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ABSTRACT BOOK

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Neuroanatomy is a journal in English, and publishes original research articles dealing with neuroanatomical sciences in animals (vertebrates and invertebrates) and humans. Papers in any of the following fields will be considered: molecular, cellular, histological and gross anatomical studies on normal and/or abnormal experimental animals and humans. Functional, morphological, biochemical, physiological and behavioral studies are considered if they include neuroanatomical analysis. Reports on techniques applicable to the above fields are also considered. Occasional reviews on subjects selected by the Editors will be published. Miscellaneous items, including essays, book reviews and commentaries may also be published on approval of the Editorial Board.

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This supplement of *Neuroanatomy* is dedicated to Professor Atila Muftuoglu.
We are deeply sorry for his sudden death.
Dr Muftuoglu will be in our thoughts and prayers.
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The implication of membrane channels and receptors in the generation of the epileptic discharges was suggested as early as in the Sixties, when high-frequency action-potential discharges superimposed to a sustained depolarising envelope were recorded for the first time from neurons belonging to an epileptogenic aggregate. This type of discharge, that was christened paroxysmal depolarising shift (PDS) by Matsumoto and Ajmone Marsan (Exp Neurol, 80, 286, 1964), was thought to be related to a dysfunction of ion-channel-dependent excitable mechanisms. Only recently, however, direct demonstrations of genetically determined ion channel defects resulting in epileptogenesis have been provided.

In 1995 Phillips et al. (Nature Genetics, 10, 117, 1995) showed evidence of a mutation in the CHRNA4 gene coding for a subunit nicotinic receptor of acetylcholine in an Australian family affected by autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE). This observation suggested that other idiopathic epilepsies of assumed genetic origin might also fall in the field of channelopathies, as it was demonstrated later. We now know at least four different epileptic phenotypes: "benign neonatal familial convulsions" (BNFC), "generalised epilepsy with febrile seizure plus" (GEFS+), "severe myoclonic epilepsy of infancy" (SMEI) and ADNFLE, which are due to genetically-related changes in K1 or Na+ channel structures or in GABA and acetylcholine receptors, and there is indirect evidence that Ca2+ channelopathies might be responsible for a fifth phenotype ("absence-epilepsy").

The relevance of recent data on epileptogenic channelopathies for understanding epilepsy genetic mechanisms and developing antiepileptic drugs is clearly demonstrated by studies on Na+ channels. The current flowing through rapidly-inactivating Na+ channels, called transient Na+ current (INaT), is the main component of the Na+ current. A small portion of Na+ channels escaping rapid inactivation is responsible for the persistent fraction of Na+ current (INaP).

Although comparatively weak, this current is functionally important in that it is virtually able to support high-frequency phasic discharges, such as those typically observed in neuronal populations of epilepsy foci. It is therefore particularly interesting to demonstrate that mutations related to GEFS+ involving β1 and α subunits of the Na+ channel cause defective inactivation of Na+ channels. This finding offers a pathogenetic explanation of this genetic epilepsy.

Finally, evidence of the possible epileptogenic role of a Na+ channel dysfunction is consistent with the knowledge that many antiepileptic drugs of proven clinical efficacy act on the Na+ current in a use- and voltage-dependent way, i.e. the higher the cell discharge frequency and the broader the neuronal membrane depolarisation, the greater the efficacy. This useful selective mode of action is further increased by the specific effect of some antiepileptic drugs (phenytoin, valproic acid, lamotrigine, and topiramate) on the persistent fraction INaP.

K2 Electrophysiological explorations of the brain’s response to novelty
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Allocation of attention to novel events facilitates adaptation to a rapidly changing environment and is likely to have played a critical role in the evolution of the mammalian brain. This bias toward responding to novelty may be one of the driving forces in primate cognitive development and learning, and may contribute to sustaining intellectual abilities as individuals get older. Novelty processing involves a complex set of neurobehavioral functions that includes orienting attention, allocating additional attentional resources, directing investigatory activity, and assessing the meaning and impact of a novel event. Event-related potentials (ERPs) have been a major tool for investigating how the brain responds to target and novel events. These patterned voltage changes in the ongoing electroencephalogram, time-locked to cognitive events, have exquisite temporal resolution of underlying cognitive processes.

The focus of this lecture will be on cortical components of the cerebral network that subserves the processing of novel events. We will emphasize results from our ERP laboratory and try to place them in the broader context of data derived from other labs.

The lecture will address the following major issues: 1) Significance of the topic of novelty processing to cognitive neuroscience and clinical work; 2) Brief overview of ERP methodology; 3) P3 ERP component: standard methods and conventional view; 4) Variant of the novelty oddball paradigm—linking the novelty P3 to viewing duration and exploratory behavior; 5) Central role of the prefrontal cortex in the allocation of attention to novel events; 6) Contribution of the parietal lobes—updating internal models of the environment.

We will review data which supports the following ideas: The orienting response and its cerebral correlate, the novelty P3 component, is part of the decision making processes that regulates the allocation of attention to stimuli. The novelty P3 may serve as a "curiosity switch," signaling that an event is worthy of further exploration. The prefrontal and posterior parietal regions are involved in the voluntary allocation of attention to novel events and comprise two nodes of a network for responding to and processing novelty. Injury to this network is indexed by a reduced novelty P3 amplitude, which is tightly associated with diminished attention to novel stimuli.

The posterior parietal lobes appear to be critically involved in the voluntary allocation of attention to infrequent stimuli regardless of their degree of novelty. However, parietal lobe injury leads to less of a disruption of the processing of novel stimuli than target stimuli. Consistent with other theories about the role of the parietal cortex in attention, the posterior P3 response may be indexing the neural activity involved in updating the parietal lobe’s highly processed model of the environment. The more that a stimulus is unusual, unexpected, or difficult to integrate into the existing model, the larger the amplitude of the posterior P3 component in response to novel events.

The prefrontal cortex plays a major role in determining the allocation of scarce processing resources based on the potential significance of an event and the context in which it occurs. The prefrontal cortex appears to be particularly engaged by stimuli that are ambiguous, for which there are no clear pre-determined responses. Damage to the prefrontal cortex results in a greater disruption of response to novel stimuli than to designated targets. Injury to the prefrontal cortex results in a failure to appropriately allocate attention and resources to environmental events. This disruption is likely to contribute to the behavioral disengagement and apathy observed after frontal lobe damage.

K3 Brain, behaviour and evolution
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I will present the outcomes of my long time studies related to comparative brain topography. I have studied in parallel the brain of experimental animals and humans in order to establish the correspondences (homologies) between them. I used the distribution of chemicals (chemoarchitecture) to obtain clues in homologies across mouse, rat, monkey, human and now bird. The brainstem of mammals is largely (95%) homologous. The cortex is homologous (close to 100%) across primates, but largely heterologous between primates and rodents. In the brainstem, birds have a far larger degree of homology with mammals than currently believed, but their pallium is a mystery.
K4
Role of NMDA receptors in axonal and dendritic development
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N-methyl-D-aspartate (NMDA) receptors play an important role in synaptic communication. In particular, associative events underlying neural plasticity, such as long-term-potentiation (LTP), long-term-depression (LTD), involve NMDA receptor activation. Aside from plasticity associated with learning and memory, newly formed synapses in the developing nervous system are also consolidated via activation of NMDA receptors. In this context, development and sculpting of axonal terminals and postsynaptic dendrites require NMDA receptor activation in systems utilizing glutamate as the main neurotransmitter. In recent years, interactions and signaling between postsynaptic density proteins, Eph proteins and cell adhesion molecules, and NMDA receptors have been underscored in morphological differentiation of synapses. This presentation will evaluate a series of electrophysiological and morphological findings on differentiation and patterning of developing presynaptic axon arbors and postsynaptic dendritic trees in mice with genetic impairment of the essential subunit of NMDA receptors, the NR1 gene.

K5
Stress and autonomic nervous system: selective activation of the sympatho-adrenal system by various stress
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The transmission of signals through particular sympathetic ganglia and to the adrenal medulla is an essential part of several important physiological processes. It might be anticipated that not all of the process controlled by sympathetic neurons by or circulating catecholamines would normally be activated concurrently; rather, one or another particular process should be activated in response to the body’s particular needs at any moment, by facilitating transmission through the relevant ganglia and accelerating impulse flow along post-ganglionic sympathetic nerves originating in these ganglia. If certain portions of the sympathetic nervous system are, in fact, capable of being activated independently of other portions, then one might anticipate that the mechanism within the central nervous system that control various sympathetic functions should also exhibit some degree of specificity. That is, distinct neurons and tracts in the brain and spinal cord, utilizing particular neurotransmitters, should, when activated, accelerate the flow of impulses through the appropriate ganglia but not others. This view of sympathetic nervous function contrast with the belief that a uniform, centrally mediated sympatho-adrenal activation occurs in response to stress and other stimuli, and causes increased impulse traffic through all portions of the sympathetic nervous system, but is supported by some electrophysiologic studies on patterns of sympathetic outflow.

It is well-established fact that the activity and the amount of tyrosine hydroxylase in the adrenal gland and in the sympathetic ganglia controlled by the impulse flow from the central nervous system through the preganglionic cholinergic nerves. The activity of this enzyme in the adrenal gland and in the sympathetic ganglia has been shown to rise following treatments thought to accelerate the firing of its preganglionic cholinergic neurons and remained increased for few days; hence, tyrosine hydroxylase activity within a ganglion or adrenal is a convenient “integral” of the impulse flow to the tissue during the few days preceding sacrifice. In early studies, by measuring tyrosine hydroxylase activity in the adrenal medulla and selected sympathetic ganglia (such as in superior cervical, stellate and coeliac ganglia), we demonstrated that the peripheral sympathetic system responds selectively to various stimuli and drugs, which are acting in the central nervous system. In my present presentation, I will be focused on effects of various stressful situations (hypoglycemic, hemorrhagic hypoxia, hypercapnic, immobilization, social isolation etc.) various stressfully condition on tyrosine hydroxylase activity in adrenal gland and various sympathetic ganglia. Rats were exposed to stress for 3 to 4 days and then they were killed 24 hours after the last treatment; adrenal gland and the sympathetic ganglia were dissected and assayed for tyrosine hydroxylase activity. Tyrosine hydroxylase activity increased in adrenal gland but not in any of the sympathetic ganglia in response to hypoglycemic stress. Under immobilization stress, tyrosine hydroxylase increased in adrenal gland and mainly in the lumbar sympathetic ganglia. Hypercapnia caused to increase tyrosine hydroxylase activity mainly in the thoracic sympathetic ganglia, where as hypoxia increased tyrosine hydroxylase only in the adrenal gland. These data show that the increase in impulse flow from central nervous system to the sympatho-adrenal system is not uniform in response to stress and the site of activation of the sympatho-adrenal system varies depending upon the type of stressfully situation.

PANELS

PN1
EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE
Moderator : Hakan Gurvit
Panelsists : Hakan Gurvit, Kirk Daffner, Gorsey Yener

The electrophysiological characterization of early Alzheimer's disease with event-related potentials
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Alzheimer’s disease (AD) is characterized by a progressive cognitive decline resulting in global dementia. The most consistent electrophysiological findings include a prolonged latency and decreased amplitude of P300 in oddball paradigms. However, these findings remain subtle and relatively undetectable in the early stages of the disease. In this study, P3b and P3a potentials in auditory oddball and novelty paradigms were measured from 15 healthy volunteers and 22 patients with early to moderate stage AD (11 early: GDS 3 and 4 and CDR 0.5 and 1, 11 moderate: GDS 5 and CDR 2) in order to look for a more sensitive marker of early AD. All patients, who were referred from the Behavioral Neurology and Movement Disorders unit of the Department of Neurology had recently been assessed with Mini Mental State Examination (MMSE) for the severity of global cognitive impairment, and with Global Deterioration (GDS) and Clinical Dementia Rating Scales (CDR) for staging the disease. In the oddball paradigm the differences in P3b amplitudes and latencies between the AD groups and the control group were not statistically significant. P3a to novel stimuli showed an overall latency prolongation in the AD groups (the latency prolongation did not reach statistical significance in the early group as compared to the controls, but in the moderate group it was significantly prolonged as compared to both the early and control group). Interestingly the group that showed no significant amplitude reduction as compared to the controls. However, the amplitude of the P3b generated by target stimuli of the novelty paradigm showed a similar pattern of highly significant decrease in parietal leads in both of the AD groups as compared to the controls. These findings suggest that there is a delay in the processing of distracting novel stimuli in the novelty paradigm, and that this causes a difficulty in focusing attention to the target stimuli. We subsequently analyzed the early component, that is P50 wave of the standard oddball ERP’s in this group, the detailed results of which will be presented by one of us in a separate paper in this meeting. Based on this analysis, which is a time-frequency decomposition, further revealed that the early group displays a significantly higher beta, but not gamma evoked responses as compared to normals (the combined AD group is significantly different than the normals in both beta and gamma responses). In this study, the oddball P3b amplitude and latency changes reported in the literature have not been observed possibly because the subjects were relatively in the earlier stages of the disease process. However, the P3b potentials obtained in the novelty paradigm are more sensitive in detecting early stage AD subjects than classical oddball paradigm. Time-frequency decomposition of the P50 wave in the classical oddball paradigm might also help to discriminate early AD patients.

Keywords: Alzheimer’s disease, event-related potentials, P3a, P3b, beta response, gamma response

Pathological and clinical dimensions of Alzheimer’s disease: implications for the concept of mild cognitive impairment
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In this talk, we will present a simple model that tries to link the pathological and clinical dimensions of Alzheimer’s disease (AD). The pathological process that underlies AD likely begins decades before the onset of clinical symptoms and dementia. By the time early dementia is recognized, there has already been a substantial amount of irreversible brain damage. The descent from normal brain function to clinical dementia can be divided into a presymptomatic phase (no observable decline in cognitive or functional status), a preclinical phase (deficits in memory and/or other cognitive functions without significant impairments in daily function), most commonly designated as Mild Cognitive Impairment (MCI), and the progressive stages of dementia (mild, moderate, and severe impairment). This schema suggests ongoing degenerative changes and a “threshold” degree
of neuropathological damage, beyond which an individual manifests cognitive and functional decline and eventually the clinical syndrome of dementia. Several observations present interesting challenges to this notion. For example, there are many reports of adults who were considered clinically normal in life, but at autopsy met established criteria for a pathological diagnosis of AD. Moreover, individuals with a similar level of pathological burden can exhibit varying degrees of cognitive impairment. Thus, the relationship between AD pathology and clinical symptoms is not necessarily a simple or linear one, and, as will be reviewed, is likely mediated by a range of factors, including cognitive reserve (e.g., as indexed by baseline intellectual capacity and education) and concomitant medical conditions (e.g., cerebrovascular disease). This complicates efforts to clinically identify individuals in the earliest stages of the illness, when new treatments that are being developed may offer the greatest opportunity to slow or arrest the underlying pathological process.

Mild cognitive impairment is, in part, being diagnosed when a person performs below published norms on specified neuropsychological tests (often >1.5 standard deviations below the mean for age). Unfortunately, this approach does not take into account an individual’s baseline intellectual capacity and performance, which often is not available because a patient has not had prior neuropsychological testing. The failure to account for a person’s baseline status is particularly problematic for individuals with high intelligence and education, or those with limited intellectual capacity or education. In this context, we discuss the slippery but important concept of cognitive reserve, which may be conceived of as the varying capacity individuals have to use neural networks efficiently or to call on alternative networks or cognitive strategies in the face of increasing task demands or physiological changes associated with aging or disease. We will review a strategy that we have developed that uses an estimate of a person’s baseline intellectual capacity to help determine whether there has been a decline in cognitive function. This approach was much more accurate than the standard one in identifying which highly intelligent elders were at greatest risk for exhibiting cognitive decline and the development of mild cognitive impairment. We will also briefly discuss how an appreciation of the complex interaction between neuropathological burden and cognitive reserve has potential implications for cultivating strategies to reduce the risk of developing MCI and dementia, even before definitive treatments for AD become available.

The early diagnosis in Alzheimer’s disease: biomarkers

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Alzheimer’s disease is a dementing disease characterized by extracellular neuritic plaques consisting from amyloid precursor protein (APP) derived peptide aggregates of α-40, α-42 and intraneuronal neurofibrillary tangles composed by hyperphosphorilated tau.

The diagnosis of AD depends on clinical features. The clinical criteria such as DSM III or NINCDS-ADRDA have shown the sensitivity of 70% at the level of 81 % specificity. The objectivity of clinical diagnosis may vary due to several factors as clinician’s experience, variations in the course of disease and background of patient. Therefore there is a need for biomarkers in AD. Total tau (t-tau), phosphorylatted tau (p-tau), α-40, α-42, AD7C-NTP are among those biomarkers. Recent studies have shown that CSF α-42 indicates the disease at the sensitivity level of 78-92% and 81-83% specificity. The corresponding ratios for t-tau are 86-95 % for sensitivity and 80-97% for specificity; and for AD7C-NTP 70% and 87%, respectively.

P-tau is a likely candidate as a more specific biomarker for AD. CSF p-tau is not increased in ischemic stroke or Jacob-Creutzfeldt disease, differently from t-tau. P-tau is found lower in depression, ALS, Parkinson disease, vascular dementia, frontotemporal dementia and dementia of Lewy body type than AD. α-42 is a well-studied, valuable biomarker. α-42 is correlated to age, while p-tau is not correlated to the severity of cognitive decline or age.

We have investigated α-40, α-42 and p-tau in AD (n=15) and age and education matched healthy controls (n=15) in Dokuz Eylul University Dementia Clinic. P-tau is found to have higher sensitivity and specificity levels than other markers and a cut-off value has been determined for AD patients. Disease duration is correlated to p-tau levels, while MMSE scores are not.

We believe there is a need for further clinical or histopathological studies on these markers before using them as a diagnostic tool.

Keywords: Dementia, diagnosis, marker, Alzheimer

PN2

ELECTRICAL OSCILLATIONS OF THE BRAIN AND COGNITION

Moderator: Tamer Demiralp

Panelists: Canan Basar–Eroglu, Christoph Herrmann

Event-related oscillations in schizophrenics and healthy controls

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The clinical history of schizophrenia shows a focus on deficits in integrative processes of the brain since Kraepelin's study 1919. In the last decade many studies have implied that event-related oscillations such as delta, theta, alpha and gamma may contribute to functional integration in the brain. Therefore, pathological changes related to schizophrenia provide an appropriate model to investigate integrative processes of the brain and their dysfunction during cognitive processes.

The aim of our study was to investigate the oscillatory brain activity in schizophrenic patients and healthy controls during various tasks requiring different perceptual and cognitive processes, i.e. visual perception and attention.

Ten patients with schizophrenia and ten healthy controls participated in our study. EEG was recorded from frontal, central, parietal and occipital locations. We employed three tasks associated with different modalities and attentional processes. An auditory continuous performance test (CPT) and sustained attention to response test (SART) assessing sustained attentional processes to auditory stimuli, and furthermore we presented the Necker-Cube for investigating attentional processes during visual perception.

The results of this study show not only a decrease of gamma, but also reduced delta, theta and alpha-oscillations at the frontal locations in patients with schizophrenia. An imbalance in the relation between gamma- and alpha-oscillations concerning of visual perception was observed.

Based on our results, we conclude that event related oscillations in patients imply impaired networks and abnormal temporal integration that lead to disturbance of perception and attention.

We suggest that event-related oscillations provide information that may help to understand the neurophysiology of psychotic disorders.

Keywords: schizophrenia, event-related oscillations, CPT, SART, delta, theta, alpha, gamma

Human EEG gamma oscillations in healthy and pathological conditions

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EEG oscillations in the frequency range of about 30-80 Hz have been coined gamma activity and have been shown to correlate with a number of cognitive functions. As we have found out in a series of experiments, the most basic of these functions seems to be memory access. Whenever perceived stimuli match with contents of either short-term or long-term memory they evoke stronger gamma activity, i.e. known objects or sounds evoked stronger gamma responses than unknown ones. This basic memory matching process is also involved in numerous other cognitive functions like directing attention and language processing. We propose a neural model which explains the generation of gamma oscillations and its modulation by memory processes. In this model, neurons of early visual cortices are connected to neurons of higher visual cortices. These connections represent stored information and exist only for known objects. If a perceived object drives such a connection it receives feedback because the connections are bidirectional. The feedback then results in enhanced gamma oscillations for known objects. This model at the same time predicts certain phenomena which are frequently observed in pathological states of cognition. The hallucinations of schizophrenic patients and the deja vu phenomena of epileptic patients are both associated with a pathological increase in gamma activity. Since the brain cannot determine whether a strong gamma oscillation results from feedback due to a memory connection or from a pathological state, strong gamma activity in visual cortex will phenomenally lead to the perception of a known object. In the absence of any object to be perceived this will be considered a hallucination. If an unknown object or situation is actually perceived this distorted perception will lead to a deja vu phenomenon.

Keywords: Gamma oscillations, memory matching, hallucination, deja vu
PN3
THE PRESENT AND FUTURE OF NEUROSCIENCES IN TURKEY
Moderator : Lutfiye Eroglu
Panelists : Sakire Pogun, Lutfiye Eroglu, Turgay Dalkara, Gonul Peker, Reha Erzurumlu, Tamer Demiralp

Neurosciences have secured an independent departmental status within Schools of Medicine, Arts and Sciences in developed countries for the past quarter century. Interdisciplinary nature of neurosciences has led to dramatic expansion of this academic discipline and to the establishment of Neuroscience Centers in almost every university. It is evident from the participants of the Turkish National Neuroscience Meetings that interest in neurosciences is growing exponentially in our Medical School Basic and Clinical Science Departments as well as in Biology, Molecular Biology and Genetics, and Psychology Departments of Faculties of Arts and Sciences. This is reflected in the numbers of neuroscience research projects and noticeable quality of publications.

Considering qualitative and quantitative increases in neuroscience research, TÜBITAK Brain Research Planning and Coordination Commission called for a joint meeting of all neuroscientists in 2000 in Uludağ, which then led to the institution of annual National Neuroscience Congresses, the 4th taking place this year here in Mersin.

In this panel, representing the TÜBITAK Commission, Turgay Dalkara will summarize our accomplishments since the first meeting in Uludağ.

Gonul Peker will present TUBAS activities and establishment of undergraduate neuroscience education in Turkey for which she has devoted considerable time and effort.

Reha Erzurumlu will discuss the need for and ways of recruiting the new generation of neuroscientists trained in developed countries to Turkish neurosciences, and benefits of active interactions between neuroscientists residing in Turkey and abroad.

Tamer Demiralp, who has been involved in drafting the Neuroscience PhD program at Istanbul University, will summarize the founding principles and basics considered during the development of this program.

Possibilities of active solicitation of research funds from abroad, in particular from European Union resources, will be presented by Sakire Pogun.

Neurosciences occupy a significant research potential in our country. We hope that discussion of questions/problems facing neurosciences in Turkey will help defining strategies for future development and advancement along new venues.

PN4
MULTIPLE SCLEROSIS
Moderator : Guher Saruhan-Direskeneli, Aksel Siva
Panelists : Guher Saruhan-Direskeneli, Aksel Siva, Selim Badur, Ayse Altintas

Antibody response in multiple sclerosis (MS)
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MS has been considered as a T cell mediated autoimmune disease directed against central nervous system (CNS) myelin. The role of T cells in MS has been supported by animal models of the disease and by some clinical observations; however, the presence of oligoclonal IgG bands in cerebro-spinal fluid (CSF) and plasma cells at the MS lesions and CSF supports the contribution of B cells in the immune response in MS. Recent studies evaluating the role of B cells and their development in MS have gained considerable attention.

The presence of mutated but oligoclonal expanded heavy chain transcripts in MS brain and CSF has revealed antigen-driven response in the disease development. Antibodies to myelin oligodendrocyte glycoprotein (MOG) has been detected at acute MS lesions with myelin detachment and anti-MOG antibodies has been shown as prognostic markers in the early phase of MS (T.Bberger N Engl J Med 2003, 349,139). An auto antibody repertoire specific for subtypes of MS has also been suggested and “α-enolase” has been assigned as possible candidate (Lefranc D, J 2004, 172, 669).

Most surprising finding is the observation of lymphoid follicles in the inflamed meninges of animals with experimental autoimmune encephalitis (EAE), although CNS is principally devoid of lymphoid tissue. In MS brain tissue, perivascular B cell infiltrations have been detected in chronic inactive lesions. Lymphoid follicle-like structures containing B cells, T cells and plasma cells were observed in leptomeninges while proliferating B cells were also present. A network of follicular dendritic cells producing CXCL13 which attracts naive B cells was detected (Serafini B, Brain Pathol 2004, 14, 164). When the B cell subsets in the CSF have been evaluated phenotypically, B cells expressing CD80, CD86, CCR1, CCR2 and CCR4, memory and plasma cells or centroblasts of secondary lymphoid tissue were detected more frequently in the CSF than peripheral blood, whereas naïve B cells were lower in both MS and other neurological diseases. Plasma cells were even more frequent in MS than other diseases (Corcoran A, PNAS 2004, 101, 11064). Another recent finding demonstrated the production and survival of B cells in the CNS by production of B cell activating factor, BAFF by astrocytes and BAFF expression was strongly up-regulated in MS to levels observed in lymphatic tissue (Krumholz M, JEM 2005, 201, 195).

Recent findings in MS reveal critical steps in maintaining humoral autoimmunity and disease exacerbation.

Multiple sclerosis and neutralizing antibodies against interferone beta
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Since first ages of 1990, the recombinant interferone (INF) has been used to therapy not only in the infectious diseases but also in the neurological disorders like Multiple Sclerosis (MS). However, it is evaluated to occur the specific antibodies against the molecules which is being protein form are one of the reason failure of the treatment by some investigators. Most research groups go on to proceed their studies in order to define the best response of the anti-interferone antibodies (anti-INF) occurring which level and explain of this issue which has no consensus on it. Although the IFN preparations and its dosages using in studies have different formation and absence of the standardization in measuring processes of the antibody, it is difficult to compare the results which are obtained.

