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ABSTRACT BOOK

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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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CONFERENCES

K1

The neurobiology of Alzheimer's Disease: behavioural studies transgenic mice targeting APP, presenilin and the impact of active immunization

Morris R.

College of Medicine and Veterinary Medicine, Edinburg

r.g.m.morris@ed.ac.uk

There is presently considerable effort worldwide to understand the neurobiology of Alzheimer's Disease. It is a complex problem with work at many different levels of analysis. Behavioural studies are contributing as they have revealed that transgenic mice, harbouring familial mutations of human genes, can also display memory loss and other cognitive abnormalities as well as pathological hallmarks of the disease such as amyloid plaques. This talk will describe some of my group's small contributions to this field, including longitudinal studies of memory loss through life, and efforts to restore memory through interference with secretase pathways that cleave APP and active immunisation against beta-amyloid itself. The lecture will conclude with a short assessment of the prospects of developing treatments that truly stem the course of the disease.

K2

The nuclear symptoms of schizophrenia and the evolution of Homo sapiens: the Broca-Annett axiom and the quadripartite brain

Crow TJ.

SANE POWIC, University of Oxford, Warneford Hospital, Oxford OX3 7JX

tim.crow@psych.ox.ac.uk

The faculty of language as a defining feature of Homo sapiens with characteristics absent in the communicative systems of the great Apes challenges Darwinian gradualism as Friedrich Max Mueller in 1873 and Noam Chomsky in 1959 clearly explained. It is more readily assimilated to a saltational account of speciation as suggested by TH Huxley and developed by R Goldschmidt.

The Broca-Annett hypothesis that cerebral asymmetry is the characteristic that defines the human brain and has enabled the evolution of language is supported by recent cross-species comparisons for directional handedness and anatomical asymmetry.

The paradox of psychosis is that inter-individual variation that is apparently genetic in origin persists at approximately the same frequency in all populations in the face of a fecundity disadvantage; it is suggested that this variation represents a component of the variation associated with the capacity for language and that the phenomena of psychosis are the key to an understanding of the neural organisation of language.

Two characteristics of human language have been suggested – the arbitrariness of the association between the signifier and its associations (de Saussure) and universal grammar (Chomsky); neither on its own has led to a clear exposition of the neural components of language and neither has been related to cerebral asymmetry.

It is suggested that the cerebral torque (the bias from right frontal to left occipital across the antero-posterior axis) defines the human brain as a four-chambered organ by comparison with the two chambers (anterior motor and posterior sensory) of the brains of other primates, and that it dictates a reversal of sign of the convergence of inter-hemispheric connexions (from left to right posteriorly and from right to left anteriorly).

These transitions are proposed as critical for the separation of the sensory and motor phonological engrams in the dominant left hemisphere from some of their associated signifiers (the sensory "meanings" and the motor "thoughts") in the non-dominant hemisphere.

Critical to the distinction between the speaker and the hearer and to what is motor and what is sensory in the neural representation of speech is the notion (associated with K Buehler) of a deictic origin ("I, here, now") to the coordinate system of speech. Related to this is the performative hypothesis that every sentence has a (usually unexpressed) superordinate clause ("I say unto you") in the first person and the present tense.

The nuclear symptoms of schizophrenia (eg thoughts spoken aloud, running commentary, thought insertion) are interpreted as anomalies of the segregation of the components of language into the four compartments of association cortex, anomalies that illustrate the importance of the separation of the motor and sensory aspects of the spoken word and of the two types of phonological engram from some of their associations.

The deictic origin is identified in Broca's area and defined by its interaction through the uncinate and arcuate bundles with Wernicke's area.

According to this concept the nuclear symptoms of schizophrenia are the primary disorders of syntax.

K3

A potential for axonal regeneration in the adult mammalian brain

Aguayo A.

albert.j.aguayo@mcgill.ca

No abstract available.

K4

Molecular mechanism of the human circadian clock

Sancar A.

Department of Biochemistry and Biophysics, University of North Carolina School of Medicine, Chapel Hill, North Carolina 27599, USA

aziz_sancar@med.unc.edu

Circadian rhythm is the oscillation in the biochemical, physiological, and behavioral functions of organisms that occurs with a periodicity of about a day. Recently four genes that control the circadian rhythm in mice and humans have been identified. The clock and BMal1 genes encode transcription factors that activate the transcription of the Cry and Per genes. These genes encode problems that inhibit the clock-BMal1 activator, generating a delayed feedback regulatory loop that results in the time-circadian expression of physiological functions. The cryptochrome genes and proteins that were discovered in our laboratory are also involved in tight-synchronization of the circadian clock. Circadian clock disruption may predispose humans to sleep disorders, depression, cardiovascular disease, and cancer.

K5

Motor nervous system of *Caenorhabditis elegans*: a platform for systems biology

Cinar H.

Department of MCD Biology, 329 Sinsheimer Labs, University of California Santa Cruz, CA 95060, USA.

hcinar@biology.ucsc.edu

Research on the vertebrate brain has to tackle the complexity that pervades every level of analysis. The nematode *C. elegans* is a genetically tractable

organism that provides a simple model to study neurobiological questions. Here, I discuss the motor nervous system of *C. elegans* as an experimental unit to analyze functions of specific neurons in molecular and behavioral terms.

The motor neuron circuit has components A, B, and D type neurons that control body movement. A fundamental question is what makes these neurons distinct from each other. Using neuron specific genomics, we described a molecular signature for the GABAergic D neurons. By coupling high throughput data to functional analysis, we identified members of a regulatory gene network specific to these cells. This approach provides access to genetic networks in a neuron type and offers a valuable tool to crack the regulatory code underlying neuronal identity and/or diversity.

Another question is how the motor neuron circuit controls movement. For this, we exploited motor-neuron-expressed nicotinic acetylcholine receptors (nAChRs). The organization of the nematode nervous system is such that loss of function in nAChR genes may disrupt neuronal circuits that control motor behavior. We took animals that carry null alleles of three nAChR genes and examined their sinusoidal movement using an automated tracking system. This analysis identified genetic interactions that suggest circuit configurations for nAChR combinations. Cell-specific rescue analysis demonstrated a function for one of the genes in GABAergic motor neurons, possibly involving neurotransmission. These observations underscore the advantage of using *C. elegans* to understand neuronal cholinergic signaling which is implied in drug addiction and Alzheimer's disease.

Lastly, using ultrashort laser technology, we described an axon regeneration paradigm in *C. elegans* motor neurons. Animal models of nerve regeneration are mostly limited to vertebrate organisms. Invertebrate models such as the nematode provide tremendous research potential because of genetics and screening methods. Laser-lesioned axons of motor neurons recover in one day and, convincingly, the behavioral defect created by severed axons improves over the same time period. We would like to use this technique to investigate the dynamics of injury and regeneration in the worm nerves. This endeavor may generate insights for human afflictions such as diabetic neuropathy and spinal cord injuries.

K6

The evolution of asymmetry: why the human brain is not unique?

Gunturkun O.

Dept. Biopsychology, Institute for Cognitive Neuroscience, Faculty of Psychology, Ruhr-University Bochum, 44780 Bochum , Germany.

onur.guentuerkuen@ruhr-uni-bochum.de

Several theories posit that the evolution of the human brain involved the introduction of a completely new architectural feature, namely cerebral asymmetries. It is assumed that only due to these left-right differences we harbour the ability to produce language, handedness, and all the other cognitive features that make us human. One implication of these theories is that we will not find animal models for our asymmetries.

I will present evidences that cerebral asymmetries are an ancient feature of the vertebrate brain. Asymmetries of communication, handedness, and visual feature analysis are shared by many species similar to humans. In addition, the general neural architecture of our brain shows no uniqueness but is part of the general pattern of the vertebrate brain. There is no doubt that humans have cognitive abilities beyond anything found in the animal kingdom. But the reason for these superior abilities is not our asymmetrical brain.

K7

New trends in genetic and epigenetic control of addictions: transcription factor "clock" genes

Uz T.

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

uz@psych.uic.edu

Recently, in addition to the genetic mechanisms that take place at the transcription level (i.e., rna), the regulatory mechanisms that occur at the dna level (i.e., epigenetic) are being considered in the field of addiction. Transcription factor "clock" genes have been proposed as regulators of addictive behaviors. Furthermore, the underlying long-term plastic changes in these behaviors, which regulate the expression of a second group of genes (i.e., clock controlled genes), such as tyrosine hydroxylase in the brain. It has also been demonstrated that clock genes themselves are regulated by epigenetic mechanisms. We have found that histone acetylation (i.e., h3) is critical for the expression of the clock gene *period1* in the brain regions implicated in the development of addictive behaviors, such as the striatal complex. It has been suggested that intracellular signaling systems (i.e., camp-mediated) regulate the expression of clock genes. Using an *in vitro* model of primary neuronal cultures prepared from the striatum, we demonstrated that in these dopaminergic neurons, g protein-coupled receptors for melatonin and dopamine and the signaling pathways mediated by these receptors regulate the expression of clock genes. Moreover, using mouse knockout for melatonin receptors and their matching wild type controls, we found that melatonin receptors are involved not only in the regulation of striatal clock gene expression but also in the development of cocaine-induced behavioral changes (i.e., diurnal locomotor sensitization). Thus, our results suggest that neuronal receptor (e.g., melatonin receptor)-mediated mechanisms are capable of controlling the long-term plastic changes involved in the development of addictive behaviors by regulating clock gene expression at both the dna (i.e., epigenetic) and the rna (i.e., genetic) levels.

K8

The effects of EEG-biofeedback on disinhibitory symptoms

Karamursel S.

I.U. Istanbul Medical Faculty, Department of Physiology, Istanbul, Turkey.

sacit@istanbul.edu.tr

Attention-deficit/hyperactivity disorder is a multifactorial disorder with complex etiology and strong genetic underpinnings. The inattention component of ADHD is manifested as daydreaming, distractibility, and difficulty focusing on a single task for a prolonged period. The hyperactivity component is expressed as fidgeting, excessive talking, and restlessness. Attention-deficit/hyperactivity disorder is a worldwide and highly prevalent disorder, estimated to affect 5%-10% of children (Faranone et al 2003). Bruxism and nail biting symptoms are also supposed to have a disinhibitory mechanism. Neurofeedback refers to an operant conditioning paradigm where participants learn to influence the electrical activity of their brain. The principal feasibility of learned self-regulation has been demonstrated for evoked potentials (EPs) (Rosenfeld et al, 1969), event-related potentials (ERPs) (Birbaumer et al, 1981), slow cortical potentials (SCPs) (Birbaumer, 1984; Hardman et al, 1997), and EEG frequency components (Kamiya, 1968). The best established clinical application of EEG frequency component training consists of the treatment of epilepsy through learned self-regulation of the 12–15 Hz sensorimotor rhythm (SMR) recorded from central scalp regions over sensorimotor cortex (Sterman, 2000). SMR activity over sensorimotor cortex is probably generated through thalamocortical interactions during burst firing activity in ventrobasal thalamic relay nuclei (Harper and Sterman, 1972), associated with the suppression of somatosensory afferent gating (Howe and Sterman, 1972). The operant enhancement of SMR, trained concurrently with suppression of slower theta (4–8 Hz) components, and/or training of higher beta band components, such as beta1 (15–18 Hz) in the treatment of attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD) (Lubar and Lubar, 1984; Lubar et al, 1995; Linden et al, 1996). P300 recordings with oddball paradigm were taken before and after EEG-biofeedback training in 16 ADHD, 14 nail biting and 10 bruxism patients. They were trained twice a week for 30 minutes. Complete relief was obtained in 10-15 sessions in nail biting and bruxism, whereas 30-40 sessions were needed for ADHD patients to obtain a significant progress. In all groups, after SMR training, SMR and P3 amplitudes increased significantly and slow potential shifted robustly from negative to positive in the time window of ca. 200-500 ms after the stimulus. The increase in P3 amplitude and shift in the slow positive potential suggest that SMR training enhances inhibitory processes that might cause resolving or improvement in the symptoms related to disinhibition.

K9

Signal transduction mechanism in melancholic depression

Akin D.

Yeditepe University, Facuty of Farmacy, Istanbul, Turkey.

demetakin2000@yahoo.com

Mood disorders are complex conditions involving widely divergent symptom elements, including dysregulation of mood, sleep, appetite, energy expenditure, hormonal function, and sex drive. This diversity, involving multiple brain regions and neurochemical systems, suggests abnormalities in regulatory aspects of neuronal function. Chief among the intracellular regulatory elements are the protein kinases such as protein kinases A (PKA) and C (PKC). Our group (Manier et al., 1996, 2000, 2001; Shelton et al., 1996;1997; Dwivedi et al., 2002a–c; Dwivedi and Pandey,2000; Manji and Chen, 2002; Mori et al., 1998, 2001;Nestler et al., 1989; Pandey et al., 1997, 1998, 1999, 2001, 2002; Perez et al., 1995, 1999, 2000, 2001, 2002; Rahman et al., 1997) have suggested that anomalies of signal transduction, could yield consequences that, at a psychopathological level, could result in depressed mood. Moreover, antidepressant drugs activate norepinephrine (NE)- and serotonin (5-HT)-receptor mediated signal transduction cascades, involving PKA and PKC (Nestler et al., 1989; Popoli et al., 2000;Shelton, 2000).

PKA-dependent phosphorylation regulates receptor function, synaptic transmission, ion channel activity, and gene transcription (Edelman et al., 1987; Feliciello et al., 2001; Meinkoth et al., 1993; Montminy,1997; Skalhegg and Tasken, 2000; Taylor et al., 1992). PKA is a tetrameric holoenzyme consisting of two catalytic subunits (C) bound to a dimer of regulatory subunits (R). cAMP binds cooperatively to two domains on the R subunits, releasing the C subunits, which then are available to phosphorylate serine and threonine residues on target proteins (Doskeland et al., 1993).

A picture of altered cAMP binding to PKA R subunits, PKA phosphorylation activity and subunit expression has emerged in patients with mood disorders. The phospholipase C (PLC)–PKC pathway also has been implicated in mood disorders (Dwivedi et al., 2000, 2002a; Dwivedi and Pandey, 1998; Hrdina et al., 1997; Hrdina and Du, 2001; Pandey et al., 1995, 1997, 1998, 2001, 2002; Sibille et al., 1997; Yatham et al., 1999). The activation of PKC results in the phosphorylation of CREB and therefore, ostensibly, would be expected to act in ways similar to PKA (Hoe.er et al., 1989). The current picture of PKC activity in mood disorders is complicated. One study showed increased PKC activity in platelets (Pandey et al., 1998) and chronic administration of antidepressants was found to decrease the activity of PKC in the cortex and hippocampus of rats (Chen et al., 1999; Mann et al., 1995). Another study indicated that there was an alteration in PLC and PKC isoform expression and activity in platelets of bipolar but not unipolar patients (Pandey et al., 2002). However, by contrast, studies of postmortem brain tissue of depressed suicide victims have found decreased PKC binding and activity (Pacheco et al., 1996; Pandey et al., 1997).

An improved understanding of the physiological bases of depressive disorders will provide new targets for invention of drugs.

K10

The role of inflammation and free radicals in neurodegenerative diseases

Yuksel M.

Marmara University, Vocational School of Health Related Professions, Department of Medical Laboratory, Haydarpasa- Istanbul, Turkey.

meralyuksel@marmara.edu.tr

Oxidative stress has long been linked to the neuronal cell death that is associated certain neurodegenerative conditions. Postmortem brain tissues from patients with neurodegenerative disorders, including Parkinson's disease (PD), Alzheimer's disease (AD), Huntington's disease (HD) and amyotrophic lateral sclerosis (ALS) clearly display increased indices of reactive oxygen species in affected brain regions. Additionally a sustained inflammatory reaction is present in acute (e.g. stoke) and chronic (e.g. PD, AD, HD) neurodegenerative disorders. Inflammation, which is fostered by both residential glial cells and blood- circulating cells that infiltrate the diseased brain, probably starts as a time and site specific defense mechanism that could later to evolve into a destructive and uncontrolled reaction. Microglia are the resident innate immune cells in the central nervous system and produce a barrage of factors (IL-1, TNF alpha, nitric oxide, PGE2, superoxide radical) that are toxic to neurons. The aim of this conference is to explain the role of inflammatory cells and mediators at an inflammatory site affects the function and structure of the nervous system. A particular focus on free radicals and nitric oxide which are produced in relatively high concentrations at inflammatory sites. At least alternative therapies which reduced the intensity of neuroinflammation in neurodegenerative disorders.

K11

Neuronal differentiation of embryonic stem cells

Dalcik H.

Kocaeli University, Department of Histology and Embryology, Umuttepe, Kocaeli, Turkey.

hdalcik@kou.edu.tr

A stem cell can be described as an undifferentiated cell that is capable of producing an identical cell having a self-renewal property. Presently, it is possible to isolate and use culture conditions to establish stem cells, and from these potent cells, various types of differentiated cells can be obtained. There are two types of stem cells; Embryonic stem cells and Adult stem cells. Embryonic stem cells are derived from iner cell mass of the preimplantation blastocysts and are able to differentiate into cellular derivations of the three primary germ layers. Adult stem cells, are derived from the adult organs. These cells can differentiate into neurons, astrocytes and oligodendrocytes.

It is difficult to obtain a homogenious population from the embryonic stem cells. Therefore, inductive signals and transcription factors made it possible to identify type and subtype of neurons.

In the process of transplantation of the embryonic stem cell-derived neurons, it would be applicable to use a defined progenitor cells giving rise to a known mature cell rather than cells that are continously dividing and giving rise to various types of cells. When the factors that are used to maintain the undifferentiated states (without LIF and feeder layer) are removed and when the cells are cultured in suspention cultures, the embryonic cells form spherical aggregates called the Embryoid Bodies. The neuronal progenitor cells are derived from the embryoid bodies by spontaneous differentiation or by induction of the neuronal agents. From the outer layer of the embryoid bodies in sequence, endodermal, mesodermal and ectodermal derived cells appear.

In our study, we investigated spontaneous differentiation and induced neural differentiation of mouse embryonic stem cells (R1 cell lines). Retinoic acid was used as neuronal inducer. Endogenous retinoic acid is a regulatory factor that controls many aspects of embryonic development and adult functions. In spontaneous differentiation, embryonic stem cells were cultured in standart embryonic stem cell media without retinoic acid. In controlled differentiation, embryonic stem cells were cultured in a media containing retinoic acid. Retinoic acid was observed to induce neuronal and astrocytic differentiation in a dose and a time dependent manner. According to our results, in spontaneous differentiation in the late stage, small amount of neurons was visualized. With low doses of retinoic acid, neuronal cells were obtained, however, distinct mesencymal cell were also observed. At high concentration of the retinoic acid, the embryonic stem cells were fully differentiated into neuronal cells and no mesenchymal derivatives was observed.

K12

The role of ETS domain transcription factors in neuronal differentiation

Aksan Kurnaz I.

Yeditepe University, Dept. Genetics and Bioengineering, 34755, Kayisdagi, Istanbul, Turkey.

iakurnaz@yeditepe.edu.tr

PC12 cells have long been used as a model system for neuronal differentiation. 3 major growth factors studied in these cells, namely NGF, EGF and bFGF, all activate the MAPK signal transduction pathway and yet generate different cellular responses: NGF (Nerve Growth Factor) and bFGF (basic Fibroblast Growth Factor) both induce neuronal differentiation as monitored by axonal outgrowth and electrical conductivity, while EGF (Epidermal Growth Factor) induces proliferation in these cells (Marshall, 1995; Traverse et al, 1994; Yaka et al, 1998; Yamada et al, 1996). This difference is mainly due to duration of MAPK signaling, where transient versus sustained MAPK activation is though to induce expression of different target genes through activation of different transcription factor subfamilies. In this study, we have observed

that two different members of the ETS domain transcription factor family can induce different cellular responses: PEA3 results in differentiation in PC12 cells, while Elk-1 factor appears to play a role in survival of differentiating neurons rather than differentiation per se.

When cells are transfected with a repressive form of Elk-1 (ElkEN), the cells show increased apoptosis. This implies that Elk-1 normally has an anti-apoptotic function in cells. Consistently, when anti-apoptotic IAP-1 protein is cotransfected with ElkEN, cells gob ack to their normal mitoti cycle. It has also been shown that promoter of another anti-apoptotic molecule, MCL-1, is regulated by Elk-1 (Townsend et al, 1999). Our findings indicate that Elk-1 protein functions in survival of PC12 cells.

PEA3 protein, however, results in a differentiation response in PC12 cells when administered in combination with EGF, which normally leads to proliferation in these cells. In addition, when cells are differentiated with NGF, the expression of PEA3 message is increased. We believe, therefore, that sustained activation of MAPK leads to an increase in the PEA3 transcription factor, which may further get phosphorylated by MAPK, eventually leading to axonal outgrowth through expression of target genes.

Understanding the molecular mechanism of neuronal differentiation at the genetic level may help us generate a particular type of neuron through genetic modifications of stem cells *in vitro*. These kind sof genetic modifications may be more effective in directing lineage-specific differentiation when compared to growth factor coctails currently used in stem cell research.

PANELS

PNL1

IMAGING OF CORTICAL REORGANISATION / ADAPTATION

Moderator : Kubilay Aydin

Panelists : Didem Gokcay, Uzay Emrah Emir, Kader Karli Oguz, Kubilay Aydin

Brain morphology as a function indicator: studies on autism, dyslexia and schizophrenia

Gokcay D.

METU, Ankara, Turkey

didem@ii.metu.edu.tr

Being one of the non-invasive imaging methods, magnetic resonance (MR) is widely used at our times to generate images of the human brain. The structural characteristics of the brain can be derived from the MR images by the use of morphological methods. Comparison of morphological features in between patient and normal populations show that there is a difference between these two groups, and in general, the differences are observed at the regions of the brain where functional differences are localized. Thereby we may say that the structural differences observed on the MR images through morphological analyses also indicate functional differences.

In this talk, 4 different morphological analysis methods (volumetric, statistical, shape analysis and VBM) will be studied first by giving examples from the normal population, and by pointing out the advantages and disadvantages of each method. The examples on the normal population will cover morphological differences observed after the aging, growth in adolescense and training processes. Later on, the research on the autism, dyslexia and schizophrenia populations that use these morphological methods will be studied, highlighting the conflicting results in the literature and comparing the morphological and functional differences.

Emerging adaptation due to retinotopic stimulation in the primer visuel cortex

Emir UE.

Institute of Biomedical Engineering, Bogazici University, Bebek, Istanbul, Turkey.

uzayemir@boun.edu.tr

Neuroimaging modalities such EEG, PET, MEG and fMRI are the most common methods that neuroscientists use for functional brain imaging. By providing high resolution images, fMRI is used for functional brain mapping in clinic and research areas. Basically, fMRI is based on a response of the brain to a specific task which activates the specialized brain region. For instance, visual stimulus activates primary visual cortex.

In animal studies, visual cortex was previously mapped by electrophysiological measurements [1]. According to these studies, it is well understood that visual cortex can be mapped by polar coordinate system, retinotopy. In addition to this, results of retinotopy studies done by fMRI are coincide with the electrophysiological measurements. Most famous method used in fMRI for this purpose is based on phase-encoded retinal stimulation and Fourier-based analyze of functional response of visual cortex [2]. With the help of this method, human visual areas V1, V2, VP, V3, and V4 can be precisely and non-invasively determined.

In this study, first, how visual areas in primary visual cortex are determined by using fMRI will briefly described and then results of the study which aims to measure the structural and functional changes in primary visual cortex of the normal subjects, trained to Retinotopy stimulus for a month.

Activitydependent cortical adaptation; from morphology to biochemical imaging

Aydin K.

Istanbul University, Department of Radiology, Istanbul, Turkey.

kubilay@kubilayaydin.com

The results of the studies published in the last decade demonstrated the ability of brain to get functional and structural adaptive changes to gain new skills which increases the advantage in nature and in his social community. Adaptation/reorganization in brain leads to the more rapid, more accurate performance of the achieved new skills. The adaptive changes in brain is an old story in human history. The early brain specimens of homo habilis who contructed the first tools, had a brain weight of 500gr in early times of his life. He started to make tools to use in his daily life. And the late fossils demonstrated that his brain weight increased to 800gr at the end of species life time period. Homo erectus was a hunter and developed some speech. The complexity of sulcal pattern in inferior frontal area (Broca area) of homo erectus increased during the period of speech development.

Until the recently, it was thought that neuronal cell proliferation (neurogenesis) was not possible in adult brain. But, thanks to the recent studies, today we know that neurogenesis is possible in adult brains. The animal studies showed the presence of adult neurogenesis in subventricular zone and dentate nucleus of hippocampus. In these studies, the degreee of the adult neurogenesis in hippocampus was higher in animals living in the enriched environment in which animals should show high activity of search to get food. This findings demonstrated the activity dependent regulaton of adult neurogenesis. The activity dependent neurogenesis is not seen only in laboratory conditons but also in nature. The songbirds provide an excellent example of activity dependent regulation of adult neurogenesis. The new neurons are inserted into the neuronal circuits in high vocal center region of birds which is the song production center. The neurogenesis in high vocal center shows seasonal changes, which shows correlation with the appearance of new songs. Black-capped chickadees are the birds living North America forrests. Their diet changes from insects to seed in early fall. They hide their food to eat during witer season. Therefore, they need high navigation memory to find their hiden seeds. In a study, there was new neuron addition in the hippocapus of black-capped chickadees and the degreee of neurogensis increased during fall period in which birds need high spatial memory. In in interesting and popular study, Maguire et al., performed voxel based morphometry in the taxi drivers of London. They found larger volumes and thickening of cortex in the right hippocampus of the taxi drivers compared to the control subjects. And there was a correlation between the volumetric changes and period of time spent as a taxi driver. They proposed that high motivation and activition in navigation might lead to the adaptive changes in right hippocampus which was accepted as a spatial memory center.

Musician brains constitute a perfect model in the adaptation and reorganization studies. The results of mant studies demonstrated the morphological and functional adaptive changes in the brain of professional musicians. Planum temporale is the center for pitch discrimination. The cortex of the left plaum temporale is thicker in the brain of musicians. In a studiy, the asymmety of left planum temporale is correlated with the age of commensement of music training. In a quantitative proton MR spectroscopy study, we searched for

the possible diffence(s) of neurometabolite concentrations in the planum temporale between musicians and those of control subjects. The N-acetyl aspartate concentration (which is produced in the mitochondria of neurons) was high in the planum temporale of musicians and the N-acetyl aspartate concentration was corrrelated with the life time period of music training and performance. The musical experience beginning in early childhood might have led to the formation of new synapsesand/orneurons in the left planum temporale of musicians, to be able to process highly complex data during music perception.

Although the strong theories have been proposed, the definition of physiological mechnism(s) of cortical adaptation/reorganization needs more clarification in future studies.

PNL2

CURRENT ADVANCES IN EPILEPSY MODELS

Moderator : Filiz Onat, Cigdem Ozkara

Panelists : Cafer Marangoz, Melike Sahiner, Safiye Cavdar, Mehmet Kaya

Audiogenic seizure models

Marangoz C.

Ondokuz Mayis University Medical School, Department of Physiology, Samsun , Turkey.

caferm@omu.edu.tr

More than 50 million people worldwide suffer from epilepsy, and 20-30% of those afflicted have seizures that are resistant to treatment with the currently available antiepileptic drugs. Studies on the epilepsy have been done in experimental models. For development of new and effective antiepileptic drugs and study of mechanisms of the epilepsies requires appropriate experimental models. An ideal model for epilepsy should show the following characteristics: (1)the development of spontaneously occurring recurrent seizures; (2) seizure types similar to seizure types occurring in human epilepsy; (3) EEG pattern similar to EEG of the respective seizure in human; (4) high seizure frequency to allow acute and chronic drug efficacy tests; (5) pharmacokinetics of antiepileptic drugs similar to those in humans; (6) effective plasma and brain concentrations of antiepileptic drugs similar to those required for control of the respective seizure in humans.

Audiogenic seizures, which are a type of generalized seizures and reflex epilepsy, occur in some species of mammals in response to exposure to intense acoustic stimulation (100-110 dB). Audiogenic seizures are produced in brainstem, and main nuclei involved in their expression include inferior and superior colliculi and periaquaductal gray. Genetically seizure susceptible animals exhibit a wild running response which terminates in either a violent generalized clonic or tonic convulsion. Electrophysiological and pharmacologic studies suggest that the inferior colliculus (IC) is the main trigger area of audiogenic seizures.

According to the results obtained from our laboratory, L-Arginin, a precursore of nitric oxide, flunerizine, nicardipine and kynurenic acid have inhibitory effects on both wild running and tonic-clonic episodes of audiogenic seizures in Wistar rats.

In an other series of experiments, unbiased stereological methods have been used to estimate neuron number in the cochlear nuclei, inferior collicular nucleus (IC), and medial geniculate body in audiogenic seizure susceptible and nonsusceptible (control) Wistar rats. A significant decrease was observed in the cell number of the IC; but there were no alterations in the cell number of the cochlear nucleus and medial geniculate body in audiogenic seizure susceptible animals compared to controls. From these results, it can be suggested that the neuronal system within IC may plays a crucial role in audiogenic seizure activity.

Key words: Animal model; Audiogenic seizure; Inferior colliculus; stereology; rats

Learning and hippocampal kindling

Sahiner M.

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

aysemelike@pau.edu.tr

Repeated electrical stimulus causes epileptic seizures in cortical and limbic structures. This phenomena is known as “kindling effect” Kindling has been shown to have dramatic effects on a variety of structures within the brain. In particular, kindled seizures have been reported to cause long-lasting effects on Hippocampal physiology and anatomy. These effects range from the subcellular level, such as altered Hippocampal gene expression, to complicated structural alterations, such as mossy fiber sprouting, neurogenesis and cellular apoptosis.

Research examining synaptic structure following LTP has typically focused on the hippocampus, where morphological changes have been found . Synaptogenesis or the formation of new synapses has not been a consistent finding following Hippocampal LTP. The hippocampus is typically involved in processes that require rapid acquisition of information, whereas other structures may display more gradual changes.

However, kindling and LTP are different phenomena, they both show similar morphological changes. Studies have shown that kindling of fully generalized seizures produces subsequent deficits in spatial tasks such as the radial-arm maze and Morris water maze. Its known that such disturbances represent a specific disruption of spatial learning/short-term memory and are preferentially induced by kindling of the dorsal hippocampus. Clearly, very little amounts of kindling are capable of disrupting spatial cognition, although it is not clear whether this deficit is a retrograde impairment of spatial reference memory or an anterograde impairment of spatial working memory. Findings on this purpose are not clear evidence that this deficit increases in severity with continued kindling, although one interpretation of the research findings is that the deficit changes in nature from one of retrograde memory to one of anterograde memory.

So the question is: Does “the kindling” creates “a different learning” in the hippocampus?

Thalamus and absance epilepsy

Cavdar S.

Marmara University, Medical School, Department of Anatomy, Istanbul, Turkey.

safcavdar@yahoo.com

There are two parts of diencephalon that play distinctive roles in the production of epilepsy. The dorsal and the ventral thalamus. They have distinct embryological origins, connections and functions. The dorsal thalamus sends messages to the neocortex and the ventral thalamus forms the thalamic reticular nucleus, which sends important inhibitory connections to the dorsal thalamus.

The dorsal thalamus is concerned with the transmission of imformation to cortex. The imputs that carry this imformation can be catagorized as drivers (eg retinal afferents, leminiscal afferets). All other afferents are modulators. They modifiy the activity of the relay cells. Wheras, the drivers form less than 10% of synapses on the relay cells, the modulators form more than 90% of the synapses.

Many thalamic nuclei receive their drivers from the cortex and these have been called “higher order relays” to distinguish them from the nuclei receiving ascending afferents, which are “first order relays” (LGN, vMGN, VPL) are first order; MD, PUL, LP, intralaminar are higher order).

Modulators come from the brainstem, hypothalamus, basal forebrain, (cholinergic; noradrenergic; serotenergic; histaminergic). In addition inhibitory modulators also come from the thalamic reticular nucleus (TRN) and from the interneurons.

Thalamic relay cells have two patterns of activity: tonic mode and burst mode. The modulators are important in controlling which mode is active. When the membrane of the relay cell is depolarised the cell will fire in tonic mode. The burst mode depends on a polarised membrane potantial. The high number of modulators allows for a fine control of the level of the membrane potentials.

Epilepsy is characterized by the burst mode occuring rhytmically in thalamic relay cells. The effect is global acting on all parts of thalamus and disrupts the capasity of the thalamus to transfer spesific information to the cortex.

Current advances in pentylenetetrazol epileptogenesis

Kaya M.

Istanbul University, Medical School, Capa, Istanbul, Turkey.

mehkaya@istanbul.edu.tr

The cellular mechanisms of eliptogenesis in humans have not been elucidated yet despite the growing number of studies that focus on the subject. Experimental animal models are particularly important in epileptogenetic research. We need to understand the interactions that occur among molecular, cellular and circuit level functions which constitute the basic mechanisms of epileptogenesis. Epilepsy, one of the most common neurological disorders, has been documented to lead to a variety of changes including ion fluctuations, kinase activation, immediated early or late gene expression, cell loss, gliosis, and mossy fiber sprouting in the brain after single or repeated seizures. Systemic administration of convulsant agents is the most widely used route to create a model of seizures. One of the convulsant agents, pentylenetetrazol (PTZ), is a selective blocker of the chloride ionophore coupled to the $GABA_A$ receptor, and produces epileptic seizures on acute intravenous administration in high doses as well as in long-term low dose administration. PTZ has significant convulsant potency in mice, rats, monkeys and humans. PTZ activates a range of seizure types, in a dose-dependent manner, with single injections of PTZ at low (<40 mg/kg), intermediate (40-70 mg/kg), and high doses (>70 mg/kg) usually eliciting absence, myoclonic and clonic, and tonic seizures. A number of studies have indicated that increased neurogenesis and neuronal death occurred in seizures induced by both acute and chronic administrations of PTZ. However, it is reported that minor or no neuronal death may occur in PTZ-induced seizures. Recent studies suggest that fMRI can be used to monitor seizure activity induced rodent brain by systemic PTZ injection together with EEG monitoring. Repeated administration of subconvulsive doses of PTZ also down-regulates the sensitivity of $GABA_A$ receptors. Animal kindling models propose the opportunity to examine alterations associated with epilepsy. The chemical kindling induced by PTZ is a popular rodent model of generalized epilepsy; this model of epilepsy could also cause cognitive disorders and neuronal loss in hippocampus appear after PTZ kindling. Kindling with PTZ can be preferred to other kindling models since it requires no indwelling electrodes and has low mortality rate. Recent evidence that cerebellar volume reduced more than cerebral and hippocampal volumes suggests that epilepsy might have a very important impact on cerebellar pathophysiology as well as in the cerebrum and hippocampus. In recent years PTZ induced kindling model has been widely utilized to elucidate the underlying mechanisms of the epileptogenesis. Finally, a better understanding of the molecular and functional basis of epileptogenesis should lead to create new antiepileptic drugs and to prevent the development of epilepsy or drug resistant epilepsia.

PNL3

ENGINEERING APPROACH

Moderator : Haluk Bingol

Panelists : Haluk Bingol, Yagmur Denizhan, Ufuk Caglayan

Complex Systems and Brain

Bingol H.

Department of Computer Engineering, Bogazici University, Istanbul, Turkey.

bingol@boun.edu.tr

Probably we are surrounded by non-linear systems. Yet the system theory starts with linear systems. The reason for that is that we have mathematical tools for modeling linear systems, more than that these models are analytically solvable. We try to attach none-linear systems, too. Even if we can model these systems, we cannot solve them analytically. So we have to live with numerical solutions. Chaotic systems, that are quite popular in recent decays, are also classified as non-linear systems.

In last decay we stated to deal with a new type of systems, called Complex Systems. These systems are composed of quite simple units, called agents. Even if the behavior of an agent is very simple, when they are allowed to interact by a large numbers, their overall behavior is unexpected. This "emergence" of behavior at the macro level not predicted from the micro level is typical for complex systems.

As a system of interacting neurons, brain can be considered as a complex system. The cumulative effect of these interactions, brain presents macro "behaviors" that is hard to explain from the macro level, namely neurons. In that respect brain is a strong candidate of Complex Systems. In this talk, current on going work of brain as a Complex System is discussed.

Code duality and the brain

Denizhan Y.

Bogazici University, electrical and Electronics Engineering Department, Istanbul, Turkey.

denizhan@boun.edu.tr

Today's biology is moving away from the traditional morphological approach, which investigates the anatomical structures of organisms, and focusing on the "biological information" contained in the genetic code. While research activities, which consider the information hidden in the DNA in terms of the Shannon information definition –typical for the Age of Information-, are continuing in full speed, 15 years ago two Danish biologists, Jesper Hoffmeyer and Claus Emmeche, have adopted a semiotic approach focusing on the contents and meaning of information rather than its amount, and have introduced a concept also applicable to other areas: Code Duality.

