiatry

1963
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2006



Sebnem Kargi, MD
Assoc. Professor of Ophtalmology

1969
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2007

This supplement of **NEUROANATOMY** is dedicated to

Murat Rezaki
Gunfer Gurer Aydin
and
Sebnem Kargi.

We are deeply sorry for their sudden deaths.
All of them will be in our thoughts and prayers.

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CONFERENCES

C1

How smart is my mouse? The genetic dissection of memory systems in the mouse

Crusio WE [1], Schwegler H [2].

[1] *Centre de Neurosciences Intégratives et Cognitives, CNRS UMR 5228, Université de Bordeaux I, Talence, France.* [2] *Institut für Anatomie, Universität Magdeburg, Germany.*

wim_crusio@yahoo.com

Male mice from several inbred mouse strains were tested in a number of different spatial and non-spatial radial maze tasks that assessed working (WM) and/or reference memory (RM). Large strain differences were obtained that were task-dependent. Other animals from the same strains were processed histologically to estimate the strain-specific extents of the hippocampal intra- and infrapyramidal mossy fibre projections (IiPMF). We estimated genetic correlations between the different behavioural and anatomical variables. The results of these experiments show that seemingly minor changes of procedure, such as turning the maze by 45 degrees between trials, can have dramatic effects on learning performance in some strains. A factor analysis rendered three factors: two representing non-spatial learning (factors I and Iii), one representing spatial learning (factor Ii). WM and RM did not dissociate on different factors. The IiPMF strongly loaded on the spatial learning factor only. We conclude that in radial maze tasks: (1) spatial learning, in contrast to non-spatial learning, is a unitary process, (2) WM and RM are possibly not related to different neuronal mechanisms in mice, and (3) variations in the extent of the hippocampal IiPMF projection underlie individual differences in spatial learning abilities in the radial maze. More in general, these results emphasize that behavioral experiments deserve the same precision and care given to, e.g., neurochemical or molecular experiments, otherwise results may be biased or misleading.

C2

How do thalamocortical pathways relate to sensorimotor views of perception and perceptual development?

Guillier RW.

Anatomy Department, School of Medicine, Marmara University, Turkey

rguiller@wisc.edu

S Murray Sherman and I have proposed a theory of cortical function that adds to and challenges existing views about information flow between cortical areas. The current text-book presentation shows information passing to cortex exclusively via thalamo-cortical connections that provide a first order entry for further, higher level processing through direct cortico-cortical paths. We argue that in addition to this there are higher order cortico-thalamo-cortical pathways which serve to pass information about the motor outputs of lower cortical areas on to higher cortical areas. Information for relay to cortex, both first and higher order, reaches the thalamus along axons that are branched; the information in the thalamic branch represents a copy of the message passing along the other branch to motor centers, thus representing a 'motor component' of sensory messages, and providing an anatomical basis for understanding the sensorimotor nature of perception. In this lecture I will present some of the evidence for this view of cortical circuitry, and will discuss evidence concerning structural and functional differences between first and higher order thalamic relays. These differences suggest that the hierarchy of cortical processing, from lower to higher cortical areas, also represents a developmental hierarchy, with the lowest thalamocortical relays

developing earliest and providing the most stable (and least surprising) inputs to cortex. Higher order relays mature later, maintaining a degree of plasticity for longer and delivering a greater proportion of unexpected messages to cortex.

C3

Melatonin and melatonin receptors in drug abuse

Uz T.

Psychiatric Institute, Department of Psychiatry, University of Illinois at Chicago, USA.

uz@psych.uic.edu

Circadian rhythms in humans may be affected by the use of addictive drugs, such as cocaine and opioids. Further, the health problems caused by these drugs demonstrate circadian rhythms and may be influenced by these rhythms. In experimental animals, the behavioral effects of psychostimulants, such as cocaine and amphetamines, are influenced by diurnal rhythms. Moreover, circadian changes were observed in cocaine self-administration in rats. The neurohormone melatonin is one of the well-known regulators of circadian rhythms. Using various models of melatonin deficiency, we have previously demonstrated that endogenous (i.e., pineal origin) melatonin is critical to regulate the development of cocaine-induced circadian behaviors, such as locomotor sensitization and drug seeking. Moreover, using a mouse knockout for melatonin receptors, we found that melatonin receptors (i.e., MT1) are required for this effect of both endogenous (i.e., pineal origin) and exogenous (i.e., administered) melatonin. As members of a G protein-coupled receptor family, melatonin receptors are involved in the regulation of intracellular signaling pathways leading to gene expression regulation and further, to long term plastic changes in the cell. Using in vivo and in vitro models, our laboratory is currently testing the intracellular signaling mechanisms (e.g., cAMP, cFos, and extracellular signal-regulated kinases) as well as the gene expression dynamics (e.g., 'clock' genes) regulated by melatonin receptors that could explain the regulatory effects of melatonin in addictive behaviors.

C4

Entering new avenues for stroke treatment: roles of vegf and abc (atp-binding cassette) transporters

Kilic E.

Brain Research Laboratory, Department of Neurology, University Hospital Zurich, Switzerland

ertugrul.kilic@usz.ch

Neuroprotection therapies have made limited progress in recent years. Several compounds shown to be efficacious in animals were tested in humans in cost-expensive trials. Unfortunately none of these studies were able to demonstrate efficacy under clinical conditions in patients. In order to establish treatments that are of benefit not only in animals but also humans, new strategies are clearly needed, comprising (I) new factors mimicking intrinsic mechanisms that the brain itself makes use of, (Ii) novel delivery techniques allowing drugs to pass the blood-brain barrier more efficaciously than before, (Iii) better, functionally relevant readouts of brain recovery and (IV) strategies that are of usefulness not only in the acute, but also post-acute stroke phase. In this presentation, research strategies pursued at the Brain Research Laboratory at the University Hospital Zurich are presented and outlooks for the future discussed.

C5

A cortical view in ALS

Ozdinler PH.

MGH-HMS Center for Nervous System Repair, Harvard Medical School/ Mass General Hospital

hande_ozdinler@hms.harvard.edu

ALS (Amyotrophic Lateral Sclerosis) is a complex neurodegenerative disorder, in which both the corticospinal neurons that project to the spinal cord, and the spinal motor neurons that project to the muscle progressively degenerate with the progress of the disease. ALS shown both hereditary (fALS) and non hereditary (sporadic) progression pattern, and this adds more complications not only to the diagnosis, but also to the therapeutic applications for the disease. In this talk, I will focus on corticospinal motor neurons and the molecular controls over their survival, differentiation and growth. Understanding the biology of corticospinal motor neurons in detail, will not only elucidate the molecular and cellular mechanisms responsible for their cell-specific death, but also will help us develop effective treatment strategies for this devastating disease.

C6

The adverse effects of prenatal and neonatal stress on physiology, morphological asymmetry, and overt behavior in infancy and adulthood

Benderlioglu Z.

Department of Evolution, Ecology, and Organismal Biology, The Ohio State University

benderlioglu.1@osu.edu

Exposure to adverse conditions, including low temperatures, food shortages, diseases, and environmental pollutants during ontogeny has enduring effects on physical development, physiology, and behavior of individuals. Prenatal stress disturbs the hormonal milieu in expecting mothers and disrupts the hypothalamic-pituitary-adrenal axis function and its response to stress in both mothers and offspring. However, the effects of environmental and genetic perturbations during postnatal development are equivocal. Some studies report ameliorating effects of postnatal stress on prenatally disturbed nonhuman animals, whereas others confirm earlier studies on adverse consequences of prolonged stress during neonatal period. This study attempts to shed light on seemingly contradictory results in the literature. Specifically, it asks whether species' differences and seasonal reproduction, where environmental conditions in terms of pathogens, temperature, and food availability determine the birth and ontogeny of offspring, play a role in this discrepancy. The study also explores whether glucocorticoids and sex steroids may in part explain physical development, physiology, and overt behavior in pre- and postnatally stressed individuals. The specific parameters studied for physical development, physiology, and behavior are symmetrical organization of bilateral traits in the body, HPA axis response to stress, and aggression. Both rodent and human models are used in studying these parameters. A final discussion will focus on buffering capacity, developmental homeostasis, and developmental stability against genetic and environmental perturbations, and morphology and behavior in adulthood.

C7

Critical periods for developmental plasticity: a look from inside the neuron

Erisir A.

University of Virginia, Department of Psychology, Charlottesville

erisir@virginia.edu

Human development is marked by multiple critical periods, during which early experiences can shape many aspects of our sensory, cognitive and social functions. The phenomenon of plasticity underlies both the adaptability and the vulnerability of the brain to the influences of the environment. Animal models displaying well-defined plastic changes during early development allow investigation of biological factors that enable critical periods. Using ferret and mice models for ocular dominance column plasticity in visual cortex, we have been involved in identifying the morphological and molecular properties of cortical development, and the contribution of NMDA type

glutamate receptors and the GABAergic circuitry on the maintenance of a critical period. Prevention of vision through one eye during early development leads to an abnormal wiring pattern for thalamocortical axons such that deprived terminal arbors shrink while nondeprived axons enlarge. Asking whether any morphological parameters of thalamocortical axon development may underlie the end of vulnerability of this input to deprivation, we studied its ultrastructural properties at the peak and the end of the critical period. These demonstrated that the end of critical period coincided with morphological maturation of thalamic axons, the loss of synaptic NMDAR subunits and a reduced sensory drive onto GABAergic circuitry. One of the main properties of critical period plasticity is its activity dependence; activity reduction paradigms, such as dark-rearing, delay the course of the critical period. Then, the development of any factor that determines the end of the critical period should also be delayed in parallel to the critical period. To test this idea, we re-examined the development of thalamocortical axons in animals that were reared in complete darkness, and allowed to recover for varying durations. Our results have shown that while thalamocortical axon development ensues independent of the plastic state of the cortex or sensory activity, their synaptic and perisynaptic interactions with the postsynaptic partners are influenced by sensory activity: The selectivity of thalamic synapses for GABAergic circuitry, and the subunit composition of synaptic NMDA receptors show delayed development in dark-rearing circumstances. The results will be discussed in the framework of developmental synaptic plasticity and life-time synaptic stability that emerges at the end of the critical period, aided by the circuit properties of GABAergic connections and perisynaptic factors that may be specific to primary or driver inputs in the central nervous system.

C8

Pharmacogenetics of central nervous system drugs (model of antiepileptics)

Eskazan E.

Marmara University Medical School, Department of Pharmacology, Turkey

eeskazan@istanbul.edu.tr

As a branch of pharmacology, pharmacogenetics studies how genetic differences of biologic unit influence individual drug responses, both in terms of efficacy and adverse drug reactions. Pharmacogenetics properties of central nervous system (cns) drugs are more complicated than other system drugs and their pharmacokinetic differences give rise more to the clinical problems. In this presentation, pharmacogenetic profile of antiepileptic drug therapy and related clinical problems were evaluated. During the speech, the knowledge on this field was examined in 4 groups; a- Drug kinetics of central nervous system (blood-brain barrier, transporter molecules, etc); b- Other genetic factors such as enzymes affecting the antiepileptic drug kinetics; c- Genetic variations of the targets of antiepileptic drugs; d- Genetic factors that play role on the adverse effects of antiepileptic drugs.

C9

In-vitro differentiation of human mesenchymal stem cells into neuronal precursors

Can A, Karahuseyinoglu S.

Department of Histology-Embryology, Ankara University School of Medicine, Ankara University Biotechnology Institute, Ankara, Turkey

alpcan@medicine.ankara.edu.tr

It was clearly demonstrated that human mesenchymal stem cells (MSCs) are able to differentiate into functional neurons when induced in vitro expressing neuron-specific cytoskeletal proteins as well as some proteins that lead to the synthesis of catecholamines. A recently isolated source for stem cells is the mesenchymal cells of human umbilical cord stroma. Although neuronal differentiation has been previously demonstrated in human umbilical cord stroma cells (HUSCs), there is still a discordance among studies regarding the potential of these cells to differentiate into neurons. The aim of this study is to differentiate HUSCs into neurons and investigate the temporal development potency of newly differentiated neuronal cells. The spatio-temporal distribution and the quantification of various proteins during differentiation, immunofluorescent single and multi-immunolabeling techniques were performed using a series of antibodies raised against major

cellular markers for neurons such as α and β tubulin, β -III tubulin, MAP-2, NF-M, GFAP, NeuN and NSE. When cells were incubated in neuronal differentiation medium after a 48-hr preinduction period, they suddenly transformed into a bipolar morphology extending long slender processes resembling to neurons. MAP-2, a dendrite specific protein found in mature neurons was upregulated and remodeled particularly at cell-cell contacts. β -III tubulin, a microtubule protein specific to neurons and increase in axonal growth was also positive throughout the differentiation. Nestin was found as a 'nest-like' structure in the juxtaneuronal perikarya. While NF-M was mainly positive along the neurites, NeuN was restricted to nuclei. GFAP was consistently negative in all experiments tested. Finally, NSE as the most abundant form of glycolytic enolases found in adult neurons and thought to serve as growth factor for neurons was partially positive both in induced and in control cells. Taken together, morphological and structural appearance of neuronally-induced cells suggests a well-shaped developing neurons. MAP-2, NF-M and β -III tubulin positivity found in cellular outgrowths indicates that these cells are forming axons and dendrites to function. However, partial lack of some functional neuronal markers such as NSE implies an incomplete neuron formation. Conclusively, it appears that throughout the differentiation of HUCSCs into neurons, expression of neuronal markers present a diversity which follows a similar progress as seen in embryological development of neurons of the body. (Grant supports: Ankara Univ. Biotechnology Inst. 2005-180 and TUBITAK-SBAG -3314)

C10

Antidromic spread and the dynamic clamp method

Purali N.

Hacettepe University Medical School, Department of Biophysics, Turkey

npurali@hacettepe.edu.tr

The neuronal function is perhaps the most fundamental research subject of the modern neurosciences. Electrical recordings performed in isolated or identified neurons are the most common methods to obtain information about the subject. However, considering the microscopic dimensions of the neurons most of the compiled data is in fact extracted by using intracellular microelectrodes. Current clamp and voltage clamp methods are some of the most well known of those methods. However, in both case recordings are obtained under some constant stimulation conditions. Though, the conditions could be optimal for some experimental purposes but not physiological. A dynamic clamp method has recently been developed to investigate the behavior of the neurons under physiological stimulation conditions. In the dynamic clamp method stimulus is actively modulated by the neuronal response via either an analogue or digital circuit. Under the dynamic clamp conditions the stimulus is not determined before the experiment but develops through the experiment (Marder 2006). The method has been employed to investigate various properties sensory neurons and some neuronal circuits (Merriam et al. 2005, Sharp et al. 1992). I have used the method in receptor neurons with two different adaptive behaviors to investigate the effects of the antidromic action potentials in receptor responses and adaptation. It was observed that both the receptor responses and the adaptation were influenced substantially by the antidromic spread of the action potentials.

C11

Sleep and rem in the context of cognitive functions

Aydin H.

GATA, Department of Psychiatry, Turkey

hamdullahydn@yahoo.com

Disorders of sleep lead to cognitive as well as biological dysfunctions. Memory and learning processes are completed while information processing continues during sleep. REM sleep is increased during the night after new information is processed and if it is interrupted, information cannot be stored and utilized properly. Thus, cognitive processes must be defined with their counterparts in sleep. In this context, it can be claimed that thinking, fantasizing and dreaming are parts of the whole cognitive process. Cognitive processes, although in different forms, persist through REM and NREM stages during sleep. Each sleep stage with its own structure differs from the other and from wakefulness in these processes. In wakeful perception, specific centers in the brain are stimulated while surrounding

areas are relatively inhibited. In this way, immediate encoding processes are implemented, after which the stimulation is spread through larger areas to be evaluated further. In a way, the first response to the stimulation is elicited (episodic information), then further evaluation is made and the process is completed. In wakefulness, images and fantasies are included in the symbols of thought processes. On the other hand, the process during REM sleep differs in two main points: firstly, the stimulation set out by the stimulus is widespread, and secondly, the stimuli are internally derived. As distinct from the wakeful state, being under the control of the dominant cholinergic activity, widespread stimulation leads to specific processes according to the characteristics of the stimulus. Because only internal stimuli are involved, they are ordered sequentially depending on the subjective importance of the experience. In waking state visual processes begin in the striatal areas while during REM sleep, extrastriatal cortex is selectively activated. Dreams during REM may be generated as a consequence of the activation of striatal cortex by the back-projection of extrastriatal cortex activation. Daily experiences take place mostly during NREM dream or dream like processes. This is explained by under utilization of encoded information because of the non-dominance of cholinergic activity. During wakefulness, perception is governed by the external reality, while responses are also perceived and readjusted according to the circumstances if needed. The disappearance of this type of processing during sleep leads to the preclusion of logical unity of cognitive processes.

C12

The effects of growth factors on neurogenesis in ischemia/reperfusion

Topalkara K.

Cumhuriyet University, Medical School, Department of Neurology, Sivas, Turkey

topalkara@cumhuriyet.edu.tr

The main focus of the treatment strategies in ischemic stroke is being kept alive of damaged neurons (neuroprotection), but the time window for that kind of therapies is narrow. Although new treatment strategies in stroke have increased the survival rate, success rate to decrease disability is still low. It has been thought that functional improvements observed in some stroke victims are due to the remodeling of neural pathways in undamaged brain regions, but this phenomenon could also be explained by adult neurogenesis which newly generated neurons might play a role in reorganisation of brain functions. There is an intense research on the subject of neurogenesis after cerebral ischemia, searching the proliferation and migration of new neurons arising from the two restricted region of adult mammalian brain, namely the subventricular zone of the lateral ventricle and the subgranular zone of the hippocampal dentate gyrus, and their capability to differentiate into the neuron phenotypes which is damaged by the ischemia, and also their capability to survive and gain function by making new synaptic connections in the damaged region. There is also a lot of studies searching the positive and negative factors affecting the processes mentioned above. In this lecture, the studies on both the endogenous neurogenesis in rodent models of focal cerebral ischemia and the effects of exogenously applied growth factors on this process will be reviewed.

C13

CART and stress response

Koylu EO.

Ege University, Center for Brain Research and School of Medicine, Department of Physiology, Bornova, Izmir, Turkey

ersin.koylu@ege.edu.tr

Number of publications has been published in recent years about the putative role of CART (Cocaine and Amphetamine Regulated Transcript) in various physiologic and pathologic processes. Abundant CART existence in all levels of hypothalamus-pituitary-adrenal (HPA) axis, as well as the other areas in central nervous system, suggests a role for this peptide in stress response. Particularly, CART expression in paraventricular nucleus of hypothalamus and locus coeruleus which are major sources of corticotrophin releasing factor (CRF) and noradrenaline respectively, is noteworthy. There is a bidirectional relation between CART and HPA axis activity. CART stimulates CRF, adrenocorticotrophic hormone and glucocorticoid secretion, whereas CRF and glucocorticoids increase the transcriptional activity of

the CART gene. Furthermore, adrenalectomy decreases CART expression in hypothalamus. Stress exposure in animal models modulates CART expression in hypothalamus and amygdala in rat brain in a region and gender specific manner. Findings suggest that CART has a role in stress response, as well as drug abuse and feeding behavior, and CART may be a mediator peptide in the interaction of these processes.

C14

Modern techniques in neuromicroscopy

Ozturk G.

Yuzuncu Yil University Medical School, Physiology Department / Neuroscience Research Unit, Van, Turkey

drgurkan@yyu.edu.tr

In this talk, I will present the basic principles and applications of three of advanced microscopy techniques, namely time-lapse microscopy, laser – scanning confocal microscopy and laser microdissection, giving examples from the studies performed in our laboratories. Time-lapse microscopy can be defined as the imaging tissues and cells in culture at desired time intervals while keeping them under physiological conditions. Beside its ability to capture many cellular and sub-cellular events, as a superiority over snap-shots, the most important advantage of this technique is inclusion of a fine-tuneable time dimension to experiments. With this method, while it is possible to develop new, less obscure alternatives to detect well-known phenomena like apoptosis, some novel notions could also be unearthed. Laser – scanning confocal microscopy is basically a highly advanced microscopy technique. Simultaneous and discrete visualization of multiple fluorescent labels, three-dimensional reconstruction of microscopic structures and time – lapse imaging capability make this technique invaluable for neuroscience studies. Confocal imaging is indispensable for living cells as well as for fixed preparations. Ion movements into and out of cells, spatial and temporal relationships between same or different cell types, dynamics of fluorescent-labelled proteins or organelles could be qualitatively and quantitatively examined. Laser microdissection is a relatively new technique and its applications in neurosciences are not yet extensive. A UV laser beam is focused on microscopic structures through an objective and they are destroyed with this energy. The diameter of the laser beam could be narrowed down to 0,3 micrometer and energy level could precisely be adjusted. In our laboratory we use this system for an in vitro neuronal injury model in which outgrown axons from cultured neurons are cut with the laser. On the other hand, the system has other applications such as isolation of live or fixed cells and subcellular structures and intracellular injections.

C15

Role of matrix metalloproteases in central nervous system physiology and pathophysiology

Gursoy-Ozdemir Y.

Hacettepe Medical School, Department of Neurology, Ankara, Turkey

yase68@hotmail.com

Matrix metalloproteases (MMP) are the enzymes located in multiple tissues as well as brain. In brain they take part in matrix reconstruction, cellular development, path finding for axons, inflammation and change blood-brain barrier opening. They are expressed as proenzymes and being cleaved to active forms by auto induction or other proteases. MMPs are expressed in BBB especially at astrocytes and endothelia. Their roles in CNS pathology are well investigated especially during reperfusion injury, tumor genesis and neurodegenerative diseases. Migraine and stroke are both important public health problems. Pathophysiological mechanisms aren't well investigated especially for migraine. Experimental cortical spreading depression model (CSD) can be used to mimic migraine aura and ischemic depolarizations. Changes induced after CSD will be discussed especially at the level of MMP-9 protein and mRNA and blood brain barrier changes induced after CSD. Implications of these changes for pathophysiology of migraine and stroke will be investigated in detail.

PANELS

NEUROETHICS

Moderator: Gonul O. Peker

Panelists: Kucuradi I [1], Koptagel Ilal G [2], Bayraktar K [3], Tuğular I [4], Peker GO [5].

[1] Maltepe University Department of Philosophy, [2] Turkish Association Psychosomatics and Psychotherapie, [3] Galatasaray University, [4] Aegean University Faculty of Medicine Department of Pharmacology, [5] Aegean University Faculty of Medicine Department of Physiology

Following establishment and rise of neuro-philosophy as a unique area of philosophy in the 1980s, neuro-ethics came by shortly to be adopted as a unique area of ethics, mainly to define (or redefine) the conscience, will, perception, attitudes and even legislative regulations, and to be argued at the universal level in 2003 as an unavoidable necessity owing to the research yielded immense knowledge and the numerous innovations in pharmaceuticals and neuro-technology, and despite the existence of bio-ethics and medical ethics, which have long been on the stage already. In 4-5 years only, a considerable amount of high impact power arguments and (re-) questionings were conducted and released in this new multi-professional and multi-disciplinary area at conferences and via publications and mass media. Neuroethics departments, chairs and graduate study programs were established and launched in several North American and European universities. Neuroethics has also been evolving to be perceived as a subject of serious concern nevertheless it has not been amending, sentencing or limiting presently. Since that it is directly related to the human existence, consciousness, will and behaviour as well as human's interactions with the society and the nature, neuroethics emerges and flourishes not only as the concern of neuroscientists, pharmacologists, neurologists, psychiatrists, neurological surgeons, rehabilitation therapists, and psychologists; but also as the potential problematic of the philosophers, ethicists, sociologists, educators, society and education engineers, decision makers, legislatives, and leaders to a great extent.

Comprising of topics, problematics, and questionings which are all subject to qualitative and quantitative change in parallel with or in dual correlation to, or as a function of the novel scientific, medical and social developments (and sometimes progress), the constantly expanding field of neuroethics will be studied and discussed within its definitions, essential content basis only with addition of several spot topics selected for this panel:

Philosophy, Philosophy of Science and (Why) Neuro-Philosophy

Ethics, Bioethics, Medical Ethics and (Why) Neuro-Ethics

Human as a Bio-Psycho-Social Entity and Salutogenesis

Enhancing/Developing Human Brain Health versus Creating 'Supermen'

Ethics, Bioethics, Medical Ethics and Neuro-Ethics from the Perspective of Law and Criminal Law

Revisiting/Redefining the Concepts of 'Free Will' and 'Culpability'

Brain Imaging: Today's First Runner to Replace 'Phrenology'

Research Ethics, Drug Development Research Ethics and Neuro-Psychiatric Drug Development Research Ethics

A Critical/Skeptic Analysis of the Global and Turkish Industry, Clinical Indications / Recipe Trends and Marketing of the Pharmaceuticals and Technology Targeting the Brain

ORAL PRESENTATIONS**O1****Behavioral and immune effects of chronic interferon alpha administration in mice**

Orsal AS, Coquery N, Blois SM, Bermpohl D, Schaefer M, Priller J, Arck PC.

Psychoneuroimmunology laboratory, Charité, Universitäts Medizin Berlin, Germany.

arif.oersal@charite.de

Interferon alpha (IFN-alpha) is a cytokine which has been used in the treatment of chronic viral infections and malignant disorders. Depression is among the most frequent side effects of IFN-alpha treatment, which occasionally even necessitates discontinuation of IFN-alpha therapy. The mechanisms by which IFN-alpha induces depression still remain elusive and a skew of the immune homeostasis towards immunity - subsequently perpetuating cell migration - may play a role in the pathogenesis of such depression-like symptoms. To address this hypothesis, we injected murine IFN-alpha (60.000 U/kg) i.p. daily over a period of 7 days into male Balb/c mice, followed by forced swim test (FST) to identify depressive behaviour. Furthermore, flow cytometry was used to identify IFN-alpha induced immune changes of blood and brain cells. We observed that chronic IFN-alpha application resulted in increased immobility behaviour in the FST, and increased percentages of the adhesion molecules CD11a, CD11b, and the activation marker CD25 on blood lymphocytes was detected. Flow cytometric analysis of the brain revealed that IFN-alpha treated group had increased percentages of CD4+ and CD8+ lymphocytes. We propose that, besides neural stimulation, an IFN-alpha advanced immunity may render the blood brain barrier more permeable for an enhanced migration of inflammatory cells, subsequently resulting in depression-like behaviour.

Keywords: interferon alpha, depression, lymphocyte migration, adhesion molecules, CD11a, CD11b

O2**Gender differences in brain oscillations**

Guntekin B, Basar E.