The first report has been shown that the immunogenetic features of human-interferone which is using to therapy by Vallbracht and his friends in 1981. In 1996 IFNB - MS study group has explained that there are specific antibodies against the interferone β-1b. Until nowadays from the first studies, it is determined that the technical procedures used for obtaining the recombinant interferone effects on the immunogenic form of the molecules. And also it is shown that anti-INF antibodies generally occurs as being binding antibody (BAB) and some of these antibodies have been detected as being neutralising antibodies (NAB) which are responsible of real neutralization. Therefore, it is suggested that the binding antibodies must be detected in the patients who have taken IFN and its failure in the therapy. If these binding antibodies have been determined in the patient sera, it is researched that these antibodies are neutralising antibodies whether or not. There are different processes which are used for measuring of the antibody levels. The ELISA processes which is contained IFN is generally used for detecting these specific binding antibodies. After BAB has been detected, it is performed the Western-blot to confirm these results. On the other hand, in order to detect the NAB two different method have been used. The first technic is that NAB can be measured by using the cytopatic effect of the virus strain in the specific cell-culture. The other one is that MXA level can be detected in the cell-culture directly. Recently European countries, especially Austria, Italy and USA have accepted to investigate the MXA protein level which is indicates the INF bioactivation in the A549 cell-culture without using virus strain. After the standardization procedures have been supplied in the anti-INF studies, it is necessary to know which level of antibody titer is more considerable, in which stage of the therapy founding of these antibodies are more important and finally it is useful to reply how should be the therapy procedure.

The optimization steps to be used for investigating anti-INF antibodies have been completed successfully in Istanbul Medical Faculty, Virology and Basic Immunology Unit. And also, it will be possible to perform the BAB and NAB assays by using specific procedures.

Demyelination and the role of oligodendrocytes in the experimental model of multiple sclerosis
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Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS) and the most common cause of disability among young adults. Much emphasis has been placed on identifying the causes and the mechanism of MS. Histopathological features of MS are characterized by inflammation, multifocal loss of myelin, oligodendrocyte (OGs) and axons. Despite years of classical histopathological study, the MS lesion is incompletely understood. Recent detailed studies on the immunopathology revealed a profound heterogeneity of the lesions with respect to the composition of the inflammatory infiltrate, immunological effector mechanisms, extent and mode of oligodendrocyte death, and occurrence of remyelination. Although remyelination occurs in many acute plaques of MS, remyelination failure becomes an increasingly prominent
feature of the pathology of chronic MS. There are extensive experimental and clinical studies to understand the mechanism of remyelination. Investigations of toxin-induced, autoimmune, and viral-mediated experimental models of CNS demyelination have provided valuable information regarding the morphological, cellular, and molecular events surrounding remyelination. Infection of susceptible mice with the Daniel (DA) strain of Thiel’s murine encephalomyelitis virus (TMEV) produces a chronic progressive immune-mediated demyelinating disease which clinically and pathologically resembles chronic MS. The target cells for TMEV are neurons, OGS, astrocytes, and macrophages. The histological appearance is characterized by primary demyelination. Like human disease, inflammatory cells and macrophages are intimately involved in the demyelinating process. There are recurrent episodes of acute demyelination superimposed on a chronic progressive disease that mimic the exacerbations and remissions observed clinically in the human disease. Remyelination in the CNS by OGS is limited, especially in animals infected with the DA strain of TMEV. In our study, we evaluated the number of PL-P-l-mRNA expressing OGS in different time points following TMEV infection in susceptible mice. Our study revealed a transient reduction in the number of OGS within the demyelinating TMEV lesions in the early phase. However, there was a reappearance of OGS during later stages of the disease. Despite the presence of numerous OGS, remyelination during chronic stages was limited. This finding suggests factors other than the availability of OGS may underlie impaired remyelination in TMEV-induced demyelination model of MS.

Keywords: multiple sclerosis, oligodendrocyte

PN5

NEW DIRECTIONS, INTERACTION OF UNIVERSITY-INDUSTRY AND TUBITAK IN THE FIELD OF NEUROSCIENCE

Moderator : Murat Emre
Panelists : Altan Demirdere, Ata Akin, Omer Cebeci

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The list of the subjects under the name of University, the Drug Industry and the Government Cooperation is presented below:

1- High-quality health service: As the government executives pointed “It is essential to present a service which complies with the idea of equal, easily reachable and high-quality health service to our citizens for our all health staff. We completely believe that our staff will provide a health service in compliance with this view to our citizens.”, they are aware of the responsibilities of the Drug Industry exclusive of the Programme of Transformation in Health as much as before. We can include the following subjects in these responsibilities; supporting the scientific projects and programmes required by both the instructors who work in the University Clinics and the physicians in the peripheral areas referred to physician-patients affair, providing accurate, upgraded and reliable information regarding to new released drugs and treatment alternatives, reporting reliable information about side effect profiles of drugs to the Ministry of Health, donating the materials required by physicians and health organizations to provide a service. The policy of high-quality health service of both government and academic peripheries is also one of the leading worries of the drug industry.

2- Clinical researches: Approximately %50 of the drug researches throughout the world has been performed in the USA. This rate is approximately %25 for the European Union and %15 for Japan. The total expenses for the researches cost roughly 40 billion USD.

13,000 new research project will be started in 2005 in the world and approximately 56,000 researchers will be needed. All countries compete for the requirement of 8,000 researchers, except 48,000 researchers locating in America and Europe. Although clinical researches are performed in our country, the drug industry has decided to increase the number of the researches. This means an income of 300 million USD per year to our clinical research centers, which the universities constitutes %90 of these centers, in case of applying only %1 of the total clinical researches in Turkey. This source can be used for many different purposes such as, studying on various researches and providing equipments for patients to have better treatment facilities. To make this possible, the organizations specified above, e.g. the Government, Universities and Drug Industry should cooperate.

3- The Principles of Drug Advertisement: The Drug Industry has a sensitive point of view about unethical drug advertisement which had remarkable discussions in the past. Regarding this aim, it has precisely applied theDrug Advertisement Regulations issued by the Ministry of Health with an exact cooperation; in addition, it has issued a Guide of Advertisement Principles in the internal structure, arranged training programmes for their employees and developed auto control mechanisms. We expect the academy’s support for our efforts in this subject.

4- The Policy of Scientific Issues: The findings obtained from the clinical researches in all issues should be considered as the property of both the drug firm which is sponsored for the research and also the researchers. The results in question should be issued without causing any doubts and should be open to the independent comments of the medical organizations. The drug industry learns unfortunately about the discussions regarding the reliability of the issues especially released lately and develops the ways of cooperation as expected. Many drug firms accepted to collect all information about the studies performed in data bases which can be followed by all parties before the results come out and try to prevent this kind of claims.

5- The leadership of thought: The drug development is not a process which only drug firms included. In the period of 14 years, various leaders of thought in the academic structure have also taken part. Their contribution forms a wide spectrum from determining the required treatment areas to discovering new molecules which will be used in this field. Some important leaders of thought in this field are also present in our country. The drug industry, our universities and the cooperation of the government will provide our leaders of thought to be used more effectively.

6- Creation of Economical Added Value: The drug industry clearly understands the importance of production in our country and the necessity of including economical added value in the country and also makes significant investments for this aim as it can be followed from the press.

However, as TUBITAK pointed, there are a lot of breakthroughs that the national industry can make. TUBITAK supports the suggestions about projects from the institutions which have a potential needed to create economical added value without regarding to their bigness and types. The rates of support and paying back are decided by the Area Committees with the direction of arbiter reports. The developments are evaluated with a report of expert in the periods of 6 months and the projects are followed by the technical personnel and the project-watchers sent by the Ministry. If the universities take place in an international project, the studies performed by the universities are supported separately. When considering these developments, the drug development activities should be included in the supported group such as, Electrical, Electronic and Information Technologies, Machine Production, Metallurgy and Chemical Technologies.

Neuroscience: a path from scientific research to industrial applications

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We have seen an increase in the number of scientific research projects hence industrial applications in the field of neuroscience after the initiation of the Human Brain Project incentive in USA in 1990’s and Neuroinformatics research group in Europe in 1996. The presentation will include a quick overview of the techniques and instruments employed in neuroscience studies as well as the ground rules and mechanisms of developing a commercial product. Funding opportunities in neuroscience research, national and international job opportunities awaiting neuroscientists and the future of neuroscience will be outlined. Major steps in technology transfer will be outlined with real-life examples.

Keywords: Neuroscience, biomedical instrument, technology transfer

ORAL COMMUNICATIONS

S1

Building healthy brains: how early brain development affects social and emotional development in young children

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It is now clear that the first three years of life are crucial for social and emotional development of children, and we know a great deal about the family, societal, and environmental factors that impact in this period. New research on the complex process of brain development before and after birth helps us understand the ways in which children learn to cope successfully with the world around them. This presentation will look at the interaction between genetic and environmental factors, the role of sensitive periods, environmental enrichment, and the effect of stress on the developing brain. These processes can be viewed from the point of view of those factors which protect the developing brain and those which increase the risk of poor outcomes. We know that very negative environments, such as those involving neglect, abuse, family violence and community violence, can have
serious impacts on brain development in the child. At the same time, it is clear that normal brain development is very robust, and it can proceed successfully even in relatively poor environments, as long as early attachment has occurred.

S2. [NOT PRESENTED]

Educational neuroscience and orchestrating the neurological symphony in a developing brain

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Studies on brain and neurobiological processes underlying learning have shown that the "absorbent mind" period seems to be the best duration for acquisition and some crucial learning to take place. By employing brain-compatible approaches and appropriate materials, infants can be given a solid foundation in all the areas of development and academic skills. In this particular paper, presenters will share the results of a three-year quasi-experimental study aimed at developing "multiple intelligences" of a 6-month baby. The findings of the study have revealed that early learning experiences and exposure to written world may result in a well established reading comprehension skill, both in mother tongue and a foreign language. The subject of the study began reading in Turkish and in English in the 18th month of the experiment, with a limited vocabulary.

Keywords: early stimulation, brain-compatible, developmental neuroscience

S3

Evaluation of corticospinal system maturation and plasticity with transcranial magnetic stimulation in children

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Plasticity of brain is an increasingly important topic in many areas of neuroscience including development, learning and repair. It is still a challenge to study plasticity directly in human nervous system. Transcranial magnetic stimulation (TMS), however, has become a suitable non-invasive and painless technique which can be applied to detect changes in cortical excitability or connectivity as indicators of plasticity. In this study, children with healthy brain development and with various types of neuronal plasticity following a brain injury were evaluated with TMS. Fifty-seven children with impaired corticospinal motor system based on the clinical neurologic examination and 46 volunteers with normal brain development, a total of 103 children were included in the study. The patients were grouped into four according to the topographic involvement of the pyramidal system: (I) unilateral pyramidal syndrome (UPS): 11 children with spastic hemiparesis, (II) bilateral pyramidal syndrome-spasticity (BPSh): 23 with spastic tetraparesis and 10 with spastic diparesis in total of 33 children, (III) BPSh+hypotonicity (IV) extrapyramidal syndrome (EPS): 7 children with dystonia + spasticity. Three types of neuronal plasticity were determined according to etiology; [1] excessive plasticity (29 children),[2] impaired plasticity (18 children), [3] achilles plasticity (27 children).

In TMS, motor evoked potentials (MEP) with cortical and radicular stimulation were recorded from contralateral and ipsilateral upper extremities (hemian muscle group) and lower extremities (tibialis ant muscle). Recordings were obtained during the rest and the facilitation. Results were compared with data obtained from healthy controls and with clinical and radiological (magnetic resonance imaging-MRI) findings of the patients. Latency, amplitude and latency jumping values of the MEP obtained in healthy volunteers displayed a strong correlation with age and height. Pathological MEP response in upper extremities was observed in 64% and 68% of children with UPS and BPSh involvement respectively; this rate was 66% and 81% respectively in lower extremities. Rate of normal response was seen. The mean values of axodendritic synapses counted in CA1 area in the 1., 2., 3., and 4. groups were 38.3 ±1.9, 35.7 ±2.2, 33.1 ±1.2, 38.7 ±2.2 respectively, and at CA3 area they were 38.1 ±1.7, 34.6 ±2.7, 31.9 ±2.6, 38.3 ±2.1, respectively.

Keywords: maternal deprivation, dendritic spine, hippocampus, limbic-hypothalamo-pituitary-adrenal stress

S4

The effects of maternal deprivation on the hippocampal dendritic structure in adult rats

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In mammals, the limbic-hypothalamo-pituitary-adrenal axis is activated during stress response. Hippocampus, whose functional importance in learning and memory is known, is the central structure of this circuit. In our study, the electron microscopic investigation of the morphological variations at hippocampus in adult rats is aimed by applying maternal deprivation as a stress factor in certain periods of limbic-hypothalamo-pituitary-adrenal axis. For this purpose, Wistar Albino rats have been mated, and pups have been divided into four groups. The first group was the control group, in which the pups did not leave the mother, the second, third and fourth groups have been separated from the mother for 24 hours at postnatal 4, 9 and 18 days respectively. Then, all groups have been settled into different cages according to their genders on the postweaning on 22th day. At the third month, when they become adult, perfusion has been done by providing deep anesthesia. After perfusion, the samples have been taken from CA1 and CA3 regions of the hippocampus, and have been prepared for electron microscope examinations. While there was no morphological variation in both areas in hippocampus on the micrographs of the first group, there were membranous whorls in some dendrites in the second group. In the ultrastructural examination of the third group, the cytoplasm and nucleus were observed normal. On the micrographs of the last group, filamentous structures and a lot of deep invaginations in the nucleus were seen. The mean values of axodendritic synapses counted in CA1 area in the 1., 2., 3., and 4. groups were 38.3 ±1.9, 35.7 ±2.2, 33.1 ±1.2, 38.7 ±2.2 respectively, and at CA3 area they were 38.1 ±1.7, 34.6 ±2.7, 31.9 ±2.6, 38.3 ±2.1, respectively.

Keywords: maternal deprivation, dendritic spine, hippocampus, limbic-hypothalamo-pituitary-adrenal axis

S5

The effect of epilepsy on the cell membrane

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Epilepsy is the group of syndromes caused by recurrent seizures due to the abnormal electrical discharging that take place in neurons. Today it is clear that epileptic seizures arise from a simultaneously activating group of neurons forming electrical discharge. However, it is not fully understood that epileptic seizures lead to changes of brain tissue in molecular level. Pentilenetetrazol (PTZ) is one of the most widely used epileptic agents in the studies for developing treatment of epilepsy. Although the mechanism of PTZ is not fully understood, there is information in the literature that it applies its effect on picrotoxin binding site of GABA receptor. In this study the molecular changes caused by epileptic seizures on the rat brain cell membranes, which are made epileptic by the application of PTZ, are investigated by Fourier Transform Infrared Spectroscopy (FTIR). FTIR is a technique which enables the monitoring of vibrational groups in the structure of different molecules found in the structure of the investigated sample, thus giving detailed information about the molecular structure of the sample. The frequency analysis of the bands in FTIR spectrum gives information about phase transition behaviour, order and hydrogen bonding of lipids in the structure of cell membranes and the specific bandwidths enable us to gather information about membrane dynamics. In this study two groups are determined as control (n=5) and PTZ (n=5). The PTZ group is injected with 60mg/kg/ml pentilenetrazol and after the fifth phase of epileptic seizures are observed brains of rats are decapitated. Brain tissues are homogenized and FTIR investigations are carried out in liquid media in 4000- 400 cm−1 frequency interval and at 4 cm−1 resolution. According to the results, there is an increase in the concentration of unsaturated fatty acids with the application of PTZ. The bands found in 3050-2800 cm−1 region (CH2 symmetric / CH3 symmetric stretching mode) are due to the lipids and proteins in the structure of membrane and Amide-I band is due to proteins and the ester (C=O) groups of lipids; according to the intensity ratios of these bands PTZ decreases the lipid to protein ratio of the system. In addition, the increase in the bandwidths of CH2 asymmetric stretching, C=O stretching and PO2 stretching which is due to the head groups of phospholipids in membrane structure, of PTZ samples showed the increasing effect of PTZ on the membrane dynamics. However the decrease in the frequency of C=O and PO2-2 stretching modes showed that PTZ has an increasing effect on hydrogen bonding on C=O groups. On the other hand this effect is not seen on PO-2 groups of phospholipids. In conclusion, although pentilenetrazol interacts with C=O groups and increases their mobility, it also alters lipid order and dynamics in the system; so these effects can be interpreted as the interaction can be formed by both hydrogen bonding and ion-dipole or ion-ion interaction. In the control group the appearance of Amide-I band in 1653 cm−1 frequency region

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may mean that the structure of proteins is mainly α-helix. The change in these bands’ frequency with the application of FTZ shows the conformational changes of proteins in the system. In conclusion according to the results obtained from this study, pentilenetrazol has an increasing effect on cell membrane dynamics by interacting with the cell membrane phospholipids, in addition to this it also changes lipid and protein concentrations.

Keywords: epilepsy, vigabatrin, topiramate, molecular biology, FT-IR spectroscopy, FT-IR microscopy, DSC

S6

Genetic absence epilepsy rats receiving kindling stimulations: a preliminary morphological study in CA3 region of hippocampus

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The genetic absence epilepsy rats from Strasbourg (GAERS) are a model of absence epilepsy. Although excessive GABAergic neuromediation within the thalamo-cortico-thalamic circuit is the accepted mechanism in absence epilepsy, neuronal networks of the hippocampus have recently received attention. The aim of this preliminary study was to investigate whether or not amygdaloid kindling stimulations in GAERS caused pyramidal neuronal degeneration in the hippocampal CA3 region. Adult Wistar rats and GAERS were instrumented stereotaxically with bilateral stimulation and recording electrodes into the basolateral amygdala and the cortex. Control groups were sham-operated. After one week of recovery period, animals were electrically stimulated twice daily at their after discharge threshold currents. Animals were considered as fully-kindled when they experienced three stage 5 seizures. Twenty-four hours after the last amygdaloid stimulation, the animals were deeply anesthetized and sacrificed by transcardiac perfusion with a fixative solution. The brains were cut into 300 μm slices and the CA3 region of the hippocampus was dissected. After applying routine electron microscopic procedures, tissues were embedded in Epon 812. Semi-thin sections were cut on a Leica Ultracut R ultramicrotome and stained with toluidine blue. GAERS did not reach stage 5 seizure state although they received more stimulus than fully-kindled Wistar rats. Kindled Wistar rats showed neuronal morphological degeneration in the CA3 region of the hippocampus, compared to Wistar sham-operated controls. Sham-operated GAERS and GAERS, which showed only stage 2 seizures after amygdaloid stimulations, revealed no pyramidal neuronal degeneration in the CA3. It is known that the hippocampus is involved in neural activity in absence epilepsy. GAERS failed to progress beyond a stage 2 seizure states even after 30 kindling stimulations. In kindling model of temporal lobe epilepsy, morphological changes occur in mesial temporal region including loss of hippocampal CA3 pyramidal neurons. We conclude that the protection of CA3 pyramidal neurons in GAERS might be related to the failure of this strain to reach stage 5 seizure states. Furthermore, GAERS may have a different plasticity. Absence of degeneration in CA3 in GAERS needs further evaluation in terms of GABA and glutamate density in this region by quantitative electron microscopy.

Keywords: GAERS, kindling, CA3, hippocampus, neurodegeneration

S7

The evaluation of the effect of prostaglandin synthesis inhibition on the development of scopolamine-induced convulsions in fasted mice after food intake

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Glutamatergic activity has been shown to contribute to the development of clonic convulsions observed after scopolamine treatment and food intake in 48 h fasted mice. Glutamatergic receptor activation and chemically-induced convulsions are associated with increased amounts of prostaglandins in brain tissues. Prostaglandins are suggested to have proconvulsant activity. Thus, this study was performed to evaluate the effect of prostaglandin synthesis inhibition on the development of scopolamine-induced convulsions in fasted mice. Mice, weighing 25-30 g, were deprived of food for 48 h. Indomethacin was used for prostaglandin synthesis inhibition. Fasted animals were given indomethacin subcutaneously or acetally. For the subacutec treatments, 5 mg/kg indomethacin or saline were given (ip) twice daily during fasting. On the day of experiments, subacutely treated animals were given the same treatments. Acutely treated animals were given 5 or 10 mg/kg indomethacin or saline. Forty min later, all animals were treated with saline or 3 mg/kg scopolamine and then individually placed in wire mesh cages. After being given food pellets 20 min later, they 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. After fasting for 48 h, animals fell to approximately 80-85% of the starting body weights. Scopolamine treatment caused convulsions in fasted animals (75%; p<0.01). Neither 5 mg/kg subacute (100%), nor 5 mg/kg (80%) or 10 mg/kg (66%) acute indomethacin pretreatments had an effect on the incidence and onset of convulsions. Present results indicate that prostaglandins seem not to contribute to the underlying mechanism of scopolamine-induced convulsions in fasted mice.

Keywords: scopolamine, prostaglandin, fasted, convulsion, mice

S8

Interactions of NO system and calcium channel blockade in pentilirin-induced experimental epilepsy: a comparison of methods

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The aim of the present study was to investigate the possible interactions of NO system and calcium channel blockade in penicillin-induced experimental epilepsy. Thirty seven healthy male Wistar rats were connected to a digital electrocorticography (ECoG) apparatus (Powerlab 4S/P, ADInstruments, Australia) following exposing the left cortical surfaces surgically. All recordings were initiated at least 10 minutes before the injections and continued throughout each experiment without interruption. Animals were divided into 7 groups randomly: 8) Penicillin G [200IU/microl; i.c.]; n=6 13) Flunarizine [10mg/kg i.p.]+ Penicillin G [200IU/microl; i.c.; n=4 10] Sodium nitroperriside (SNP) [100microg/kg i.p.]+ Penicillin G [200UI/microl; i.c.; n=4 11] N-L-nitro arginine methyl ester (L-NAME) [50mg/kg, i.p.]+ Penicillin G [200IU/microl; i.c.; n=5 12] Flunarizine [10mg/kg i.p.]+ L-NAME [50mg/kg i.p.]+ Penicillin G [200IU/microl; i.c.; n=6 13] Flunarizine [10mg/kg i.p.]+ SNP [100microg/kg i.p.]+ Penicillin G [200IU/microl; i.c.; n=5 14] Flunarizine [10mg/kg i.p.]+ L-Ariginine [1000mg/kg i.p.]+ Penicillin G [200IU/microl; i.c.; n=5 Results obtained from ECoG recordings summarized as follows: A) The mean latency of the onset of epileptiform activity in the 3rd group was significantly higher than control group (p<0.05; anticonvulsant-like effect) while the mean latency values obtained from groups 4, 5 and 6 were significantly lower than control (p<0.05; proconvulsant-like effect). B) Group 2 has a higher mean latency value when compared to groups 4, 5 and 6 (p=0.05; relative anticonvulsant-like effect). C) Comparing the mean epileptiform spike amplitude values during the first minute of epileptiform activity onset showed that group 2 displayed a significantly diminished amplitude (p<0.05) while group 4 had a significantly higher (p<0.05) spike amplitude compared to controls. D) Comparing the mean epileptiform spike frequency values during the first minute of epileptiform activity onset showed that the groups 3, 4, 5 and 6 displayed a significantly higher spike frequency when compared to control values (p<0.05; proconvulsant-like effect). E) Comparisons between total spectral power values taken in successive time windows revealed that the mean total power in 25-50Hz region of the spectral profile belonging to the 5th group was significantly higher than all other groups in the study (p<0.05; proconvulsant-like effect). Results indicate that, pharmacological calcium channel blockade together with nonspecific NOS inhibition before the onset of penicillin-induced epileptiform activity results in a significant increase in the intensity of epileptiform brain activity. Although the mechanism of this phenomenon is not clear, we think that the spectral analysis should be used as a complementary method since this phenomenon was revealed as a result of spectral analysis rather than the routine spike/latency analysis.

Keywords: penicillin-induced experimental epilepsy, spectral analysis, nitric oxide, calcium channel blockers, electrocorticogram

S9

Amygdaloid kindling in genetic absence epilepsy rat models

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Coexistence of idiopathic generalized epilepsy in patients with partial epilepsy is only exceptionally reported. The kindling model in rats with genetic absence epilepsy is highly suitable for studying mechanisms involved in the propagation and generalization of seizure activity for convulsive and non-convulsive
components of epilepsy. In this study we aimed to evaluate and to compare the kindling process in two different genetic absence epilepsy rat models namely GAERS (genetic absence epilepsy rats from Strasbourg) and WAG/Rij (Wistar Albino Glaxo / Rijswijk). Three groups of animals were used in this study: non-epileptic control Wistar rats, GAERS and WAG/Rij rats. All animals were stereotaxically instrumented with bilateral stimulation and recording electrodes into the basolateral amygdala and recording electrodes on the cortex. After one week recovery period animals were electrically stimulated twice daily at their afterdischarge thresholds. The seizure severity was evaluated using Racine’s 5-stage scale. Stage 1 and 2 (limbic seizures) were characterized by immobility, facial automatisms, head nodding, stage 3 by unilateral forelimb clonus, stage 4 by rearing and bilateral forelimb clonus, and 5 by rearing and falling accompanied by generalized tonic-clonic seizures. Animals were considered as fully-kindled when they experienced five stage 5 seizures. All Wistar rats were fully kindled and the mean number of stimulations for the development of stage 5 seizure was 12±0.6. GAERS remained at stage 2 although 30 stimulations were applied. Fifty percent of the WAG/Rij rats showed stage 5 seizures, but these rats needed more stimulation to reach stage 3 seizures compared to non-epileptic rats, whereas half of the animals stayed at stage 2 even at the end of 30 stimuli. Although limbic structures are not generally thought to contribute to the brain circuitry in which spike-and-wave discharges are generated, our results suggest that the mechanisms involved in absence epilepsy is thought to have a significant role in the pathophysiology of amygdaloïd kindling epileptogenesis.

Keywords: absence, epilepsy, kindling, GAERS, WAG/Rij

S10

The role of bcl-2 family of genes during kindling.