In the light of this concept, considering DNA both as a morphological structure and as a "program" (code) they have come across a circular causality. When considered as a program code, DNA must "mean something" to a subject. This subject is the organism itself, which is thought to be coded by the program. This is exactly the point where circular causality is hidden. Consequently, Hoffmeyer and Emmeche have abandoned the traditional Neodarwinist genetic approach, which considers the DNA as the only code, and have asserted that *an evolvable system must have two mutually interacting codes, or better to say a pair of codes.* One of these codes must be digital (the genetic code in the DNA or RNA) and the other one must be analog (the dynamic environment that interprets and realises the digital code). Here the digital code stores the system knowledge as truthful as possible, thus serves as a memory. On the other hand, the analog code (eg. the intracellular environment) somewhat deciphers the meaning hidden in the digital code and expresses it.

The interpretation of the dynamic nature of the organism as a code may sound strange to the ears of the contemporary audience, which is conditioned by the Shannon information definition and is used to a measure of information in terms of bits. However, if we keep in mind that the meaning of the digital code is hidden in this dynamics such an interpretation may seem acceptable.

Furthermore, Hoffmeyer and Emmeche have applied the concept of code duality to another evolvable system: the human culture. They present the human language as the digital code, while the socio-cultural dynamics, within which the contents of language is interpreted and realised, is considered as the analog code.

In this paper, an attempt will be made to apply the concept of code duality to the human brain, which is a complex evolvable system with many organisational levels.

Developments in computer processors and memory

Caglayan UM.

Department of Computer Engineering, Bogazici University, Bebek, Istanbul 34342, Turkey.

caglayan@boun.edu.tr

In this paper, we first cover the short history of computer processor and memory technologies and present example landmark contributions in the past. Research in areas such as microelectronics, material science and software engineering resulted in revolutionary developments in processor and memory technologies. Especially following the year 2000, previously unimaginable computer processor and memory structures and products were possible at a very low cost. In this paper, we present how LSI and VLSI technologies are being used in processor and memory design and production, then we briefly cover the operation of fundamental low level structures such as gates and flip-flops and we explain how the main units of a processor and memory such as adders, logic units and control units are designed and constructed by using the fundamental low level structures. Finally, we present modern

processor and memory structures, multi-processor and parallel structures, memory hierarchy, give state-of-the-art examples and discuss the future of processor and memory technologies in the framework of Moore's Law and phsical limits.

PNL4

TRANSCRANIAL MAGNETIC STIMULATION

Moderator : A. Emre Oge

Panelists : A. Emre Oge, Raif Cakmur, Nebil Yildiz

Transcranial magnetic stimulation: methods, excitability studies

Oge AE.

Department of Neurology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey.

aemreoge@ttnet.net.tr

In less than twenty years after its invention, transcranial magnetic stimulation (TMS) has become an essential brain research tool and it has also found to possess some therapeutic potential due to the lasting effects of repetitive TMS. In this part of the workshop, the role of TMS in neuroscience research will be summarized under the subheadings of 'basic mechanisms of magnetic neural tissue stimulation' and 'principal methods of TMS studies'. The methods used in 'cortical excitability studies' and the physiological mechanisms which they are based on will be described in more detail and our experience with paired TMS and cortical silent period on normal children, patients with involuntary facial movements and blind subjects will be mentioned.

Repetitive transcranial magnetic stimulation

Cakmur R.

Dokuz Eylul University, Medical School, Department of Neurology, Izmir, Turkey.

As a low-risk method for direct and localised stimulation of the cerebral cortex, transcranial magnetic stimulation (TMS) has played an important role in neurophysiology for several years. Further technical and methodological developments, such as high-frequency (rapid rate TMS/repetitive TMS) stimulation, have led to broad scientific application of this method again in recent years. Repetitive TMS (rTMS) has the potential to either directly or transsynaptically modulate neuronal circuits. Due to its ability to modulate cortical excitability, rTMS is currently being used to investigate cortical processes and as a treatment tool in disorders such as depression, schizophrenia, Parkinson disease, spinocerebellar degeneration, epilepsy, urinary incontinence, dystonia, chronic pain, migraine and chronic tinnitus, etc. Although it is generally accepted that rTMS is a safe and well tolerated method, the most serious side effect of high-frequency rTMS is seizures. rTMS represents an exciting new frontier in neuroscience research, providing insights into the pathophysiology and treatment of various neuropsychiatric disorders.

Transcranial magnetic stimulation of the cranial nerves and related cortical areas

Yildiz N.

Department of Neurology, Abant Izzet Baysal University, Izzet Baysal Faculty of Medicine, Bolu, Turkey.

Transcranial magnetic stimulation (TMS) evoked motor potentials recorded from cranial muscles are particularly useful in neurophysiological studies. They provide information on corticobulber pathways and extraaxial nerve segments that can not be easily accessed by standart nerve conduction studies. Stimulation of the cranial nerves in their proximal intracisternal parts may be of considerable value for the assesment of lesions induced by tumors, neurovascular compressions, cranial neuritis, or metabolic neuropathies (1, 2).

The general principle for cortical control of cranial motor nuclei V, VII, IX, X and XII is that there is a predominantly contralateral and variable but important ipsilateral influence. The importance of the bilaterality of innervation is clearly different from that for limb motor control and is helpful in understanding clinical phenomena such as recovery from stroke(1,2). Magnetic fields induced over skull elicit distinct types of responses in the muscles supplied by the cranial nerves both on the ipsilateral and contralateral sides. When the coil was positioned 4-8 cm lateral to the vertex on a line from the vertex to the external auditory meatus, bilateral responses in the masseter, orbicularis oculi, mentalis, and SCM muscles occured with a delay of about 10-14 ms after the stimulus. The finding of long latency corticonuclear responses, also recordable on the ipsilateral side, confirms the results of a number of anatomical investigations and the view of various neurologist. Similar to the transcranially evoked muscle responses in hand muscles, the responses in the cranial muscles can be influenced in latency and amplitude by background excitation (3).

Ertekin et al recorded the motor evoked potentials (MEP) of cricopharyngeal (CP) muscle which is important in swallowing . They postulated that when the pathway is affected by a pathological process (i.e. ALS or pseudobulbar palsy) the CP sphincter becomes hyperreflexic due to disinhibition, and the cortical MEP of the CP muscle disappears due to degeneration of the corticobulbar pathway (4). They recorded stylohyoid and digastricus muscle complex MEPs in another study (5). Khedr and associates (6) obtained bilateral MEPs from the thyroarytenoid and cricothyroid muscles. The latency was shorter in the ipsilateral than contralateral and, in the thyroarytenoid muscle, shorter on the right than on the left side. Shon et al (7) elicited o.oculi responses to medial frontal TMS. With TMS applied to the midfrontal scalp position, they recorded a small response in the orbicularis oculi muscles with latencies ranging from 6 to 8 ms which were interpreted as MEPs.

Oge et al (8) stimulated the facial nerves of patients with hemifacial spasm (HFS) and post-facial palsy synkinesis by TMS and found decreased amplitudes as well as increased latencies. They emphasized the importance of TMS to diagnose the intracranial facial nerve lesions. They also presented a case with facial myokymia in whom segmental demyelination was demonstrated in the extramedullary course of the facial nerve with the aid of TMS (9).

Another characteristic of the cranial nerve motor neurons is that they lack axon collaterals and do not undergo recurrent inhibiton. Many muscles are devoid of muscle spindles and consequently antagonist muscles do not undergo reciprocal inhibition. Cranial nerve motor neurons seem to be mostly regulated by superficial reflex input and by the motor cortices. The TMS induced silent period (SP) is entirely produced by inhibition of the motor cortex (1). In small hand muscles, after the early CMAP evoked by TMS, a period of EMG silence lasting some 200 ms can be found if the target muscle is tonically active. After unilateral TMS, there is a bilateral SP in tonically active muscles supplied by cranial nerves in normal subjects. The experiments in normal subjects and the results in patients, however, strongly suggest that the SP results from local inhibitory actions in the primary motor cortex (10). Cruccu et al also recorded SPs in mentalis, orbicularis oculi and masseter muscles (11). They conclude that the SP induced in facial muscles by TMS results from the excitation of cortical inhibitory interneurons surrounding the upper motoneurons, because the SPs in facial muscles elicited by facial or cutaneous nerve stimulation are incomplete and have shorter duration.

Von Giesen and coworkers, (12) analyzing 30 patients with lesions of different brain areas, showed that the duration of the SP depends on whether the primary motor cortex is directly involved in the lesion or whether there is damage to areas projecting to the primary motor cortex. Oge et al. (13) showed that the SP could not be recorded in most of the patients with post-facial palsy synkinesis. Curra et al.(14) demonstrated that facial SPs were significantly shorter in patients with cranial dystonia.

By paired transcranial magnetic stimulation, it was shown that intracortical inhibition and facilitation patterns in lower and upper facial muscles observed in short and long interstimulus intervals (ISI) are not different from hand muscles (15,16). In the report of Celik et al.(17), ISI's of 20, 25, 30 ms revealed facilitation of the test MEP in control subjects at rest. Test MEP facilitation on the symptomatic sides of HFS patients was significantly less than the resting controls.

TMS of the cranial nerves and related motor cortex are used also in plasticity studies. Hamdy et al (18) demonstrated that the organization of swallowing function can be altered after electrical sensory stimulation of the pharynx. We studied the corticonuclear innervation to facial muscles in patients with stroke and central facial paresis (CFP) (19) in Ege University Neurophysiology Department. We found that the amplitudes of the MEPs recorded from the intact side in response to the unaffected hemisphere

TMS were enhanced especially in the first week following the stroke. We demonstrated that perioral muscles are innervated by the corticobulbar tracts bilaterally and CFP caused by a stroke is generally incomplete and mild because of the ipsilateral cortical and multiple innervations out of the infarction area, and recovers quickly through cortical reorganisation. In another study performed in Ege University (20), we demonstrated that topical anesthesia to the lower facial region leads to cortical modulation and fast plastic changes in both hemispheres that are directed to the normal side. In a recent unpublished study on patients with peripheral facial paresis, we found that mean amplitude of the MEPS recorded from the intact perioral muscle in response to stimulation of the hemisphere contralateral to the paretic side were significantly higher than those of the normal controls.

PNL5

NEUROGENETIC

Moderator : A. Nazli Basak

Panelists : Nazli Basak, Murat Gunel, Ebru Bodur

Genetics of autosomal-dominantly inherited spinocerebeller ataxias

Basak AN.

Bogazici University, Department of Molecular Biology and Genetics, Neurodegeneration Research Laboratory, Istanbul, Turkey.

basak@boun.edu.tr

Spinocerebellar ataxias (SCAs) are a heterogeneous group of neurodegenerative disorders, which are inherited in an autosomal-dominant manner. Most SCAs are genetically characterized by an expanded CAG repeat motif. Until recently, ataxias were considered to be some of the most intriguing neurogical disorders, regarding their molecular pathologies and differential diagnoses. Although the discovery of several new gene loci and the definition of different SCA subtypes made precise molecular diagnosis possible, and also explained clinical phenomena, like anticipation and variable phenotypes, the continious increase in the number of new SCA loci seems to give rise again to a new confusion among scientists. The presentation will focus on these aspects, with a special emphasis on the molecular pathologies and differential diagnoses of dominantly inherited SCAs.

Molecular genetic of serebral vascular diseases

Gunel M.

Yale University School of Medicine Dept. of Neurosurgery, USA.

murat.gunel@yale.edu

No abstract available.

Silencing butyrylcholinesterase: a new approach to co-regulation through RNAi

Bodur E.

Hacettepe University, Faculty of Medine, Department of Biochemistry, 06100, Ankara, Turkey.

bodurebru@yahoo.com

RNA interference (RNAi) is a process of sequence specific post-transcriptional gene silencing (PTGS) in animals and plants, initiated by double-stranded RNA homologous in sequence to the silenced gene. According to the prevailing model, the transfected double-stranded RNA is processed into small RNAs (siRNAs) of 21-25 nucleotides. The siRNAs associate with a multi-component nuclease, the RNA-inducing silencing complex (RISC) to guide this enzyme for sequence specific degradation of mRNA. This process is promptly utilized as a gene function analysis tool in molecular biology and has the further potential to be used as gene therapy. Here RNAi was employed to analyze the Cholinesterase (ChE) proteins in developing neurons. Cholinesterases are ubiquitous enzymes classified into two types through a preferential specificity of inhibitors and substrates: acetylcholinesterase (AChE; E.C. 3.1.1.7) and butyrylcholinesterase (BChE; E.C. 3.1.1.8). Whereas AChE is defined as the classical enzyme that terminates acetylcholine triggered neural transmission, BChE is clinically significant as a bioscavenger enzyme through its ability to hydrolyze a wide variety of ester containing compounds. Apart from this classical role, both ChEs are involved in novel functions in developing neurons. Sequence specific siRNAs against BChE was designed and successfully employed to knock down BChE in the rat retinal embryonic cell line R28. Of the siRNAs designed against BChE, one pair resulted in total knockdown of BChE. The knockdown of BChE resulted in an up-regulation of AChE, displaying that there is a co-regulation between the ChE proteins which can be put into affect at the mRNA level. This process provides a novel tool for investigating the conditions during retinal development.

PNL6

NEUROTROPHIC FACTORS

Moderator : Guher Saruhan-Direskeneli

Panelists : Emel Ulupinar, Rasit Tukel, Murat Rezaki, Banu Anlar, Guher Saruhan-Direskeneli

The role of neurotrophic factors and their receptors on the nervous system development

Ulupinar E.

Eskisehir Osmangazi University, Faculty of Medicine, Department of Anatomy, Eskisehir, Turkey.

eulupi@ogu.edu.tr

During the development of the nervous system, neuronal populations go through a naturally occurring cell death process when their axons are innervating target areas. This mechanism ensures a balance between the size of the innervating neuron population and the size of its target territory. The production of limited amounts of survival factors regulates this matching process. Nerve growth factor (NGF) and its family members were identified during a search for such survival factors. More recent studies have revealed that neurotrophins not only control the growth of axons, but also possess acute regulatory effects on neurotransmitter release, synaptic strength and connectivity. These different actions are dictated via a complex, dual receptor system consisting of two classes of cell surface receptors; the Trk family of tyrosine kinases and the p75 neurotrophin receptor ($p75^{NTR}$). While Trk receptors are responsible for most of the survival and growth promoting properties of the neurotrophins; $p75^{NTR}$ can mediate survival versus apoptotic outcomes. The unconventional mechanisms for Trk activation, identification of novel ligands for $p75^{NTR}$ and unique intracellular signalling mechanisms further stress the complex nature of neurotrophin functions. In this talk, recent surprises of how ligand-receptor coupling may affect such diverse developmental events will be summarized.

The effects of neurotrophic factors and neuroplasticity in anxiety and depression

Tukel R.

Istanbul University, Istanbul Faculty of Medicine, Deparment of Psychiatry, Istanbul, Turkey.

rtukel@superonline.com

Neuronal effects of brain-derived neurotrophic factor (BDNF) are mediated through the tyrosine kinase reseptor, TrkB. Hippocampus and hypothalamus contain the highest BDNF protein levels and possess a high degree of plasticity in the brain.

Stress is the known to influence neurogenesis in depression and anxiety. The decrease of neurogenesis itself may be an important cause of depression. Clinical studies have demostrated that the volume of the hippocampus and volume of its gray matter were reduced in patients with major depression.

It has been shown that hippocampal and hypothalamic BDNF levels are decreased by stress. Mitogen activated protein (MAP) kinase signaling pathways may be important for BDNF and antiapoptotic protein bcl-2 functioning, and also may play a role in depression. The expression of the BDNF has shown to be regulated by the cAMP response element binding protein (CREB) gene transcription factor that may contribute to the regulation of mood state and neuroplasticity. CREB activation may arise through increased 5-HT activity that would facilitate BDNF production and ultimately modulate plasticity and hence positive mood change. If CREB is inactivated through stress, this process is not maintained.

5-HT neurotransmission has been shown to play an important role in anxiety and depression. The majority of the antidepressants increase the level of 5-HT

and therefore increase the rate of neurogenesis in hippocampus. It is possible that the agents which modulate CREB/BDNF/bcl-2 cascade, may have positive effects in anxiety and mood disorders. Many novel strategies including CRH antagonists, glucocorticoid receptor antagonists, antiglutamatergic agents and phosphodiesterase inhibitors have been investigated for anxiety and depressive disorders. It would be expected that these agents exert trophic effects in addition to their effects on neurochemical systems.

BDNF in psychiatric animal models

Rezaki M.

Hacettepe University, Medical School, Department of Psychiatry, Ankara, Turkey.

smrezaki@yahoo.com

Brain derived neurotrophic factor (BDNF) is the most prevalent neurotrophin in the brain. It is recognized that it has important functions in adult brain as well as in brain development. In adult brain it has an important roles in learning and memory, and in some psychological functions. In animal models for stress, BDNF levels in hippocampus have been decreased while antidepressant treatments were found to restore BDNF levels. Increased BDNF in hippocampus has been proposed to contribute to the antidepressant treatment effect. The important role of BDNF in brain development has put it among the candidate proteins to take part in developmental disorders observed in schizophrenia models. Some antipsychotic treatments decrease the BDNF levels in hippocampus. In contrast some second-generation antipsychotics reverse the decrease in BDNF levels in stressed animals. Mood stabilizer lithium also alters the BDNF levels in the brain. This presentation will focus on the studies in animal models of depression and schizophrenia and on the role of BDNF in mechanisms of actions of psychiatric treatments.

Neurotrophic factors in the brain: normal and pathological conditions

Anlar B.

Hacettepe University Faculty of Medicine, Department of Pediatric Neurology, Ankara, Turkey.

banlar@hacettepe.edu.tr

Neurotrophic factors (NTFs) and their receptors are expressed throughout the nervous system. They regulate physiological cell death and elimination of neurites during development. In adult neurons, they modulate adaptive changes, presynaptic and postsynaptic mechanisms, and synthesis of neurotransmitters and their receptors. The expression levels of NTFs and their receptors are altered in pathological conditions, suggesting a role in traumatic or degenerative processes. Expression by CNS cells is generally reduced during degenerative CNS diseases such as Parkinson's and Alzheimer's disease. NTFs enhance oligodendrocyte survival and support remyelination after peripheral and central nervous system injury and viral infection. In CNS inflammation, infiltrating immune cells and activated microglia provide neurotrophic support to limit the extent of secondary degeneration.

The expression of NTFs is developmentally regulated: it occurs at specific times and locations in the nervous system. For this reason, NTFs may be involved in the pathogenesis of certain neurodevelopmental disorders. Lower levels of nerve growth factor have been demonstrated in Rett syndrome, an autistic syndrome due to MECP2 gene mutations. Our recent data suggest alterations of insulin-like growth factor (IGF) excretion in early childhood autism. The effect of exogenous insults may also be mediated through NTFs. Hypertension in pregnancy impairs fetal development: offsprings of pre-eclamptic mothers are small-for-gestational age and show neurological problems. Because NTFs are involved in the pathogenesis of certain forms of hypertension, we investigated IGF and glia-derived neurotrophic factor (GDNF) expression in fetal brain by Western blotting. Preliminary results suggest altered expression of GDNF in the brain of fetuses of pre-eclamptic mothers.

NTFs are the agents of physiological attempts at neuroprotection and repair. For this reason, animal studies on their therapeutic use have been conducted in neuroinflammatory disorders, CNS demyelination or degeneration. Various methods of NTF delivery to the CNS are being investigated. Pharmacological manipulation of post-receptor signaling pathways of NTFs is another, perhaps more specific and tolerable way of altering NTF actions.

Genetic polymorphisms of the neurotrophic factors and interactions with the immune system

Saruhan-Direskeneli G.

I.U. Istanbul Medical Faculty, Department of Physiology, Istanbul, Turkey.

gsaruhan@istanbul.edu.tr

Trophic factors affecting the nervous system are mediating their effects with neuroprotective mechanisms and the lack of trophic support is linked mainly with neurodegeneration. Both neurotrophins, nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF), are important for the survival and maintenance of different types of neurons. These factors play an important role in neural repair and plasticity.

Although BDNF is highly concentrated in the nervous system, it is present in human serum as well. BDNF is known to be stored in human platelets and neurons are the main source of this neurotrophin. However, BDNF production has also been shown to occur from inflammatory cells and a neuroprotective effect of BDNF during the treatment of inflammatory diseases of the nervous system has been proposed as a bystander activity of the immune cells which may help to repair/ remyelination in disease. Conversely, BDNF and NGF exert partial modulating effects on cytokine expression of immune cells.

Lower levels of BDNF in the patients with psychiatric diseases as depression and in the serum and cerebrospinal fluid of the multiple sclerosis (MS) patients have been reported. Moreover treatment related changes in the BDNF levels could be detected in both disease groups. In MS, glatiramer acetate and to some extent interferon beta have been shown to reverse the decrease of BDNF.

Several genetic polymorphisms of BDNF have been demonstrated and the single nucleotide polymorphism (SNP) at the 196. codon (rs6265) is also causing an amino acid substitution (Val/Met) at the 66. residue of the protein. Different associations with this particular BDNF polymorphism are reported with various diseases as like mood disorders, bipolar disorders, Alzheimer disease, Parkinson disease and others. In MS the polymorphism of BDNF was not associated with the disease development.

The functional implications of genetic polymorphisms of BDNF will be discussed in relation to the interactions of nervous and immune systems.

PNL7

NEUROENDOCRIN CONTROL OF THE APPETITE AND OREXINE SYSTEM

Moderator : Haluk Kelestimur

Panelists : Haluk Kelestimur, Ahmet Ayar, Bayram Yilmaz

The interaction between appetite and reproductive functions

Kelestimur H.

Firat University, Faculty of Medicine, Department of Physiology, Elazig Turkey.

hkelestimur@firat.edu.tr

Regulation of appetite and reproductive functions and thus maintenence of optimal body weight and fertility depends on complex interactions in the brain and especially hypothalamic neuro-circuitry. Feeding behavior and reproductive function are closely linked. It is well known that deficiency of body fat resulting from malnutrition or high intensity exercise causes a delay in puberty onset. It has been recently understood that leptin, which is mainly secreted by adipose cells, sends signals to the hypothalamus about body fat stores and thus provides a link between nutrition and reproduction. Discovery of leptin has remarkably contributed to the understanding of not only the interaction between and feeding but also physiopatology of obesity. Leptin exerts its effects on gonadotrophin releasing hormone (GnRH), pulsatil secretion of which triggers puberty, and appetite by altering hypothalamic neuropeptid circuits. Leptin stimulates alfa-melanocyte stimulating hormone (MSH) and cocaine and amphetamine regulated transcript (CART) neurons whereas it inhibits neuropeptid Y (NPY) and agouti related peptide (AgRP) neurons in arcuate nucleus. NPY/AgRP neurons activate melanin-concentrating hormone (MCH) and orexinergic neurons in lateral hypothalamus. MCH has a stimulating effect on food intake whereas orexins (hypocretins) are especially related to motivational aspects of feeding behavior. Ghrelin, which is secreted by stomach and also hypothalamic

neurons, antagonizes the effects of leptin. Melatonin, a neuroendocrine hormone secreted by mainly pineal gland, may have modulatory effects on appetite and reproduction since it decreases leptin secretion. I will discuss the neuroendocrine mechanisms controlling appetite and reproduction in the lights avaliable literature including our recent studies.

Orexinergic System

Ayar A.

University of Firat, Faculty of Medicine, Department of Physiology, Elazig, Turkey.

aayar@firat.edu.tr

Orexins, also called hypocretins, are the common names given to novel neuropeptides that were simultaneously discovered by two independent reseach groups. The two highly-related peptides (Orexin A and B, or Hypocretin-1 and -2) are produced from a single precursor protein. Because the orexinergic neurons are found exclusively in the lateral hypothalamic area, initially they considered to be involved only in the control food intake. But discovery of broad projections of their fibers to the entire central nervous system have let to the idea and later discovery of involvement of orexinergic system in variety of physiological functions including in the regulation of life sustainig processes such as feeding, circulation, body temperature, and the sleep-wake cycle. It has been discovered that orexins and orexin receptors (OX-1R and OX-2R) are also expressed in neurons and endocrine cells in the gut suggesting that these novel neuropeptides might play an important a role in the motility of digestive system. The discovery that narcolepsy-cataplexy is associated with orexin/hypocretin dysregulation indicated that the research on orexins is still in an early phase and this system may have still undisclosed important role(s) in many health and disease states. Additionally, emerging evidence suggests that orexins modulate pain transmission. The topic of orexinergic system will be reviewed with presentation of our recent findings on the electrophysiological effects of orexin A in cultured rat sensory neurons.

Kisspeptin

Yilmaz B.

Firat University, Medical School, Department of Physiology, 23119, Elazig, Turkey.

bayram2353@yahoo.com

The kisspeptins are the peptide products of the KiSS-1 gene and the endogenous agonists for the GPR54 receptor. KiSS-1 was initially discovered as a metastasis suppressor gene (and therefore the protein was named metastin) in late 1990s, however, recent evidence suggests the kisspeptin/GPR54 complex is a key regulator of the reproductive system and may also be involved in the regulation of energy metabolism. Kisspeptin is expressed in the central nervous system, testis, ovary, pancreas and intestine, but is most concentrated in the placenta. GPR54 receptors are widely distributed in the CNS and have recently been visualized on gonadotrophin releasing hormone (GnRH) neurons in the hypothalamus. Kisspeptin directly stimulates GnRH release via GPR-54 receptors. Central or peripheral administration of kisspeptin potently stimulates the hypothalamic-pituitary-gonadal axis, increasing circulating gonadotrophin concentrations in a number of animal models. Conversely, injection of anti-kisspeptin antibody into the brain of female rats stopped their oestrous cycle. It has been shown that hypothalamic KiSS-1 expression is modulated by circulating sex steroids. In view of all these findings, it is believed that kisspeptin may play an important role in the onset of puberty. Indeed, patients with loss-of-function mutations in GPR54 have idiopathic hypogonadotropic hypogonadism, and mice lacking GPR54 similarly fail to undergo puberty and have immature reproductive organs and low levels of sex steroids and gonadotropins. Leptin modulation of KiSS-1 mRNA expression in the mouse hypothalamus implicates that kisspeptin neurons are also involved in the central regulation of energy homeostasis. Results from our laboratory have shown that intraperitoneal administration of kisspeptin-10 decreases serum levels of ghrelin, a hormone released from the stomach in response to hunger that exerts inhibitory effects on gonadotrophin secretion. These findings suggest that kisspeptin neurons may serve as a cellular conduit to integrate circulating indices of energy metabolism to the neuroendocrine reproductive axis. The discovery of the role of kisspeptin and GPR54 opens exciting new possibilities in the treatment of a variety of conditions including delayed or advanced puberty.

PNL8

SLEEP MECHANISMS

Moderator : Erbil Gozukirmizi

Panelists : Sabri Derman, Hakki Onen, Derya Kaynak, İbrahim Oztura

Physiology of sleep

Derman S.

Sleep Disorders Clinic, VKV American Hospital – Istanbul, Turkey.

derman@amerikanhastanesi.com.tr

We spend nearly a third of lifes asleep. Not only humans, but all creatures from a single cell organism up, have regular activity/rest cycles. İn animals higher than reptiles, sleep/wake cycle and it's inner architecture is finely regulated by complex neurological mechanisms, resulting in a REM/nonREM cycle of about 100 minutes. Recent research shed more light on these regulatory mechanisms and possible role of sleep for brain's optimum functioning. Better understanding of neurological circuits, neurotransmitter systems, hormonal influences and predisposing genetic factors help us better appreciate basic physiology of sleep while providing new ground for diagnosis and treatment of various sleep disorders. This brief introduction of physiology of normal human sleep will highlite basic elements of neurophysiology of sleep/wake and REM/nonREM cycles, circadian rhythms, hereditary factors and environmental influences.

Sleep, aging and dementia

Onen H.

Geriatric Sleep Unit, Hopital Geriatrique Universitaire A. Charial 40, avenue de la Table de Pierre, 69340 Francheville France.

saban-hakki.onen@chu-lyon.fr

Sleep disturbances are common and significant complaints of older people. Disturbed sleep may be caused by many factors such as physical illness, psychiatric disorders, dementias, increased use of medications and changes in social patterns (retirement, death of a spouse or loved one). However, normal aging also may induce changes in sleep patterns. Compared with young adults, the elderly tend to have delayed sleep onset, fragmented sleep, early-morning awakening and decreased time in sleep stages 3 and 4 (slow wave sleep). The rapid eye movement (REM) sleep occurs earlier and the first REM period duration increases (1).

Patients with Alzheimer's disease (AD) may have the same sleep disturbances seen in other non demented seniors, and, early in the course of AD, their sleep may not differ markedly from age-matched controls. Patients with AD experience more frequent nighttime awakenings, daytime sleep increases, and both slow-wave sleep and REM sleep are decreased (2). Sleep-related problems generally increase as AD progresses.

It is important to note, however, that the sleep disturbances seen in AD are nonspecific and can also be seen in vascular dementia and other neurodegenerative conditions such as dementia with Lewy bodies (DLB) and Parkinson's disease. These other dementing diseases are also associated with high rates of insomnia and daytime sleepiness. Parasomnias are also more likely to occur in non-AD disorders. Some patients with dementia experience loss of muscle atonia during REM sleep that can result in dramatic motor activity and dream-enactment behavior. The syndrome, called *REM behavior disorder*, is not typically seen in AD, but is characteristic of DLB (3). Its development may even precede the dementia.

In demented patients, controlling sleep-wake disturbances with sedative drugs often increases the risk of falls, respiratory depression and cognitive impairment. A chronobiological approach with bright-light therapy, melatonin administration, restricted time in bed, and diurnal activity may be an interesting therapeutic alternative in the management of sleep-wake disorders in demented patients. The aim of these therapeutics is to improve sleep and diurnal activity and consequently to increase the quality of life of both patients and care givers.

Parkinson's disease and restless legs syndrome-dopaminergic bridge

Karadeniz Kaynak D.

Istanbul University, Cerrahpasa Faculty of Medicine, Deparment of Neurology, Istanbul, Turkey.

deryakaynak@uykum.com

Restless legs syndrome (RLS) and Parkinson's disease (PD) exhibit striking similarities in impairment of central dopaminergic transmission and response to dopamine replacement strategies.The links and also similarities and differences between RLS and PD in respect to epidemiology, clinical features, pathophysiology, neuropharmacology, neurophysiology, neuroimaging, iron metabolism and genetics were reported below.

Epidemiologic studies RLS was present between 7 and 20 % of PD patients that is more than controls. On the other hand the prevalance of PD in RLS patients was reported between 5 and 65 %. Though most epidemiological studies suggest an association between RLS and PD, there are conflincting results in terms of this association and not incompatible with the large prevalance of RLS in general population. It is not clear yet whether RLS patients may be more prone to develop PD. It will have to be confirmed using larger samples that are population based with control group and long term follow up.

From the clinical point of view, RLS symptoms in PD appeared to be milder in severity than reported for idiopathic cases. It was reported that age of onset was older, positive family history was less likely and serum ferritin levels were lower in RLS associated with PD compared to idiopathic form. In addition demographic factors, treatment, disease duration, disease severity may be related with RLS in PD. In an other point of view, PD symptom or treatment related complications may mimic or provoke RLS.

It is well established that symptom of PD are based on a disturbance of central dopaminergic transmission mainly in nigrostriatal motor system. The improvement of RLS with the appropriate treatment of PD suggest the involvement of nigrostratal system in RLS too. Amelioration of RLS symptomatology following pallidotomy in a patient coesting PD provides an evidence that basal ganglia sensoriomotor circuits modulates RLS expression. However involvement of nigrostriatal system was not supported by neuropathological studies. Pathological examination of the Substantia Nigra Pars Compacta in RLS patients has not shown dopamineric cell depletion**.**

In respect to neuropharmacology, there is a general aggrement in the literatur that levels of HVA, the principal metobolite of dopamine, is decreased in lumbar CSF in PD which is due to degenerating dopamine containing neurons. Studies with RLS patients however showed normal CSF HVA levels. In addition, the absence of L-dopa induced dyskinesias in RLS, which is well known phenomenon in PD suggest that the beneficial effect of L-Dopa in RLS is not mediated through the same patways or receptors as in PD. However both PD and RLS patients respond strongly to both L-Dopa and dopamine agonists but only RLS patients benefit from opiates. On the other hand, other drugs of second choice in RLS such as gabapentin, carbamazepine, valproic acid, benzodiazepines are of no value in PD.

Neurophsiological studies showed significant reduction in intracortical inhibition in PD. Decrease of intracortical inhibition for foot and hand muscle was also shown in RLS patients.Therefore impairment in nigrostriatal motor system (A8 and A9 systems) excitability may be attributed to the role of striatal dopaminergic system in RLS. However the prominent involvement of lower limbs and lack of facial involvement in RLS suggests the impairment of the other dopaminergic system caudal to the pons or in spinal cord. Mesocorticolimbic dopaminergic neurons (A 10 system) plays a role in regulation of sleep and responsible of disturbances in sleep and wakefullness in PD. These neurons are also particularly sensitive to opiate agonists which may mediate the therapeutic effects of opiates in RLS. Another neuronal population possibly involved in the pathogenesis of RLS is diencephalic dopaminergic cells (A11 system). The A11 cell group in the dorso-posterior hypothalamus and subparafasicular thalamus is the largest sole of spinal dopamine. A11 neurons recieve diffuse projections from suprachiasmatic nucleus which largely control circadian rhyms. A11 cell bodies project mainly into the dorsal horn and intermediolateral tracts. Exact role is not known but has been speculated to participate nociceptive control and flexor reflex as well. Spinal reflex studies in RLS demonstrated lower threshold and greater spatial spread of the flexor reflexes more prominent during sleep reflecting increased spinal cord excitability. One preliminary experimental study suggests that, dopaminergic diencephalospinal pathway lesion in rats can induce RLS. (rat model of RLS). Posible selective degeneration of dopaminergic spinal innervation with aging may also cause RLS independently of PD in PD patients. An additional argument in favor of A11 source for RLS is its anatomical connection with the suprachiasmatic nucleus which largely control circadian rhythms.

In PD, significantly decreased signal for 18F-dopa uptake and 123 I-β-CIT SPECT binding and a mostly unchanged D2 receptor binding using 123 IBZM-SPECT and 11 C-raclopride PET were well established. However studies which concerns nigrostriatal system in RLS reveal conroversial results. Conflicting results might be due to an intermittant decrease in dopamine turnover with relatively normal intrasynaptic dopamine levels or performing these studies in the morning when patients are asymptomatic. In addition, no structural changes or degenerating signs have been detected in patients with RLS in MRI but functional MRI showed bilateral activation of the cerebellum and the contralateral activation of the thalamus during sensory symptoms and in the pons and red nucleus when sensory events were accompanied by movements

Iron metabolism has an important role in pathophysiology of PD and RLS as well. There is evidence that this abnormal iron metabolism may contribute to oxidative stress and dopaminergic degeneration in PD. On the other hand RLS conversly is associated with iron deficiency. It was shown reduced iron content in substantia nigra and putamen of RLS patients compared to controls. Long term treatment of RLS with IV iron leads to sustained remission of symptoms. Conversly, reduced dopaminergic activity might cause a reduced iron concentration. There is a possibility that, in RLS there is perhaps a common factor causing both iron and dopamine dysfunction.

Analzing the 8 genes coding for receptors and enzymes related to dopaminergic transmission did not reveal vulnerability to RLS in genotypic or allelic distributions of D1 to D5 receptors dopamin transporter (DAT) gene, thyrosine hydroxylase or the dopamine beta hydroxylase gene. On the other hand it was also shown an excess of high activity alleles of the MAO-A gene resulting in an elevated MAO-A activity contributes to susceptibility of RLS in females.

In summary, both RLS and PD appear to involve disturbance in central dopaminergic system. PD is a prototypcal disorder of brain dopamine cell loss while there is dopamine dysfuntion in RLS. In RLS the changes in dopaminergic system seem to be relatively discrete . Other dopaminergic systems rather than nigrostriatal dopaminergic system appear to play the key role. RLS may be novel form of neural disorder one in which the structural elements are relatively unaffected but the functional activities of key neuronal systems are altered in a state dependent manner.

Circadian rhythms and advancing age

Oztura I.