Istanbul Culture University, Brain Dynamics, Cognition and Complex Systems Research Unit, Faculty of Science and Letters.

b.guntekin@iku.edu.tr

There are only few studies describing the gender differences in Event Related Oscillations. The present report aims to demonstrate the differences in Event Related Oscillations (EROs) between female and male subjects during a simple visual stimulation. The electrical recordings of 32 (16 males, 16 females) healthy subjects were recorded at thirteen different scalp locations (F3, F4, Cz, C3, C4, T3, T4, T5, T6, P3, P4, O1, O2). The analysis was performed in alpha (9-13 Hz), beta (15-24 Hz), delta (0.5-3.5 Hz), gamma (28-48 Hz), theta (5-8.5 Hz) frequency windows. The results showed that the maximum peak to peak (p-p) delta amplitudes of the female subjects were significantly higher than the maximum p-p of the male subjects on the Cz, T5, P3, P4, O1 and O2 locations. The maximum p-p beta amplitudes of the female subjects were significantly higher than the maximum peak to peak beta amplitudes of the male subjects at the O1. Further the maximum peak to peak beta and gamma amplitudes of the female subjects were significantly higher than the maximum peak to peak amplitudes of the male subjects at O2 locations. Clear differentiations at the primary sensory visual area (O2) between female and male subjects in the delta frequency range has a considerable importance, since these results could be used as a standard in the future experiments, also in order to compare reaction to cognitive loads.

Keywords: Event Related Oscillations, Gender, alpha, beta, delta, theta, gamma, VEP

O3**Behavioral despair in young and adult male Wistar rats**

Tunc Ozcan E, Canbeyli R.

Psychobiology Laboratory, Department of Psychology, Bogazici University

canbeyli@boun.edu.tr

There are age-dependent differences in the sensitivity of depression in both humans and animals. A noticeable increase in the prevalence of depression during adolescence is well-documented. In young people depression dramatically increases between the ages of 13 and 15 years and reaches a peak at the age of 17 years with a subsequent decline. There are remarkable differences in the occurrence, treatment and neurobiological correlates of depression among children, adolescents and adults. Similarly, juvenile rats show more vulnerability to stress compared to adults; therefore, differences in induction, progress and the treatment of depression among different age groups are to be expected. Accordingly, in the present study, it was hypothesized that juvenile rats would exhibit aggravated behavioral despair compared to adult rats. Behavioral despair is an animal model of depression based on two forced tests separated by 24 hours; immobility and decreased struggling in the second test compared to the first have been shown to be an indicator of depression that can be alleviated by antidepressants.

Approximately, 1.5 and 4.5 months old experimentally naive male Wistar rats were used in the experiment (n=8 for both groups). Individual rats were tested in two swim tests (15 min for the first, 5 min for the second) separated by 24 hours and their behavior was video recorded.

Results indicated that juvenile rats displayed longer duration of immobility, shorter duration of swimming, fewer head shakes and instances of total struggling in the second swim test compared with adults. These findings suggest that juvenile rats are more susceptible to behavioral despair than adult rats. While no biochemical assays were conducted in the present study, our findings may be due to higher basal glucocorticoids levels, longer duration for returning to basal level of glucocorticoids in response to a stressor, higher levels of anxiety and/or lower levels of habituation in juvenile rats compared to adults. Additionally, recent studies show that testosterone is a protective factor against depression that rapidly reduces anxiety and despair in male rats. Consequently, lack of sexual maturity in juvenile rats may be a factor in determining susceptibility to stress effects in the male animals. (Supported by Bogazici University BAP Fund 05B0702 to RC).

Keywords: Behavioral despair, juvenile, adult, depression, Wistar rats.

O4**Brain regions associated with suppressing a spatial image**

Kocak OM [1], Cicek M [2], Yagmurlu B [3], Atasoglu C [4].

Kirikkale University Faculty of Medicine, Department [1] Psychiatry, [3] Radiology Department, Ankara University Faculty of Medicine, Department of [2] Physiology, [4] Psychiatry.

orhanmuratkocak@gmail.com

Cognitive control (CC) includes parallel or sequential processes that are keeping the relevant memory (and suppressing the irrelevant), directing attention, response selection, producing goal directed behavior (1,2). If we take a thought or an image in to account, apart from being a part of complex cognitive process, it is not clear whether they are controlled by the mechanisms involved in the CC or not. Even a simple mental process like keeping the image of an object in mind or suppressing it is not easy (3). The aim of this study was to determine the brain regions associated with suppressing an image of object. We used functional magnetic resonance imaging (fMRI) while the subjects were performing a thought suppression paradigm. Twelve healthy subjects were participated in the study. Mean age was 25.7±2.6 (mean± SD) and participants' education was more than eleven years. Subjects viewed a paper with a shape first and then they went in to the scanner to perform four task conditions while functional images were acquired. These four conditions are as follows: 1) Imagine the paper with the shape 2) Imagine the paper without the shape 3) Erase the shape from the paper with an eraser and 4) Freely imagine. The 'imagine without shape' condition is a thought suppression paradigm and 'erase' is also a suppression task but it contains a visuospatial manipulation rather than a direct suppression. The brain activities related to suppressing, erasing and imagining were obtained by subtracting the free imagine related activity from these conditions. The contrast between suppressing versus erasing given the differences between two thought suppression tasks. fMRI analysis showed that suppressing; erasing and imagining conditions all activated the parietal and prefrontal regions with different extent. Erase versus suppress

contrast, which might unveiled spatial manipulation related processes, showed left intraparietal sulcus and right inferior parietal lobe activity. These results suggest that the regions associated with CC (4) were also activated while a simple mental process is performed. Additionally the results showed that the parietal lobe is the key region for suppression of a mental image by spatial manipulation. Finally, our novel fMRI paradigm for thought suppression might be a candidate as a tool to investigate psychiatric diseases that is proposed to include CC related disturbances.

Keywords: Cognitive control, prefrontal cortex, parietal lobe, functional mri, thought suppression.

O5

The effects of n-methyl-d-aspartate receptor blockade in the last maturation period of brain development on the anxiety-related behaviors in adult rats

Kocahan S, Babar E, Melik E.

Cukurova University, Medical Faculty, Department of Physiology, Division of Neurophysiology, Adana, Turkey.

sayad_han@hotmail.com

It is known that N-methyl-D-aspartate (NMDA) type of glutamate receptors in the brain play an important role in the development of neuronal migration, dendritic arborization and establishment of synaptic connections. Blockade of NMDA receptors in adult age produced deficits in learning and memory, as well as the neuro- and psychopathological abnormalities. Cognitive and social interaction deficits usually take place directly after weaning, it seems reasonable to suggest that behavioral abnormalities in adult age could be induced by blockade of NMDA receptors in the last maturation period of brain development. In the present study, rats pups were treated with saline or MK-801 (0.25 mg/kg, s.c.) at postnatal between 20-30 days for 10 days. Behavioral patterns related to anxiety were examined in adult Wistar rats (3 month) in the 'open-field' (OF), White/Black Box (WBB) and elevated plus-maze (EPM). MK-801 treatment in the OF test produced a significant decrease in peripheral grooming ($P<0.01$) and an increase in immobility ($P<0.01$), whereas in the WBB test MK-801 treatment had no effect. In EPM, MK-801 treatment significantly increased time spent in open arm, open arm entries, and head dipping ($P<0.01$) and decreased time spent in the enclosed arm ($P<0.01$) with decreasing vertical activity ($P<0.05$). This finding could suggest that postnatal blockade of NMDA receptors between 20-30 days of brain maturation period impacts information-processing that resulted in diminishing, during adult age, an anxiety on the environmental novelty but not on the natural threatening stimuli.

Keywords : NMDA, Anxiety, Neurodevelopment, MK-801, Neonatal Treatment , Rat

O6

Effect of the correlation in synaptic background activity on the latency of neocortical neurons

Erkaymaz O [1], Uzuntarla M [2], Ozer M [2].

Zonguldak Karaelmas University, [1] Karabuk Technical and Educational Faculty, Department of Electronics and Computer Education, [2] Engineering Faculty, Department of Electrical and Electronics Engineering, 67100 Zonguldak, Turkey.

okanerkaymaz@hotmail.com

Neurons transmit information about input signals by transforming them into the spike trains. The information provided by spike trains may be encoded in spike timing or in average rate of firing. However, codes in spike timing can make more efficient use of the capacity of neural connections than those simply rely on the average rate of firing. In this context, the determination of the latency of the first spike constitutes a physiologically important subject. Neocortical neurons in vivo are subject to synaptic background activity, which is called synaptic noise. Synaptic background activity is particularly intense during the active states of the brain. In this study, we investigate the effect of the correlation of the synaptic background activity on the latency of first-spike. Different computational models have been previously proposed to reproduce the stochastic membrane potential fluctuations and high-conductance state characterizing the dynamics of neocortical

neurons in vivo. We use the simplest one that was proposed recently by Destexhe et al. (2001) and called as a point-conductance model. The model considers single-compartment neuron with global excitatory and inhibitory conductances that represent the sum of a large number of synaptic inputs. Time-dependent global excitatory and inhibitory conductances are described by one-variable stochastic processes similar to the Ornstein-Uhlenbeck process. We determined the latency by a time taken for the first upward crossing a certain threshold value of membrane potential. The mean latency of first spikes is computed by averaging the latencies of the first spikes over an ensemble of N realizations. We changed the correlation of the background activity without affecting the average conductance due to the background activity. Therefore, the neuron received the same amount of random input with different correlation at each trial. We conducted simulations for seventeen different values of the correlation and computed the mean latency over an ensemble of 6000 realizations for each level of the correlation. Obtained results suggest that the neocortical neuron can detect the change of correlation in its input and encode it by decreasing the latency for the increasing correlation. Standard deviations of the latency take large values indicating that the latency of the first-spike is highly variable as expected from spiking activity of cortical neurons in vivo to a repeated stimulus.

Keywords: Neocortical neuron, synaptic background activity, point-conductance model, correlation, latency

O7

What does learning-related hippocampal neural activity tell us about hippocampal information processing?

Okatan M.

Massachusetts General Hospital, Department of Anesthesia and Critical Care, Neuroscience Statistics Research Laboratory, Boston MA, USA.

murat@neurostat.mgh.harvard.edu

The temporal difference learning algorithm (TD) is a popular learning algorithm in machine learning. It has also been widely used in explaining learning-related changes in neural activity and behavior across multiple species and in various neural systems, particularly in the reward pathway. This study uses the TD algorithm to interpret recent findings on learning-related neural activity recorded from the hippocampus of monkeys performing an associative-learning task. The algorithm is trained on the location-scene association task of Wirth et al. (2003), *Science* 300, 1578–1581. In this task, a monkey learns to associate pictures of complex visual scenes with target locations that are superimposed on the pictures, in order to receive reward. After viewing a picture with superimposed target locations, the monkey chooses one of the locations by shifting its gaze to that location. The monkey's behavioral responses were recorded at each trial as correct or incorrect, while the spiking activity of hippocampal neurons was recorded simultaneously. The neural activity of certain neurons (changing cells) changes with behavioral learning in this task, and this change leads, lags, or occurs simultaneously with changes in behavioral learning (Wirth et al., 2003). A mechanism that explains the temporal effects that are observed in neural activity and behavioral performance in this task during learning has been lacking. The present study shows that the TD algorithm may serve as a link between neural activity and behavioral performance and explain the findings on the relative timing of learning-related changes in these two processes. It constitutes the centerpiece of a model for the joint probability density of the neural activity and behavioral responses. The model suggests that the activity of changing cells may be explained in terms of the predictive value signal of the TD algorithm. This provides the first direct evidence suggesting that individual hippocampal neurons may participate in a network that implements a temporal difference-like algorithm. The results are interpreted to suggest that changing cells may signal the reward-predictive value of prefrontal goal representations that are triggered by visual scene stimuli in this task.

Keywords: Hippocampus, prefrontal cortex, electrophysiology, learning, artificial intelligence

O8

Comparison of point counting and planimetry methods for the assessment of cerebellum volume on MR images: A stereological study.

Acer N [1], Sahin B [2], Usanmaz M [3], Tatoglu H [4], Sankur S [4], Kabadayi T [5], Goktas A [6], Abban T [7].

Mugla University, [1] School of Health Sciences, Mugla; Ondokuz Mayıs University Faculty of Medicine, Department of [2] Anatomy, Samsun; Mugla State Hospital [3] Neurosurgery Clinic; [4] Metamar MR Merkezi, Mugla; Mugla State Hospital, [5] Patology Laboratory Mugla; Mugla University, Faculty of Art and Sciences, [1] Statistic Department; Mugla University, [7] Medical Clinic, Mugla, Turkey.

nacer@mu.edu.tr

There is evidence that the cerebellum is involved in motor learning and cognitive function in human. The effect of gender on cerebellar size has not been fully established yet. To understand this effect, many of studies have been conducted to assess the cerebellar volume. However, we have not seen a study evaluating the efficiency and the accuracy of point-counting and planimetry methods of the Cavalieri principle. For this purpose the volume of cerebellum was estimated using serial magnetic resonance images (MRI) of 50 Turkish young volunteers (aged between 20 and 25; 25 males, 25 females) free of any neurological symptoms and signs. The cerebellar volumes were determined on films using the point-counting and planimetry methods. Our results suggest that female subjects had smaller cerebellar volumes compared with males, however, there was no statistical significant difference between the genders ($P > 0.05$). Total cerebellar volumes obtained by two different methods were not statistically different ($P = 0.84$) and strongly correlated with each other ($r = 0.97$). We concluded that both methods could be used for the assessment of cerebellar volume. However, the point-counting method takes less time (7-12 minutes; minimum and maximum, respectively) than the planimetric method.

Knowledge of the detailed normal anatomy of the cerebellar volume on sagittal MR images can assist in the identification of various pathologic alterations.

Keywords: Cerebellar volume, MRI, Stereology, Cavalieri principle, Point-counting, Planimetry.

O9

Relationship between 2D:4D Ratio and aggression and anger

Dogan A [1], Barut C [2], Konuk N [3], Bilge Y [4].

[1] Dept of Interdisciplinary Forensic Medicine, Health Sciences Institute, Ankara University, Ankara, Turkey; [2] Dept of Anatomy, School of Medicine, Zonguldak Karaelmas University, Zonguldak, Turkey; [3] Dept of Psychiatry, School of Medicine, Zonguldak Karaelmas University, Zonguldak, Turkey; [4] Dept of Forensic Medicine, School of Medicine, Ankara University, Ankara, Turkey

aslidgn@gmail.com

In studies aiming to determine aggression and anger level, anthropological and biological factors are investigated together. The studies evaluating the relation between the 2D:4D and aggression and anger become more popular because the digit length ratio is suggested to reflect the effects of exposed prenatal androgens during development. One of the mechanisms underlying this is Hoxa and Hoxd genes. These genes are not only responsible for the development of both the digits but gonads as well. The aim of this study is to investigate the relation between the digit length ratio and aggression and anger.

377 university students (195 women, 182 men) aged between 18-24 years participated in the study. A digital compass with a resolution of 0.01 mm was used for hand anthropometric measurements, using standard anthropometric methods. State Trait Anger Scale (STAS) and Aggression Questionnaire were used to evaluate the aggression and anger in individuals. Independent samples test was used for comparisons according to gender. The relation between the 2D:4D and STAS and Aggression Questionnaire were evaluated with Pearson Correlation Analysis and Multiple Regression Analysis. 2D:4D ratio was found to be smaller for males than females ($p < 0.05$). There was only a positive, weak, significant correlation between 2D:4D and

physical aggression ($r = 0.158$, $p < 0.05$), which was a sub-scale of aggression questionnaire, in males. The relation between 2D:4D and physical aggression was observed to be weaker when possible psychopathology, which can be diagnosed with SCL-90-R test, was excluded. There were no correlations between 2D:4D and STAS and Aggression Questionnaire subscales in females. These results indicate that there is a weak correlation between finger length ratio and aggression and anger. Taking other factor that have role in formation of aggression and anger into account, digit ratio may be used as a pre-assessment method regarding physical aggression. However, digit ratio is not an ideal biological marker reflecting the brain development.

Keywords: 2D:4D, aggression, anger

O10

The network identification of the anticonvulsant and proconvulsant regions placed in substantia nigra in adult Sprague Dawley rats

Gulcebi M [1], Yananli HR [1], Aker R [1], Cavdar S [2], Onat F [1].

Marmara University School of Medicine [1] Pharmacology and Clinical Pharmacology Department, [2] Anatomy Department, Istanbul, Turkey.

mgfarma@yahoo.com

The substantia nigra (SN) which takes place in mid-brain is divided into two main regions called pars compacta (SNpc) and pars reticulata (SNpr). SNpr is one of the components of basal ganglions and forms the big subunit of SN. SNpr has GABA-ergic neurons that project to ventrobasal nucleus of thalamus, intermediate and deep layers of superior colliculus, pedunculopontine and laterodorsal nucleus of ventral tegmentum. SNpr plays an important role on the control of epileptic seizures. SNpc is the small region above the SNpr that has dopaminergic neurons projecting to striatum.

SNpr has been divided into two GABAA-sensitive regions topographically which shows different effects on epileptic seizures. The GABAA-sensitive anticonvulsant region takes place in SNpr anterior and GABAA-sensitive proconvulsant region exists in SNpr posterior. The different projections of these two regions can cause opposite effects on epileptic seizures.

This study has an aim to demonstrate the different afferent projections of SNpr anterior and SNpr posterior.

Male adult Sprague Dawley rats were used in the study. The rats were placed to stereotaxic device and 2% Fluorogold (Fluorochrome, Inc, Englewood, CO, USA) dissolved in the cacodylic acid was injected with iontophoretic method to the anterior and posterior regions of SNpr. After a 7-10 latent period the rats were perfused with physiological saline and 4% paraformaldehyde solution. The sections of the whole brain were evaluated under the fluorescent microscope.

The differences about the projections between the SNpr anterior and SNpr posterior were observed. There was a connection between SNpr posterior and cortical (motor) regions although we couldn't establish this kind of connection between SNpr anterior and cortical regions. There were topographical projections from subthalamic nucleus to SNpr similar to striatum and SNpr. Also in the lateral injections to SNpr, we determined unilateral painting in the amygdala and bilateral painting in red nucleus however there were no Fluorogold painted neurons in both of nucleus in the medial injections. Therefore the topographical structure of SNpr is important both in anteroposterior and mediolateral direction. Thus in order to understand the topographical structure and order of SNpr, detailed localized injections are being planned. The obtained results from this study will clarify the mechanisms playing a critical role in the generation of epileptic activity and will participate to the development of the medical and surgical treatment of epilepsy.

Keywords: Fluorogold, iontophoresis, epileptic seizure, projection, afferent

O11

Effects of hypothermia on conduction velocity distribution of isolated rat sciatic nerve

Guney O [1], Tuncer S [2], Ilık MK [1], Dalkılıç N [2], Ayaz M [2].

Selçuk University, Meram Faculty of Medicine, Departments of [1] Neurosurgery, [2] Biophysics, Konya, Turkey.

ayaz72@yahoo.com

Like all tissues the peripheral nervous system is also temperature sensitive. In clinical studies, effects of changes in temperature on rat sciatic nerve have been investigated by using conventional techniques. In this study, effects of the lower temperature values than the physiological one on fiber groups having different conduction velocities and constituting rat sciatic nerve were investigated. To assess the alterations on nerve preparation, compound action potentials (CAP) were recorded with suction electrodes and conduction velocity distributions were obtained by collision technique. Up on each tested temperature (33, 32.5, 32, 31.5, 31, 28, 25 °C) nerve conduction velocity distributions were determined and electrophysiological parameters like latency (L), chronaxie, maximum depolarization value (MD) and the time required to reach this value (TP) were calculated. This study have shown that, the first effects of decrease in temperature are seen on faster conducting fiber groups and these effects are more prominent in absolute temperatures (28, 25 °C). Furthermore, the decrement in temperature makes latency elongation more clear which carries information about fastest conducting fiber groups and this situation contributes relative decrement on conduction velocity of whole fiber groups. Significant changes in the time required to reach maximum depolarization point (TP) which gives information of alterations on nerve fibers with sub maximal conduction velocity is occurred in 28 and 25 °C temperatures.

Keywords: Sciatic nerve, compound action potential, conduction velocity distribution, hypothermia, collision

O12

The mechanism of Pea3 protein in neuronal differentiation

Caglayan B [1], Demir, O [1], Oney P [2], Aksan Kurnaz I [1].

Yeditepe University, Faculty of Engineering and Architecture, Department of Genetics and Bioengineering, Istanbul, [1], Ankara University, Faculty of Science, Department of Biology [2] Ankara, Turkey.

iakurnaz@yeditepe.edu.tr

Pea3, ER81 and ERM belong to the PEA3 subfamily of ETS transcription factors and these proteins are expressed at different time points within the nervous system. We have significant evidence that PEA3 proteins, activated by the MAPK pathway in response to external stimuli such as NGF or bFGF, are involved in neuronal differentiation and axonal extensions. Using PC12 cells as a neural differentiation model, the effect of growth factors such as NGF and bFGF on neurite formation in response to PEA3 protein expression are analyzed. We have shown that transcriptional activity of PEA3 proteins are upregulated in response to external stimuli, and we have also shown that PEA3 proteins can result in neurite formation as an indicator of neural differentiation when stimulated by growth factors. Currently we are investigating the neural differentiation abilities of oestrogen receptor (ER) fused chimeras of ERM and ER81 in order to regulate the expression of these proteins through induction. Potential target genes of PEA3 proteins are currently under investigation, and we have preliminary evidence that PEA3 proteins may generate the differentiation response through regulation of neurofilament gene expression.

Keywords: PEA3, PC12, differentiation, growth factor

O13

Preparation and characterization of biopolymeric nerve guide structures

Denkbas EB.

Hacettepe University, Chemistry Dept., Biochemistry Div., Beytepe-Ankara, Turkey.

denkbas@hacettepe.edu.tr

Peripheral nerve damages and defects are encountered more often and are of particular importance as a problem in today's emergency nerve surgery operations as a result of frequent traffic accidents and fire weapon wounds. Repairing the peripheral nerve damages is still a major problem by nerve surgeons. In cases where end-to-end repair is not possible and in cases where a large wound and a large defect cannot be repaired via proximation of the ends, a possibility for a complete healing chance is extremely low. Even in cases where an end-to-end repair is possible, the expected functional recovery is only up to 50 to 60%.

One alternative approach is placing the nerve ends in silicon tubing and expecting the defect to recover. The healing mechanism depends largely on the nerve sprouting from the proximal end to find the distal myelinated sheet for recovery. Various neurotrophic factors are added to the tubing material to facilitate the healing mechanisms.

In this proposal, the aim is to fabricate and test synthetic nerve guide polymers with micro-tubular structure to serve as a nerve guide to the peripheral nerve fascicles. While the researchers in biotechnology field and the nerve surgeons at the clinics are seeking for alternative approaches, the polymer sciences are creating a new horizon to explore as new candidate materials and new approaches to facilitate the nerve guidance. The context of this study is to test the application potentials of biopolymeric structures such as alginate-chitosan microtubular polymers and characterized to be employed in *in vivo* experimental studies.

Keywords: Biopolymeric, nerve guide, biotechnology

O14

Measurement of local cerebral blood flow during amygdala kindling process in rats with genetic absence epilepsy (GAERS)

Carcak N [1], Ferrandon A [2], Koning E [2], Aker R [3], Ozdemir O [1], Onat F [3], Nehlig A [2].

[1] Istanbul University Faculty of Pharmacy Department of Pharmacology, Istanbul, Turkey; [2] INSERM U 666, Louis Pasteur University, Faculty of Medicine, Strasbourg, France; [3] Marmara University Faculty of Medicine Department of Pharmacology and Clinical; Pharmacology, Istanbul, Turkey
nihan.carcak@gmail.com

GAERS are resistant to the progression of kindling seizures beyond stage 2. The quantitative autoradiographic measurement of local cerebral blood flow (LCBF) by the [¹⁴C] iodoantipyrine autoradiographic ([¹⁴C]IAP) technique allows the precise mapping of brain regions in which the paradigm studied leads to perfusion changes. In the present study the brain regions involved in stage 2 seizures in both GAERS and non-epileptic rats (NEC) were mapped to define the nature of the brain areas involved in resistance to kindling.

Adult NEC (n=14) and GAERS (n=14) male rats were stimulated with electrodes implanted into the amygdala until they reach stage 2. LCBF rates were measured by the quantitative [¹⁴C]IAP technique bilaterally in 43 brain regions. Tracer infusion lasted for 60 s and started at 15 s before seizure induction.

Rates of LCBF increased in GAERS and NEC-stimulated groups compared to their respective non-stimulated controls. LCBF increase in stimulated GAERS was larger and more widespread than in stimulated NEC. LCBF increase in the somatosensory cortex, ventrobasal and anterior thalamic nuclei, hypothalamus, subthalamic nucleus, piriform, entorhinal and perirhinal cortex, amygdala, CA2 region of hippocampus, and substantia nigra was statistically significantly larger in stimulated GAERS compared to stimulated NEC. The present study shows that more brain regions are activated by kindling stimulation in GAERS compared to NEC. This widespread activation in GAERS concerns both the somatosensory cortex and thalamus which are involved in the mechanism of absence seizures as well as numerous limbic regions where spike-and-wave activity is not observed.

Keywords: Cerebral blood flow, [¹⁴C]iodoantipyrine, amygdala kindling, absence epilepsy, GAERS

O15

Effect of kainic acid on spike-and-wave discharges in rats with genetic absence epilepsy

Gurbanova A [1], Aker R [1], Sirvanci S [2], Demiralp T [3], Onat F [1].

Marmara University, School of Medicine, [1] Department of Pharmacology and Clinical Pharmacology, [2] Department of Histology, Istanbul University, School of Medicine, [3] Department of Physiology.

aytenazizova@yahoo.com

In this study we investigated the effects of intraamygdaloid injection of kainic acid (KA) upon spontaneous spike-and-wave discharges (SWDs), upon transition from the interictal to SWD state and the synaptic reorganization of

dentate gyrus mossy fibers as a marker of epileptogenesis in genetic absence epilepsy rats from Strasbourg (GAERS).

Five adult GAERS were stereotaxically equipped with a cannula into the right amygdala and EEG electrodes into the right hippocampus and cortex. KA (750 ng/ 300 nl) was injected unilaterally into the amygdala after one week recovery and basal EEG recording on the preinjection day. The number and duration of convulsive seizures and EEG recordings on the injection day and every other day for 2 months were evaluated. To analyse EEG changes during transition from interictal to SWD state, the power-spectrum of 2-second epochs immediately before and 10 seconds before SWD onset were computed. Then animals were perfused and vibratome brain sections were stained with neo-Timm's method.

During preinjection recordings a significant increase in 16-32 Hz frequency range was observed in the 2-second epoch immediately preceding SWD onset but was absent in the 10-second preceding SWD onset. After KA administration, animals had convulsive seizures for at least 3 hours. Time to first convulsive seizure was 107.3 ± 13.3 minutes and number of convulsive seizures during 3 hours was 50.8 ± 5.9 . Basal SWD activity disappeared immediately after KA injection for at least 24 hours. The cumulative SWD duration was 907.0 ± 174.9 seconds/hour in preinjection period whereas was 67.6 ± 37.9 seconds/hour in the first and 400.5 ± 165.5 seconds/hour in the fourth week after KA administration. The increased 16-32 Hz EEG power preceding SWD activity disappeared in the first week after KA injection. The spectral changes observed positively correlated with the number of SWDs. Mossy fiber sprouting was present in the dentate gyrus.