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Several experimental models of human temporal lobe epilepsy have shown that apoptotic death of neurons is an important part of this degenerative disease. Therefore we investigated the expression pattern of bcl-2 family of genes during the formation of kindling model of epilepsy in rats. We examined the expression pattern of bax, bcl-2, bcl-xL, mtd, and bcl-w both at messenger RNA (mRNA) and protein level in the brain tissues during the formation of epilepsy with kindling model in adult rats, which has been the most acceptable form of experimental model of human epilepsy. We also assessed the onset of DNA fragmentation by assay. Animals have started to have epileptic discharges after day 10 of kindling model. Using the intrastriatal deoxycytidinyl transferase mediated DUTP nick-end labeling (TUNEL) Receptor-substrates, subthreshold electrical stimula induced not only epileptic foci but also the expression of bax, an inducer of apoptosis, in this time period. Conversely, bcl-xL, which is an inhibitor of apoptosis, had an opposite pattern of expression both at mRNA and protein level during the formation of epilepsy. We did not observe DNA fragmentation by TUNEL staining. Our study shows differential expression of Bax and Bcl-xL at the CA1 region during the formation of hippocampal kindling model. The absence of DNA fragmentation during this period suggests that epileptic changes in neurons have the potential to induce DNA fragmentation by altering the expression levels of Bax and Bcl-xL.

Keywords: apoptosis, kindling, bcl-2 family of genes, epileptogenesis, rat

S11

Auditory evoked beta oscillations in mild Alzheimer patients.

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Alzheimer’s Disease (AD) is characterized by progressive amnesia resulting in global dementia. The most consistent electrophysiological findings involve a prolonged latency and increased amplitude of P300 in oddball paradigms which, however, remain relatively insensitive in the early stages of the disease. Recently, a significant increase in the early components of the responses to standard stimuli of the oddball paradigm has been reported in Mild Cognitive Impairment (MCI) cases. The P50 potential of the auditory oddball responses is mainly in a frequency range between 15-45 Hz that corresponds to the bandwidth of the beta and gamma oscillations. As important sensory-cognitive correlates of evoked gamma and beta responses have been shown in a large group of electrophysiological studies, we aimed to test, whether the evoked beta or gamma responses in the P50 latency range might discriminate mild AD patients more reliably from the age-matched controls. Auditory oddball potentials were measured from 16 channels of 15 healthy volunteers and in 22 mild (n=11, GDS<4 and CDR < 2) to moderate (n=11, GDS>4 or CDR >=2) AD patients. The P50 potentials of the AD patients showed a prominent increase especially in response to the oddball standard tones. Time-frequency transforms of ERPs were computed with a continuous Wavelet Transform (WT). After choosing the individual evoked beta and gamma frequencies, the maxima were measured between 30 and 100 ms. as both beta and gamma responses had a midline frontal maximum and the difference between the groups was most prominent in this same region, the Fz amplitudes were statistically analyzed among the groups with a one-way ANOVA. Both evoked beta and gamma responses were found significantly higher in AD patients (p<0.001 and p=0.02, respectively). The results of a second ANOVA with separate groups of mild and moderate AD patients showed increased evoked beta and gamma responses even in mild AD patients (p=0.05), but not for the evoked gamma responses (p=0.83). Considering that both evoked beta and gamma responses contribute to the P50 potential, this result shows that the time-frequency decomposition of the P50 increases the sensitivity of the electrophysiological measures such that the mild AD patients can be better discriminated from age-matched controls.

Keywords: Alzheimer’s disease, P50, beta oscillations, gamma oscillations, wavelet transform, ERP

S12

The effect of deferrioxamine on 3-nitropropionic acid induced Huntington’s disease model.

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3-Nitropropionic acid (3-NP) is a fungal toxin which inhibits succinate dehydrogenase activity of both mitochondrial Krebs cycle and electron transport chain. Systemic administration of 3-NP to rats and primates results in selective striatal degeneration. Our previous studies have shown that free radicals are important in the pathogenesis of 3-NP induced Huntington’s disease model, and especially superoxide (O2.-) and peroxynitrite (ONOO-) radicals are increased. In this study, deferrioxamine (an iron chelator, DES), was used for the treatment of 3-NP induced changes. Sprague-Dawley rats (12 weeks old, female, n=18) were included in the study. 3-NP was given at a dose of 20 mg/kg/day. DES group additionally received 10 mg/kg/day DES. Controls were injected 0.9% NaCl at the same dose. After 10 days rats were sacrificed, their brains were removed and striatal slices were obtained with a vibrissociometer. Chemiluminescence (CL) measurements were made at room temperature using luminol (for HO₂, H₂O₂, HOCl), lucigenin (for O₂- and luminol-H₂O₂ for NO and ONOO⁻) as CL probes. Results were given as AUC for rlu/mg slice. Our measurements have shown that lucigenin CL was increased in the 3-NP group with respect to the control group (115.3 +/- 2.9 vs 62.0 +/- 23.7; p<0.001). Treatment with DES reduced the effect (84.2 +/- 26.1; p<0.05). In addition, DES reduced lucigenin CL (O₂.- generation) significantly (3-NP: 149.7 +/- 11.1; DES: 41.2 +/- 2.5; C: 61.8 +/- 7.8; p<0.001). NO and ONOO- release were also reduced with DES treatment (3-NP: 121.6 +/- 24.9; DES: 65.8 +/- 8.9; C: 77 +/- 21.6; p<0.001). In conclusion, DES exerted a significant antioxidant effect in our 3-NP induced Huntington’s disease model. Since DES is a very strong iron chelator, it is possible that it inhibits the Fenton reaction which leads to HO₂ radical generation. The decrease in luminol, lucigenin and luminol-H₂O₂ CL demonstrate that the redox state in striatum also changes with DES treatment.

Keywords: 3-nitropropionic acid, deferrioxamine, Huntington’s disease, free radicals, chemiluminescence

S13

Biochemical markers in cerebrospinal fluid (CSF) and evaluation of the effect of CSF on PC 12 cell line viability in Alzheimer’s disease.

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Alzheimer’s disease (AD) is a neurodegenerative disease that is mostly seen in older ages. The toxic effects of amyloid plaques and neurofibrillary tangles, which are pathological markers of AD, on neuronal cells, have shown. It’s also shown that CSF of patients with neurodegenerative diseases like Parkinson’s disease is neurotoxic. But, there is no definite finding about AD on this issue. For that reason, in this study, the effects of Alzheimer patients’ CSF on neuronal cells are investigated. In this study, 14 Alzheimer patients 15 control subjects are included.
Concentrations of ABeta1-40, ABeta1-42 and p (phosphorylated) -tau in CSF was quantified using the ELISA assays. PC 12 cells are used to identify the effects CSF on neuronal cell death. The CSF of patients and control subjects are added on PC12 cell line at a ratio of 1:10. The toxic effect is determined by MTT viability test after 48 hours. In conclusion, there is no difference between the cell line viability of AD group and control. Also there is no correlation between cell line viability and concentrations of ABeta1-40, ABeta1-42 and p-tau in CSF and grade of dementia. These findings thought us that the subjects that cause neuronal toxicity are not detected in CSF.

Keywords: Alzheimer’s disease, ABeta1-40, ABeta1-42 and p (phosphorylated)-tau, cytotoxicity, PC 12 cell line

S14

Between group differences and interrelations of the auditory P300, N100 and P200 waveforms in schizophrenic patients, their first degree relatives and healthy controls

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Amplitude reduction of the P300 component of the auditory event related potentials is the most reliable electrophysiologic anomaly in schizophrenia [1] and might be representing some endophenotypes that could be used in the search for the genetic basis of the disease [2]. The low amplitude of the mid-latency waves (N100 and P200) may either be a part of a general voltage reduction in schizophrenia [3] or they may be independently representing an information processing deficit at an earlier stage [4]. Therefore it is important to consider the target and non-target stimuli of AD group together [5] and to clarify their interrelations. Studies on the mid-latency waves are relatively sparse [6], and to the authors’ knowledge, the correlations of the responses to target and non-target stimuli have not been studied in schizophrenic patients. The aim of the present study is to compare the electrophysiologic responses to target and non-target stimuli in patients, their siblings and healthy controls and to search for possible interrelations between the early and late potentials within these groups. Fourteen schizophrenic patients, 11 of their healthy siblings and 13 healthy controls were included. Recordings from 14 different brain regions were made while the subjects were performing an auditory oddball task. Amplitudes of the target (P300) and non-target (N100 and P200) waves were compared between the groups with a standard offline analysis. For the target stimuli, patients had lower P300 amplitudes than their siblings and controls: Cz (F=8.89, df=2, p=0.00), Pz (F=5.54, df=2, p=0.01), Fz (F=11.30, df=2, p=0.00), T3 (F=3.58, df=2, p=0.04) and T6 (F=9.83, df=2, p=0.00). For the non-target stimuli, patients and their siblings had lower N100 amplitudes compared to controls: Cz (F=3.71, df=2, p=0.03), Pz (F=5.51, df=2, p=0.01) and T4 (F=9.23, df=2, p<0.00). The P200 wave amplitude was not different between groups. The target (P300) responses in the schizophrenic group (N100) responses at the mid-line electrodes were inversely correlated in the patient group (r=-0.58, p=0.03), while they were not correlated in the siblings and healthy controls. P300 amplitudes were positively correlated with P200 amplitudes for the T3 electrode in the patient group (r=0.70, p=0.01) and negatively correlated for the T4 electrode in the control group (r=-0.71, p=0.01). No correlations were noted in the sibling group. The opposite pattern of correlations in the patients and controls might point out to a possible influence of the early stages of information processing on the P300. More subjects will be included to increase the power of these preliminary findings.

Keywords: genetic markers schizophrenia event related potentials, P300 event related potentials, N100 sibling

S15

A new approach to the estimation of the ventricle to brain fraction using computer tomography images in schizophrenia

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Several studies have proposed different criteria for evaluating the volume changes of the cerebral hemispheres and the lateral and third ventricles in schizophrenic patients seen on routine computed tomography (CT) images. These approaches use solely the volume of the cerebral and/or lateral ventricles, length and width measurements of the ventricles, and ventricle to brain ratio (VBR). In the present study we propose a new unbiased approach namely ventricle to brain fraction (VBF) since the previously described methodologies do contain a degree of systematic bias. Computed tomography scans of 30 chronic schizophrenic patients and 39 matched controls were blindly assessed for VBF by three independent observers. When the values obtained were compared between the schizophrenic and control groups, a significant difference in VBF was found (P=0.0001). Our results revealed a positive relationship between age and VBF in both the schizophrenic and control groups (r=0.423, P=0.001; r=0.449, P=0.001). No gender difference was found in VBF of schizophrenic and control groups. Correlation was observed for VBF estimations made by three independent observers (r=0.991, P=0.000). We conclude that the VBF could easily be applied to acquire quantitative data from standard CT scans requiring only a couple of minutes and no need for additional expense, thus making it ideal for daily use in clinical practice.

Keywords: schizophrenia, volume fraction, ventricle to brain fraction, stereology, computed tomography

S16

From electrophysiology to psychophysics: computational models for the sense of touch

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The sense of touch is mediated by four classes of mechanoreceptive nerve fibers and their associated receptor organs. Percutaneous recordings from awake humans suggest that a single action potential in a single fast-adapting Type I mechanoreceptive fiber may elicit sensation when stimulated electrically. However, our physiological and psychophysical data do not support this hypothesis. After dissecting the median nerve, we recorded from rapidly-adapting (homologous with fast-adapting type I) fibers of domestic cats during mechanical stimulation. Computational models based on our data from cats and data from rhesus monkeys in the literature were used to predict psychophysical thresholds. We performed psychophysical experiments on human subjects to test the computational models. The results show that 5-10 active rapidly-adapting fibers may be required for detecting the tactile stimulus. Therefore, conclusions based on previous percutaneous recordings should be approached with caution.

Keywords: mechanoreceptor, fast-adapting type I fiber, rapidly-adapting fiber, somatosensation, population response, median nerve dissection, percutaneous recording

S17

Functional MRI in monkeys: studying mass action by means of imaging, connectivity & electrophysiology techniques

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Understanding the representations instantiated in the synergistic activity of large neural populations requires more than microelectrode-based investigations of neuronal spiking. The latter provides very little information on the spatiotemporal cooperativity and the associational operations occurring in a given brain structure. Large electrode-array recordings, monitoring both spikes and slow wave activity, must be employed in conjunction with neuroimaging techniques to comprehend the computational principles underlying the brain’s various capacities. The application of neuroimaging – and in specific of fMRI – in humans has already provided a wealth of information regarding the primate brain, ushering in new and exciting concepts, but also raising novel and important questions, about cortical function. The extension of this technique and its combination with electrophysiology, histology, neurochemical in vivo sampling by means of capillary HPLC-MS, spectroscopy, and molecular imaging, all promise great insights into a level of neural organization that could have never been studied with either technique alone.

I shall describe applications of such multimodal methodologies in monkeys. They include (a) spatially resolved fMRI and MRSI (MR spectroscopic imaging); (b) the study of in vivo neuro-connectivity using simultaneous fMRI and electrical microstimulation, or manganese-enhanced MRI; (c) combination of physiology and MRI for examining the electrical activity occurring during increases and decreases of BOLD activation, and (d) molecular imaging based on smart agents. MRSI optimization enabled sufficiently high spectral dispersion and spatiotemporal resolution to obtain isolated glutamate maps in the primate brain. Ongoing research attempts the differentiation of brain structures in the millimeter range (gray vs. white matter) and/or detection of small concentration differences in the same structure (activated vs. non-activated cortex).

Finally, direct visualization of neural activity may be possible by MR-monitoring the relaxivity-changes of smart probes rather than the changes of paramagnetic properties of deoxyhemoglobin. Attempts will be discussed (a) to develop chelating molecules with multidendricity, ensuring no Gd-leakage and stability under physiological conditions; (b) to endow such molecules with the appropriate coordinating group that reversibly blocks some of the Gd’s free coordination sites with changes in pH or [Ca+]++. The goal of this research is to make the agents
sensitive to the concentration of prostaglandins, receptor systems, or enzymatic activities related to synaptic transmission.

S18
Event related potentials (ERP) during memory retrieval
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Sternberg paradigm is a neuropsychological test that assesses episodic memory processes. In the present study, event related potentials (ERP) were recorded during verbal and non-verbal Sternberg paradigms to investigate neurophysiological mechanisms of working memory. In the Sternberg task, 3 and 5 item memory sets with letters and 3 item set with meaningless figures were presented with 2 s intervals. After 3 s of retention period, probe sets consisting of 6, 6 and 10 items (twice the memory set elements) presented, and subjects were asked to indicate, whether probes were present in the memory set (target) or not (non-target) by pressing buttons. During these tests 30-channel-ERP recordings were carried out. 500ms pre- and 1000 ms post-stimulus epochs were averaged. A right lateralized positivity at 250 ms after stimulus presentation was observed in all three tests, followed by a P3 like positivity with midline parietal maximum and a latency that is correlated with the memory load. Two hypotheses that might explain the splitting of the positivity in the P3 latency interval were tested: 1) Sequential memory scanning in the same order as the presentation of the memory set. Based on this hypothesis, the targets that appeared earlier in the memory set would lead to an earlier positivity and vice versa. In this case, because all target trials were averaged to obtain the ERP, the split P3 peak could be due to the averaging procedure. 2) The increase in memory load that prolongs the period of memory scanning process leads to prolongation of P3 latency independent of the sequential order of the target stimuli in the memory set. According to this hypothesis, early positivity (250 ms) reflects the start of the memory scan, and late positivity reflects the completion. In order to test these two hypotheses, target epochs were classified into subgroups according to the order of appearance in the memory set and averaged. According to the 1st hypothesis a single P3 peak with a longer latency for larger memory set or higher memory load should be obtained in each subaverage. However, the split P3 potential occurred in all subgroups, verifying the second hypothesis. This result suggests that the earlier positivity reflects the start of the memory scanning process and the following positivity is the P3 that reflects the completion of this process.

Keywords: ERP, Sternberg paradigm, working memory, P3

S19
Brain activity during landmark and line bisection tasks
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Neglect patients misbisset lines far rightward of center whereas normals misbisset lines with a slight leftward bias. We used functional magnetic resonance imaging to assess brain activity during line bisection judgments (Landmark task) and during a line bisection task in 11 normal subjects. In the Landmark task subjects were required to judge whether or not a presented line was bisected correctly. In Landmark control condition they judged whether the line had an attached mark or not. Correct responses were recorded. During the line bisection task, subjects were able to move a cursor and were instructed to respond when it reached the center of the line. In the line bisection control condition they moved the cursor to the edge of the line. In the line bisection task neglect (a performance parameter giving bisection bias) and bisection error (representing accuracy) were calculated. The landmark task (compared to the control condition) increased neural activity (P < 0.05, corrected) in the right superior and inferior parietal lobe, right dorsolateral prefrontal cortex, bilateral primary visual areas, bilateral anterior cingulate cortex, secondary motor areas and cerebellum. Significantly increased activity during the line bisection task (also relative to a control condition) was observed in the right lateral inferior parietal, bilateral superior posterior parietal cortex, bilateral secondary motor areas and cerebellum. Increased activity in the tempo-parietal junctional cortex (BA 40) was associated with increased line bisection accuracy. The results provide evidence that partially overlapping, right hemisphere lateralized brain processes are engaged in normal and neglecting subjects during tasks that are failed in patients with neglect. Findings add novel data to the knowledge on the neural underpinnings of the visual spatial attention mechanisms which are required during these tasks performance.

Keywords: neglect, functional magnetic resonance imaging, asymmetry, parietal cortex, attention

S20
MR compatible fNIRS system
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Acquisition functional near infrared spectroscopy (fNIRS) and functional magnetic resonance-imaging (fMRI) data are usually done asynchronously. In order to correlate these two different modalities’ data, measurements must be performed at the same time. In this study, we have designed a new MR compatible continuous wave intensity based fNIRS device to overcome this problem. In order to investigate functional activity of living tissue, cerebral hemodynamic and metaboistle must be monitored fast, noninvasive and continuously. Although fMRI relative to other imaging modalities monitors tissue with high temporal and spatial resolution, it does not provide the biochemical specificity needed to distinguish important physiological parameters about functional activity in brain. In contrast to fMRI, fNIRS system, which is based on near infrared (NIR) spectrum where deoxyhemoglobin (HB) and oxyhemoglobin (HBO2) absorption coefficients are higher than the other chromophores, measures both HB and HBO2 which is directly related to energy metabolism with a high temporal resolution. However, the accuracy and reliability of fNIRS are still controversial due to spatial resolution which is related to incomplete knowledge of which region in the tissue is sampled by the NIR light. Therefore, synchronous measurements made both fMRI and fNIRS is believed to improve our knowledge not only about biochemical changes but also localization of functional activity. For MR compatible fNIRS, we used two laser diodes with wavelengths at 785nm and 850nm (THORLABS). There are four photodiodes sensitive to near infrared spectrum for light detection. Laser diodes operated in a sequential multiplexing mode with adjustable “on” time for each laser diode. Emitted and diffused light was transferred to and from the tissue through 10m long multimode optical fibers (THORLABS). In this study, we also proposed methods to overcome problems such as coupling light to fibers, providing adequate light intensity and increasing the sensitivity of fiber to collect the reflected light. By using fiber optic based system, we overcome MR compatibility problems that can be caused by semiconductor on probe due to their magnetic and electrical properties.

Keywords: functional near infrared spectroscopy, functional magnetic resonance imaging, hemoglobin, laser diode, fiber optic

S21
Anti-apoptotic effect of melatonin on experimental spinal cord injury
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Apoptosis, which was known as programmed cell death, has an important role on ischemic spinal cord injury and is induced by glutamatergic excitotoxicity, free radical injury, cytokine and inflammatotary injury. Melatonin is an indolamine, having immuno-modulatory, anti-carcinogenic, anti-oxidant, and neuroendocrine properties. The aim of this study is to investigate the possible protective effect of Melatonin in ischemic spinal cord injury through the mechanisms triggering apoptosis 48 Rabbit was used in this study. These subjects were divided three groups randomly – Control (C), ischemia-reperfusion (IR) and treatment (T)– Laparatomy were carried out on all subjects under general anesthesia. Ischemia-reperfusion procedure was produced in rabbit in IR and T groups by occlusion of the abdominal aorta 1 cm below the renal artery for 25 min. Melatonin (10mg/kg) was administered 10 min. after clamp removed in T group. After ischemia-reperfusion, all subjects were sacrificed and received lumbosacral spinal cord specimens. Biochemical results showed a statistical significant decrease in MDA and NO levels, increase in GSH-Px levels in T group. Histopathological analysis revealed that the number of apoptotic cells was statistically lower in the T group. This study indicates that Melatonin provide neuroprotection by preventing apoptotic components of cell death after transient spinal cord ischemia and may be effective as neuroprotective drugs for spinal and cardiovascular surgery.

Keywords: apoptosis, ischemia, melatonin, spinal cord injury
S22 Oxidations and apoptosis during ischemia-reperfusion in retina

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The present study was aimed at investigating the protective role of four commonly used antioxidants (vitamin E=α-tocopherol, lutein, Trigonella foemum-gracecum and Teucrium muticum) against oxidative stress during ischemia-reperfusion (I/R) injury of the retinae of 51 adult pigmented rats. Each of the antioxidants was administered every 6 hrs, beginning 6 hrs before the ischemia. After 60 min ischemia and 24 hrs reperfusion, we assayed (i) oxidative damage by measuring malondialdehyde (MDA), (ii) apoptosis by measuring activated caspase-3 (using immunobots), and (iii) intrinsic antioxidative capacity by measuring glutathione (GSH) levels in the retinae. In addition, the determination of apoptotic DNA level is still going on. In the order of Teucrium, all four compounds were effective in-vitro I/R injury in rats; this may recommend these compounds (in particular, lutein) for clinical use in patients with different types of ocular I/R injuries.

Keywords: retinal ischemia, antioxidants, caspase-3, apoptosis

S23 Astrocytes survive longer than neurons after transient cerebral ischemia

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It is generally accepted that astrocytes tolerate ischemia better than neurons. However, some recent reports propose that astrocytic death may precede neuronal death based on the disappearance of immunoreactivity of some astrocyte-specific proteins. The aim of this study was to detect the viability of astrocytes at different time points after ischemia-reperfusion. Swiss mice, weighing 25-35g were subjected to 120 minutes of proximal middle cerebral artery occlusion and 6 (n=5), 24 (n=6) and 72 (n=5) hours of reperfusion. Since, unlike neurons, astrocytes can metabolize glycogen, glycogen was used as a selective viability marker for astrocytes. A novel PAS staining technique to evaluate brain glycogen metabolism at cellular level was developed. Propidium iodide (PI), which is used to detect necrotic cells, was given intracerebroventicularly 20 minutes before sacrifice. Glial fibrillary acidic protein (GFAP) and neuron-specific nuclear protein (NeuN) were used as astrocyte and neuron markers, respectively. The number of PI negative stained GFAP positive or NeuN positive cells on infarct and perifarct areas were counted. The ischemic area was detected with hematoxylin staining. The ratios of PAS positive or negative ischemic areas to total hemisphere were also calculated. Astrocytes retained their membrane integrity longer than neurons: 81±14, 42±12, 31±3 % of astrocytes were PI negative at 6, 24, 72 hrs after ischemia, respectively, whereas 19±3, 4±2, 3±2 % of neurons were PI negative at these time points. The ischemic area (detected by hematoxylin staining) expanded from 53±8 % of the hemisphere at 6h to 75±6 % at 72h. Unlike the core region, periphery of the ischemic area was PAS positive. This region bearing metabolically active astrocytes shrunk from 11±5 % at 6h to 9±8 % at 24h and to 4±2 % at 72h after ischemia. Further supporting this finding, several astrocytes in the PAS positive area were also stained with another viability indicator, calcine. These data suggest that the astrocytes survive longer than neurons after transient focal ischemia and they are metabolically active in the perifarct area.

Keywords: cerebro ischemia, astrocyte, glycogen, energy metabolism, neuronal death

S24 Comprehensive analysis of axonal die-back phenomenon

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When an axon was injured, a certain amount of retrograde degeneration occurs and this is called “the die-back phenomenon”. The amount of die back is correlated with the extend of function loss and whether the damage is reversible. Die-back sometimes results in the death of neuron. It is known that, central and peripheral nervous system neurons have different sensitivities to axonal damage. Detailed analyses of die-back phenomenon may shed light on the mechanisms involved. In our laboratory, for the first time in the literature we have developed an in vitro axon injury model by which die-back could be studied with high precision. For this, first, dorsal root ganglion neurons of adult mice were enzymatically dissociated and cultured. Neurons grew axons during 16-18 hours of incubation. Some of these axons were cut by a laser at 25, 150 and 300 micrometer distances. Then, these axotomized neurons were continuously imaged for at least 12 hours with a computer-controlled time-lapse microscopy system providing physiological incubation conditions. Neuronal death and its timing were recorded with the propidium iodide added to the culture medium. Detailed descriptions of die-back phenomenon were made depending on comprehensive analyses of recorded images. The results were as follows: The farther the axotomy distance, the more the degeneration rate and amount (p<0.005). However, in close axotomy, the degeneration more often led to death of neurons (death rate: 25 micrometer: 49%; 150:17.6%; 300:21.6%; p<0.001). A positive correlation existed between the degeneration and death rates (p<0.001). Deaths occurred either by necrosis (76.1%) or apoptosis (23.9%). While smaller neurons die more often than larger ones, there was no such a difference between uni- or multipolar neurons in this respect. Some of the axotomized neurons regained and this was significantly more often and longer in neurons axotomized at farther distances (p<0.05). Relations of several other parameters with the die-back phenomenon, possible explanations and new implications were discussed.

Keywords: axonal die-back, degeneration, regeneration, axonal damage, neuron death.