Dokuz Eylul University, Faculty of Medicine, Department of Neurology, Izmir, Turkey.

ibrahim.oztura@deu.edu.tr

Sleep is arranged by both homeostatic and circadian mechanisms. Although homeostatic mechanisms have been known for long years, circadian mechanisms have been defined recently. One of the most important main features of humans and other organisms is the rhythm they have. The addition of this feature to the four main qualities of life (growth, reproduction, movement and irritability) is proposed. These rhythms can be in different durations ranging from seconds to years. Organisms which are active at daytime and resting at night are defined as diurnal. This rhythm is endogenous in several living species and arranged by pacemaker which is also known as internal timing mechanisms or biological clock. Circadian rhythms are the best known endogenous rhythm and last for 24 hours. Word circadian comes from the Latin circa-diem meaning about a day. Suprachiasmatic nucleus (SCN) located within anterior hypothalamus receives retino-hypothalamic projections. Circadian pacemaker (biological clock) in mammals has been shown to be localized at SCN. Suprachiasmatic nucleus includes a pacemaker sensitive to light. Direct and indirect retinal projections are combined with environmental and endogenous rhythms. Melatonin release from pineal gland is controlled by the efferents from SCN.

In the pineal gland and plasma, melatonin which is at basal level at day time reaches its highest level at night.

Another factor affecting the circadian and sleep-wake pattern is advancing age. The prevalence of sleep disorders increase significantly with age. The majority of sleep complaints consist of the difficulty to start and continue sleeping and early awakenings. Changes in circadian pacemaker or sleep homeostasis or both are considered to cause this clinical presentation. Body temperature and melatonin rhythm with low amplitudes and an earlier circadian rhythm have been reported in literature. A more important issue is that while circadian rhythm in younger adults creates sleep in a wider range, internal circadian rhythm in older people causes an earlier awakening.

ORAL PRESENTATIONS

O1

Genetic absence epilepsy rats (GAERS) receiving kindling stimulations: hippocampal granule cell degeneration

Akakin D [1], Sirvanci S [1], Azizova A [2], Aker R [2], Onat F [2], San T [1].

Marmara University, Faculty of Medicine, Department of Histology and Embryology [1], Pharmacology and Clinical Pharmacology [2], Istanbul, Turkey.

dilekbangir@yahoo.com

Gliosis, apoptosis, neuronal loss, mossy fiber sprouting and related synaptic reorganization are the histopathological changes observed in hippocampus after amygdaloid kindling. The Genetic Absence Epilepsy Rats from Strasbourg (GAERS), which show spontaneous spike and wave discharges developing at about 30 days of age, is a model of absence epilepsy. In this model of epilepsy, high metabolic activity, increase in extracellular glutamate, GABA and glutamate co-localization and increased glutamate in the mossy fiber terminals and Ca^{+2} dependent neural activity were reported in the hippocampus. In a study in which GAERS were stimulated to induce amygdaloid kindling, they failed to show spontaneous convulsive seizures. In the present study, Fluoro Jade B (FJB) was used in order to investigate whether or not morphological degeneration in GAERS hippocampus was present. Adult Wistar rats and GAERS were instrumented stereotaxically with bilateral stimulation and recording electrodes into the basolateral amygdala and the cortex. Racine scale for grading seizures was used. Experimental groups were Wistar sham-operated control, Wistar kindling stimulation, GAERS sham-operated control and GAERS kindling stimulation. Twenty-four hours after the last amygdaloid stimulation, the animals were deeply anesthetized and sacrificed by transaortic perfusion. The brains were cut into 300 µm slices using a vibratome. After electron microscopic preparation, the brain tissue sections were embedded in Epon 812. Serial semi-thin sections (1 µm) were cut on a Leica Ultracut R ultramicrotome and stained with toluidine blue and FJB. Sections were photographed with the light and fluorescein microscope. GAERS did not reach stage 5 seizure state although they received more stimuli than fully-kindled Wistar rats. Kindled Wistar rats showed neuronal morphological degeneration in the dentate granular layers of the hippocampus, compared to Wistar sham-operated controls. GAERS, which could not reach stage 5 seizure state after amygdaloid stimulations, revealed no neuronal degeneration in those layers, similar to that of sham-operated GAERS. It is known that the hippocampus is involved in neural activity in absence epilepsy. The finding that GAERS failed to progress beyond a stage 2 seizure state even after 30 kindling stimulations gives a new approach to the debate on how absence and temporal lobe epilepsy in humans were rarely seen together. In this study, the absence of neuronal degeneration in the dentate granule cell layer of GAERS that show strain to kindling suggests that the morphological findings should be considered in parallel with opposite transmitter mechanisms and plasticity.

Key words: Wistar, GAERS, kindling, hippocampus, fluoro-Jade B

O2

Phenotypic features of glial satellite cells and differences from Schwann cells: an invivo and invitro investigation

Erdogan E [1, 2], Gunduz C [1], Ozturk G [2, 3], Cengiz N [1, 2], Ragbetli MC [1].

Yuzuncu Yil University, Medical Faculty, Department of Histology and Embryology[1], Neuroscience Research Center[2], Department of Physiology[3], Van, Turkey.

drender@hotmail.com

Glial satellite cells (GSCs) are ganglion cells surrounding neurons as an envelope or sheet. And they are connected with adjacent neurons via gap-junctions. The histological and structural changes of nerve cells in dorsal root ganglia (DRG) fallowing axotomy have been studied intensively. But, studies about the origins and detailed morphology of satellite cells are restricted. Some of the authors suggested that these cells are a type of Schwann cells (SCs) while others classify them as astrocytes. This study was aimed to determine the detailed structural phenotypic features of GSCs of DRG. For this purpose, L4 and L5 spinal ganglions were taken bilaterally from hemilateral axotomised mice. After fixation (paraformaldehyde 4%) and sucrose (30%) processing, 5-30 µm thickness sections were taken by frozen section and then labeled with DAPI, Laminin, Neun, NFH, GFAP, S100, P75, Vimentin, SMA and MBP primary and fluorescent conjugated secondary antibodies or avidin-biotin DAB. Tissue samples were examined with confocal and light microscopes. In addition, phenotypes of dissociated cells in culture condition were compared, in vitro. In the confocal microscopic examination of sections: DAPI and NeuN were expressed by nuclei and Laminin was expressed by perineuronal sheets and basal membranes. In some satellite cells; S100 and GFAP immunoreactivity were quite strong. On the other hand, NFH, MPP, P75, SMA and vimentin were expressed very weakly. Strong S100 and GFAP staining of GSCs indicate close phenotypic relationship with SCs. The light microscopic data were consistent with the confocal microscopic data. In culture, significant morphological differences between GSCs and SCs were observed. Being prominent in the third day, GSCs became larger and had more processes, while the SCs maintained their initial fusiform morphology.

Key words: glia, satellite cells, dorsal root ganglia, confocal microscopy, immunhistochemistr, in-vitro, cell culture

O3

Melatonin phase advances the neuronal activity peak in SCN of the Syrian hamster

Karakas A, Sumbul A, Gunduz B.

Abant Izzet Baysal University, Faculty of Arts and Sciences, Department of Biology, Bolu, Turkey.

karakas_a@ibu.edu.tr

In mammals, endogeneous circadian rhythm of several physiological parameters (e.g., locomotor activity, body temperature, reproductive responses to photoperiod and release of some hormones) are generated and controlled by a circadian oscillator located in the hypothalamic suprachiasmatic nuclei (SCN). These rhythms disappear by the ablation of the SCN region and some of them (e.g., locomotor activity) reappear upon transplantation of fetal SCN tissue. The neuronal firing rate in SCN is high during day-time in both nocturnal and diurnal species and the peak of the neural firing rate in SCN of the Syrian hamster occurs at nearly circadian time (CT) 6. In mammals, melatonin (5-acetyl-N-methoxytryptamine) is synthesized primarily by the pineal gland and the retina and is released in a circadian fashion with high levels during the night. Melatonin modulates a myriad of physiological functions, including sleep, as well as circadian, visual, reproductive, neuroendocrine and neuroimmunological functions. In the present study, we aimed to investigate the effects of exogeneous melatonin administration on the rhythm of the neuronal firing rate in SCN of the Syrian hamster. For this aim, we recorded the neuronal firing rate of the in vivo SCN at two hour intervals throughout the day-time (CT 24-12) by using a Powerlab ML 750 Data Acquisition System. The anesthetized hamsters were placed in a stereotaxic instrument, a hole was opened in the skull by a dental drill and a glass capillary microelectrode filled with 2 M NaCl was placed to the SCN (coordinates; 0,1 mm anterior, ± 0.3 mm lateral to the bregma and 7.8 mm below the dura). The experimental group was injected with melatonin (25 mg/kg) and the controls were intraperitoneally injected with saline (0.9 % NaCl) at CT 0. The spikes were amplified (10.000 x) and filtered (300 hz – 3 khz) by the Dagan A-4200 amplificator. The individual firing rates were then used to calculate 2 h running averages. The time of peak neuronal

activity was defined as the time of symmetrically highest activity. Student's t-tests were used to test for significant differences between the means with significance set at $p<0.05$. Melatonin phase advanced the neuronal activity peak. In controls the neuronal activity made peak near at CT 6 ($p>0.05$) however in melatonin injected hamsters the neuronal activity made peak nearly at CT 3.30 representing an advance of about 2.30 h ($p<0.01$). The results have shown that the rhythm of the SCN activity in Syrian hamster may be regulated by the timed exogeneous melatonin administrations.

Key words: Melatonin, SCN, Syrian hamster, Neuronal firing rate

O4

Effect of stimulus presentation frequency on BOLD response

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

Istanbul University, Istanbul Faculty of Medicine, Department of Physiology[1], Bogazici University, Institute of Biomedical Engineering[2], 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 activity patterns of neural systems during cognitive processes. Within this framework, a correct modeling of the neurovascular coupling is still a very important gap 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.

It is well known, that regular oscillations at the stimulation frequency and its harmonics occur in the EEG, when the brain is stimulated in any sensory modality with stimuli at high presentation frequencies. 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, the BOLD responses during visual stimulation with stimulus presentation rates between 1-20 Hz have been systematically studied and the change of the BOLD response in relation to the stimulus presentation frequency has been analyzed.

The visual stimulus was the reversal of a checkerboard produced on a computer screen. The stimuli were projected with a video projector located outside of the MRI room through a semi-transparent panel located in the room onto a mirror fixed in front of the eyes of the subject.

The BOLD measurements were conducted with 3 Tesla Philips MRI System. A single shot T_2^* weighted gradient echo planar imaging sequence was used for BOLD measurements. Ten transverse slices of 64x64 were acquired with a slice thickness 3.5 mm positioned through the visual cortex. At the end of the fMRI scan 180 images were acquired. A 3D MPRAGE sequence was used for high resolution anatomic scan. Subject's head stabilized during scans to eliminate movement artifacts. The stimuli were presented at 0.5, 1, 2, 4, 5, 6, 7, 10, 12, 14, 16, 18, 20 Hz.

It has been observed that the BOLD response showed two peaks at 5 and 10 Hz. The decreasing BOLD amplitude with increasing frequencies built another peak around 18 Hz. The fact that the BOLD response did not show a linear increase or saturation with increasing frequencies, but displayed increases and decreases around certain frequencies, shows the presence of a relation ship between the metabolic activity and the electrical oscillations in the EEG. For a more comprehensive description of this relationship, the measurements are currently extended by applying stimulus presentation frequencies between 1-100 Hz on a larger group of subjects.

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

O5

Brain potentials during encoding and retention processes of short term memory

Ergen M [1], Uslu A [1], Yildirim E [2], Bayraktaroglu Z [1], Gurvit H [3], Demiralp T [1].

Istanbul University, Istanbul, Department of Physiology [1], Istanbul University Institute for Forensic Medicine [2], Istanbul University, Istanbul Faculty of Medicine, Department of Neurology [3], Istanbul, Turkey.

mehmet.ergen@gmail.com

In order to investigate electrophysiological correlates of encoding and retention phases of Sternberg paradigm, which is a short term memory test, EEG (electorencephalogram) sweeps recorded during these test phases were analyzed. To apply two levels of memory load we used two versions of this paradigm with memory sets consisting of 3 and 5 letters. During the encoding phase, single letters were presented sequentially with 2 s intervals on a computer screen. Following this phase, retention phase started and lasted for 3 seconds. In the third phase, probe stimuli were presented and subjects were asked to recognize the letters that were present in the memory set. During the repeated trials of this paradigm EEG was recorded from 30 channels according to 10/20 system to obtain sweeps starting from 1 s before the first stimulus of the memory set until the end of the whole encoding and retention phases. Evoked acitivity that is phase-locked with stimuli was calculated by applying wavelet transform on average responses of each subject, and total activity, which additionally contains signal components that are not phase-locked to the stimuli, was calculated by applying wavelet transforms of single trials and averaging the absolute values of these transforms. In both tests with 3 and 5 letters, a gradual decrease in the alpha amplitude was observed in the total time-frequency transform of the poststimulus EEG of the occipital area during the presentation of stimuli to be encoded, that gradually increased with each item being added to the memory set. However, during the retention period, mean amplitude of alpha band in the total time-frequency transform was higher in the 5 letters paradigm than in the 3 letters paradigm. As alpha desynchronization is generally suggested to be proportional to the amount of cortical resources allocated to a mental process, increased alpha desynchronization observed by each additional item during encoding of the memory set could be interpreted as increased allocation of cortical resources for the encoding of stimuli. Besides, establishment of load dependent alpha oscillations with higher amplitudes in the 5 letters test, suggests that alpha oscillations in this phase reflect another distinct functional mechanism for the maintenance of stimulus representations. This dichotomous pattern observed during enconding and retention phases implies the co-existence of alpha acitivities reflecting distinct functions.

Key words: short term memory, electroencephalography (EEG), evoked potentials, alpha rhythm, cortical synchronization

O6

Sexual dimorphism in medial vestibular nucleus of adult rats: a stereologic study

Ayyildiz M [1], **Kozan R [1]**, Agar E [1] , Kaplan S [2].

Ondokuz Mayis University, Faculty of Medicine, Department of Physiology [1], Department of Histology [2] Samsun, Turkey.

rkozan@omu.edu.tr

The vestibular system helps to maintain equilibrium. There are four vestibular nuclei within the brain stem (superior, lateral, medial, and inferior). The medial vestibular nucleus (MVN) is a largest of them. In this study, we used five-month-old 5 male and 5 female Wistar rats (weighing 180-220 g). The animals were deeply anaesthetized with urethane (1.25 g/kg, i.p.) and perfused intracardially. Thereafter, the brains were immediately removed from the cranium and treated in routine tissue processing, were embedded in paraplast and sectioned at 40-µm-thickness in the horizontal plane. The slides were stained with Cresyl violet staining. The volume and the total number of neurons in the left and right MVNs of adult male and female rats were estimated using stereological techniques. Data were analysed by Wilcoxon Signed Ranks test and Mann Whitney U test. The volumes of MVN were 0,67±0,03 and 0,71±0,02 in the left and right MVNs of female, and 0,61±0,03 and 0,55±0,02 in the left and right MVNs of male rats, respectively.

Total neuron numbers were 19364±791 and 20978±784 in the left and right MVNs of female, and 16905±229 and 15547±439 in the left and right MVNs of male rats, respectively. It was found no asymmetry in volume between the left and right sides in both sexes; a significant difference in volume was only observed in volume comparison of the right MVN, but not between the left MVNs of male and female subjects. A significant difference in both side comparison of total neuron number of the left and right MVNs in the female and male rats between the right and the left sides was observed, in male left>right; in female right>left. There was also a significant difference in comparison of the total neuron numbers of the right and left MVNs between male and female, since both MVNs in female have more neuron than male, i.e. female > male. These results indicate that neuron number in MVN shows laterality in the same sex, and a female-based sexual dimorphism.

Key words: Rat, mvn, neuron number, sexual dimorphism, stereology

O7

A novel adult spinal motoneuron culture: Survival record in serum and growth factor – free medium.

Ozturk G, Bektas S.

Yuzuncu Yil University, Medical School, Department of Physiology and Neuroscience Research Unit, Van, Turkey.

drgurkan@yyu.edu.tr

To be able to keep spinal motoneurons alive in vitro is crucial for investigation of pathologies affecting these cells under controlled conditions. On the other hand, available culture methods either require the use of embryonic animals or supplementation of serum, muscle extract or various growth factors. The related literature reports the survival in other cultures to be only 24 hours. In this study, we aimed to extend the in vitro life span of adult mouse spinal motoneurons without any serum, extract or growth factor. For this, the motoneurons dissociated from spinal cord of adult mice were cultured. The novelties we applied in this technique were the performance of enzymatic dissociation at +4°C, with papain and agitation during the last part, "cold-hibernating" cells at +4°C for three days in L15 supplemented with B27 following the dissociation and then replacement of medium with Neurobasal A supplemented with B27 and continuing incubation at 37°C afterwards. Neurons cultured under these conditions started to grow neurites, which continued for 4-5 days. By showing immunoreactivities for spinal motoneuron markers choline acetyl transferase, TrkA and calcitonin gene related peptide, the identity of the cells was verified. The viability test done with propidium iodide demonstrated that motoneurons live up to six days after they were transferred to 37°C. In conclusion, by extending the in vitro survival of adult mouse spinal motoneurons to 9 days, we have broken a record and developed a new model for many new studies.

Key words: Motoneuron, culture, adult, serum-free

O8

The effect of ethosuximide on the kindling process

Gurbanova A, Ozkaynakci A, Aker R, Onat F.

Marmara University, School of Medicine, Department of Pharmacology and Clinical Pharmacology, Istanbul, Turkey.

aytenazizova@yahoo.com

Ethosuximide (ETS), a well-known antiabsence drug, has no consistent efficacy for any convulsive type of epilepsy. In this study, we aimed to evaluate the effect of ETS on epileptogenesis in the kindling model. In the experiments Wistar animals were instrumented stereotaxically with bilateral stimulation and recording electrodes into the basolateral amygdala and recording electrodes on the cortex. After one week recovery period, animals were injected intraperitoneally with physiological saline (control group,n=7), ETS 50 mg/kg (n=5) or ETS 100 mg/kg (n=4) an hour before each electrical stimulation. Animals were electrically stimulated twice daily at their afterdischarge thresholds. The seizure severity was evaluated using Racine's 5-stage scale. Animals were considered as fully-kindled when they experienced five stage 5 seizures. All animals in the control group were fully kindled and the mean number of stimulations for the development of first stage 5 seizure was 13 ± 0.6. Wistar rats treated with the dose of 50 mg/kg of ETS showed similar rate and pattern of kindling with control group. ETS delayed the development of forelimb clonus in the rats treated with 100 mg/kg. Two out of four Wistar rats in this group remained at stage 3 or 4 although 30 stimulations were applied. The mean number of stimulations for the development of first stage 5 seizure in the rest of the animals was 25 ± 2.1. Although ETS is considered as ineffective agent on convulsive seizures, it delayed the development of convulsive seizures in amygdala kindling model.

Key words: ethosuximide, kindling, epilepsy, convulsive seizure, clonus

O9

Investigation of the effect of valproic acid and ceftriaxone to cortical spreading depression.

Gurer G [1], Gursoy–Ozdemir Y [1], Dalkara T[2].

Hacettepe University Institute of Neurological Sciences and Psychiatry [1], Department of Neurology [2], Ankara, Turkey.

gunfer@hacettepe.edu.tr

Cortical spreading depression (CSD) is a neuronal depolarizing wave with a propagation speed of 3-4 mm/min. Neuroimaging studies suggested that migraine visual aura may be caused by an electrophysiological event like CSD. In experimental models of migraine, trigeminovascular afferents were found to be sensitized after CSD showing that CSD can trigger migraine attacks.

Fanilial hemiplegic migraine (FHM) is genetically transmitted from of migraine. Recent mutations detected in P/Q calcium channels and Na+, K+ ATPaseII pump underlined the role of exitatory amino acid glutamate release and its uptake by astrocytes in migraine pathophysiology. Supporting this view, glutamate and its analogs can trigger CSD. Recently, it was reported that VA could decrease hyperexitability in occipital cortex of patients and cefrixone could induce expression of glutamate transporter GLT1 in astrocytes in cell cultures. For this reason, we aimed to study the effects of valporic acid and ceftriaxone on CSD threshold in the mouse.

VA (100mg/kg) was administered for 40-80 days and ceftriaxone (200mg/kg) was administered for 5-13 days intraperitoneally to Swiss albino mice. Control group received SF for the same time period. Also, CSD were recorded after single injections of the same time period VA (n=6) and ceftriaxone (n=6).

The effect of the drugs on CSD threshold and CSD propagation speed was investigated. To demonstrate the mechanism of action of VA, the changes in the hippocampal evoked potentials were also evaluated. CSD induced by applying topical potassium (1mM) to the cortex for 2 hours. Hippocampal CA1 evoked potentials were obtained by stimulation of anterior commissure in vivo.

Chronic exposure to VA significantly decreased the number of CSDs, which is 17±1 in the control group (n=6) to 12±3 and also the propagation speed from 2.7±0.6 mm/min in to 1.8±0.4min. The acute injection group (n=6) showed no difference from the control group (CSD number: 18±1.1, CSD speed: 2.6±0.8). The number of CSDs was 20±0.9 and the propagation speed was 2.5±0.3 mm/min in acute ceftriaxone injection group (n=6) but, in the chronic injection group the animals come out of urethane anesthesia faster and it was not possible to get stable recordings for two hours. Hence, only the data from the first hour (n=4) was evaluated. The preliminary studies showed that the number of CSDs was 6 in the day 5, 9 in the days 9 and 13, 8 in the day 11. In hippocampal recordings, VA decreased the slope of population excitatory post-synaptic potentials (epsp).

This data showed that chronic treatment with VA decreased the frequency and propagation speed of CSD. Preliminary data suggested that chronic ceftriaxone treatment had the same effect.

Key words: cortical spreading depression, valproic acid, migraine

O10

Amygdala kindling in rat pups and young adults with genetic absence epilepsy

Carcak N [1], Aker R [2], Ozdemir O [1], Onat F [2].

Istanbul University Faculty of Pharmacy Department of Pharmacology[1], Marmara University Faculty of Medicine Department of Pharmacology and Clinical Pharmacology[2], Istanbul-Turkey.

fonat@marmara.edu.tr

A recent kindling study in rats with genetic absence epilepsy showed that Genetic Absence Epilepsy Rats from Strasbourg (GAERS) failed to progress beyond stage 2 after the application of 25 electrical stimulations. In the models of Genetic Absence Epilepsy spike-and-wave discharges start to appear on postnatal day (PN) 40. In order to evaluate age-related changes on the kindling progress in GAERS pups, we examined the amygdala kindling rate and afterdischarge characteristics of PN30 and PN60 GAERS. Electrodes for stimulation and recording were stereotaxically implanted into the basolateral amygdala and cortex of male Wistar (n=6 each group) and GAERS (n=6 each group). After a recovery period, animals were stimulated every 90 min at 400 μA. Animals received kindling stimulation until they reached five stage 5 or the maximum number of stimulations (45). The seizures were scored by using Racine's 5-stage scale. All of non-epileptic control rats and five out of six (83.3 %) PN30 GAERS achieved stage 5, whereas one (16.7 %) PN30 GAERS stayed at stage 2 after 45 stimulations. Four out of six (66.6 %) PN60 GAERS reached stage 5, two of six (33.4 %) PN60 GAERS stayed at stage-2 and no motor seizures was observed after the application of 45 stimulations. Additionally, the amygdala kindling rate of five PN30 and four PN60 GAERS was significantly slower when compared to non-epileptic control rats. In GAERS groups, afterdischarge durations recorded from cortex and amygdala, were found to be increased compared to control group only when they reached stage 5 seizure. The results of our study demonstrate that resistance to the secondary generalization of limbic seizures during amygdala kindling in GAERS is age-related.

Key words: Pup, GAERS, Amygdala Kindling, Absence Epilepsy.

O11

Parasympathomimetic analgesia: antinociceptive effects of physostigmine and arecolin combined with hyoscine n- buthyl bromide in mice

Tekol Y, Eminel S.

Erciyes University, Faculty of Medicine, Department of Pharmacology, Kayseri, Turkey.

ytekol@erciyes.edu.tr

The unwanted effects (e.g. dependence, respiratory depression and tolerance development) of opioids, which are effective analgesics used in severe painful situations necessitates discovering new analgesic agents. In this regard, parasympathomimetics may be an alternative to opioids, because their antinociceptive action is very powerful. Parasympathomimetics produce several unwanted effects at the same doses as those necessary for analgesia, so they are not useful in clinical practice for this purpose. Neostigmine may produce some unwanted effects such as nausea, vomiting, urinary, and fecal incontinence, even when used clinically by the intrathecal route. In order to eliminate the unwanted side effects of parasympathomimetics, and thereby providing the use of these drugs as systemic analgesics, tertiary amine parasympathomimetics, physostigmine (physo) and arecoline (arec), that crosses blood- brain barrier easily were combined with quaternary amine hyoscine n- buthyl bromide, which can not penetrate central nervous system. All drugs were administered intraperitoneally and totally 120 mice were used. The antinociceptive effect was determined by tail-flick response. When compared to SF (saline), while hyoscine N- buthyl bromide (0.15 and 4.00 mg/kg) did not produce antinociception ($P>0.05$), physo (0.3 mg/kg) and arec (8.00 mg/kg) exerted significant antinociceptive effect ($P<0.05$). In combined applications, physo + hyo (0.075 + 0.15; 0.15 + 0.30; 0.30 + 0.60 mg/kg) and arec + hyo (1.00 + 0.50; 2.00 + 1.00; 4.00 + 2.00; 8.00 + 4.00 mg/kg), respectively, produced significant antinociception ($P<0.05$), and the tail flick latencies produced by physo 0.30 + hyo 0.60 mg/kg and arec 8.00 + hyo 4.00 mg/kg were not significantly different ($P>0.05$) from those of physo 0.30 mg/kg and arec 8.00 mg/kg, respectively, showing that hyo did not antagonise the antinociceptive effects of physo and arec.As a result, the peripherally acting hyo does not change the antinociceptive effects of physo and arec, and consequently, the peripheral unwanted effects of parasympatomimetics applied as analgesic may be prevented by hyo.

Key words: Antinociception, Analgesia, Physostigmine, Arecoline, Hyoscine n butylbromide, Mice

O12

Alpha-synuclein A30p mutation increases sensitivity to focal cerebral ischemia

Yemisci M [1], Gurer G [1], Unal-Cevik I [1], Kahle JP [2], Dalkara T[1].

Hacettepe University Department of Neurology, Institute of Neurological Science and Psychiatry [1],Laboratory of Alzheimer's and Parkinson's Disease Research, Department of Biochemistry [2], Ludwig Maximilians University of Munich, Germany.

myemisci@hacettepe.edu.tr

Alpha-synuclein is a presnaptic protein that has a role in neuronal plasticity. Marked alpha-synuclein accumulation is found in neurodegenarative diseases like Alzheimers Disease, Parkinson Disease and Lewy-body dementia and may be involved in their pathogenesis. In vitro oxidative stress and pH changes causes alpha-synuclein aggregation and these conditions are present in ischemia.

Transgenic mice expressing mutant human alpha-synuclein (A30P) has a tendency to form synuclein fibrils and is thought to be an in vivo model for synucleinopathies. They may be more sensitive to ischemia than age-matched controls, thus may be vulnerable to cell death hence develop larger infacts.

Focal cerebral ischemia (30 minutes) and reperfusion (24 hours) was performed on 8-week old transgenic mice [C57Bl6(Thy1)-h[A30P]alphaSYNmice,line3 1H] (Tg) and 8-9 week-old wild type (WT) C57Bl6 mice with intraluminal filament method under ketamin and xylasine anesthesia. In another set of mice, selective neuronal necrosis was induced by compressing distal middle cerebral artery for 20 minutes with a glass pipet inserted through a cranial window. These mice were sacrified 72 hours after ischemia. Regional cerebral blood flow and body temperature were monitored. Infact volumes and the number of selectively necrotic neurons were calculated on hematoxyline and eosin stained brain sections.

Infarct volumes of transgenic mice were larger when compared to WT ($15\pm2mm^3$ versus $8,5\pm1mm^3$, respectively, mean±SE, $p<0.05$). Number of selectively necrotic neurons were also higher in the transgenic group (79±14% versus 38±5%, data expressed as percentage of total neurons). Physiological parameters were not significantly different between the groups, so the increased vulnerability of Tg mice to ischemia was thought not related to hemodynamic factors.These data implicates that A30P Tg mice have increased vulnerability to ischemia due to tendency to form synuclein aggregates. Recent studies suggest that protein aggregates may cause cell death by blocking ubiquitin-proteosome pathway. We are currently investigating this potential mechanism.

Key words: alpha-synuclein, focal cerebral ischemia, A30P mutation, selective neuronal necrosis

O13

The role of ETS domain transcription factors in neuronal differentiation

Aksan Kurnaz I [1], Demir O [1, 2], Sharrocks, A [3].

Yeditepe University, Dept. Genetics and Bioengineering[1],İstanbul, Istanbul Technical University, Dept. Molecular Biology and Genetics[1,3], İstanbul, University of Manchester, School of Biological Sciences, Manchester[1], UK.

iakurnaz@yeditepe.edu.tr

PC12 cells have long been used as a model system for neuronal differentiation. 3 major growth factors studied in these cells, namely NGF, EGF and bFGF, all activate the MAPK signal transduction pathway and yet generate different cellular responses: NGF (Nerve Growth Factor) and bFGF (basic Fibroblast Growth Factor) both induce neuronal differentiation as monitored by axonal outgrowth and electrical conductivity, while EGF (Epidermal Growth Factor) induces proliferation in these cells (Marshall, 1995; Traverse et al, 1994; Yaka et al, 1998; Yamada et al, 1996). This difference is mainly due to duration of MAPK signaling, where transient versus sustained MAPK activation is though to induce expression of different target genes through activation of different transcription factor subfamilies. In this study, we have observed that two different members of the ETS domain transcription factor family can induce different cellular responses: PEA3 results in differentiation in PC12

cells, while Elk-1 factor appears to play a role in survival of differentiating neurons rather than differentiation per se.

When cells are transfected with a repressive form of Elk-1 (ElkEN), the cells show increased apoptosis. This implies that Elk-1 normally has an anti-apoptotic function in cells. Consistently, when anti-apoptotic IAP-1 protein is cotransfected with ElkEN, cells gob ack to their normal mitoti cycle. It has also been shown that promoter of another anti-apoptotic molecule, MCL-1, is regulated by Elk-1 (Townsend et al, 1999). Our findings indicate that Elk-1 protein functions in survival of PC12 cells.

PEA3 protein, however, results in a differentiation response in PC12 cells when administered in combination with EGF, which normally leads to proliferation in these cells. In addition, when cells are differentiated with NGF, the expression of PEA3 message is increased. We believe, therefore, that sustained activation of MAPK leads to an increase in the PEA3 transcription factor, which may further get phosphorylated by MAPK, eventually leading to axonal outgrowth through expression of target genes.

Understanding the molecular mechanism of neuronal differentiation at the genetic level may help us generate a particular type of neuron through genetic modifications of stem cells *in vitro*. These kind sof genetic modifications may be more effective in directing lineage-specific differentiation when compared to growth factor coctails currently used in stem cell research.

Key words: PC12, neuronal differentiation, ETS, Elk-1, PEA3

O14

Analyzing and decoding neural ensemble spiking activity using a multivariate point process likelihood model.

Okatan M [1], Wilson MA [2], Brown EN [1, 2, 3].

Massachusetts General Hospital, Department of Anesthesia and Critical Care[1], Massachusetts Institute of Technology, Department of Brain and Cognitive Sciences[2], Harvard Medical School, Harvard/MIT Division of Health Sciences and Technology[3], Boston, MA, USA.

murat@neurostat.mgh.harvard.edu

We present a multivariate point process likelihood model for analyzing the functional connectivity among a group of simultaneously recorded neurons. The model is used in analyzing the functional interactions among a group of rat hippocampal place cells (PCs) during a spatial task. The spiking activity of 33 PCs was recorded simultaneously in hippocampal area CA1 using 12 tetrodes for 23 minutes while the animal was foraging for randomly delivered food pellets in a familiar circular environment of 70 cm diameter. We divided the session into two equal parts and estimated the functional connectivity among the neurons in each part independently. Each cell's spiking behavior was modeled as a function of the animal's instantaneous position and the 30 ms history of the ensemble spiking activity. We find that the functional connectivity patterns were significantly similar in both parts of the session ($P<10^{-7}$). The place fields (PFs) of the cell pairs that were present in the connectivity patterns in both parts of the session had significantly larger overlaps compared to other cell pairs ($P<0.004$). In a previous study, the functional connectivity was determined using only the history-dependent component of the model. The new model fits the spike trains significantly better as indicated by the Kolmogorov-Smirnov plots. Using the model fit in part I, we determined the animal's position in part II by decoding the ensemble neural activity. We find that taking account of the functional neural interactions reduces the median decoding error significantly ($P<0.001$). The significant relation between functional interactions and PF overlaps suggests the presence of further position-dependent signals that control the relative spike timing in these cells. PCs tend to fire at particular phases of the hippocampal theta rhythm, and the preferred phase of each cell varies (phase precession) as the animal moves through the cell's PF. This phenomenon will be included into the model in future studies. Our results show that point process likelihood models are convenient and efficient tools for analyzing the information encoded in neural ensemble spiking activity.

Key words: Hippocampus, electrophysiology, action potentials, neural networks, memory.

O15

Regularity in the response of a single-compartmental neuronal model with stochastic ion channels for subthreshold periodic stimulus

Agaoglu N, Ozer M.

Zonguldak Karaelmas University, Engineering Faculty, Department of Electrical and Electronics Engineering, Zonguldak, Turkey.

nihal_agaoglu@yahoo.com

Excitable membranes generate electrical signals and propagate them due to voltage-gated ion channels. Ion channel proteins change their conformations thermally and so open and close randomly. The stochastic behavior of the ion channels results in a certain level of internal noise. Finite population of the stochastic ion channels may cause random current fluctuations due to the fluctuations of the number of open ion channels around the corresponding mean values. The fluctuations can modify excitability, cause spontaneous firing, and result in variability of spike threshold, spike timing and interspike intervals. In this study, we investigate the regularity in the response of a single-compartmental neuronal model with stochastic ion channels for subthreshold periodic stimulus. The effects of the channel noise have been included into the model by using different computational algorithms. We use the Jung-Shuai computational algorithm for modeling the stochastic behavior of the channels. The Jung-Shuai algorithm is called a channel-state-tracking (CST) algorithm since it determines the state of each channel based on the states of the channel gate particles at each time increment. To measure the regularity we use the coefficient of variation (CV) defined as a relative dispersion of the interspike interval distribution. CV, which is also called as a relative fluctuation, assumes a value between 0 and 1. When CV=1, the generated spike train is fully uncorrelated. As the CV gets smaller values, the spiking activity becomes more ordered. We computed the CV values for seven different frequencies of the subthreshold periodic stimulus in the range of 0.1-0.7 ms^{-1} and nine different membrane patch sizes in the range of 0.16-64 μm^2. The simulation duration is taken as a 1000 second for each trial. We observed that the CV exhibits a resonance behavior. The CV exhibits a minimum at an optimal size of the patch near 1 μm^2. This means that the spike train becomes distinctly more ordered. We also observed that the CV exhibits another minimum at an optimal stimulus frequency near $\omega=0.4$ ms^{-1} for the larger patch sizes. Consequently, it is shown that the resonance is independent of the stimulus frequency for the very small patch sizes while it is dependent on the frequency for larger sizes. The obtained results indicate that the responses of a single-compartmental neuronal model in subthreshold periodic regime reflect frequency selectivity rather than overall stimulus power for the larger patch sizes in context of the regularity.

Key words: Excitable membranes, noise, subthreshold stimulus,resonance, spike train

O16

Spatial frequency separation of brain potentials

Bayram A [1], Yildirim E [2], Demiralp T [2], Ademoglu A [1].

Bogazici University, Bio-Medical Eng. Institude [1], Bebek, Istanbul Istanbul University, Istanbul Faculty of Medicine, Department of Physiology[2], Capa, Istanbul, Turkey.

ali.bayram@boun.edu.tr

The highest temporal resolution, which is crucial for temporal localization of activities in the brain, is achieved by event-related potentials (ERP), but spatial resolution of scalp topography is low while comparing to fMRI and PET. To overcome the resolution limitation of scalp topography, current-density estimation techniques were emerged whose goal is to find the possible locations of the three-dimensional intracerebral activities by solving an inverse problem. However, it is known that, during stimulus processing in the brain, many different generator configurations could interfere the ERP topography at the scalp. That is, scalp topologies constituted by multiple sources which makes the inverse problem more complicated.