The KA-induced loss and re-appearance of SWDs and change in power of the 16-32 Hz frequency band preceding SWDs indicate an initiation and progress of epileptogenesis and an alteration in mechanisms related to the transition from interictal to SWD state. Our observation of mossy fiber sprouting supports these findings.

Keywords: GAERS, spike-and-wave discharge, kainic acid, epileptogenesis, power-spectrum.

O16

Formation of cerebral cavernous malformation expression pattern of PDCD10/Ccm3

Tanriover G [1], Louvi A [2], Demir N [1], Gunel M [2].

Department of Histology and Embryology [1], Akdeniz University School of Medicine, Antalya, Turkey; Department of Neurosurgery, Neurovascular Surgery Unit, Yale University, School of Medicine, New Haven, CT, USA [2].
gamzetanriover@yahoo.com

Cerebral cavernous malformation (CCM) is a neurovascular disease, resulting focal neurological deficits. This disease lesion is comprised of grossly dilated capillary-like vascular regions, maintained by a single layer of endothelium with little or no intervening neural parenchyma. Three CCM loci have been mapped which are Ccm1 (Krit 1), Ccm2 (Malcavernin), Ccm3 (PDCD10). Mutations in these genes cause autosomal dominant familial cerebral cavernous malformations (CCM). As just little is known about the function of this gene in disease pathogenesis so far, this study was focused on a well known programmed cell death gene 10 (PDCD10), Ccm3. The mRNA expressions of Ccm3 in the embryonic and postnatal mouse brain were analyzed by in situ hybridization and CCM3-specific polyclonal antibodies confirming their specificity. Thereafter CCM3 protein expression in cerebral and extra-cerebral (kidney, liver, lung, skin) tissues was examined by using immunohistochemistry. In embryonic mouse brain, Ccm3 mRNA was seen in the neural tube, ventricular zone, subventricular and intermediate zones, the cortical plate, the developing septum, striatum, midbrain, pons, cerebellum and medulla. In the post-natal mouse brain, Ccm3 expression in the olfactory bulb, neocortex, striatum, septal nuclei, hippocampus, dentate gyrus, thalamic and hypothalamic nuclei, inferior colliculus, the Purkinje cell layers and deep nuclei of the cerebellum and in many cells and nuclei in the medulla was detected. Similar to CCM1 and 2, the CCM3/PDCD10 protein was expressed in the neurovascular unit which is arterial endothelium, but not in venous structures in cortical, sub-cortical, and brain stem structures. In addition CCM3/PDCD10 was expressed in arterial, but not venous endothelium in extra-cerebral tissue. The expression pattern of CCM3/PDCD10 in multiple organ systems displays similarities and differences

to CCM1 and CCM2. Our results demonstrated that the Ccm3 gene was highly expressed in the neurovascular unit and in the arterial endothelium of structures within multiple organ systems including the brain. Our data suggest that provide further information about CCM lesion development and the role PDCD10 in angiogenic activity as a whole.

Keywords: Cerebral cavernous malformation, PDCD10, neurovascular unit, in situ, immunohistochemistry.

O17

An in-vitro model of transneuronal degeneration

Him A [1], Ozturk G [1], Cengiz N [2].

Yuzuncuyil University, Faculty of Medicine, Department of [1] Physiology, [2] Histology and Embryology, Van, Turkey.

ahim@yyu.edu.tr

Injury in some parts of the nervous system may result in damage and eventually death of the afferent and the efferent neurons as well as directly injured neuron itself. Investigation of this phenomenon called transneuronal degeneration could contribute to the understanding of the mechanisms of neuronal death which occurs with a delay after the traumatic and degenerative nervous system pathologies. The mechanisms of transneuronal degeneration have not fully been explained because there is no in-vitro model of transneuronal degeneration and it has been studied only in-vivo. In this study, to develop an in-vitro model of transneuronal degeneration, neurites of the dorsal root ganglion neurons cultured from young adult mouse were injured by cutting with a laser micro dissection device and the effect of this injury on the survival of the other neurons in the culture were analyzed. At the 48th hour of each culture neurites of about 3 neurons near each other were cut from a distance of 100-150 micron from the soma. Twenty four hours after the injury the ratios of the dead neurons were determined within an area of 2000 micron diameter around the injury center. These ratios were evaluated in two groups; close to the center (closer than 1000 micron) and far from the center (1000-2000 micron far). While the ratio of the dead cells was 7% in the cultures in which no injury was performed, it was 37% in the cultures in which neuronal injury was performed. The ratio of the dead cells near the center of the injury was 46% whereas this ratio was 29% in the area far from the center. These results showing that the injured neurons caused a significant increase in the death of the other cells in the culture compared to the cultures in which no injury was made ($p < 0.05$) indicate the presence of transneuronal degeneration. The finding that the ratio of the dead cells near the injury center is significantly higher than the ratio in the area far from the center ($p < 0.05$) shows that the effect of the injury decreases with distance and this could be related to the presence of more synaptic connections between the injured neurons and the neurons closer to the injury center. When the neurons were injured in calcium-free cultures there was no significant difference between the ratios of dead cells in the areas near center and far from center (39% and 33% respectively, $p > 0.05$). This finding suggests that transneuronal degeneration could spread through synaptic connections. Since the model developed in this study is practical and reliable, and since that it also allows the control of the in-vitro conditions, it can provide opportunity to test the hypothesized physiopathological mechanisms of transneuronal degeneration.

Keywords: degeneration, transneuronal, cell culture, mouse, dorsal root ganglion

O18

Advanced analysis of finger-tapping performance: A Preliminary Study

Barut C [1], Kiziltan E [2], Gelir E [3].

[1] Zonguldak Karaelmas University, School of Medicine, Department of Anatomy, Zonguldak; [2] Zonguldak Karaelmas University, School of Medicine, Department of Biophysics, Zonguldak; [3] Hacettepe University, School of Medicine, Department of Physiology, Ankara
cagbarut@yahoo.com

Finger-tapping test is extensively employed in quantitative assessment of upper extremity motor performance after rehabilitation and hand skill in occupations regarding hand usage that can affect work performance. Various systems including electromechanical counters or computer keyboards using word processing software are known to be employed in such tasks determining

total number of finger taps and intertap interval with a low time resolution. However, these systems did not take into account the time changes between consecutive taps. Aiming to encounter with this weakness, we designed this study in which single finger tapping test was applied to 38 male participants aged between 20-28 years using TanTong FingerTap system for right and left hands. Synchronous mean values of intertap intervals were calculated and the alteration patterns of intertap intervals with tap numbers were evaluated using numerical analysis methods.

Intertap interval value was detected to have periodic alterations within 20-30 ms intervals. Single finger tapping task is a complex motion which is known to be affected from audio and visual external stimuli, mood and physical status, physical and chemical factors which influence muscle, skeletal and nervous systems. Hence, explaining the movement with a single mean intertap interval value may give a general idea but this may lead to neglect the temporal effects of the aforementioned factors. For this reason, temporal alterations of the intertap intervals were evaluated by best curve fit method. The evaluations were performed using exponential and polynomial up to sixth degree curves. Although may not be the best fit, exponential and linear equations gave an idea about the general tendency of the motion ($R^2 < 0.50$). As the degree of the polynomial equation increased, correlation was also increased (6th degree polynomial, $R^2 = 0.71$), and it also reflected the alterations during the task together with the general tendency. Thus this reflected the multi factorial nature of the finger tapping task.

In conclusion, we suggest that it would be better to perform this test in isolated environments in which the aforementioned factors could be controlled during the studies evaluating motor coordination and hand performance. In addition, the evaluation of temporal alterations would bring new insight for future studies.

Keywords: Finger-tapping test, performance, motor coordination

O19

Effect of selenium on the compound action potentials of rat sciatic nerve

Ayaz M [1], Dalkilic N [1], Tuncer S [1], Bariskaner H [2].

Selcuk University, Meram Faculty of Medicine, Departments of [1] Biophysics, [2] Pharmacology, Konya, Turkey.

ayaz72@yahoo.com

The nervous system provides communication between various organs, governs the reactions to stimuli, processes information, and generates elaborate patterns of signals to control complex behaviors. Although selenium has been shown to induce some beneficial effects in several pathological conditions, it is still considered as a toxic mineral with a fairly small therapeutic window. In the present study, direct effects of sodium selenite ranging from 10-8 to 10-4 M were tested on rat sciatic nerve preparations. To assess the alterations on nerve preparation, compound action potentials were recorded with suction electrodes, and conduction velocity distributions were performed by collision technique. Measured parameters compared with Student t-test and $p < 0.05$ values were taken as significant. The evidence of toxicity was detected at 10-8 M concentration, and the degree of alterations was found to be dose dependent. Among all the parameters, the total compound action potential area ($A_{start} = 3.70 \pm 0.16$ ms x mV and $A_{-8M} = 3.04 \pm 0.14$ ms x mV), and the maximum depolarization points ($MD_{start} = 6.70 \pm 0.22$ mV and $MD_{-8M} = 6.04 \pm 0.18$ mV) were first to be affected by 10-8 M selenite induced toxicity. Latencies and conduction velocity distribution measurements showed that nerve fibers having intermediate conduction (20 – 35 m/s) velocities were first to be affected by the toxic doses. We conclude that despite the recent reports claiming the positive aspects of selenite administration, it is evident that the dose of supplementation must be fine-tuned to avoid the possible side effects.

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Keywords: Sciatic nerve, compound action potential, sodium selenite, conduction velocity group, toxicity

O20

Oscillatory components of visual Oddball responses in schizophrenia

Ergen M [1], Marbach S [2], Brand A [3], Basar-Eroglu C [2], Demiralp T [1].

Istanbul University, Istanbul Faculty of Medicine, Department of Physiology, Istanbul, Turkey [1]; Bremen University, Institute of Psychology and Cognition Research, Bremen, Germany [2]; General Hospital Bremen-East, Center for Psychiatry, Bremen, Germany [3]

mehmet.ergen@gmail.com

Impaired functions and the underlying dynamics in schizophrenia is still a matter of debate and impairments in working memory and attention has been widely considered as the crucial cognitive deficits in this disease. P3, an event related potential (ERP) that reflects the incorporation of a sensory stimulus into memory representations and the context in which it occurs, is reported to be reduced in schizophrenia. In the present study, chronic schizophrenia patients and their matched healthy controls performed an oddball task, in which two types of visual stimuli were repeatedly presented, and performers were required to count the rare stimulus type (25%) mentally, within a train of standard ones. Electroencephalography (EEG) epochs were recorded from 12 channels according to 10/20 system while they performed the oddball task. Amplitude and latency of the positive maximum in post stimulus 300-800 ms (P300) was measured. Oscillatory activity in EEG responses was investigated by wavelet transform (WT). To obtain the total power that includes both phase-locked and non-phase-locked activity WT was applied to single epochs and the absolute values of WT magnitudes were averaged, evoked activity was obtained by application of WT on average of the epochs. Late delta band (1-3 Hz) response, proved most pronounced time frequency component correlating with the P300, was evaluated by measuring the mean amplitude of the activity in post stimulus 300-800. ms. Evoked delta activity and P300 amplitude were both significantly reduced in schizophrenic group ($p = 0.022$, $p = 0.046$, respectively). However, the difference in total activity was non-significant. Differing in evoked activity that reflects phase locked activity, and non-significant difference in total activity that is sensitive to changes in amplitude of the oscillation, regardless of phase locking, suggests that the delta band response is weakly phase-locked to stimulus, i.e. the latency of the delta response is more variable across trials, in schizophrenic patients. Therefore, reduced P300 might be interpreted as disruption in temporal integration of neural circuits to the stimulus input, rather than neuronal loss in structures that are involved in P300 generation.

Keywords: Schizophrenia, electroencephalography (EEG), event related potentials (ERP), P300, Delta rhythm

O21

Stereologic cell counting on dorsal root ganglia of rabbits; an experimental study

Erdogan AR [1], Cevli SC [1], Malkoc I [1], Diyarbakir S [1], Gundogdu C [2], Aydin MD [3].

Department of Anatomy [1], Pathology [2], Neurosurgery [1], Medical Faculty of Ataturk University, Erzurum, 25240, Turkey.

elifcan@rocketmail.com

There are many studies mentioning the degeneration or cell depletion of dorsal root ganglia due to several diseases. Rabbits are generally preferred as the easiness of study and availability. In these studies the degeneration level is either given in the form of cell count or percentage. Eventhough the precise volume and number of cells in a ganglion must be known as a starting point to understand the changes in dorsal root ganglia morphology no publication is present in the literature giving those values as a standart. In this study we aimed to count the number of the cells in the dorsal root ganglia of 20 male hybrid rabbits which were two years old each, in order to show the effectiveness of this method and to predict the mean volume and cell number of T5-L10 dorsal root ganglia which may constitute a standart for further studies. We preferred the stereologic method as described by Cavalieri for the counting method. This method is very cheap and easy to apply and capable of giving precise cell count. These specimens were fixed in 10% formaline solution and embedded in paraffin blocks. They were stained with hematoxylin-eosin and they were observed under light microscope.

Ganglion volumes and number of the neurons (GNs) were counted with physical dissector method. The mean values were calculated as a result and standart deviaton was also reported. The numeric density which is the cell count in each volume unit was predicted and the number of total neurons was calculated by multiplying with volume of ganglia. In this study, the mean total volume of the spinal ganglions was calculated as $1.2 \pm 0.3 \text{ mm}^3$, the mean numerical density value was estimated as 20480 ± 250 (Neuron number/mm³) and the total number of cells was 20500 ± 3500 .

Keywords: dorsal root ganglions, cell count, Cavalieri, stereology.

O22

The protective effect of sildenafil in spinal cord ischemia

Kiyamaz N [1], **Yilmaz N** [1], **Mumcu M** [1], **Anlar O** [2], **Ozen S** [3], **Demir I** [1].

Yuzuncu Yil University, Faculty of Medicine Department of [1] Neurosurgery, [2] Neurology, [3] Pathology, Van, Turkey.

nejmikiyamaz@yahoo.co.uk

Prospective study of the neuroprotective activity of sildenafil in a rat spinal ischemia model. The present study involved 21 male Sprague-Dawley rats. The animals were divided into three groups. Serum physiologic was administered intraperitoneally to the eight rats in the control group at the beginning of reperfusion for a period of 20 minutes after abdominal aortal occlusion. Sildenafil (Viagra®) was administered as a 10 mg/kg/day intraperitoneal single dose to the eight rats in the sildenafil group at the beginning of reperfusion after 20 minutes of abdominal aortal occlusion. No occlusion was performed and no agent was administered to the five rats in the sham group, but the abdominal aorta was reached by means of surgical intervention. Before the animals were sacrificed, several physiological and biochemical parameters were investigated preoperative and postoperative motor functions were also assessed, and somato-sensory evoked potential (SEP) monitoring and histopathological examinations were carried out. No differences were found between the physiological and biochemical parameters in each of the three groups. Neurological scoring performed after reperfusion demonstrated a significant improvement in the neurological results relative to those of the control group over 48 hours in subjects that received sildenafil. These animals also showed better 24-hour SEP results, measured in terms of extended latency and decreased amplitude, than the control animals. A histopathological study showed reduced ischemic symptoms in rats that received sildenafil compared with those in the control group. However, no anomalies were observed in the sham group with respect to the histopathological and neurological findings. These results indicate that neurological damage due to spinal-cord ischemia–reperfusion injury can be reduced by sildenafil.

Keywords: Sildenafil, Somatosensory evoked potentials, spinal cord ischemia

O23

The effects of oral administration of Aloe Barbadensis on the central nervous system of rats

Kosif R [1], **Aktas R G** [2], **Oztekin A** [2].

Karaelmas University, Faculty of Medicine, Department of [1] Anatomy, [2] Histology-Embriology, Zonguldak, Turkey.

rengink@yahoo.com

Aloe Barbadensis is the most widely used both commercially and therapeutic properties. It has been used for an array of ailments since ancient times as a medicinal plant. There are more than 360 different species of Aloe Vera. Its products have been used in health foods for medical and preservative purposes. The objective of this study was to search the effects of Aloe Barbadensis on the rat's central nervous system; since there are limited studies on that issue. Gel form of Aloe Barbadensis is used in the study. It is commercial, preserved but otherwise untreated form of Aloe Barbadensis gel capsul. Female Wistar Albino rats were divided into three groups. Both study and control group were fed with standard chow and water ad libitum. In addition, 25 mg. (100mg/kg) Aloe Barbadensis and soybean oil had been given daily to the rats in the one group orally with gavages for 3 weeks. Soybean oil had been given daily to the rats in the other group and standard chow and water ad libitum

had been given third group. Tissue specimens from cerebrum, cerebellum, hippocampus and ventricular area were processed for the microscopic examination. All sections from each group were stained with Hematoxilene Eosin and Crezyl Violet. Our results indicate that Aloe Barbadensis did not have any clear toxic effects on both neurons and glial cells of the central nervous system in different areas. Cytoplasmic features of the neurons, Nissle bodies, axonal hillock, and nuclei of neurons were the same after the treatment. However; the relationship between the purkinje cells and the surrounding cerebellar tissue was decreased in the treated group. The other important finding was the change of ependimal cells at the ventricular zone: The number and the height of these cells were obviously increased. The single layered epithelium changed into the stratified epithelium in certain areas. It was also evident that microvilli and the cilia on the apical side of these cell increased dramatically. The capillaries in the region of choroid plexus were also dramatically increased. We believe that further studies related with these morphological changes will be helpful to understand the mechanism(s) of the similar transformation of the cells in different conditions.

Keywords: Aloe Barbadensis, rat, Central Nervous System, histologic examination.

O24

Hypothalamic ultrastructure of female rat during menstrual cycle.

Demir N [1], **Naftolin F** [2].

Akdeniz University Medical Faculty, Department of Histology and Embryology, Antalya, Turkey [1]; New York University School of Medicine Department of Obstetrics and Gynecology, New York, USA [2].

ndemir@akdeniz.edu.tr

There are some evidences which suggest that, the alterations estrogen causes on the structure of hypothalamic morphology affects the regulation of secretory functions of gonadotrophin releasing hormone-secreting neuroendocrine cells. It is thought that estrogen mediates the mechanisms that regulate synaptic plasticity of hypothalamic nuclei which are located at the top of the hypothalamic-pituitary-gonadal axis. In the present study, arcuate, paraventricular and ventromedial hypothalamic nuclei of female rats at proestrus, estrus and metestrus of menstrual cycle were investigated by electron microscopy. The differences that occur in these nuclei during menstrual cycle was determined by investigating synapse numbers and intercellular distances of the hypothalamic nuclei. As also shown by other studies, we have found significant differences in synapse numbers, especially in the axosomatic inhibitive synapse numbers according to the menstrual cycle phase. Moreover we have also found differences in measured intercellular distances. We have detected a significant increase in the distances between nuclei, and a significant decrease in inhibitive synapse numbers in the stages where estrogen levels were high. The morphological changes in periventricular hypothalamic site and the possible mechanisms involved in these changes were discussed according to the literature. As a result we conclude that the changes in estrogen levels during the menstrual cycle affect astroglial and neuronal morphology in the hypothalamic nuclei and that these effects may play important roles in cyclic hormonal regulation in the hypothalamic-pituitary-gonadal axis.

Keywords: Hypothalamus, morphology, estrogen, astroglia, neuron

O25

Capability of brain perfusion parameters in tissue classification

Bayram A [1,2], **Firat Z** [2], **Ozkan M** [1], **Kovanlikaya I** [2].

Bogazici University, Bio-Medical Eng. Institute[1], Bebek, Istanbul Yeditepe University Hospital, Radiology Department[2], Kozyatagi-Istanbul.

ali.bayram@boun.edu.tr

Perfusion-weighted MR imaging technique is based on indirect measurement of metabolite and oxygen exchange of a tissue in the capillary and venule scale, which is named perfusion, by tracking passage of an injected agent (bolus) through the brain tissue during MR scan.

Blood flow, blood volume, time to peak, mean transit time, which can be calculated via time based change of MR signal (perfusion curves) due to the contrast agent for each voxel, are widely used basic MR perfusion parameters. Thanks to these parameters and their relative increase or decrease, functional

or structural change within the same type of tissue could be separated, while other MRI techniques couldn't. Also perfusion curves makes separation of different tissue types possible to some extent.

Aim of this study is to probe specificity of MR perfusion curves and their derived parameters for basic tissue types by evaluating their success in tissue classification. Beside that, deriving new perfusion parameters from perfusion curves is aimed to increase the tissue classification.

Four patients were studied at 3T MR (Philips) machine. 5ml/sn flow rate of 0.2 mmol/kg contrast agent (Gd-DTPA) was administered with a power injector. 10 base total 60 GRE-EPI based images were acquired and used in analysis.

There are three stages in this work. First, 60 voxels were selected from the healthy artery, vein, gray matter, white matter regions were selected by a professional radiologist. Corresponding perfusion curves and basic parameters of these points were calculated offline at Philips ViewForum. Second, new perfusion parameters were achieved by modeling the dynamics following time to peak of perfusion curve. Summation of two exponentials was fitted to the data by Levenberg-Marquardt algorithm in this modeling procedure. In the final stage, raw perfusion curves, basic perfusion parameters and new perfusion parameters achieved at the second stage were separately used to classify tissues. Classification was performed by using backpropagation based neural networks. Success of classification was evaluated according to correct test outputs of neural network.

As a result, perfusion curves gave 72% correct classification beside that due to the modeling capability of basic perfusion parameters, correct tissue classification increased to 83%. New perfusion parameters represented in this work gave 90% correct tissue classification which shows that deriving new parameters from raw perfusion curves might represent tissue types more successfully.

Keywords: Perfusion weighted mri, Nonlinear models, nerve tissue, classification, Neural Networks.

POSTER PRESENTATIONS

P1

Imaging of neurons by atomic force microscopy: a literature review and the project started at Bilkent University

Gundogan M [1], Un M [2], Kacici OU [3]

Bilkent University Department of Physics [1], Department of Molecular Biology and Genetics [2], Ataturk University, Faculty of Medicine [3]
gmustafa@ug.bilkent.edu.tr

Since its invention in 1986 by Binnig, Quate and Herber [1], AFM became an interdisciplinary tool for imaging non-conducting surfaces with sub-nanometer resolution. Its major advantage over STM [2] is that, AFM can be used to imaging and manipulating biological samples. AFM is also a potential tool for nanosurgery [4]. In this study, we summarize the previous works done by Parpura et. al [3] and McNally et. al. [4]. Comparison of AFM imaging of biological structures with other imaging techniques such as scanning electron microscope (SEM) [5] [6] showed that AFM is as successful as other techniques in imaging the general morphology and would be more accomplished for getting information about vertical structures [6]. Finally we discuss sample preparation procedures and present the project that is just started at Bilkent on imaging neuron cells.

Keywords: neuroscience, neurons, AFM, nanotechnology, nanosurgery

P2

Effects of various parameters on binocular rivalry

Bolukbasi G, Guclu B.

Biomedical Engineering Institute, Bogazici University, Istanbul, Turkey.
gamzebolukbasi@gmail.com

In daily life, two eyes see similar images and there is no perceptual competition. The inputs from the eyes are compatible and the images are fused with stereopsis in the brain. On the other hand, if two eyes are presented with incompatible visual stimuli, binocular rivalry occurs in the

brain. In this condition, the visual perception alternates every few seconds from one monocular stimulus to the other or an unstable piecemeal mixture is seen. Binocular rivalry is affected by many parameters like contrast, form and motion velocity. In this study, the effects of flickering frequency (0.25 Hz or 0.5 Hz), duty factor (%37.5, %50, %62.5, %75, %87.5), diameter of the target (2.5 cm, 5 cm or 7.5 cm) and luminance of the monocular image (24.2 cd/m², 21.3 cd/m² or 18.3 cd/m²) on binocular rivalry were tested. It was expected that the temporal rivalry percentage would be decreased when the stimuli is flickered in contrast to static stimuli. It was also expected that the rivalry percentage would be increased as the duty factor is increased, but would stay constant with respect to frequency. The visual stimuli used in the experiments were a square and a disc. Six subjects determined binocular fusion times by pressing a button. The mean rivalry percentage value of static stimuli was 12.49 % ± 10.09 % (mean ± SD, n=16). The mean rivalry percentage of flickering stimuli was 1.97 % ± 3.30 % (mean ± SD, n=240). The results showed that the rivalry occurrence was reduced when stimuli were flickered in contrast to static stimuli (t-test; P=0.013). However, the frequency (ANOVA; P=0.921) or duty factor of the flicker (ANOVA; P=0.204) did not have any effect on the total rivalry time. Moreover, the locations of the monocular images were interchanged in order to test visual asymmetry effects. No such effects were found. Additionally, changes in the size (ANOVA; P=0.898) and the luminance of the target (ANOVA; P=0.509) did not cause any differences in the total rivalry time. The results of the study may be helpful for binocular contrast experiments, because the temporal rivalry percentage is greatly reduced with flickering stimuli.

Keywords: vision, perception, flickering stimuli, frequency, duty factor, luminance

P3

Classification of single tactile units of frogs by using von Frey monofilaments

Ucar K, Guclu B.

Biomedical Engineering Institute, Bogazici University, Istanbul, Turkey.
korcanucar@gmail.com

Twenty-four single mechanoreceptor afferent units with fast conducting axons in the sciatic nerve innervating the plantar surface of the hind foot were isolated for electrophysiological recording in pithed frogs. Ten rapidly adapting (RA) units and fourteen slowly adapting (SA) units were classified based on their discharge patterns. In the neural response to von Frey indentations, RA units had rapid transient discharges with maximally five sequential action potentials. SA units had sustained activity during steady pressure on the receptive field. Two types of SA units were distinguished. One group of SA units (SA type I) generated irregular discharge patterns with gradually decreasing rates when ramp stimulus was applied. The other group (SA type II) generated fewer transient discharges followed by sustained regular discharges lasting more than two seconds. SA I and SA II units were further differentiated based on several other features: spontaneous firing, transient response and interspike interval histograms. The property of regularity in firing was determined quantitatively by calculating coefficient of variation. SA type I units had high coefficients of variation (0.24-0.75), but the SA type II units had lower coefficients of variation (0.02-0.16). SA units generally discharged with higher latencies than the RA units. RA units also differed from SA units by their higher conduction speeds. The average latency of the first spike was 33 ms for RA units and 45 ms for SA units. There was a significant difference between the conduction speeds of RA and SA units (t-test; P=0.039). There was no significant difference between the conduction speeds of SA I and SA II units (t-test; P=0.082). The thresholds were calculated as grams. RA units had an average threshold of 0.169 ± 0.167 g (mean±SD, n=10). The average threshold of SA units was 0.162 ± 0.143 g (mean±S.D). No significant difference was found between the thresholds of RA and SA units (t-test; P=0.057), and between the thresholds of SA Type I and Type II units (t-test; P=0.500). Spike counts for RA units did not change as a function of the indentation level, but SA spike counts increased as a function of the indentation amplitude (r=0.927, P=0.023). The results indicate that frog tactile units are similar to mammalian tactile units.