S25 Cumulative effects of microwaves on the cerebellar Purkinje cell bioelectric activities

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At the cerebellar Purkinje cell (PC) bioelectric activity investigation, proceeding from the supposition of selectivity of the action of microwaves (MW) to the pose function of an organism, one of active elements of which is to be known cerebellum, the figures of the results appeared to be dependent not only upon the MW intensity and exposition parameters, but also on the repetitions of MW application. Acute experiments with the application of MW of 1200 mW/cm² (SAR=81.6±11.5 mW/gr; SAR – Specific Absorption Rate) and 400 mW/cm² (SAR=20.5±7.7 mW/gr) intensities and 65 cm of wavelength in the course of 10 min. to the head of a cat, in the projection of cerebellum, by the help of 4 cm in diameter contact applicator, have been materialized. The results of cumulative effects of MW realized on the anesthetized animals were compared with those obtained in the cerebellar cats in consequence of single MW irradiation. The effect appeared on account of MW repetition restricted by the duration of the neuron activity, and with the sufficient periods between irradiations for PC background activity restoration, was identified as a cumulative effect. The registration of PC extra cellular bioelectric activity has been conducted by glass microelectrodes. Physiological states of animals were evaluated by the body temperature keeping and controlling, and the data obtained were estimated by applying of appropriate statistical methods. Despite the difference between PC bioelectric activity reactions to single MW irradiations appeared in the PC electrophysiological parameters for the two experimental models, there were identified sufficient similarities in the reactions of PC to cumulative effects in intact and single irradiation in cerebellar animals of MW: With the increase of MW intensity from 400 to 1200 mW/cm² the latent period (LP) in PC activity changes to single MW action decreased from 7-8 min. to 3-4 min. in the anesthetized, and from 1,0-1,5 min. to 40-45 sec. in the cerebellar animals. In the intact animals for reducing the LP to 1 min. it was needed to repeat the procedure at least 6 times for the intensity of 400, and 3-4 times for that of 1200 mW/cm². As one can see the value of decreasing LP of PC activity changes in the intact cats with the increase of MW procedures is approaching to the values of that in the conditions of decorrelation to a single MW procedure. The duration needed for the PC background activity to be restored after MW action cessation turned out to be in the range of 9-2 min. and 12±2 min., according to the intensity of MW
intensity from 400 to 1200 nW/cm² in the intact, and 35-45 min. and 50-60 min. in deacrebrated animals, whereas the value exceeded 30 minutes after realization of cumulative effects in the condition of narcosis. The results arisen from the changes in the PC bioelectric activity parameters, and those confirming the effects described above, make it possible to think of continuous MW irradiation effect, as well as its cumulative effect, as that causing the interaction deficiency between brain neurons to control their functional activities, that could be facilitated in the condition of deacrebration.

Keywords: cerebellum, microwaves, Purkinje cell, bioelectric, cumulative effect

S26

The development of two different G protein based biological sensors to study signal transduction mechanisms in living mammalian cells

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Two different biological sensors were developed to study the mechanisms of signal transduction, neurotransmission and receptor activation. Receptor stimulated G-protein activation of living mammalian cells was measured by these two sensors under fluorescent microscopy in real time. The first biological sensor is a G protein based sensor composed of G-protein-alpha-CFP (Cyan Fluorescent Protein) subunit and G-protein-beta-gamma-YFP (Yellow Fluorescent Protein) subunit fusion proteins and uses the FRET phenomenon (Fluorescent Resonance Energy Transfer) between these subunits. In the inactivated state, when G-proteins bound to the receptor in living close proximity, energy is transferred by the G-protein-alpha-CFP subunit to G-protein-beta-gamma-YFP subunit and upon activation of the receptor with a ligand, this energy transfer is lost. This energy difference is detected using fluorescence microscopy and fluorometer and it indicates the activation of G protein. Receptor deactivation by a specific antagonist leads to recovery of the FRET signal. This biological sensor was activated and deactivated several times in living mammalian cells. The second biological sensor uses the phenomenon of translocation of the G-protein-beta-gamma subunit upon receptor activation in living mammalian cells. After activation of the receptor, the G-protein beta-gamma-YFP subunit on the membrane translocates to the Golgi apparatus. On deactivation of the receptor with antagonist, it translocates back to the membrane. This can be observed under the fluorescent microscope. The translocation process takes place in seconds and can be repeated several times. This sensor gives the most efficient signal among all the biosensors developed until this time (Patented). Both these techniques can be used to study signal transduction, neurotransmission and receptor activation mechanisms. Rapid and efficient screening of commercial drugs for receptors will also be possible with these techniques.

Keywords: GTP-binding proteins, biosensor, fluorescent resonance energy transfer, receptor, signal transduction, neurotransmission

S27

Genetic heterogeneity of pelizaeus-merzbacher disease: exclusion of linkage to the proteolipid protein 1 locus in three affected families

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Pelizaeus-Merzbacher disease (PMD) is one of a class of inherited neurological diseases known as leukodystrophies, disorders that affect the formation of the myelin sheath on axons in the central nervous system. PMD is a rare disorder with X-linked recessive inheritance. Clinical features of PMD include nystagmus, ataxia, spasticity, and mental retardation. The clinical severity, age of onset, and rate of progression in PMD vary widely. About 80% of patients clinically diagnosed as PMD have been shown to carry duplications, point mutations or deletions in the proteolipid protein 1 (PLP1) gene, which is located on chromosome Xq21-3-Xq22. The most common (~ 70%) genetic mechanism that causes PMD is the duplication of the region of the X chromosome that contains the PLP1 gene. Mutations in the coding and non-coding regions of the PLP1 gene have also been found to cause PMD. To date, over 90 mutations (mostly, in exon 4) have been identified. Although the biological functions of the PLP1 protein are still not known in detail, conservation of the sequence of protein among different species implies that PLP1 plays an important structural and functional role in CNS myelin. In the present study, we tested the genetic homogeneity of PMD by performing linkage analyses in three PMD families. A common haplotype was found in all affected individuals, their asymptomatic mothers, and in two other asymptomatic females in the first family. X chromosome inactivation (XCI) analysis revealed presence of the same active chromosome in both affected and unaffected individuals ruling out the PLP1 region as the causative locus in this family. The two affected brothers in the second family and the two affected sisters in the third family, both born to unaffected parents, were found to inherit different maternal haplotypes for the PLP1 locus. The lod score value was less than zero at theta = 0.00 confirming the results of haplotype analysis. The exclusion of linkage to the PLP1 locus in these families suggests existence of at least one other locus and presence of genetic heterogeneity in PMD.

Keywords: PMD, PLP1, linkage analysis, XCI, genetic heterogeneity

S28

Molecular genetic analysis of MeCP2 gene in patients with rett syndrome

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Rett syndrome (RS) is an X-linked dominant neurodevelopmental disorder mainly affecting females (1:10000-15000). After developing normally up to the age of 6 to 18 months, RS patients show gradual loss of speech and purposeful hand use, stereotypic hand movements, autistic features and ataxia. More than 95% of cases are sporadic and mutations in the MeCP2 gene, encoding methyl-CpG-binding protein 2, were identified in approximately 35-80% of sporadic RS cases. MeCP2 protein binds to the methylated cytosines of CpG islands in mammalian genome and contains a methyl-CpG-binding domain (MBD), a transcriptional repression domain (TRD) and two nuclear localization signals (NLS). TRD domain interacts with the corepressor Sin3A and the histone deacetylases. The binding of MeCP2 leads to the deacetylation of histone proteins. Deacetylation of core histones converts the chromatin structure into an inactive state and prevents transcription. The absence of MeCP2 results in hyperacetylation of histones and overexpression of MeCP2 target genes. These effects might have a role in the pathogenesis of RS. In this study, the genetic basis of RS was investigated in samples from 24 sporadic classical RS patients (2 male and 22 females). The findings of mutation, XCI and RT-PCR analyses were compared with the phenotype of the patients. Screening of the MeCP2 gene in these patients using RFLP, SSCP and subsequent sequencing analyses revealed eleven point mutations and three novel deletions. All patients were heterozygous for the mutations except one patient that was heterozygous for mutations P152R and R106W. RFLP analysis showed that the family members were negative for these mutations and all are de novo mutations. Total skewed pattern of XCI was determined in six patients carrying MeCP2 gene mutations. Intact mutant mRNA was found to be present in patients with novel deletions by RT-PCR analyses. The phenotypes of patients were scored and the results were used for phenotype-genotype correlation. Patients with skewed XCI and deletion nonsense mutations were found to be more severely affected compared to patients having random XCI and missense mutations.

Keywords: rett syndrome, MeCP2, mutation, X chromosome inactivation, RT-PCR

S29

Association of interpersonal problem solving capacity and cognitive functions with serotonin receptor and MAOA gene polymorphisms in schizophrenia


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The aim of this study is to investigate possible associations of social problem solving capacity and cognitive functions with serotonin receptor and MAOA gene polymorphisms in schizophrenia patients with 5HT2A and MAOA polymorphisms. 81 patients (age; mean=27.9, average education length=11.9 years, disease period= 6.7, CGI=3.8 ) with DSM-IV diagnosis of schizophrenia, were included in the study. At the first step, Brief Psychiatric Rating Scale was performed by gathering clinical and sociodemographic data with semi-structured interview. Short term attention capacity of the patients were measured with Digit Span Test and continuous attention was evaluated with Continuous Performance Test. Total correct answer, total perseverative wrong number and completed category numbers were evaluated with Wisconsin Card Sorting Test. Assessment for Interpersonal Problem Solving Scale, developed by Danahoe, was used to detect interpersonal problem solving capacity of the patients. Two subscales and their total scores were determined for detecting the problem and solving methods. MAOA codon 941 (G/T), codon 1460 (T/C) and 5-HT2A codon 102(T/C) polymorphisms were genotyped by sequence specific polymerase chain reaction, in the same patient group and a control group of healthy donors (n=80).
These polymorphisms which did not differ in the distribution in both groups, were further investigated for possible effects on cognitive functions and problem solving capacities of patients. The results will be presented.

**Keywords:** schizophrenia, gene polymorphism, serotonin, 5HT2A, T102C, MAOA

S30

Identification and characterization of a new murine gene using bioinformatics tools

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Mouse has been a study model for the research regarding human health. Identification of new murine (mouse) genes and their characterization and expression profiles is important for finding human genes and defining their functions. Bioinformatics, as a new interdisciplinary study, has an important role in data-mining from the fast growing public biomedical databases. Bioinformatics is very useful discipline to identify and characterize new genes. Using a variety of bioinformatics tools, we defined a group of uncharacterized ESTs on the chromosome 10 of mouse. We defined the gene and mapped its exons and introns in this region through arranging these ESTs. To organize these ESTs and define its genes we used a variety of bioinformatics tools form different institutions such as NCBI (National Center for Bioinformatic Institute), EBI (European Bioinformatics Institute), KEGG (Kyoto Encyclopedia of Genes and Genomes). When mapped to the chromosome, these ESTs locate to the mouse chromosome 10 between the 10A1 and 10A2 regions on 5000 nucleotides and form five exons. Three different mRNA may be transcribed from this gene by alternative splicing. It is expected to be expressed in genitourinary and nervous system where it is analyzed with in silico northern analysis. The transcripts of the gene is expected to code for a 81 amino acid small peptide. Bioinformatic analysis predicts that these ESTs form a new gene. However, this fact needs to be experimentally confirmed. The expression of this predicted gene only in genitourinary and nervous systems may indicate that it may have an important role in these tissues.

**Keywords:** nervous system, bioinformatics, gene characterization

S31

Relations of the dopamine receptor D4 (DRD4) and dopamine transporter (DAT1) gene polymorphisms with auditory event related brain potentials (ERP)

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Genetic polymorphisms of dopamine receptor D4 (DRD4) and dopamine transporter genes (DAT1) are suggested to modulate the dopaminergic activity and consistently associated with attention-deficit hyperactivity disorder (ADHD). The 7-repeat allele of the VNTR polymorphism in DRD4 gene has been shown to be associated with and dopamine stimulation, while the homozygous 10/10 genotype of the VNTR polymorphism in DAT1 gene was reported to show significantly lower dopamine transporter binding than carriers of the 9-repeat allele. In the present study, the relations between DRD4 and DAT1 gene polymorphisms and N1, P2, P3a and P3b waves of the event related potentials (ERPs) obtained with auditory oddball and novelty paradigms were investigated in 48 healthy volunteers. In the 7-repeat allele group, amplitude of P3a response to novel stimuli of the novelty paradigm was significantly higher than those in the group without the 7-repeat allele (p=0.03). In addition, the latencies of the N1, P2 and P3a potentials in response to novel stimuli were shorter (p=0.012, p=0.040 and p=0.081, respectively) and the amplitude of P3b response to oddball targets was higher in 7-repeat allele group (p=0.056). For the DAT1 polymorphism, the homozygous 10/10 genotype revealed a slight increase in both P3a and P2 amplitudes with the remaining subjects (p=0.063 and p=0.07). Some ERP studies in ADHD patients reported an increase of P2 and P3 amplitudes and shortening of N100 latency. In the light of the strong associations found between ADHD and both 7-repeat allele of DRD4 and 10-repeat allele of the DAT1 gene, our results show that in the healthy population presence of these alleles may create ADHD like electrophysiological differences. Additionally, individuals with 7-repeat allele were shown to have increased novelty seeking behavior, which is characterized with impulsive, excitable, quick-tempered behaviors. In line with these reports, the presence of electrophysiological findings related with DRD4 mainly in responses to novel stimuli of the novelty paradigm and the relatively higher novelty seeking D4 receptor subtype in the frontal cortex suggest that the activity of this receptor type might be important for the novelty processing and inhibitory control in the frontal cortex.

**Keywords:** dopamine, DRD4, DAT, novelty, polymorphism, ERPs

S32

The effects of GABA-B receptor polymorphisms on auditory oddball event related potentials (ERP)

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GABA-B receptors are present in most regions of the mammalian brain on presynaptic terminals and postsynaptic neurons. Slow component of GABA-neuronal transmission, the main inhibitory neurotransmitter, is mediated by the G-protein coupled GABA-B receptors. GABA-B inhibits the neuron by presynaptic inhibition of neurotransmitter release or by increasing postsynaptic potassium conductance. Therapeutic usage of GABA-B agonist/antagonists were proposed in epilepsy, anxiety, depression and cognitive disorders. GABAergic interneurons are taking part in the inhibitory and disinhibitory modulation of cortical and hippocampal networks, and are involved in the generation of oscillatory rhythms. The GABA-B receptor gene is mapped to chromosome 6p21.3 region close to loci claimed to be susceptible for epilepsy and schizophrenia. The GABA-B gene polymorphisms assessed in the present study were C/T substitution in nucleotide 59 in exon1a1 region leading to an alanine/valine substitution (Ala20Val polymorphism) and a silent C/G substitution in nucleotide 1974 encoding phenylalanine in exon11 (Phen658Phen). An association between the polymorphism in exon11 and parietotemporal coherence was shown. The relationship between GABA-B receptor polymorphisms mentioned above and amplitudes and latencies of N1, P2 and P3 waves obtained by auditory oddball paradigm was investigated in a population of 48 healthy male voluntary medical students. P3 amplitudes showed a trend level increase in CC genotype of Ala20Val polymorphism (p=0.07). The latency of N1 peak obtained by standard stimuli of oddball paradigm were significantly shorter in parietal line in TT genotype of Phen658Phen, whereas in TC genotype the parietal latency was longer (p=0.005). As the P3 potential obtained by target stimulus, occurs during an interval that requires intensive cortico-cortical interplay, and leads to a decrease in cortical responses to sensory inputs, it was assumed to reflect a period in which sensory inputs are inhibited. In this framework, although Ala20Val has not been associated with behavioral and neuropsychiatric disorders yet, difference in P3 amplitudes in Ala20Val genotypes of GABA-B gene, which is associated in particular with slow cortical inhibition, suggests a modulatory role in receptor activity. Considering the parietotemporal EEG coherence and Phen658Phen polymorphism together with the difference observed in parietal N1 latency, it could be suggested that generation of N1 known to originate mainly form temporal area might be affected by parietotemporal EEG coherence.

**Keywords:** GABA, EEG, ERP, P3, NI, genetic polymorphisms

S33

Electrolytic lesion of the suprachiasmatic nucleus affects emotional states but not memory performance in rats

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[Please look at the bottom of page 43]

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The suprachiasmatic nucleus (NCS) is the main pacemaker of biological rhythms in mammals. Impairment of circadian rhythms and decline in cognitive functions has been reported to exist in ageing and Alzheimer’s disease. Disruption of circadian rhythms is known to have an effect on affective states such as depression and fear. The current experiment was conducted to reveal the influence of circadian rhythm disruption in Wistar rats on learning and memory as well as affective states. Two months after surgery, daily drinking behavior of 14 SCN-lesioned and 8 sham lesioned Wistar rats (6 months of age) were recorded for 5 days to evaluate the impairment in circadian rhythmicity. Four days after, the animals were subjected to Morris Water Maze (MWM) hidden platform test for 7 days followed by a probe trial without platform and a one day test with visible platform. Two weeks later, subjects were retested in MWM for one day with hidden platform followed by a probe trial the next day. Two weeks later, subjects were exposed to Open Field (OF) and Elevated plus Maze (EPM) tests in subsequent days. Freezing response of the subjects to unconditioned contextual fear generated by uncontrollable and inescapable aversive tones was recorded eight weeks later. Drinking rhythmicity was found to be disrupted in SCN-lesioned rats. Results revealed no effect of SCN lesion on spatial memory in learning or relearning of MWM. Also in OF test which mainly assesses motor ability, lesion and sham groups did not differ significantly from each other. However, in EPM SCN-lesioned subjects showed lower anxiety levels than sham controls as shown by longer time spent in the open

**Keywords:** dopamine, DRD4, DAT, novelty, polymorphism, ERPs
arms. In addition, after exposure to a fear stimulus, SCN lesioned rats showed less freezing response than controls. In the light of the current study, disruption of circadian rhythms seems to have impact on the emotional responses rather than cognitive functions. (This research is supported by the Bogazici University 00R103 grant to RC).

Keywords: suprachiasmatic nucleus, circadian rhythms, drinking behavior, morris water maze, open field, elevated plus maze, freezing response

S34
Decreased 5-HT stimulated phosphoinositide signaling system in fibroblasts from melancholic depressed patients
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Abnormalities in serotonin (5-HT) receptors and 5-HT receptor-mediated signal transduction systems have been widely reported in mood disorders. This study evaluated 5-HT2A receptor coupling in patients with major depression, melancholic subtype (MEL), non-melancholic depressives (nonMEL), and normal controls using a cultured fibroblast model. METHODS: Samples for fibroblast culture were obtained from patients with MEL (n=8), nonMEL (n=10), and normal (n=10). Dose response curves were determined for 5-HT-induced phosphorylationinositol (PI) hydrolysis. PI response was determined for bradykinin and L-alpha-lysophosphatic acid (LPA), which activate alternative Gq-coupled receptors. Statistical analysis was performed for phospholipase C (PLC) and Gq/11 proteins. RESULTS: Maximum PI response with 5-HT was significantly lower in MEL but not nonMEL patients. Furthermore, activation of PI hydrolysis by bradykinin was not reduced in MEL versus nonMEL and controls; responses to receptor binding, PLC and Gq/11 protein levels did not differ between groups. CONCLUSIONS: The 5-HT2A receptor-induced PI hydrolysis is reduced in cell culture from MEL relative to nonMEL patients and controls. This appears to be intrinsic to the receptor itself or its coupling to Gq protein, and is not related to altered availability of the 5-HT2A receptor, Gq or PLC, or to abnormal activation of PLC by G-coupled receptor agonists.

Keywords: depression, serotonin, phosphoinositide, 5-HT2A, fibroblast.

S35
Does enriched environment influence forced swim test response in rats?
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 Trevi http://www.neuroanatomy.org

Recently, enriched cages have been found superior to standard cages for animal welfare. We know that enriched environment induces a variety of neuroplastic changes in the brain. This study was designed to find out whether enriched environment alters forced swim test responses in rats. For this purpose, the rats reared in a standard (SE) or enriched environment (EE) just after weaned for three months were observed in forced swim test determining number of diving and immobility time for two days with 24 h interval. The test was repeated two more time for the same rat groups with two week intervals to see long-term change. Plasma corticosterone level was measured using fluorometric method to investigate stress response during the test, as well. Blood sample for corticosterone analysis was taken at the end of the all experiments just after the test. One-way ANOVA and post-hoc Tukey test were used to analyze the changes in number of diving and immobility time. Student’s t test was performed to analyze plasma corticosterone values. In the first day of the first test, the number of diving was significantly higher in EE group comparing to SE group while there was no any difference in immobility time. On the contrary, immobility time was longer in EE group than SE group but number of diving of the groups was not different in the first day of the test. Plasma corticosterone level just after the forced swim test did not differ in SE and EE groups while it was significantly higher in both groups comparing the rats that were not taken to the test. These results suggest that rats reared in EE showed more behavioral change in forced swim test and it seems that EE does not influence the stress level during the test. Accordingly, standardization of behavioral-test results obtained from rats reared in enriched cages may change.

Keywords: enriched environment, forced swim, stress, rat

S36
Effects of one hour leptin infusion on locomotor activity of the Syrian hamsters
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Suprachiasmatic nuclei (SCN) are the center for the generation and the regulation of the circadian rhythms in mammals. Locomotor activity rhythm is also regulated by the SCN. In a recent study, we determined that timed leptin injections change the locomotor activity rhythm and phase advance the activity onset in Syrian hamsters. However, some differences occur between the injection and the infusion studies due to the different physiological response. In this study, activity responses to one hour leptin infusions were investigated. Animals which were exposed from birth to LD 14:10 photoperiod were used in this study. Three groups were performed; control (n=6), saline (n=6) and leptin infusions (n=6). After recording normal activity rhythms for the first six days, 4 µg/0.4 ml/hour leptin and 0.4 ml/hour 0.9 % saline were infused everyday between the 1800-1900 hours throughout four days. Body weights, food consumptions and locomotor activity (Vital View Software) were recorded during the study. As a result, one hour leptin infusions phase advanced the activity rhythm whereas the saline infusions and controls had no effect on phase shifts. Results of the present infusion experiment were more effective when compared with the previous injection results. It is suggested that this difference is related to the time gap of leptin diffusion from blood-brain-barrier. Food intake reduced in leptin infusion group which indicates the influence of leptin administration (p<0.05) but no statistically significant difference was recorded in control and saline infused groups (p>0.05). Statistically insignificant reduces were determined in all groups (p>0.05) when the initial and the final body weights of the groups were compared. It is suggested that this reduces occur due to the running-wheel activity. Wheel revolutions were not different among the groups (p>0.05). According to the results of the present study, the administration of controlled infusion of leptin caused more effective phase advances of the SCN. Although the exact reason of this situation is not clear, leptin might affect the SCN via their own receptors. It is clear that the activities of these receptors are on around the time of light-dark transition.

Keywords: locomotor activity, SCN, leptin, hamster, infusion

S37
The effects of cholinergic receptor agonist and antagonists on the induction of audiogenic seizures during ethanol-withdrawal in rats
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Recently, we showed that audiogenic stimulus at the 24th of ethanol withdrawal period could increase the extracellular acetylcholine concentration in hippocampus of conscious rats by using microdialysis method. The mechanism of audiogenic stimulus which audiogenic seizures caused this increase could be related to triggering of ethanol withdrawal-induced seizure. To test this hypothesis, and determine the role of cholinergic system, we investigated the effects of muscarinic receptor agonist (pilocarpine) and antagonists (atropine and scopolamine) on the ethanol withdrawal syndrome in rats. Ethanol (7.2 % v/v) was given to the rats by a liquid diet for 21 days, and then ethanol was withdrawn from the diet. At the 2nd ant 6th hours of withdrawal, pilocarpine (6.25-20 mg/kg), scopolamine (0.5-2 mg/kg), atropine (2-4 mg/kg) or saline (0.9 % NaCl) were injected intraperitoneally to the individual groups rats and observed for 30 min as a cut-off time. Additionally at the 6th h of ethanol-withdrawal, an audiogenic stimulus (100dB) was given to rats 10 min following treatments. The incidence of audiogenic seizures was evaluated. No seizure observed in rats at the 2nd of the withdrawal. Exposure to audiogenic stimulus at the 6th of withdrawal precipitated seizures with an incidence of 59% in control rats. However, the administration of pilocarpine (12.5-50 mg/kg) significantly increased the incidence of audiogenic seizures compared to the control (X^2=3.927, p < 0.05), but at the dose of 6.25mg/kg it was ineffective (X^2=5.126, p > 0.05). Only, the high dose of scopolamine (2 mg/kg) significantly prevented the induction of audiogenic seizure during ethanol withdrawal (X^2=7.770; p < 0.01). Atropine did not affect the audiogenic seizures. These results indicate the role of cholinergic system in the induction of audiogenic seizures during ethanol withdrawal, and support our previous microdialysis data.

Keywords: pilocarpine, scopolamine, atropine, audiogenic stimulus, acetylcholine

S38
The effects of botulinum toxin-a on bladder function and histology of transected rats: is there any advantage between application on acute or chronic period?
Spinal cord injury (SCI) leads to detrusor external sphincter dyssynergia (DSD) and detrusor hyperreflexia (DH). In References 3, 7 Botulinum-A toxin (BTX-A) is a selective blocker of acetylcholine release from nerve endings and accordingly blocks neural transmission. BTX-A binds tightly and rapidly to the intramuscular nerve terminals and causes a prolonged local effect when injected directly into the muscle. It is used principally in the management of focal dystonia, spasm, and spasticity. We investigated both the acute and chronic effects of BTX-A on bladder functions and histology of transected rats. We used twenty six, female Sprague-Dawley rats in this study. Experimental SCI was induced at level T8-T9 by total transection in lamincotomised animals. We performed intravesical BTX-A injections by first diluting 200 to 300 units Botulinum-A into 20 ml preservative-free saline. Using a collagen injection needle, BTX-A is injected into 30 to 40 sites, at the 12, 3, 6, and 9 o’clock positions, within the detrusor muscle, targeting the trigone, base of the bladder and lateral walls. Groups: 1- Sham (n=5), 2- SCI (n=5), 3- SCI+BTX-A injection after 7 days, acute period, (n=5), 4- SCI+BTX-A injection after 28 days, chronic period, (n=5), 5- SCI+saline injection after 7 and 28 days (n=6). Baseline pressure and uninhibited detrusor contraction amplitude were markedly restored after the BTX-A injections (p<0.01). There was no positive therapeutic effect on maximum bladder capacity and opening pressure in SCI treated groups. Fibrosis and hyperplasia were significantly decreased in this group (p<0.01). When we compare the acute and chronic BTX-A treated periods, cystometry data and histology did not show significant difference. In conclusion, our results indicate that BTX-A is an effective treatment for detrusor-sphincter dyssynergia in SCI and also it can provide an alternative treatment for detrusor hyperreflexia.