The core objective of the present study is to separate spatial frequency components of scalp topography by 2-D wavelet transform and to interpret spatial frequency formation via corresponding current-density estimations. In addition, by achieving less complex scalp maps, obstacle of the inverse problem due to the multiple sources might be lessen. In this work, 30-channel-ERP recordings were taken during Sternberg paradigm with 3 item memory set (3 letters) from 18 healthy volunteers. 500ms post-stimulus epochs (100 samples) were averaged and used in analysis. First, main topologies of

ERP recordings were investigated by hierarchical clustering algorithm and significant clusters were defined. Second, in order to see the topographic variations in neurocognitive processes and to make the 2-D wavelet transform possible, the ERP recordings were spatially enhanced by interpolation. After that different spatial frequencies of main topologies were separated by 2-D wavelet transform. Finally, main topological maps and topographic maps of different spatial frequencies derived from them were used to find corresponding cortical activities (cortical activity maxima) by LORETA (Low Resolution Electromagnetic Tomography). The most important finding of this study is the significant separation of source locations in the brain, thanks to spatial frequency separation of the scalp topographies on the surface. As a result, we could say that, spatial frequency separation of ERP topographies by 2-D wavelet transform increases the success of the methods that are used to find sources in 3-D.

Key words: ERP, scalp topography, spatial analysis, 2-D wavelet, LORETA.

O17

Synchronization between neuronal spiking activity and subthreshold periodic stimulus for two different noise models

Uzuntarla M, Ozer M.

Zonguldak Karaelmas University, Engineering Faculty, Department of Electrical and Electronics Engineering, Zonguldak, Turkey.

muzuntarla@yahoo.com

Voltage-gated ion channels are crucial components in the generation and propagation of action potentials. The ion channels open and close stochastically. Therefore, the random channel events introduce channel noise into the system. The effects of the channel noise have been included into the system by using different computational algorithms. One of the neuronal systems widely used is the FitzHugh-Nagumo model (FHNM). The FHNM was proposed as a simplification of the Hodgkin-Huxley neuronal model. The aim of the present study is to compare the responses of the FHNM driven by two different noise models for subthreshold periodic stimulus, and to examine the phase relation between the fired action potentials and the stimulus. In the first case, the noisy driving term is modeled as a Gaussian white noise with a zero mean. Therefore, it is characterized by only a variance parameter. In the second case, it is modeled as an Ornstein-Uhlenbeck (OU) noise, which is a zero mean, Gaussian noise with an exponentially decaying correlation function, and characterized by two parameters: the variance and correlation time. In order to investigate the synchronization between the spiking activity and subthreshold periodic stimulus for two different noise models, we obtain the phase probability density of the spiking events for four different noise intensities and four different frequencies of the stimulus. The simulation duration is taken as 1000 periods of the subthreshold periodic stimulus and each simulation is repeated 100 times. In each period, timing of the spikes is determined relative to stimulus period. Then, by making necessary normalization the phase probability density of the spiking events is obtained. In the case of Gaussian white noise, the phase probability density becomes relatively flat on both positive and negative phases of the stimulus for all frequencies as the intensity of the noise becomes stronger. On the contrary, in the case of OU noise, the phase probability density takes very small values on the negative phase of the stimulus for all frequencies. With decreasing the intensity of the noise for both cases, a peak of the probability density on the positive phase is getting more visible. This means that the noise looses its strength and external stimulus becomes dominant at smaller noise levels. Consequently, the timings of the spiking events concentrate on a specific phase of the stimulus, the phenomenon is called as a phase locking behavior.

Key words: Fitzhugh-Nagumo model, noise, synchronization, ion channel

POSTER PRESENTATIONS

P1

The absence of musculacutaneous nerve

Arican RY, Coskun N, Sarikcioglu L, Sindel M.

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

aricanry@akdeniz.edu.tr

During the routine dissection studies in the upper limbs of a 56-year-old female cadaver, we encountered variations in the biceps brachii muscle and musculocutaneous nerve. Additionally, there was a communicating branch between the middle trunk and the medial root of the median nevre. The knowledge of such variations may become significance during diagnostic and surgical procedures.

P2

Determination of hand, foot and eye preferences in young adults: A descriptive study

Barut C [1], Ozer CM [1], Yunten Z [2] , Sumbuloglu V [2].

Zonguldak Karaelmas University, School of Medicine Department of Anatomy[1], Biostatistics[2], Zonguldak, Turkey.

cagbarut@yahoo.com

Procedures such as determination of hand preference, foot preference and eye preference are important in the evaluation of cerebral lateralization. The aim of this study was to determine the hand, foot and eye preference of individuals in order to maintain support for future studies regarding cerebral lateralization. The hand preference of individuals was detected using Edinburgh Inventory, depending on Geschwind score. Foot preference was detected by asking the individual which foot he/she preferred to kick a ball. Eye preference was detected by asking the individual which eye he/she preferred in order to look through a telescope. 633 individuals (343 male, 290 female) aged between 18-42 years (22.11±2.07) participated the study. 17.85% of the individuals were strong right-handers, 61.3% were weak right-handers, 5.21% were ambidextrous whereas 10.74% were weak left-handers and 4.9% of them were strong left-handers. 71.57% of the individuals preferred their right foot, 14.69% preferred left foot and 13.74 preferred both feet. 56.08% of the individuals preferred right eye, 3.65% left eye and 13.27% preferred both eyes. The results regarding the hand, foot and eye preference in a sample of Turkish population were suggested to bring insight for future studies.

Key words: Lateralization, hand preference, foot preference, eye preference

P3

The arterial supply of the upper thoracal-lower cervical regions of the spinal cord of the Guinea pig

Demirel BM [1], Sarikcioglu L [1], Yildirim FB [1], Demir N [2], Acikbas C [3], Ucar Y [1], Oguz N [1].

Akdeniz University Faculty of Medicine,Departments of Anatomy [1], Histology and Embryology [2], Neurosurgery [3], 07070 Antalya, Turkey.

bmdemirel@akdeniz.edu.tr

Spinal cord is affected by mechanical traumas or pathologies. These compressions are important to be caused to the neural deficiencies. It has been known that vascular structures of the spinal cord are associated with spinal cord injuries by direct or indirect ways. Vascularization of the lower cervical and upper thoracic segments of the spinal cord is poor (watershed zone). Therefore it is important to preserve vascular structures during surgical procedures in this region.

In the present study, we aim to form a vascular cast made by polyester resin of the vascular structures in the upper thoracic-lower cervical region in the 20 adult male Guinea pigs. After perfusion and fixation of the animals, polyester resin was injected transcardially. After polymerization of polyester resin, the tissues were macerated and then vascular corrosion casts exposed. The casts were examined by stereomicroscope and photographed.

We observed that the spinal cord in the Guinea pig was supplied by a. spinalis anterior, a. spinalis posterior, a. spinalis anterolateralis, a. spinalis posterolateralis and a. vertebralis. The watershed zone was also found in the upper thoracic and lower cervical segment of the *Guinea pig* as reported in man.

We think that our findings should be kept in mind during surgical procedures in the guinea pig and are worthy of note for researchers dealing with vasculature of the spinal cord of the small laboratory animals.

P4

Tethered cord syndrome: an anatomical point of view

Demiryurek D [1], Yagmurlu B [2], Tuccar E [3], Bayramoglu A [1].

Hacettepe University Faculty of Medicine, Department of Anatomy [1], Radiology [2], Ankara, Turkey; Ankara University Faculty of Medicine, Department of Anatomy [3], Ankara, Turkey.

mdeniz@hacettepe.edu.tr

The spinal cord is located within the spinal column, cushioned by cerebrospinal fluid, and is attached at its lower end to a strand of elastic tissue, the filum terminale, which is in turn attached to the lower end of the spinal column and which secures the lower end of the cord but allows it to be stretched without injury. Tethered spinal cord syndrome is a motor, sensory, and autonomic nervous function disorder. It is due to an inelastic structure anchoring the caudal end of the spinal cord and limiting its movement within the vertebral canal. The symptoms may include back pain , deformity of the spine, loss of sensation and weakness in the lower extremity, progressive loss of control over urinary bladder functions (incontinence). This presentation aims to inform about the anatomical structures related to this syndrome and to analyse the neurological findings of the tethered cord syndrome from an anatomical point of view.

Key words: Tethered, spinal cord, syndrome, anatomy

P5

Morphometry of the rhomboid fossa as a guide for transtegmental surgical approach

Kayalioglu G, Erturk M.

Ege University, Faculty of Medicine, Department of Anatomy, Bornova, Izmir, Turkey.

kayali@rocketmail.com

The transtegmental approach is used in interventions to intrinsic brainstem lesions via the fourth ventricle floor. In this study, we used 45 adult human brainstems fixed in 10% formalin to examine the morphometry of constant brainstem structures to provide safe entry via the fourth ventricle floor. We measured the length and width of the rhomboid fossa as 34.65±2.51 mm and 22.61±1.77 mm, consequently. The length and width of the facial colliculus were 5.8±0.73 mm and 3.66±0.41 mm, consequently. The distance between the obex and the lower border of the facial colliculus was measured as 12.84±1.37 mm. The distance between the facial colliculus and the median sulcus was 0.62±0.07 mm. We measured the distance between the upper border of the hypoglossal triangle and the obex as 9.42±1.28 mm, and the distance between the upper border of the hypoglossal triangle and the lower border of the facial colliculus as 4.42±0.65 mm. The distance between the two sulcus limitans incisures was 9.52±1.15 mm. We measured the distance between the obex and the the sulcus limitans incisure as 18.4±1.51 mm. These measurements reveal two safe approach zones as the infrafacial and suprafacial approach zones, and give detailed knowledge of the anatomical structures of the region for the neurosurgeon approaching intraaxial space-occupying lesions via the rhomboid fossa.

Key words: rhomboid fossa, anatomy, morphometry,cadaver, surgery

P6

Wegener's granulomatosis and neurological complications

Koc F [1], Yerdelen D [1], **Ozcan F** [1], Bozdemir H.

Cukurova University Medical School, Department of Neurology [1], (Present address: Baskent University Faculty of Medicine, Adana Teaching and Medical Research Center, Department of Neurology [1], Adana-Turkey)

zaferkoc@superonline.com

Wegener's granulomatosis is characterized by necrotising granulomatous vasculitis of the upper and lower respiratory tracts, glomerulonephritis, and generalized vasculitis of small vessels. It develops generally at 40 years old, but it can affect people of all ages and men more than women. In this report, a case with wegener's granulomatosis presenting with multipl cranial neuropathy. A 33-year old female was accepted to the clinic with a complaint of headache. She was diagnosed as wegener's granulomatosis 10 years ago and had immunosuppresive therapy. But she wasn't on any therapy at that time. Neurological examination revealed left semiptosis, anisocoria (right pupil > left pupil), partially internuclear ophthalmoplegia while looking right side, bilateral facial paralysis, and bilateral decrease in hearing. Visual evoked potentials showed bilateral prolongation of P_{100} latency, and brainstem evoked potentials showed loss of first response. Cranial mangetic resonans imaging and EEG werenormal. Initial pressure and biochemical examination of cerebro spinal fluid were normal. Peripheral electromyography (EMG) revealed normal findings, however, facial EMG showed denervation potentials. Immunsupressive therapy was started and the patient was discharged. The control examination after 20 days, headache of the patient was improved. In wegener granulomatosis, neurological involvement is not rare and the ratio is 22-54 %. Neurological complications are limited to central nervous system, peripheral nerves, and lower group cranial neuropathies. In this report, a case with upper group and lower group cranial involvement is presented.

Key words: Necrotising granulomatous vasculitis, neurological, electrophysiological, and radiological findings.

P7

Comparison of growth and development in patients with cerebral palsy and normal people of 18 years of age

Kosif R [1], Sunter AT [2].

Karaelmas University, Faculty of Medicine, Department of Anatomy[1], Ondokuzmayis University, Faculty of Medicine, Department of Public Health[2], Samsun, Turkey.

rengink@yahoo.com

The patients with cerebral palsy may encounter nutrition difficulties related to mental retardation, motor dysfunction, speaking difficulties, impaired coordination, impaired equilibrium and abnormal motions, learning difficulties, attention problems, troubles in swallowing and hearing, and communication problem. As a result of this situation, growth and development can be effected. In this study, the anthropological measurements of healthy male indiviuals of 18 years of age and those of peer male patients with cerebral palsy were compared and the growth and development of the patients with cerebral palsy were evaluated. The anthropological measurements of healthy male indiviuals of 18 years of age and peer male patients with cerebral palsy were performed and the skin fold thickness values were noted. The anthropological measurements were length, weight, head circumference, arm circumference, biacromial diameter, nipple diameter, the diameter of areola mamma, the distance of the nipple from the median line, sitting height, fathom length, chest circumference, thoracic outlet diameter, thorax depth. The skin fold thicknesses used were subscapular, triceps, suprailiac. The study was performed with 45 healthy young males of 18 years of age and 16 patients of the same age with cerebral palsy. The study group was selected among the young patients with cerebral palsy appropriate for the study (GMFCS 1 and 2) in Spastic Children Center in Zonguldak and Sari Basak Special Education Center in Kozlu and their measurements were done. The healthy controls were the students in the central campus of Zonguldak Karaelmas University. When the measurements of the normal individuals and those with cerebral palsy were compared, significant differences were found in head circumference (57.37±3.32, 54.81±3.64 cm), distance of nipple from the median line (11.47±1.05, 9.83±1.52 cm) and sitting height (90.44±7.08, 84.65±6.96 cm). The measurements were smaller in the patients withvcerebral palsy. No significant diffferences were found for skin fold thickness.

Key words: cerebral palsy, 18 age, anthropologic measurements, growth, comparison

P8

Stereological methods in the volumetric analyzes of brain structures

Mas N [1], Pelin C [1], Zagyapan R [1], Inceli O [2], Kelesoglu Y [2].

Baskent University Department of Anatomy [1], Baskent University Term I students [2], Ankara, Turkey.

nmas@baskent.edu.tr

Differential changes due to aging in human brain exhibit a complex pattern. Volumetric changes in brain structures caused by several pathological disorders besides aging are recently of importance for the clinicians. In the present study the contribution of stereological methods for the detection of pathological or abnormal changes in brain structures has been evaluated.

It is well known that many neurological disorders are characterized by the volumetric abnormalities in cortical or subcortical regions. In the behavioral and anatomical studies on Alzheimer's disease, schizophrenia, senile

dementia, multiple sclerosis, cerobrovascular disorders, tumors, epilepsy, bipolar disorder, it is reported that such disorders could cause morphological changes in brain structures. So, quantitative volumes of the intracranial structures could be useful for an objective assessment of the pathological changes. Up to date, in order to determine the changes in the volume or surface area of the brain structures or tissue composition some radiological techniques such as MRI or CT imaging have been used.

Stereological methods based on the Cavalier's principle offer many opportunities for noninvasive in vivo measurement of the structures in human brains. By the technique, brain volume can be estimated without bias by randomly translating a point grid over a uniform random cross-sectional image and then the points on the area of interest is counted. Later the volume is calculated by multiplying the area per point, by the surface area of the certain region and later by the tissue thickness. Stereological method is preferable when compared with the other methods since it is unbiased and efficient. Besides since it does not need extra software computer program, though extra time and technical staff it is rapid and economical. In addition to this it increases the inter- and intra-observer accuracy. However this method is not good in reflecting the minor volumetric changes.

Key words: Stereology, morphometry, Cavalier's principal, anatomy, intracranial volumetric analysis.

P9

Morphometric analysis techniques in neuroscience

Mas N [1], Zagyapan R [1], Pelin C [1], Akgun Arda [2], Tastekin Y [2].

Baskent University Department of Anatomy [1], Baskent University Term I students [2], Ankara, Turkey.

nmas@baskent.edu.tr

Morphometric analysis techniques are of importance in neuroscience for metric or picksel estimation of volume or surface area in digital images. The discrimination of the volumetric changes due to aging or pathological factors is without doubt important for clinicians. Therefore in the present study the morphometric evaluation of the normal or pathological masses in the radiographic images of the brain tissue has been studied.

It is well known that some neurological disorders such as Parkinson, Alzheimer's disease, post traumatic stress syndrome, hydrocephalus, aneurysm, schizophrenia, senile dementia, multiple sclerosis, tumors, epilepsy or cerobrovascular disorders could cause morphometric changes. In recent studies computer based (MIDAS, UNIX, SIENAX, STEREO, OSIRIS etc.) morphometric techniques such as thresholding, tracing or stereological methods are used in estimating volumetric changes.

The thresholding is a volume analyzes method depending on the color differences on the radiographic images. Tracing is an other method for volume analyzes technique by measuring the surface area of the countered region on the subsequent images. Either in thresholding or in tracing method require software computer programmes such as Unilog, Histometrics, Photoshop, Image J, Osiris, Matlab etc. On the other hand stereological technique, different from the above-mentioned methods, depends on the amount of the points on a certain surface area on the radiographic images or histological samples. Volume is calculated by multiplying the area per point, by the surface area of the certain region and later by the tissue thickness.

All these volume analyze techniques with their advantages and disadvantages according to each other are preferable for the morphometric analyzes of vital brain structures.

Key words: Intracranial, morphometric analysis, thresholding, tracing, stereological, Cavalier's principal

P10

Morphological and ultrastructural examination of the areas with demyelinization after sciatic nerve anoxia: a pilot study

Sarikcioglu L [1], Demirel BM [1], Demir N [2], Yildirim FB [1], Oguz N [1].

Akdeniz University Faculty of Medicine, Departments of Anatomy [1], Histology and Embryology [2], Antalya, Turkey.

Neural tissue requires a significant amount of oxygen to function properly, and, as a result, peripheral nerves have an extensive blood supply composed of both external and internal blood vessels. The external vessels run through the perineurium and segmentally supply the intrinsic vessels via the arteriae nervorum. The intrinsic vessels are arranged in a longitudinal plexus made from the vasa nervorum that run through the outer epineurium, inner epineurium, and perineurium. A series of endoneurial vessels that supply the axons themselves is also present. In the present study, we aimed to study the effect of anoxia on ultrastructure of the peripheral nerve after stripping of the vasa nervorum and found demyelinization in certain area of the nerve.

Key words:ischemia, dejeneration, rejeneration, sciatic nerve

P11

Assessment of atlanto-occipital junction in MRI of subjects with cervical disc herniation

Is M [1], **Sevinc O** [2], Safak A [3], Barut C [4], Yazici B [3].

Abant Izzet Baysal University, Duzce School of Medicine, Departments of Neurosurgery [1], Anatomy [2], Radiology [3], Duzce, Turkey, Zonguldak Karaelmas University, Department of Anatomy [4] Zonguldak, Turkey.

ozdemirsevinc2@yahoo.com.tr

Atlanto-occipital dislocations (AOD) are rare and generally fatal traumatic injuries. It is difficult to identify AOD on plain lateral cervical radiographs especially with multiple traumas because of the peculiar anatomy and bony overlap which may lead to misdiagnosis. In suspicious cases additional imaging with computerized tomography (CT) or magnetic resonance imaging (MRI) is recommended to achieve the secondary findings like subarachnoid and prevertebral hemorrhage or ligamentous disruption of the cervical spine There are different methods for assessing AOD like Powers ratio (PR), X-line method, Harris method and basion-dens interval (BDI) which was applied on plain lateral cervical radiographs of normal subjects. In the presented study our aim was to assess the normal limits of PR and BDI which are mostly used methods, on mid-sagittal MRI images of patients with cervical disc herniation. 445 patients who have neck pain without history of trauma were chosen. Four groups were identified according to the number of disc herniations. The normal limits of powers ratio and basion dens interval were 0.77±0.15, 0.80±0.66 in group 0, 0.76±0.14, 0.81±0.76 in group 1, 0.75±0.13, 0.80±0.71 in group 2, 0.76±0.14, 0.81±0.74 in group 3, and 0.77±0.16, 0.81±0.66 in group 4 respectively. The relationship between the number of disc herniations and powers ratio and basion dens interval was not statistically significant. Our results were in concordance with the previous studies concerning the powers ratio and basion dens interval. These two methods can be used in magnetic resonance images of atlanto-occipital dislocation suspected patients with disc herniations.

Key words: Atlanto-occipital dislocation, cervical disc herniation, magnetic resonance imaging, spine, measurement

P12

Obtaining embryonal neural stem cells from rat brain to study the effects of H_2O_2 toxicity and plausible prevention by antioxidant treatment

Akinturk SS [1], Dagci T [2, 3].

Ege University, Faculty of Science Department of Biology, (student) [1], Center for Brain Research [2], Ege University School of Medicine, Department of Physiology [3], Izmir, Turkiye.

serra.akinturk@mail.ege.edu.tr

Research in the field of neural stem cells (NSCs) is rapidly advancing, driven by the potential to provide new therapies for neurodegenerative diseases, stroke, and trauma. A NSC is defined as a cell with the ability to proliferate, exhibit self-maintenance or renewal over the lifetime of the organism, and generate clonally related neural progeny. NSCs give rise to neurons, astrocytes, and oligodendrocytes during development and can replace a limited number of neural cells in the adult brain and spinal cord. An imbalance between antioxidants and reactive oxygen species (ROS) results in oxidative stress, leading to cellular oxidative damage. Hydrogen peroxide is a common ROS, which is a by-product produced during the degradation of fatty acids and other molecules. Exposure of neurons to H_2O_2, decreases

cellular ATP, disrupts DNA strands, and inhibits protein synthesis. Lim et al. (2002) have reported H_2O_2 induced nuclear DNA breakage in Aplysia sensory neurons and dramatic morphological changes, such as neurite fragmentation, disintegration of the cell body, and a change in the resting membrane potential caused by high concentrations of H_2O_2. The poster will provide the methodological details of obtaining NRPs and GRP's, isolated from Sprague Dawley rats at embryonic day 13.5. This technique is currently employed in our laboratory. The composition of the NRP/GRP cultures, with respect to the absence of mature cells, will be verified by staining for the mature neurons [neuronal-specific nuclear protein (NeuN)], astrocytes [glial fibrillary acidic protein (GFAP)] . These cells will be used to evaluate the effects of antioxidants (Vitamin E, Vitamin C, 7-nitro indazole and dially disulfide) following H_2O_2 toxicity. Although the current poster will describe only the methodology, the ultimate aim of the study (SA's thesis work) is to determine whether NRP/GRP would survive and differentiate in the H_2O_2 environment and whether antioxidants will provide local neuroprotection.

Key words: stem cell, toxicity, antioxidants, Hydrogen peroxide, Vitamins

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P13

Interleukin-18 as a potential diagnostic marker for Alzheimer's disease

Aykan S [1, 2], Egrilmez MY [1], Yaka E [3], Cavdar Z [1], Genc S [1], Yener GG [3], Genc K [1].

Dokuz Eylul University Faculty of Medicine, Research Laboratory [1], Department of Neuroscience [2] Department of Neurology [3], Izmir, Turkey.

simge.aykan@deu.edu.tr

Alzheimer's disease (AD) is the most common form of dementia in elderly. It is characterized by progressive deterioration of cognitive functions. In clinical practice, current criteria for diagnosis of AD are still largely based on the exclusion of secondary causes and other dementive disorders. The golden standard of diagnosis is the identification of typical neuropathological changes in the brain of a patient who has suffered from clinical AD. Studies have shown that the accuracy of clinical diagnosis is between 65% and 96%. In view of this, the need for spesific AD marker is great.

TNF-related apoptosis-inducing ligand (TRAIL) is a recently discovered cytotoxic member of TNF ligand superfamily that mediates apoptotic cell death by interactions with its cognate receptors. Interleukin-18 (IL-18) is a proinflammatory cytokine that induces IFN stimulation in T and NK cells. In this project, we aimed to search whether these two molecules are possible diagnostic and prognostic biomarkers for AD. Cerebrospinal fluid (CSF) and serum samples were obtained from patients with AD. CSF samples were collected from 15 patients and 15 control subjects. Serum samples were collected from 24 patients and 12 control subjects. Both serum and CSF protein levels of IL-18 and TRAIL were determined by enzyme linked immunosorbent immunoassay (ELISA). CSF IL-18 and TRAIL levels of AD patients and control subjects were under detection limit. There were no significant differences in the serum levels of TRAIL between patients and control subjects, but we observed lower levels of IL-18 in the serum of patients as compared to control subjects ($p=0.043$). Taken together, these results indicate that IL-18 can be a candidate diagnostic biomarker for AD.

Key words: Alzheimer's Disease, Interleukin-18, TNF-related apoptosis-inducing ligand, biological markers, Cerebrospinal fluid, serum

This study was supported by the Scientific & Technological Research Council of Turkey.

P14

Erythropoietin upregulates NF-E2 related Factor 2 expression in human neuroblastoma cell line.

Aykan S [1, 2], Egrilmez MY [2], Tarcan-Avci S [3], Genc S [2], Genc K [2].

Dokuz Eylul University Faculty of Medicine, [1] Department of Neuroscience, [2] Research Laboratory [3] Department of Basic Oncology, Izmir, Turkey.

simge.aykan@deu.edu.tr

Erythropoietin (Epo) is a hematopoietic growth factor and cytokine which stimulates erythropoiesis. In recent years, Epo has been shown to have important nonhematopoietic functions in the nervous system. Actions of Epo include a critical role in the development, maintenance, protection and repair of the nervous system. A wide variety of experimental studies have shown that Epo has neuroprotective characteristics following ischemic, hypoxic, metabolic, neurotoxic and excitotoxic stress in the nervous system. Epo acts in a coordinated fashion at multiple levels in the nervous system showing its protective effect by different mechanisms, including attenuation of oxidative stres. NF-E2 related Factor 2 (Nrf-2) has been demonstrated to play a central role in the gene expression of phase II detoxification enzymes and some antioxidant genes. In this study, we assessed whether Epo regulates expressions of Nrf2, its cytoplasmic inhibitor Keap-1 and target genes in human neuroblastoma cell line. SHSY-5Y cells were treated with 10 U/ml EPO for 6 and 24 hours. RT-PCR was performed to measure mRNA levels of Nrf2, Keap-1 and target genes. Our study showed that Epo increased expressions of Nrf-2 and its target genes after 6 hours treatment with Epo. However, treatment with Epo for 24 hours maintained the elevation of its target genes' expression levels. The present work demonstrates that Epo can offer cytoprotection through direct modulation of Nrf2 signaling.

Key words: Erythropoietin, oxidative stress, NF-E2 related Factor 2, gene expression, SHSY-5Y cell line

P15

Interleukin 10 (IL-10) and Interleukin 1beta receptor antagonist (IL-1ra) attenuates the early ischemic response in an experimental rat model of spinal cord ischemia-reperfusion injury: a functional, biochemical, histopathological and ultrastructural preliminary study

Oruckaptan HH [1], **Atilla P** [2], Tuncel M [3], Muftuoglu SF [2], Kilinc K [4], Ozdemir Geyik P [5], Basaran N [6], Ozcan OE [1].

Hacettepe University Faculty of Medicine, Department of [1] Neurosurgery, [2] Histology and Embryology, [3] Anatomy, [4] Biochemistry, [5] Biostatistics, [6] Pharmacology, Division of Toxicology, Ankara, Turkey.

patilla@hacettepe.edu.tr

The production of proinflammatory mediators during perfusion and induction of neutrophils migration is important in ischemia-reperfusion injury. The aim of the study is to determine neuroprotective effects of antiinflamatory cytokine IL-10 and interleukin-1beta receptor antagonist (IL-1ra) in early ischemia-reperfusion injury.

Transient aortic balloon occlusion model was used. Study groups were; Control-A (sham-operated), Control-B (ischemia), IL-10 (IL-10 treated after ischemia-reperfusion), IL-1ra (IL-1ra treated after ischemia-reperfusion). They were sacrificed after twenty-four hours. Six points lower extremity walking scale, was used for neurological evaluation. Difference between early-late MDSs was recorded as motor recovery score (MRS) and analyzed statistically. Tissue lipid peroxidase (LPO) activity, was measured. Inflammatory, glial and degenerated neuronal cells were counted and analysed. Ultrastructural findings (neuronal cytoplasm, neuronal nucleus, neuronal mitochondria, axon, myelin, endothelium) were scored 0-3 and statistically analyzed. DNA fragmentation was evaluated by Comet assay and graded in 4 stages.

Analysis of MDSs revealed no statistical difference among Control-B, IL-10 and IL-1ra groups. Statistical analysis of MRS showed significant difference between Control-B and IL-10 groups, but insignificant between Control-B and IL-1ra groups. LPO levels in IL-10 and IL-1ra groups were statistically different than Control-A and Control-B. Difference between IL-10 and IL-1ra groups were insignificant.

Histologically Control-A, was completely preserved. In Control-B, white and gray matter were edematous. Glial cells were more in white matter. Dilatation of vessels, congestion, inflammatory cell infiltration were remarkable. Picnotic neurons were observed. Some neurons had chromatolysis, but others were more degenerated and shrunk. White matter was preserved in IL-10 group. Edema, vascular congestion, inflammatory cells were absent. White and gray matters was partially preserved in IL-1ra groups; but disorganized and edematous than IL-10 groups.

Ultrastructurally; impairment of cell-membrane integrity, decrease in Nissl substances, nuclear chromatin, loss of intra-cytoplasmic organelles, mitochondrial edema were remarkable in Control-B. In IL-10 and IL-1ra groups, most neurons were preserved, but intra-cytoplasmic and mitochondrial edema, decreased cytoplasmic organelles, nuclear chromatin substance, focal impairment of cell-membrane integrity were infrequently observed. In control-B, myelin degeneration with slimming, crackling, axon-myelin disintegration, resulting honeycomb pattern were frequent. Decreased axoplasmic density, mitochondrial edema, scarce bundles of neurofilaments were remarkable. Despite the presence of minimal changes such as occasional myelin fragmentations, crackling, mitochondrial edema, axonal integrity spared better in IL-10 and IL-1ra groups than in control-B. Endothelial cells preserved better than neurons and axons in Control-B. In IL-10 and IL-1ra groups, endothelial impairment was less prominent.

Results of single cell gel electrophoresis had no statistical difference in categorical distributions of comet formation in all groups.

In this study we conclude that IL-10 and IL-1ra attenuates early ischemic response in spinal cord ischemia-reperfusion injury .However there is need to further studies about role of interleukins in ischemia-reperfusion injury for clinical significance.

Key words: Spinal cord, Ischemia, Ischemia reperfusion injury, Interleukin, Inflammation

P16

Insulin-like growth factor (IGF-1) and glial cell line derived neurotrophic factor (GDNF) expression in fetal brain: effect of maternal hypertension

Beken S [1], Kose MF [2], Ozturk E [2], Gursoy-Ozdemir Y [3], Zeybek D [4], Anlar B [1].

Hacettepe University, Faculty of Medicine Department of Pediatrics [1], Ankara Diskapi Hospital Department of Obstetrics and Gynaecolgy[2], Hacettepe University, Faculty of Medicine Department of Neurology [3], Hacettepe University, Faculty of Medicine Department of Histology and Embryology [4], Ankara Turkey.

serbeken@yahoo.com

"Insulin-like growth factor" (IGF-1) and glial cell line derived neurotrophic factor (GDNF) are two growth factors affecting brain development in embryonic life. GDNF is a member of the transforming growth factor- (TGF-) superfamily, and promotes the survival and morphological differentiation of dopaminergic neurons. Their expression in rat hippocampus starts in early embryonic life and continues throughout adulthood, expression being much higher in the perinatal period. GDNF expression in humans is observed from fetal period to adult life. Both factors have neurotrophic and supportive role for many neural cells. Fetal nervous maturation can be accelerated in certain conditions including maternal hypertension. Mechanisms are not well understood: they can be mediated through glucocorticoids and catecholamines elevated in preeclampsia. In this study, the growth factors GDNF and IGF-1 in fetal brain are investigated. The study group consists of preeclampsia (n=2, gestational week 24-31), spontaneous abortions (n=2 gestational week 18-20) and therapeutic abortions for hydrocephaly (n=2, gestational week 21-22). Fetal brain frontal necropsy materials were homogenised and studied for IGF-1 and GDNF by western blotting. IGF-1 expression was not different between three groups. GDNF showed two bands at approximately 37 kDA and 20 kDA in the hydrocephaly and control groups while the preecclampsia group had two more bands at approximately 35 kDA and 24 kDA. These additional bands were interpreted as monomers of GDNF whose active form is a dimer, or isoforms of GDNF. These results suggest preeclampsisa may affect fetal brain maturation by altering the expression of growth factors in the brain: further studies of these growth factors can be helpful in pathogenesis and treatment.

Key words: IGF-1, GDNF, preeclampsia, moleculer weight, isoform

P17

Sex-related differences in spatial learning in juvenile rats after fetal alcohol exposure

Dursun I. Jakubowska-Dogru E.

Middle-East Technical University, Department of Biological Sciences, Ankara, Turkey.

dilknur@metu.edu.tr

In adult rats, there were found significant sex differences in ethanol actions at the molecular as well as the behavioral level (Devaud et al., 2003). These differences correspond probably to the sexual dimorphism in the brain architecture and the hormonal milieu. Sex-related differences in the sensitivity to alcohol intoxication were also reported after prenatal exposure to ethanol in rats tested as young adults. Observed memory deficits were generally, although not always, greater in female offspring (Lee and Rabe, 1999, Neese et al., 2004, Zimmerberg et al., 1991). The aim of the present study was to examine whether similar trend toward slower task acquisition in females exists when animals are tested as juveniles. Alcohol was delivered to the pregnant dams intragastrically, throughout GD 7-20, at the dose of 6g/kg maternal body weight /day resulting in peak BAC of 340 mg/dl as assessed on GD 20. A pair-fed isocaloric and untreated control groups were included. Place learning in the Morris water maze task was carried out for 4 consecutive days (4 trials daily) beginning on PD 32; a probe trial was given on the fifth day. Another group of male rats was tested in the same memory task on PD 82 to compare spatial learning between the two age groups. At this stage, female rats were not taken into experiments to avoid fluctuations in mnemonic capacity related to estrus cycle and changing estrogen levels. Performance of alcohol-exposed juvenile rats, both males and females, was significantly worse as compared to alcohol-exposed young adult subjects what is in line with the notion that adverse behavioral effects of fetal alcohol intoxication ameliorate with maturation. Among juvenile rats, female subjects showed significant deficits both in the task acquisition and probe trial performance relative to control animals and alcohol-exposed male rats. According to the present results, females are selectively more vulnerable to the alcohol-induced damage in neural areas supporting spatial reference memory.

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Key words: fetal alcohol, spatial learning, sexual dimorphism, juvenile and adult rat

P18

The effect of intrathecal ropivacain and ketamine on spinal cord in rabbits

Guven A [1], Demiraran Y [2], Sezen G [2], Sevinc O [3], Cam M [1].

A.I.B.U. Medical School of Duzce. Department of [1] Histology and Embryology, [2] Anesthesiology and Reanimation, and [3] Anatomy Duzce, Turkey.

drayselguven@yahoo.com

Ropivacaine is used as an epidural anesthetic in routine and intrathecal use as alternative to bupivacaine is being suggested and studied. Its lower lipid solubility and S-stereoisomere in its structure increases its central system tolerence and safety profile. Ketamine that is used intrathecally is also an anesthetic substance with a strong anesthetic activity. Development of neurologic sequelae after spinal and epidural anesthesia renders its neurotoxicity important. Though ropivacaine and ketamine are used currently, in this study it was aimed to determine the neurotoxic effects of ropivacaine and ketamine in different doses because there are relatively few studies on neurotoxicity.

30 New Zealand albino female rabbits were included in the study. After anesthesia with intramuscular 25 mg/kg ketamine and 5 mg/kg xylazine, in prone position and sterile conditions a spinal catheter was introduced between L_7- S_1 vertebrae using a 20 G Tuohy needle after making a skin incision of 0.5 cm. The distal end of the catheter, that is left 0.5 cm inside, was sutured to the back of the neck through a subcutaneous tunnel. Later the rabbits were divided into 5 groups and ropivacaine % 0.2 to group 1, ropivacaine % 0.75 to group 2, ropivacaine %1 to group 3, ketamine to group 4 and 0.09 % NaCl to group 5 was given eachtime with a volume of 0.3 ml. Signs of irritation, changes of defecation and urination were observed for the following five days. At the end of this time euthanasia was applied with a high dose intracardiac anesthetic 100 mg/kg pentothal. Spinal cord was

evacuated with spinal dissection and specimens taken from 0.5- 1 cm above the introduced spinal catheter were fixed with 10 % formaldehyde, embedded in paraffin. 5 µm thick sections were stained with hematoxylene and eozine and their histopathologic examination was performed. In histopathologic examination parameters of axonal degeneration, degeneration in neurons, increase in glial cells and hemorrhage were evaluated as present and absent and statistics was done. In histopathologic examination axonal degeneration was observed more in the group of 1 % ropivacaine than that of other groups but this difference was statistically not significant. The observed axonal degeneration was in the form of a diffuse degeneration in the white matter of the posterior horn and this was more intense around the catheter. The present study supports that ropivacaine and ketamine are appropriate anesthetic agents for intrathecal administration.