Keywords: mechanoreceptor, rapidly adapting unit, slowly adapting unit, frog skin

P4

Creutzfeldt-Jacobs Disease: An occupational risk for anatomists

Demiryurek D [1], Bayramoglu A [1], Tuccar E [2].

Hacettepe University Faculty of Medicine, Department of [1] Anatomy, Ankara, Turkey; Ankara University Faculty of Medicine, Department of [2] Anatomy, Ankara, Turkey.

mdeniz@hacettepe.edu.tr

Like all other occupations, being a member of an anatomy department has its own risks. Cadavers are the main studying materials of anatomists but may pose infection risks to people who handle them during embalming procedures or dissections. Prions cause transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease (CJD) and Gerstmann-Straussler-Scheinker syndrome (GSS). This infectious pathogen present particular risk for those who handle and dissect cadavers. Specific safety precautions are necessary to avoid accidental disease transmission from cadavers before and during dissection and to decontaminate the local environment afterward.

This presentation aims to give detailed information about the disease and to suggest safety guidelines for the protection of all who handle cadavers.

Key words: Creutzfeldt-Jacobs Disease, cadaver

P5

Morphometry of the cervical vertebral pedicles as a guide for transpedicular screw fixation

Kayalioglu G [1], Erturk M [1], Varol T [2], Cezayirli E [2].

Ege University, Faculty of Medicine, Department of Anatomy [1] Izmir, Turkey, Celal Bayar University, Faculty of Medicine, Department of Anatomy [2], Manisa, Turkey.

gulgun.kayalioglu@ege.edu.tr

Anatomical measurements of the cervical pedicle in a large series of human cervical vertebrae from 48 individuals were obtained to reduce the incidence and severity of complications caused by transpedicular screw placement. The greatest pedicle length was at C-3 and the greatest pedicle width was at C-6. Pedicle width and lateral mass thickness gradually increased from C-3 to C-6. Pedicle height and interpedicular distance increased from C-3 to C-5, and decreased slightly at C-6. The lateral mass-pedicle length was greatest at C-4. The present study found right-left differences for the pedicle-spinous process distance at C-6 ($p < 0.05$). Pedicle width and height were smaller than those reported in earlier studies, especially at C-3 and C-4, whereas the increasing pedicle widths at C-5 and C-6 were appropriate for pedicle screw fixation.

Key words: cervical pedicle, anatomy, right-left difference, morphometry

P6

Innervation features of the extraocular muscles

Erdogmus S [1], Govsa F [2], Celik S [2].

[1]Mustafa Kemal University, Tayfur Ata Sokmen Medical Faculty, Department of Anatomy, Antakya, Turkiye; [2]Department of Anatomy, Faculty of Medicine, Ege University, Izmir, Turkiye.

senemerdogmus@gmail.com

Several surgical approaches have been used for exposure of lesions within the orbit. Most authors have not focused on the exposure of specific structures within the orbit, such as retroorbital region, optic nerve and deep orbital apex. Many large lesions especially tumors, arteriovenous malformations, hematomas can cause damage on the orbital part of the oculomotor nerve. During surgical approaches are important detailed anatomy knowledge regarding neural, muscular, vascular and neighboring structures.

A total of 44 cadaver fixed in formalin were dissected for this study. The vascular structures were perfused with colored latex to facilitate their definition. In this anatomic study, orbit was investigated at two divisions as superior and inferior. In the superior division, the levator palpebrae superioris muscle, the superior rectus muscle, the superior oblique muscle were examined. In the inferior division, the medial rectus muscle, the lateral rectus muscle, the inferior rectus muscle, the oblique inferior muscle and the ciliary ganglion were examined. The diameter of the oculomotor nerve within the superior orbital fissure was measured as 2.10 mm on the right

and 2.09 mm on the left. The diameter of branch innervating the superior rectus muscle was measured as 1.0 mm on the right and on the left. The area nervosa of the inferior rectus muscle was 2.42 mm on the right and 2.64 mm on the left. The area nervosa of the lateral rectus muscle was 3.55 mm on the right and 3.43 mm on the left. In this study, detailed knowledges regarding innervation features of the extraocular muscles were attained.

Key words: orbit, extraocular muscle, innervation, anatomy, surgery

P7

Assessment of head and neck development in children with hemiplegic cerebral palsy using anthropometric measurements

Uygun R, Ozen OA, Bas O, Caglar V, Songur A.

Afyonkarahisar University Faculty of Medicine, Department of Anatomy, Afyonkarahisar, Turkey.

fztramazan@mynet.com

Cerebral Palsy is a neuro-developmental disorder resulting from non-progressive injury of immature brain tissue. Permanent and also changeable movement disorders and impairment of posture are also seen in CP. Our objective was to study the effects of hemiplegic cerebral palsy (HCP) on the development of head and neck. We measured the anthropometric parameters such as head circumference, neck circumference, head width, head length, face height, distance between the pupils both in the children with HCP and in the normal children. The results were compared. We found that head circumference was 49.1 ± 2.4 cm, head width was 13.8 ± 0.8 cm, head length was 15.8 ± 1 cm, face height was 11 ± 1 cm, face width was 7.8 ± 1 cm, distance between the pupils was 5.4 ± 0.6 cm and neck width was 7.9 ± 0.8 cm in the children with HCP. The results of these same parameters in normal children were 51.1 ± 1.6 cm, 14.6 ± 0.6 cm, 16.1 ± 0.7 cm, 11.2 ± 0.6 cm, 8.9 ± 0.6 cm, 5.5 ± 0.4 cm, 8.6 ± 0.7 cm respectively. Head circumference, head width, face width, neck width values were significantly higher in normal children than those in the children with HCP. We think that impairment of the brain development due to neurodegeneration accounts for the low values seen in the anthropometric measurements of the head in the children with HCP and decreased neck width values may be associated with poor nutrition in the same group.

Keywords: hemiplegic cerebral palsy, anthropometry, measurement, head development, neck development.

P8

Investigation of fibre structure of olfactory tract in human

Akcer S [1], Ozen OA [1], Songur A [1], Bas O [1], Sahin O [2], Kucuker H [3], Uzun I [4].

Kocatepe University School of Medicine, Department of [1] Anatomy [2] Pathology [3] Forensic Medicine, Afyonkarahisar, Turkey.; [4] Council of Forensic Medicine, Ministry Justice, Istanbul, Turkey.

sakcer@gmail.com

Nervus olfactorius (1st cranial nerve) is a collection of sensory nerve fibres. Olfactory cells of N olfactorius (bipolar ganglion cells) is present in the nostrils (regio olfactoria) from where they extend to the bulbus olfactorius. The aim of this study was to investigate the fibre structure of the tractus olfactorius, which is an important neuronal junction.

Forty bulbus and tractus olfactorius tissue samples were obtained from 20 cadavers for analysis. Tissue samples were stained with H&E (Hematoxylin-Eosin) and histologically examined. Macroscopic examination revealed that the lengths of left and right bulbus olfactorius were 0.74 ± 0.02 cm; while the length of left and right tractus olfactorius, located in the sulcus olfactorius, was 4.82 ± 0.13 cm. When examined microscopically, a layered structure of the olfactory bulb was immediately apparent. These layers ($n=6$) were; the layer containing olfactory nerves without myelinated axons, the glomerulus layer, molecular and outer granular layer, mitral cell layer, inner granular layer and the layer of tractus olfactorius.

In the light of our findings and information available in literature, it was found that the fibrous structure of tractus olfactorius contains, in addition to mitral and tufted cells in the bulbus olfactorius, efferent axons leaving higher brain regions from the anterior nucleus olfactorius and the opposite bulbus olfactorius.

Key words: The olfactory tract structure, olfactory bulb, olfaction

P9

Facial pain, vertigo and tinnitus due to vascular compression of multiple cranial nerves

Yerdelen D [1], Koc F [2], Koc Z [3].

Baskent University Faculty of Medicine, Department of Neurology [1], Adana, Turkey, Cukurova University Faculty of Medicine, Department of Neurology [2], Adana, Turkey, Baskent University Faculty of Medicine, Department of Radiology [3], Adana, Turkey.

vahidedenizy@gmail.com

Compression of 5, 7 and 8. cranial nerves by abnormal changes like loop, tortuosity, and ectasia in vascular structures that form vertebrobasilar system may develop different neurological symptoms like vertigo, tinnitus, hypoacusia, hemifacial spasm and trigeminal neuralgia. A 52-years-old man was admitted to the clinic with complaints of pain located to upper and left part of face triggered by stress, making awake from sleep and becoming intensified through evening for 18 years, tinnitus prominent on the left, and positional vertigo developing occasionally for 5 years. Headache was recurring once a 10-15 days while taking 200 mg/day carbamazepine, and without this treatment, the frequency and severity was increasing. He and his family didn't have any other diseases. The physical and neurological examinations were normal. Cerebral MRI and MR angiography showed tortuosity in both of the vertebral arteries and basilar artery, and external compression of trigeminal (5) ve 7, 8. nerve complex by intradural segment of left vertebral artery. Internal acoustic channel MRI revealed compression of 7,8. nerve complex by left basilar artery. Brainstem evoked potential study was normal. Audiometric test was normal except a mild asymmetry (right 3 decibel, left 5 decibel).

As a result; neurological symptoms due to compression of one or two of 5, 7 and 8. cranial nerves by vascular abnormalities of vertebrobasilar system have been reported. This case shows difference because of presenting compression of 3 nerves together.

Key words: facial pain, vertigo and tinnitus, vascular compression and cranial nerves.

P10

Investigation of the course of trigeminal nerve in the cranial base and histological analysis

Songur A [1], Acar T [1], Bas O [1], Uzun I [4], Sahin O[2], Kucuker H [3], Ozen OA [1].

Kocatepe University, School of Medicine, Department of [1] Anatomy [2] Pathology [3] Forensic Medicine, Afyonkarahisar, [4] Council of Forensic Medicine, Istanbul, Turkey.

tolgahanacar@hotmail.com

Trigeminal nerve (Cr5) is root part and trigeminal ganglia (TG), locates to area, where important attachments expose to surgeries, often. Anatomical and histological studies of the Cr5 and TG were aimed to increase success of the surgery. Additionally, in this study, it was aimed to investigate anatomical details and variations of the related connections or structures which effect Cr5.

In our study totally 40 Cr5's intracranial parts were examined and taken sample structure from 20 forensic autopsy cadaver. The intracranial course of Cr5 was noted carefully, and the possible types of variation were investigated. Then, tissue examples were taken and these were painted with Hematoksilen-Eosin and Mallory's anilin blue collagen stain to make histological investigation of the tissues.

Macroscopically, Cr5's length was found as 25.32±2.90 mm and TG's wideness as 13.5±1.2 mm. In two cadaver motor roots were located at the bottom of the radix sensory, and the other cadavers were located at medial. Cr5 located nearly especially to vascular structures.

Microscopically, the total number of bundles was found as 71.75±8.20. The diameter of the fibers of the big fasciculus was found as 9.11±0.98 µm, and the diameter of the fibers of the small fasciculus was found as 3.17±0.26 µm. Fibers with big diameter observed as motor fibers, and the fiber with small

diameter observed as sensory fibers. Histologically, satellite cells were observed more in TG. Additionally, the difference between ganglion (2/5) and neurons (1/6) according to the ratio of the neuron and collagen cause to think us about making deeper investigation on this topic.

In the conclusion, we think that the result of our survey will contribute to country's demography, to success on surgery, and to clarify possible different diseases.

Keywords: trigeminal nerve, trigeminal ganglia, anatomy, histology.

P11

A methodological study to induce optic nerve crush

Sarikcioglu L [1], Demir N [2,3], Demirtop A [1].

Akdeniz University, Faculty of Medicine, Department of Anatomi [1], Histology and Embryology [2], Akdeniz University, Faculty of Medicine Electron Microscopy Unit [3], Antalya, Turkey.

sarikcioglu@akdeniz.edu.tr

Various crush methods are available in the literature. It is often difficult to compare results obtained by different investigators on nerve compression injuries, owing to differences in method of pressure application and noncomparable pressure levels. In the present study, we described a new method to crush the optic nerve by using a specially designed and commercially available device. We think that standardization of the compression methods is necessary to compare interlaboratory results.

Keywords: optic nerve, crush injury, crush time, yasargil aneurysm clip

P12

Macroscopic evaluation of the sciatic nerve neovascularization after stripping of the vasa nervorum

Sarikcioglu L, Demirel BM, Yildirim FB.

Akdeniz University, Faculty of Medicine, Department of Anatomy, Antalya, Turkey.

sarikcioglu@akdeniz.edu.tr

Peripheral nerve trunks are well-vascularized structures where a well-developed collateral system may compensate for local vascular damage. Vasculitis in nerve has a predilection for epineurial vessels and causes to the peripheral neuropathy, which is a major clinical feature of primary and secondary systemic vasculitides. In the present study, we created a vasculitic neuropathy model and for this purpose vasa nervorum were stripped. We examined neovascularization by three days interval using stereomicroscope. Therefore, we found that the model we described is an appropriate method. Additionally we tried to find if the neovascularization was originated from internal plexus to external plexus, or vice versa.

Keywords: vasculitic neuropathy, sciatic nerve, neovascularization

P13

The variations of vertebrobasilar arterial system

Songur A [1], Gonul Y [1], Bas O [1], Ozen OA [1], Toktas M [1], Kucuker H [2], Uzun I [3].

Kocatepe University Medical School Department of [1] Anatomy and [2] Forensic Medicine, Council of Forensic Medicine, Istanbul.

yucelgonul@yahoo.com

Vertebrobasilar system (VBS) is an important structure which supplies blood to the posterior parts of the brain stem, spinal cord, cerebellum and cerebrum. Many kind anomalies are seen in VBS like all the other vessels. Clinicians must consider the possibility of variations while making diagnosis or giving treatment. The aim of our study was to demonstrate the possible variations of VBS in Turkish population and to discuss these comparing with the literature. VBS which were taken from 109 forensic autopsies and 1 cadaver in Afyonkarahisar and Istanbul regions were studied and photographed. The widths of vertebral artery (VA) and basilar artery (BA) were measured; dominance and hypoplastic arteries and also the types of variations and their sites were determined. Proportional correlations were established.

In 21.2% of the cases left VA, in 17.3% of cases right VA were dominant. Hypoplastic VA was observed as 20.2% in the right, 14.4% in the left and

4.8% bilaterally. Vertebrobasilar junction (VBJ) was found to be at the level of medullopontine sulcus (20%), below the sulcus (67%) and above the sulcus (12%). BA variations were observed as the duplication of the proximal segment (0.9%) and the duplication of the distal segment (1.8%). Anterior spinal arteries (ASA) were originating as a single trunk in 12.5% of the cases and it was arising from a transverse anastomosis connecting VA's in 6.3% of the cases. Furthermore 15.6% of the ASA were double. In 3.6% of the cases left superior cerebellar artery (SCA), in 7.2% of cases right SCA was dominant. The variations of SCA were early bifurcation (7.2% in the right, 12.7% in the left), fenestration (4.5% in the right, 7.2% in the left), duplication (14.5% in the right, 12.7% in the left), and origin as a common trunk (6.3% in the right, 10% in the left). In 20% of the cases left posterior cerebral artery (PCA), in 15.4% of cases right PCA was dominant. Furthermore many atheroma plaques were observed in various arteries especially in older cases. The incidence was found to be 30% in BA.

Our results show that a high percentage of variations can be seen even in a small number of cases. We believe that our data are clinically important because variations are a factor which increases the incidence of aneurysm and thrombus. We also think our results will contribute to the demography our country and to clinical medicine.

Keywords: variation, artery, vertebral, basilar, vertebrobasilar system.

P14

Volumes estimation of brain and medulla oblongata using stereology on MR images, in 2nd decade

Keles ON [1], Malkoc I [2], Kaciki OU [1], Unal B [1].

Dept. of Histology and Embryology [1], and Anatomy [2], Medical Faculty, Ataturk University, 25240, Erzurum, Turkey.

imalkoc@atauni.edu.tr

Stereology is a sampling technique used to generate mathematically unbiased estimates of geometric properties of three-dimensional structures based on two-dimensional slices of the object. The purpose of this study is to estimate brain and medulla oblongata volumes were obtained from sections of MR images using the Cavalieri estimator in combination with point counting which is one of stereological methods.

In this study, we evaluated brain MR images of 10 health volunteers and groups were constituted 5 female and 5 male in the 2nd decade. Transfer MR brain images (5 mm section thickness and 1,5 gap, approximately 16-17 sections for brain and 3-5 section for medulla oblongata) were used for estimation. Stereological software (version 6.0, Microbrightfield, Colchester, VT) was used to estimation volumes. The size of the point counting grid was predicted to receive a coefficient of error (CE) in an appropriate range which was less than 5%. Handled data was analyzed statistically by SPSS for Windows version 13.0 (independent samples T test).

At the end of our stereological estimations, mean brain volumes and were 1131 cm³ and 1015 cm³ in men and women, respectively. Also mean medulla oblongata were 503 cm³ in men and 438 cm³ in women. There was found many statistical differences in terms of both brain and medulla oblongata volumes ($p < 0.05$). The ratio between volume of brain and medulla oblongata were 2,24 and 2,10 in men and women, respectively.

It is concluded that MRI estimated brain and medulla oblongata volumes in vivo may provide an index of anatomical structures.

Keywords: Brain; Medulla Oblongata; MRI; Volume; Stereology

P15

An interdisciplinary approach to consciousness

Atabay KD.

Anadolu University, Department of Biology, Eskisehir, Turkey.

kdatabay@gmail.com

Consciousness can be defined as state of mind that is formed by self-awareness, intentionality, intelligence, sentience and emotional codes. Basically, consciousness has two phenomenal properties; active consciousness which comprises self-awareness and passive consciousness that leads us to 'qualia' (properties of sensory experiences). A general definition like that conceals many aspects about consciousness. During the processes of mind; some

occurrences like circular reasoning (different mental levels affecting and determining each other), non-computability, quantum entanglement, chaos interactions, parallelism and simultaneousness are effective on consciousness. In order to acquire a universal point of view, we can use reductionism for the application of physics and philosophy on consciousness. According to the incompleteness theorem of Godel; if a system tries to define itself by using its own elements, this will produce a paradox for that system. This shows us that we may not manage to define the consciousness concept because of the existence of circular reasoning -like a man thinking about the dynamics of his own mind or a book that is about books-. At this point, the definition for consciousness will always be incomplete because one will use his/her own consciousness to define consciousness and this will produce circularity. However, this study observes the correlation of Hameroff-Penrose theorem claiming neuronal microtubules produces quantum mechanical properties in brain, Godel's incompleteness theorem, circularity, light cones and lastly chaos theory on consciousness and tries to acquire a new synthesis on the understanding of consciousness.

Keywords: consciousness, microtubules, Hameroff-Penrose, Godel's incompleteness theorem, circular reasoning.

P16

Effects of embryonic neural stem cell therapy on DNA damage levels of different tissues in acute and chronic spinal cord injured rats

Dagci T [1,2], Konyalioglu S [3], Guleli S [3].

Ege University, Department of Physiology, School of Medicine [1], Center for Brain Research [2], Department of Biochemistry, Faculty of Pharmacy [3], 35100, Bornova Izmir Turkey.

taner.dagci@ege.edu.tr

The embryonic neural stem cell (ENSC) therapy are being applied experimentally to a wide range spinal cord injury (SCI), however, the effects of the ENSC therapy on oxidative stress and cell death, have not known. For this purpose, DNA damage of different tissues and spinal cord (SC) of lesioned, and the SCI+ENSC therapy groups were analyzed by using Comet assay. The parameters used to evaluate DNA damage are the 'tail%' (T %), 'tail moment' (TM) and 'tail length' (TL) levels. Thirty adult male Sprague Dawley rats were used in four experimental groups (n=5): Acute sham, chronic sham, acute SCI, chronic SCI, acute SCI+ENSC and chronic SCI+ENSC. DNA-damage levels were found to high in all regions of SC in the chronic and acute injured animals compared to the acute and the chronic sham-operated controls (A-sham and C-sham). The ENSC therapy significantly decreased DNA-damage levels in both of study groups. Furthermore, we found significant increases of these parameters levels in brain and kidney of chronic SCI group compare to C-sham. Thus, the chronic SCI was resulted in the generation of oxidative-DNA damage in brain and kidney of rats. However, oxidative DNA damage of acute SCI rats remained unaltered in brain and kidney. The ENSC transplantation decreased the comet assay parameters in brain, but this therapy has not found to effect kidney tissues. The ENSC therapy found effective DNA damage in all the SC in chronic and acute injury, meantime, this therapy was decreased DNA damage of only brain tissue samples in the chronic SCI rats.

Keywords: spinal cord injury, embryonic neural stem cell therapy, tissue-DNA damage, Comet assay

P17

The interaction between Elk-1 and neurocytoskeleton

Demir O [1,2], Karabay A [1], Aksan Kurnaz I [2].

Istanbul Technical University, Department of Molecular Biology and Genetics [1], Yeditepe University, Department of Genetics and Bioengineering [2], Istanbul Turkey.

odemir@yeditepe.edu.tr

TCF subfamily of ETS-Domain transcription factors, Elk-1, Net and Sap1 are commonly known to be involved in regulation of cell proliferation in response to MAPK signalling. However, it has been previously shown that Elk-1 mRNA and protein is present in the adult rat brain, and in particular the presence of Elk-1 protein in axons and dendrites indicates that Elk-1 might have a different role in neurons. Regardless of its functional role,

Elk-1 -being a transcription factor- has to be transported to the cell's nucleus in order to carry out this function. To investigate this possibility, we have studied whether there is any interaction between Elk-1 protein and neurocytoskeletal elements such as microtubules. We successfully show that bacterially expressed GST-Elk-1 fusion protein can directly interact with purified and reconstructed microtubules from brain in GST-pulldown assay. This interaction is currently being investigated in immunoprecipitations with various neural and non-neural cell lines. In addition to that, we observed that Elk-1 co-localizes with beta tubulin in proximal and distal axon regions in SH-SY5Y neuroblastoma cell lines using confocal microscopy. These data will be confirmed in primary neural cells, and we are also currently carrying out similar interaction and colocalization studies with neurofilaments. The data altogether indicates that Elk-1 can indeed interact with neurocytoskeleton, however we are yet to unveil the relevance of these interactions and how signaling cascades might regulate Elk-1 binding and/or transport.

Keywords: Elk-1, neuron, neurocytoskeleton

P18

Radio frequency radiation (CW) effects on blood brain barrier (BBB) of female rats

Sirav Aral B, Seyhan N.

Gazi University, Faculty of Medicine, Department of Biophysics, Ankara, Turkey.

bahriyes@gazi.edu.tr

Increasing use of mobile phones and associated base stations are becoming a widespread source of Radio Frequency Radiation (RFR) which is the part of non-ionizing radiation. Mobile phone's antenna is very close to the user's head during normal use of the telephone and there is concern about the level of RFR emissions to which the brain is being exposed. There are some studies on the relation between the use of mobile telephones and headaches, brain cancer and the permeability of Blood Brain Barrier (BBB).

We investigated effects of CW – continuous wave - 900 MHz and 1800 MHz RFR on the permeability of BBB of female rats. Twenty seven wistar albino female rats (216.85 ± 24.72 g) were used in the study. They were divided into 3 groups; in the first group, animals used as control (Group I, n = 9), in the second and third groups (Group II, n = 9, Group III, n = 9) exposure to 900 MHz (13.9 V/m – 12.8 V/m) & 1800 MHz (13 V/m – 12.3 V/m) RFR, respectively, in the near field condition with 20 minutes of exposure period was used. The permeability of BBB was determined by Evans Blue (EB) dye. It was given by i.v. injection via tail vein prior to the exposures and had been used as a tracer for serum albumin. EB solution was given to all groups. After the exposure, cardiac perfusion was performed and then brains were taken out. Samples were analyzed using spectrophotometric method. Evans blue dye content was found to be 0.14 ± 0.013 mg % in the whole brain in the control animals, 0.13 ± 0.03 mg % in the 900 MHz exposed group and 0.11 ± 0.02 mg % in the 1800 MHz exposed group. No statistical variance found between the two exposed groups (p > 0.01). There was no statistically significant difference between exposed the groups and the control group (p > 0.01), either.

Sex differences have been reported for many structures and functions of central nervous system. In this study, results have shown that 20 minutes of RFR exposure of 900 MHz and 1800 MHz did not induce any effect on the permeability of BBB in female rats. Female BBB permeability is higher than male BBB permeability thus; females could be more vulnerable to RFR than males.

This study was supported by grant from Gazi University Research Foundation, No: 01/2005-78.

Keywords: Permeability of the Blood Brain Barrier (BBB), Evans Blue (EB), Radio Frequency Radiation (RFR), Spectrophotometric Method, Mobile Phones

P19

Searching the mechanism of conditioning lesion effect in mouse primer neuron culture

Kaval Oguz E [1], Cengiz N [2], Ozturk G [3].

Yuzuncu Yil University, Education Faculty, Department of Biology [1], Van, Turkey, Yuzuncu Yil University, Faculty of Medicine, Department of Histology&Embryology[2], Van, Turkey, Yuzuncu Yil University, Faculty of Medicine, Department of Physiology[3], Van, Turkey.

nurettincengiz@hotmail.com

Once a peripheral nerve is injured, a second injury increases nerve regeneration. The primary lesion causing this increase is referred to as 'conditioning lesion'.

In this study, to investigate conditioning lesion effect, two groups of mouse were used. In the first group sciatic nerves were cut and waited for 3 days to let DRG neurons to be conditioned. At the end of 3 days L4-L5 DRG from these animals and the animals of the control group that had not been conditioned were removed and primer sensory neurons were cultured. The cultures of these two groups were imaged by time lapse microscopy system. The images were analysed for several axon regeneration parameters. It was observed that around the 12. hour conditioned cells had a significantly higher rate of regeneration that was not seen in control group and that this rate was reduced to a basal level by the 24. hour and a second peak was observed around the 40. hour. Control preparations on the other hand had a peak that was progressively reached over 30. hours which was not seen conditioned neurons. Control cells then had reduction in regeneration rate and exhibited another peak around 45. hours. The results suggest that the conditioned neurons contain some protein or their m RNAs at their disposal; they can have a much earlier and faster regeneration.

Keywords: dorsal root ganglion, conditioning lesion, regeneration

P20

The effects of non-selective NMDA receptor antagonist memantine on learning during the 'kindling' procedure

Sahiner M, Erken G, Kursunluoglu R, Genc O.

Pamukkale University, Medical School, Department of Physiology, Denizli, Turkey.

aysemelike@pau.edu.tr

Hippocampal kindling is a well defined epilepsy model but there are few studies showing the changes in learning parameters accompanying neuroplastic changes in hippocampus of kindled rats. In our study we aimed to observe the effects of non-selective NMDA antagonist memantine on water maze learning parameters in early kindling time period.