Keywords: spinal cord injury, botulinum toxin-A, bladder, cystometry.

S39 Evaluation of neuromuscular transmission by using monopolar needle electrode
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Single fiber EMG (SFEMG) with SFE is still gold standard for each electrode, in the same volunteer. In the MG group the mean jitter values for each electrode in every muscle. At least 50 consecutive potential pairs were recorded to calculate these values. Repetitive nerve stimulation (RNS) test on transperoneus muscle was applied to 15 patients. In controls the mean jitter values were 27.6±9 (10-58) usec with SFE, and 21.7±2.0 (9-56) usec with MNPE (p=0.001). Of 200 individual jitter values only one was high, in the same volunteer. In the MG group the mean jitter values were 52.4±38 (12-221) usec with SFE, and 51.8±34.7 (12-179) usec with MNPE. Both electrodes identified junction dysfunction in ten patients. RNS revealed decrement in 4 patients but 1. Both SFE and MNPE could identify additional 5 patients of remaining eleven patients. SFEMG with SFE is still gold standard however, SFEMG with MNPE is superior to RNS.

Keywords: neuromuscular junction, single fiber EMG, jitter, single fiber electrode, monopolar needle electrode.

S40 Investigation of the neuromuscular transmission in primary headache syndromes
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Dysfunction of neuromuscular transmission (NMT) has been shown in migraine and cluster headache by using single-fiber electromyography (SFEMG). This abnormal NMT is due to genetically modified P/Q Ca 2+ channels in subgroups in migraine with aura. Cluster headache (CH) is a primary headache disorder in which genetic factors may, at times, play a strong role. In this study, we investigated any dysfunction of NMT by SFEMG in migraine, CH and other primary headaches. One hundred twenty nine patients (43 with migraine with aura, 5 with chronic CH, 46 with episodic CH, 18 with sporadic hemiplegic migraine, 3 with hemicrania, 4 with familial hemiplegic migraine, 6 with basilar-type migraine, 4 with migraine without aura) and 10 healthy control subjects recruited. All subjects underwent nerve conduction studies, concentric needle electromyography and SFEMG during voluntary contraction of (EDC) muscle. For each subject, twenty different potential pairs were recorded and twenty individual jitter values were calculated. Numbers of abnormal individual jitter values of primary headache patients were compared with the one calculated from the normal controls. Twenty of 129 patients with primary headaches showed pronounced NMT abnormalities. Another 18 patients had borderline dysfunction of NMT. Transmission was clearly normal in 91 patients. None of the control subjects had abnormal NMT. The number of abnormal NMT values exceeding upper normal limit was significantly higher in the patients group. This study showed abnormal NMT in primary headache patients. An abnormality of ion channel might be proposed as an underlying pathophysiology.

Keywords: ion channel, neuromuscular transmission, cluster headache, migraine, SFEMG.

S41 Middle-finger reflex
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I discovered a new reflex as I was a medicine student in 1956: “Middle-Finger Reflex” elicited by percussion of tendon insertion of musculus extensor digitorum communis in forearm. Following percussion using a reflex hammer, two EMG responses from the belly of the muscle were recorded: a short-latency (M1) monosynaptic reflex with a mean latency of 31.4 (SE = 1.5) ms, and a long-latency (M2) reflex with a mean latency of 64.8 (SE = 6.31) ms, the former being a monosynaptic extensor reflex, and the latter belonging to a spino-cortico-spinal reflex circuitry. It was suggested that the middle-finger-extensor-reflex elicited by radial nerve afferents (C7-CS) would be of clinical and theoretical importance.

Keywords: reflex, extensor, middle finger, short-latency reflex, long-latency reflex.

S42 Neuromuscular transmission alterations in experimental sepsis
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The etiopathogenesis of Critical Illness Polynuropathy (CIP) seen in critical care units is the final stage of sepsis is unclear. Related research on this topic, is limited to clinical electrophysiological and histopathological evaluation. The aim of this study is to investigate neuromuscular transmission alterations in the experimental acute sepsis in rats. 30 male Sprague-Dawley rats (250 gr), fed ad libitum and housed in a constant temperature room with 12h12h light-dark cycle, were used in the experiments (sepsis group= 20, sham group= 10). Cecal perforation and ligation (CPL) was performed to induce experimental sepsis under 100 mg/kg ketamine and 10 mg/kg xylazine (i.p.) anesthesia. Before and 24 hours after surgery, right sciatic nerve was stimulated (10V, 0.1ms, 1Hz) with Biopac HST01 surface stimulation electrode from the sciatic notch and compound muscle action potentials (CMAP) were recorded from the gastrocnemius muscle (BIOPAC Systems). Data were evaluated with the Biopac BSL Pro program, v. 3.6.7 regarding latency, amplitude and duration of CMAP. In the sepsis group, 5 rats died during the first 24 hours and excluded from the study. The results were analyzed with the SPSS statistical program, using Repeated Measures (ANOVA), Factors were session (preoperative and 24 hour after surgery) and treatment (CPL and sham operation). Dependent variables were latency, amplitude and duration. The groups were compared by paired-samples t-test and results were given as Mean±SD. Latency measures in the sham group were 0.076±0.010 ms, and 0.080±0.015 ms, while measures were prolonged in the in the sepsis group (0.094±0.015 ms, and 0.149±0.054 ms) during preoperative and 24 hours post-surgery respectively. Latency data showed significant difference only in the sepsis group, regarding factors and interacted for session (F1,23=15.37, p=0.001) and treatment (F1,23=15.86, p=0.001) (F1,23=11.96, p=0.002) CMAP amplitudes in the sham group in the pre-op and 24 hours after post-surgery were 8.41±0.79 mV and 8.28±1.92, while in the sepsis group the amplitudes were declined to 7.60±1.75 mV and 4.87±3.44 mV, respectively. The amplitude data displayed the

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same paradigm as in the latency. Session (F1,23 = 5.56, p = 0.027) and treatment (F1,23 = 8.40, p = 0.008) were significantly interacted (F1,23 = 4.38, p = 0.047) and the effect was observed only in the sepsis group. CMAP durations during pre-op recordings were 0.45±0.05 ms and 0.48±0.05 ms at the post-op 24h hour in the sham group. Respective values were 0.46±0.05 ms and 0.55±0.01 ms in the sepsis group. The ANOVA results revealed statistically significant difference in CMAP duration only for session (F1,23 = 7.49, p = 0.012), but not for treatment (F1,23 = 4.02, p = 0.057) assuming no effect of sepsis. Overall, experimental results indicated that neuromuscular transmission alterations appear in the first 24 hour period following experimental sepsis and were characterized by an increase in the latency and a decline in the amplitude. In conclusion, these experimental findings suggested that, neuromuscular transmission deficits seen in the CIP patients might be appeared before the clinical signs.

Keywords: critical illness polyneuropathy, sepsis, action potential, electrophysiology

S43

Effects of antineoplastic agents on the peripheral nerves under a surgical tissue expansion procedure: an experimental study

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Elongation of peripheral nerve by the use of a tissue expander is helpful to repair nerve defects. The present experimental study was designed to investigate the effects of some antineoplastic agents on the peripheral nerves under a surgical tissue expansion procedure. Twenty-five Wistar rats were used in this study. Under general anesthesia through a longitudinal posterior incision, the sciatic nerve was exposed over a distance of 40 mm and two 10-0 nylon sutures were placed in the epineurium a measured 20 mm apart. A tissue expander was then placed under the sciatic nerve. Inflation of the expander accomplished then the expander was removed. Wistar rats were randomly divided into five groups, each consisting of five rats: Cyclophosphamide, cisplatinum, mitomycin-C, 5-fluorouracil and control groups. These agents were administered to each group intravenously via the tail vein on 30 minutes before expansion, 48 and 96 hours after removal of expander. The incision was reopened the third and seventh postoperative days, and the sciatic nerve was exposed. Then the pinching test was distroproximally achieved to measure regeneration distance. The portion of the sciatic nerve between two sutures was removed for histological evaluation. Excluding the retraction portion, the elongation rate was 18.97 %, 19.11 %, 19.94 %, 19.06 %, and 18.88 % in the groups respectively. Histologic evaluation showed that inflammatory changes, vacuolization, intraneural edema, demyelination, axonal changes in the control group, the cisplatinum group, and the mitomycin-C group. These changes were significantly decreased in the cyclophosphamide group and the 5-fluorouracil group. These results suggest that these changes in the two groups, the cyclophosphamide group and the 5-fluorouracil group, may depend on their beneficial effects on the ischemia-reperfusion injury of peripheral nerves.

Keywords: antineoplastic agents, peripheral nerve, ischemia-reperfusion, expansion, injury

S44

CPAP, REM sleep rebound, and corneal thickness in patients with OSA

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Many physiologic changes are associated with rapid-eye-movement (REM) sleep, including: atonia, poikilothermia, nocturnal penile tumescence, middle ear muscle activity, and increased cerebral blood flow. Recently, corneal thickening was added to the list of physiologic properties affected by REM sleep. The hypothesis is advanced by Maurice (1998), proposes that eye movements in REM sleep help corneal oxygenation. According to Maurice thermal circulation of the aqueous humor is needed for adequate corneal respiration, this circulation is suppressed when the lids are closed, and REM is required to stir the anterior chamber and thus prevent corneal anoxia during sleep. Obstructive sleep apnea (OSA) is associated with airway collapse and breathing cessation or reduction. The standard, first-line treatment for OSA is continuous positive airway pressure (CPAP). In the present study we aimed to test Maurice's hypothesis by measuring corneal thickness in sleep apnea patients. We evaluated 21 patients. Patients are divided into 3 groups as No-CPAP, With-CPAP and Split-Night-CPAP. We measured corneal thickness by pachymeter before going bed and in ten minutes after waking. In No-CPAP group, corneal thickness increased significantly in one night sleep. The two-tailed P value is 0.0025, considered very significant for left cornea. The two-tailed P value is 0.0001, considered extremely significant for right cornea. In With-CPAP group, corneal thickness did not increase significantly in one night sleep. The two-tailed P value is 0.9608, considered not significant for left cornea. The two-tailed P value is 0.847, considered not significant for right cornea. In Split-CPAP group, corneal thickness did not increased significantly in one night sleep. The two-tailed P value is 0.9153, considered not significant for left cornea. The two-tailed P value is 0.2510, considered not significant for right cornea. According to our results, there is a significant increase in corneal thickness in No-CPAP group. This finding is very consistent with the Maurice's hypothesis. Because of REM sleep decrease in this group, corneal oxygenation has been endangered. The decrease in corneal oxygenation revealed itself as an increase in corneal thickness.

Keywords: REM sleep, corneal thickness, aqueous humor, OSA, CPAP

S45

Quantitative EEG analysis in patients with severe COPD: some clues of chronic hypoxemic degeneration

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This prospective clinical and electrophysiological study was performed in order to determine the electroencephalographic correlates of cognitive disturbances in patients with severe chronic obstructive pulmonary disease (COPD), using quantitative electroencephalographic (QEEG) measurements. Electroencephalograms (12 channels) were obtained from 33 patients with severe or very severe COPD and from 20 age and sex matched controls. Patients showed mild cognitive impairment (mean MMSE score was 24.6±3.7), unrelated to depression, especially in the construction, language and memory areas. Electroencephalograms revealed fronto-temporal slow waves especially in the left hemispheres. QEEGs revealed higher frequency slow wave-bands and lower frequency beta activity, predominantly in the bilateral fronto-temporal localizations, in addition to decreased global relative beta power in patients with COPD. Analysis of variance of QEEG parameters and clinical characteristics showed that age, PaO2, PaCO2 and FEV1 had significant correlation with QEEG variables in different cerebral localizations. Supported with the first detailed QEEG findings, it was concluded that cognitive impairment in COPD patients was far from being a coincidence and some important clues about its degenerative basis, especially in data processing areas, existed.

Keywords: chronic obstructive pulmonary disease, cognitive impairment, quantitative EEG, slow wave asymmetry, chronic hypoxemia

S46

Comparative analysis of impairment in cognitive processes in multiple sclerosis and neuro-Bechet's diseases as revealed by event related potentials (ERPs)

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Multiple sclerosis (MS) and Neuro-Bechet’s (NB) diseases are similar from the neurological perspective as somatic neurological signs predominate in both. As both disease processes cause exclusively subcortical involvement, it might be expected that they would lead to similar cognitive impairment patterns. It is reported that this pattern is characterized by executive dysfunction, memory impairment with relatively intact recognition attentional problems. In a previous study at Istanbul Faculty of Medicine, Department of Neurology, the performance of the NB patients (mean age: 36) on neuropsychological tests such as Verbal Fluency Test, Stroop Test, California Verbal Learning Test and Frontal Behavior Inventory was significantly worse than that of age and education-matched MS patients (mean age: 41), and it was concluded that the frontal dysfunction in NB patients was more severe compared to MS patients. In this study, Event Related Potential (ERP) recordings sensitive to frontal system function were used in the two groups of these patients with the aim of revealing the electrophysiological correlates of the above-mentioned difference in severity. ERP recordings were performed using Continuous Performance Test (CPT), Novelty paradigm and Contingent Negative Variation (CNV) paradigm as experimental paradigms. While no significant difference was found in CNV potentials between MS and NB patients, the amplitudes of Go and No-Go P3 potentials in the CPT paradigm and P3a potentials recorded with novel stimuli along with P3b potentials recorded with
target stimuli in the Novelty paradigm were significantly reduced in the NB group compared to the MS group. Among the electrophysiological differences found, the largest was amplitudes of No-Go P3 potentials in the CPT paradigm. The topographic distribution of P3a potentials displayed a maximum P3a amplitude at centro-parietal localization in MS patients similar to the normals whereas, in NB patients frontal P3a amplitudes were reduced and instead parietal maximization was observed. In the light of these findings, we conclude that cognitive processes such as sustained attention, response inhibition, working memory and novelty detection in NB patients are more affected than those in MS patients. This conclusion is in line with the previous study in which the same groups were compared with neuropsychological measures.

Keywords: multiple sclerosis, neuro-Bechter’s disease, ERP, CPT, P3a, P3b, CNV

S47
Treatement of malignant glioma with mitoxantrone-loaded microspheres
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One of the limiting factors in malignant glioma treatment is the difficulty to achieve therapeutic concentrations of antineoplastic drugs in tumor without inducing unacceptable systemic side effects. Implantable, biodegradable polymers may maximize the efficacy of antineoplastic treatment by providing local and sustained drug delivery directly to the tumor. Mitoxantrone is a potent antitumor and antibiotic drug that has not been used in treatment of gliomas before because of mitoxantrone brain barrier penetration. In this study poly(lactide-co-glycolide) (PLGA) microspheres were loaded with mitoxantrone and its effect on malignant gliomas in the rat brain were investigated. Fisher rats (180-205g) were randomized into three groups. The first group (n=6) was implanted concomitantly with rat glioma (RG2) cells and empty PLGA microspheres in the frontal cortex stereotactically. The second group (n=3) was implanted stereotactically with rat glioma cells and mitoxantrone-loaded PLGA microspheres at the same coordinates. The third group (n=6) was implanted with rat glioma cells and, after 7 days, were injected stereotactically with mitoxantrone-loaded PLGA microspheres to the same brain area. Fifteen days after implantation, rats were sacrificed; brains were formalin fixed and embedded in paraffin. Tumor volumes were measured after hematoxyline-eosin staining. The tumor volume was (76±11mm3) (mean±SE) in glioma and empty PLGA microsphere implanted group, and was significantly reduced (17±4mm3) in gliomas treated with mitoxantrone loaded PLGA microspheres 7 days later. No tumor formation was observed when glioma cell and mitoxantrone-loaded PLGA microspheres were implanted concomitantly. No systemic side effects were observed in either group of rats. These data demonstrate that mitoxantrone-loaded PLGA microspheres can deliver therapeutic concentrations of drug to the tumor without causing side effects and prevent glioma formation. This treatment method could increase the efficiency of antineoplastic therapy and positively impact the survival.

Keywords: malignant glioma, rat glioma (RG2) cells, mitoxantrone, poly (lactide-co-glycolide) (PLGA), microsphere

S48
A neural network model for syntactic processing: Sensory-motor representations can be plotted for association of verb, object and time of action
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In the steps of evolution, language and fine hand movements are evolved together. The acquisition of bipedal during the evolution of early hominids has freed the hands and arms from primary involvement in locomotion and lent the upper body a new potential for expressive communication. Moreover, the concentration of areas specialized for language in the same hemisphere of the cerebral cortex as controlling hand has been placed to facilitate precise manipulative tasks may demonstrate the intimate connections between the two functions. The relationship between language development and motor performance suggests the presence of common pathways. In the literature, many studies show evidences for sensory and motor regions related to action and verb generation. In the verb generation stage, displayed activities in frontal and temporal areas suggest that verb generation occurs in sensory-motor processing. How is verb object relationship processed? When a sensory cue (object) was presented, a motor activation (verb) related to it could occur. By this way shaped sensory-motor activation becomes a template for language expression. This might be ensured with a distributed network. Many activities of us do not consist of one action segment. For example if we mention about smoking, we must realize consequent activities like holding the cigarette box, taking cigarette out of the box, bringing it to mouth, firing a lighter e.g.. All of these activities have mental motor representations. At the same time all of them place in one motor programming which proceed this actions keeping in step. Every action step is controlled by distributed neural networks which consist of areas that execute motor programs. Among these areas, SMA, ventral and dorsal premotor cortex and Broca’s areas are consistently displayed. Interestingly this areas control the language production and comprehension. The presence of areas related to execution of action and to language suggests that a time reference of action (past tense or future tense) is defined by action’s place in the motor program which is processed actually. That is to say that we place any action in time dimension with preceded and followed actions. Because of whole motor program for any activity is determined, this become template for index action and its position. A neural network model is created for integrating the sensory-motor representations with verb, object and time of verb. The processing of network and neural equivalents were discussed.

Keywords: neural networks, syntax, sensorial representation, frontal lobe, Broca’s area, syntax first model.
Large classes, overloaded curriculum and inefficient instruction hinder academic achievement, durable gain, and general satisfaction. Since 1998, we have pursued vertical integration by early clinical exposure, case-based modules, multidisciplinary panels, and lively multimedia sessions in our Second Year Neuroscience Blocks. Cerebral stroke case and car accident spinal injury scenario, celebrated movie and “The Secret Life of the Brain” (SLB) viewings, interactive large group conferences (Introduction to Neurology, Psychiatry, Anesthesiology, Pain and Addiction) and a panel on Neurodevelopment & Neurogenetics were conducted. In the usual 100 MCQ end-block exam, 3-12 MCQs per specific learning issue/general theme were constructed to test the reinforcement efficiency of each teaching atmosphere/technique/tool strategy. A questionnaire followed the exam. Different teaching-learning activities and their respective MCQs were categorized in 10 groups. RM-ANOVA, DG-1, Friedman and Post-hoc Wilcoxon tests revealed the following: * Significance in % correct answer ratios (lowest: car accident scenario; highest: the movie, “Birdy”); and in positive perceptions (highest: Integrated Conference on Introduction to and Management of Addiction; lowest: “SLB”). * No significance of preference between the strategies; and in positive perceptions pertaining to a) knowledge and instruction, b) enjoyment and e) psycho-social issues. * Significance in negative perceptions (lowest: SLB). In conclusion, instructors’ personal attitudes and the language (Turkish is favorable) of the films influence the effectiveness of the teaching-learning experiences and their outcomes. A deeper integration of basic & clinical neuroscience and additional movies are desired.

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Keywords: basic neuroscience curriculum, vertical integration, multimedia in learning, reinforcement learning, bio-psycho-social approach, innovative medical teaching

POSTER PRESENTATIONS

P1

GABA and glutamate levels in hypothalamus of rats with genetic absence epilepsy

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The vital role of posterior part of the hypothalamus through GABAergic and glutamatergic neurotransmission in the regulation of homeostatic processes of the internal environment and furthermore, in the regulation of blood pressure and heart rate has been reported in various species. Previous studies have indicated that tonic GABAergic inhibition through GABAA receptors in several nuclei of the hypothalamus but specifically dorsomedial hypothalamic nucleus (DMH) is responsible for the control of cardiovascular responses. The purpose of the present study was to examine blood pressure and heart rate effects of bicuculline (BMI), a GABAA antagonist, and the basal and bicuculline induced GABA and glutamate levels in hypothalamus of rats with genetic absence epilepsy (GAERS). This study was performed to examine the role of BMI in cardiovascular system and the hippocampus because there is an influence of BMI on cardiovascular responses. The effects of BMI were determined in the dorsomedial and posterior (PH) nuclei of the hypothalamus of GAERS and Wistar rats. Stereotaxic surgery was performed to implant icv cannula and concentric microdialysis probes into DMH and PH in different groups of animals. All experiments were performed on conscious rats. In the first group, iliac artery was cannulated to record blood pressure and heart rate. After recording the basal blood pressure and heart rate values, the rats were treated with ivc aCSF or 0.3 nmol BMI. In the second group of experiments, the day after placement of microdialysis probes, basal microdialysis samples were collected and rats were treated with ivc aCSF or 0.3 nmol BMI and four more samples were collected. GABA and glutamate concentrations in samples were analysed using HPLC. Continuous EEG recording was made throughout the experiment. IvC 0.3 nmol BMI significantly increased mean arterial pressure (MAP) in GAERS (p<0.05), but no change in MAP was observed in Wistar rats. No significant effect on heart rate of Wistar and GAERS was observed. Glutamate concentration in DMH increased in [20-40] min interval after BMI injection in GAERS (p<0.01). GABA concentration in DMH showed a tendency to decrease in [40-60] min period of BMI injection. This decrease was not statistically significant. Glutamate concentration in PH of GAERS increased after BMI injection, but this increase was not found statistically significant. GABA concentration significantly decreased in [20-40] min interval of BMI injection in PH of GAERS (p<0.05). ACSF injection did not cause any change in neurotransmitter levels. There was no change in neurotransmitter levels in either DMH or PH region of Wistar rats. Changes in GABA and glutamate levels and cardiovascular responses imply that hypothalamic region has a role in the mechanisms of absence epilepsy in GAERS.

Keywords: GABA, glutamate, absence epilepsy, hypothalamus, DMH, cardiovascular regulation

P2

The brain trace elements changes in experimental epilepsy induced by topical penicillin application in rabbits

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The aim of this study was to investigate the role of zinc (Zn) and copper (Cu) on physiopa-thology of epilepsy. For this purpose, experimental epilepsy model was formed by penicillin application in rabbits. Forty rabbits were used and divided into equal two groups as experi-mental epilepsy group and control group. Screw electrodes were applied in four different cor-tical regions in rabbits. Electrophysiological and clinical seizures were observed after 6000 IU penicillin dropped in posterior sensory motor area, and their electrocorticograms were re-corded. The animals were decapitated two hours later and their brains were evaluated. Brains were homogenized in nitric acid solution and the levels of Zn and Cu were measured using atomic absorption device. We found that Zn levels in rabbits induced epilepsy were lower and Cu levels were higher than control groups. But these differences were not statistically significant. In conclusion, topical penicillin application had no significant effect Zn and Cu levels in brain of rabbits.

Keywords: Epilepsy, zinc, copper, trace elements, penicillin.

P3

Morphological changes in hippocampus of rat exposed to in utero radiation and postnatal febrile convulsions: a preliminary study

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Hippocampal sclerosis (HS) is characterized by gliosis, neuronal loss and synaptic reorganization in mesiotemporal structures and occurs with medically intractable seizures. It constitutes a major part of adult patients that have undergone epilepsy surgery. Etiology and pathophysiology of mesiotemporal sclerosis is not well understood. Studies demonstrated that hippocampal sclerosis and hippocampal sclerotic reorganization is more frequently seen in patients that had febrile convulsions in their childhood. Some authors accept that patients with HS have hippocampal cortical developmental anomaly and physiopathologic processes start with secondary effects. It is also known that the immature brain is more resistant to epileptic seizures. Previous experimental studies showed that the convulsions caused by hyperthermia is more frequent and have higher mortality rates in the rats with cortical dysgenesis and the cases with neuronal migration defects had a higher neuronal loss. The aim of this preliminary study was to investigate the role of hyperthermia in the hippocampal sclerosis in the infantile period in the rats that are made cortically dysgenetic by in utero radiation. In this study, the rats in the 17th day of in utero development were exposed to 225 cGy radiation and had febrile convulsions induced by hyperthermia in postnatal 10th day. Radiation and hyperthermia were not induced in control groups. Five months after the experimental procedure, the animals were perfused with 3 % paraformaldehyde and 0.2 % glutaraldehyde. Forty µm cryostat sections were obtained and then stained with 1 % cresyl violet and examined with the light microscope. Control group showed normal hippocampal morphology. The hippocampus was atrophic in the rats exposed to radiation and hyperthermia. Neuronal loss in CA1, CA3 and CA4 regions except CA2 and dentate granular regions and ectopic neurons were observed in this group. The present preliminary study showed that the radiation and hyperthermia caused severe degeneration in the hippocampus. The results need further evaluation by EEG recording, electron microscopy and morphometry such as cell count and measuring of hippocampal area.

Keywords: Hippocampus, mesiotemporal sclerosis, radiation, hyperthermia, morphology

P4

The effects of lipopolysaccharide on blood-brain barrier permeability during pentylenetetrazol-induced epileptic seizures

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Lipopolysaccharide (LPS), major component of the gram negative bacteria cell wall, has been shown to exert effects on the blood-brain barrier (BBB) under a variety of pathological conditions in addition to its dose dependant epithelial protective effects in recent studies. In this study, the effects of LPS and pentylentetrazole (PTZ) on the BBB permeability were investigated. LPS was intraperitoneally injected to Wistar albino female rats at the dose of 5 mg/kg at hours 0, 6 and 12. PTZ (80mg/kg) was administered to induce epileptic seizures 24 hours after the first injection of LPS. The functional changes of BBB were determined by measuring the Evans blue (EB) dye content in the brain regions. In the PTZ and LPS+PTZ groups, the blood pressure was recorded by a catheter inserted into the femoral artery before and after PTZ administration. Plasma nitric oxide (NO), superoxide dismutase (SOD), catalase and malondialdehyde (MDA) levels were measured in control, PTZ and LPS+PTZ groups. EB dye content in the left cerebral cortex, right cerebral cortex, diencphalon and cerebellum regions of animals increased in the PTZ group (p<0.01). LPS caused a decrease in the EB dye content in all brain regions of animals treated with PTZ (p<0.01).