Key words: Ropivacain, ketamin, intrathecal, spinal cord, histopatology

P19

The effect of memantine on harmaline-induced tremor in rats

Karson A [1], Iseri P [2], Akman O [1], Ozdamar C [2], Yardimoglu M [3], Ates N [1].

Kocaeli University, Faculty of Medicine, Department of [1], Physiology, [2] Department of Neurology, [3] Department of Histology, Kocaeli, Turkey.

karson.ayse@gmail.com

Harmaline, a neurotoxic β-carboline, produces a reversible, postural/ kinetic tremor that mimics the pharmacological and clinical properties of essential tremor in rodent and human.

Additionally, harmaline produces exitotoxic lesion in cerebellar purkinje cells, due to excessive olivo-cerebellar burst-firing at the higher dosage. Memantine is a specific, moderate affinity, uncompetitive NMDA-receptor antagonist. Unlike high-affinity NMDAR blockers, it has been stated that memantine only acts under pathological conditions without having any side effect on normal function. Memantine has been used for the treatment of neurodegenerative disorders such as Alzheimer and Parkinson's disease because of its good tolerability in clinical practice.

The aim of this study was to evaluate the effect of memantine on harmaline-induced tremor. The anti-tremor efficiency of memantine was compared with ethanol.

Female Wistar Albino rats (3-month old, weighing 250–350 g) were used. Experimental tremors were produced by a single intraperitoneal injection of harmaline (20 mg/kg). Next to the saline injected control group, ethanol (1/10 dilute with saline, 2 g/kg; ip, group 1), and memantine (5 mg/kg, ip, group 3) were given 10 and 15 min before harmaline, respectively. The latency, intensity and duration of tremor were evaluated in all groups. The clinical grading of the intensity of tremors was done as follows:No tremor-0, mild tremor-1, moderate intermittent tremor-2, moderate persistent tremor-3 and pronounced severe tremor-4.

There were no differences in latency and duration of tremor among the three groups. However ethanol significantly reduced the intensity of tremor within one hour, while there were no differences in the intensity of tremor between memantine and control groups. It has been recorded the 4rd grade of tremor lasted very shorly in the memantine group. In contrasto to the harmaline and ethanol groups, memantine did not induced behavioral immobility apperantly.

In this study, the lack of anti-tremor effect of memantine on harmaline-induced tremor might be related with dose of memantine used in this study and its selective effect on NMDA receptor subtypes. To clarify the effects of memantine on harmaline-induced tremor, different dosages of memantine will be used and purkinje cell degeneration will be evaluated.

Key words: harmaline, memantine, essansiyel tremor, NMDA receptor, rat

P20

Role of matrix-metalloproteinases in the mechanism of action of electro-convulsive treatment

Eren-Kocak E [1], Gursoy-Ozdemir Y [1], Rezaki M [2], Dalkara T [1, 3].

Hacettepe University (1) Institute of Neurological Sciences and Psychiatry, (2) Faculty of Medicine Department of Psychiatry, (3) Faculty of Medicine Department of Neurology, Ankara, Turkey.

eminedr@yahoo.com

Electroconvulsive treatment (ECT) is an effective antidepressant treatment. ECT leads dendritic restructuring in hippocampal regions of experimental animals, however its mechanism of action is still unknown. Matrix metalloproteinases (MMPs) are proteases that cleave extracellular matrix proteins, neurotrophins and cytokines to modify their activity. The facts that BDNF has antidepressant properties and proBDNF is one of the MMP substrates suggest that MMPs might have a role in the mechanism of action of ECT. Supporting this idea, MMP expression is increased by kainate-induced seizures.

Electrical stimulation was applied through transcorneal electrodes to induce tonic-clonic seizures in swiss albino mice studied in three groups (n=4/group). Acute ECT group received single electrical stimulation, whereas chronic ECT group received once daily electrical stimulation for 10 days. Sham-stimulated group received the same treatment as acute ECT group except that no electrical stimulation was applied. Mice were sacrificed 6 hours after the last treatment. In situ gelatinolytic activity was determined from 10 micrometer thick brain sections. The fluorescence intensities of the photographs obtained from the sections were analyzed by Image J-software (NIH). In order to determine if there is a change in MMP-9 protein expression following ECT, Western blotting will be performed and results will be discussed accordingly.

Key words: depression, Antidepressants, Electroconvulsive treatment, Matrix metalloproteinases, In situ zymography

P21

The effects of endogenous opioids on the neurons injured in vitro

Ozturk M [1], Cengiz N [2], Ozturk G [3], Kaval Oguz E [4].

Yuzuncu Yil University, Faculty of Medicine, Department of [1], Internal Medicine, [2] Histology, [3] Physiology, Faculty of Education Department of [4]Biology, Van, Turkey.

cengiznurettin@yahoo.com

Nothing is known about the role of endogenous opioids on the survival of injured neurons whose levels increase in the cerebrospinal fluid after a trauma. In this study, we investigated the effects of dynorphin A, endomorphin-2, beta-endorphin and metenkephalin on the survival of mouse primary sensory neurons that were injured by neurite cuts. For this, adult mouse primary sensory neurons were dissociated and cultured and after 24 hours, the dominant outgrown neurite was cut with a laser beam at 25 micrometers. Twenty-four hours after that, live/dead cell ratios were determined using propidium iodide. Interestingly, all factors added to the medium before the lesioning increased the death rate of injured neurons. These effects were significant between the control (21,9%) and endomophin-2 (83,8%), beta-endorphin (80%), dynorphin A (70.6%) and metenkephaline (32,7%). Endogenous opioids did not affect the survival of uninjured neurons. In conclusion, this study has revealed a novel effect of endogenous opioids, which would implicate a new insight into the understanding of the mechanism of traumatic damage in the nervous system.

Key words: dinorfin A, endomorfin-2, beta-endorfin ve metenkefalin, neuron injury

P22

Immunolocalisation of MMP-2, MMP-3 and MMP-9 during the early stages of focal brain ischemia in rats

Tatlisumak E [1], Inan S [2], Comert A [3], Kose C [2], Hayretdag C [1], Tekdemir I [3].

Celal Bayar University, Faculty of Medicine, Department of [1] Anatomy, [2] Histology and Embryology [3], Manisa, Turkey; Ankara University, Faculty of Medicine, Department of Anatomy, Ankara, Turkey.

ertugrul40@yahoo.com

Matrix metalloproteinases (MMPs) are Ca^{++} dependent endopeptidases that contain Zn^{++} at their active sites. They are secreted in latent form, require activation of proteolytic activity and are inhibited by spesific tissue inhibitors

of metalloproteinase (TIMPs). They are capable of degrading almost all proteinaceous components of extracellular matrix and involved in a variety of physiological and pathological conditions. The integrity of blood-brain barrier (BBB) protects the neuronal microenvironment in brain and the events occurring by the loss of this integrity during brain ischemia complicates the pathology. Basal lamina is an important component of BBB and is composed of type IV collagen, fibronectin, laminin which are well-known substrates for MMPs and various proteoglycans. The role of MMP-2 and MMP- 9 is well-defined in the opening of BBB during ischemia/reperfusion and there are implications for the role of MMP- 3.

Male adult Wistar rats weighing 250-350 grams were used. Anaesthesia were induced by ketamine and medetomidin. Permanent focal ischemia was applied by the suture occlusion model. Harvested brains which had visible well-demarcated infarcts were used for the study. The animals were divided in to 7 study groups (n=4) with time schedules including 1.5, 3, 6, 12, 24 and 72 hours and the sham. Immunohistochemistry was performed for investigating the distribution of MMP-2, MMP-3 and MMP-9 in the ischemic brain. Formalin fixed, paraffin embedded, 5 µm sections of frontoparietal cortex were used for the study. anti-MMP-2, anti-MMP-3 and anti-MMP-9 primary antibodies and indirect immuno peroxidase technique were used. Intensity of immunostaining was scored as minimal (-/+), mild (+), moderate (++) and strong (+++).

Minimal immunostainings of MMP-2, 3 and 9 were observed in brains of sham-operated animals. Immunostainings were increased in the ischemic side of the rat brain after 1.5, 3, 6, 12, 24 and 72 hours. Stainings were first appeared in the endothelial cells of the cerebral vessels. Immunostaining were observed increased mild to moderate from 1.5 to 3 h,. Increases were more pronounced, diffuse and observed in the parenchyma at 6 h. At 12, 24 and 72 hours all MMPs were strongly stained. Immunostainings were increased delayed and less in the contralateral sides.

Experimental studies are indicating the beneficial effects of the inhibition of MMPs on the disruption of BBB and survival. MMP inhibition may provide new opportunities in the treatment of stroke and immunolocalisation of MMPs in ischemia is valuable for the development of new strategies for drug therapy.

Key words: Brain, Rat, Focal Ischemia, Blood- Brain Barrier, Matrix Metalloproteinase

P23

Observation with Nissl staining and neuron specific enolase (NSE) immunocytochemistry of neuroprotective effects of magnesium sulfate treatment after hypoxic ischemic reperfusion injury

Yardimoglu M [1], Turker G [2], **Costur P** [1], Tugay M [3], Dalcik H [1], Gokalp SA [2].

Kocaeli University, Medical Faculty, Department of Histology and Embryology [1], Department of Pediatrics [2] , Department of Pediatric Surgery [3], Kocaeli, Turkey.

docdrmelda@yahoo.com

We planned to evaluate histologically protective effects of magnesium sulfate (MgS04) after hypoxic ischemia (HI). Eight each seven-day-old rats were employed into the treatment and HI-control group. All rats were exposed to unilateral carotid artery ligation and one hour hypoxia. Thirty minutes after HI, 300 mg/kg MgS04 was given to the treatment group intraperitoneally at one dose bolus injection. Serum physiologic at same dose were injected to the HI-control group. At 24.hour and 7.day after HI, rats were sacrified and removed brains embedded paraffin and serail sections (5µm) were stained with Cresyl Violet and Neuron Specific Enolase (NSE) immunohistochemistry performed and examined light microscopically. Neurons were divided into three groups according to the amount of cytoplasmic Nissl bodies in hippocampus and Parietal cortex (PC). It was observed that treatment of MgS04 has a protective effect Nissl amount in neurons according to the HI-control group. NSE immunoreactivity was not seen in several neurons of examined brain regions at Hİ-control group. NSE (+) neurons were seen often in the brains of MgS04 treatment group rats. Decreasing of Nissl amount showed a tendency to be less stained by anti-NSE antibody. Hippocampal neurons clearly lost NSE immunoreactivity with the progression of decreasing of Nissl. Anti-NSE immunostaining was lost in the injured areas of the PC while neurons in the intact areas were better stained in brain injury. These results indicate that NSE immunostaining could reflect metabolic reaction of neurons and MgS04 treatment could be useful in neuroprotective in the brain regions after HI damage.

Key words: Hypoxia, magnesium sulfate, Neuron Specific Enolase (NSE), Nissl, rat brain.

P24

Protective effects of posttreatment with linoleic acid: histochemical and Neuron-spesific enolase (NSE) immunohistochemical observations

Yardimoglu M [1], **Yazir Y** [1], Basim B [2], Tugay M [3], Turker G [2], Gokalp AS [2], Dalcik H [1].

Kocaeli University Medical Faculty [1] Department of Histology and Embryology, [2] Department of Pediatrics, [3] Department of Pediatric Surgery, Kocaeli-Turkey.

docdrmelda@yahoo.com

Histopathological processes in cell such as insufficient energy, asidosis, free radicals, i.e after hypoxic ischemia (Hİ) and maintain of these processes after reoxigenation, recirculation play an important role in brain injury. It was reported that LA has a neuroprotective effect. Treatment of perinatal asfixia can only be applied just after asfixa. Therefore, LA was administered to after hypoxia. Unilateral carotid artery was ligated to 11 each rat and they were exposed one hour hypoxia. 30 minutes after hypoxia, LA was given to 1st and 2nd treatment group as 100 nmol/kg and 500 nmol/kg repectively i.p at one dose. Serum physiologic at same dose was injected to HI group. Animals were sacrified in 7th day after HI and brains were removed and sections were performed Nissl staining and Neuron Specific Enolase (NSE) immunohistochemistry. Neurons were examined in the cerebral corteks, hippocampus and thalamus by light microscopy. In these regions, it was observed that nissl amont of neurons were more protected, especially in 2nd treatment group according to HI group. In the HI group, in several regions nissl of neuroplasm was low and it was not seen NSE immunoreactivitiy. Hippokampus was the most affected region from hypoxia and NSE immunoreactivitiy was also poor in treatment groups. In another regions, it was seen that dose of 500 nmol/kg LA has a neuroprotective effects. It was concluded that preventing depolarization by blocing Na and Ca chanels and activating K chanels may cause to more protective effect in the case of LA administration before HI.

Key words: neonate, hypoxic-iscemia, linoleic acid, Neuron Specific Enolse (NSE), rat brain.

P25

Immunohistochemistry of neuron specific enolase (NSE) in the rat brain after single and repeated pentylenetetrazol (PTZ) induced epileptic seizures

Yardimoglu M [1] , Ilbay G [2], Dalcik C [3], Dalcik H [1], Sahin D [2], Ates N [2]**.**

Kocaeli University, Medical Faculty, Department of Histology and Embryology [1], Department of Physiology [2] , Department of Anatomy [3], Kocaeli, Turkey.

docdrmelda@yahoo.com

Neuron specific enolase (NSE) is a sensitive marker of neuronal damage in central nervous system (CNS) diseases including epilepsy. While multiple reports have documented elevation in NSE levels following neuronal injury in various neurologic disorders, limited knowledge is available about localization of NSE in human different brain regions after chemically induced seizures. Changes in NSE localization have not been analyzed clearly in the CNS after epileptic seizures. Therefore, the present work was designed to investigate changes in NSE immunoreactivity in different brain regions after pentylene tetrazol (PTZ) induced acute and chronic epileptic seizures in rats. Male Wistar rats were divided into three groups: 1- single dose of PTZ group; 2-repeated dose of PTZ group; 3-control group. Following PTZ injections, generalized seizures started with the clonus of the facial and the forelimb muscles, and continued with the neck and tail extensions, loss of straightening reflex. Eeach rat was sacrified and removed brains for microscopic examination. Serial paraffin sections (5 µm) were stained with cresyl fast violet (CFV) and NSE immunocytochemistry. The

NSE immunoreactivity was expressed in the neuronal perikarya with dendrites in the control and seizing animals. In thalamus, the number of immunoreactive cells were significantly (p=0.006) increased in PTZ groups compared to the control group. In single dose of PTZ group, the number of NSE (+) neurons increased significantly ($p<0.05$) in hypothalamus compared to the other groups. However, in the repeated-PTZ group, the number of NSE(+) neurons decreased significantly ($p<0.05$) in the hypothalamus compared to the single dose of PTZ group. It was seen a possible correlation between the NSE immunoreactivity and Nissl staining in the neurons of the same brain regions. It was revealed that Nissl staining was less with CFV in repeated dose of PTZ group in these regions compared to the other groups. In conclusion our results indicated that in animal models NSE immunoreactivity is a valuable marker in determining the changes in the number of metabolically active neurons in various brain regions after single and repeated seizures.

Key words: Epileptic seizures; Pentylene tetrazol; Neuron Specific Enolase; Nissl; Rat brain.

P26

Light and electron microscopic examinations in the hippocampus of the rat brain following epileptic seizures

Yardimoglu M [1] , Ilbay G [2], Kokturk S [3], Durmaz Onar F [4], Sahin D [2], Alkan F [3], Dalcik H [1].

Kocaeli University, Medical Faculty, Department of Histology & Embryology [1], Department of Physiology [2] , Kocaeli; Istanbul University, Cerrahpasa Medical Faculty, Department of Histology& Embryology [3], Istanbul, Istanbul University, Istanbul Medical Faculty, Department of Histology & Embryology [4], Istanbul, Turkey.

docdrmelda@yahoo.com

The epilepsy worldwide affects more than 50 million people. Epileptic seizures begin simultaneously and several histopathological changes occur in both cerebral hemispheres. The changes leads to abnormally increased excitability and synchronization, and eventually to the occurrence of spontaneous seizures. Our understanding of the cellular mechanisms underlying epilepsy remains incomplete. Therefore, we aimmed to evaluate hippocampal neurons in the rat brain after pentyleneterazol (PTZ)-induced generalized seizures at microscopically. Male Wistar albino rats were divided into three groups: 1-acute PTZ group; 2-chronic PTZ group; 3-control group. After experimental protocols all rats were sacrified and removed brains and processed. Paraffin sections (5μm) were stained with Toluidin blue and Cresyl fast violet and examined by light microscopy. For electron microscopy (EM), tissues were embedded in Vestopal and sections sections were stained with uranyl acetate. The number of cells was quantified in $765x10^2$ μm^2 fields of hippocampal regions in the X40 objective using a grid for determination of the sampling volume via Cavalieri method and analyzed using the SPSS statistical software package and compared using an ANOVA ($p<0.05$). Ischemic neurons were observed in the PTZ groups, especially in the chronic epileptic animals. Histological changes were perikaryal swelling, chromatolysis and decreasing of Nissl. In EM, necrotic and apoptotic hippocampal neurons were observed in the PTZ groups. EM revealed that a few dying neurons at the CA1 showed an apoptotic morphology as described by Portera-Cailliau et al.(1997). These findings demonstrated a significant decrease in the number of hippocampal neurons (neuronal loss) in the PTZ-induced epileptic rat groups.

Key words: Epileptic seizures, pentylenetetrazol (PTZ), Nissl, electron microscopy, rat brain.

P27

The comparison of calculated and measured osmolality in intracranial hemorrhage and head trauma patients

Acikgoz S [1], Can M [1], Sumbuloglu V [2], Gul S [3], Mungan AG [1], Ataymen M [1].

ZKU Faculty of Medicine Department of Biochemistry [1], ZKU Faculty of Medicine Department of Biostatistics [2], ZKU Faculty of Medicine Department of Neurosurgery [3], Zonguldak, Turkey.

serefdenacikgoz@yahoo.com

Osmolality is defined as the number of particles present in one Kg water. Blood and urine osmolality measurements are used to evaluate electrolyte and acid-base disorders. The main osmolar substances in normal serum are sodium (Na), potasium (K), glucose and urea. Osmolality can be calculated by using concentrations of serum Na, K, glucose and urea or it can be measured directly by freezing point depression with an osmometer. The difference between measured and calculated osmolality is defined as osmolar gap and it can be important to detect the presence of exogenous substances.

We measured serum osmolality of 40 head trauma (HT) and 31 intracranial hemorrhage (IH) patients. The patients were treated at neurosurgical clinic between 01/2004 and 09/2005 years. Direct osmolality measurements were done using Model 3300 Micro-Osmometer (Advanced Instrument). The concentrations of Na, K, glucose and urea were measured with same samples on Integra 800 autoanalyzer (Roche Diagnostic). Calculation of the serum osmolality levels and osmol gap were done with the formulas below (1, 2, 3, 4).

(1) Osm=1,86(Na)+1,86(K)+Glucose+Urea

(2) Osm= 1,86(Na+K)+Urea+1,15(Glucose)+1,2(Ethanol)+14

(3) Osm= 2(Na)+Urea+1,15(Glucose)+1,2(Ethanol)

(4) Osm=1,86(Na)+Urea+Glucose+Ethanol+9

Statistical comparisons between groups were performed by the analysis of variance. Linear regression analysis was used to evaluate the relationship between measured osmolality and calculated osmolality.

Results were given as mOsm/Kg. Equation 1 and 4, equation 2 and 3 gave similar results when compared with each other. Equation 1 and 4 gave similar results with the measured osmolality in IH patients when compared with HT patients where mannitol was not used. Equation 1 and 4 had same bias with the measured osmolality in IH and HT mannitol treated patients. Equation 2 and 3 had higher bias than equation 1 and 4 when compared with measured osmolality and gives falsely high results. In conclusion equation 1 and 4 can be used in IH mannitol untreated patients.

Key words: Osmolality, Osmometer, Osmol gap, Intracranial hemorrhage, Head trauma.

P28

Role of renal nerves on ischemia reperfusion injury

Ozsoy U [1], Sindel M [1], Akbas H [2].

Departments of Anatomy [1], Biochemistry [2], Akdeniz University Faculty of Medicine, 07070 Antalya, Turkey.

ozsoyu@akdeniz.edu.tr

The purpose of this study was to characterize the time course of renal ischemia-reperfusion injury and the role of renal nerves on renal functions in the rat kidney.

Thirty-six male wistar rats were randomized into six groups. All rats underwent right nephrectomy to create a single kidney model. Renal denervated and innervated rats were subjected to renal clamping for 30 min and 60 min. Group I (n=6) only underwent right nephrectomy, group II (n=6) underwent right nephrectomy and left renal ischemia by occlusion of the renal artery for 30 minutes, group III(n=6) underwent right nephrectomy and left renal ischemia by occlusion of the renal artery for 60 minutes, group IV (n=6) only underwent right nephrectomy and left denervation, group V (n=6) underwent right nephrectomy, left denervation and left renal ischemia by occlusion of the renal artery for 30 minutes, group VI (n=6) underwent right nephrectomy, left denervation and left renal ischemia by occlusion of the renal artery for 60 minutes. After reestablishment of blood flow 24-h urine collected from each groups and blood samples were taken for analysis of blood urea nitrogen (BUN), creatinine, sodium, chloride, potassium and nitric oxide.The function of kidney was assessed by glomerular filtration rate (GFR), and fractional excretion of sodium (FENa), following reperfusion (24hr).

The serum creatinine and BUN levels were significantly higher in G-II, G-III, G-V and G-VI when compared with the G-I. There was a significant decrease in GFR in G-III, G-V, and G-VI without significant change in G-II when compared with the G-I. FeNa was over 1 in group V and group G-VI.

Our results indicate that at physiological conditions denervation doesn't affect renal functions but it is worsening the injurious effect of ischemia-reperfusion injury.

Key words: ischemia reperfusion injury, denervation

P29

The macromoleculer oxidation in cerebellum of rat exposed to Mk-801 and the protective effects of cape

Ozyurt B [1], Ozyurt H [2] , Ekici F [3], Erdogan H [3], Sarsilmaz M [4].

Gaziosmanpasa University Faculty of Medicine, Departments of Anatomy [1], Biochemistry [2], Physiology [3],Tokat, Firat University Faculty of Medicine Departments of Anatomy [4], Elazig, Turkey..

birsenozyur05@hotmail.com

The aims of this study are to investigate the contribution effect of oxidative stress in MK-801 induced neurotoxicity, and to show that prevention of oxidative stress may improve prognosis. MK-801 was shown to be one of the most neurotoxic NMDA receptor antagonists.

Wistar Albino rats were divided into three groups: 1. group: MK-801, 2. group: MK-801+CAPE group, 3. group: control group. MK-801 was given intraperitoneally for five days. CAPE was given to the treatment group while exposed MK-801. In control group, saline was given intraperitoneally at the same time. After 7 days, rats were killed by decapitation. Cerebellum was removed biochemical analyses. Malondialdehyde, protein carbonyl, as well as nitric oxide levels as oxidative parameters , levels was found to be increased significantly in cerebellum of MK-801 group compared to control group. In CAPE treated rats, cerebellum tissue malondialdehyde, protein carbonyl, nitric oxide levels were significantly decreased when compared to MK-801 groups. The results of this study revealed that oxidative stress in cerebellum may play an important role in the pathogenesis of MK-801-induced neuronal toxicity. This experimental study also provides some evidences for the protective effects of CAPE on MK-801-induced changes in cerebellum.

Key words: MK-801, CAPE, MDA, PC, NO

P30

Inhibition of Glutathione Reductase By Calcium Chloride

Tandogan B, Ulusu NN.

University of Hacettepe, Faculty of Medicine, Department of Biochemistry, 06100 Ankara, Turkey.

tandogan@hacettepe.edu.tr

Glutathione reductase (GR, type IV, Baker's yeast, EC 1.6.4.2) is a flavoprotein that catalyzes the NADPH-dependent reduction of oxidized glutathione (GSSG) to reduced glutathione (GSH). This enzyme is essential for the GSH redox cycle which maintains sufficient levels of reduced cellular GSH. Glutathione reductase requires NADPH for its activity, and any disruption in the level of NADPH may have a profound effect on this enzyme. Glutathione is essential for the antioxidant system and cellular homeostasis. GSH plays a role in such a number of biological processes as protein synthesis, enzyme catalysis, transmembrane transport, receptor action, intermediary metabolism, and cell maturation. The GSSG/GSH ratio may be a sensitive indicator of oxidative stress. Oxidative stress has been implicated in aging and in the pathogenesis of a number of disorders such as Alzhemier's disease, atherosclerotic vascular degeneration, cataract, lung insufficiencies, Parkinson's disease, and many others. Glutathione reductase deficiency is characterized by hemolysis owing to the increased sensitivity of erytrocytes membranes to H_2O_2. In this study, we have investigated the effects of $CaCl_2$ on the Baker's yeast glutathione reductase. Glutathione reductase activity was determined by spectrophotometric method. Decrease in the absorbance of NADPH at 340 nm was monitored at 37ºC. A unit of activity (U) was defined as the amount of enzyme that catalyses the oxidation of 1 □mol of NADPH in 1 min under these conditions. Inhibiton assay were measured adding at different concentrations of $CaCl_2$ in the assay mixture. Enzyme added to the incubation mixture last. We have established that glutathione reductase is inhibited by $CaCl_2$ concentration dependent manner. Kinetic characterization of the inhibition effects of Ca^{2+} on glutathione reductase was also investigated. The data were analyzed by a nonlinear curve fitting program. It was found that the inhibition was non-competitive with respect to GSSG and uncompetitive with respect to NADPH. Inhibition constants were calculated as Ki_{GSSG} 1,476 ± 0,195 and Ki_{NADPH} 2,993 ± 0,227.

Key words: Glutathione reductase, calcium, inhibition

P31

Protective Effect of EDTA on Glutathione Reductase Inhibition

Tandogan B, Ulusu NN.

University of Hacettepe, Faculty of Medicine, Department of Biochemistry, 06100 Ankara, Turkey.

tandogan@hacettepe.edu.tr

Ethylenediamine tetraacetate (EDTA) is a powerful hexadentate chelating agent. The EDTA is simply binding and removing divalent metals, thereby improving metabolic functioning in a variety of conditions. It binds heavy metal ions that are dissolved in water and provides protection of the enzyme activity. Chelation therapy uses EDTA has been helping people with heavy metal toxicosis, heart disease and many other circulatory diseases for decades. Glutathione reductase (GR, type IV, from Baker's yeast, EC 1.6.4.2) is a crucial antioxidant enzyme which catalyzes the reduction of oxidized glutathione (GSSG) to reduced glutathione (GSH). Glutathione reductase requires NADPH as reducing power, resulting in the reduction of GSSG to GSH and the corresponding oxidation of NADPH to NADP. This enzyme contains flavin adenine dinucleotide and, which is sensitive to riboflavin deficiency. Glutathione is an essential cofactor for antioxidant enzymes and has profound importance for cellular redox balance. The tripeptide thiol glutathione has facile electron-donating capacity, linked to its sulfhydryl (-SH) group. In this study, we have investigated the effects of EDTA on the Baker's yeast glutathione reductase inhibition. Glutathione reductase activity was determined by spectrophotometric method. Decrease in the absorbance of NADPH at 340 nm was monitored at 37ºC. First we have inhibited the enzyme by calcium ion and we have found that this inhibition effect increased according to the increasing calcium concentration. IC50 of glutathione reductase inhibition with $CaCl_2$ was determined as 5mM. We have suggested that EDTA recovers of the GR activity, which was inhibited by $CaCl_2$ In order to determine this protective effect, to the assay mixtures containing 2,5 mM $CaCl_2$, (0- 12 mM) EDTA concentrations were added and the initial velocities were determined. We have found that EDTA recovers the GR activity completely.

Key words: Glutathione reductase, EDTA, calcium, inhibition, IC_{50}

P32

Effects of taurine on young and middle aged rat cerebellum AOPP levels

Yildirim Z. [1], Kilic N. [1], Ozer C [2].

Gazi University Faculty of Medicine, Department of Medical Biochemistry, Ankara, Gazi University Faculty of Medicine, Department of Physiology; Ankara, Turkey.

zyildirim2004@yahoo.com

Aging is a biological status of progressive functional loss and decreasing stress resistance of the organism. It is well known that oxidative reactions increase by age. Taurine is a prooxidant as well as an antioxidant amino acid. In this study, advanced oxidation protein products (AOPP) were measured in order to investigate the effects of taurine on protein oxidation in the cerebellum of young and middle aged rat brain. Twenty 13-14 months middle aged male Wistar albino rats (400±20g) were divided into two groups as middle aged control and middle aged taurine groups.Twenty 6-7 weeks male Wistar albino rats (170±10g) were divided into two groups as young control and young taurine groups. While the rats in the control groups were given 0.5ml of isotonic sodium chloride, the others (taurine groups) were given taurine intraperitonally at a single dose of 200mg/kg/day for 7 days, dissolved in 0.5ml of isotonic sodium chloride. Anestesia with Na-Thiopenthal was performed 24 hours after last injection. AOPP levels were measured by a spectrophotometric method. Statistical analyses were carried out by ANOVA and Mann Whitney U tests. $p<0.05$ was taken as significant. Following the seven days of taurine administration, higher cerebellum AOPP levels were detected than the control groups in both aged groups. However that increase was higher in the young group than the middle aged group.

Key words: Taurine, AOPP, cerebellum, aging, rat

P33

On righ handed and left handed patients with prediagnosos schizophrenia; investigation of dermatoglyphic and cytogenetic analyses Nd evaluation about laterization

Kutlu N [1], Altintas N [2], Arslan E [2], Orenay S [2], Asci M [2], Esen Danaci A [3].

Celal Bayar University Faculty of Medicine, Department of [1] Physiology, Medical Biology and Genetic [2], Psychiatry, [3] Manisa, Turkey.

nkutlu@bayar.edu.tr

Dermatoglyphic were investigated in some illnesses and syndromes, chromosome aberations, cancer and non-chromosomal illnesses. In a polygenic illness like schizophrenia, determinating the differences in finger edge samples , atd angle and sample line number show that dermatoglyphic analysis can be a scaning method which makes the diagnosis. It's thougt that schizophrenia which had 1% prevalance for all live long had a complex inheritance. Dermatoglyphic studies were used in schizophrenia before but now schizophrenia illness is investigated with cytogenetic anh molecular level. While searching genetic studies in schizophrenia although there are a lot of hypothesis, the ethiology and pathophysiology aren't exactly known. Ethiology has a side which is supported strongly and renewly ; this is the genetic component that lays under of it . Dermatoglyphic analysis has an important role for finding a relationship between genetic susceptibility and asymmetric dispersion and to prognose in the first degree relatives of cases. In this study with laterization foresight, it was intended to determinate chromosome abnormalities as polymorphic varient chromosome , inheritance abnormalities and de novo changes , and studying dermatoglyphic print as loop, whorl and arch samples in schizophrenia cases.

Hand Preference ise was determinated by Edinburg poll. Study material was prepared from right handed (R) female (F) (n=38), right handed (R) male (M) (n=18) and left handed (L) male (M) (n=4) patients for dermatoglyphic analysis. Dermatoglyphic samples which are taken from right and left hand were determainated by comparing control groups (n=38RF, n=19RM, 3LM) about whorl, loop and arch samples. The differences between atd angles from palms were determainated by comparing with control groups.

Study material for cytogenetic analysis was determinated from blood. Standart peripheral blood method and Giemsa-Trypsin Banding (GTG) method was applied.. Caryotype analysis was done by determinating 15-20 metaphases for Cytogenetic Nomenclature. In dermatoglyphic study, it was found that the number of finger edge line in left hand II,III and right hand IV,V were increased in patients by comparing control groups ($p<0.05$). However, in female schizophrenia patients left hand II,III,IV and right hand I,V finger edge line numbers were increased in male patients left hand I,III,IV and right hand II finger edge line numbers had a meaningful increase by comparing control groups ($p<0.05$). Increases in atd angles of the palms were seen. 25 schizophrenia cases who had cytogenetic analysis, it's found that one of the female patients had 45,X caryotype in 6 metaphases, the other one had 46,X,fra(X) in 2 metaphases and rest of them had normal caryotypes.

We thought that ; dermal samples in schizophrenia patients have important differences from the control group and also thought that results can be ethiologically useful. Cytogenetic analyse and differences in dermal samples between right handed and left handed people can be seen with the increasing the number of the patients and so that laterizationally estimation can be meanfull.

Key words: Dermatoglgyphics, handeded, schizophrenia, laterization, chromosome cytogenetic analysis

P34

Association between extracellular metalloproteinase-3 polymorphism and migraine disease

Orhan N [1], Ozkok E [1], Aydin M [1], Cetinkaya Y [2], Gencer M [2], Tireli H [2], Kara I [1].

Department of Neuroscience, Istanbul University Institute of Experimental Medicine [1], Neurology Clinic of Haydarpasa Numune Hospital [2], Istanbul, Turkey.

norhan@istanbul.edu.tr

Migraine that affects %12 of general population can be characterized chronic neurovascular disorder. Recent studies have suggested that there is relationship between extracellular metalloproteinase (MMP) and neurodegenerative diseases. MMP-3 is one the member of the MMP family. In the present study, we investigated the possible relationship between the polymorphism of 5A6A promoter region of MMP-3 gene and migraine disease. This study was carried out in 149 patients who applied to Neurology Clinic of Haydarpasa Numune Hospital and 86 age-matched healthy controls. DNA was isolated from blood containing EDTA by salting out method. This polymorphic DNA region was amplified by polymerase chain reaction (PCR) using the primers designed for 5A6A. The amplified PCR products were digested by appropriate restriction enzyme. Under UV light the genotypes were read on agarose stained with ethidium bromide by independent individuals. The genotype analyses were performed with the use of Pearson's chi-square test. Although there were not significant differences in 6A6A and 5A6A genotype frequencies, the frequencies of 5A5A genotypes were significantly higher in patients when compared to healthy controls ($p<0.05$). While the distributions of genotypes in patients with migraine were detected 6A6A %42.3, 5A6A %32.9 and 5A5A %24.8, distributions in controls were 6A6A %46.5, 5A6A %43 and 5A5A %10.5. Our findings have suggested that there is relationship between MMP-3 polymorphism and migraine disease.

Key words: Migraine, MMP-3, polymorphism, promoter, PCR

P35

Demyelination in subacute sclerosing panencephalitis (SSPE): an experimental study

Beken S, Talim B, Kale G , Anlar B.

Hacettepe University, Faculty of Medicine Department of Pediatrics, Ankara, Turkey.

serbeken@yahoo.com

Subacute sclerosing panencephalitis (SSPE) is a chronic disease caused by measles virus. Approximately 50-80 new cases per year are reported in Turkey: this number is higher than the classically known figure of 1/100000 measles cases. Demyelination occurs in the course of SSPE: the pathogenesis is unknown. Demyelination can be caused by inflammatory cells, endogenous or exogenous toxins, antibody- or complement-mediated myelin breakdown. In this study the presence of demyelinating soluble substances (cytokine, antibody, complement...) in the cerebrospinal fluid of SSPE patiens was investigated experimetnally by injeciton of CSF samples from patients into mice. Adult swiss albino mice received an intraperitoneal injection of 0,5 ml CSF for two consecutive days. Groups were: SSPE (n=3) control (n=3, control CSF, metabolic disease). To disrupt the blood brain barrier, 10 ng pertussis toxin (PT) was given intraperitoneally before the CSF injections. In addition 2 mice received only PT. Totally 14 mice were follwed-up for 6 days (n=7), or 21 days (n=7). Daily examinations were done for tail tone, gait, and paralysis. After the follow-up period, the brain and sciatic nerves were studied histopathologically (hematoxylene-eosine and luxol-fast blue) for peripheral or central demyelination.

None of the mice developed clinical signs during follow-up. On histopathological examination sciatic nerves revealed no difference in morphology, myelin thickness, myelin morphology between groups. There was no difference in ventricle width, cortex thickness, grey and white matter thickness, myelin morphology in brains either.

In this study we found no evidence that the CSF in SSPE patients' contained substances causing demyelination. Demyelination in SSPE may be caused by oligodendrocyte death in progressive disease rather than myelin degradation.

Key words: SSPE, measles, demyelination, oligodendrocyte, histopathology

P36

Distinct morphological and immunohistochemical features in Schwannomas: report of a case with osseous metaplasia

Bektas S [1], Bahadir B [1], Colak S [1], Gun Dogan B [1], Acikgoz B [2], Ozdamar SO [1].