40 male Wistar rats were taken to the study in 5 groups (8 in each group: Control, sham, memantine, kindling, kindling+memantine). We used modified water maze learning model for the learning procedure. Memantine has been applied intraperitoneally as follow: 20 mg/kg for once and then 2x1 mg/kg/day for 7 days.

Our findings has shown that memantine has a positive effect on water maze learning parameters. Escape latencies and path length are both better in memantine, kindling and kindling+memantine groups than in control and sham groups. In the 13th 'choice day' only the kindling group's PL and EL performance was impaired. We emphasize though memantine is a non-selective NMDA receptor antagonist, its' non-selective properties might be the reason for the modulating effects on learning.

Keywords: kindling, epilepsy, NMDA receptor, learning, memantine

P21

Investigations on analgesic actions of venoms of *Androctonus* and *Mesobuthus* species

Aydin S [1], Caliskan F [2], Bektas N [1], Cakmak A [1].

Anadolu University Faculty of Pharmacy Department of Pharmacology [1] 26470 Eskisehir, Turkey, Eskisehir Osmangazi University Faculty of Science and Letters Department of Biology [2], 26040 Eskisehir Turkey.

saydin@anadolu.edu.tr

Venom of *Androctonus* species is known as one of the most toxic ones on the earth. Due to previous reports of scorpion venoms on analgesia and ion channels, analgesic actions of venoms of *Androctonus* and *Mesobuthus* species of Turkey are comparatively investigated in this study. Freeze dried

venoms (0.01 mg/kg i.p.) of *Androctonus crassicauda* (Olivier 1807) and of *Mesobuthus gibbosus* (Brulle 1832) were studied on mice using in vivo tail-clip and tail-immersion (52.5 °C) methods. *Mesobuthus gibbosus* venom was observed devoid of activity on both tests. The results suggested an activity of the venom of *Androctonus crassicauda* but because of its high standard deviation values, further fractionation of the venom and new investigations on central and analgesic effects of the fractionated venom samples are required.

Keywords: *Androctonus crassicauda*, *Mesobuthus gibbosus*, venom, analgesia, tail-clip, tail-immersion

P22

The role of nitrenergic system on the antinociceptive effect of tramadol in neuropathic pain

Kahriman C [1], Ozbek H [1], Mete S [2], Daglioglu K [3], Yalcin I [2,4], Aksu F [2].

Cukurova University Faculty of Medicine, Department of Anesthesiology and Reanimation [1], Pharmacology [2], Medical Sciences and Experimental Research Center [3], CNRS Institut des Neurosciences Cellulaires et Integratives Department Nociception et Douleur., Strausburg [4].

faziletaksu@gmail.com

Tramadol, a centrally acting analgesic relieves the symptoms in neuropathic pain. Opiatergic, serotonergic and noradrenergic mechanisms were well established but the mechanism of action of tramadol in neuropathic pain is not well established.

The present study was designed to investigate effect of tramadol in a model of chronic peripheral neuropathic pain – loose ligation of the sciatic nerve (chronic constriction injury, CCI) and possible role of nitric oxide (NO) in this effect. CCI was created by ligation of right sciatic nerve of mice. Nociceptive and antinociceptive threshold in mice were evaluated by using hot-plate latency time. The evaluations were made on postoperative day 15, and 30 minute after drug administration. In the first part of experiments, hot-plate test was performed in control, sham, neuropathy control, tramadol dose-response (25, 50, 75 mg/kg, ip), L-arginin (50 mg/kg, ip), L-NAME (NG-nitro-L-arginine-methyl ester, 150 mg/kg, ip) and tramadol + L-arginine (or L-NAME) groups.

Hot-plate latencies in the neuropathic mice were statistically different from control and sham groups. Tramadol enhanced hot-plate latency in a dose dependent manner. L-arginine both reduced the neuropathic pain and enhanced the antinociceptive effect of tramadol slightly. The same action on the neuropathic pain and tramadol effect was observed with L-NAME but more significantly than L-arginine.

The results of this part of the study show that both NO precursor L-arginine, and a NOS inhibitor L-NAME have antinociceptive effect in neuropathic pain and they enhance the antinociceptive effect of tramadol. The effects of these two NO modulators were quantitatively different. The other compounds which include in the L-arginine-NO synthase pathway and different NO donors and NOS inhibitors will be evaluated to interpret these results and investigate the role of NO in neuropathic pain and tramadol action.

Keywords: Tramadol, neuropathic pain, NO, L-arginine, L-NAME

P23

Effect of amiodarone in pentobarbital induced sleep in rat

Ozbakis Dengiz G.

Karaelmas University, Medical Faculty, Pharmacology Department, Zonguldak, Turkey.

gunnuozbakis@myynet.com

Amiodarone is a Na⁺, Ca⁺⁺ and K⁺ channels blocker drug used as an antiarrhythmic. It passes to blood-brain barrier and it has been reported that amiodarone increased the inhibitory amino acids (GABA and glycine) in brain. Hypnotic drugs causes sleep by stimulating GABAergic activity. Aim of the study is to evaluate the effects of amiodarone on pentobarbital induced sleeping.

Our study was performed on male rats weighed 150-200 gr. Animals were separated into five groups. Distilled water to first group (control), diazepam to second group (1 mg/kg), 50 mg/kg amiodarone to third group, 100 mg/kg amiodarone to fourth group and 200 mg/kg amiodarone to last group were administered intraperitoneally (ip), 30 minutes later 35 mg/kg pentobarbital were injected to all groups(ip). Following pentobarbital injections, latency time of sleep (time to lose the righting reflex) was measured as second (sec), and sleeping time (duration of loss of the righting reflex) was measured as minute. Results were evaluated with Dunnett t-test, p< 0.05 value was significant statistically.

The latency times were 142.33±8.65 sec, 125.83±4.36 sec, 274.00±13.45 sec (p=0.000), 267.50±18.70 sec (p=0.000) ve 209.65±20.54 sec (p=0.010) in the group 1, 2, 3, 4 and 5, respectively. The sleeping times were 27.00±3.78 min, 120.00±6.87 min (p=0.000), 183.00±17.07 min (p=0.000), 196.40±6.19 min (p=0.000) in the group 1, 2, 3 and 4, respectively. Since all animals in the group be treated with high dose of amiodarone (200 mg/kg) died, the sleeping time could not be measured in this group.

In conclusion, amiodarone prolonged the latency times compared to control group, but dose increasing caused shortening of these times in animals. Amiodarone prolonged the sleeping times; all of the animals at 200 mg/kg administration died. This drug presented hypnotic activity in the central nervous system; we think that this effect may be through ion channels and/or increasing at levels of inhibitory amino acids in the brain.

Key words: Amiodarone, pentobarbital, sleeping, rat.

P24

Chronic emotional stress increases infarct size in rats: A heart rate variability study

Mercanoglu G [1], Eroglu L [2].

Yeditepe University, Faculty of Pharmacy, Department of Pharmacology[1]; Istanbul University, Istanbul Medical Faculty, Department of Pharmacology and Clinical Pharmacology [2] Istanbul, Turkey.

gmercanoglu@yeditepe.edu.tr

Although the link between emotional state and cardiovascular events was shown, exact mechanisms underlying this relationship have not been identified yet. We investigated the level of sympathetic hyperactivity in response to stress exposure in acute myocardial infarction (AMI) model and possible effects of this hyperactivity on infarct size. Rats were assigned as non stress and stress groups. Different chronic emotional stress factors (daylight / darkness exposure for 24 hours; overcrowding; isolation of the rats; new hierarchy; tilting the cage; restriction of water or food for 1 hour) were applied regularly in the stress group during 20-day period. After chronic stress application, AMI was induced by surgically. Infarct size was determined by tri-ethyl-tetrazolium (TTC) stain. Before the surgical operation and 6-hour of AMI ECG records were taken. From these records, HRV was calculated as the standard deviation of R-R intervals (SDNN index). The LF region is considered a measure of both sympathetic and parasympathetic activity whereas HF region is associated with parasympathetic activity. LF/HF ratio was used as a measure of sympatho-vagal balance. Compared to non-stress group, SDNN index was low and heart rate values were high in stress induced group before the induction of AMI (p<0.05 for both comparison). The increase in the LF/HF ratio was insignificant also (p=0.08). Mean infarct size of stress group was significantly larger (44.6 % versus 53.1%, p<0.05). After induction of AMI while SDNN index was decreased, LF/HF ratio and heart rate values were increased in both two groups, these changes were more significant in stress induced rats (p<0.05 for both comparison). Chronic emotional stress is deteriorating factor for induction and prognosis of myocardial infarction. Exaggerated sympathetic activity might be the major contributing factors.

Keywords: Emotional stress, MI, sympathetic hyperactivity, heart rate variability

P25

AT1 receptor blocker candesartan-induced attenuation of brain injury of rats subjected to chronic cerebral hypoperfusion

Ozacak VH [1], Sayan H [1], Cetin A [2], Akyildiz-Igdem A [2].

Zonguldak Karaelmas University, School of Medicine, Department of Physiology [1], Zonguldak, Turkey. Taksim Training and Research Hospital, Department of Pathology [2], Istanbul, Turkey.

vhaktan@yahoo.com

One of common pathophysiological states associated with central nervous system is chronic cerebral hypoperfusion (CH) that frequently occurs in conditions such as vascular dementia and Alzheimer's disease. Long term blockage of angiotensin II type 1 (AT1) receptor provides protection from ischemia induced injury of brain as well as reduction of cerebrovascular inflammation. Examining effect of the blockage on reduced glutathione (GSH), ascorbic acid (AA), and lipid peroxidation were of purpose in the present study. Modeling CH, rats were subjected to permanent occlusion of common carotid arteries bilaterally. AT1 receptor antagonist, candesartan, was given daily for 14 days after surgery. CH caused a significant increase in lipid peroxidation and decrease in GSH content of cerebral hippocampal tissue with no change in AA level. Candesartan (0.5 mg/kg, oral) not only reduced lipid peroxidation but also restored GSH significantly besides elevating AA and improving histopathological alterations. In conclusion, long term AT1 receptor blockage may be considered as novel therapeutic approach for protection from damage associated with CH. Underlying mechanism(s) may in part be related to suppressing oxidative stress and preserving brain antioxidant capacity.

Keywords: Ascorbic acid, AT1 receptor blockage, chronic cerebral hypoperfusion, glutathione, oxidative stress.

P26

Developmental and neuroendocrine effects of postnatal monosodium glutamate toxicity

Eken B [1], Yamanturk-Celik P [2].

Yeditepe University, Faculty of Medicine, Department of Psychiatry, Istanbul, Turkey [1]; Istanbul University, Istanbul Faculty of Medicine, Department of Pharmacology and Clinical Pharmacology, Istanbul, Turkey [2].

beken@yeditepe.edu.tr

Glutamate as monosodium salt (MSG) has been used widely as a food additive. It produces excitotoxic damage to different brain regions when it is administered to newborn rats. The present study evaluated developmental and neuroendocrine effects of postnatal administration of MSG. The study was performed on male Wistar albino rats divided into two groups, each containing eight animals. Animals were treated with subcutaneous injections of MSG (4 mg/g body weight) or the same volume saline (0.9 % NaCl) on postnatal days 2, 4, 6, 8, and 10. Body weight and food consumption of animals were recorded up to 16 weeks of age. At the end of 4 months, all rats were sacrificed under ether anaesthesia and cardiac blood samples were collected for plasma corticosterone levels. Liver and adrenals were removed and weighed. Data were analyzed using the Student's t test. MSG treated rats were exhibited decreases in body weight and food consumption. Absolute liver and adrenal weights were less in MSG-treated rats compared to controls. Liver weights corrected for 100 g body weight were not less in MSG-treated rats than controls but adrenal weights corrected were. Plasma corticosterone levels elevated in MSG-treated group. The results indicate that glutamatergic system seems to be involved in eating behaviour and hypothalamo-pituitary-adrenal axis activity.

This study was supported by Istanbul University Research Fund (Project No: T-558/21102004)

Keywords: Monosodium-L-glutamate, postnatal toxicity, development, hypothalamo-pituitary-adrenal axis, rat

P27

Effect of caffeine on brain lipid peroxidation in rats

Ofluoglu E [1], Pasaoglu H [1], Demirtas C [1], Pasaoglu A [2].

Gazi University Faculty of Medicine, Department of [1] Medical Biochemistry, [2] Neurosurgery, Ankara, Turkey.

ebruofluoglu@yahoo.com

Caffeine, known as methylxanthines (1,3,7 trimethylxantine), is widely consumed by people as a component of many beverages and food (such as coffee, tea, chocolate), stimulates central nervous system. According to researchers, caffeine is a psychomotor stimulant and it enhances dopaminergic activity which causes addiction. After oral administration caffeine is quickly and almost completely (99 %) absorbed by the gastrointestinal system and the hydrophobic properties of caffeine allow its passage through all biological membranes into cells. Previous studies in rats have shown that caffeine, protects membranes against oxidative damage induced by oxidant agents and reduces lipid peroxidation. On the other hand, some researchs in rats and human have suggested that caffeine ingestion increases blood pressure and causes secretion of epinephrine. Repeated daily blood pressure elevations increase stress reactions caused by caffeine consumption and also cause an increase in lipid peroxidation.

In our study, effects of caffeine on lipid peroxidation in short-term and orally given two different doses of caffeine as 30 mg/kg and 100 mg/kg (high non-toxic dose) in rat brain were investigated. The malondialdehyde (MDA) levels of brain tissue and serum in the caffeine groups decreased significantly compared by the control group. There was a statistically significant decrease in tissue MDA levels between 30 mg/kg and 100 mg/kg dose caffeine groups. But there was no statistical significance between the changes in serum MDA levels of caffeine groups. TNF- α levels were also investigated in rat serum. There was no statistical significance in the difference of TNF- α levels between caffeine groups and control group. In conclusion; our study indicates that brain MDA levels decreases with short-term 30 mg/kg dose and 100 mg/kg dose of caffeine administrations. Our findings provide strong evidences for possible antioxidant effects of caffeine.

Keywords: Rat, caffeine, brain, malondialdehyde, TNF- α

P28

Anoxia-induced dopamine release from rat striatal slices: Effects of some phenolic compounds present in red wine.

Gursoy M, Dogru HH, Buyukuyal RL.

Uludag University, School of Medicine, Department of Pharmacology and Clinical Pharmacology, Bursa, Turkey.

lrbuyuk@uludag.edu.tr

It is known that dopaminergic neurons in CNS are highly sensitive to anoxia and similar conditions. Since enhanced dopamine release with other possible mechanisms probably contributes to resultant tissue damage, attenuation the neurotransmitter release induced by anoxia and anoxia-like conditions seems to be important in decreasing the tissue damage. In recent years, it has been shown that some phenolic compounds present in red wine exert antioxidant activity and can decrease the tissue damage induced by ischemia. In this study we aimed to investigate the effects of some phenolic compounds found in red wine on anoxia-induced dopamine release from rat striatal slices. Striatal slices (0.3 mm thickness) prepared from rat brain were first incubated in normoxic Krebs for 90 min (equilibration period) and then transferred to anoxic medium (anoxic period) for 60 min. During this period, incubation medium was changed at 10 min intervals with fresh anoxic medium and collected samples were pooled and acidified with HClO₄ (final concentration 0.4 N). Incubation of the slices were terminated by transferring them in 2 ml of 0.4 N HClO₄. Dopamine and DOPAC released into the medium were first extracted with Al₂O₃ and then measured with high pressure liquid chromatography. Dopamine remained in the tissue was measured with high pressure liquid chromatography systems without purification. While one hour of anoxia significantly increased dopamine release (40±15 from 554±39), DOPAC output was determined to be declined by 50%. Resveratrol (1, 10 and 100 μ M) added into the incubation medium dose dependently protected the slices against anoxia-induced dopamine release. DOPAC output, however, was further declined by resveratrol. Other phenolic compounds (Catechin, Epicatechin, Morin hydrate ve Quercetin dihydrate), on the other hand, failed in decreasing the dopamine release under anoxic condition. These results indicate that resveratrol exerts a decreasing effect on anoxia-induced dopamine release and thus may have a therapeutic potential under anoxia and/or anoxia-like conditions.

Keywords: Anoxia, dopamine release, glutamate receptors

P29**The protective effects of melatonin hormone on morphological changes induced by exposure of formaldehyde in rats**

Kus MA [1], Ozen OA [1], Kus I [2], Alkoc O [1], Songur A [1].

Afyonkarahisar Kocatepe University Faculty of Medicine, Department of Anatomy [1], Afyonkarahisar. Firat University Faculty of Medicine, Department of Anatomy [2], Elazig, Turkey.

muratkus@canada.com

In our study, toxic effects of formaldehyde on testicular tissue and protective effects of melatonin hormone against these toxic effects were investigated at biochemical and immunohistochemical levels. For this purpose, 21 male Wistar-Albino rats were divided into three groups. Rats in group I were used as control. Rats in group II were injected every other day with formaldehyde. Rats in group III were administered melatonin with injection of formaldehyde. At the end of one month experimental period, all rats were killed by decapitation. Then the testes of rats were removed and dissected from the surrounding tissue. The activities of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px) and the levels of malondialdehyde (MDA) were determined in the some of testicular tissue specimens by using spectrophotometric methods. The remaining testicular tissue specimens were used for immunohistochemical examination.

The activities of SOD and GSH-Px were significantly decreased, and MDA levels were significantly increased in rats treated with formaldehyde compared to control. Additionally, apoptotic changes were occurred in testicular tissue after exposure of formaldehyde. It was seen that increase of SOD and GSH-Px enzyme activities and decrease of MDA levels in rats administered melatonin with exposure of formaldehyde. Furthermore, apoptotic changes caused by formaldehyde were regressed in this group.

In conclusion, it was determined that oxidative damage and apoptosis in testicular tissue caused by exposure of formaldehyde were suppressed by administration of melatonin.

*Key words : Formaldehyde, melatonin, testis***P30****The effects of streptozotocin-induced diabetes and insulin treatment on anxiety-related behaviors in wistar rats**

Kocahan S, Babar E, Emre M, Kavak S, Akillioglu K, Melik E.

Cukurova University Medical Faculty, Department of Physiology and Biophysics, Balcali, Adana, Turkey.

sayad_han@hotmail.com

Diabetes Mellitus is the most common serious metabolic disorder in humans; clinical studies reported impairments in cognitive functions of brain in diabetic patients, however the influence of diabetes on emotional functions of brain remains unclear. The present studies are investigated anxiety-related behaviors in streptozotocin (STZ, 45 mg/kg, iv)-induced diabetic Wistar rats with or without insulin treatment in the 'open-field' (OF), White/Black Box (WBB) and elevated plus-maze (EPM). Results showed that in the OF test, STZ-diabetic rats (n=12) exhibited significant enhancement of immobility ($P<0.01$) and decreased exploratory behavior ($P<0.05$) with tendency to increase thigmotaxis ($P=0.06$) when compared to the sham animals (n=11). In the EPM test, STZ-diabetic rats showed decreased risk assessment ($P<0.01$) and exploratory behaviors ($P<0.01$), but WBB behaviors did not change, compared to sham rats. Insulin treatment (1 IU, ip) 1 h before behavioral test had no effect on OF and WBB behaviors in STZ-diabetic rats (blood glucose level before insulin treatment 354 ± 8 mg/dl, 1 h after insulin treatment 124 ± 5 mg/dl, n=5 per group), but produced significant decreases in entries to open arms in EPM. These findings indicate that STZ-diabetic rats suffer enhancement of anxiety and insulin treatment did not diminish anxiety.

*Keywords : Anxiety, Diabetes, Open-Field, Elevated Plus Maze, White-Black Box, Rat***P31****Evaluating the antidepressant effect of valeriana officinalis root extract with porsolt forced swim test**

Dogan YH [2], Aran C [1], Yildirim NC [1], Dogan S [1], Demireoren S [2].

Gaziemir Anadolu High School, Ministry of National Education [1], Izmir, Turkey, Ege University, School of Medicine, Department of Physiology [2], Izmir, Turkey.

hakan.dogan@ege.edu.tr

Herbs originated treatment methods are used as a traditional medicine from the ancient times, especially in Egypt, in Sumerian and in old China. Today herbal medications are used also for many different reasons. One of these herbs is valeriana officinalis used for anxiolytic and gastrointestinal spasmolytic effect and for sleep aid. Although more than 150 constituents have been identified, none appears to be solely responsible for valerian's effects, suggesting many compounds may act synergistically. This study was performed to investigate especially the antidepressant effect of valerian extract used for insomnia.

Twenty male Sprague-Dawley albino rats were used for this study. They were divided into two groups randomly and every morning at 09:00-10:00 hours for 12 days one group took valeriana officinalis root extract resuspend in 5% dextrose solution and the other group took 5% dextrose solution equal volume. At 11th and 12th days Porsolt forced swim test was applied. Rats swam 15 minute at 11th day and 6 minutes at 12th days. Both of the days some of the behaviors like swimming, diving, struggle and freeze duration of the rats were recorded.

The evaluations of the first day of records showed that, there is no statistically difference between groups in swimming, struggling and diving durations, but there is a significant difference in freeze duration between valerian root extract group and sham group (42.4 ± 27.1 and 145 ± 91.3 sec. respectively) and the freeze duration of the valerian group was shorter than the sham group ($p=0.00963$). When compared first 5 minutes of first and second day there was no difference between swim, struggle and diving duration, but there is a statistically significance between groups ($F=8.941$, $p=0.009$) and treatment ($F=6.888$, $p=0.018$) according to freeze duration. The first five minutes freeze duration of valerian group in first day was 3 ± 3.92 sec. and it was 14 ± 25.5 sec. in second day whereas in sham group it was 20.9 ± 23.1 sec. in first day and 44.9 ± 32.1 sec. in second day.

The less freeze duration in valerian group in the first five minutes and in the total period of the first day declares the existence of anxiolytic effect, and beside the increase of the freeze duration in the second day in valerian group, its was statistically less than the freeze of the sham group that can be indicate antidepressant effect.

*Key words : valerian, depression, porsolt, forced swim test, herbals***P32****The effects of enriched environment and memantin on reference memory performance in aged rats**

Ugur E, Yamanturk-Celik P.

Istanbul University, Istanbul Faculty of Medicine, Department of Pharmacology and Clinical Pharmacology, Istanbul, Turkey.

elifugurl304@yahoo.com.tr

It is well-known that enriched environment induces some morphologic and functional changes in neurons. In this study, we investigated the effects of enriched environment together with non-competitive N-methyl-D-aspartic acid receptor antagonist, memantine (MEM) on reference memory performance in aged rats. For this purpose, 26 months old Wistar Albino male rats were held in impoverished environment (IE) or enriched environment (EE) for two months. At the end of this period saline (SAL, 0.9 % NaCl) or MEM (5 mg/kg) intraperitoneal injections was performed both in IE and EE groups for two weeks. Along with injection period, they were housed in their IE or EE and reference memory performance of them was assessed by three-panel runway test. In three-panel runway test, rats taken a food restriction schedule were observed for the time required to obtain food-pellets (latency) and the number of poking doors which were prevented to open as errors. Statistical analysis was performed using Student's t-test. Both in EE and MEM groups, number of errors and latency reduced compared to IE and SAL, respectively while MEM injections in rats held in EE, did not alter number of errors and latency compared to SAL injections in rats held in EE. The results indicate that both EE and MEM improves the memory performances

of aged rats but their combination does not cause further change in these experimental conditions.

This study was supported by Istanbul University Research Fund (Project No: T-554/21102004).

Key words: Aging, enriched environment, memantine, reference memory, rat

P33

Multiple cavernous malformations presenting with epilepsy

Koc F [1], Yerdelen D [2], Koc Z [3].

Cukurova University Faculty of Medicine, Department of Neurology [1], Adana, Turkey, Baskent University Faculty of Medicine, Department of Neurology [2], Adana, Turkey, Baskent University Faculty of Medicine, Department of Radiology [3], Adana, Turkey.

zaferkoc@superonline.com

Cerebral cavernous malformations (CCM) are a group of intracerebral vascular malformations developing secondary to developmental defects of vascular bed. CCMs form 1% of intracranial vascular lesions, and 15% of cerebrovascular malformations. The prevalence has been reported 0.02-0.53% in autopsy studies, and 0.39-0.9% in cerebral magnetic resonance imaging (MRI) studies. In sporadic cases, multiple CCMs are seen in 15-33% of patients with CCM. CCMs locate in cerebral hemispheres in 63-90% of cases, and in posterior fossa in 7.8-35.8% of cases. They can be seen in every ages and sex, and are generally asymptomatic. However, they can present with epilepsy, intracerebral hemorrhage, focal neurological findings, and headache at ages of 20-40.

A 25-years-old woman was admitted to the clinic with complaints of headache lasting for 24-48 hours recurring occasionally and seizure continuing for 3 years. Based on the history, her seizure was diagnosed as complex partial epilepsy. Seizures were not under control with 600mg/day carbamazepine treatment taken for 3 years. She and her family didn't have any other diseases. The physical and neurological examinations were normal. Cerebral MRI showed multiple millimetric nodular hypointens lesions in especially bilateral cerebral hemisphere, cerebellum, and brainstem, prominent in T2-weighted gradient-echo images. According to Zabramski classification, most of the lesions compatible with type 4 cavernous malformations were not visualized in standard T1 and T2-weighted MR images except gradient-echo MR, only few of them were poorly seen or mild hypointens.

As a result, CCMs are rarely seen vascular malformations and located generally in supratentorial areas. Infratentorial localization is rare. This case is attractive because of presence of both supra and infratentorial lesions and because of being multiple.

Keywords: Cerebral cavernous malformation, neurological and radiological findings

P34

Hemifacial spasm and hypoacusia due to vascular loop compression

Yerdelen D [1], Koc F [2], Koc Z [3].

Baskent University Faculty of Medicine, Department of Neurology [1], Adana, Turkey, Cukurova University Faculty of Medicine, Department of Neurology [2], Adana, Turkey, Baskent University Faculty of Medicine, Department of Radiology [3], Adana, Turkey.

vahidedenizy@gmail.com

Vascular loop compression is the term used to classify a group of conditions though to be caused by the compression of cranial nerve by vessel. The vascular abnormality is usually an atherosclerotic aberrant or ectatic intracranial artery, most commonly the anterior and posterior cerebellar artery or the vertebral artery. Relationships between hemifacial spasm (HFS) and cochleovestibular symptoms due to vascular compression have been reported.

A 50-year-old man was admitted with a complaint of 4-month history of left sided hemifacial spasm which exacerbated by speaking and anxiety. He had any chronic medical and ophthalmologic problems. Neurological examination disclosed an updrawn left nasolabial fold, a vertically narrowed left palpebral fissure, and typical hemifacial spasm provoked by speaking.

There was no facial weakness. In diapason test (512 cps), Weber test was lateralized to the right side. Rinne was negative and no other neurological signs were detected.