Although LPS injection alone, caused an increase in EB dye content in the brain, this difference failed to reach significance when compared with control values (p>0.05). The blood pressures of LPS treated and untreated animals elevated during PTZ-induced epileptic seizures (p<0.01). Although LPS administration alone decreased the blood pressure, the difference was not statistically significant when compared with control values (p>0.05). Plasma NO and MDA levels increased and plasma catalase levels decreased in animals treated with PTZ and LPS+PTZ when compared with control values (p<0.01). However, no significant difference was found between PTZ and LPS+PTZ groups when the decreases in antioxidant activity was compared (p>0.05). This study indicates that LPS, when administered before inducing epileptic seizures by PTZ, can exert protective effects on the endothelial cells of BBB, at least partly, by causing an increase in plasma NO level, and hence may decrease the extravasation of EB dye into the brain.

Keywords: Blood-brain barrier, Evans blue, Lipopolysaccharide, Pentylentetrazole, Epileptic seizures

P5

The effects of the adenosinergic system on experimental epilepsy induced by penicillin in rats

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Adenosine is an important signaling molecule that has evolved to modulate physiological responses in all mammalian tissues. It has been shown to have powerful inhibitory actions on neuronal activity and release of excitatory transmitters. Furthermore, adenosine is involved in the modulation of seizures and several findings support the notion that adenosine is an endogenous anticonvulsant. In the present study, we investigated the effects of adenosine and theophylline injections on penicillin-induced epileptiform activity. Sixteen Wistar rats for perform experiments were anaesthetized with urethane. The epileptic activity was produced by intracortical injection of penicillin (200 IU/1 ml microlitre). Adenosine (100 microM) or theophylline (1 mM) administered via icv after 30 minute (min) following epileptiform activity. The ECoG activities were recorded from left somatomotor cortex via two Ag-AgCl ball electrodes. These recordings were displayed and stored on the computer. Data were analyzed offline to compare spike frequencies, spike amplitudes and power spectra of epileptiform activity before and after ATP injection. The mean of spike frequency were calculated as 25.75±3 per min and 18.75±4 per min before and after the injection of ATP, respectively. However, the difference between two groups was not significant.

Keywords: Epilepsy, GABRA1, Mutation Analysis, PCR, SCCP

P6

The effects of ATP on power spectra of brain signals and epileptiform activity in penicillin-induced experimental epilepsy

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ATP is an important molecule in activity-dependent signaling between neurons and glia at the synapse and non-synaptic regions. The role of ATP as a pheripheral and central neurotransmitter is mediated by P2 purinoceptors. Recent studies suggest that purinergic receptors may participate in the pathophysiology of temporal lobe epilepsy. In this study, the effects of ATP on power spectra of brain signals and epileptiform activity in penicillin-induced experimental epilepsy were investigated. Experiments were performed on seven adult male Wistar rats anaesthetized with urethane (1.2 g/kg). ATP (100 microM) administered by icv after 30 min following epileptiform activity.

Extracellular ATP is an important molecule in activity-dependent signaling between neurons and glia at the synapse and non-synaptic regions. The role of ATP as a pheripheral and central neurotransmitter is mediated by P2 purinoceptors. Recent studies suggest that purinergic receptors may participate in the pathophysiology of temporal lobe epilepsy. In this study, the effects of ATP on power spectra of brain signals and epileptiform activity in penicillin-induced experimental epilepsy were investigated. Experiments were performed on seven adult male Wistar rats anaesthetized with urethane (1,2 g/kg). ATP (100 microM) administered by icv after 30 min following epileptiform activity.

Epileptic seizures in Behcet syndrome

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Behcet Syndrome (BS), is a chronic vascular-inflammatory multisistemic disease. Its etiology and pathogenesis are unknown. According to the diagnostic criteria formed by the International Study Group, two of oral and genital ulcerations, skin lesions, uveits and pathergy test are necessary for definite BS diagnosis. The incidence of nervous system involvement ranges from 2.2 to 49 percent. Headache, intracranial and cerebellar signs, sensory symptoms, intracranial hypertension, dementia, change in personality and seizure are some of the presentations. In large series of patients with BS, seizure has been rarely reported. In this study, seizure types and electrophysiological features of patients with BS are evaluated. The frequency of seizures in 40 patients diagnosed with BS (26 males (% 65), 14 females (% 35)) is examined retrospectively and found in 4 of them. All of 4-patients had been diagnosed as NeuroBehcet Syndrome (NBS) and treated because of this disease before seizures started. The age of NBS onset was 30.3 ± 7.6 (25-39) years, and duration of disease was 17.5 ± 11 (8-32) years. The age of seizure onset...
was 41 ± 6.6 (36–47) and it had been started after 9 ± 2.5 (6–12) years after NBS onset. Partial with complex symptomatology in 5 of the patients and secondarily generalized seizures in one of them were determined. EEG findings of 3 subjects were background abnormality and slow activity localized to frontotempocentral areas; EEG of one of them was normal. Epileptic seizures were not associated with deterioration of neurological findings. Cranial MRI showed ischemic changes in left cerebral peduncle, left temporal lobe unicus, and left occipital region; ischemic changes in right frontotemporal, bilateral periventricular areas, brainstem, and cerebral and cerebellar atrophy; and ischemic lesions in the right anterior region of medulla oblongata in 3 patients respectively. One of them had normal findings. None of our patients had status epilepticus. Seizures were controlled in 3 of them but it was recurring once a year in one of them and this patient’s treatment had been changed with carbamazepine and followed up by our clinic. As a result, it is seen that both the neurobehavioral syndrome should be investigated for the etiology of partial epilepsy by evaluating other symptoms and clinical signs of patients.

Keywords: Behcet Syndrome, epileptic seizure, EEG, radiological findings

P9
Comparison of two seizure scales on the audiogenic seizures during ethanol withdrawal in rats
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Ankara Many previous studies on ethanol withdrawal syndrome in rats have been reported various seizure scores. These varieties in seizure scores might originate using different scales. Observing the best scale, which represents the severity of seizures, would be important. This scale should include significant neuroethological properties of audiogenic seizures during ethanol withdrawal in rats. The present study has been designed to evaluate the neuroethological properties of audiogenic seizures during ethanol withdrawal in rats. Ethanol (7.2% v/v) was given to the rats by a liquid diet for 21 days, and then ethanol was withdrawn from the diet. At the 6th hour of the withdrawal period, rats were subjected to an audiogenic stimulus (100dB) with a 60 sec cut-off time. For a more detailed analysis of audiogenic seizures, we used the limbic and the brainstem seizure index to evaluate audiogenic seizures during ethanol withdrawal.

Keywords: Ethanol Withdrawal, Seizure, Audiogenic Stimulus, Limbic Seizure Index And The Brainstem Seizure Index

P10
The effect of experienced generalized tonic-clonic seizures on ischemia-reperfusion induced arrhythmias
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Epilepsy in humans is associated with autonomic abnormalities that affect heart rate variability, but it is not known whether seizure experience increases the complications for myocardial ischemia-reperfusion (MI/R). That is why, the goal of this study was to examine acute effect of experienced generalised tonic-clonic seizures on MI/R induced arrhythmias. Animals divided into two groups: 1) saline- treated group + MI/R (n=7), 2) seizure group + MI/R (n=7). Myocardial ischemia was produced by ligation of left coronary artery and reperfusion by releasing of this artery. Generalised tonic-clonic seizures induced by 70 mg/kg pentylenetetrazol (PTZ). PTZ or saline was given i.p., 2h before coronary artery ligation. Electrocardiogram and arterial blood pressure were recorded during experimental procedure. As a result, the total length of arrhythmia observed following ligation and reperfusion was found to be significantly lower in PTZ-induced seizure + MI/R group than only MI/R induced group (238±36sec vs 77±23sec respectively, p<0.05). It is probable that seizure experience before MI/R can create an ischemic preconditioning effect which, in turn, can induce a significant decrease in observed arrhythmia parameters such as ventricular fibrillation and ventricular tachycardia. The mechanism for this protection remains to be further evaluated.

Keywords: Epilepsy, arrhythmia, PTZ.

P11
Spontaneous burst activity induced by lidocaine effect on crayfish receptor neurons: an electrophysiological study
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In the slowly adapting receptor neuron of the crayfish abdominal stretch receptor organ high dose (5 mM) lidocaine causes spontaneous activity. Where as similar effects were not observed in the rapidly adapting neurons. Similar effect was observed by the perfusion of equivalent concentrations of Benzocaine but not by Procaine and Prilocaine. In the presence of TTX which is a specific sodium channel blocker, lidocaine application did not evoke impulse activity. However, a dose dependent depolarization was observed in both types of neurons. The depolarizing effect of lidocaine did not change when the receptor neurons were perfused with a specific potassium channel blocker tetraethylammonium (TEA, 20 or 200 mM) solution. Also it was shown by the voltage–clamp experiments that the potassium currents were not affected by perfusion of lidocaine. Crayfish stretch receptor neurons receive GABA-mediated inhibitory input. Presence of an interaction between lidocaine and the GABA mediated system has been investigated by preventing pre-synaptic GABA release by verapamil, or blocking the post-synaptic GABA action by picrotoxin. In both types of applications depolarizing effect of lidocaine was similar to that in control conditions. Also persistence of the depolarizing effect in the presence of ouabain, indicated that the effect is mediated by a mechanism independent of the Na/K ATPase. May be the depolarizing effect of lidocaine is due to a change in the physical properties of the membrane. It was observed that lidocaine increased the membrane resistance in a dose dependent manner when membrane resistance was measured both in control solution and in the presence of high dose of lidocaine Spontaneous activity evoked by lidocaine in the slowly adapting neuron was due to the slow depolarising effect of lidocaine. The effect was observed solely in the slowly adapting cell since the depolarization developed slowly. It was proposed that the principal mechanism of the effect could stem from a change in the physical properties of the membrane.

Keywords: Local anesthetics, stretch receptor, membrane depolarisation

P12
BDNF protein expression following repetitive electroconvulsive shocks in mouse nucleus accumbens
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Most of the studies on mechanism of action of antidepressant treatment modalities emphasizes the role of intracellular signalling pathways. Among these, brain-derived neurotrophic factor (BDNF), which has important functions in neuron survival, has been most extensively studied. BDNF expression in hippocampus is increased in laboratory animals after chronic antidepressant use, and in samples in post-mortem studies of antidepressant users. Direct application of BDNF had antidepressant-like effects in animal models. There are findings indicating an association between BDNF increase and neurogenesis and plasticity. However, there are also studies implying regional differences with respect to BDNF change following chronic antidepressant treatment. While CREB (cAMP response element binding protein) is increased in hippocampus with antidepressant treatment, CREB inhibition has antidepressant-like effects in nucleus accumbens. BDNF administration to nucleus accumbens also results in depression like responses in mice. Our aim in this study was to examine in mice the effects of repetitive electroconvulsive shock (ECS) on BDNF protein expression in nucleus accumbens. Electrical stimulation was applied to mice through transcorneal electrodes, resulting in a generalized tonic-clonic seizure lasting 5-10 seconds. In order to model electroconvulsive treatment applied in clinical management of depression in humans, ECSs were repeated 7 times with regular intervals. The sham group was subjected to similar procedure but the electrical stimulation was missing. Mice were fixed with intracardiac perfusion of paraformaldehyde under high dose pentobarbital anesthesia, then the brains were removed. Forty micron thick sections were stained for BDNF according to immunohistochemistry protocols, and dianinobenzidine was used as the chromogen. Sections were digitally photographed at X40 under microscope, then a group of photographs were selected so that in each mouse at least around 0.5 mm2 of nucleus accumbens could be covered (6x0.093 mm2). Immunoreactive cells in each photograph were counted. The results were compared by using Student’s t-test. The number of immunoreactive cells was significantly lower in nucleus accumbens in the ECS group compared to the sham group, (p<0.01). This result is in accordance with the
findings in literature, suggesting depression like effects of BDNF administration into nucleus accumbens.

Keywords: Depression, antidepressants, electroconvulsive shock, BDNF, nucleus accumbens

P13
Auditory evoked N100 and P200 potentials in Alzheimer's disease

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Alzheimer’s disease (AD) is the most common neurodegenerative disorder and the most prevalent cause of dementia. Prolonged latency and decreased amplitude of P300 in oddball paradigm are well known neurophysiological parameters. However, reports on the changes of N100 or P200 potentials in AD are rather rare and contradictory. In the present study, N100 and P200 waves that are mainly generated in sensory and unimodal association cortices were investigated in order to search for electrophysiological changes arising from these regions that are assumed to be affected in later stages of the disease. N100 and P200 potentials of the auditory event-related potentials of 15 healthy volunteers and 22 patients at early (n=11), GDS<4 and CDR <2 to moderate (n=11, GDS=4 or CDR =2) stages of AD were analyzed. The differences among the three groups were statistically tested with a repeated-measures ANOVA. It was observed that N100 potentials of the moderate AD group to target stimuli of the novelty paradigm peaked later than those of the control group (p<0.01). This effect had a topographical pattern such that the latency was especially prolonged in the fronto-central sites but not in the parietal site (p=0.009). In both oddball and novelty paradigms, N100 potentials of the early stage AD patients to standard stimuli peaked significantly earlier over the left hemisphere (p=0.044 in the novelty paradigm, p=0.051 in the oddball paradigm). No other significant differences were found among the groups. The N100 latency changes between moderate AD patients and controls, but not between controls and mild AD patients, is in accordance with the later onset of damage in sensory and unimodal association cortices. The lateralization effect in N100 latencies to standard stimuli found between control group and mild AD patients might reflect top-down modulation of N100 by structures claimed to be damaged earlier.

Keywords: Alzheimer’s disease, dementia, N100, P200, auditory evoked potential

P14
Polymorphisms at the ligand binding site of the vitamin D receptor gene and Alzheimer’s disease

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Interleukin-1 alpha gene promoter region polymorphism in Alzheimer’s disease

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Interleukin-1 is a pluripotent immunomodulatory cytokine that has an initiating role in cellular and humoral immunity in the periphery. It is reported that a polymorphism in the 5′-flanking regulatory region at −889 of the interleukin-1 alpha (IL-1α) gene may cause an over expression of IL-1 α alpha, which is also shown to be associated with inflammatory diseases and Alzheimer’s disease. In this preliminary study, our aim was to determine if there is an association between IL-1 α gene and late-onset Alzheimer’s disease. We collected blood samples from 52 cases of dementia of Alzheimer type and from 35 age-matched controls (mean ages 75.1±5.7, and 72.7±7.3, years respectively). Patients are clinically diagnosed by Istanbul University, Cerrahpasa Faculty of Medicine, Department of Geropsychiatry and Istanbul University, Istanbul Faculty of Medicine, Department of Neurology, Behavioral and Movement Disorders Unit according to DSM-IV criterias. Salting-out method with 5M NaCl is used for DNA isolation. We used polymerase chain reaction-confronting two-pair primers (PCR-CTPP) to test for an association between Alzheimer’s disease and a polymorphism at −889 of the IL-1 α gene. After genetic analysis of the IL-1 α gene, we found 62.5% genotype C/C, 32.7% genotype C/T, 3.8% genotype T/T for patients, and 46.6% genotype C/C, 45.7% genotype C/T, 7.5% genotype T/T for healthy control. When the control and patients were compared for C/C, C/T and T/T genotypes we saw that the distribution of genotypes and alleles did not differ according to Chi-square test (p=0.39). Our preliminary results show no significant increase in the risk for the T/T or C/T genotype in late-onset cases. Thus, we were unable to find an association between the C –889T transition on IL-1 α gene and late-onset Alzheimer’s disease.

Keywords: IL-1, Alzheimer disease, inflammation, polymorphism, PCR-CTPP

P16
Evaluation of the effect of blood and urine samples on Pe 12 cell line viability in Alzheimer’s disease

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Alzheimer’s disease (AD) is a neurodegenerative disease mostly seen in older ages. The toxic effects of pathological markers, namely amyloid plaques and neurofibrillary tangles, on neuronal cells have been shown. Also, there is a probability of being neurotoxic agents in urine and blood in Alzheimer’s disease. For that reason, in this study, it’s aimed to investigate the effects of Alzheimer patients’ urine and blood samples on neuronal cells. In this study, 15 Alzheimer patients 15 control subjects are included. PC 12 cells are used to identify the effects of blood and urine samples on neuronal cell death. The blood samples of patients and control subjects are added on PC12 cell line at a ratio of 5%, 10%, 15%. The urine samples of patients and control subjects are added on PC 12 cell line at a ratio of 1/10. The toxic effect is determined by MTT viability test after 48 and 72 hours for blood and urine samples respectively. As a result, it’s concluded that there is no neurotoxic or neuroprotective effect of Alzheimer patients’ urine samples. It’s determined that Alzheimer patients’ blood samples which are added at a ratio of 15% have neuroprotective effect. These results show us that there may be some materials in Alzheimer patients’ blood samples which cause neuroprotection.

Keywords: Alzheimer’s disease, blood sample, urine sample, neurotoxicity, neuroprotection

P17
The antiangiogenic effect of centrally administered CDP-Choline in rats

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CDP-choline (Cytidine-5’-diphosphate choline, citicoline) is a drug to treat several cerebral ischemic situations and neurodegenerative disorders. Exogenously administered CDP-choline is rapidly hydrolyzed to choline and cytidine. Choline, a precursor of neurotransmitter acetylcholine and increases cholinergic neurotransmission. Activation of cholinergic pathways by cholinergic agonists elicits antinociceptive effects in a variety of species and pain tests. In this study we investigated the antinociceptive effect of intracerebroventricularly (icv) injected CDP-choline in rats. Experiments were performed on male Sprague-Dawley rats (Experimental Animals Breeding and Research Center, Uludag University, Bursa, Turkey) weighing 300-350 g. The experimental protocols were approved by the Animal Care and Use Committee of Uludag University. Animals were anaesthetized with ether 21 gauge guide cannula was implanted to the left lateral ventricle and allowed yto recover from anaesthesia for 3-4 h. The pain sensitivity of rats was determined using latency to withdrawal to a heat stimulus provided by a focused light on the hindpaw. After the baseline latency were obtained CDP-choline, saline or other drugs were administered icv. Then paw withdrawal latency were measured at 5, 10, 15, 20, 30, 40, 50 and 60 minutes. icv injected CDP-choline (0.5, 1, 2 µmol) increased the paw withdrawal latency dose and time dependent manner. Equimolar dose of CDP-choline (1 µmol) and choline (1 µmol) caused similar increases in paw withdrawal latency while cytidine produced small, but significant increase in paw withdrawal latency in rats. Hemicholinium-3 (1 µg), a high affinity choline uptake blocker, and mecamylamine (50 µg) nicotinic cholinergic receptor antagonist, pretreatment abolished the antinociceptive effect of CDP-choline (1 µmol) while atropine (10 µg) muscarinic cholinergic receptor antagonist, failed to alter the antinociceptive effect of CDP-choline. These results indicate that centrally administered CDP-choline induced dose and time dependent antinociception in rats by activating central nicotinic cholinergic receptors through the activation of presynaptic cholinergic mechanisms. This study is supported from the Research Fund of Uludag University (T-2003/37).

**Keywords:** Acute pain, cholinergic, CDP-choline, nicotinic receptors, antinocicep

**P18**

**Analgesic effect of allopurinol in acute pain and the possible role of serotoninergic system in this effect**

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Serotonin is a mediator which stimulates nociceptive effect at sensory nerve ending. This mediator effect includes 5-HT3 receptors in peripheral nerve system, particularly within the nociceptive sensory neurons. Tryptophan, the precursor substance of serotonin, in high doses, significantly increases the threshold level of pain. It has been shown that allopurinol, a xanthine oxidase inhibitor, manifests its effect by elevating the activity of serotoninergic system. Selective serotonin reuptake inhibitors (SSRIs) are used as co-agonists in treating various severe pains. Although modulation of serotoninergic pathways considerably explains their clinical efficacy, various reports indicate the direct or indirect role of the opioidergic pathway in SSRIs-induced analgesia. Our aim is to investigate effect of allopurinol on nociception and role of serotoninergic system and its 5-HT3 receptors. Experiments were carried out with both sexes of Balb/c mice weighing 25-30g. 4 groups of mice were established, and each group included 8 to 10 mice; group I (control), group II (allopurinol, 50 mg/kg), group III (granisetron, 10 mg/kg) and group IV (allopurinol + granisetron). Analgesiometric tests were carried out by tail flick tests because of its good reflection of pain in spinal level and the most sensitive test hot plate. These two tests were applied 30 minutes before and 60 minutes after the drug administration. Antagonist was applied 5 min before the drug. Firstly, animals underwent to tail flick test followed by the hot plate test 5 minutes later. In hot plate test, animals were individually place on a hot plate with the temperature adjusted to 55±0.5°C. A cut-off time of 30 seconds was chosen. In tail flick test, the intensity of the radiant heat was adjusted to the baseline tail withdrawal of mice within 3-5 seconds. A cut-off time of 15 seconds was chosen. Measurements were converted to percent maximum possible effect (% MPE). Application of allopurinol or granisetron had no significant effect in hot plate and tail flick tests compared to the control. Granisetron and allopurinol application respectively reduced the effect of granisetron application alone but these preliminary data were not statistically significant. This study will be continued with allopurinol and SSR1 drugs.

**Keywords:** Analgesia, allopurinol, serotoninergic system, granisetron, hot plate, tail flick

**P19**

**The role of potassium channels and nitrergic system on the antinociceptive effect of tramadol**

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It has been considered that tramadol, centrally acting analgesic, shows its effect via opiateergic, noradrenergic, serotonergic systems. It has a low affinity for opioid receptors and its effects can be partly blocked by naloxone. Noradrenergic and serotonergic mechanisms are still unknown so that the other systems which are associated with pain and analgesia may have a role on the antinociceptive effect of tramadol. It has been known that the modulation of both K+ channels and nitrergic pathways has a role on the perception of pain and the effects of analgesics. The aim of this study is to evaluate the effects of K+ channels and nitrergic systems on the antinociceptive action of tramadol. For this purpose, the antinociceptive effects of tramadol were determined by hot-plate test, and non-specific voltage-dependent K+ channel blockers 4-aminopyridine (4-AP) and tetraethylammonium (TEA), L-arginine, a nitric oxide (NO) precursor, and the NO synthase inhibitor NG-nitro-L-arginine methyl ester (L-NAME) were used to examine the effects of K+ channels and nitrergic system on the antinociceptive action of tramadol. Our results indicated that K+ channel blockers 4-AP ve TEA reduced the antinociceptive effects of tramadol. L-arginine diminished the analgesic effect of tramadol, however L-NAME augmented these effects. The reduction of the effects of tramadol by L-arginine were reversed by L-NAME. In conclusion we suggest that non-specific voltage-dependent K+ channels and nitrergic systems may have a role on the antinociceptive effects of tramadol in hot-plate test in mice.

**Keywords:** Tramadol, potassium channels, nitrergic system, hot-plate, mice

**P20**

**The use of tramadol and gabapentin in acute pain and drug interaction**

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To examine effects of gabapentin (Neurontin) and/or tramadol (contramal) in acute pain and to examine the interaction between two drugs. After having the approval of Animal Ethics Committee; 88 Swiss albino mice divided into 11 equal groups. Without injection (Group I), distilled water (Group II), Tramadol 30 mg/kg (Group III), gabapentin 30 mg/kg (Group IV), 100 mg/kg (Group V), 200 mg/kg (Group VI), 300 mg/kg (Group VII) respectively given intraperitoneal. To determine interaction of gabapentin and tramadol, mice received 30 mg/kg tramadol also injected 30-100-200-300mg/kg gabapentin (Group VIII-XI). Mice received 0.1ml solution per 10g of their weights. Thirty minutes after the drug injection tail-flick and hot-plate tests were done. Tail-Flick was set for 55% power and hot-plate was set for 56°C. No extension was detected in the tail-flick and hot-plate tests in low doses with the addition of gabapentin to the tramadol. However, the period lasted longer in the 300 mg/kg gabapentin addition than Tramadol alone (p<0.001). Whereas tail-flick periods stayed the same when gabapentin doses increased except 300 mg/kg. Tail-flick test determined that acute pain lasted longer with tramadol. Also in hot-plate tests, tramadol and gabapentin groups lasted longer than Group I.11 and gabapentin groups. With 30-100-200 mg/kg doses; gabapentin was found non-effective while 300 mg/kg gabapentin was effective in acute pain. In neuropathic and chronically pain’s acute pain attacks we should take into consideration that gabapentin added to tramadol would not increase the analgesic effect.

**Keywords:** acute pain, tail flick, hot plate, tramadol, gabapentin

**P21**

**Communicating brain health, brain science, and brain research with the public: brain health promotion and brain literacy improvement by employing the brain awareness weeks in Turkey since 1998**

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Today, the issues related to autonomy, independence and irresponsibility of science and the scientist versus their pragmatic and translational concerns are debated more irascibly than ever. Confronted by the shortage of public resources, high measures for protection of intellectual property, and the strong drives of the market economy, scientists and professionals from various age and rank concerned with human mentality and behaviors, and its creativity and outputs are seriously challenged by a major responsibility in their respective communities.

Undergoing this controversy, today’s neuroscientist is committed to payback to his/her community by awakening brain consciousness, and developing brain literacy and brain health promotion targeting the public in the largest spectrum from preschool children to the interested/perceptive aged persons. To serve and materialize this vision, the American Society for Neuroscience and the Dana Foundation (DANA Alliance for Brain Initiatives) pioneered in taking action and launching the first Brain Awareness Week (BAW) in 1995 in North America. In 1997, Europe joined in by establishment and activation of EDAB (European DANA Alliance for the Brain). The following year, Neuroscience Society of Turkey (TUBAS), on behalf of Turkish Neuroscience, began observing BAW annually in various cities and institutions in Turkey. BAW has boomed in the whole world since then.