Karaelmas University, Faculty of Medicine, Department of Pathology [1], Neurosurgery [2], Zonguldak, Turkey.

sbektas@mynet.com

Schwannoma is a benign nerve sheath tumor that may be encountered at all age groups and has a predilection for the head, neck and flexor surfaces of the upper and lower extremities.

The sections from a thoracolomber mass of a 50-year-old male patient with pain in his left leg for a month, revealed focal osseous metaplasia occasionally detected in schwannomas. Accordingly, histomorphological and immunohistochemical features of nine previously diagnosed cases of schwannoma between 2002-2005 were considered to be worth presenting.

All the slides diagnosed in the Department of Pathology of Zonguldak Karaelmas University Faculty of Medicine, were retrospectively rewieved on histomorphological grounds, and reactivity for S-100 protein, vimentin, glial fibrillary acidic protein ve epithelial membran antigen were investigated.

Histomorphologically, two ancient schwannomas with intensive degenarative changes, one plexiform schwannoma, and six ordinary schwannomas were observed. Encapsulation, and cellular Antoni A and hypocellular Antoni B areas were consistently present in all cases. The case with osseous metaplasia and a surrounding hyalinized zone demonstrated an ordinary schwannoma with additional areas of epithelioid appearence; moreover this was the unique case reactive for glial fibrillary acidic protein. The mitotic counts for all cases were three or less per 10 high power fields. All cases were positive for S-100 protein and vimentin whereas no reaction with epithelial membran antigen was noted.

Schwannoma is benign nerve sheath tumor with occasional malignant transformation. Osseous metaplasia is usually determined in malignant peripheral nerve sheath tumor; only a few cases of schwannoma with osseous metaplasia were reported. In this study of nine schwannomas including two ancient schwannomas, one plexiform schwannoma and six ordinary schwannomas, an ordinary schwannoma demonstrating both focal osseous metaplasia and glial fibrillary acidic protein expression was observed. From our point of wiev, because of distintive features in addition to its ordinary cellular composition the current case is among the peripheric nerve sheath lesions requiring long term follow-up.

Key words: Schwannoma, osseous metaplasia, glial fibrillary acidic protein

P37

The nervous system tumors between 2002-2006 in the department of Pathology in Zonguldak Karaelmas University Faculty of Medicine

Dogan Gun B, Bahadir B, Numanoglu G, Mocan Kuzey G, Acikgoz B, Ozdamar SO.

Zonguldak Karaelmas University, Faculty of Medicine, Department of Pathology, Zonguldak, Turkey.

banudogangun@yahoo.com

In this study central and peripheral nervous system tumors from January 2002 to February 2006 have been reviewed in the Pathology Department of Zonguldak Karaelmas University, Faculty of Medicine and the number as well as the ratio of the tumors, the distribution of age and sex, the locations, biological behaviors and histological types were determined.

In the five years period, excluding cytological material, total number of the biopsy and operation specimens was 13511 and nervous system tumors was 69 (0.51%). When grouped as to their biological behavior 55% (38) was benign, 43.5% (30) was malignant and 1.5% (1) was borderline.

Of the all nervous system tumors, the percentages of central and peripheral nervous system tumors was 78.3% (54) and 21.7% (15), subsequently. The female population was 40.8% (22), male population was 59.2% (32) in all central nervous system tumors. The minimum age was 11 months, maximum age was 76 years with an average of 45.81. The number of malignant, benign and borderline tumors of 54 cases was 30 (55.6%), 23 (42.6%) and 1 (1.8%), consequently. Males constituted 66.7%, females constituted 33.3% of all malign central nervous system tumors. The most frequent location was cerebrum (57.4%), followed by pituitary, cerebellum, spinal cord, posterior fossa and pontocerebellar region. Between the primary brain tumors, the distribution of histological types was astrocytoma (26.7%), pituitary adenoma (22.2%), meningioma (17.8%) and other tumors (33.3%). The proportion of metastatic tumors was 16.7% (9/54) in all central nervous tumors. And the proportion of childhood central nervous system tumors was 7.4%, the most frequently seen histological type was medulloblastom (50%).

When peripheral nervous system tumors were evaluated 80% (12) of them was male, %20 (3) of them female, average of age was 40.4 (range 7-73). All of the cases were benign and histopathological diagnosis were as neuroma (46.6%), schwannoma (26.7%) and neurofibroma (26.7%).

In this study, diagnostic and epidemiologic data of nervous system tumors have been determined and constituting systematic and continuous data transfer from Zonguldak Karaelmas University Pathology Department, which represents the Western of Black-Sea population was aimed.

Key words: Nervous system, central nervous system, peripheric nervous system, epidemiology

P38

Choroid plexus carcinoma: differential diagnosis in central nervous system papillary tumors

Numanoglu G [1], Gun B [1], Bahadir B [1], Sonmez A [1], Acikgoz B [2], Kalayci M [2], Ozdamar SO [1].

Zonguldak Karaelmas University Faculty of Medicine Department of Pathology [1], Neurosurgery [2] Zonguldak, Turkey.

gamzenu@yahoo.com

Choroid plexus carcinoma which is a rare malign tumor of central nervous system is more frequent in infants compared to adults. These tumors constitue 20-30% of the primary choroid plexus tumors and are more frequently situate in the lateral ventricle. In contrast to choroid plexus papilloma, choroids plexus carcinoma is invasive and involves areas of necrosis and hemorrhage.

Our case is a 4 year old girl who was admitted to university hospital presented with headache, stupor and lethargy. In cranial computerized tomography, a solid tumor with cystic areas was detected in right temporoparietal lob and the patient was operated. Histopathologically the tumor cells were composed of branching papillary structures surrounding a fibrovascular core and infiltrate in brain parenchyma. Large areas of necrosis was detected within the tumor. High mitotic activity was also present. Tumor were not showed to react with mucicarmen, but diffuse reaction for S-100 and focal positive reaction for GFAP, pankeratin (Clone AE1/AE3) and CK7 were observed. Finally, the tumor was diagnosed as choroid plexus carcinoma.

This case is presented here, because of its rarity and importance in differential diagnosis of papillary tumors of central nervous system.

Key words: Choroid plexus carcinoma, immunohistochemistry, central nervous system, glial tumor, brain metastase

P39

Traumatic neuromas: a histopathologic and immunohistochemical study

Ozdamar SO, Dogan Gun B, Barut F, Bahadir B.

Zonguldak Karaelmas University, Faculty of Medicine, Department of Pathology, Zonguldak, Turkey.

banudogangun@yahoo.com

Traumatic neuroma is an exuberant, probable non-neoplastic proliferation of a nerve occurring in response to injury or surgery. Under ideal circumstances the ends of a severely injured nerve reestablishes continuity by an orderly growth of axons from proximal to distal stump through tubes of proliferating Schwann cells. However if close apposition of the ends of the nerve is not maintained, a disorganized proliferation of the proximal nerve gives rise to a neuroma lesion.

We studied six cases of traumatic neuroma by light microscopic, histochemical and immunohistochemical methods to assess the cellular compositions of these lesions. Sections from the formalin-fixed parafin-embedded tissues were stained with hematoxylin-eosin, Gomori's trichrome, Verhoeff elastica-von Gieson, reticuline, and S–100 protein, Epithelial Membrane Antigen, CD34 and CD68. All cases revealed large numbers of small and haphazardly arranged regenerating nerve fascicles within a densely collagenous and fibroblastic stroma. A focal chronic mononuclear cell inflammatory reaction was seen in three of the cases. In all of the cases, Gomori's trichrome revealed

collagen. Axonal morphology was detected in nerve fibers, histochemically by reticulin. In all the cases, fascicles were stained diffusely with S–100 protein, and Epithelial Membrane Antigen showed a positive reaction in a thin band of cells surrounding the fascicles in three of the cases. CD34 positive cells were present in five cases. Only in two of the specimens the cells contained positive cells with CD68.

In traumatic neuromas specifically staining of fascicles with S–100 protein, perineural cells reactive for Epithelial Membrane Antigen and also CD34 positive cells probable of endoneural fibroblasts origin might help to understand their pathogenesis and would provide to differentiate these lesions from the mimickers.

Key words: Traumatic neuroma, Schwann cell, perineural cell, histochemistry, immunohistochemistry

P40

An experimental invastigation of the histological effects of epidural hematomas on cerebral parenchima in early and late period.

Balikci M [1], Koc K [1], **Yazir Y** [2], Anik I [1], Ceylan S [2], Ceylan S [1].

University of Kocaeli, School of Medicine, Department of Neurosurgery, [2] Department of Histology and Embriyology, Kocaeli, Turkey.

yusufhanyazir@yahoo.com

Even the developments in the treatment and diagnosis of epidural hematomas, traumatic epidural heamatomas are one of the important causes of mortality and morbidity especially in young population. In the recent years, the number of the litreture suggesting conservative management has been increasing.The experimental studies that have been performed are based on especially about the effects of epidural heamatomas. The purpose of this study is to determine the effects of epidural heamatomas histologically those had not increased CPP and not caused brain shift.

This experimental study has been performed in 3 experimental groups. In the first group (control) 10 rats to which EDH has not been performed. In the second and third group: EDH has been performed via administrating 0,1 ml autolog blood to each 10 rats. Histological observation has been done by sacrifing the second group after 6 hours (early period) and 21 days (late period) in the third group.

Results of the study demonstrated neuronal distortion, oedema and eosinophilia in the paranchyma neighbouring the heamatoma in the second group, histologically. It is found out that these changes have been recovered in the third group.

In our experimental study epidural heamatoma that did not cause shift and without cerebral perfusion decrease was performed via 0.1 ml enjection of autolog blood. The finding of the oxidative stress and cell destruction that was seen in the parenchyma beneath the heamatoma in early period was not continued in the late period revealed the conclusion of that conservative approach does not cause pathophsyological process of the brain parenchyma.

Key words: Epidural hematoma, brain, cerebral cortex, histology, rats.

P41

The effects of levetiracetam on mouse hippocampal electrical field responses and LTP

Aksoz E, Sara Y, Onur R.

Hacettepe University Faculty of Medicine Department of Pharmacology Sihhiye, Ankara, Turkey.

eaksoz@hacettepe.edu.tr

Levetiracetam is a novel antiepileptic drug and its mechanism of action is still remains to be determined. Suggested mechanisms are high voltage-activated Ca^{2+} channel inhibition, SV2A synaptic vesicule binding and indirect $GABA_A$ channel activation. In order to evaluate the contribution of these mechanisms to its antiepileptic action, we investigated the effects of levetiracetam on synaptic transmission in mouse hippocampus, *in vivo*. Electrical field responses were induced by fimbria-commissure stimulation and were recorded from CA1 region. Alterations in presynaptic release was assessed by paired pulse facilitation (PPF) and excitatory postsynaptic potential slopes. GABAergic activity evaluated by PPF. Population spike amplitudes and synaptic input-output curves were used as a measure of neuronal excitability. Long term potentiation (LTP) was studied to determine the changes in long term synaptic plasticity. Levetiracetam (10-100 mg/kg i.p.) did not change presynaptic release, excitability, GABAergic activity and LTP induction. These results indicate that single dose of levetiracetam has no effects on Ca^{2+} channels and GABAergic system and does not alter hippocampal neuronal activity in mice.

Key words: Hippocampus, Levetiracetam, LTP, Synapse, Epilepsy

P42

The effect of enriched environment on reference memory performance in aged rats

Ugur E, Yamanturk-Celik P

Istanbul University, Istanbul Faculty of Medicine, Department of Pharmacology and Clinical Pharmacology, 34390, Capa, Istanbul, Turkey.

ugurelif1304@yahoo.com

Enriched environment, leads morphologic and functional changes in neurons and improves learning-memory functions in animals. In this study, we investigated the effect of enriched environment on memory performance in aged rats. For this purpose, male aged Wistar Albino rats (26 months) have been taken impoverished (IE) or enriched environment (EE) for two months and at the end of this period their reference memory performance was assesed in three-panel runway test. Both groups were observed in open-field before memory test procedure to investigate if there is any change in locomotor activity, exploration and emotional state of animals which may affect their memory performance. In open-field test, numbers of square crossing, rearing, head-dipping and defecation were recorded within 5 minutes. For reference memory performance in three-panel runway test experimental groups were taken a food deprivation schedule and during training period the time required for the animals to obtain food pellets (latency) and the number of errors were recorded. Habituation and training process took 14 days totally for three-panel runway test. Statistical analysis was performed using Mann-Whitney *U*-test for open-field and Student's *t*-test for three-panel runway results. There was no any significant difference in both groups for square crossing, rearing, head dipping, and defecation in the open-field test. Latency and number of errors decreased in EE group compared to the IE group. It seems that EE does not change locomotor activity, exploration, emotional state while it improves memory performance in aged rats.

Key words: aging, enriched environment, reference memory, open-field, three-panel runway, rats

P43

The effect of postnatal monosodium glutamate toxicity on forced swim test in rats

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

Yeditepe University, Faculty of Medicine, Department of Psychiatry, 34755, Kayisdagi, Istanbul, Turkey [1], Istanbul University, Istanbul Faculty of Medicine, Department of Pharmacology and Clinical Pharmacology, 34390, Capa, Istanbul, Turkey [2].

beken@yeditepe.edu.tr

It has been reported that drugs related with glutamatergic system make changes in behavioural response pattern in experimental models and there are interactions with the hypothalamo-pituitary-adrenal axis (HPA) and glutamatergic system. Present study attempts to investigate the effect of glutamatergic system toxicity induced by postnatal monosodium glutamate (MSG) on widely used depression model forced swim test in male Wistar Albino rats. For this purpose, glutamatergic system toxicity was induced by subcutaneous injections of MSG at the dose of 4 mg/g body weight on postnatal days 2, 4, 6, 8, and 10. The control group received subcutaneous injections of saline solution (0.9 % NaCl) at the same time as the experimental group. Rats were exposed to the forced swim test at four months of age. Both groups were observed in open-field test to evaluate if there is any change or not in locomotor activity, exploratory behaviour, emotional state that may affect the response of forced swim test. Immediately after forced swim test, cardiac blood samples were collected under ether anesthesia for plasma corticosterone measurement. In open-field test the observed parameters were number of square crossing, rearing, head-dipping and defecation

within 5 minutes. Immobility time and number of diving were measured for 5 minutes in forced swim test. Data were statistically analyzed using the Mann-Whitney *U* test for open-field and Student's *t* test for forced swim test and plasma corticosterone levels. Number of square crossing increased in MSG-treated group compared to the control group while no significant differences were observed between two groups in number of rearing, head-dipping and defecation. In forced swim test, immobility time decreased in MSG-treated group compared to the control group while number of diving was not different between two groups. Plasma corticosterone levels were found higher in MSG-treated group than control group. These findings may indicate crucial role of glutamatergic system development in behavioural and stress responses in rats.

Key words: Monosodium glutamate, postnatal toxicity, open-field, forced swim, rats

P44

Effects of omeprazole in caffeine and phentylenetetrazole-induced convulsion models in mice

Ozbakis-Dengiz G [1], Halici Z[1], Bakirci A[2]

Ataturk University, Medical Faculty, Pharmacology Department, Erzurum -Turkey [1], 100. Yil University, Medical Faculty, Infection Diseases and Clinical Microbiology Department, Van, Turkey [2].

gunnurozbakis@mynet.com

Omeprazole is an antiulcerogenic drug for treating peptic ulcer, and is inhibiting both H+-K+ ATPase enzyme and carbonic anhydrase enzyme in the gastric mucoza. In our study, since omeprazole has a carbonic anhydrase inhibitor activity, we wanted to evaluate whether omeprazole has protected on caffeine and phentylenetetrazole (PTZ)-induced generalise seizures in the mice, and whether the tolerance has developed upon continued administration of omeprazole. In the first step of the study, animals used in this study were separated at control (distilled water), diazepam and omeprazole groups. Omeprazole, diazepam and distilled water were administrated intraperitoneally (ip), 30 minutes before PTZ (100 mg/kg, ip) or caffeine (300 mg/kg, ip) injections. Following the caffeine or PTZ injections, animals were observed for 30 minutes, and the time taken for the onset of the animals' first generalize colvulsive attacks was measured as second, and was accepted as a latency period. In the second step of the study, tolerance study was done. The most effective anticonvulsant dose of omeprazole, in the first step of the study, had been determined as 0.5 mg/kg in caffein model, and was administrated once for following 6 days in the same model. On the following days, six mice were distinguished from the group on each day, and omeprazole was injected 30 minutes prior to caffeine injections (300 mg/kg). The latency periods were also measured. In the first step in the study, compared to own control groups, while omeprazole dose dependently prolonged the latency periods in the PTZ model, at low doses (0.25 - 0.50 mg/kg) prolonged the latency periods in the caffeine model ($p < 0.05$). Omeprazole had showed more effective in caffeine model than in PTZ model and presented the most protective effect at 0.5 mg/kg dose (prolongation in latency period, 307.47 %) in caffeine model. At second step, in the tolerance study, latency periods were shortened by omeprazole on the following days. In conclusion, single dose administration of omeprazole showed the protective effect on both caffeine- and PTZ-induced seizures and it was more effective in especially caffeine model at low doses. Its effect may be through by inhibiting of carbonic anhydrase enzyme, or by vasodilating on the cerebral vessels like the other CA inhibitors, or by decreasing the intracranial pressure via blocking the K+, H+-ATPase enzyme. In repeated doses administrations of omeprazole, tolerance developed against its anti-convulsant action like the other carbonic anhydrase inhibitor drugs.

Key words: Omeprazole, caffeine, PTZ, convulsion, carbonic anhydrase inhibitors.

P45

The investigation of behavioral changes and effects of naloxone in 24 h food-deprived rats

Firtina M, Hatipoglu I, Enginar N.

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

izzetmeftun@yahoo.com

It was shown that exposure to 24 h food deprivation gave rise to analgesia in rats. This effect was antagonized by naloxone and was greatly reduced after five exposures to periods of 24 h food deprivation, indicating the development of tolerance. Depending on these findings, food deprivation was suggested to increase pain threshold by inducing an activation in opioidergic system. As opioidergic system has also effects on behaviors in animals, behavioral differences may also occur after exposure to food deprivation. Thus, the behavioral effects of food deprivation and naloxone were investigated in 24 h food-deprived rats with the measurements of anxiety, exploratory activity and behavioral despair. In the study, Wistar albino male rats were used. After a 15 min pretest session for the forced swimming test, the animals were assigned to two groups as fed (free access to food) and fasted (24 h food deprived). On the day of experiments, fed and fasted animals were treated (i.p.) with saline or 10 mg/kg naloxone. Following treatments, animals were individually placed in wire mesh cages for the novelty-induced grooming. Total time spent by scratching body and face and licking body fur, tail, limbs and genital area was determined for 20 min. Then exploratory activity was recorded in an exploration cage by counting number of squares crossed, head dippings and rearings for 5 min. Finally, the total duration of immobility was measured during a 5 min forced swimming test. Grooming and immobility were analysed using Student's *t*-test. Exploratory activity was evaluated with Mann-Whitney U test. Compared with fed rats, number of head dippings was higher in fasted rats ($p=0.05$), but changes in number of squares crossed, number of rearings and time spent in grooming were not significant. There was also no difference in the duration of immobility between fed and fasted rats. Naloxone reduced number of rearings in fasted rats ($p<0.05$) and time spent in grooming in fed ($p<0.01$) and fasted ($p<0.01$) rats, but had no effect on square crossing, head dipping and duration of immobility in both groups. Present results show that exposure to 24 h food deprivation did not alter measures of anxiety and behavioral despair in rats. But, possibly reflecting the food seeking behavior of the animal, it caused an increase in the exploratory activity. The antagonizing effect of naloxone implies the contribution of an opioidergic activation in this effect. On the other hand, the reduction in grooming caused by naloxone in both fed and fasted rats supports the previous findings indicating the contribution of opiodergic system to novelty-induced anxiety.

Key words: food deprivation, naloxone, novelty, grooming, exploratory activity, forced swimming test, rat

P46

The effects of intracerebroventricular injection of NMDA to genetic absence epilepsy rat model on cardiovascular system

Gulcebi M, Alsen S, Aker R, Onat F.

Marmara University, School Of Medicine, Pharmacology and Clinical Pharmacology Department, Istanbul, Turkey.

mgfarma@yahoo.com

Glutamate is an excitatory neurotransmitter widely found in central nervous system. Glutamate and glutamate receptors are placed in the areas that are especially involved in the central control of blood pressure and heart rate. The receptors of glutamate are classified as ionotropic and metabotropic. Ionotropic subtypes are NMDA, kainate and AMPA. Epilepsy leads to changes on blood pressure, heart rate, respiratory system, vasomotor activity, gastrointestinal motility and sphincter tonus by affecting autonomic functions. In this study, in order to understand the roles of glutamatergic NMDA receptors, the effects of intracerebrovascular (i.c.v.) NMDA on cardiovascular system by measuring blood pressure and mean arterial pressure of the rats which are genetic models of absence epilepsy were investigated. GAERS (Genetic Absence Epilepsy Rats from Strasbourg) as a model of genetic absence epilepsy and Wistar rats as a control group were used. Guide cannula was stereotaxically unilaterally implanted to the lateral ventricle so as to inject artificial cerebrospinal fluid (aCSF) and NMDA. After a recovery period of 3-5 days, polietilen catheter was placed into iliac artery for measurement of blood pressure and heart rate. aCSF and NMDA (1 nmol) were injected to both groups at the same time and mean arterial pressure and heart rate were calculated. Administration of NMDA increased blood pressure and heart rate in both groups. There was no difference observed between two groups. Previously, a significant increase in the i.c.v. and parenchimal injections of biccuculine, $GABA_A$ receptor antagonist, in epileptic rats has been shown. So, GABA- and NMDA- mediated trans-

mission are thought to have different roles in the regulation of cardiovascular system in epileptic and non-epileptic rats. In order to understand the roles of non-NMDA receptors, icv injections of non-NMDA receptor agonists and i.c.v. and parenchimal injections of NMDA and non-NMDA receptor agonists into the dorsomedial hypothalamus which has a pivotal role in cardiovascular regulation are being planned.

Key words: glutamate, NMDA, GAERS, blood pressure, heart rate

P47

Anoxia-induced dopamine release from rat striatal slices: Involvement of glutamate release and glutamate receptors.

Gursoy M, Buyukuysal 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 against anoxia and similar conditions. With other possible mechanisms, enhanced dopamine release under these conditions is believed to contribute to resultant tissue damage. We have previously shown that reversal of dopamine uptake carrier is a significant contributor to anoxia-induced dopamine release from rat striatal slices (Buyukuysal and Mete, J. Neurochem., 72, 1507-1515, 1999). In this study we aimed whether glutamate release and/or glutamate receptors are involved in anoxia-induced dopamine release. 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 at10 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 and glutamate released from the slices were measured with high pressure liquid chromatography systems without purification. While 60 min of anoxia caused almost 100 times increase in dopamine release, DOPAC output under this condition was determined to be declined by 50%. Involvement of glutamate in anoxia-induced dopamine release was tested by measuring glutamate release and by adding the glutamate receptor antagonists into the medium. In contrast to dopamine release, anoxia failed in enhancing the glutamate release from the slices. While MK-801 and CNQX, which block the NMDA and kainat/AMPA receptors, respectively, caused partial inhibition, sigma receptor antagonists ifenprodil and haloperidol almost completely protected the slices against anoxia-induced dopamine release. These results clearly indicate that, 1) anoxia causes a great increase in dopamine release, b) this increase seems to be related with enhanced glutamate receptor activity rather than enhanced glutamate output and 3) sigma binding sites on glutamate receptor complex might preferentially involved in anoxia induced glutamate receptor activation.

Key words: Anoxia, dopamine release, glutamate receptors.

P48

Oxidized low-density lipoprotein accumulated in rat brain tissue after mesenteric ischemia-reperfusion

Isikdemir F [1], Sipahi YE [1], Tekin OI [2], Acikgoz S [3], Numanoglu G [4], Comert M [5], Alkan C [6].

Departments of Pharmacology [1], Immunology [2], Biochemistry [3], Pathology [4] and General Surgery [5], Medical student [6], Faculty of Medicine, Karaelmas University, Zonguldak, Turkey.

drfulden@mynet.com

Intestinal ischemia/reperfusion is a serious disorder that is prevalent in elderly patients and has been shown to be associated with multiple organ damages. Oxygen-derived free radicals have been implicated as possible mediators in the development of tissue injury induced by ischemia and reperfusion. Furthermore, lipid peroxidation mediated by free radicals is believed to be one of the important causes of cell membrane destruction and cell damage. The aim of this study was to evaluate the possible participation of the oxidative modification of low density lipoproteins in brain damage induced by experimental mesenteric ischemia-reperfusion in rat. Rats underwent 30 min of superior mesenteric artery occlusion followed by 24 h of reperfusion. Oxidized low-density lipoprotein, malondialdehyde level, superoxide dismutase activity and inducible nitric oxide synthase expression in brain tissue were evaluated. While there was no staining in the control group, ischemia/reperfusion resulted in positive oxidized low-density lipoprotein staining in brain tissue. Compared with control rats, ischemia-reperfusion group showed significantly higher malondialdehyde level and lower superoxide dismutase activity. There were no significant differences for inducible nitric oxide synthase expression. This study demonstrated for the first time that oxidized low-density lipoprotein accumulates in intact rat brain tissue after local extracranial ischemia and reperfusion. This may be an important indicator of ongoing oxidative stress and enhanced lipid peroxidation in the brain after mesenteric ischemia-reperfusion.

Key words: Brain damage; intestinal ischemia-reperfusion; lipid peroxidation; oxidative stress; oxidized low density lipoproteins

P49

Prophylactic effect of nilvadipine on biochemical and behavioral changes induced by repeated 4-vessel occlusion ischemia in rats

Kaya E [1], Yilmaz E [1], Bolukbasi Hatip F [1], Sert S [2], Demir S [2], Hatip I [1].

Pamukkale University, Faculty of Medicine, Departments of [1] Pharmacology and [2] Biochemistry, Denizli, Turkey.

drekaya@yahoo.com

Nilvadipine is a dihydropyridine derivative antihypertensive drug with emanating neuroprotective properties. Repeated 4-vessel occlusion ischemia induces memory impairment and selective hippocampal degenerative changes. This study aimed at investigating the prophylactic effect of nilvadipine on memory impairment and biochemical changes caused by 4-vessel occlusion (4-VO) ischemia in rats.

In this study, the vertebral arteries were cauterized, and the bilateral common carotid arteries were twice occluded for 10 min at 60 min interval. At the end of the study, the rats were decapitated and the hippocampus was dissected out. The memory was evaluated by measuring the correct and error choices in 8-armed radial maze. The ischemia-reperfusion-induced damage was evaluated by measuring level of malondialdehyde (MDA) in the hippocampus using thiobarbituric acid method.

The study included three groups: 1; Sham (n=8), 2; ischemia-control (n=7), 3; nilvadipine-ischemia (3,2 mg/kg/day i.p.) before ischemia for seven days (n=7). The rats were decapitated at the end of the experiments, and the level of MDA in hippocampus.

Ischemia impaired memory performance by decreasing the correct choices and increasing the error choices ($p<0,001$). Nilvadipine improved the performance by increasing the correct choices ($P<0.002$) and decreasing the error choices ($P<0.05$). On the other hand, ischemia elevated MDA level ($P<0.001$), whereas nilvadipine decreased the elevated MDA ($P<0.001$).

In conclusion, prophylactic treatment with nilvadipine improves memory impairment and decreases MDA increment caused by 4-VO in rats.

Key words: Ischemia, maze, nilvadipine, memory, malondialdehyde

P50

Prophylactic effect of minocycline on biochemical and behavioral changes induced by repeated 4-vessel occlusion ischemia in rats

Kaya E [1], Yilmaz E [1], Bolukbasi Hatip F [1], Sert S [2], Demir S [2], Hatip I [1].

Pamukkale University, Faculty of Medicine, Departments of [1] Pharmacology and [2] Biochemistry, Denizli, Turkey.

drekaya@yahoo.com

Minocycline is a second generation tetracycline that has high lipophilic property. Recently, it has been found that, this drug could provide neuroprotection in animal models of global brain ischemia and other neurological disorders. Repeated 4-vessel occlusion ischemia induces memory impairment and selective hippocampal degenerative changes. This study aimed at investigating the prophylactic effect of minocycline on

memory impairment and biochemical changes caused by 4-vessel occlusion (4-VO) ischemia in rats.

In this study, we used Wistar male rats (n=22) weighing 230-280 g. For 4-VO ischemia induction, the vertebral arteries were cauterized, and the common carotid arteries were twice occluded bilaterally for 10 minute at 60 minute interval. At the end of the experiments, the rats were decapitated and the hippocampus was dissected out. The memory was evaluated by measuring the correct and error choices in 8-armed radial maze. The ischemia-reperfusion-induced damage was evaluated by measuring level of malondialdehyde (MDA) in the hippocampus using thiobarbituric acid method.

The study included three groups: 1; Sham (n=8), 2; ischemia-control (n=7), 3; minocycline-ischemia (45 mg/kg/day i.p.) before ischemia for seven days (n=7). The rats were decapitated at the end of the experiments, and the level of MDA in hippocampus.

Ischemia impaired memory performance by decreasing the correct choices and increasing the error choices ($p<0,001$). Minocycline improved the performance by increasing the correct choices ($P<0.001$) and decreasing the error choices ($P<0.04$). On the other hand, ischemia elevated MDA level ($P<0.001$), whereas minocycline decreased the elevated MDA ($P<0.001$).

In conclusion, prophylactic treatment with minocycline improves memory impairment and decreases hippocampal MDA increment caused by 4-VO in rats.

Key words: Ischemia, maze, nilvadipine, memory, malondialdehyde

P51

Effect of erythropoietin on memory impairment and hippocampal malondialdehyde in rats with repeated ischemia

Yilmaz E [1], Kaya E [1], Bolukbasi-Hatip F [1], Sert S [2], Demir S [2], Hatip I [1].

Pamukkale University, Faculty of Medicine, Departments of [1] Pharmacology and [2] Biochemistry, Denizli, Turkey.

efdikbas@yahoo.com

Erythropoietin (Epo) is a peptide derivative being used in treatment of anemia in dialysis patients. Plethora of new studies reveal the neuroprotective activity of Epo.

Of the ischemia models 4-vessel occlusion , that is known to induce hippocampal neurodegeneration and impaired memory, is used in this study. In this study, the correct (CC) and error choices (EC) of rats, that reflect memory, were recorded in 8-armed radial maze test. 4-VO ischemia was induced by cauterization of the vertebral arteries and bilaterally occluding the carrotid arteries twice for 10 min repeated at 60 min interval.

The study included four groups: 1. Sham (n=8), 2. Control-ischemia (n=7), 3. Epo-1; ischemia –Epo (20 U/kg i.p.) after one h (n=7), and 4. Epo-6; ischemia-Epo (20 U/kg I.P.) after 6 h, (n=7). The rats were decapitated at the end of the experiments, and the level of malondialdehyde (MDA) in hippocampus (HC) was measured by thiobarbituric acid method.

The results showed that 4-VO decreased CC ($P<0.0002$) whereas increased the EC ($P<0.001$). Epo-1 and Epo-6 increased the CC ($P<0.003$), whereas decreased EC at $P<0.002$ and $P<0.02$ levels respectively. No significant difference was detected between Epo-1 and Epo-6 for their efects on CC and EC. The level of MDA detected in HC of sham rats was 317.70±20.5. 4-VO increased MDA to 567.01±24.9 ($p<0.0004$). Epo-1 and Epo-6 decreased MDA to 359.43±25.5'e ($p<0.0003$) and 471.8±25.4 ($p<0.03$) respectively. The effect of Epo-1 was greater than Epo-6 ($p<0.003$).

In conclusion, repeated 4-VO impaired memory. Epo-1 and Epo-6 improved memory and lowered the increased MDA in HC. However, the effect of Epo-1 on MDA was greater than Epo-6.

Key words: Ischemia, Memory, Maze, Malondialdehyde, Erythropoietin

P52

Inhibition of spinal reflexes by doxycycline and minocycline in rats.

Kortunay S [1], Genc O [2], Erken HA [2], Turgut S [2], Turgut G [2].

Pamukkale University, Faculty of Medicine, Department of [1] Pharmacology *and [2] Physiology, Denizli , Turkey.*

skortunay@pamukkale.edu.tr

We have investigated the effects of doxycycline and minocycline, which inhibit phospholipase A2, on spinal monosynaptic reflexes in rats. Adult rats (n=48) weighing 150-200 g were anaesthetized with ketamine. A laminectomy was performed in the lumbosacral region. Following electrical stimulation of the sciatic nerve by single pulses, the reflex potentials were recorded from the ipsilateral L5 ventral root. Doxycycline (50 and 90 mg/kg) and minocycline (50 and 90 mg/kg) were administered intraperitoneally. Also we used 90 mg/kg doses of these two drugs locally to the spinal cord. Locally administered neomycine sulphate (40mg/kg) phospholipase A2 inductor, also significantly decreased the amplitude of reflex response ($p<0.05$). The all dosages of doxycycline and minocycline significantly decreased the amplitude of reflex response ($p<0.05$). The mechanism of these dose-dependent inhibitions remain unknown. Our results suggest that the products of arachidonic acid may play an important role in regulating the reflex response.

Key words : Doxycycline, minocycline, spinal reflexes, rat

P53

Evaluation of the relationship between emotional stress and myocardial infarction in rats: the role of cortisol and oxidative stress

Mercanoglu G [1], Safran N [2], Sezgin C [3],Uzun H [3],Gungor M [1], Eroglu L[1].

Istanbul University, Istanbul Medical Faculty [1]Pharmacology and Clinical Pharmacology Department, [2] Microbiology and Cilinal Microbiology Department, Virology and Immunology Unit [3] Cerrahpasa Medical Faculty, Biochemistry Department, Istanbul, Turkey.

guldemiko@yahoo.com

Observational studies have shown that negative psychological factors are risk factors for coronary artery disease. Despite large number of studies investigating the relationship between physiological stress and the activation of neurohormonal and sympathetic system, limited data is present related to the possible relation between emotional stress and coronary artery disease. In this study we aimed to evaluate the relationship between the chronic emotional stress and acute coronary disease in rats. 12 weeks old young adult Sprague Dawley Rats used in the study were assigned as control and stress groups. Different chronic risk 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. After chronic stress application, rats were infracted surgically by the ligation of the left anterior descending coronary artery (LAD) for 30 minutes. In the 24th hour of AMI the rats were sacrificed and heart was isolated. The infarct size was measured by three-ethyl-tetrazolium bromide (TTC) dye. Oxidant parameters were measured in heart tissue. The cortisol, LDH, troponin T and CK levels were measured in plasma specimens (before and after AMI). In stress group the serum-cortisol levels before and after AMI were found higher than that of the control ($p<0.05$). Mean infarct size in stress group was significantly larger (%44,6 and %49,8 respectively; $p<0.05$). Compared to the control group, trophonin T levels that marker of necrosis were higher in the stressed group (2.13 and 3.35 ng/ml respectively; $p<0.05$). Chronic emotional stress increased the infarct size in rats. The significant increase in cortisol and oxidative stress levels in stress exposed rats may indicate that these mechanisms are highly responsible from the worsening effects of the stress.

Key words: Emotional stress, MI, oxidative stress, cortisol

P54

Evaluation of the depressive like behavior in rats after myocradial infarction

Mercanoglu G [1], Safran N [2], Gungor M [1], Eroglu L [1].

Istanbul University, Istanbul Medical Faculty [1] Pharmacology and Clinical Pharmacology [2] Microbiology and Clinical Microbiology Department, Virology and Immunology Unit, Istanbul, Turkey.

guldemiko@yahoo.com

Correlation between the inflammatory cytocines (IL-6, TNF-alfa) and depression is well kwon. These cytocines are also risk factors for cardiovascular diseas (CVD). The aim of the study is the determinetion of

depression and anxiety in rats after myocardial infarction. 12 weeks old young adult Sprague Dawley Rats was used. Rats were infarcted surgically by the ligation of left anterior descending coronary artery for 30 min. In the 3,5,7,14,21 and 28th days of infarction anxiety and deprresive behavior were studied in the elevated plus-maze test (EPM) and in the forced swimming test (FST), respectively. In EPM, during the 5-min test period, the number of open and enclosed arms entries, plus the time spent in open and enclosed arms, was recorded.Entry into an arm was defined as the point when the animal places all four paws onto the arm. In FST test, during the 5-min test, swimming and immobility behaviors were recorded in the pre-treated animals (15 min duration and 24 hour before the original test). Results were represented as the average of 8 animals' results per group. In the infarcted group, a decrease of percentage of entries and in the percentage of time spent in the open arm was seen in EPM, This decrease was significant especially for first two weeks. Similiarly increased immobility was also seen in infarcted group in FST test. As a results however anxiety was observed in the acute phase of infarction, depressive like behavior was significant in the chronic phase. Both the effects on the quality of life and the progression of the CVD, it is very important to adding the antidepressant/anxiolytic theraphy to the reperfusion strategies in patients after myocardial infarction.