In laboratory tests, total blood count, liver and renal function tests, lipid profile, thyroid hormone levels, vitamin B12 and folate were normal. Brainstem evoked potentials were normal. Caloric test with 300C water stimulation for 40 seconds showed prolonged response in the left-sided ear. Audiometric examination was convenient with increased threshold in the left. Coronal T2 weighted magnetic resonance image (MRI) showed signal void vertebral arteries and tortuous loop of basilar artery. Axial and coronal T2 weighted MRI showed the tortuous course of basilar artery impinging on deep cerebellopontine angle in area of root exit zone of facial nerve and proximal part of the auditory nerve. The patient was given oxcarbazepine 600 mg/day and planned to follow up as an outpatient.

In our patient, in addition to the hemifacial spasm, hypoacusia was present confirmed by clinical, otological and neurootological examination findings. However, any case with unilateral hypoacusia and hemifacial spasm due to basilar vascular loop has not been described yet, according to our literature data.

Keywords: Hemifacial spasm, hypoacusia, vascular loop compression.

P35

Idiopathic femoral nerve mononeuropathy

Koc F [1], Yerdelen D [2].

Cukurova University Faculty of Medicine, Department of Neurology [1], Adana, Turkey, Baskent University Faculty of Medicine, Department of Neurology [2], Adana, Turkey.

zaferkoc@superonline.com

Femoral nerve is formed by taking branches from 2nd, 3rd and 4th lumbar roots and enters into inguinal channel by passing psoas major muscle fibers. It passes through inguinal ligament with external iliac artery and provides sense of anterior of thigh. Saphenous nerve, extension of femoral nerve downward, provides the sense of anterior of patella, anteromedial part of leg and mid part of foot. Motor innervation of quadriceps femoris muscle maintains the extension of the knee. Femoral neuropathy is a pathological condition characterized by pain in anterior part of thigh, paresis and sensory dysfunction caused by focal injury of femoral nerve. Diabetic amyotrophy and frequently seen hemorrhages due to anticoagulant therapy may cause femoral neuropathy. Femoral nerve injury has been also reported with various conditions and procedures, including hip replacement, femoral vessel catheterizations, obstetric and gynecologic procedures, general and urologic surgery explorations, ilioinguinal nerve blocks, and hematologic or neoplastic conditions. As neuropathy progresses, weakness of knee extension, difficulty in ascending stairs, and atrophy of quadriceps muscle develop. The patellar reflex is typically weak or absent. Sensory loss over the anterior thigh and most of the medial thigh is typical with extension to the saphenous area.

A 44-years-old man was admitted to the clinic with complaints of weakness and slimming of left lower limb. His complaints were present for 3 years. He didn't have a history of any illness. Anybody had a similiar complaint or another diseases in his family. In physical examination, his left calf was 15 cm thinner compared with right one. Neurological examination showed monoparesis of left lower limb prominent in the proximal muscle groups. Other examination findings were normal. Lumbosacral MRI showed any pathological findings. Total blood count and biochemical panel were normal. ENMG showed denervation potentials in left rectus femoris muscle, neurogenic unit changes and decrease in unit density. Left femoral nerve was inexcitable and right femoral nerve distal latency was 4,15, and amplitude was 7 mv.

In this report, we aimed to mention that idiopathic femoral nerve neuropathy may develop without an etiological factor and draw attention to the electrophysiological findings.

Keywords: femoral nerve mononeuropathy

P36

Effect of BNST lesions on behavioral despair and navigational learning in female Wistar Rats

Pezuk P [2], Aydin E [1], Kutlu MG [1], Iyilikci O [1], Unal G [1], Gungor Z [1], Canbeyli R [1].

Psychobiology Laboratory, Department of Psychology, Bogazici University, 34342, Istanbul, Turkey [1] Department of Biology, University of Virginia, Charlottesville, Virginia 22904-4328, USA [2].

canbeyli@boun.edu.tr

The bed nucleus of the stria terminalis (BNST) is involved in many motivational processes especially in coping with stressful situations. Previously we reported that in male rats BNST lesions aggravated behavioral despair but did not interfere with navigational learning as tested by performance in the Morris water maze (MWM) task. Since the BNST is a sexually dimorphic structure, in the present study we tested female Wistar rats in both behavioral paradigms after bilateral electrolytic BNST lesions. Two weeks after surgery, lesioned animals (n=8) and sham-operated controls (n=7) underwent two forced swim tests separated by 24 hr to assess behavioral despair. A week later, animals were tested in the MWM with a hidden platform task for 10 days (5 trials per day) followed by a probe trial test with the platform removed. One day after probe trial, the animals were tested in a one day visible platform MWM. To assess locomotor activity, an open field test was administered two weeks after termination of the MWM task. Our results indicated that female rats also showed aggravated behavioral despair after BNST lesions which did not impair acquisition in navigational learning in the MWM task. The BNST lesions did not affect performance in probe trial of MWM or in open field test.

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Keywords: BNST, electrolytic lesion, rats, sex differences, depression, navigational learning, Forced swim test, Morris water maze

P37

The influence of clozapine on regional cerebral blood flow and cognitive functions

Ertugrul A [1], Ergun-Lay E [2], Basar K [1], Volkan-Salanci B [2], Demir B [1], Ulug B [1], Erbas B [2].

Hacettepe University Faculty of Medicine, [1] Department of Psychiatry, [2] Department of Nuclear Medicine, Ankara, Turkey.

aertugru@hacettepe.edu.tr

Clozapine is a prototypical atypical antipsychotic which has been shown to be the most effective treatment in schizophrenic patients who are treatment refractory. The purpose of this study is to investigate the influence of clozapine on regional cerebral blood flow (rCBF) and the relation between response to treatment and change in rCBF. Twenty-two patients with DSM-IV criteria for schizophrenia whose treating psychiatrist decided for initiation of clozapine were included in the study. Patients were given clozapine treatment after one week of drug free interval. Psychopathology and neurocognitive functioning were assessed at baseline and 8 weeks after initiation of clozapine treatment. Psychopathology was assessed by Positive and Negative Syndrome Scale (PANSS). The neurocognitive functions such as attention, executive functions, memory, verbal fluency and working memory were evaluated by a neuropsychological test battery. Radionuclide imaging (SPECT) was performed before and 8 weeks after clozapine treatment. There were significant improvement in PANSS total score, positive, negative, general psychopathology subscores and cognitive tests such as digit spanforward, verbal fluency, Rey's Auditory Verbal Learning Test and visual reproduction-1 after 8 weeks of clozapine treatment. The right frontal/caudate perfusion ratio has increased significantly with treatment. The left superior frontal perfusion has increased and right caudate perfusion has decreased in responders to clozapine treatment compared to non-responders. In addition frontal/caudate perfusion ratio increased bilaterally in treatment responders. Frontal/subcortical perfusion ratio increased in patients who respond to clozapine treatment. This result supports the previous findings which suggest that atypical antipsychotics increase perfusion in frontal region. The results of this study may increase our understanding of the mechanism of

action of clozapine, may lead us to find new treatment strategies and predict who will respond to a particular treatment.

Keywords: schizophrenia, clozapine, SPECT, regional cerebral blood flow, cognitive functions

P38

The effects of Ms/vdb lesions on behavioral despair and navigational learning

Aksoy Aksel A [2], Iyilikci O [1], Yildirim Y [1], Kutlu MG [1], Aydin E [1], Avlar B [1], Canbeyli R [1].

Psychobiology Laboratory, Department of Psychology, Bogazici University, 34342, Istanbul, Turkey [1], University of Bochum, Bochum, Germany [2].

canbeyli@boun.edu.tr

The present study aimed to investigate the consequences of partial hippocampal denervation by means of irreversible medial septal lesions on behavioral despair and navigational learning. To that purpose medial septum / vertical diagonal band of Broca (MS/VDB) lesions were achieved electrolytically or with 980-nm diode laser application in male Wistar rats. The animals were tested in forced swim test followed a week later by Morris water maze task to assess behavioral despair and navigational learning, respectively. Histochemical evaluation revealed lower acetylcholinesterase (AChE) content in the hippocampus of some of the lesioned animals compared to sham-operated control animals as a functional outcome of MS/VDB lesions. Animals with low AChE content in the hippocampus showed aggravated behavioral despair determined by increased duration of immobility in the second swim test. On the other hand, the temporal aspect of acquisition in the Morris water maze task rather than learning capability was affected by medial septal area lesions. Behavioral findings in the present study appear not to be due to possible sensorimotor impairment in lesioned animals since the latter did not differ from sham-operated controls in the visible platform version of MWM task or open field activity test. Electrolytic lesions appear to be more efficient than laser lesions in terms of AChE decrease in the hippocampus. In conclusion, reduction of hippocampal AChE content via irreversible lesions of MS/VDB area aggravates behavioral despair but fails to induce navigational learning impairments in rats.

Keywords: 980-nm diode laser, electrocoagulation, neurosurgery, acetylcholinesterase, Forced swim test, Morris water maze

P39

The comparison of psychologic features in medical students who have different subjective sleep quality

Vardar SA [1], Vardar E [2], Ersoz E [3], Molla T [3], Kaynak C [3].

Trakya University, Faculty of Medicine, Departments of [1] Physiology, [2] Psychiatry, [3] Third Grade Students of Trakya University School of Medicine, Edirne, Turkey.

arzuwardar@trakya.edu.tr

Sleep problems are common in young medical students. The relationship between impairment of sleep quality and psychopathologic features such as depression in university students is well-known phenomenon (De Gennaro et al. 2004). The aim of this study was to explore the psychologic features in medical students who have poor and good subjective sleep quality.

Sixty three male and 79 female students aged between 17 and 23 yrs were participated voluntarily in the study. All participants were students in Trakya University School of Medicine. They completed Turkish versions of the Pittsburg Sleep Quality Index (PSQI), and psychological features and psychopathologic symptoms were evaluated with the self reported symptom inventory (SCL-90-R). Participants were categorized as poor sleepers (PSQI global score > or = 5) or good sleepers (PSQI global score < 5) using the total sleep quality score. Differences in psychological features between poor and good sleepers were compared each other.

Out of 141 students, 68 (48%) were poor sleepers, 73 (51%) were good sleepers. SCL-90-R general severity index, positive-symptom distress index and positive-symptom total scores of SCL were higher in poor sleeper than the good sleepers. Poor sleepers scored significantly higher SCL-90-R subscale scores for somatization (p<0.05), obsessive-compulsiveness

($p < 0.05$), depression ($p < 0.05$), anxiety ($p < 0.01$), hostility ($p < 0.05$), phobia ($p < 0.05$) and paranoid ideation ($p < 0.01$) features.

Our findings suggest that medical students who have poor sleep quality suffer from more psychopathologic features than the students who have good sleep quality.

Key words: sleep quality, anxiety, depression

P40

Relationship between matrix metalloproteinase-3 and schizophrenia

Orhan N [1], Kucukali CI [2], Aydin M [1], Zengin A [1], Ozkok E [1], Kara I [1].

Istanbul University Institute for Experimental Medicine, Department of [1] Neuroscience, [2] Erenkoy Psychiatric and Neurological Disorders Hospital, Istanbul, Turkey.

norhan@istanbul.edu.tr

It has been suggested that free radical-mediated damage plays an important role in psychiatric disorders. Recently, the generation of free radicals has shown to stimulate the expression/activity of matrix metalloproteinases (MMPs). MMPs are a family of calcium-requiring and zinc-containing endopeptidases that are major components of the enzyme cascade responsible for the degradation of the extracellular matrix in a variety of physiological and pathological processes. Nervous system MMPs are synthesized primarily by astrocytes, microglia, and neurons. The functional promoter polymorphism of MMP-3 has been associated with some diseases. The aim of our study was to investigate the relationship between MMP3 polymorphism and schizophrenia. MMP-3 -1171 5A/6A polymorphic variants were studied by a polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis. One hundred and eleven schizophrenic patients, 134 first-degree relatives of schizophrenic patients and 117 controls were included in the study. The distributions of 6A6A genotype and 6A allele were significantly lower in patients and relatives than in controls. However, the distributions of 5A5A genotype and 5A allele were over-presented in patients and relatives as compared to controls. Our data have suggested that MMP-3 genetic variants might be related to the schizophrenia.

Keywords: Free radicals, MMP-3, PCR, polymorphism, Schizophrenia

P41

Evaluation of working memory in recent-onset schizophrenia patients by event related potentials

Keskin-Ergen HY [1], Ertekin E [2], Uocok A [2], Devrim-Ucok M [1].

Istanbul University, Istanbul Faculty of Medicine, Department of Physiology [1], Department of Psychiatry [2], Istanbul, Turkey.

h_yaseminkeskin@yahoo.com

Deficits in working memory processes have been repeatedly observed even in the early phases of schizophrenia. This study aimed to investigate working memory processes in recent-onset schizophrenia patients, who were relatively free of confounding factors such as the long-term effects of antipsychotics and chronicity by using event-related potentials obtained during visual n-back task. N-back task is a test that permits to impose a parametrically variable load upon working memory, while other task demands are kept constant. Additionally, this task is considered as a dual task including working memory updating and matching subtasks. In this study, P300 and post-P300 period slow wave obtained with four different load levels of n-back task (0-, 1-, 2-, and 3-back) were evaluated in recent-onset schizophrenia patients ($n=22$) and healthy controls ($n=24$). Participants were required to indicate whether a currently presented letter on the computer screen matches or not with the one presented 'n' trials before by pressing left and right button of the mouse, respectively. Amplitude and latency of P300 peak, and mean amplitude of positive slow wave between 0.7 – 1.5s were measured for correctly responded match trials. Performances of both groups were decreased with increasing working memory load ($p < .001$). Patients performed significantly worse compared to controls in all levels of n-back task ($p < .01$). While the latency of P300 did not differ, amplitude of P300 reduced with increasing working memory load in both groups ($p < .001$). P300 amplitudes and latencies were comparable between the groups. Reduction in P300 amplitude with increasing memory load might be reflecting

reallocation of attention and processing capacity away from P300 generating processes to increasing working memory requirements. The finding of no amplitude difference between patients and controls might be considered as schizophrenia patients could perform matching task that involve comparison of a currently presented stimulus with a previous one already selected in working memory. In contrast to P300 amplitude, amplitude of slow wave increased as the working memory load increased ($p < .001$). Amplitude of slow wave was significantly lower in patients compared to controls in all load levels ($p < .001$). Considering that slow wave has been associated with different processes including updating and maintenance of working memory and sustained attention depending on task conditions; slow wave difference between the groups, which was not affected by memory load, might reflect a deficit in a cognitive process engaged in all memory load levels, such as deficit in maintenance or central executive system component of working memory in schizophrenia patients.

Keywords: Schizophrenia, working memory, n-back task, event-related potential, P300, slow wave.

P42

The effects of alternating magnetic field on the biomechanic parameters of streptozotocin-induced diabetic rat diaphragma muscles

Demirkazik A [1], Emre M [2], Gulturk S [1], Demir T [1].

Cumhuriyet University Medical Faculty Department of Physiology [1] Sivas-Turkey; Cukurova University Medical Faculty Department of Biophysics [2] Adana-Turkey.

dmrkzk@yahoo.com

In this study, it was aim to determine the effects of alternating magnetic field on the resting membran potentials of streptozotocin (STZ) induced experimental diabetic rat diaphragma strips.

Wistar type albino rats were used ($N=27$). Half of the rats were injected 45 mg/kg streptozotocin (STZ) solved in 0,1 M cold sitrat buffer solution ($pH=4,5$) in the juguler veins. The other half were injected 0,1 M cold sitrat buffer of the same volume mentioned. Half of the diabetic group was left in selenoid within a magnetic field of 50 Hz frequency and 5.0 mT strenght for 165 min.long everyday. They were exposed to two through non-stop pulses of 30 min, following 15 minute durations. Half of the healty group ,-injected sitrat buffer,-was exposed to the MMF at the same time every day. At the end of this time, the rats were decapited and dissected phrenic nerve-diaphragm muscle preparation. Intracellular records were taken by microelectrode recording technique. Resting membran potential were recorded.

Muscle resting membrane potential in control group compared to the other groups, has decreased significantly ($p < 0.05$). However, there is no significantly difference between D and DMA groups.

Keywords: magnetic field, diabetes, membrane potential, rat

P43

Evaluation of corticosterone and 5-hydroxyindoleaceticacid parameters in experimental anxiety induced rats

Kucuk A [1], Golgeli A. [2], Koc N. [3], Saraymen R. [4].

Hospital of Dumlupinar University, Department of Physiology[1], Kutahya, Turkey; University of Erciyes, Faculty of Medicine, Department of Physiology [2], Kayseri, Turkey; University of Erciyes, Faculty of Medicine, Department of Microbiology [3], Kayseri, Turkey; University of Erciyes, Faculty of Medicine, Department of Biochemistry[4], Kayseri, Turkey.

kucukaysegul@hotmail.com

The aim of this study was to assess the changes in corticosterone (CORT) and 5-Hydroxyindoleaceticacid (5-HIAA) parameters in two different anxiety induced young and aged rats. For this purpose 40 Sprague Dawley rats, 20 of which as experiment group and the remaining 20 as control group, were used. Rats were firstly exposed to cat odor and then to elevated T-maze for developing anxiety. Baseline, avoidance 1, avoidance 2, and escape latencies were analyzed. Before and after these experiments, locomotor activity, exploratory activity and autonomic functions of the rats were tested in open field area. At the beginning and at the end of behavior tests, urine samples of those rats kept in metabolism cages for 18 hours were collected to determine

5-HIAA levels. Following these tests, rats were anesthetized and their serum CORT levels were analyzed.

The differences between the groups were analysed by Kruskal-Wallis and Friedman tests. Changes in behavioural parameters, before and after the anxiety state were analyzed by Wilcoxon test. 5-HIAA and CORT parameters were analyzed by ANOVA and T tests.

Anxiety that is induced by elevated T maze and cat odor in young rats reflected as high CORT levels compared to control groups, implying that effective level of anxiety had been really induced. In aged rats, CORT and 5-HIAA levels did not change implying that either 1) anxiety affected the young rats more than the aged ones or 2) the age related physiological decreases in old ages compared to younger ages. The 5-HIAA level differences in the young rats group were in parallel with behavioural parameters. However, there were no differences in 5-HIAA levels in the aged group. Taken together, these results may imply that 5-HIAA measurements is a reliable tool for showing the effects of anxiety in young rats whereas it is not so in the aged rats.

Key words: learning-memory, anxiety, age, 5-Hydroxyindoleaceticacid, corticosterone

P44

Relationship of BOLD response with steady state evoked potentials

Bayraktaroglu Z [1], Emir UE [2], Uslu A [1], Ozturk C [2], Ademoglu A [2], Demiralp T [1].

[1] *Istanbul University, Istanbul Faculty of Medicine, Department of Physiology, [2] Bogazici University, Institute of Biomedical Engineering, Istanbul, Turkey.*

zbay@istanbul.edu.tr

The joint use of the EEG as an electrophysiological technique with a high temporal resolution and neuroimaging techniques such as fMRI and PET that reflect neural activity with a high spatial resolution will help to understand better the neural activity patterns observed. Within this framework, a correct modeling of the neurovascular coupling is a very important for revealing the relationship between the BOLD response and functional neural activity patterns.

Tonic neural discharges can be expected to generate increases in BOLD response, whereas it is not yet systematically investigated how the metabolic activity changes during regular oscillations in the EEG bands such as alpha and gamma. The analysis of changes in the BOLD response under the conditions which synchronized neural activity generated will improve the understanding about neurovascular coupling.

It is well known that the brain stimulation in any sensory modality with stimuli at high presentation frequencies generates regular oscillations in the EEG at the stimulation frequency and its harmonics. The steady-state evoked potentials obtained with this type of stimulation show increased amplitudes at stimulus presentation frequencies close to the peaks in the EEG spectrum (10, 20, 40 and 80 Hz).

In this study, changes in the relationship between SSVEP (Steady State Visual Evoked Potentials) and BOLD responses during visual stimulation have been systematically studied with 24 stimulus presentation rates (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44 Hz) between 1–44 Hz. The diffuse light modulated by computer generated square waves were used for stimulation. The photic stimulation was applied using LEDs coupled to fiber bundle which transferred the light into the magnet and EEG room. The BOLD measurements were conducted with 1.5 Tesla Siemens Symphony MRI System. A single shot T2* weighted gradient echo planar imaging sequence was used for BOLD measurements. Twenty slices of 64x64 were acquired with a slice thickness 3.5 mm positioned through the visual cortex. EEG has been recorded from 32 channel with Brain Amp MR+ amplifier. The signals were analog filtered between 0.1–250 Hz and digitized at 1000 samples/sec.

The analysis of the relationship between BOLD responses and SSVEPs power showed similar local maxima within the alpha range (around 8 and 10 Hz stimulation frequencies) and in the gamma range (around 40 Hz). But, in the beta band and below the alpha range, power of the EEG signals and BOLD percentage changes seem to be uncorrelated. Such differences in SSVEP and

BOLD responses to different stimulus frequencies suggest that energetic cost of electrical oscillations differ across frequency ranges.

At the current stage of the study, we can conclude that the investigation of the influence of neurons synchronized with stimulus frequency on hemodynamic response provides further understanding about the relationship between electrophysiology and hemodynamics of neuronal activity.

Keywords: Electroencephalogram, Functional Magnetic Resonance Imaging, Event-Related Oscillations, Steady-state Evoked Potentials, BOLD, SSVEP

P45

The effect of familiar environment on scopolamine-induced convulsions in fasted mice after food intake

Zengin A [1], Ozunal ZG [2], Nurten A [1], Enginar N [2].

Istanbul University, [1] Department of Neuroscience, Institute for Experimental Medicine, [2] Istanbul Faculty of Medicine, Department of Pharmacology and Clinical Pharmacology, Istanbul, Turkey.

aslizenginn@yahoo.com

Mice treated with scopolamine after fasting for two days develop convulsions soon after allowed to eat ad lib. Animals also develop convulsions after deprived of food for shorter periods. Neuroadaptive changes during food deprivation have been suggested to underlie the occurrence of convulsions. It has been shown that due to an increase in the anxiety level, latency in food intake increases and amount of food consumption decreases in animals reared in novel environment. Thus, food intake in unfamiliar environment may contribute to the development of convulsions in fasted animals. In the present study, the effects of food intake in familiar and novel environments on convulsions were investigated in 48 h fasted mice. Albino Balb/C mice housed 3 per cage were deprived of food for 48 h. On the day of testing, half of the animals was kept in the housing room (familiar environment) and the other half was transferred to the testing room (novel environment). The animals were treated i.p. with saline (control) or 3 mg/kg scopolamine. After treatments, animals in the familiar environment remained in their home cages whereas animals in the novel environment were placed in an observation cage (3 animals per cage). Twenty min later, they were given food pellets and allowed to eat ad lib. All animals were observed for 30 min for the incidence and onset of convulsions. Seizure activity was quantified by staging 1-5 (Enginar et al., *Neuropharmacology* 44:199, 2003). Incidence of convulsions was expressed as the percentage of animals displaying forelimb clonus with rearing (either stage 3, 4 or 5). Fisher's Exact test and Student's t-test were used to evaluate the incidence and onset of convulsions, respectively. The body weights of the mice fell to approximately 80-82% of the initial body weights after fasting for 48 h. Scopolamine treatment caused convulsions both in animals fed in observation cages (78%; $p < 0.01$) and in home cages (34%; $p > 0.05$). Eating in familiar environment increased latency in onset of convulsions (5.5 ± 1.1 to 18.0 ± 7.5 min; $p < 0.05$). Present results show that the incidence of convulsions decreases and the onset of convulsions delays when food is given to fasted animals in familiar environment. However, the significant incidence of forelimb clonus (stage 2) in home cage animals indicates that familiar environment could not prevent the occurrence of convulsions in a significant manner.

Key words: food deprivation, familiar environment, scopolamine, convulsions, mice

P46

Cyp effect in adult rats which had free access to oral nicotine since adolescence

Yararbas G, Nesil T, Kanit L, Pogun S.

Ege University, Center for Brain Research and Department of Physiology Bornova, 35100 Izmir, Turkey.

gorkem.yararbas@ege.edu.tr

Although the harmful effects of smoking are known, the average age for initiating smoking is decreasing. Nicotine is known to be the main addictive substance in tobacco and therefore is used in animal models to study smoking addiction. The addictive aspects of nicotine can be evaluated regarding reward, conditioning, deprivation, tolerance etc. Individual differences in

nicotine addiction should be elucidated in order to better understand and cope with smoking behavior. In this study, adolescent rats were given a choice of nicotine and water from a free access two bottle system. The rats were grouped according to their preferences in nicotine consumption as minimum or maximum nicotine preferring rats. The control groups received water in both bottles. In our previous studies we have shown that nicotine induces CPP in male rats but not in females. The aim of the present study was to study the nicotine induced CPP effect in animals which freely accessed to nicotine since adolescence. The CPP apparatus consisted of black and white chambers with different floor textures and a third neutral chamber. The chambers were separated by guillotine doors which were open during the pre- and post-conditioning sessions and closed during conditioning. Time spent in each chamber during pre- and post- conditioning was monitored. Adult Sprague Dawley rats were initially allowed to explore all three chambers for 30 minutes to depict preference. In 8 conditioning sessions that followed, nicotine (0.2mg/kg base, s.c.) or saline were administered alternatively and rats were placed in appropriate chambers for 15 minutes. Nicotine was paired with the non-preferred chamber, and control animals received saline in both chambers. During the final assessment, rats were placed in the neutral chamber and time spent in each chamber was monitored for 30 minutes. Our results show that: (1) Female groups did not show CPP effect (2) Significant CPP effect was observed in control males ($p < 0.005$) but not in minimum or maximum male groups (3) Time spent in the compartment paired with nicotine was lower in the maximum male group than the control male group ($p < 0.005$). These data indicate that the male rats which were exposed to nicotine since adolescence do not show nicotine-induced CPP effect. The role of conditioning in addiction may be more important in early stages of addiction.

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Keywords: Nicotine, CPP, addiction, sex differences

P47

Analysis of nicotine preference in male and female rats with free access to oral nicotine during adolescence and adulthood.

Nesil T [1,2], Mola GD [3], Kanit L [2,3], Pogun S [2,3].

Ege Univ. Faculty of Science Institute Biotechnology Department[1], Ege Univ. Center for Brain Research [2], and Department of Physiology [3], Bornova, 35100 Izmir, Turkey.

tanselinesil@gmail.com

Smoking is an addiction with detrimental effects on society. Nicotine is the addictive component of tobacco and underlies the addictive properties of tobacco use. While tobacco use among adults is decreasing in developed countries, adolescent smoking, especially among girls is increasing. Tobacco use in adolescence is a major problem which has significant impact on public health. In view of these observations, the present study was designed to test voluntary nicotine consumption of rats which had free access to nicotine starting during adolescence until adulthood. Sprague Dawley rats obtained from Ege University Experimental Animal Breeding Facility were used. A total of 90 female and male rats were monitored from their birth until 4 weeks, when they were separated from their mothers and individually housed in plexiglas cages; nicotine was self administered via 'two bottle free choice' method for 6 weeks, with 24 h free access. Nicotine and water consumption were recorded. Control rats received only water from both bottles. The taste of nicotine was masked by saccharin, which was also used in water. At the end of the 6 weeks nicotine administration was discontinued until the rats reached adulthood. At 4 months of age, nicotine administration was resumed and continued for 6 weeks, using the same procedure as in adolescence. At the end of the experimental period nicotine consumption data was analysed by Ward test to depict individual differences; results showed that rats were divided into 3 different groups (maximum, median and minimum) both during adolescence and adulthood. Rats were able to discriminate nicotine from water and showed individual differences in nicotine consumption both as adolescents and adults. Group means showed that nicotine consumption was higher in adolescent rats than adults ($p < 0.001$). Furthermore, female rats increased nicotine consumption as adults compared to their adolescent consumption rates ($p < 0.001$) and there was a correlation between adolescent and adult nicotine in consumption in female rats but not in males ($p < 0.001$).