The objectives and expected added values of BAW can be summarized as follows:

To promote the responsibility of the neuroscientist as “an educator of the public” in the community.

Communicate with the public concerning brain research in his/her country and in the world.

Translate the community the applicable results of brain research directly concerning brain health promotion (prevention, treatments, management).

Discuss with the public the costs, benefits, failures, weaknesses and the added values of the resources invested for brain research.

Develop consciousness for a) the contextual nature of the brain, its states and its products, especially in the practices concerning modern medication, high technology and law; b) neuroethics in issues related to human and patient rights, confidentiality, free will, informed consent and penal liability; c) good conduct of brain health practices.

Evolve curiosity about brain function, health and research in the community starting from preschool stage, and help construct progressive public opinion effective on the government, civil society, mass media and the individuals.

Provoke the government, state, civil and the private sectors for better investment of resources for brain research and brain health practices.

Elaborate on the potential “super” power of function and plasticity of the brain for promotion and betterment of the understanding of rationality, liberty, self-respect, individuality, higher level intellectualism, empathy, aesthetics, human rights and democracy in the community.

Introduce the public with the multi-disciplinary, multi-professional, above-national and above-governmental nature of brain science; advertise the various sub-fields of neuroscience, and encourage and convince the children, youngsters, tutors and families for studies and careers related to brain science, brain education and brain health.

The aim of our poster is to:

Present a bird’s eye view of the multi-disciplinary, multi-professional and multi-institutional BAW endeavours and activities accomplished since 1998.

Motivate, encourage and guide the neuroscientists and future neuroscientists in adoption of this responsibility and commitment to the community.

Benefit from the constructive criticism and the novel, original and creative opinion/suggestions of our peer spectators.

Keywords: brain awareness week (BAW), community brain health, brain awareness, brain consciousness, brain literacy, brain research, neuroscience teaching, neuroethics

P22 Effects of prenatal alcohol exposure on activity, anxiety and learning in young adult wistar rats

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Evoke curiosity about brain function, health and research in the community starting from preschool stage, and help construct progressive public opinion effective on the government, civil society, mass media and the individuals.

The objective of the present study was to examine the effects of prenatal exposure to alcohol on sensorimotor coordination, emotionality, learning and memory in young adult Wistar rats. Most of the up date reports concerning behavioural effects of fetal alcohol exposure referred to the juvenile period of life and very few studies simultaneously investigated different aspects of behaviour in the same subjects. In the current study, alcohol was delivered to the pregnant dams by intragastric infusions, throughout gestation days (GD) 7-20, at the dose of 6g/kg maternal body weight/day. This dose resulted in relatively high peak blood alcohol concentration (340 mg/dl) as assessed on GD 20. A pair-fed isocaloric and untreated control groups were included. Prenatal alcohol administration significantly retarded dams’ weight gain, and adversely affected pups’ weight at birth but not in adulthood. No between-group differences were observed in the litter size and in the pups’ mortality. Rats prenatally treated with ethanol when tested as adults were not impaired in sensorimotor coordination and/or did not show muscle weakness as assessed by rotarod/accelerated tests. Their behaviour in the open field and plus maze suggested alcohol-induced increase in anxiety level and some decrease in behavioural flexibility, but hyperactivity level was not observed. In cognitive tasks, alcohol treated rats when tested at 3 month of age showed slightly slower rate of initial place learning in the Morris water maze. However, memory retention tested after 1 and 10-day delay, reversal learning, rate of extinction of place preference, as well as working memory capacity appeared to be the same in alcohol exposed and control rats. The results of this study confirm that effect of prenatal alcohol intoxication on behaviour is age-dependent, and if there is a function recovery during maturation, it refers equally to both motor and cognitive aspects of behaviour. Elucidation of the mechanisms of recovery from deteriorating behavioural effects of perinatal alcohol exposure in the adulthood requires further investigations.

Keywords: prenatal alcohol, activity, anxiety, learning, rat

P23 The effect of social isolation stress on learning in male juvenile rats

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Learning is a complex function and it is influenced from variation of physiological conditions. So, it is thought that the stress which was affect inside and outside environment of the organism affects learning as causes biochemical and functional changes in endocrine and nervous system. In this study, we investigated searched the effect of social isolation stress on learning in male juvenile rats which were 21 days old. The study was done with 25 Wistar Albino male juvenile rats which were 28 days old. Five of them were at preexperimient group, 10 of them were at control group and 10 of them were at social isolation group. The rats were experienced social isolation stress four hours in a day during 21 days. As take refuge in different cages, at the end of this period, learning was tested at morris water maze if they learn how to find the place. After a three days learning period, learning test was done at fourth day. The total duration of time spent to find the platform and the duration of time spent in half area of the tank including the platform in a value representing the percentage in the total time were compared statistically within and between the rats included in the control and social isolation experiment groups so as to assess the effect of social isolation stress on the ability of learning position in rats. The comparison on the learning phase for learning performances displayed on each day within groups was statistically analysed by means of repeated measurement with the ANOVA test and benferroni test whereas the test phase was compared between groups with the unpaired t-test. P<0.05 was accepted for significant level. Comparing of findings within groups, the different between days is meaningful, but comparing of findings between groups is unmeaningful. As a result, it was found that social isolation stress, at applied for 21 days, is not affect on learning in male juvenile rats and it was concluded that the effect of stress on learning is related to period and degree of the stress.

Keywords: social isolation, learning, rats, morris water maze, stress

P24 Nitric oxide synthase inhibition does not modify nicotine-induced conditioned place preference in rats

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We have previously shown that nicotine (NIC) treatment induces conditioned place preference (CPP) in male and female Sprague Dawley rats; and that the effect is stronger in males than in females. CPP is observed when NIC is paired with the initially preferred or non-preferred chambers. We have also shown that NIC increases NO levels in rat brain. In the current study, we studied the effects of Nitro-L-Arginine, L-NA; 50 mg/kg) on NIC-induced nitric oxide synthase inhibition (N (0.2)
mg/kg, base) induced CPP in adult male and female Sprague Dawley rats. The CPP apparatus consisted of black and white chambers (associated with drugs or saline=SAL), and a third neutral chamber. Rats were initially allowed to explore all three chambers for 30 minutes and time spent in each chamber was monitored to depict preference. In 8 sessions that followed rats received LNA or SAL 12 hours prior to NIC=SAL, administered alternatively, or SAL=SAL, injections, thereby the groups were SAL=SAL, LNA – SAL, SAL – NIC, LNA- NIC. Rats were placed in appropriate chambers (NIC was paired with the unpreferred chamber) for 15 minutes. After conditioning trials, during the final assessment, the doors between the chambers were opened, rats were placed in the neutral chamber, and time spent in each compartment was monitored for 30 minutes. In males CPP was observed in SAL-NIC and LNA-NIC groups while SAL-LNA had no effect. In females CPP was not observed at the dose employed. Although NO may modulate the rewarding or cognitive aspect of nicotine, our results suggest that NO is not involved in its conditioning effects. Supported by Ege University Research Fund grant 2002/ TIP/ 014

Keywords: Nicotine, conditioned place preference, addiction, nitric oxide synthase, sex differences

P25

Behavioural parameters in phasic pain suffered mice; importance of sex differences

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In this study, the changes in behaviour and the response to phasic stimuli in female and male mice, were investigated. Locomotor activity, exploration behaviour, avoidance and escape responses were examined before and after noxious stimuli. A hot-plate was used for phasic pain and behavioural parameters were observed in open field area. There were no differences in the latency of paw licking between male and female mice when they were placed on a hot plate (maintained at 52°C) (p>0.05). The number of cross section area, rearing, grooming and defecation were not different in male and female mice before and after noxious stimuli. Although baseline and escape latencies were similar in both male and female mice, avoidance latency was longer in female mice than male mice (p<0.05) prior to noxious stimuli. In both groups avoidance and escape latencies lengthened; especially avoidance 2 was longer in female mice than in male mice following noxious stimuli (p>0.03).

We observed that the phasic pain did not change locomotor and exploratory activities, autonomic responses, baseline, avoidance and escape latencies in female and male mice. However avoidance latencies were prior to stimuli in female mice, but escape latency was longer following stimuli in male mice. It was concluded that phasic pain did not change behavior in mice.

Keywords: Phasic pain, behaviour, sex differences, mice

P26

Effects of valid stress related symptoms and coping strategies on sleep quality parameters in doctors and nurses

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Stressor induced cognitive and physiological responses reveal the components of general adaptation syndrome such as alarm reaction, resistance-normalization and/or loss of resistance-exhaustion. Prolonged and/or uncontrollable stressors render this adaptive period ineffective, increasing the likelihood of sleep and mood disturbances. Influences of previous waking period events on sleep architecture and of depression, post-traumatic stress disorder, panic disorder, emotion-focused coping behavior and personality features on sleep quality were reported by studies. Chronic sleep restriction and shift work with a combination of high demand and low control over workload were shown to induce psychosocial stress by disturbing the coping strategies and the reactivity of stress systems playing a critical role in adapting to a new environment. This study was performed to investigate stress-related symptoms, coping-strategies and sleep quality of 159 doctors-nurses in Mugla. Stress Related Symptoms Scale (Sahin-Durak), Ways of Coping Inventory (Folman-Lazarus, 1980; Sahin-Durak, 1995) and Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989; Ajarqın et al., 1996) were applied to evaluate musculoskeletal, parasympathetic, sympathetic, emotional, cognitive, endocrine and immune symptoms; self confident, optimistic, submissive, helpless, seeking social support strategies and subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction components of sleep quality. SPSS 10.0 was used to analyze data via Independent t, ANOVA, Tamhane and Pearson correlation tests. Stress symptoms were higher in women and A type personality. Marriage was found to negatively effect musculoskeletal, parasympathetic and endocrine measures. Primary health care/out patient clinics staff had more musculoskeletal, parasympathetic, sympathetic and cognitive symptoms. Self-confidence and optimism in women, submission in B type personality, optimism and social support seeking in smokers were less popular. Scores of daytime dysfunction in younger, sleep disturbances and use of sleeping medication in married subjects and women, habitual sleep efficiency in single subjects and men; subjective sleep quality in smokers and drinkers were found to be high signifying the poor sleep quality. Sleep quality and stress symptoms were positively correlated with each other, and together they were also positively correlated with submissive-helpless strategies and negatively correlated with self-defensive strategies. Stress symptoms, coping strategies and sleep quality seem to be influenced by common variables such as gender, marital status, personality features and work environment.

Keywords: Stress, coping, sleep quality, personality, health staff

P27

The assessment of foot motor asymmetry and the relationship between motoric dominance and turning preference

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In the present study, the correlation between turning direction with two measures of motoric dominance—handedness and footedness was examined. Also the reliability and the validity of the footedness measurements were investigated. Fifty subjects (23 men, 27 women) were randomly selected from medical school students. Handedness assessment: a) the subjects completed a 13-item questionnaire adapted from Chapman and Chapman. b) Finger-tapping task: The subjects attempted to tap with their index finger on a mouse as many times as possible within 10 sec. After three trials for each hand, the average number of taps/sec. was calculated. Footedness assessment: a) The subjects were performed 14 unilateral foot activities. The task was given in two trials and on each item, the subjects received a score of 0 or 1, for using the right and the left foot respectively. Thus the score could range from 0 to 28. b) Foot-tapping task: A foot tapper that similar to a car’s accelerator pedal was used to measure tapping rates. The subjects were seated and asked to tap on the pedal with their foot as many times as possible. The task was performed under the same trials as done for finger-tapping. The average number of taps/sec. was calculated for each foot. For reliability of the foot-tapping and the foot preference tasks, 20 subjects attended the test-retest study 3–4 weeks later. Rotation task: Four loudspeakers were placed on the walls of a room and each time one of the loudspeakers emitted a ring sound. The subjects were asked to turn to the loudspeaker which they heard the ring sound. The direction of turnings was recorded. Percentage of turning to the left was computed. There was no significant correlation between the handedness score and finger-tapping performance. Also the correlation between foot preference and foot-tapping performance was not significant. The test-retest reliability and internal consistency were found to be high for both foot preference and foot-tapping tasks. Many of the items were correlated significantly with total score of foot preference task. The correlation between turning bias and motoric dominance was not significant. The results show that the foot preference and foot-tapping tasks are reliable in measuring footedness. These findings suggest that turning preference may be independent from motoric dominance.

Keywords: Footedness, handedness, turning bias, foot-tapping, finger-tapping

P28

Raloxifen has an antidepressant effect and enhances spatial memory in ovariectomised rats

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During the postmenopausal period, deficiencies are observed in multiple systems, probably due to reduced estrogen levels. Cognitive deficits and mood disorders are among these problems and have a negative impact on this stage. Experimental and clinical studies provide evidence for the antidepressant and cognitive enhancing effects of estrogen. Currently, due to the side effects of hormone replacement therapy reported recently, the use of alternative pharmaceuticals acting on the estrogen receptors (E) is preferred. Selective ER modulators
have variable agonistic or antagonistic effects depending on the tissue. Within this frame, Raloxifen acts as an agonist in the bone but as an antagonist in the breast and uterus; therefore raloxifen is used in the treatment of postmenopausal osteoporosis. The aim of the present study was to investigate the effects of Raloxifen on cognition and depression in an animal model. Adult female Sprague Dawley rats (n=39) were used. Menopause was obtained by ovariectomy and after 21 days rats received daily injections of Raloxifen or placebo for 12 days. At the end of drug administration, two groups of rats (Raloxifen and control) were subjected to Porsolt forced swim test (FST) for mood assessment while the other two groups were trained in the water maze (MWM) for spatial learning and memory testing. Drug treatment was continued for an additional 2 days in the FST and 7 days in the MWM groups. Raloxifen decreased immobility (p<0.001) and increased struggling (p<0.001) in the FST, suggesting the prevention of depression. There were no significant differences were depicted between the groups regarding swim speed or acquisition of place learning. However in the memory test, Raloxifen group had an advantage over controls (p<0.5). Our results demonstrate that Raloxifen acts as an antidepressant in rats subjected to surgical menopause and supports memory although the effects on spatial learning are negligible. This study was supported by the 2004 TÜBİTAK/BAD Research Grant awarded to CMT.

Keywords: Raloxifen, Porsolt forced swim test, Morris Water Maze, Spatial learning, menopause, estrogen, depression, cognition.

P29
Effect of taurine on lipopolysaccharide-induced spatial learning deficits
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Lipopolysaccharide (LPS) is derived from the cell wall of gram-negative bacteria and is a potent endotoxin that causes the release of cytokines. LPS is thought to activate both the neuroimmune and neuroendocrine systems; it also blocks long-term potentiation in the hippocampus. Spatial learning requires integrative control functions of hippocampus. LPS administration results in physiological and behavioral disturbances; including fever, anorexia, body weight loss, induction of slow-wave sleep, suppression of locomotor and exploratory activity, reduction in social and sexual behavior, impairment in spatial learning performances. These changes might be interpreted as an acute stress reaction to the LPS. Taurine is one of the most abundant free amino acid in mammalian cells and play a role in variety of physiological functions (osmoregulation, Ca++ modulation, antioxidant and membrane stabilizer) pharmacological actions (neurotransmission, inhibition neomroduction and pathological states. Taurine is present in the mammalian brain and is known to decline with aging. It has been demonstrated that taurine administration improves the oxidative stress-induced short-term and long-term memory defects in experimental animals. The aim of this study is to investigate the effects of taurine on LPS-induced spatial learning deficits in rats. In the present study, therefore, we studied the effects of LPS (10, 100, 500 μg/kg, i.p.) and taurine (500 mg/kg) on spatial learning performances using Wistar-Albino male rats. In the Morris’s water-maze task, spatial learning performances were examined in four trials of the training for six consecutive days. LPS-treated rats had a longer time to reach the hidden platform than control rats (p<0.05 at 500 μg/kg). Taurine administration prevented the spatial learning impairments in LPS-treated rats (p<0.05). On the other hand, taurine also impaired spatial learning performances in LPS- non treated rats (p<0.05). Our results indicate that taurine may play an important role in the hippocampal functions as the spatial learning and memory.

Keywords: lipopolysaccharide, spatial learning, morris water maze, memory, taurine

P30
Effect of channel noise on the recovery from inactivation of the stochastic sodium channels
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Ion channels provide conduction pathways for specific ions and constitute the fundamental elements for electrical signaling in nerves. Voltage-gated ion channels, which form an important class of such channels, are involved in the generation and propagation of electrical signals in the excitable cell membranes. The voltage-gated ion channels fluctuate randomly between open and closed states. The fluctuations between conducting and non-conducting states give rise to noisy membrane currents and sub-threshold voltage fluctuations. The sub-threshold voltage fluctuations contribute to the reliability of spike timing since they near threshold affect precisely when an action potential is initiated. In this study, we examine the relation between the sub-threshold voltage fluctuations and ion channel blocking based on the squid giant axon. For this purpose, we characterize the sub-threshold noise for sodium and potassium ion channels by using linearized quasi-active approximations and compute the variance, power spectral densities and resonant frequencies of voltage noise for the Hodgkin-Huxley model embedded in a 1000 mm² patch of membrane. The total number of involved sodium and potassium ion channels is scaled by a scaling factor in order to disregard the blocked channels. We found that the variance of the voltage noise decrease exponentially with the decreasing amount of the blocked potassium channels while the decreasing amount of the blocked sodium channels leads to an increase in the variance of the voltage noise. We also obtained the power spectral densities of voltage noise for a variable scaling factor. We then determined the resonant frequencies by using the power spectral densities for sodium and potassium channels, and observed that the resonant frequencies decrease with the increasing the amount of the blocked sodium and potassium channels. The resonant frequencies provide information at which frequency the maximal power of the voltage noise occurs. Our results indicate that the resonant frequencies, approximately range from 55 Hz to 61 Hz for sodium channels and from 31 Hz to 61 Hz for potassium channels at a membrane voltage of ~65 mV.

Keywords: ion channel noise, subthreshold voltage fluctuation, ion channel blocking

P31
The relation between the sub-threshold voltage fluctuations and ion channel blocking
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Ion channels provide conduction pathways for specific ions and constitute the fundamental elements for electrical signaling in nerves. Voltage-gated ion channels, which form an important class of such channels, are involved in the generation and propagation of electrical signals in the excitable cell membranes. The voltage-gated ion channels fluctuate randomly between open and closed states. The fluctuations between conducting and non-conducting states give rise to noisy membrane currents and sub-threshold voltage fluctuations. The sub-threshold voltage fluctuations contribute to the reliability of spike timing since they near threshold affect precisely when an action potential is initiated. In this study, we examine the relation between the sub-threshold voltage fluctuations and ion channel blocking based on the squid giant axon. For this purpose, we characterize the sub-threshold noise for sodium and potassium ion channels by using linearized quasi-active approximations and compute the variance, power spectral densities and resonant frequencies of voltage noise for the Hodgkin-Huxley model embedded in a 1000 mm² patch of membrane. The total number of involved sodium and potassium ion channels is scaled by a scaling factor in order to disregard the blocked channels. We found that the variance of the voltage noise decrease exponentially with the decreasing amount of the blocked potassium channels while the decreasing amount of the blocked sodium channels leads to an increase in the variance of the voltage noise. We also obtained the power spectral densities of voltage noise for a variable scaling factor. We then determined the resonant frequencies by using the power spectral densities for sodium and potassium channels, and observed that the resonant frequencies decrease with the increasing the amount of the blocked sodium and potassium channels. The resonant frequencies provide information at which frequency the maximal power of the voltage noise occurs. Our results indicate that the resonant frequencies, approximately range from 55 Hz to 61 Hz for sodium channels and from 31 Hz to 61 Hz for potassium channels at a membrane voltage of ~65 mV.

Keywords: ion channel noise, subthreshold voltage fluctuation, ion channel blocking

P32
The factors affecting F response in normal population
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F wave is a late response which is evoked by supramaximal stimulation of the periferal nerve showing antidromic motor neuron discharge of alpha motor fibres.
and reflects the latency over the afferent and efferent arces of the motor fibers from the stimulating site and anterior horn cells. In this study, F responses of bilateral median, fibular and posterior tibial nerves are examined in 74 healthy individuals (34 females, 30 males) the mean age of which is 44.2 ± 16.3 (17-73). The distribution of data according to the age, sex, height and weight is evaluated. The subjects are divided in three age groups: 15-35, 35-55, 55 and >55. The effect of age, weight and height on F latency in males and females are examined by regression analyze. Mean F reflex latency of nerves was found as following: N. Medians 25.9 ± 2.2 msn, N. Ulnaris 26.0 ± 1.8 msn, N. Fibularis 47.4 ± 4.1 msn (3.8-5.5), N. Tibialis posterior 48.7 ± 3.8 msn (1.6-18.1). The values of N. Medianus, N. Ulnaris, Fibularis and Posterior tibialis in females in 15-35 age group were respectively: 24.30 ± 2.3 msn, 24.70 ± 1.9 msn, 44.34 ± 2.01 msn, 44.8 ± 1.9 msn, in 35-55 age group: 25.2 ± 1.3 msn, 24.6 ± 1.0 msn, 45.3 ± 2.8 msn, 46.8 ± 3.0 msn and in >55 group: 26.1 ± 1.9 msn, 47.9 ± 5.1, 50.1 ± 3.4. In males, respectively in 15-35 age group 25.4 ± 3.2 msn, 26.8 ± 1.2 msn, 48.6 ± 3.4 msn, 48.9 ± 2.6 msn, in 35-55 age group 27.2 ± 1.7 msn, 27.2 ± 1.9 msn, 48.7 ± 3.6 msn, 49.9 ± 3.6 msn and 55 and >55 age group 27.8 ± 1.2 msn, 28.2 ± 1.5 msn, 52.2 ± 4.9 msn, 52.9 ± 3.9 msn were found. As a result, it is seen that F latency is not affected by weight and sex (p=0.18), but there can be variations due to height and age (p<0.001).

Keywords: F response, weight, sex, age, height.

P33
The factors affecting H reflex in normal population
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Hoffman reflex (H reflex); is a reflex response obtained from the calf muscle after stimulation of the posterior tibial nerve with lower stimulus than that of compound muscle action potential in adults. The effect of age, weight and height on H reflex in males and females are examined by regression analyze. In this study bilateral H reflex are examined in 74 healthy individuals (34 females, 30 males), the mean age of which is 44.2 ± 16.3 (17-73) and distribution of the data according to age, sex, height and weight is evaluated. The subjects are divided in three age groups: 15-35, 35-55, 55 and >55. In 15-35 age group the results were as following: H reflex distal latency 27.9 ± 1.9 msn (28.3-34.3), H amp. 1.7 ± 0.8 mV (1.6-2.5), M latency 4.3 ± 0.5 msn (3.8-5.5), in 35-55 age group: H reflex distal latency 28.6 ± 1.8 (27.8-32.8), H amp. 1.3 ± 0.6 mV (0.5-2.5), M latency 4.5 ± 0.5 msn (5-5.7), in 55 and >55: H reflex distal latency 31.5 ± 2.9 msn (25.7-36.8), H amp. 0.6 ± 0.5 mV (0.1-2.1), M latency 4.6 ± 0.6 msn (3.5-5.8). It is observed that while age and height in males and age in females affect latency of H reflex, H amplitude varies associated with age in males and females (p<0.001).

Keywords: H reflex, weight, sex, age, height

P34
Effect of a single day of light: light (L-L) regimen on behavioral despair in aged rats
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Exposure to bright light has been commonly used in phototherapy for Seasonal Affective Disorder (SAD) in humans. A potential explanation for the therapeutic effect of light in the treatment of SAD may be the capacity of light to entrain the circadian rhythms. Previously we have described that a single day of Light: Light (L-L) exposure is sufficient to ameliorate depressive symptoms of young female rats in two forced swim tests (FSTs), frequently used as an animal model of behavioral despair in rodents. Since the circadian rhythms in aged humans and rodents have been shown to be defective, the present study was conducted to further elucidate the effect of a single day of L-L exposure in old male rats in FST and navigational learning. Forty male Wistar rats from our breeding colony maintained on a 12:12 light:dark (L:D) lighting schedule were used. Aged subjects were 24 months old whereas young subjects were 3 months old. There were 5 groups of Wistar rats (n=8 each). The aged L-L group were placed overnight in an insutulated chamber illuminated by 60 watts lamp under 12:12 L:D cycle. The aged chamber control group was put in the chamber under a 12:12 L:D cycle. A week later, they were exposed to a 2-day FST followed by a 7-day hidden platform, 1 day probe trial and 1 day visible platform test in the Morris Water Maze (MWM). An aged control group and another one consisting of young rats were not put in the chamber but tested in FST and MWM. Another aged control group was tested only in the MWM task. None of the old rat groups was ‘depressed’ as assessed by the fact they displayed shorter duration of immobility in the second FST compared to the first. Light treatment did not affect the behavioral despair state of old animals.

In contrast, young rats were immobile for a significantly longer duration in the second swim test compared to the first. In the MWM, all aged rat groups behaved similarly and performed significantly worse than the young rats. (This research is supported by the Boğaziçi University 09IR03 grant to RC).