Key words: MI, depression, anxiety

P55

The investigation of the effect of repeated food deprivation on the convulsions induced by scopolamine treatment and food intake in fasted mice

Uslu ZG [1], Nurten A [2], Enginar N [1].

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

zguslu@istanbul.edu.tr

Scopolamine treatment and access to food induce convulsions in mice fasted for 24 or 48 h. On the other hand, it has been shown that food deprivation gives rise to analgesia and this effect is greatly reduced after five exposures to periods of 24 h food deprivation, indicating the development of tolerance. Although repeating food deprivation after 40 days does not alter the development of convulsions, similar repeated exposures may cause a decrease in susceptibility to convulsions. Thus, the present study was performed to investigate the effect of repeated food deprivation on the convulsions in mice fasted for 24 or 48 h. For this purpose, inbred albino Balb/C male mice were divided into single or repeated food deprived groups. For single exposure, animals were deprived of food for 24 or 48 h. For repeated exposures, animals were exposed to periods of 24 or 48 h food deprivation 5 times (alternating with 24 or 48 h free access to food). On the day of testing, animals were treated (i.p.) with saline (control) or 3 mg/kg scopolamine. Following treatments, they were individually placed in wire mesh cages and were given food pellets 20 min later. All animals were observed for 30 min for the incidence and onset of convulsions. The frequency of the incidence of convulsions was evaluated using Fisher's Exact test. The onset of convulsions was evaluated with Student's *t*-test. Single and repeated food deprived animals developed convulsions after scopolamine treatment. The incidence of convulsions was significant when compared with the saline injected control groups. However, when single and repeated food deprived groups were compared with each other, no significant difference was found in the incidence of convulsions both in 24 and 48 h fasted animals. On the other hand, repeated food deprivation decreased latency to the onset of convulsions in 48 h fasted mice. Present results indicate that repeated food deprivation does not reduce the susceptibility to convulsions in 24 and 48 h fasted mice. On the contrary, exposure to repeated food deprivation facilitates the onset of convulsions in mice fasted for 48 h.

Key words: food deprivation, scopolamine, fasting, convulsions, mice

P56

The effect of venlafaxine on intraplantar glutamate induced nociception in rats

Yaba Gulay [1], Tekol Yalcin [1], Sezer Zafer [2].

Erciyes University, Medical Faculty, Department of Pharmacology [1], Kayseri. Gulhane Military Medical Academy, Medical Faculty, Department of Pharmacology [2], Ankara, Turkey.

gulayy@erciyes.edu.tr

It is now well established that the excitatory amino acid glutamate plays a significant role in nociceptive processing and all glutamate receptors participate in induction, modulation or maintenance of pain. Antidepressants' analgesic effects have been known for a long time and an antidepressant drug venlafaxine is now under clinical trials in some painful conditions. In this study we investigated the role of venlafaxine on glutamate induced pain in rats. For this purpose male Sprague Dawley rats (n=6) were injected with 35 µl 5 µmol glutamate (pH:7.4) solution intraplantarly (i.pl) under the ventral surface of hindpaw. Animals were treated with venlafaxine (20 mg/kg) or saline (control group) intraperitoneally 20 minutes before glutamate injection. Immediately after glutamate injection rats were observed for 15 minutes and the amount of time spent for licking or biting the injected paw was timed. Differences between venlafaxine and control groups were compared by Student's t-test. Glutamate induced significant nociceptive response in saline treated rats and this effect was antagonised by venlafaxine. The present study demonstrates, to our knowledge for the first time, that systemic administration of venlafaxine produced a significant inhibition of the nociceptive response caused by intraplantar injection of glutamate in rats. Because it was supposed that substances which block glutatamate receptors may have important clinical potential in the management of some painful states it may be beneficial to investigate the possible effect of venlafaxine on glutamate receptors for the treatment of pain.

Key words: Venlafaxine, glutamate, antinociception, rat

P57

The antioxidant effects of ketamine and propofol anesthesia on spinal cord trauma model in rats

Yuksel M [1], Adil M [2], Haklar G [3].

Department of Medical Laboratory [1], Vocational School of Health Related Professions, Marmara University, Departments of Anesthesia [2] and Biochemistry [3], School of Medicine, Marmara University, Haydarpasa-Istanbul, Turkey.

meralyuksel@marmara.edu.tr

Peripheral nerve injury is a significant clinical problem that is often difficult to treat. The primary traumatic mechanical injury to the spinal cord causes the death of a number of neurons that cannot be recovered and regenerated. The secondary neuronal death may be caused by substances released from cells in response to the primary injury. It is well reported that destruction of neurons and glial cells are associated with production of reactive oxygen species. In the present study, we evaluated the antioxidant effects of ketamine and propofol in a model of spinal cord injury that was induced by the application of vascular clips to the dura via a fur-level T5-T8 laminectomy. After one hour of the laminectomy operation ketamine was induced in a dose of 100 mg/kg ip. to the ketamine-laminectomy group or propofol was induced in a dose of 40 mg/kg ip to the propofol-laminectomy group (n=8). A control group without a trauma injury (n=8) and a laminectomy group (n=10) was also included. Spinal cord tissues are removed after the injuries. Thiobarbituric acid reactive substances (TBARS), luminol (specific for ·OH, H_2O_2, HOCl), and lucigenin (selective for superoxide radical) enhanced chemiluminescence (CL) measurements are used for detecting free radical damage.

TBARS measurements are increased in spinal trauma group with respect to the control group (59,4±10,1 vs 17,6±3,6 nmol MDA/g tissue; $p<0,001$). Ketamine and propofol administration have decreased TBARS measurements significantly (19,8±4,1vs 24,9±2,5nmol MDA/g tissue; respectively). Luminol and lucigenin enhanced CL measurements are also increased in spinal cord trauma injury in contrast to the control group (luminol 129,5± 49,7 vs 26,3±9,3 rlu/mg tissue; lucigenin 105,3 ± 29,1 vs 23,3 ± 8,1 rlu/mg tissue; $p<0,001$). Propofol (28,9 ± 7,3 and 24,4 ± 8,8 rlu/mg tissue) and ketamine (22,8 ± 18,1 and 15,2 ± 4,8 rlu/mg tissue) anesthesia have reduced the effects.

Our results have shown that ROT induced spinal cord damage is decreased with ketamine and propofol anesthesia. Additionally, lucigenin enhanced

superoxide radicals and luminol enhanced ·OH, H_2O_2, HOCl radicals are reduced with ketamine and propofol injections.

In conclusion, ketamine and propofol administrations have reduced oxidative damage in spinal cord injury.

Key words: Spinal cord injury, reactive oxygen species, ketamine, propofol, oxidative stress.

P58

The attractors of complex visual evoked potential signals

Agbulut Y [1], Seymen O [2], Aytac E [2], Ogullar S [2], Yalcin GC [1], Akdeniz KG [1].

Istanbul University, [1] Faculty of Science, Physics Department, [2] Cerrahpasa Faculty of Medicine, Physiology Department, Istanbul, Turkey.

yilmazagbulut@gmail.com

The Chaos Theory offers us the new techniques for the non-linear phenomenology to understand the behaviours and mechanical modelling of autonomous and complex systems. Recently, as autonomous and complex system the local physiological systems were also examined by the signal attractors in reconstructed phase-space. In this work, we have investigated the attractors of the high sensitive recorded complex visual evoked potential (VEP) signals in reconstructed phase-space to get more physiological information about the visual centre of human brain. For this purpose, we have used VEP signals of fifteen human brain (sent one hundred flash to eyes of each human) obtained by electroencephalogram (EEG) method. VEP signals were recorded in time series forms by a MP150 unit, with Nonlinear Dynamics Toolbox (NDT) and Time Series Analysis (TISEAN) softwares. The fractal dimensions and embedding parameters of the EEG recorded VEP signals from representative fifteen humans were found by TISEAN method and the attractors of VEP signals in reconstructed phase space were investigated. And the diversity of the attractors through the representative VEP signals were noted and they were compared with other data analyzed techniques examinations.

Key words: Non-linear analysis, Chaos theory, Physiological systems, EEG, VEP

P59

Difference of toluene induced reward-seeking behavior at day and night in mice

Akhisaroglu M, Topcu A, Aksu I, Semin I.

Dokuz Eylul University, Faculty of Medicine, Department of Physiology Izmir, Turkey.

m.akhisaroglu@deu.edu.tr

Abuse of organic volatile substances in children has become a social health problem that is increasing in the recent years. Toluene can be use via inhalation, intraperitoneal or intravenous for experimental research on rodents. In animal experiments, acute exposure to toluene at low to intermediate doses can increase locomotor activity, with an observable behavioral difference. A conditioning paradigm of toluene inhalation was developed the rewarding effect in mice and rats. The aim of this study was to evaluate the toluene induced reward seeking behaviorin circadian manner. We used shuttlebox (22x44x22 cm), which was divided into two compartments of equal size. One compartment was white with a smooth floor, and the other was black with a textured floor. Toluene was injected for conditioned place preference test in C3H strain at day and night time points. C3H mice were injected to 800 mg/kg of toluene in white compartment during 30-min pairing sessions given every other day alternating with olive oil for the total of eight pairings for each treatment. Test sessions were carried out 1 day after the final injection session with mice in a drug-free state. The time spent in each compartment during a 15-min session was measured using a video camera. Our results indicate that C3H mice demonstrate significant decrease in toluene-induced conditioned place preference at night compared to daytime. Such difference between night and day time may be related to the melatonin secretion.

Key words: Toluene, Reward, Conditioned Place Preference, Circadian, C3H

P60

The interactions of leptin and L-arginine on penicillin-induced epileptiform activity in the rat

Aslan A, Yildirim M, Ayyildiz M, Agar E.

Department of Physiology, Faculty of Medicine, University of Ondokuz Mayis, 55139 Samsun, Turkey.

draslan@yahoo.com

Leptin is a hormone that is controlled body mass by regulating energy balance. This hormone is mostly secreted by white fat tissue which reduces appetite and increases using energy by interaction with hypothalamus. There are several reports suggest that leptin changes the nitric oxide (NO) levels. NO is a regulating and transmitter molecule that can act as a physiological molecule that regulates blood circulation and learning-memory or pathophysiological molecule which is connected with epilepsy. The aim of this study was to find out the interactions of leptin and L-arginine on penicillin induced epileptiform activity in the rat. Nineteen female rats were used in this study divided into three groups; penicillin treated, penicillin +leptin, penicillin+leptin + L-arginine groups. Epileptiform activity was started after 4-5 minutes from intracerebral (i.c.) penicillin injection. After 30 minutes from penicillin injection, saline was injected intracerebroventricular (i.c.v.) to penicillin treated group, after 30 minutes from penicillin injection 1 microgram (i.c.v.) leptin was administrated to penicillin+ leptin group, after 30 minutes from penicillin injection 1000 mg/kg L-arginine was administrated intraperitoneally (i.p.) and 1 microgram leptin (i.c.v.) was injected to penicillin+ L-arginine + leptin group 30 minutes after from L-arginine administration. The electrocorticogram (ECoG) activity was recorded by PowerLab data gaining unit was returned to numerical data and than analyses was performed using Dunnett's *t*-test for comparisons. The spike frequency was statistically increased in penicillin+ leptin used group after 95 minutes from leptin application compared to penicillin treated group ($p<0.05$). The frequency increase after leptin injection was prevented by L-arginine injection (i.p.). We may conclude that leptin causes an increase in the frequency of epileptiform activity via NO system in the rat.

Key words: Leptin, NO, L-Arginine, Epilepsy, ECoG

P61

Effect of flunarizine, a calcium channel blocker on iron-induced cerebellar Purkinje cell loss in rat

Bagirici F, Bostanci MO, Kozan R.

Ondokuz Mayis University Faculty of Medicine Department of Physiology 55139 Samsun Turkey.

fbagirici@yahoo.com

Iron is a metal highly concentrated in brain and liver tissue, and known to induce neuronal hyperactivity and oxidative stress. It has been reported that there is a link between neuronal death and intracellular excessive calcium accumulation. The aim of the present study was to investigate the effects of flunarizine on the neurotoxicity induced by intracerebroventricular (i.c.v.) iron administration in rats. Animals were divided into three groups. Rats in iron (n=7) and iron+flunarizine (n=7) groups received i.c.v. $FeCl_3$ (200 mM, 2.5 µl), while rats in control group (n=7) received the same volume of saline. Rats in iron+flunarizine group also received i.c.v. 2 µl (1 mg/kg) flunarizine following $FeCl_3$ injection. All animals were kept alive for ten days following the operation and animals in iron+ flunarizine group were intraperitoneally injected flunarizine (10 mg/kg/day) once a day during this period. After ten days, all rats were perfused intracardially and then sacrificed. Brain tissues were removed and standard histological techniques were performed. The total numbers of cerebellar Purkinje cells of all rats were estimated with unbiased stereological techniques. Data were analyzed by Student's t Test. Iron group display a marked decrease (27.8 ± 3.9 %) in cerebellar Purkinje cell number when compared to controls ($p<0.001$). Purkinje cell loss in iron+flunarizine group with respect to controls was also significant and was 8.7 ± 2.7 % ($p<0.05$). Flunarizine appears to attenuate the iron-induced Purkinje cell loss from 27.8 % to 8.7 % and seems to have a significant neuroprotective effect against the iron neurotoxicity ($p<0.001$). Findings of the present study suggest that a calcium channel blocker, flunarizine has neuroprotective effect

on iron-induced Purkinje cell loss in rat cerebellum via blocking calcium ions into neurons.

Key words: Iron, Purkinje cell, cell death, flunarizine, stereology.

P62

Inducible nitric oxide synthase and neuronal nitric oxide synthase expressions in the brain after intrahippocampal beta amyloid peptide administration in rats

Cetin F, Dincer S.

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

ferihan@yahoo.com

Cognitive impairment and neurodegenerative disorders that mimicks Alzheimer's disease can be reproduced in some animal models via intracerebral or intracerebroventricular administration of beta amyloid peptide (A-beta) derivates. Although neurophysiologycal functions of enzymatically derived nitric oxide are known, its implication in neurodegenerative diseases still remains unclear. There are some contradictory results in the literature about inducible nitric oxide synthase (iNOS) and neuronal nitric oxide synthase (nNOS) expressions in Alzheimer's disease pathophysiology. The aim of this study was to investigate iNOS and nNOS expressions after intrahippocampal administration of A-beta $_{1-42}$ in the temporal cortex. 18 male adult Wistar albino rats were used in the study. The groups were formed as sham (n=6), control (n=6) and A-beta $_{1-42}$ (n=6). Stereotaxic surgery was performed under xylazine(10mg/kg,i.p) and ketamine (80mg/kg,i.p) anesthesia. Stereotaxic coordinates were determined as: AP=-4.8mm, L=-3.5mm from the bregma and H=-4mm. from the dura. A-beta $_{1-42}$ peptide (20micrograms/4microliters) was administered as a single injection bilaterally into the hippocampal fissure by a hamilton microsyringe. By using the same procedure, distilled water was administered to the control group and only the stereotaxic surgery was applied to the sham group. 21 days after the of A-beta $_{1-42}$ peptide application, the rats were decapitated and rat brains were rapidly removed on ice. iNOS and nNOS expressions were evaluated in the temporal cortex by western blotting. According to densitometric analyses of bands, there was no significance between the groups for nNOS expression. We showed that iNOS expression was not induced by A-beta $_{1-42}$ peptide application. There are some studies in the literature which had demonstrated neurodegenerative changes and inflammatory responses due to A-beta $_{1-42}$ peptide application. However in this study, we found that 20micrograms/4microliters of single A-beta $_{1-42}$ peptide application did not affect iNOS and nNOS expressions after 21 days of its administration. This might depend on the type of A-beta peptide, its application way (acute or chronic) and region of application (intracerebroventricular or parenchyma).

Key words: Alzheimer's disease, beta amyloid peptide, temporal cortex, inducible nitric oxide synthase, neuronal nitric oxide synthase, western blotting.

P63

Preliminary study on the involvement of perirhinal cortex in the short-term auditory recognition memory in rat.

Jakubowska-Dogru E [1], Wesierska M [2], Elibol B [1], Gunay G [1].

Middle-East Technical University, Department of Biological Sciences, 06531 Ankara, Turkey [1]; Nencki Institute of Experimental Biology, Department of Neurophysiology, Pasteura 3, Warsaw, Poland [2].

bioewa@metu.edu.tr

Recognition memory represents a kind of memory that is central to behavioral adaptation in both man and animals. Therefore, studies on the anatomy of this memory carry a great importance. It has been postulated that medial temporal lobe in general and perirhinal cortex in particular is involved in higher order processing of polymodal sensory information and is important for the familiarity discrimination aspect of recognition memory. In earlier studies carried out on different animal species such as rats, dogs and monkeys, it was demonstrated that the medial temporal lobe structures including perirhinal cortex, are mediating visual, tactile, and olfactory recognition memory. Interestingly, results from the recent experiments on dogs and monkeys indicate that damage to perirhinal cortex do not affect auditory recognition memory. This would suggest that auditory memory in these animals is organized differently from the memory in other modalities. The aim of the present study was to compare the effects of the perirhinal lesions on the auditory recognition memory in rats with those in dogs, and monkeys. Prior to any behavioral testing, bilateral neurotoxic lesions or shame surgeries were done in a group of young Wistar rats. Throughout the experiment, rats had free access to water but were put on the food deprivation schedule. Prior to the sound recognition training, an object recognition task was carried out as a behavioral test of lesion location. Visual recognition was tested in the delayed nonmatching to sample task with trial unique junk objects and variable delays (10 s and 15 min). Sound recognition was tested in a runway according to the matching to sample procedure with short, 3 s, delay between trial unique sample and test stimuli. In the present study, lesions within the medial temporal lobe destroying perirhinal cortex had no effect on simple discrimination of visual stimuli but disturbed short-term object recognition memory at longer (15 min) delay. Lesioned animals did not show impairment in the sound recognition task with trial- unique auditory stimuli at the tested short delay. However, overall response latencies (both on positive and negative trials) were significantly longer in Lesion than in Control Group.

This study was supported by METU Scientific Research Found (BAP-2004-07-020013) and TUBITAK/BAYG group.

Key words:, object recognition, sound recognition, delayed matching / non-matching to sample, perirhinal cortex, rat

P64

The effects of linoleic acid on generalized convulsive and non-convulsive epilepsies

Ekici F [1], Ates N [2], Gurol G [2].

Medical Faculty of Gaziosmanpasa University, Department of Physiology, Tokat, Turkey [1]; Medical Faculty of Kocaeli University, Department of Physiology [2] Kocaeli, Turkey.

ekicifatih@hotmail.com

Studies in resent years reported that polyunsaturated fatty acids (PUFAs), which includes linoleic acid, has a protective effects against of epileptic seizures, brain ischemia, depression and various coroner heart disease. PUFAs have realized their effects, inhibition of glutamergic synaptic transmission and activation of 2-P domains K+ channels via pre/post synaptically. Although the role of the PUFA's have been looked for some convulsive seizures created chemically, their effects on absence epilepsy have not been understood exactly. For this reason, in this study the effects of PUFA's on convulsive and non-convulsive epileptic seizures were compared. In convulsive epilepsy group, fallowing the pentilenetetrazole (PTZ) injection, during 30 minutes, epileptic seizure activity was evaluated. The experimental group given linoleic acid + PTZ was evaluated, too. When the group applied linoleic acid was compared with PTZ group, we found that this treatment delayed the onset of seizures, increased the major seizure latency and decreased major seizure duration ($p < 0.05$). These results are good agreement with the results of limited study related to linoleic acid usage in convulsive epilepsies and known effect mechanisms of linoleic acid. In the group with spontaneous non-convulsive absence epilepsy, from the WAG/Rij rats who where equipped EEG electrode with steriotaxic basal EEG records were taken. When mean value of spike- wave discharges (SWDs) number and duration, in the rats to whom 100 nmol/kg, IV, linoleic acid was given compared with control group, although there was a significant increase statistically in the 1st and 6th hours ($p<0.05$), there was not a significant increment in the 24th hour. Our results showed that linoleic acid prevents the PTZ-induced convulsive seizures into a great degree, that it increased the major seizure decreased major seizure duration, latency and delayed the onset of seizures. On the other hand, in the WAG/Rij rats with absence seizure was increased the number and duration of seizure by linoleic acid. Our study demonstrated pharmacological differentiation between the convulsive and non-convulsive epilepsy. In the clinical and experimental studies to date, it is shown that various approaches should be used since the change of balance between excitatory and inhibitory systems create different effects. Our results have shown that while linoleic acid application reduces convulsive type epilepsy, it increases non-convulsive absence epilepsy.

Key words: Linoleic acid, absence epilepsy, EEG, PTZ

P65

Moderate and strenuous running exercise alters trace element distribution in brain liver and spleen of rats

Ergen K [1], Ince H [2], Duzova H [3], Karakoc Y [3], Emre MH [3].

Department of Biophysics, Faculty of Medicine, Faculty of Medicine, Kocaeli University, 41380 Kocaeli, Turkey [1]; Department of Chemistry, Faculty of Science and Literature, Istanbul Technical University, 34469, Maslak, Istanbul- Turkey [2]; Department of Physiology, Faculty of Medicine, Inonu University 44280 Malatya, Turkey [3].

kergen@hotmail.com

In this study, we aimed to investigate the effects of moderate and strenuous running exercise on manganese (Mn), cobalt (Co) and chromium (Cr) metabolism in brain areas, liver and spleen of rats. The control (n=8), 30 min (moderate) exercise (n=7) and 60 min (strenuous) exercise (n=6) groups of rats were housed in three groups in colony cages, at ambient temperature of 23 ^{0}C with a 12-h/12-h light/dark cycle. Training consisted of treadmill running 5 days per week during a period of 13 weeks. The rats in moderate and strenuous exercise groups adapted to the treadmill exercise with a minimal progression during a week. In this period, running time was gradually increased from 15 min to 30 and 60 min per session for moderate and strenuous exercise groups, respectively. Ten min after the last session exercise training session (13 weeks), the rats were scarified and, samples of tissue were taken. Mn, Co and Cr levels of the frontal lobe, temporal lobe, brain stem, liver and spleen were determined by a Perkin-Elmer Zeeman Z/3030 atomic absorption spectrophotometer equipped with a HGA-600 graphite furnace. Co level significantly decreased in brain stem of rats in moderate exercise group and in frontal lobe of rats in strenuous exercise group ($p<0.01$ for both) when compared to controls. Mn level significantly decreased ($p<0.01$) in brain stem of rats in strenuous exercise group of which Co and Cr levels were not detected, when compared to that of moderate exercise group. Co seems to decrease in the body especially in the brain stem and Co supplementation for athletes may be helpful to prevent Co deficiency in the body, because of the consumption by running exercise.

Key words: trace element, brain, liver, running exercise, oxygene free radical.

P66

Design and implementation of the eye movement detection system in investigation of spatial neglect

Nalcaci E [1], Gunes E [1], Erdogan M [2], Telatar Z [3], Ari F [3], Ozturk O [3].

Ankara University School of Medicine, Physiology Department[1], Ankara University, Biology Department [2], Ankara University, Engineering Faculty, Department of Electronics [3] 06100 Tandogan Ankara, Turkey.

nalcaci@tr.net

Some types of lesion in the human brain cause to neglect of hemispace. In the normal individuals, a slight neglect is also detected due to the asymmetric functions of the human brain. The main problem was to understand that whether the reason of neglect depends on an asymmetric attention in space or an asymmetric mental imaginary of space. To answer this question, an eye movement detection system was aimed to develop during line bisection task, which is sensitive of spatial neglect.

In this study, a measurement system was developed in order to detect and track the eye movements. In general, the system includes a video camera sensitive to IR (Infra-Red), IR illuminator, computer for data recording and analysis, and subject monitor. A special device to make fix the head of the subject and an experiment platform have been developed together with the system. For the imaging technique used in the system, the eye region of the subject is illuminated by an IR point source harmless for the human eye and is recorded by an IR sensitive camera. In the first step of the experiment, a test image is shown to the subject on the monitor as a first visual stimulus for calibration purpose and the anatomic characteristics of the subject are extracted. At the second step of the experiment, visual stimulus, which are prepared by the expert physician, are automatically presented to the subject on the monitor and subject responses to these stimulus through a stimpad are recorded together with current eye positions. Pupil and cornea characteristics are examined in the analyses of recorded video sequence. Special trigger codes produced by system (Neuroscan STIM compatible) which is related to the visual stimulus presented to the subject, and the trigger codes giving the subject responses are synchronously recorded to the digital media together with real time image records. For this purpose, a micro controller based port monitor device is used in the system in order to read the codes coming from the stimulus server and to realize integration between different parts of the system. The image analysis algorithm computes the location of the pixel points in which the subject focuses on the stimulus monitor (gaze point). From these computations, the exact location of the pixel being focused is defined as a function of time and the statistical distribution is plotted in horizontal and vertical directions separately.

In this study, bisected horizontal lines were presented to subjects, who were asked to decide whether bisection is in the left or the right of the midpoint of lines. During this process, eye movements of subjects could be recorded between the beginning of stimulus presentation and the response of subject. Analyze of eye movement depends on how many periods gazes are spent in the right or in the left of midpoint of the lines.

Key words: Neglect, Eye movements, Line bisection task, Attention

* This study was supported by Ankara University with the research project (2003.08.09.095).

P67

Design and Implementation of the system detecting uninterrupted turning movements (ROTOMETER)

Gunes E [1], Nalcaci E [1], Erdogan M [2], Telatar Z [3], Ari F [3], Ozturk O [3].

Ankara University School of Medicine, Physiology Department [1], Ankara University, Biology Department [2], Ankara University, Engineering Faculty, Department of Electronics [3] 06100 Tandogan Ankara, Turkey.

emel_onal@hotmail.com

It is well known that human subjects tend to turn to the right or to the left, and this preference has been thought to be related to an asymmetry of dopaminergic activity. Detection of turning preference in human has been studied by different methods. One of these methods is human rotometer, which is applied to belt in order to evaluate spontaneous turning preference in daily life. However, this method was used by very limited researchers, because of it is not commercial equipment.

In this work, a measurement and recording system was developed for counting the behavior of uninterrupted turning movements of human. An electronic compass was used working with the principle of the magnetic field of the earth. Digital values measured at the output of the compass are processed by the algorithm running on the micro controller device in order to compute the uninterrupted turning movements. In other words, uninterrupted turning movements on the left and the right directions as 90°, 180°, 270° and 360° are discriminated and recorded to the memory. A threshold level of 5° tolerances was introduced in order to prevent from erroneous decision. The other property of the device is to not perceive the turning below a certain velocity as an uninterrupted turning. In that sense, turning around below the definite velocity is considered as an erroneous movement. The software developed for this system has a flexibility depending upon the application and can be adapted to realize different scenarios (e.g. measurement for different turning angles) The device is properly used for measurement during the daytime activity of subject, as it has ergonomic structure like small size with own carrying case and rechargeable internal battery of long duration. Measurement values during the experiments can be saved in the EEPROM system memory. The measurements can be interrupted at any time and device can be shutdown for any time interval. After the wait period, the experiments and recording can be proceeded. At the end of the complete exercise period, the data recorded is transferred to a computer and turning movements are evaluated by using software run by MATLAB.

Key words: Turning Preferance, Human rotometer, Dopaminergic asymmetry

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P68

Effects of acute and subchronic alcohol intake on non-convulsive genetic absence epilepsy

Gurol G [1], Sahin D [1], Duman C [2], Ilbay G [1], Ates N [1].

Kocaeli University Faculty of Medicine, Department of [1] Physiology, Department of [2] Biochemistry, Kocaeli, Turkey.

gonulgurol@superonline.com

Although the effects of acute and chronic administration of ethanol on the generalized convulsive epilepsy are well known, its effects on the non-convulsive generalized epilepsy are not well known. Therefore, we aimed to investigate to the acute and subchronic administration of alcohol on SWD (spike-wave discharges) in genetically absence epileptic WAG/Rij rats. Following a one-hour-record of basal EEG (electroencephalogram) activity in all groups, 50 mg/kg, 250 mg/kg, and 1 g/kg, i.p. alcohol was injected to the rats in acute alcohol groups, and %0,09 serum physiologic was injected to the rats in control group. Then the EEG records were continued for three hours. Ethanol was injected i.p. (intraperitoneal) subchronically to the group, on which the effects of subchronic alcohol were investigated, twice daily during the periods of 13 days. After an hour, the EEG records were done. Following an abstinence period of 12 hours, EEG records were done for an hour at fourteenth day. After the last alcohol injection fourteenth day EEG records were done and analyzed for the evaluation of the number and total duration of SWD. Spontaneous behaviors of rats were also observed before and after an alcohol administration. Their horizontal locomotor activities were recorded automatically. After the records, blood samples were taken to determine their blood alcohol levels. According to our results, acute and chronic administrations of alcohol significantly decrease to the occurrence of the SWD. However, abstinence period of twelve hours increase both of the number and duration of SWD significantly. On the other hand, our results also showed that administration of low level alcohol increased locomotor activity, whereas high dose and chronic alcohol administration reduced locomotor activity ($p<0,05$). Our results showed that, alcohol can induce a decrement in absence epileptic seizure by changing the consciousness level and modulating excitatory neurotransmitter system.

*Key words***:** *electroencephalogram; epilepsy, absence ; ethanol; models, genetic*

P69

Isolation and culture of adult mouse medial vestibular nucleus neurons

Him A, Altuntas S, Ozturk G.

Yuzuncuyil University, Medical School, Department of Physiology, Van, Turkey.

ahim@yyu.edu.tr

Primary culture of vestibular nucleus neurons has only been successfully described in embryonic and early postnatal ages. This study describes a method for culture of vestibular nucleus neurons from young adult (6-8 weeks) mice. The culture system is based on Neurobasal medium supplemented with antioxidant rich B27. Neuronal survival was optimized by replacing glutamine with GlutaMaxI and by using ice-cold culture medium to increase neuronal survival during tissue dissection. Density gradient was used for enrichment of neurons and to separate neurons from debris and non-neuronal cells. Neuronal survival was increased in culture supplemented with fetal calf serum (FCS); while neuronal survival in culture without the serum was 69%, 11% and 5% at 1, 2, and 3 days in vitro (div), respectively, neuronal survival in culture with %20 FCS were 92%, 68% and 33% at 1, 2, 3 div, respectively. Supplementing the medium with 10% FCS was less effective; neuronal survival in culture with %10 FCS was 92%, 29% and 1% at 1, 2, 3 div, respectively. From the first day in culture some neurons grew neurites. Using FCS in medium increased the number of neurons with neuritis; while 2% of the neurons grew neurites in the medium without FCS at 24 h in culture, 8% of the neurons grew neurites when 20% FCS supplement was used. The neurons with neurites survived longer in culture.

Key words: medial vestibular nucleus, neuron, culture, mouse, adult

P70

Electrophysiological features in organophosphate poisoning: a case report

Yerdelen D [1], Koc F [1], **Ozcan F** [1], Bozdemir H [1].

Cukurova University Medical School, Department of Neurology [1], (Present adress: Baskent University Faculty of Medicine, Adana Teaching and Medical Research Center, Department of Neurology [1], Adana-Turkey)

zaferkoc@superonline.com

Organophosphates are used in industry as insecticides, and miticides. The pharmacologic and toxicologic effects of organophosphates are due predominently to inhibition of acetylcholinesterase and accumulation of acetylcholine at the synapse. The excess acetylcholine can cause various neurological signs and symptoms by paralyzing the cholinergic synaptic transmission within the central nervous system (CNS), somatic nerves, autonomic ganglia, parasympathetic nevre endings, and some sympathetic nevre endings such as the sweat glands. These signs and symptoms are; 1) muscarinic or hollow-organ parasympathetic manifestations, 2) nicotinic or autonomic ganglionic and somatic motor effects, and 3) CNS effecst. CNS effects include restlessness, emotional lability, headache, tremor, drowsiness, confusion, slurred speech, ataxia, generalized weakness, delirium, psychosis, seizures, neuronopathy, axonopathy, myelinopathy, conduction neuropathy, and death. A 20-year old female ,working as a agriculture worker for 8 years and took agricultural drugs to commit suicide, was accepted to the clinic with complaints of impairment of conciousness and weakness in the four limbs. Neurological examination showed asymmetrical quadriparalysis, prominent on the right side. Deep tendon reflexes were normoactive, babinski sign was bilateral negative. Superficial and deep sensorial examination couldn't be performed because of insufficient cooperation. Computedbrain tomography was normal. Electromyogram with repetitive nerve stimulation revealed normal findings. Electromyography performed on the 25 th day showed neurogenic unit changes and decrease in the motor unit potential density. Sensorial nevre conduction studies were normal. There were prolongation of right peroneal and bilateral posterior tibial nevre distal latencies and total conduction block in the left peroneal nevre. As a conclusion, we wanted to emphasize the importance of electrophysiological studies and draw attention to the features of the examination in cases accepted with organophoshate poisoning encountered frequently in agriculturel areas.

Key words: Organohosphore, poisoning, neurological and electrophysiological findings.

P71

Analysis of motor unite potentials in healthy subjects

Yerdelen D [1], Koc F [1], **Ozcan F** [1], Bozdemir H.

Cukurova University Medical School, Department of Neurology [1], (Present adres: Baskent University Faculty of Medicine, Adana Teaching and Medical Research Center, Department of Neurology [1], Adana-Turkey)

zaferkoc@superonline.com

Motor units consist of anterior horn cell, its peripheral axon and muscle fibres innervated by related motor neuron. In this study, 27 females (54 %) and 23 males (56 %) (total 50 healthy subjects) at a mean age of 41.9 ± 14.1 (the age range of 18-69) were examined. Twenty motor unit potential examples from each of M. Abductor pollicis brevis, M. Biceps and M. Tibialis anterior were collected and amplitude, duration and number of turn parameters were evaluated. The data were compared statistically according to the gender, height and age. In males the values were as following; in M. Abductor pollicis brevis; amplitude 7.9 ± 1.8 mV (5-11), number of turns 3.6 ± 0.4 (2-5), duration 7.3 ± 0.9 (5.4-9), in M. Biceps; amplitude 7.4 ± 3.0 (3.7-19.5) mV, number of turns 3.2 ± 0.6 (2-5), duration 7.9 ± 0.8 (6-10), in M. Tibialis anterior; amplitude 8.5 ± 1.9 (4.8-12.8) mV, number of turns 3.4 ± 0.6 (2-5), duration 8.5 ± 1.1 (6.6-11.6). In females the values were as following; in M. Abductor pollicis brevis; amplitude 8.1 ± 2.2 mV (5-12), number of turns 3.6 ± 0.5 (3-5), duration 7.5 ± 0.6 (6.5-9), in M. Biceps; amplitude 6.2 ± 1.5 (3.9-10.9) mV, number of turns 3.1 ± 0.4 (3-4), duration 7.7 ± 0.9 (6-10), in M. Tibialis anterior; amplitude 6.9 ± 1.3 (4.7-9.7) mV, number of turns 3.4 ± 0.4 (3-4), duration 8.2 ± 1.1 (6.2-9.8). Height was statistically different between males and females ($p<0.001$). And mean amplitude values were higher in males

than females (T test and Mann-Whitney test) (0.005, 0.063). As age increased, mean amplitude values decreased. As a result we concluded that hight and age are important parameters affecting amplitude.

Key words: Electroneurography, motor unit, gender, age, height.

P72

Mitochondrial oxidative stress after carbon monoxide treatment in rat brain

Taskiran D [1], **Nesil T** [1, 2], Alkan K [3].