Present findings suggest that female rats are more vulnerable to nicotine as adolescents and adolescent exposure predicts higher nicotine consumption as adults in females.

This study supported by Ege University Research Fund Grant (001 BAM 2006)

Keywords: Nicotine, sex difference, adolescent, self administration oral nicotine

P48

Physiological approach to the effect of gender hormones to verbal skills, visual and hearing reaction time and mental rotation

Kutlu N [1], Ekerbicer N [1], Taneli F [2], Cullu E.[1], Ulman C [2], Ari Z [2], Ozlen N [2].

Celal Bayar University Faculty of Medicine, Department of [1] Physiology, [2] Biochemistry, Manisa, Turkey.

nkutlu@bayar.edu.tr

In this study we investigate the interaction between gender hormone levels at follicular and luteal phase of the menstrual cycle and high functions like hand preference, verbal intelligence, visual and hearing reaction time and mental rotation in right handed women.

28 volunteer university student aged 19-22 and right handed women were enrolled in this study. Hand preference of each subject was detected by Edinburgh Handedness. Verbal skill, visual and hearing reaction time were measured by 'finger tapping' in follicular and luteal phase of the menstrual cycle. Total steroid hormone levels in serum were detected by enzymatic method. All measurements were performed at the same place and same time period. Obtained data were evaluated by SPSS program.

There were statistically significant differences between the verbal skills in follicular and luteal phase of the menstrual cycle ($p < 0.005$). In both phases, motor reply data was different obtained from right and left hands was statistically significant ($p < 0.005$). It was shown that there was a positive correlation between estrogen and verbal skills. Progesteron, FSH-LH hormone levels were correlated with the high functions of the brain. Also there was a statistical tendency between visual, hearing reaction time, mental rotation values and the values in the menstrual cycle.

In women certain periods of time in menstrual cycle there was an interaction between steroid hormones and verbal, perception and problem solving skills

Keywords: Estradiol, follicular phase, luteal phase, progesteron, LH, FSH, woman, menstrual cycle, hand preference, brain, high function.

P49

The effects of KCl-induced cortical spreading depression on the kindling process

Akman O [1], Karson A [1], Aker R [2], Ates N [1], Onat F [2].

Kocaeli University, School of Medicine, Department of Physiology[1], Kocaeli, Marmara University, School of Medicine, Department of Pharmacology and Clinical Pharmacology [2], Istanbul, Turkey.

ozlemakman@yahoo.com

Cortical spreading depression (CSD) produces propagating waves of transient neuronal hyperexcitability followed by depression, and is characterized by temporary disruption of ion homeostasis and EEG depression. In this study, we aimed to evaluate the effects of CSD on epileptogenesis in the amygdala kindling model. This study was performed on male 6- to 12-month-old Wistar rats. Rats under ketamine and xylazine anesthesia were implanted with electrodes into the right and left basolateral amygdala and bilaterally in the skull over frontal and parietal cortices. To induce CSD, a 22-gauge cannula guide was implanted over the right frontal cortex. Ten days following surgery, animals in the control group ($n=4$) were electrically stimulated twice daily at their afterdischarge (AD) thresholds. The seizure severity was evaluated using Racine's 5-stage scale. In KCl group ($n=5$), 2 μ l KCl was infused above the frontal cortex through the cannula guide 3 min before each of the first 15 electrical stimulations. Animals received kindling stimulation until they reached stage 5 or the maximum number of stimulation (30). All animals in the control group reached stage 5, and the mean number of stimulations to reach the first stage 5 seizure was 13 ± 0.8 . None of the animals in the

KCl group exceeded stage 2, and motor seizures were not observed after 15 stimulations. Additionally, afterdischarge durations in cortex and amygdala decreased in the KCl group, compared to the control group. The results of this study suggest that repetitive induction of CSD in the cortex block the convulsive seizure expression, and affect the AD duration.

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Keywords: Cortical spreading depression, kindling, epileptogenesis, cortex, rat

P50

Investigation of the effect of axotomy on neuronal morphology via in-vivo retrograde tracing

Erdogan E, Cengiz N, Ozturk G.

Yuzuncu Yil University Medical Faculty Neuroscience Research Unit, Van, Turkey.

dreder@yyu.edu.tr

Several histochemical tracers can be used for demonstrating anatomical relationships between groups of cells or individual neurons. These are classified as anterograde and retrograde tracers. The retrograde tracers can be hydrophilic as well as lipophilic in character. Of these, Dii is a lipophilic fluorescent dye of carbocyanamine group. Since it is liposoluble, it can be transported via axonal flow through plasmalemma, passively. It can be applied to live or fixed tissue, both retrogradely and anterogradely. In this study, we investigated the acute effect of axotomy on neuronal morphology. For this purpose, sciatic nerves of BALB-c mice were exposed and stained with red Cell Tracker-CM Dii (Molecular Probes Cat. Nr: N22883) tissue labeling paste via a pipette tip or needle. After four days incubation period to allow the retrograde transport, a unilateral sciatic nerve cut was performed. Contralateral side was left intact as control. After an hour, animals were perfused with 4% paraformaldehyde solution. Under a stereomicroscope, L4 and L5 dorsal root ganglia, which receive most of their fibers from sciatic nerve, were removed. Ganglia were kept in 30% sucrose solution overnight and then 20-30 μm – thick frozen sections were taken. Samples were immunohistochemically labeled with anti-NeUn and anti-laminin primary antibodies and alexa fluor 488 antimouse + antirabbit IgG secondary antibodies. The sections were examined with confocal microscopy. The surface areas of the neurons that had been stained with neurotrace dye were imaged at the level where nucleoli were measured. According to measurements pooled from L4 and L5 ganglia, measured surface areas of neurons of the axotomy and control side were $709 \mu\text{m}^2 \pm 26,9$ (SEM) and $815 \mu\text{m}^2 \pm 40,4$ (SEM), respectively. There was a significant difference between two groups ($p < 0,002$). We conclude that axotomy causes a significant reduction in neuronal size in the acute period. The explanation of the mechanism of this pathological condition needs further studies.

Keywords: neuronal tracing, retrograde tracing, dorsal root ganglion, neuron, axotomy

P51

The effect of long-term changes in routine physiologic requirements on attention and memory

Dolu N, Yapislar H, Suer C.

Erciyes University Medical Faculty Physiology Department Kayseri, Turkey. handeyapislar@hotmail.com

During the month of Ramadan, Moslems abstain from drinking and eating daily between sunrise and sunset. This study is designed to investigate whether these changes in one day period have an effect on attention and memory of these people whose biologic rhythms change as a result of abstaining from routine physiologic requirements. Directed attention and memory activities are associated with P300 generation. Event related potentials (ERPs) originate in the subcortical areas as response to a stimuli, and are recorded on the scalp with electrodes. In our study, we aimed to investigate the effects of one day Ramadan fasting on directed attention and memory by comparing the P 300 measures in fasting and control subjects.

Sixteen healthy non-smoking male volunteers (medical students) were included in the study (19.75 ± 0.17). P300 records were taken from each students twice; once, during fasting ($n=16$), and once when not fasting

($n=16$). Blood glucose levels were also determined in each group. P300 record was taken from 4 (Ag/AgCl) electrode locations (Fz, Cz, Pz, Oz of the international 10/20 system). The currents were amplified and transferred to the Brain-Data station. Standard oddball paradigma was used as a stimulant. The latencies and amplitudes of P300 waves recorded during fasting and non-fasting states and respective blood glucose levels were compared by using Student t test.

There was a significant difference ($p < 0.05$) in blood glucose levels at different states. Also we found P300 latency reduced and P300 amplitude increased in non-fasting group when compared to fasting group.

Long-term changes in routine physiologic acquirments may affect given attention and memory in a bad way.

Key words: P300, ERP, attention, memory

P52

The comparison of the skin potential habituation rates in the sedentary subjects and the trained sportsmen

Yildiz A [1], Gulturk S [1], Demirkazik A [1], Kaya T [2], Demir T [1], Altun A [2], Arslan A [3]

sgulturk@yahoo.com

The aim of the present study was to investigate the habituation rates of the skin potential response in the sedentary subjects and the trained sportsmen, and to find out if there was any difference between these two groups. A total of 52 voluntary male students (30 sedentary subjects, 22 trained sportsmen) participated in the experiment. The mean pulse rates of the sedentary subjects and the trained sportsmen were $73.03 \pm 2.31/\text{min}$ and $56.04 \pm 1.08/\text{min}$, respectively. In order to initiate the skin potential responses 16 square-wave electrical shock stimuli (1200 μs duration, 5mA intensity) with 20-50s random interstimulus interval were presented to each subject over the ulnar nerve of the right arm. The skin potential responses of the subjects to repeated stimuli were recorded on Nihon Kohden polygraph in sound isolated Faraday cage (under dim light and at $20 \pm 2^\circ\text{C}$ temperature) between the hypotenar eminence and volar forearm surface with nonpolarizable Ag/AgCl electrodes (an inner diameter of 7 mm).

Although the sedentary subjects had higher means of skin potential response amplitudes than the trained sportsmen, these differences were not statistically significant ($p > 0.05$) according to Student-t test among the groups. But when the habituation rates were compared with ANOVA and Tukey test within the groups the difference was found to be statistically significant ($p < 0.05$). The sedentary subjects and the trained sportsmen showed no statistically importance after 10th and 7th stimuli, respectively. Depending upon this we can say that the trained sportsmen showed a more rapid habituation than sedentary subjects. This finding is in appropriateness with our previous knowledge of the sympathetic tonic activity is more effective in the sedentary subjects while the vagal tonic activity in the trained sportsmen.

This study was supported by a grant from CUBAB of Cumhuriyet University.

Keywords: Sedentary, Trained Athlete, Skin Potential, Habituation, Electrodermal Activity

P53

Acute prenatal stress induces behavioural despair during both adolescence and adulthood in rat offspring

Yildirim E [1,2], Saylam C [1,3], Koylu EO [1,2], Pogun S [1,2].

Ege University Center for Brain Research [1] and School of Medicine, Departments of Physiology [2] and Anatomy [3], Bornova, 35100 Izmir, Turkey.

emre.yildirim@ege.edu.tr

The effect of prenatal stress on the affective status of the offspring is emphasized in both experimental and clinical trials. Related literature is mostly focused on chronic stress administration and adolescence. The aim of the present study was to assess putative behavioural changes in the rat offspring during adolescence and adulthood following a short-term acute prenatal stress. Adult Sprague-Dawley rats obtained from Ege University Experimental Animal Breeding Facility were housed to mate (4 females to a

male). Pregnancy status of female rats was controlled by daily vaginal smears and pregnant rats were caged alone. On the 15th day of pregnancy, only one session of restraint stress was administered to the stress group between 10:00-11:00 a.m., for one hour, under intense light and in well-ventilated glass cylinders. The pregnant rats of the control group were not exposed to any stressful experience until birth. Until postnatal day 30, pups were caged with their mothers. On the 30th day, same sex pups were caged together. Rats were tested in Forced Swim Test (FST) on postnatal days 45 and 120, for adolescence and adulthood, respectively ($n=7$ in each group). In FST (Day 1, 15 mins. and Day 2, 6 mins.), behaviour were recorded semi-automatically. For each individual, freezing duration between 2nd and 6th minutes of experiment were assessed statistically by variance analysis and post-hoc tests. Increase in freeze duration was considered as an index for behavioural despair. Our results show a significant increase in freeze durations in prenatal stress group both in adolescence and adulthood and in both sexes ($p<0.001$). Post-hoc tests revealed an increase in freeze duration in Day 2 of adolescent stress group compared to control. This pattern was also observed in adulthood and was independent of sex. Additionally, Day 1 freeze durations were significantly increased in adult stress groups compared to controls. Taken together, our results depict behavioural changes in both adolescent and adult offspring prenatally exposed to acute stress and these results might be interpreted as a predisposition to depressive disorders.

Keywords: Prenatal stress, forced swim test, depression, adolescence, rat

P54

The effects of chronic exercise on anxiety and emotional memory in rats

Altan M, Mengi M, Metin G, Yurdakos E, Cakar L.

Istanbul University, Cerrahpasa Faculty of Medicine, Department of Physiology, Istanbul, Turkey.

ertanyurdakos@myynet.com

It has been suggested that exercise has anxiolytic effects in some experimental models used in mice and rats. In this study we aimed to investigate the effect of chronic swimming exercise on the emotionality of male wistar albino rats. Animals were divided into two experimental groups: control group ($n=9$) and exercise group ($n=8$). The control group was allowed only home cage activity. Exercise group swam in a water tank 30 minutes a day and 4 days a week for 9 weeks. After 9 weeks of exercise procedure all animals were tested for their level of emotionality using the, open field test (OF), hole board (HB), elevated plus maze (EPM) and Porsolt swimming test (PST). In the OF, exercise group showed a significant decrease in both the number of squares crossed ($p<0,05$) and the rearing ($p<0,01$). By using HB, exercise group showed a significant decrease in the number of head-dips ($p<0,001$) and rearing ($p<0,001$) compared to control group. In the EPM immobilization time ($p<0,05$) and time spent ($p<0,01$) in closed arm increased significantly whereas number of rearing ($p<0,05$), number of entries ($p<0,01$), time spent ($p<0,01$) on open arm and the number of entries to closed arm ($p<0,01$) in the exercise group significantly decreased compared to control group. In the PST the control group animals exhibited the well documented learned helplessness by a significant increase in the immobilization time ($p<0,01$) and a decrease in duration of struggle ($p<0,01$) compared to pretest. On the other hand, exercise group did not display learned helplessness.

These results suggest that this exercise procedure has anxiogenic effects and impairs learned helplessness. Although it is generally suggested that exercise has mood-enhancing effects, our results conflicts with the previous results, and suggests that the anxiogenic effects of the experimental exercise models should also be considered.

Keywords: exercise, anxiety, open field, hole board, elevated plus maze, Porsolt swimming test

P55

Modulation of neuronal nitric oxide synthase by nicotine and forced swim stress in rats

Keser A, Balkan B, Kanit L, Pogun S.

Ege University Center for Brain Research and School of Medicine Department of Physiology, Izmir, Turkey.

aysegul.keser@ege.edu.tr

Nitric oxide (NO) modulates secretion of stress hormones and exposure to various stressors increases activity of NO synthase (NOS) in limbic-hypothalamo-pituitary-adrenal axis. There are sex differences in stress response, brain NO levels and central effects of nicotine. Our aim was to determine effects of chronic nicotine administration on behavioral despair, nNOS levels in rat brain and elucidate sex differences in these effects.

8-10 adult Sprague Dawley rats were used in each group in a 2x2x2 factorial design with sex (male, female), stress exposure (forced swim, handling) and nicotine treatments (nicotine, saline) factors. Rats received nicotine (0.4 mg/kg, s.c.) or saline injections for 15 days. On 14th and 15th days, stress groups were subjected to forced swim stress. Behavior during forced swim was monitored and semiautomatically recorded: Struggle, freeze, diving and swimming. After 2nd day of forced swim test rats were decapitated, frontal cortex, hippocampus and amygdala were dissected on ice and frozen. NOS expression was determined by Western Blotting, using beta-actin as internal protein control. Tissue protein concentrations were determined with Lowry technique. Bands obtained, were evaluated with Image J program of NIH (density and area). In Western blotting, one sample from each group was run on a single gel and results were expressed for each group as percentage of respective controls. Data was analyzed by multifactorial ANOVAs, followed by post-hoc tests.

In forced swim test, freezing parameter (measure of behavioral despair), a significant effect of days ($p=0.001$, longer freeze duration in second day) emerged and interacted with sex and nicotine ($p=0.05$); effect of nicotine on preventing behavioral despair was more prominent in females. Freeze duration in males was shorter than females, but difference did not reach significance ($p=0.058$). NOS expression was higher in saline treated male rats than females. However, following nicotine and/or saline treatment, sex emerged as a significant effect in hippocampus ($p=0.013$) and frontal cortex ($p=0.001$) with females having higher values than same sex controls; similar trend was observed in amygdala ($p=0.078$). Nicotine and stress did not emerge as significant main effects. Overall our results show sexually dimorphic effect of nicotine and stress with more pronounced effects on females.

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Keywords: Nitric oxide synthase, nicotine, stress, gender difference, nitric oxide metabolites

P56

Effects of neuropeptid Y (NPY) on penicillin model experimental epilepsy in rats

Orallari H [1], Gokce FM [2], Demir S [2], Ankarali S [3].

Abant Izzet Baysal University, Institute of Health Sciences, Department of Physiology [1], Bolu, Turkey, Duzce University, School of Medicine, Department of Physiology, [2], Duzce, Turkey, Zonguldak Karaelmas University, School of Medicine, Department of Physiology, [3], Zonguldak, Turkey.

fmg1@myynet.com

Epilepsy is one of the frequently observed central nervous system disorder. This disorder is characterized by partial or generalize uncontrolled activation of central nervous system. Pathologically, simultaneous and noncontrolled discharge of neurons is same in all epilepsy types and the mechanism that triggers is not known yet. Balance between excitation and inhibition during epileptic seizures favours to excitation side and various neurotransmitter substances are secreted. Some of these secreted neurotransmitters have an increasing effect on excitation, while some have decreasing effect. One of the substance that decreases excitation, having various metabolic functions, being endogen anticonvulsant and mostly found in central nervous system is neuropeptid Y (NPY). NPY was found by Tatamoto and Mutt in 1982. NPY has thirty-six amino acids and five functional receptors. It is secreted and stored in GABA-ergic interneurons with GABA. It was explained that calcium ions has an important role in epileptic seizures. Intercellular intake of calcium results in secretion of excitatory neurotransmitters. Some in vitro studies show that; flow of calcium in presynaptic terminals and glutamate secretion in hippocampal region is suppressed by NPY. In this study effects of NPY on penicillin model experimental epilepsy which is one of the basic partial epileptic model was explored. Our aim was to explore whether NPY

has an anti-epileptic effect on epilepsy just same as in other epileptic models and its effective mechanism. For this experiment male, Wistar, albino, having weight of 230-270 g rats were used. Subjects were separated into two groups; while the second group was accepted as a control group, first group was used for NPY experiments. Electroencephalographic brain bioelectrical potentials (EEG) were recorded digitally by PowerLab/8SP data acquiring system. Results were analysed by independent t test. Decrease in both amplitude and frequency measured in different times, analysed was found statistically significant. Decrease in amplitude was much more than compared to control group in NPY group after the 40-45. minute measurement. Likewise, decrease on spike-wave activities in NPY group after the 50-55. minute measurement was found statistically significant ($P < 0.05$). As a result; just as in other epileptic models, NPY inhibits epileptic seizures in penicillin model experimental epilepsy.

Keywords: *Neuropeptid Y, epilepsy, electrocorticography (EEG), GABA, anticonvulsant effect*

P57

Effects of simvastatin on pyramidal neurons of the hippocampal CA1 and CA2 areas in rats

Baytan SH [1], Okuyan M [1], Yulug E [2], Yenilmez E [2], Alkanat M [1], Erdogmus E [1], Akgun A [1].

Blacksea Technical University, School of Medicine, Department of Physiology [1], and Histology [2], Trabzon, Turkey.

cbaytan@gmail.com

Simvastatin, an inhibitor of hydroxymethylglutaryl-CoA reductase enzyme (HMG-CoAR) is used widely for preventing cardiovascular diseases' risks in dyslipidemias. Simvastatin is a lipophilic drug that crosses the blood-brain barrier, and it effects HMG-CoAR metabolism and synaptic membrane structures and also its cytotoxic effects on neuron and glial cells were shown in several studies. Simvastatin is also shown to affect memory in humans. In this study, effects of the simvastatin on pyramidal neurons of the hippocampal CA1 and CA2 areas affecting memory is studied in rats. 12 male Sprague-Dawley rats aged between 5-6 months old with initial weights of 220-280 gr were used for the tests. Subjects were divided as a vehicle ($n = 6$) and simvastatin ($n = 6$) groups randomly. When vehicle groups administered only sterile normal saline, simvastatin group administered simvastatin 10 mg/kg/day dissolved in saline orally. The administered solution volume each time was 0.5 ml in all groups. Subjects were sacrificed after six weeks of drug or vehicle administration then their brains were dissected and slices from the hippocampal areas were prepared and stained for histological observation. Normal and atrophic pyramidal neurons were counted from the slices and rate of atrophic neurons to the normal neurons were calculated.

Results revealed that there were more atrophic neuron rates in the both CA1 and CA2 areas in the simvastatin group than in the vehicle group (CA1 : %10.02, %6.16, $p < 0.002$ and CA2 : %32.60, %9.11 $p < 0.002$, respectively). This results might suggest that simvastatin use might affect memory and learning by effecting hippocampal pyramidal neurons.

Key words: *Simvastatin, pyramidal neuron, hippocampus, atrophy, memory*

P58

The effect of melatonin and darkness on qEEG analysis in mild traumatic brain injured rats

Ozkaya YG [1], Ucar T [2], Onal MZ [3].

Akdeniz University, School of Physical Education and Sports [1], Faculty of Medicine, Department of Neurosurgery [2], Antalya, Turkey; Ufuk University, Faculty of Medicine, Department of Neurology [3], Ankara, Turkey.

gulozk@yahoo.com

We investigated the effect of light-dark changes and melatonin administration on quantitative EEG analysis in mild traumatic brain injured rats. Male Wistar rats were applied trauma by dropping a constant weight and then divided into four groups as; trauma (sham) group (T), dark group (D), melatonin group (M) and melatonin group under darkness (MD). Animals at D group were kept constant darkness for 48 hours after trauma. M and MD animals were injected melatonin with a dose of 50 mg/kg, i.p. EEG recordings were

obtained at three times: One day before trauma (pre-trauma), immediately after trauma (post-trauma) and 48 hours after trauma (48 h). Offline EEG power was performed from recorded values. Statistical significance between groups and measurements were determined by repeated measures of ANOVA. Results were given as mean \pm SE and a level of $p < 0.05$ was accepted as statistical significance. Results of our experiment has shown that EEG power was found decreased in all groups immediately and 48 hours after trauma ($p < 0.001$). Darkness or melatonin administration were found unaffected on EEG power decrement after trauma. Instead, animals injected melatonin under darkness had prominent decrement on EEG power after 48 hours after trauma. In conclusion, although melatonin or darkness administration alone following mild traumatic brain injury did not change the decrement of EEG power, melatonin injection under darkness was found worsened EEG power following trauma.

Keywords: *Mild traumatic brain injury, rat, melatonin, darkness, qEEG*

P59

NO and CO2 effect on neurovascular coupling

Yucel MA [1], Akin A [1], Demiralp T [2].

Bogazici University, Bio-Medical Engineering Institute, Istanbul, Turkey [1], Istanbul University, Istanbul Faculty of Medicine, Department of Physiology, Istanbul, Turkey [2].

meryem.yucel@boun.edu.tr

Hemodynamics is the study of blood flow properties which are directly affected by the arterial/venous diameter, blood consistency, and vasculature. Specifically, the study of hemodynamics with regard to neuronal function is called the hemodynamic response. The hemodynamic response is controlled by either physical factors (temperature, electrical potential) or neurogenic factors or biochemical signals (nitric oxide (NO), adenosine, K, CO₂, bicarbonate) induced by neuronal activation that travels and regulates vascular tone. The latter phenomenon is called neurovascular coupling. Brain hemodynamics is intensely studied using different modeling tools. While biochemical models in literature cover the chemical reactions and signal transduction pathways within the individual cells, mechanical and electrical models cover the fluid dynamics throughout the capillaries and voltage changes across the membrane of the cell. However there is no model linking neuron, astrocyte, smooth muscle of the blood biochemically. Therefore, the biochemical linkage between the changes in the neuronal energy metabolism (via a neural activity) and the changes in the smooth muscle (of the vessels) metabolism leading to a constriction or dilation of that muscle should be further investigated. We try to construct a preliminary model coupling neuron-smooth muscle-and-vascular system biochemically which would hopefully give more insight to our knowledge in brain energy metabolism and hemodynamics. Model basically consists of mitochondrial respiration, Na-K-ATPase, metabolite exchanges between the cells and the capillary, Na and Ca entries during an action potential. The flow rate of the blood is dependent on NO (nitric oxide), CO₂ which are the products of intracellular signaling and the energy metabolism respectively. Our preliminary results show that NO effect on vascular vasodilation is more pronounced than the CO₂ effect. In addition to this NO effect duration is limited with that of the stimulus, whereas more time is needed for CO₂ effect to diminish.

Keywords: *Neurovascular coupling, hemodynamics, NO, CO2*

P60

Effects of cSs on spatial learning and hippocampal neuronal density

Sahiner M [1], Ozdemir MB [2], **Kursunluoglu R** [1], Yonguc GN [2], Sen Turk N [3], Kucukatay V [1].

Pamukkale University, Medical Faculty, Department of Physiology [1], Anatomy [2], Pathology [3], Denizli, Turkey.

aysemelike@pau.edu.tr

Cysteine-S-sulfate (cSs) is not normally present in human body. This metabolite is produced by sulfite reacting with free cysteine amino acids in SOX deficiency. It has structural features in common with the excitotoxic amino acids such as glutamic, aspartic, cysteine and homocysteic acids. It is suggested that cSs, which is a brain damaging metabolite in SOX deficiency may be responsible for observed detrimental effects of sulfite. In this study

we aimed to observe the effects of cSs on spatial learning and hippocampal neuronal density. For this purpose, 4 groups of 36 rats (8 in each group) were taken to the study. The groups were as follows: 1-Control group; 2-Sham group, which the animals had a medial septal cannula but have no cSs injection; 3- S15 group, which the animals had a medial septal cannula and have 0.15 micro molar cSs injection; 4- S30 group, which the animals had a medial septal cannula and have 0.30 micro molar cSs injection; The anesthetized rats were taken to the stereotaxic apparatus and all injections were done with a Hamilton injector. After a post-operative period of one day, the animals were taken to the 6 day water maze protocol. According to our preliminary results S15 and S30 groups' hippocampal volumes were lesser than the control and sham group. Water maze performance of these two groups were also impaired.

Keywords: cysteine-S-sulfate, water maze, hippocampal volume, learning

P61

Genetic Factors in Development of Anxiety: studies on two Strain mice, BALB/C AND C57BL/6j

Akillioglu K, Babar E, Kocahan S, Melik E.

Cukurova University, Medical Faculty, Department of Physiology, Division of Neurophysiology, Adana Turkey.

kakillioglu@cu.edu.tr

In the present comparative study, we examined anxiety yielded in the open field (OF) and elevated plus maze (EPM) with recording conventional and ethological parameters of behaviors on two strain mice, BALB/c and C57BL/6j. Anxiety-related behaviors were observed in OF for 10 min and in EPM for 5 min. Avoidance from opening forced by novelty was examined in the OF. BALB/c mice, compared to C57BL/6j mice during 10 min OF test, showed an increased in time spent center of apparatus ($P<0.05$), a decrease in peripheral locomotor activity near the wall ($P<0.05$), decreased rearing ($P<0.05$), tendency to increase in latency first enter to center and increased grooming behavior and number of fecal boli ($P<0.05$). These findings indicate that BALB/c mice have higher anxiety level together with higher ability of adaptation to unprotected opening. In the EPM, when compared to C57BL/6j, it was found that in BALB/c mice, time spent in the open arms of the apparatus was significantly shorter ($P<0.001$), and head stretching, stretched attend posture to the open arms as risk assessment behaviors increased ($P<0.01$). These results indicate that C57BL/6j mice showed higher level of avoidance response and BALB/c mice have higher anxiety response to novelty. This suggests that these differences consist of that C57BL/6j strain has a low ability of risk assessment and exploratory functions of brain than BALB/c mice.

Keywords: Anxiety, Elevated Plus Maze (EPM), Open-Field (OF), BALB/c, C57BL/6j

P62

Friedreich's ataxia; clinical findings, and GAA tri-nucleotide expansion

Koc F [1], Kocaturk Sel S [2], Guzel AI [2], Kasap H [2], Sarica Y [1].

Cukurova University Faculty of Medicine, Department of Neurology[1], Adana, Turkey; Cukurova University Faculty of Medicine, Department of Medical Biology[2], Adana, Turkey.

zaferkoc@superonline.com

Friedreich's ataxia (FRDA), the most common subtype of early onset hereditary spinocerebellar ataxia (SCA), is an autosomal recessive neurodegenerative disorder caused by unstable GAA tri-nucleotide expansions in the first intron of FRDA gene located at 9q13-q21.1 position.

Friedreich's ataxia (FRDA) is an autosomal recessive neurodegenerative disease involving the central and peripheral nervous systems and heart. It is the most common subtype of early onset hereditary spinocerebellar ataxia (SCA). The FRDA gene, also called X25, was mapped to 9q13 by linkage analysis. It has approximately 80 kb of genomic DNA with six exons transcribing the major mRNA isoform, which encodes a 210 amino acid mitochondrial protein, frataxin. FRDA is caused primarily by unstable expansion of GAA repeats in the first intron of the gene which accounts for 96% of mutant alleles.

The study was performed on 35 patients (male n:20, female n:15) with FA and some of them family members. And we determined GAA tri-nucleotide expansion in 51 subject. Clinical findings; First complaining was gait disturbs (n:23), imbalans (n:19) and, gait disturbs and imbalans (n:9) respectively. In neurological examination, there was findings of cerebellar, pyramidal and lemniscal system involvement in all of them. In power examination; we reported paraparesia (n: 27) and tetraparesia (n: 9) respectively. Power examination was normal in 15 patient. Deep tendon reflexes were absent in 24 of them, hypoactive of upper extremities and absent of lower extremities in 27 of them. Vibration sensation was decreased in the upper extremities, and absent in the lower extremities. We determined optic atrophy (n:18), electrocardiographic findings (mitral valve prolapse, hypertrophia of left ventricle, left ventricular diastolic dysfunction and mitral failure) (n: 9), and mental retardation (n:6) in our patients. Physical examination revealed skeletal deformities (pes cavus, scoliosis, kyphoscoliosis, and hammer toes).

40 patients were confirmed as FRDA on molecular basis; 41 (80.3 %) were homozygous for GAA repeat expansions and 10 (19.6 %) heterozygous. All heterozygous patients showed typical Friedreich's ataxia symptoms indicating that these patients were compound heterozygous. In homozygous patients, repeat numbers ranged from approximately 425 to 1300. Ten patients with heterozygous GAA expansions had 7–34 GAA repeats in the normal allele and 66–900 repeats in the mutant alleles.

In conclusion, these results also confirm earlier findings about the correlation between the clinical features and GAA tri-nucleotide expansion of FRDA phenotype.

Key words: Friedreich's ataxia, clinical findings, GAA tri-nucleotide expansion

P63

A large family with restless leg syndrome

Koc F [1], Yerdelen D [2].

Cukurova University Faculty of Medicine, Department of Neurology [1], Adana, Turkey; Baskent University Faculty of Medicine, Department of Neurology [2], Adana, Turkey.

zaferkoc@superonline.com

Restless Leg Syndrome (RLS) is characterized by necessity to move legs and disturbing or unpleasant sense in the legs. Frequently, these complaints are bilateral, however can be unilateral and sometimes upper limbs are also affected. In this study, a large family with RLS is presented.

A 52-year-old woman applied to the clinic with complaints of paraesthesia and abnormal sensation disorder in legs and right arm which she could not define well. Her history revealed that her complaints had started as pain and abnormal sensation in below of the right knee spreading to end of the fingers 30 years ago and similar symptoms had started to occur in left leg and right arm for 10 and 2 years, respectively. While these complaints were prominent during rest, were decreasing with movement. Pain and abnormal sensation were starting mildly in the afternoon and increasing in the evening and before going to sleep. Abnormal sensation (dysesthesia) was causing to motor anxiety and necessity to move. It was learned that she was moving her legs continuously while going to sleep and turning in the bed frequently. So, she was feeling drowsy, concentration difficulty, headache and nervousness in the morning, as not slept never during the night. In her family, 17 subjects were determined to have RLS among 35 men and 28 women. The physical and neurological examination of the index case were normal.

Total blood count, fasting blood glucose, urea, iron, iron binding capacity, ferritin, vitamin B12, folate, free T3-T4 and TSH levels, sedimentation, blood electrolyte levels were normal. Electromyoneurography revealed normal findings. The psychic examination demonstrated a depressive emotion, decreased careful attention and concentration, difficulty in going to and continuing sleep. Antidepressant therapy (SSRI-paroxetine 20 mg/day) was given and pergolide 0.25 mg/night, a dopamine agonist, for RLS was started. It was planned to follow the patient as an outpatient and adjust the dose of pergolide by observing the improvement. Three weeks later, during control examination, her anxiety in her legs decreased and prominent improvement with pergolide 0.25 mg/day was recorded.

With this case, it is aimed to stress that RLS, seen in both of the genders and with an autosomal trait, should be kept in mind by clinicians in case of patients with abnormal sensations that can not be well defined in lower limbs.

Keywords: familial restless leg syndrome

P64

Neurofibromatosis type 1 and polymorphism

Koc F [1], Kocaturk Sel S [2], Yerdelen D [3].

Cukurova University Faculty of Medicine, Department of Neurology[1], Adana, Turkey; Cukurova University Faculty of Medicine, Department of Medical Biology[2], Adana, Turkey; Baskent University Faculty of Medicine, Department of Neurology[3], Adana, Turkey.

zaferkoc@superonline.com

Neurofibromatosis type 1 (NF1) is a rather rare multisystemic disease with generally autosomal dominant trait. Diagnosis is established by presence of at least 2 of 7 criteria including 6 or more café-au-lait spots, 2 or more cutaneous neurofibromas, axillary and inguinal freckles and Lisch nodules, slimming in cortex of long bones, pseudoarthritis, optic glioma and first degree relative with similar disease.

A 20-years-old woman was admitted to the clinic with complaints of headache without nausea or vomiting continuing for 4 years. She was diagnosed as NF1 2 years ago and her father and sister had similar disease. Neurological examination was normal and physical examination showed 15-20 café-au-lait spots, axillary and inguinal freckles and Lisch nodules. Cerebral MR imaging revealed approximately with a 1.5 cm diameter of hamartoma compatible with neurofibromatosis, mildly hyperintense in T1A and T2A series and could not be differentiated completely from adjacent paranchima in left basal ganglion inferior regions. As a result of molecular genetic examination of blood samples of our patient, her ill sister and mother, diagnosed as NF1 according to the National Health Institute (NIH) criteria, NF1 gene polymorphism haplotype analysis were obtained. By using one RFLP (Restriction part lengthiness polymorphism) marker, and four intragenic microsatellite marker for intron 27 and intron 38, haplotypes were created. These siblings with NF1 were showed to get allele, thought to be responsible for carrying disease in the family, from their father.

In this study, it is aimed to emphasize the importance of genetic studies in patients with NF with regard to determining polymorphism frequency in our community, identifying carrier individuals in the family and giving consultancy service.

Keywords: neurofibromatosis type 1, polymorphism

P65

Genetic study of demyelinating form of autosomal-recessive Charcot-Marie-Tooth diseases in a large Turkish family

Sahin-Calapoglu N [1], Soyoz M [1], Calapoglu M [2], Ozcelik N [1].

Suleyman Demirel University, Faculty of Medicine, Department of Medical Biology, Isparta, Turkey [1], Kafkas University, Faculty of Education, Department of Science Education, Kars, Turkey [2].

nilufersahin@yahoo.com

Charcot-Marie-Tooth disease (CMT) is a clinically and genetically heterogeneous group of inherited peripheral motor and sensory neuropathies, affecting 1 in 2500. CMT disease clinically characterized by distal muscle weakness and atrophy predominantly in the lower extremities, diminished or absent deep tendon reflexes and skeletal deformities such as pes cavus. The majorities of CMT cases are autosomal dominantly or X-linked dominantly inherited. Autosomal recessive CMT (CMT4) is a less frequent disorder and clinically similar to the dominant forms, but usually more severe with an earlier age of onset. To date, nine demyelinating loci have been implicated in CMT4 and seven genes have been identified. It has been screened by PCR-SSCP technique in this study for the presence of mutations in the coding region of GDAP1 (ganglioside-induced differentiation-associated protein-1) (CMT4A) and hasn't been found any mutations. Genetic linkage analyses of CMT4B1, CMT4B2, CMT4C, CMT4D, CMT4E and CMT4F loci were tested. Eleven members of this seven generations and three branches consanguineous ARCMT family were examined for molecular

genetic studies. Haplotype analyses at the loci were performed with STR polymorphic markers. PCR products were loaded onto 12% polyacrylamide gel. Genetic linkage was excluded by the absence of homozygosity for these six demyelinating genes loci. These findings show that another locus may be associated with this disease. In a further study we want to examine genetic linkage to CMT4G, CMT4H. If there is not a potential linkage to one of these loci, we thought that this large and consanguineous Turkish family will be helpful to identify a new gene for AR-CMT.

Keywords: Charcot-Marie-Tooth disease, autosomal recessive, linkage analyses, STR polymorphic markers, haplotype analyses

P66

PS1, IL1A and VDR gene SNPs and late-onset Alzheimer's disease

Dursun E [1], Gezen-Ak D [1], Uysal O [2], Ertan T [3], Bilgic B [4], Gurvit H [4], Emre M [4], Eker E [3], Engin F [3], Yilmazer S [1].

Istanbul University, [1] Cerrahpasa Faculty of Medicine, Department of Medical Biology, [2] Cerrahpasa Faculty of Medicine, Department of Biostatistics; [3] Cerrahpasa Faculty of Medicine, Department of Geropsychiatry; [4] Istanbul Faculty of Medicine, Department of Neurology, Behavioral and Movement Disorders Unit, Istanbul, Turkey.

erdincdu@hotmail.com

Alzheimer's disease is the most common cause of cognitive decline in the elderly, being characterized by progressive loss of memory and other cognitive functions, commonly occurring in late life but also seen in cases as young as 30 years of age. Single nucleotide polymorphisms (SNPs) in the intron 8 of Presenilin 1 (PS1) gene and promoter region (-889) of interleukin-1 alpha (IL1A) gene, are thought to be candidates for late onset Alzheimer's disease susceptibility. In our previous studies we also determined a strong association with vitamin D receptor (VDR) gene polymorphisms and AD. In this study our aim was to compare the genotype distribution of these three genes in AD patients and their age matched healthy controls. Sixty-two cases of dementia of late onset Alzheimer type and 48 age-matched controls have been included in this study. PCR and RFLP performed for determining the PS1 and VDR single nucleotide polymorphisms (SNP) and PCR-CTPP for IL1A SNP. When the control and patients were compared for the genotypes we saw that the distribution of PS1 and IL1A genotypes did not differ according to Chi-square test ($p=0.3$ and $p=0.5$, respectively). In contrast when the ApaI genotypes of the VDR gene compared, the frequency of the patients with Aa genotype observed significantly higher than that of the healthy individuals with the same genotype ($p=0.01$). Comparison of patients and controls having VDR gene Aa genotype with the IL1A genotypes showed a slight increase in the frequency of CC genotype, with 70% in patients and 41% in controls, though this was not statistically significant. Our results show no significant association for the suggested susceptibility alleles of neither PS1 nor IL1A in the condition of having Aa genotype for VDR gene in Alzheimer's disease.

Keywords: Alzheimer's Disease, SNP, VDR, presenilin 1, IL1

P67

SNPs at the ligand binding site of the vitamin D receptor gene and Alzheimer's disease

Gezen-Ak D [1], Dursun E [1], Ertan T [2], Hanagasi H [3], Gurvit H [3], Emre M [3], Eker E [2], Ozturk M [1], Engin F [2], Yilmazer S [1].

[1] Istanbul University, Cerrahpasa Faculty of Medicine, Department of Medical Biology, [2] Cerrahpasa Faculty of Medicine Department of Geropsychiatry, Istanbul University, [3] Istanbul Faculty of Medicine, Department of Neurology, Behavioral and Movement Disorders Unit, Istanbul, Turkey.

duygugezenak@yahoo.com

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that effects whole regions of the brain. The key aims in therapeutic strategies of AD are to decrease the neuronal damage, maintenance or regeneration of neurons. 1,25(OH)2D3 (vitamin D3) could mediate its neuroprotective effects via the modulation of neuronal calcium homeostasis and production of neurotrophins. By the way, single nucleotide polymorphisms (SNPs) which could effect the relationship between vitamin D3 and its receptor (vitamin

D receptor-VDR) may be important on the period and impact of therapy. In addition, the polymorphisms which can be effective on the affinity of vitamin D3 to its receptor may influence the synthesis of NGF and calcium channels. VDR gene polymorphisms can be related with neurodegenerative diseases and neuronal damage. In this study, our aim was to determine if there is an association between VDR gene and late-onset AD. Eighty four cases of dementia of Alzheimer type and 84 age-matched controls (mean ages 74.7, and 72.2 years, respectively) have been included in the study. Patients are clinically diagnosed according to DSM-IV criterias. We used PCR and RFLP to test for an association between AD and Apal and TaqI polymorphisms at VDR gene. When the controls and patients were compared for their TaqI genotype a nearly significant difference was observed ($p=0.07$). On the other hand when the Apal genotypes compared, the frequency of the patients with Aa genotype observed significantly higher than the frequency of the healthy individuals with the same genotype ($p=0.0018$). We concluded that having 'Aa' genotype may increase the risk of developing AD 3 times when compared with having 'AA' ($p=0.00075$, $OR=3.05$, 95% CI 1.583-5.907). With the AA genotype as a reference the Aa+aa together was associated with a 2.5 times increased in risk of AD ($p=0.003$, $OR=2.574$, 95% CI 1.370-4.837).

Keywords: Vitamin D, VDR, Alzheimer's disease, Apal, TaqI, polymorphism

P68

The effects of acute immobilization stress on spatial memory and learned helplessness

Yurtsever OD [1], Mengi M [2], Yurdakos E [2].

Istanbul University, Institute Of Social Science Psychology[1], Cerrahpasa Medical Faculty, Department of Physiology [2] Istanbul, Turkey.

ertanyurdakos@mynet.com

Considerable experimental and clinical data indicate that stress can influence emotional and spatial memory. The amygdala and hippocampal complex, two medial temporal lobe structures, are linked to two independent memory systems, each with unique characteristic functions. The hippocampus is considered to play a central role in the formation of explicit/declarative types of memories, where as amygdala has a role in emotional memory. In this study, we investigated the effects of acute immobilization stress on spatial memory and learned helplessness by using Morris water maze and Porsolt's swim test (PST) in rats. Wistar albino male adults rats weighting 250-300g. were divided into 4 groups:

The groups that Morris water maze test were applied:

1. Control group: (n=10)
2. Acute immobilization stress+Morris water maze group: in this group, rats were exposed to 10 minutes of immobilization stress daily for two days (n=10).

The groups that Porsolt's swimming test were applied:

3. Control group: (n=10)
4. Acute immobilization stress+Porsolt's swimming test group: in this group, rats were exposed to 10 minutes of immobilization stress daily for two days (n=10).

Results are analyzed with Mann-Whitney U test for inter-group comparisons and Wilcoxon Signed Ranks Test for intra-group comparisons.

There were no statistically significant differences among the daily learning performance of the experimental and control groups in the Morris water maze test.

Control group displayed longer immobilization and significantly shorter struggle time ($p<0.01$) on the second swimming test (PST 2) compared to first test (PST 1) conducted 24 hours before. No significant differences were observed for the experimental group on immobilization and struggle parameters between PST 1 and PST 2. These results suggest that acute immobilization stress 10 minutes for two days have no effect on spatial memory but prevents learned helplessness.

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Key words: acute stress, immobilization, spatial memory, emotional memory, learned helplessness

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Effect of ketamin application at a sub-anesthetic dose for 5 days on emotional and spatial learning

Karsli TA [1], Mengi M [2], Yurdakos E [2].

Istanbul University, Department of Psychology [1] Istanbul, Turkey; Istanbul University Cerrahpasa Medical Faculty, Department of Physiology [2] Istanbul, Turkey.

ertanyurdakos@mynet.com

Ketamin, a non-selective NMDA receptor antagonist, is known to induce psychosis-like symptoms. This study is conducted to find out whether i.p ketamin application for 5 days at a sub-anesthetic dose, which is proposed to be a new schizophrenia model, simulates the endotypic cognitive and emotional problems observed in schizophrenics by using Morris Water Maze and Porsolt Swimming Test (PST). Male rats of Wistar strain weighing 230 to 250gr., which were allocated randomly to one of two experimental and two control groups, were used in this study. First experimental group (n=9) was injected with 35mg/kg i.p ketamine for 5 days which was followed by Porsolt swimming tests starting 15 days after the last day of injection. The second experimental group (n=9) was also injected with 35mg/kg i.p ketamine for 5 days which was followed by Morris Water Maze starting 15 days after the last day of injection. Both of the control groups were injected with 0,35ml i.p saline for 5 days which then followed by the same procedure applied to the experimental group. Results are analyzed with Mann-Whitney U test for inter-group comparisons and Wilcoxon Signed Ranks Test for intra-group comparisons. There were no statistically significant difference among the daily learning levels of the experimental group on the Morris Water Maze, which was applied for 4 days, whereas for control group there were significant differences among the daily learning levels. Control group displayed significantly longer immobilization and shorter struggle time on the second swimming test (PST 2) compared to first test (PST 1) conducted 24 hours before. No significant differences were observed for the experimental group on immobilization and struggle parameters between PST 1 and PST 2. Our results indicate that injection with i.p ketamin at a subanesthetic dose for five days, which is proposed to be a new animal model of psychosis, actually models the deterioration in cognitive and emotional learning problems observed in schizophrenics.

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Keywords: Ketamin, schizophrenia, glutamate, Morris water maze, Porsolt swimming test

P70

Neuropeptide Y alters stress-induced changes in trace element concentrations of brain in chronically immobilized rats.

Karakoc Y [1], Turhan S [2], Yildirim EA [3], Mengi M [2], Yurdakos E [2], Barutcu UB [4].

Department of Physiology, Inonu University Faculty of Medicine, Malatya, Turkey [1]; Department of Physiology, Istanbul University Cerrahpasa Faculty of Medicine, Istanbul, Turkey [2]; Department of Anxiety Disorders, Bakirkoy Research and Training Hospital for Psychiatry and Neurology, Istanbul, Turkey [3]; Department of Biophysics, Istanbul University Cerrahpasa Faculty of Medicine, Istanbul, Turkey [4].

ertanyurdakos@mynet.com

Central administration of neuropeptide Y (NPY) produces anxiolytic-like behavioral responses in the conflict test, elevated plus maze, fear-potentiated startle paradigm, and in the chronic restraint stress. Exogenously administrated NPY also protects against the anxiogenic effects of corticotropin-releasing factor. In the present study, we aimed to determine the effects of centrally administered NPY on the trace element disturbances in brain tissues (frontal and temporal lobes and brain stem) and the other major organs including liver, spleen (zinc [Zn]-, copper [Cu]-, and iron-rich tissues), kidney, and stomach in chronically immobilized rats. The immobilization stress was performed in special cages in which the animals were not able to move. The rats in chronic stress and chronic stress+NPY groups were kept in the cages daily for 7 min for 15 consecutive days. Intracerebroventricular (ICV) cannulas were placed to the right lateral ventricles of the rats by using

stereotaxic method. In the control and chronic stress groups, 5µL of saline (NaCl 0.9%), and in the chronic stress +NPY group, 8µg NPY/5 µL saline solutions, were administered into the brain via ICV cannula, respectively. Controls and immobilized rats were decapitated 30 min after the injections were over and samples of tissue were taken. Zn, Cu, and iron levels of the frontal lobe, temporal lobe, brain stem, liver, spleen, kidney, and stomach were determined by flame atomic absorption spectrophotometer. Zn and Cu levels were significantly increased in the frontal lobe, temporal lobe, and brain stem in response to chronic immobilization stress daily for 7 min for 15 consecutive days. The administration of NPY inhibited the elevation of Zn in these three parts of brain but did not affect the elevation of Cu in the frontal lobe and brain stem. Increases in Zn and Cu levels of frontal, temporal lobes, and brain stem may be related to induction of MT-I mRNA expression by chronic immobilization stress, and NPY may affect this induction of MT-I, altering corticotropin-releasing factor release in the stress conditions.

Key words: restraint stress, zinc, copper, iron, neuropeptide Y

P71

The effects of intermittent hypobaric conditions on anxiety and learned helplessness of rats

Mengi M, Altan M, Metin G, Yurdakos E, Cakar L.

Istanbul University, Cerrahpasa Faculty of Medicine, Department of Physiology, Istanbul, Turkey.

ertanyurdakos@mynet.com

As the altitude increases oxygen content of the ambient air decreases gradually. It is well known that nervous system is very sensitive to hypoxia and %25 of body O₂ needed is consumed by the brain. Intermittent hypobaric exposure has been used extensively for altitude preacclimatization, enhancing exercise performance and for the treatment of a variety of clinical disorders. Despite the studies investigating the effects of hypoxia on brain functions there are a few studies investigating the effects of intermittent hypobaric exposure to emotionality. Previous studies that used different protocols of hypobaric conditions provide limited data on this topic. In this study we aimed to investigate the effect of intermittent hypobaric conditions on the emotionality of male wistar albino rats. Animals were divided in to two experimental groups: control group (n=9) and intermittent hypobaric group (IH) (n=10). IH group experienced hypobaric conditions 2 hours a day and 4 days a week for 9 weeks in the hypobaric chamber which has the atmospheric pressure of an altitude of 3000 meters. After 9 weeks of IH procedure all animals were tested for their levels of emotionality using the open field test (OF), hole board (HB), elevated plus maze (EPM) and Porsolt swimming test (PST). In the OF, IH group showed a significant decrease in the number of squares crossed ($p < 0,05$) compared to control. By using HB, IH group showed a significant decrease in the number of head-dips ($p < 0,05$) and rearing ($p < 0,01$) compared to control group. In the EPM time spent in closed arm ($p < 0,05$) increased significantly whereas number of rearing ($p < 0,05$), number of entries ($p < 0,01$), time spent ($p < 0,05$) on open arm and the number of entries to closed arm ($p < 0,05$) in the IH group significantly decreased compared to control group. In the PST the control group and IH group animals exhibited the learned helplessness by a significant increase in the immobilization time ($p < 0,01$) and a decrease in duration of struggle ($p < 0,01$) compared to pretest.

These results suggest that IH procedure has anxiogenic effects; however this experimental condition have no effect on learned helplessness. As a result while using intermittent hypobaric exposure for altitude preacclimatization, enhancing exercise performance and for the treatment of a variety of clinical disorders the anxiogenic effect of IH conditions should be considered.

Keywords: intermittent hypobaric, anxiety, open field, hole board, elevated plus maze, Porsolt swimming test

P72

Effects of radio frequency radiation (RFR) on the permeability of blood brain barrier

Sınav Aral B, Seyhan N.

Gazi University, Faculty of Medicine, Department of Biophysics, Ankara, Turkey

bahriyes@gazi.edu.tr

With developing industry and technology, communication tools take place in our daily life densely. Most of these tools use the Radio Frequency Radiation (RFR) in the electromagnetic spectrum. Scientific world has focused on the biological effects of RFR for more than 30 years. One of the most important biological effects of RFR is the increase in the permeability of blood brain barrier (BBB). Although, some researchers such as Merritt and Preston had found no change, Salford's group, Töre and many others found increase in the permeability of BBB of rats after RFR exposure. Lin, who is very famous in RF studies, explained that the increase was observed due to the temperature rise in the tissue after the exposure. This study's aim is to search the effects of 900 MHz and 1800 MHz CW – continuous wave - radio frequency radiation on the permeability of BBB of rats. Twenty five wistar albino male rats (268.13 ± 41.92 g) were used in the study. They were divided into 3 groups; in the first group, animals used as control (Group A, n = 8), in the second and third groups (Group B, n = 8, Group C, n = 9) exposure to 900 MHz (max 13.9 V/m – min 12.8 V/m) & 1800 MHz (max 13 V/m – min 12.3 V/m) RFR, respectively, in the near field condition with 20 minutes exposure period was used. The permeability of BBB was determined by Evans Blue (EB) dye. It was given by i.v. injection via tail vein and had been used as a tracer for serum albumin. EB solution was given to all groups. After the exposure, cardiac perfusion was performed and then brains were taken out. Samples were analyzed using spectrophotometric method. Evans blue dye content was found to be 0.072 ± 0.010 mg % in the whole brain in the control animals, 0.1325 ± 0.0200 mg % in the 900 MHz exposed group and 0.1123 ± 0.0235 mg % in the 1800 MHz exposed group. In both exposed groups the permeability of BBB found to be increased wrt control group ($p < 0.01$). No statistical difference found between the two exposed groups ($p > 0.01$). Results have shown that 20 minutes RFR exposure of 900 MHz and 1800 MHz induced an effect and increased the permeability of BBB. Our studies on the GSM Modulated RFR and the permeability of BBB are on the way.

This study was supported by grant from Gazi University Research Foundation, No: 01/2005-78.

Keywords: Permeability of the Blood Brain Barrier (BBB), Evans Blue (EB), Radio Frequency Radiation (RFR), Spectrophotometric Method, Mobile Phones.



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