Ege University, Faculty of Medicine Department of Physiology and Center for Brain Research [1], Institute of Natural and Applied Sciences Department of Biotechnology [2], Faculty of Science Department of Biology [3], Izmir, Turkey.

dilek.taskiran@ege.edu.tr

Carbon monoxide (CO) is the most common cause of fatal poisoning in industrial countries. At cellular level, a combination of tissue hypoxia and direct damage underlie the pathophysiology of CO toxicity. Binding of hemoglobin to CO results in tissue hypoxia, because carboxy hemoglobin (COHb) cannot bind and carry oxygen to the tissues. However, levels of COHb during CO poisoning do not correlate well with the clinical status of the patients. Recent studies indicate mitochondrial processes in the development of CO toxicity via binding of reduced cytochrome c reductase (Complex IV) in the brain. The purpose of this study was to determine the effect of CO treatment on oxidative stress parameters in mitochondria isolated from male and female rat brains. Adult male (n=8) and female (n=8) Sprague- Dawley rats were used for the experiments. Mitochondria were prepared from frontal cortex, hippocampus and corpus striatum and treated with 0.1 % of CO at 37 °C for 30 minutes; control samples were not exposed to CO. Cytochrome c oxidase activity (COX), lipid peroxidation (thiobarbituric acid reactive species= TBARS), protein oxidation (protein carbonyls), glutathione (GSH) levels were measured in the CO treated and control samples. Data were initially analyzed by multifactorial or one-way analyses of variance (ANOVA) for each parameter, with sex and CO treatment as factors. CO treated and control groups were compared by paired samples *t*-test. Statistical results were summarized in the table below. Our results confirmed previous studies reporting the inhibition of cytochrome c oxidase activity by CO in rat brains. Furthermore, CO treatment significantly increased protein carbonyl levels in hippocampus and striatum in male rats and decreased GSH levels in all brain regions related with sex. ANOVA test revealed a significant main effect of sex in the striatum for TBARS levels. Taken together, our data supported mitochondrial oxidative stress may play a role in CO toxicity at cellular level during CO poisoning.

This study was supported by the grant from Ege University Research Fund 03/TIP/005.

Key words: Carbon monoxide, mitochondria, oxidative stress, cytochrome c oxidase, toxicity

P73

The effect of vitamin E on the blood-brain barrier permeability in aged rats during seizures

Seker FB [1], Yorulmaz H [2], **Oztas B** [1].

I.U. Istanbul Faculty of Medicine, Physiology Department [1],Halic University School of Nursing [2], Istanbul, Turkey.

burcuseker@gmail.com

In our previous experiments we have shown that vitamin E, which is an important antioxidant for endothelial cells, has protective effects on blood-brain barrier permeability in young and adult rats during experimentally-induced seizure. In the present study, we wanted to investigate whether the supplementation of vitamin E has any protective effect on the blood-brain barrier permeability in aged rats.

We used 23-24 months old male Wistar-albino rats. The experimental groups were divided into; I. control group (n=7), II. convulsion group (n=7), III. vitamin E (70 mg)+ convulsion group (n=7), IV. vitamin E (700 mg)+ convulsion group (n=7). Evans-blue dye was used as a blood-brain barrier tracer. Convulsions induced by intravenous pentylenetetrazole (100 mg/kg). Vitamin E was injected intraperitoneally 30 minutes before pentylenetetrazole injection. The brain tissue was removed and divided into right hemisphere, left hemisphere and cerebellum+brain stem and homogenized. Trichloroaceticacid was added into homogenized brain regions and centrifugated. Evans-blue amount in the supernatant was measured at 620 nm wavelenght. Arterial blood pressure was also recorded by a computer through a cannula from the arteria femoralis.

Unpaired t-test was used for statistical analyses. Rats in group II (convulsion group) showed a higher increase in blood-brain barrier permeability of all brain areas ($p<0,01$). 70 mg vitamin E did not provide a protective effect ($p>0,05$), 700 mg vitamin E provided a significant proteictive effect on cerebellum+brain stem regions ($p=0,01$). There was a significant increase in the arterial blood pressure after the pentylenetetrazole injection ($p<0,01$).

Our findings reveal that the protective effects of vitamin E on blood-brain barrier permeability is related to doses of vitamin E.

Key words: Blood-brain barrier,Evans-blue, Vitamin E

P74

The protective effect of nicardipine on iron-induced Purkinje cell loss in rat cerebellum

Kozan R, Bagirici F, Bostanci M.O, **Sefil F**.

Ondokuz Mayis University Faculty of Medicine, Department of Physiology 55139 Samsun Turkey.

fsefil@omu.edu.tr

There are many studies about iron-induced neuronal hyperactivity and cell death. However, high dose iron-induced neurotoxicity and effects of nicardipine on cerebellar Purkinje cell death have not been investigated up to now. The aim of the present study was to investigate the effects of nicardipine on the neurotoxicity induced by intracerebroventricular (i.c.v.) iron administration in rats. Animals were divided into three groups. Rats in iron (n=7) and iron+ nicardipine (n=7) groups received i.c.v. $FeCl_3$ (200 mM, 2.5 µl), while rats in control group (n=7) received the same volume of saline. Rats in iron+ nicardipine group also received i.c.v. 2 µl (1 mg/kg) nicardipine following $FeCl_3$ injection. All animals were kept alive for ten days following the operation and animals in iron+nicardipine group were intraperitoneally injected nicardipine (10 mg/kg/day) once a day during this period. After ten days, all rats were perfused intracardially and then sacrificed. Brain tissues were removed and standard histological techniques were performed. The total numbers of cerebellar Purkinje cells of all rats were estimated with unbiased stereological techniques. Data were analyzed by ANOVA and Post-Hoc Tukey Tests. The total Purkinje cell number in the cerebellum were found 301242 ± 9667; 209002 ± 7836; 265659 ± 8291 in control, iron and iron+ nicardipine groups, respectively. There were significant differences between all groups ($p<0.001$). Findings of the present study suggest that nicardipine probably protected Purkinje cells from iron-induced toxicity via blocking Ca^{++} influx into neurons.

Key words: Iron, Purkinje cell, cell death, nicardipine, stereology.

P75

Effects of methyl alcohol exposure on visual evoked potentials (VEP) and electroretinogram (ERG) in human (case report)

Seymen P [3], Aytac E [2], Ogullar S [1], **Seymen HO [1]**.

Istanbul University, Cerrahpasa Medical Faculty, [1] Department of Physiology, [2] 6th year medical student [3] T.C. Ministry of Health, Haydarpasa Numune Education and Research Hospital, Department of Internal Medicine, Istanbul, Turkey.

seymeno@istanbul.edu.tr

We faced Pseudo raki which has methyl alcohol, events in 2005 as the past. When pseudo raki is drunken liver damage, coma and death could occur. The nervous system functions and structure are suffered seriously. When the visual neuronal symptoms are observed after alcohol exposure, methyl alcohol toxicity recurs to the mind. The effects of ethyl alcohol on visual evoked potentials (VEP) and electroretinogram (ERG) have been investigated in several studies but our knowledge is limited about methy alcohol toxicity in human, because same standards could not be able to achieve at the same time. 2 cases of methyl alcohol toxicity were examined in Cerrahpasa Medical Faculty, Department of Physiology VEP-ERG Laboratory in 2005.

We have prepared this case report to share our results and conclusions on this topic. The VEPs recording procedure was performed according to the recommendations of the International Society for Clinical Electrophysiology of Vision (ISCEV). VEP-ERGs were recorded with MP150 Manager Version 3.7.3 software (Biopac Systems, Inc., Santa Barbara, USA). N_2 and P_2 latencies (millisecond), N_2-P_2 (microvolt) amplitudes were evaluated. The patients were sent to our laboratory after their emergency aids had been done. VEP-ERG of the patients were recorded immediately after methyl alcohol exposure. Both cases were called back for their second VEP-ERG recordings after 3 months later.

The latencies were longer and amplitudes were lower than normal in both eyes in VEPs of first patient. Both eyes of amplitudes were low in ERG. In second patient, P_2 wave was a bit longer and other parameters were normal in VEPs. Both eyes of amplitudes were low in ERG. 3 moths after methyl alcohol exposure, the P_2 wave was longer and other parameters were normal in VEPs of first patient. Right eye were normal and the latencies were low in ERG. In second patient, P_2 wave of VEPs was a bit longer and the other parameters were normal. Both eyes of amplitudes were low in ERG. Methyl alcohol exposure affected VEP-ERG pathogically but not specifically. It has been shown that degree optic neuropathy in methyl alcohol toxicity correlates with the abnormal electro physiologic changing. Methyl alcohol damages the other parts of the brain with visual neuronal system such as basal ganglia. All these could impair VEP-ERG. More studies which have wide number of cases with standardized methods are needed for exact foresights and data about methyl alcohol exposure.

Key words: Methyl alcohol toxicity, ERG, VEP

P76

The effects of NMDA receptor antagonist memantine on learning during the "kindling" procedure

Sahiner M, Erken G, 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. None of these studies considered the time period to be kindled. 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 1mg/kg/day for 7 days. Control, sham and memantine groups' data have been obtained. Experiments are going on and "Kindling" and "kindling"+memantine groups are being prepared for water maze learning procedure.

Our first findings has shown that memantine has a positive effect on water maze learning parameters. Escape latencies and path length are both slower in memantine group than in control and sham groups.

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. In the next stages of our study we hope to strength our hypothesis with new findings of memantine effects during early "kindling" procedure.

P77

Interactions between the theta and gamma oscillations in human EEG

Bayraktaroglu Z [1], Uslu A [1], Lenz D [2], Junge S [2], Busch N [2], Maess B [3], Ergen M [1], Demiralp T [1], Herrmann CS [2].

Istanbul University, Istanbul Faculty of Medicine, Department of Physiology, Turkey [1]; Magdeburg University, Department of Biological Psychology, Germany [2]; Max-Planck-Institute for Human Cognitive and Brain Sciences, Leipzig, Germany [3].

zbay@istanbul.edu.tr

Human subjects typically keep about seven items (plus or minus two) in short-term memory (STM). A theoretical neuronal model has been proposed to explain this phenomenon with physiological parameters of brain oscillations in the gamma and theta frequency range, i.e. roughly 30-80 and 4-8 Hz, respectively. In that model, STM capacity equals the number of gamma cycles (e.g. 25 ms for 40 Hz), which fit into one theta cycle (e.g. 166 ms for 6 Hz). The model is based on two assumptions: 1) theta activity should modulate gamma activity and 2) the theta/gamma ratio should correlate with human STM capacity. The first assumption is supported by electrophysiological data showing that the amplitude of gamma oscillations is modulated by the phase of theta activity. However, so far this has only been demonstrated for intracranial recordings. We analyzed human event-related EEG oscillations recorded in a memory experiment in which 13 subjects perceived known and unknown visual stimuli. The paradigm revealed event-related oscillations in the gamma range, which depended significantly on the phase of simultaneous theta activity. Our data are the first scalp-recorded human EEG recordings revealing a relationship between the gamma amplitude and the phase of theta oscillations, supporting the first assumption of the abovementioned theory. Interestingly, the involved frequencies revealed a 7:1 ratio. However, this ratio does not necessarily determine human STM capacity. Since such a correlation was not explicitly tested in our study, our data is not conclusive about the second assumption. Instead of theta phase modulating gamma amplitude, it is also conceivable that focal gamma activity needs to be downsampled to theta activity, before it can interact with more distant brain regions.

Key words: EEG, oscillations, theta, gamma, memory

P78

The effect of fluoxetine on behavioral despair and BDNF expression in the limbic system of rats in an animal model of depression precipitated by stress

Yildirim E [1, 3], Gozen O [1, 3], Eker OD [2], Dogan YH [1, 3], Koylu EO [1, 3], Eker C [2], Gonul AS [2,3], Pogun S [1, 3].

Ege Univ. School of Med. Depts. of [1]Physiology and [2]Psychiatry; and [3]Center for Brain Research, Izmir, Turkey.

emre.yildirim@ege.edu.tr

Brain-derived neurotrophic factor (BDNF) is implicated in depression. Antidepressants, increase monoamine neurotransmitters in the synaptic cleft, and are reported to increase BDNF levels in rat brain. The aim of the present study was to assess the effects of fluoxetine (FLX) in a rat model of depression precipitated by chronic stress. Adult male Sprague Dawley rats were used. Restraint stress was applied in glass cylinders, 60 min/day for 30 days. Drug treatment (5mg/kg/day FLX or 1 ml/kg Saline) began on the 8th day of stress and continued for 23 days. During the last 2 days of treatment, stress was discontinued; rats were tested in the Porsolt Forced Swim Test (FST). BDNF expression was measured by immunocytochemistry in the amygdala and prefrontal cortex. Data were evaluated by multifactorial ANOVAs and t-tests.

In FST, FLX decreased freeze duration and increased swimming, thereby preventing despair, as expected. Stress elevated BDNF expression in both regions ($p<0.05$) in saline treated animals. FLX increased BDNF expression in rats not exposed to stress, but decreased expression in stressed animals. Overall, our results indicate that FLX has a positive effect in preventing behavioral despair precipitated by previous stress exposure. However, the clinical efficacy of FLX reported in depression may be independent of BDNF.

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Key words: Depression, Forced Swim Test, Fluoxetine, Brain-derived Neurotrophic Factor (BDNF), Amygdala, Prefrontal Cortex

P79

Effects of ketamin application at a sub-anesthetic dose for 5 days on emotional learning process

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

Istanbul University, Faculty of Literature, Dept.of Psychology [1], Istanbul University, Faculty of Medicine, Dept. of Physiology [2], Istanbul, Turkey.

ertanyurdakos@mynet.com

Ketamin, a non-selective NMDA reseptor antagonist, is known to induce psychosis-like symptoms. This study is conducted to find out whether i.p ketamin application at a sub-anesthetic dose models malfunctioning state of emotional memory, which is a common observation in schizophrenic individuals, by using Porsolt, open field and holeboard tests.

Male rats of Wistar strain weighing 230 to 250gr. were used in this study. Experimental group (n=9) was injected with 35mg/kg i.p ketamine for 5 days which was followed, in turn, by open field, hole board and Porsolt swimming tests starting 15 days after the last day of injection. Each of these tests were seperated from one another by 24 hours. Control group was injected with 0,25ml i.p saline for 5 days which then followed by the same procedure applied to the experimental group. Results are analysed with Mann-Whitney U and paired-samples t-tests via SPSS.

Time spent immobile in both open field and holeboard tests were significantly shorter for the experimental group compared to control group; there were no statistically significant differences on any of the other parameters in both tests fort he experimental group. 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 deterrioration in emotional learning as observed in schizophrenic individuals.

P80

Effects of prenatal stress on depression and anxiety related behaviors in rats

Eren-Kocak E [1], Ayhan Y [2], Rezaki M [2], Dalkara T [1, 3].

Hacettepe University Institute of Neurological Sciences and Psychiatry[1], Faculty of Medicine Department of Psychiatry[2], Faculty of Medicine Department of Neurology[3], Ankara, Turkey.

eminedr@yahoo.com

There is evidence suggesting that maternal exposure to stress during pregnancy can lead to depression and anxiety-related behaviors later in life. Accordingly, prenatal stress has been proposed as a risk factor for several psychiatric diseases seen in adulthood. We studied the behaviors and weight of male rats subjected to prenatal stress. Pregnant rats were forced to swim in cold water at 22 centigrade degrees for 10 minutes daily beginning from the 10th day of pregnancy until parturition. Depression and anxiety related behaviors of the male offsprings were evaluated on the 8th month. Behavioral despair as a measure of depression was evaluated by Porsolt's forced swimming test whereas anxiety was assessed by both open field and social interaction tests. Each rat was weighted at 2nd, 6th and 8th months. There were no differences in any of the behavioral measures, however, the prenatal stress group weighted significantly less than the control group at all three time points. Prenatal stress and control groups weighted 161 gr (SD=21) and 187 gr (SD=16) respectively at the 2nd month ($p<0.0001$) whereas at the 6th month they weighted 318 gr (SD=21) and 340 gr (SD=25), ($p=0.012$). Finally at the 8th month stress and control groups weighted 374 gr (SD=28) and 403 gr (SD=28) respectively ($p=0.005$). These findings suggest that exposure to this magnitude of stress in prenatal life causes lower weigths in offsprings of the stressed mothers but does not cause any alterations in depression and anxiety related behaviors. This last finding is in accordance with some studies in the literature reporting that prenatally stressed male rats do not show any differences in behavioral despair and open field tests than control animals in contrast to female rats.

Key words: Prenatal stress, Depression, Anxiety, Body weight, Social interaction

P81

Screening hypertensive patients with psychiatric scales

Uresin Y, Kiziltan E, Sabirli S, **Uslu ZG**.

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

zguslu@istanbul.edu.tr

Cardiovascular disease and depression are common diseases resulting loss of quality of life. They are found together more frequently than expected alone. There are both clinical reasons and, physiopathological mechanisms as they partially share same biochemical processes. In this study, the randomly selected records of hypertensive patients followed and treated in İstanbul Faculty of Medicine, Department of Pharmacology and Clinical Pharmacology Research Policlinics assessed in order to determine the frequencies of psychiatric comorbidities.Frequency analysis were perfomed on sociodemograpic data and results obtained by psychiatric rating scales, Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I) for DSMIV, Hamilton depression rating scale (HDRS), Hamilton anxiety rating scale (HARS) and the Sheehan disability scale (SDS). For the preliminary invastigation records of seventy two hypertensive outpatients were examined. Patients were predominantly woman with the ratio of 81.9%. Considering the education level 32.4% were primary school, 21.1% secondary school, 21.1% high school and 18.3% university graduate, 7% had no education. 23.6% of patients were working, 76.4% were not working because of other reasons, there was not any patients who did not work because of the illness. According to their economical states 1.4% of the patients were in very high income group, while 11.1% had high, 73.6% had moderate and 13.9% had low income. When the paitents evaluated using SCID-1 psychiatric scale, 21.1% diagnosed as major depression. Past major depression was present in %33.3. Past mania was diagnosed in 1.4%, no patients were diagnosed as mania at the time course which the evaluations performed. The frequency of dystimia was 11.6%. When the alchohol and substance usage examined 4.3% of the patients were diagnosed as addicted. Panic disorder was present in 16.9% of patients. While social phobia was seen in 2.9%, the frequency of patients diagnosed as general anxiety disorder was 5.9%. Specific phobia was determined in 15.7% of the patients. In the 14.7% of the patients participated in the study current illness does not cause any disability in work subscale of Sheehan Disability Scale, while 64.7% had mild and 20.6% moderate disability. In social life subscale, 23.5% had no, 66.2% had mild, 8.8% moderate and 1.5% severe disability. In family subscale, the ratio of patient who had no disability was 20.6%, mild disability was 64.7%, moderate 13.2% and severe disability was 1.5%. As a result, there is a need of clinical research to explain the relationship between depression and hypertension and compare the data with normal population. Thus, more attention is needed for hypertension in neuroscience.

Key words: Hypertension, depression, psychiatric rating scale, anxiety, retrospective studies

P82

The effects of selenium toxicity on the conduction velocity distribution of isolated rat sciatic nerve

Ayaz M [1], Kiziltan E [2], Bariskaner H [3], Tuncer S [1], Dalkilic N [1].

Selcuk University, Meram Medical Faculty, Biophysics Department Konya, turkey [1]; Zonguldak Karaelmas University, Medical Faculty, Biophysics Department Zonguldak, Turkey [2]; Selcuk University, Meram Medical Faculty, Pharmacology Department, Konya, Turkey [3].

dalkilic@selcuk.edu.tr

Action potential is the basic information unit within the central nervous system. The linear summations of action potentials originating from each active nerve fiber make up Compound Action Potential (CAP). The analysis of CAP, which is recorded from peripheral nerve evoked by supra-maximal stimulation, can be successfully used to determine the functional state of that particular nerve, to diagnose some nerve disease, and to assess conduction velocity distribution. Present study demonstrates the adverse effects of sodium selenite toxicity on the conduction velocity of isolated rat sciatic nerve fiber. After proper isolation of rat sciatic nerves they were transferred into the temperature controlled standard organ bath. All the recordings were performed in modified Krebs solution at 37 ^{o}C which was gassed with 95 %O_2 and 5 %CO_2 mixture. Stimulations of sciatic nerves were done from the proximal end and the recordings were done from the distal end by a suction electrode method. To test the toxic effects of sodium selenite on the sciatic nerve fibers, cumulative doses ranging from 10^{-7} M -10^{-3} M were used. Recordings were performed with an custom made software (BiosigW) and

stored on a computer harddisk for further analysis. Preliminary results of the experiments have shown that all the tested concentrations of the sodium selenite have toxic effect on rat sciatic nerve fibers. It was observed that the most significant alteration was on the conduction velocity and on the amplitude of CAPs.

Key words: sciatic nevre, conduction velocity, compound action potential, sodium selenite, toxicity

P83

A high precision low cost system for evaluating finger tapping tasks

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

Karaelmas University, School of Medicine, Department of [1] Biophysics, [2] Anatomy, Zonguldak, Turkey, [3] Hacettepe University, School of Medicine, Department of Physiology, Ankara, Turkey.

cagbarut@yahoo.com

Finger-tapping test is extensively employed to assess motor asymmetry in brain damaged patients and also to study the relationship between handedness and performance in normal subjects. The aim of this study was to develop a computer based finger-tapping system that could provide quantitative measures of finger-tapping performance. The system is designed to be used in a standard personal computer without the need of any other hardware. The software is written in Borland Delphi® 6.0 for Microsoft® Windows 98® or higher operating systems. Beginning with the Pentium® processor, it could be possible to access a time-stamp counter. The time-stamp counter is a 64-bit machine specific register, which is incremented by every clock cycle, and keeps an accurate count of every cycle that occurs on the processor. By using a computer with 1 GHz processor speed, it is possible to reach a high precision time resolution of 1 μs. This user friendly software also enables to detect the reaction time upon a visual/auditory stimulus and to perform mental rotation test. Our future prospects for the system are to improve it with various tools such as synchronized recording of electromyography, tapping force monitoring, monitoring of finger angle and the response to different stimulus parameters by adding appropriate hardware and procedure.

Key words: finger-tapping, handedness, software, performance, method

P84

Contrast perception in glaucoma

Guclu B [1], Utine CA [2], Perente I [3], Farell B [4]

Biomedical Engineering Institute, Bogazici University[1], Turkiye Hospital [2], Beyoglu Eye, Research and Training Hospital [3], Istanbul, Turkey; Institute for Sensory Research, Syracuse University [4], Syracuse, NY, USA.

burak.guclu@boun.edu.tr

We tested perceived contrast in 5 normal and 5 glaucomatous subjects by using modified simultaneous-contrast stimuli. Each stimulus consisted of a target circle with randomized diameter (0.5, 2.5, 4.5, 6.5, 8.5, or 10.5 cm) and lightness (25, 50, or 75 % luminance-calibrated gray level) appearing on either a black or a white square (side length: 11 cm). The experiment was balanced with respect to the stimulus parameters and the subjects judged the gray level of the target circle in each condition by matching it to one of 21 standard grays appearing on cards arranged by decreasing luminance. Matching errors were recorded and Michelson contrast values of perceived gray levels were calculated. Two-factor ANOVA with 5 replications showed no interaction between target size and luminance. There was no significant effect of target size for either normal or glaucomatous subjects. The main effect of input contrast was significant, as expected. All subjects overestimated contrast decrements (gray target on white background). Normal and glaucomatous subjects did not differ significantly in this perceived enhancement of contrast decrements (two-sample t-tests: $p > 0.28$). However, they did differ in their perception of contrast increments (two-sample t-tests: $p < 0.03$), except for the largest increment. Normal subjects enhanced contrast increments at low contrasts (two-sample t-tests: $p < 0.001$), whereas glaucomatous subjects showed no enhancement. When matching errors are directly compared, both normal and glaucomatous subjects perceive targets on white backgrounds as darker than the veridical gray level. Normal subjects perceive targets on a black background as lighter than veridical, but not fully symmetric with the effect on white background. However, glaucomatous subjects still match darker than the veridical gray level to targets on black backgrounds, which suggests an assimilation effect. In every condition and for both subject groups, a robust simultaneous-lightness-contrast effect was observed overall, even though complementary test stimuli with black and white backgrounds were not presented simultaneously.

Key words: simultaneous contrast, lightness constancy, contrast enhancement, assimilation, Michelson contrast

P85

Comparison of software packages used for EEG source localization

Sengul G [1], Baysal U [1], Yagcioglu S [2] Ungan P [2].

Hacettepe University, [1] Faculty of Engineering, Department of Electrical & Electronics Engineering, [2] Faculty of Medicine, Department of Biophysics, Ankara, Turkey.

sengul@ee.hacettepe.edu.tr

Source localization, that can be defined as the determination of positions and amplitudes of electrical dipole sources by using bioelectromagnetic field data from scalp measurements, is widely used in order to understand basic mechanisms of cognitive processes and better characterization of pathologies in the brain. However, it is an ill-conditioned inverse problem because the small errors in EEG data or patient-specific volume conductor model introduce relaticely large localization errors. For the accurate localization; one must use EEG with small noise, patient-specific head model (electrot locations and realistic geometry) and patient-specific electrical parameters (resistivities) of the tissues. In addition to this, the mathematical computations required for the inverse problem solutions must be done fast and with small errors by using some software. There are several software packages used for for the solution of bioelectromagnetic forward/inverse problem.

In a typical source localization procedure, first the forward problem is solved by assuming a known dipole position and strength. The measured EEG data and results obtained from the forward solution are compared and the dipole parameters are updated to make the difference small. Although there are some software packages available for EEG analysis and source location, there are no study in the literature that compares usability and performance of these software packages.

In this study, two different software packages developed for bioelectromagnetic problem solution are compared in the following aspects: usability of EEG data gathered from different EEG systems and electrode locations in different formats, processing and segmentation capabilities of MRI data gathered from high-resolution MRI systems, the capabilitiy of creating realistic head model from MRI data, the integreability of patient-specific resistivity values to the software packages and usability of the softwares by the non-technical personnel. The functionality and performance of the softwares are evaluated also.

As a result of this study; it has been observed that both of the software packages are capable of using patient-specific resistivity values and electrode locations can be integrated to the system easily. Both softwares have some menus for creating realistic head models and by using these menus realistic head models can be obtained easily. However, one of the packages can use 42 different EEG data formats directly while the other uses only a small number of EEG data formats. For the second package, the unknown file formats are entegrated to the system assuming the data to be an ASCII file and the other parameters are entered manually. Another difference between the two software packages is the file format type used to store 3-D electrode locations. In this study a method is developed for the conversion of file formats used for storage of electrode locations between two software packages. In a future study it is planned to compare the performance of the sofware packages in forward and inverse problem solutions.

Key words: source location, EEG, forward/inverse problem, neuroscience, volume conductor model.

P86

Atypical meningioma: case report

Bahadir B [1], Dogan Gun B [1], Kertis G [1], Kalayci M [2], Ozdamar SO [1].

Zonguldak Karaelmas University, Faculty of Medicine, Department of Pathology [1], Neurosurgery [2], Zonguldak, Turkey.

burakbahadir@yahoo.com

Tumors derived from meningothelial cells are the most common non-glial intracranial neoplasms of the central nervous system. Although histologic subtypes of meningiomas are well established, classification of meningiomas into benign, atypical and anaplastic groups has been inconsistent. The recent grading scheme proposed by World Health Organization in 2000 suggested histologic criteria primarily based on mitotic counts.

Magnetic resonance imaging of a 72-year-old male patient presented with stupor, headache, urinary incontinence, nausea and vomiting revealed a right temporoparietal mass consistent with meningioma. Histologic examination of the 8x5x4 cm tumoral mass demonstrated hypercellular areas composed of fusiform cells with indistinct cell borders and prominent nuclei growing in a patternless fashion and dispersed small cells with sparse cytoplasm. Three mitotic figures per 10 high-power fields were noted. Neighboring typical areas of meningioma characterized by clusters of syncytial cells occasionally forming whorls were also seen. Immunohistochemically, vimentin and epithelial membrane antigen were positive whereas no expression of S100 and glial fibrillary acidic protein were observed. The case was considered and reported as an atypical meningioma.

Atypical meningioma is an uncommon tumor with a more aggressive behavior and a higher rate of recurrence than its benign counterpart. The extent of resection and tumor grade appears as the major determinants for recurrence. On the other hand, the subjective nature of some of the criteria of the current World Health Organization classification may allow substantial interobserver variability. Therefore, the criteria should be taken into consideration while grading a meningioma beyond its diagnosis, and previous meningiomas diagnosed before application of the World Health Organization criteria should be reevaluated to generate a basis for the forthcoming studies.

Keywords: meningioma, atypical meningioma, immunohistochemistry

P87

The normal limits of ligamentum flavum in healthy subjects

Safak A [1], Is M [2], **Sevinc O** [3], Barut C [4], Eryoruk N [3], Erdogmus B [1], Gezen F [2].

Abant Izzet Baysal University, Duzce School of Medicine, Departments of Radiology[1], Neurosurgery[2], and Anatomy[3], Duzce, Turkey; Zonguldak Karaelmas University, School of Medicine Department of Anatomy[4] Zonguldak, Turkey

ozdemirsevinc2@yahoo.com.tr

In many studies, ligamenta flava were evaluated according to the pathological and clinical perspectives. But the normal limits were not widely studied. We designed an anatomy study of the ligamentum flavum (LF) using magnetic resonance imaging, to determine the normal limits of the thickness of LF in lower lumbar levels of the spine.

Sex, age and thickness of totally 1340 LF at L4-L5 and L5-S1 levels without pathology were determined in magnetic resonance images.

Three hundred thirty five patients (161 males [48%] and 174 females [52%]) in the age group from 13 to 82 years were screened. There were no significant differences in LF thickness with respect to gender ($p>0.05$). Age showed no correlation with the thickness of LF. The right LF of L4-L5 and L5-S1 levels were thicker than the contralateral sides and the differences were statistically significant ($p<0.05$). Furthermore, the bilateral LF thickness at L5-S1 were more than the corresponding sides at L4-L5 levels and the differences were statistically significant ($p<0.05$).

As a result, LF is an important anatomical structure which might cause low back or leg pain. Therefore, the thickness of LF should be measured and evaluated carefully in the case of spinal stenosis.

Key words: Ligamentum flavum, thickness, Magnetic Resonance Imaging, normal range, spine

P88

Retinoic acid isomers protect hippocampal neurons from apoptosis induced by amyloid beta-peptide

Sahin M [1], Berker Karauzum S [2], Perry G [3], Smith MA [3], **Aliciguzel Y** [1].

Akdeniz University, Faculty of Medicine, Department of Biochemistry[1] and Department of Medical Biology and Genetics[2], Antalya- Turkey; and Institute of Pathology[3], Case Western Reserve University, Cleveland, Ohio USA

yakup@akdeniz.edu.tr

The aim of this study was to investigate whether apoptosis which is induced by amyloid beta-peptide 25-35 (Abeta25-35) is prevented by retinoic acid (RA) isomers in different concentrations in cultured primary hippocampal neurons or not. All-trans retinoic acid (t-RA), 9-cis retinoic acid (9-c-RA) and 13-cis retinoic acid (13-c-RA) were used as retinoic acid isomers. Apoptotic nuclei formation characterized by condensed chromatin and fragmented DNA was monitored in neurons treated with or without retinoic acid 24 hours after treatment with Abeta.

Abeta increased the percentage of apoptotic neurons from 16 % in controls to 81 % ($p<0.01$). t-RA in concentrations of 0.01, 0.1 and 1 uM decreased the percentages of apoptotic neurons from 81 % in Abeta treatment to 33 %, 25 % and 21 %, respectively. 9-c-RA at the same concentrations decreased the percentages of apoptotic neurons from 81 % in Abeta treatment to 35 %, 26 % and 23 %, respectively. Similarly, 13-c-RA at the same concentrations decreased the percentages of apoptotic neurons from 81 % in Abeta treatment to 38 %, 28 % and 24 %, respectively. ($p<0.01$ for all concentrations and isomers).

Our results suggest that retinoic acid isomers may play an important role in protection neurons from Abeta25-35 –induced apoptosis.

Keywords: Apoptosis, all-trans retinoic acid, 9-cis retinoic acid, 13-cis retinoic acid, amyloid-beta, hippocampal neurons

P89

The effects of sodium valproat and SNP on penicillin induced epilepsy in rats

Nacar T, Yildirim M, Ayyildiz M, Agar E.

Ondokuz Mayis University Medical Faculty, Department of Physiology 55139 Samsun, Turkey

tnacar@omu.edu.tr

Epilepsy is a common nervous disease and affects approximately 1% of world population. Epileptic seizures occur when a group of neurons begin to discharge together abnormally. Factors causing abnormal discharges include trauma, stroke, bleeding, hypoxi, anoxi, vascular malformations, infection, and metabolic disorders. But it is impossible to find the etiology in nearly half of the patients. We have investigated the effect of Sodium Nitroprussid (SNP), a nitric oxide donor, on sodium valproate (Na-Valproate) which was used as antiepileptic drug, in the present study.

Eighteen adult female Wistar Albino rats weighing 175-225 gm were used in this study. After the anesthesia with 1,25 gr/kg urethan, their cranium were opened. Two ball electrodes were placed on left somatomotor cortex. Penicillin (500 IU) were injected intracortically (i.c.) to induce epileptiform activity in the rats. Na-Valproat (300 mg/kg, i.p) and SNP (6mg/kg, i.p) were injected to the animals. In addition, SNP (6 mg/kg, i.p) was administered in one group of animals 30 minutes before Na-Valproate (300 mg/kg) injected. ECOG records were analyzed and evaluated statistically.

Na-Valproate suppressed penicillin-induced epileptic activity. SNP significantly decreased the frequency of epileptiform activity from 34.4 spike/minute to 24.8 spike/minute and 11.2 spike/minute in the SNP and SNP + Na-Valproate groups, respectively ($P<0.05$).

The present study was the first, in which the interaction between SNP and Na-Valproate on the penicillin-induced epileptiform activity in the rat has been investigated. It can be concluded that nitric oxide potentialized the anti-epileptic effect of Na-Valproate in penicillin-induced epilepsy in the rat.

Key words: Sodium Valproate, Epilepsy, SNP, Nitric Oxide, Penicillin Model

P90

Antidromic potential signals and the receptor function

Purali N.

Hacettepe University, Medical Faculty, Department of Biophysics 06100 Sihhiye Ankara Turkey

npurali@hacettepe.edu.tr

Concept of dynamic polarization has conventionally been used to describe the sequential development of the neuronal function. Accordingly, receptor or synaptic currents, generated in the dendritic region, evoke receptor or generator potential, spreading passively to soma. Eventually, action potential, generated in axon hillock, propagates in the direction of the axon to the presynaptic site. However, the action potential has a significant magnitude which can passively propagate from the axon hillock through the soma and to the dendrites. In the present work the consequences of the antidromic action potentials in the developing receptor responses has been investigated comparatively in the rapidly and the slowly adapting stretch receptor neurones of the crayfish. The receptor responses were recorded when the driving force of the current stimulus was constant and when the on line recorded membrane potential was allowed to influence the driving force for the receptor current. In the slowly adapting neuron membrane potential reduced the magnitude of the driving force for the receptor current, and kept the receptor responses within the active range even when excessive amplitudes of permeability levels were used. Thus, irrespective of stimulus magnitude, adaptation of the impulse response was not observed. In the rapidly adapting neuron, membrane potential substantially influenced the adaptive properties of the impulse responses. Membrane potential has been shown to modulate the receptor response so that the rapid adaptation is facilitated. Results were compatible with those calculated in a digital model representing the rapidly and the slowly adapting neurones. Thus, it was concluded that the antidromic action potentials should be considered as an important mechanism contributing to the adaptive properties of the receptor neurones.

Keywords: Antidromic action potential, stretch receptor neuron, neuronal modelling.

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10th NATIONAL ANATOMY CONGRESS

with international participation

September 6 – 10, 2006

Bodrum

TURKEY

The 10th National Anatomy Congress with international participation, organized and hosted by the Hacettepe University Faculty of Medicine Department of Anatomy and the Turkish Society of Anatomy will be held in Bodrum, on September 6–10, 2006.

Our aim is to present to our colleagues a congress that together with its scientific and social programs, will be one to be remembered for many years to come. We are planning to hold the congress fee under 100 Euro and would like to thank all participants in advance for giving us the honor of hosting such a congregation.

Final deadline for the abstracts will be June 15, 2006; and the accepted English summaries will be printed as a supplement of the NEUROANATOMY journal which is scanned by many international scientific indexes [http://www.neuroanatomy.org]. Awards will be given to selected oral presentations and posters. The fact that this congress is organized together with the Turkish Society of Anatomy will make it possible to discuss Education in Anatomy for a duration of half a day.

Congress language will be Turkish and English. Colleagues who wish to take part in the scientific evaluation boards should contact us by March 31, 2006 at congress@anatomy.web.tr e-mail address.

With the hope of getting together in a very pleasant congress in Bodrum...

Contact Information
10th National Anatomy Congress
Hacettepe University Faculty of Medicine
Department of Anatomy 06100, Ankara–TURKEY
+90 312 305 21 01 (telephone)
+90 312 310 71 69 (fax)
congress@anatomy.web.tr
http://www.anatomy.web.tr

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M. Mustafa Aldur, MD, PhD
Hacettepe University
Faculty of Medicine
Department of Anatomy
06100 Ankara–Turkey
editor@neuroanatomy.org

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