Keywords: Aging, Wistar rats, Light Treatment, Forced Swim Test, Morris Water Maze

P35
Cognitive success in primary-school pupils: gender differences and predictability by height and weight
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It is known that some cognitive abilities show gender differences: women are better than men in verbal intelligence, men are better than women in spatial intelligence. However, during last years, Tan and his co-workers have shown that spatial abilities are associated with height, weight, and lung capacities, not with gender; if these bodily measured are taken into consideration, gender differences entirely disappeared. In these works, cognitive abilities were assessed by intelligence tests. The aim of the present work was to study gender differences in verbal and spatial abilities under natural conditions, i.e., scores at schools; if so, to predict these abilities using height and weight. This study included 265 female and 273 male pupils. The height and weight were accurately measured. The scores for Turkish, maths, social knowledge, science, drawing, and music lessons were taken from teachers. Mean age was 12.2 (SE = 0.12), mean weight 40.8 Kg(SE = 0.65), mean height 145.5 cm (SE = 0.77). There were no significant difference between these parameters.Results showed that scores were significantly better in females than in males, except maths which was nearly equal in males and females. There was no significant difference in right- and left-handers for verbal and spatial cognitive abilities. Scores significantly declined with age, height, and weight. Taking height and weight as covariates did not change these results. The results of the present work suggested that females outperformed males in verbal and spatial abilities, under natural conditions, i.e., without using intelligence tests; cognitive abilities can be predicted using height and weight

Keywords: success, height, gender difference, weight, intelligence

P36
A sequence design and visualization techniques for DT-MRI
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Recent improvements in the MR based neuroimaging methods have led to design of numerous imaging techniques. One of these is Diffusion Tensor MRI (DT-MRI), which measures water molecules diffusion in three dimensions (x, y and z). This method has recently been used to diagnose neurodegenerative diseases, neural development and functional connectivity. In structured tissue such as fibers in brain and muscles, water molecules show directional diffusion. In DT-MRI Apparent Diffusion Coefficient (ADC) is used as a parameter to describe direction dependencies of water molecules. According to this, ADC is larger along the structure. DT-MRI measures the ADC in six directions, from the ADC in these six directions are a symmetric diffusion tensor matrix is derived. After diagonalization of the diffusion tensor matrix three eigenvectors and three corresponding eigenvalues are obtained. The eigenvector with the largest eigenvalue corresponds to the main diffusion direction. The other two eigenvectors correspond to directions perpendicular to this direction. By using the main diffusion direction, we can find trajectory that water molecules follow. The found trajectory can be a bundle of nerve fibers or muscle fiber. In order obtain the diffusion tensor image, simple bipolar pulsed gradient is applied before and after the 180° pulse in the spin-echo sequence. This causes the static spins to be all in phase, which gives a maximum signal where as diffused spins lead to signal attenuation. In this study we are going to give brief description of DT-MRI sequence and visualization tool developed at BUMIL (Bogazici University Medical Imaging Laboratory). In order to acquire diffusion tensor image, a pulse sequence was developed by using IDEA software. VTK (Visualization Toolkit) and ITK (Insight Segmentation and Registration Toolkit) are use in order to calculate and visualize diffusion information.

Keywords: diffusion tensor magnetic resonance imaging, tensor analysis, trajectory, sequence, VTK-ITK
P37
Wavelet analysis of FNIRS signal in breath-holding task
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Functional Near Infrared Spectroscopy (fNIRS) has been used to investigate changes in cerebral hemodynamics induced by hypercapnia challenges, such as carbon dioxide (CO2) inhalation and breath-holding. The aim of this study was to investigate the changes in the frequency spectrum of cerebral hemodynamic oscillations measured by fNIRS during breath-holding task. Clinicians have been investigating the cerebrovascular reactivity of brain by changing its vasodilatory or vasoconstrictory capacity of the resistance arterioles. Cerebrovascular reactivity of the cerebral circulation can be assessed by CO2 inhalation or alternatively by simple breath-holding. fNIRS of the human brain is possible because there is a window of transparency of biological tissue to light in the near infrared part of the spectrum. Near-infrared (NIR) light from approximately 700-900 nm is much more weakly absorbed by tissue than the visible light. Changes in the intensity of transmitted light in NIR range allow us to calculate concentration changes of deoxy-hemoglobin ($\Delta$HbR) and oxy-hemoglobin ($\Delta$HbO2) in the tissue. Measurements of $\Delta$Hb are performed on three healthy subjects during four breath-holdings of 30 s each, interleaved with 90 s of normal breathing. fNIRS probe is placed on the forehead of the subjects. In a typical breath-holding task, $\Delta$HbR increases during breath-hold interval which is followed by a decline after breath-holding. $\Delta$HbO2 increase and decrease are called hold and recovery periods, respectively. The periods where $\Delta$Hb is stable are called baseline periods. We investigate CO2 pressure changes dependence of frequency subbands ($[0.88-0.44]$, $[0.44-0.22]$, $[0.22-0.11]$, $[0.11-0.055]$, $[0.055-0.0275]$ Hz) of cerebral hemoglobin oscillations during breathing-holding task for three periods, normal, up and down. To separate the frequency of $\Delta$Hb signal to its subbands we use wavelet decomposition. Of the three periods, Recovery period is much more sensitive to vasoreactivity response than the others. We have observed that subband medium frequency recovery period is statistically different (P<0.05) between first and fourth breath-hold interval in four of the five subbands. This difference could be due to the physiological adjustment of cerebral dynamics to the last breath-holding task. We conclude that the frequency dynamics of the recovery period can be an important indicator that can reveal the auto regulation mechanism of the brain during breath-holding.

Keywords: Near infrared spectroscopy, wavelet analysis, frequency analysis, hypercapnia, breath-holding.

P38
An anaglyphic three dimensional (3D) investigation of SEM images taken from the olfactory region of rat
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Smelling differs from the other special senses of being reached to cerebral cortex without passing through the thalamus. Smell fibers and their connections with limbic system could have regulatory effect of smell sense over the emotional functions in primitive mammals by the means of smelling. Because of this situation, investigation of the micro-structural pattern of the formation of olfactory nerve will allow us to better understand the functions of this nerve. One female albino rat 250-300 g in weight was used in the study. The specimens were fixed in 2.5% glutaraldehyde for 24 hours, washed in phosphate buffer (pH:7.4), post-fixed in 1% osmium tetroxide in phosphate buffer (pH:7.4) and dehydrated in increasing concentrations of alcohol. After dehydration, the specimens underwent to critical point drying and mounted on metal stubs with double-sided adhesive tape. Then the samples were sputtered with 150 Å thick layer of gold in BIO-RAD sputer apparatus. The images were taken as stereo pairs by JEOL SEM ASID-10 (Uapplied electron microscope. After having the stereo pairs, we held anaglyphs in RGB format using Adobe Photoshop © 7.0 Mac version software. The aim of this study as methodological and as originally will be reported is to investigate the scanning electron microscope image of the Olfactory Area of Rat by a technique called anaglyph, in which the images were initially recorded as stereo pairs and then converted to the dimensional images in red blue channels that would be seen by the use of special anaglyph glasses.

Keywords: SEM, anaglyph, stereopair, olfactory, 3 dimensional.

P39
Investigation of the brain hemispheric asymmetry by the Cavalieri principle using CT images in the schizophrenics
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It is known that the brain hemispheres have the functional asymmetry since they have different functions. The existence of the morphological asymmetry in terms of volume and surface area of the brain is still controversial. Besides the studies reporting that the hemispheric volume of the schizophrenic patients has volumetric asymmetry, there are some studies having contrary findings. The asymmetry model expected for schizophrenics is thought that it is the product of feral developmental anomalies. In this study, the brain volumes of 30 chronic schizophrenic patients and 39 control subjects were examined stereologically for the existence of the interhemispheric asymmetry. The volumes of the brain hemispheres were estimated by three independent observers using the Cavalieri principle on routine CT images. The findings of three observers were correlated well each other (P<0.001). The difference of the brain volume between the schizophrenics and control groups were statistically significant (P<0.005). The volumetric asymmetry in the brain hemispheres was statistically significant for the schizophrenics and control groups (P<0.001). The volumetric decrease of the left hemisphere volume depending on the increase of the age for both group were statistically significant (P<0.005). The findings of volume values in the present study that were obtained by using unbiased approach may provide contribution for the discriminative diagnosis of the schizophrenic patients.

Keywords: Cavalieri principle, schizophrenic, CT, hemisphere, asymmetry.

P40
Determination of normal electrooculography standards: a preliminary study
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The electrooculography (EOG) measures the potential that exists between the posterior pole of human eye and cornea. This standing potential is generated largely by the transepithelial potential across retinal pigment epithelium (RPE). Retinal illumination causes alteration in this potential. The EOG measures the amplitude of the standing potential and light response. The EOG was recorded in accordance with Standardization Committee of the International Society for Clinical Electrophysiology of Vision (ISCEV) standards on 25 healthy individuals to determine normal values of our laboratory. The Arden ratio, the ratio of light peak to dark trough, was used to evaluate the EOG measurements as ISCEV suggested. The mean value of Arden ratio is around 2.10. We found that the Arden ratio in the male subject is lower than that of in the women subject. Thus, EOG can be used for the diagnosis of disease of RPE. In addition, the Arden ratio has diagnostic value for some clinical disorders such as Best Vitelliform Macular Dystrophy.

Keywords: electrophysiology, electrooculography, arden ratio, retinal pigment epithelium, Biopac MP100 data acquisition system.

P41
3-D reconstruction of the layers of the eyeball from serial light microscopic images
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The eyeball is one of the most interesting subjects of the neuroscience. In this study, we aimed to obtain the 3-D image of the layers of the eyeball of a rat, by using semi-thin serial. After removal of the eyeball of the rat, the tissue specimen was put into 2.5% glutaraldehyde for fixation and then, routine transmission electron microscopic tissue preparation technique was used for post-fixation, dehydation and embedding procedures of the tissue sample. Following this procedure, the semi-thin sections of the tissue were cut with a glass knife. These sections were 2 µm in thickness and they were stained with methylene blue. The photographs of the images were taken with a Nikon Optiphot light microscope. All the serial images were transferred into a computer, their wire frame images and the rendered form of these wire frame images were obtained by the help of a computer program named Surf Driver. From these rendered form of images, the 3-D reconstruction of the organ was done. Totally 20 serial semi-thin sections were taken from the specimen and the interval in between two serial sections was 20 µm. Therefore, the 3-D reconstruction of the organ was done from a tissue sample, which was 420 µm in thickness. In conclusion, the 3-D image of this organ from
serial semi-thin sections will be very helpful for the understanding of the three dimensional appearance of the organ and relations of the layers of it at the light microscopic level.

Keywords: Light microscope, 3-Dimensional, Eye ball

P42
Microdialysis and gene cloning and their application in pharmacologic and biomedical sciences
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Microdialysis is a powerful in vivo sampling technique that enables researchers to investigate endogenous neurochemical changes without tissue removal. It is as though an artificial blood vessel is surgically inserted into the tissue. The changes are also detected in awake animals. This technique is used while investigating mechanism of drug dependence, also during drug phase studies. In this study, the effect of neuroenin on dopamine metabolism is investigated in the nucleus accumbens of rats. The use of gene cloning techniques has increased sharply during the recent years. The cloning of the lactate hydrogenase gene and the expression of the lactate dehydrogenase enzyme are accomplished in this study. Many drugs can be cloned by using the gene cloning technique. Further use of gene cloning experiments will be discussed.

Keywords: Microdialysis, Gene cloning

P43
Dopamine receptor D4 (DRD4) and dopamine transporter (DAT1) gene polymorphisms modulate human gamma band responses
Demirag T [1, 2], Hermans C [2], Ergençöl T [4], Erdal ME [3], Keşkin HY [1], Ergen M [1], Beydagi H [4].
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Evoked gamma oscillations (30-80 Hz) following sensory stimuli are modulated by attention, object recognition, and working memory. However, little is known about the neurochemical basis of their modulation during cognitive processes. Schizophrenia and Attention Deficit Hyperactivity Disorder (ADHD) introduce changes in gamma responses and have significant associations with genetic polymorphisms of dopamine receptor D4 (DRD4) and dopamine transporter (DAT1) and catechol-O-methyltransferase (COMT) enzyme that are responsible for the termination of dopaminergic neurotransmission. Therefore, we investigated whether direct relations exist between these polymorphisms and the amount of gamma oscillations in a healthy population with an auditory attention paradigm. The 7-repeat allele of the VNTR polymorphism in DRD4 gene has been shown to be less responsive to dopamine stimulation, and subjects homozygous for the 10-repeat allele of a VNTR polymorphism of the DAT1 gene showed significantly lower dopamine transporter binding than carriers of the 9-repeat allele. A G/A transition polymorphism in COMT that specifies which COMT enzyme is expressed was also studied. It was found that the 10-repeat allele of the COMT polymorphism was associated with lower amplitudes of P3 potential compared with subjects who were homozygous for the 11-repeat allele. Therefore, we suggest that the 7-repeat allele of DRD4 may be a useful marker for reduced gamma responses and that the 10-repeat allele of the DAT1 polymorphism is associated with reduced gamma responses to auditory stimuli. These results suggest that genetic polymorphisms of DRD4 and DAT1 are involved in modulation of gamma responses in healthy subjects.

Keywords: DRD4, DAT1, evoked gamma response, ADHD, schizophrenia

P44
The genetic polymorphisms of the receptor SIGMA-R1 affect the latency and amplitudes of P3 potential
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Although no endogenous ligand for SIGMA-R1 has been identified, there is some evidence showing its interaction with neurotransmitters and neuromodulators. In the present study, the investigated polymorphisms of SIGMA-R1 gene were GC-241-240TT and T-485A, which were suggested to be associated with the regulation of transcription, and Gln2Pro (61. nucleotide A-C), may alter the transportation of sigma receptors from the endoplasmic reticulum to the plasma membrane. A-485 allele and TT-241-240/Pro haplotypes may be protective factors against the development of alcoholism, and this was attributed to its’ modulatory role in ethanol stimulated dopamine release from nucleac accumbans. NMDA response in hippocampal CA3 pyramidal neurons was also reported to be potentiated by SIGMA-R1. Binding of antipsychotic agents such as haloperidol, and induction of delusions and hallucinations similar to those seen in schizophrenia by SIGMA ligand SKF 10 047, supports the evidence for a potential link between sigma receptors and the etiology of schizophrenia. In several studies, TT-241-240 and Pro allele were reported to have a role in genetic predisposition to schizophrenia. In the present study, the relation between N1, P2 and P3 event related potentials obtained by auditory oddball paradigm and GC-241-240TT and Gln2Pro polymorphisms of the SIGMA-R1 was investigated in 48 healthy volunteers. In line with the literature, a linkage disequilibrium between GC-241-240TT and Gln2Pro was present. While no significant association was found between genotypes of T-485A polymorphism and ERP components, GC/TT and Gln/Pro genotypes of GC-241-240TT and Gln2Pro polymorphisms lead to an earlier P3 peak in all channels (p<0.019) and higher F3 amplitudes over left hemisphere (p<0.005). These results show that T-485A polymorphism alone does not affect the cognitive electrophysiological measures. However, TT haplotype of GC-241-240TT and/or Pro haplotype of Gln2Pro polymorphism have a shorter P3 latencies and enhance P3 potentials of left hemisphere. This result suggests that SIGMA-R1 has effects on the processes of P3 generation. Although it is not yet possible to explain which neurotransmitter system is modulated causing these differences, the inferences about these changes would be more reliable as the effects of glutamate and dopamine on P3 parameters become clear.

Keywords: SIGMA-R1, ERP, N1, P2, P3, genetic polymorphism

P45
Association analysis of the functional MAOA gene promoter and MAOB gene intron 13 polymorphisms in tension type headache patients
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Tension Type Headache (TTH) is one of the most frequently observed causes of the primary headaches. Exact pathophysiology of this disease is not clearly known. Monoamine Oxidase A (MAOA) is an enzyme that has done inactivation of epinefrine, norepinefrine and catecholamines by their oxidation. MAO has two isoenzymes that have known MAOA and MAOB. For propose of this study, the significance of MAOA and MAOB genes polymorphism was assessed in TTH. We studied MAOA gene promoter 30bp VNTR and MAOB gene intron 13 SNP polymorphisms in 120 TTH patients and 168 healthy volunteers (control group). We used Polymerase Chain Reaction and Restriction Fragment Length Polymorphism (PCR-RFLP) methods. The genotype distribution of MAOA and MAOB genes polymorphisms in TTH patients and controls were not found to be statistically different (p=0.162). Result of this study, we have not found any association between TTH patients and MAOA, MAOB genes polymorphism. The factors like, less number of men patients, genes of other neurotransmitters that playing role in the etiology of tension type headache and, because of TTH is frequently in women, estrogen dose may lead to statistically significant data.

Keywords: Monoamine Oxidase A (MAOA), Monoamine Oxidase B (MAOB), Tension Type Headache (TTH), Genetic polymorphism, PCR-RFLP

P46
Electroencephalographic properties of a rat during long term cerebral ischemia/reperfusion
Ozerman R [1, 2], Nanten A [1], Ozcan I [1], Karı I [1].
P47 The effect of long term cerebral ischemia/reperfusion on event related potentials of rat

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In this study we aimed to investigate the effect of the long term cerebral ischemia/reperfusion on event related activity of a Wistar albino rat. It has been placed symmetrically eight pairs of cortical electrodes to medial and frontal localisation of pre and post frontoparietal and occipital regions. Basal EEG records carried out by Neuroscan. The record continued for five and half-hour of bilateral common carotid artery occlusion. At the end of the long term ischemia EEG record lasted during reperfusion for ninety minutes. Records repeated on the third and thirtieth day after ischemia/reperfusion. EEG records were divided into 2 seconds epochs and analysed by averaged frequency spectra (0-50 Hz). Comparing to the basal EEG during the first 30 min of ischemia the amplitudes of 4-7 Hz and 20 Hz frequency bands were decreasing and the peak point of 15 Hz frequency band was shifted to 16 Hz. The increase of amplitudes of 8 Hz, 17 Hz, 23 Hz and 40-43 Hz frequency bands was found during the last 30 min of ischemia. It was resulted that the most prominent dynamic properties of five and half-hour of ischemia were the increase in the amplitude of 40-45 Hz and the decrease in the amplitude of 6-8 Hz frequency bands. In the first 30 min of reperfusion 16-18 Hz frequency bands became evident and its amplitude had risen maximum during the second half an hour of reperfusion. The amplitude of 35 Hz frequency band kept its elevation during 90 min of reperfusion. Comparing to basal activity a prominent increase in the amplitude was detected for 12-13 Hz between 36-60 min and for 14 Hz and 22 Hz frequency bands during 60-90 min of reperfusion. In the third day of postischemia it was found an increase in the amplitude of 4-6 Hz frequency bands only. In the thirtieth day of postischemia it was detected the increase in the amplitude only for 6-8 Hz frequency bands and the decrease in the peak point of frequency bands with high amplitude recorded in basal EEG. The properties of EEG during long term ischemia/reperfusion of the rat showed alterations in one month. It was concluded that further electrophysiologic investigations and studies are needed in order to elucidate neurochemical basis of alterations in frequencies during postischemia.

Keywords: EEG, ischemia, reperfusion, carotid artery, rat

P48 The effect of enoant on oxidative stress in ischemia / reperfusion


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Free radicals have been implicated in neuronal injury during ischemia reperfusion. Polyphenolic compounds found in grapes and wines has recently been shown to have neuroprotective activity against oxidative stress. In the present study, the effect of enoant, extract of grape consisting of polyphenols such as resveratrol, catechin and quercetin, on oxidative stress was evaluated in ischemia/reperfusion in Wistar albino rats. Rats were divided into three groups. Ischemia was induced by occlusion of bilateral common carotid artery. After two hours occlusion reperfusion was allowed. 1st group were ischemic group. 2nd group received 1.25 g/kg/day enoant for 2 weeks before ischemia. 3rd group received 1.25 g/kg/day enoant for 2 weeks before and after ischemia. Enoant was freshly prepared in drinking water and administered orally. Malondialdehyde (MDA) was measured as an oxidant marker; glutathione (GSH), superoxide dismutase (SOD), glutathione reductase (GR) and glutathione peroxidase (GPX) were measured as an antioxidant makers in brain homogenates. The values of superoxide dismutase, glutathione reductase and glutathione peroxidase were expressed as U/mg protein. The malondialdehyde value was expressed as nmol/mg protein. The malondialdehyde levels in 3rd group were significantly reduced compared to ischemia group (<0.05). In contrast, glutathione levels in 3rd group were significantly increased as compared to ischemic group (<0.05). Our results show that enoant is an effective antioxidant to reduce oxidative stress following ischemia/reperfusion.

Keywords: Ischemia/reperfusion, enoant, MDA, GSH, SOD, GR, GPX, rat

P49 The effect of intrauterine hypoxic-ischemia on fetal brain development

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Cell death is usually classified as apoptotic or necrotic based on biochemical and morphological criteria. In the fetal central nervous system, a large number of cells die by apoptosis. Apoptosis is a form of physiological cell death moulding the developing nervous system which also occurs in pathological conditions, observed more frequently in the immature brain. Hypothetic episodes in pregnancy are among frequent causes of fetal circulatory defect and constitute a potential risk factor for fetal hypoxic-ischemic injury. The aim of the present study was to investigate the effect of transient hypotension on cell death in the fetal central nervous system. Twenty pregnant 3-6-months-old Wistar rats were included in the study. Hypotension was produced for 30 minutes by blood withdrawal until mean arterial blood pressure dropped to 50% of the initial level on the 15th day of pregnancy. The same procedure was performed in the control group without producing hypotension. On the 17th or the 19th days of pregnancy, fetuses were delivered by cesarean section. One fetus from each mother was randomly chosen which was decapitated and the brains were removed. Brain sections were examined with hematoxylin-eosin for general structure, necrosis and/or hemorrhage. Apoptosis was evaluated by Terminal Transfere Mediated –UTTP Nick End Labelling (TUNEL) and caspase-3 activation by immunohistochemistry. The histological sections including telencephalon, diencephalon, and metencephalon were evaluated by two blinded observers: positively stained cells were counted under high-power magnification in 10 fields in each brain area. The hypotension group examined on day 19 showed significantly more active caspase-3 positive cells in the telencephalon than those on day 17 (P < 0.05). Although the hypotension groups had more TUNEL positive and active caspase-3 positive cells than the control group, the difference was not statistical significant. A linear correlation may exist between physiological and pathological apoptosis. In fetal brain, 96 hours after hypotension; caspase-3 activation and apoptosis increased. This interval between the injury and the prominent caspase-3 activation may provide a therapeutic window in which neuroprotective agents especially caspase inhibitors may be effective in preventing brain damage. The most appropriate time for prophylactic intervention may be determined by a series of detailed studies.

Keywords: apoptosis, rat, hypotension, fetal brain, caspase

P50 The effect of enoant on proinflammatory mediator in ischemia/reperfusion in rat

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Free radicals have been implicated in neuronal injury during ischemia reperfusion. Polyphenolic compounds found in grapes and wines has recently been shown to have neuroprotective activity against oxidative stress. In the present study, the effect of enoant, extract of grape consisting of polyphenols such as resveratrol, catechin and quercetin, on oxidative stress was evaluated in ischemia/reperfusion in Wistar albino rats. Rats were divided into three groups. Ischemia was induced by occlusion of bilateral common carotid artery. After two hours occlusion reperfusion was allowed. 1st group were ischemic group. 2nd group received 1.25 g/kg/day enoant for 2 weeks before ischemia. 3rd group received 1.25 g/kg/day enoant for 2 weeks before and after ischemia. Enoant was freshly prepared in drinking water and administered orally. Malondialdehyde (MDA) was measured as an oxidant marker; glutathione (GSH), superoxide dismutase (SOD), glutathione reductase (GR) and glutathione peroxidase (GPX) were measured as an antioxidant markers in brain homogenates. The values of superoxide dismutase, glutathione reductase and glutathione peroxidase were expressed as U/mg protein. The malondialdehyde value was expressed as nmol/mg protein. The malondialdehyde levels in 3rd group were significantly reduced compared to ischemia group (P<0.05). In contrast, glutathione levels in 3rd group were significantly increased as compared to ischemic group (P<0.05). Our results show that enoant is an effective antioxidant to reduce oxidative stress following ischemia/reperfusion.

Keywords: Ischemia/reperfusion, enoant, MDA, GSH, SOD, GR, GPX, rat
Cerebral ischemia is associated with an acute triggers the production of additional cytokines such as IL-6. A growing body of literature indicate that polyphenols are active ingredients in dietary plants and traditional medicine used for the treatment of disorders related to the oxidative stress and inflammation. In the present study, we investigated the effect of enoant, extract of grape consisting of polyphenols such as resveratrol, catechin and quercetin, on TNF-alpha, IL-beta and IL-6 proinflammatory cytokines in ischemia/reperfusion in Wistar albino rats. Rats were randomly divided into 3 groups. Ischemia was induced by occlusion of bilateral common carotid artery. After two hours occlusion reperfusion was allowed. 1st group was ischemic control; 2nd group received 1.25 g/kg/day enoant for 2 weeks before ischemia; 3rd group received 1.25 g/kg/day enoant for 2 weeks before and after ischemia. Enoant was freshly prepared in drinking water and administered orally. TNF-alpha, IL-1 beta and IL-6 levels were measured in whole brain homogenate by using enzyme linked immunosassay techniques. TNF-alpha and IL-6 concentrations in 3rd group were significantly reduced when compared with 1st group. On the other hand there was no significant difference in IL-1 beta levels among three groups. Our data have suggested that enoant reduce the proinflammatory mediator production following ischemia/reperfusion.

**Keywords:** Enoant, inflammation, ischemia, rat, polyphenols

### P51

The effect of enoant, a natural polyphenolic compound, on cortical electroencephalography in rats subjected to cerebral ischemia/reperfusion

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It has been shown that many polyphenolic compounds have a neuroprotective effect against neuronal damage following ischemia/reperfusion in rats. In this study, we aimed to examine the effects of enoant, extract of grape consisting of polyphenols such as resveratrol, catechin and quercetin, on ischemia/reperfusion in rats subjected to cerebral ischemia by electroencephalography. We placed symmetrically eight pairs of cortical electrodes to the frontal, pre and post parietal and occipital regions of medial and lateral of Wistar albino male rats’s hemispheres. Eight days after operation, continuous EEG records were taken in freely moving rats with Neuroscan for ten minutes. Then rats were divided into three groups, while the rats in the first and second groups were drinking water, the others were drinking water freshly prepared with Enoant (1.25 g/kg/day). After 15 days, EEG records were taken and under ether anaesthesia, ischemia was induced by occlusion of bilateral common carotid artery of all animals. Two hours after occlusion, reperfusion was allowed. Later the rats in the first group continued to drink water, while the rats on the second and third group were drinking water with enoant. After 15 days, EEG records were taken. Continuous EEG records were divided into 2-second epochs and analysed by averaged frequency spectra (0.5-50 Hz). In animals with ischemia-reperfusion 30 days after, the amplitudes of 0.5-2 Hz frequency bands decreased, while the amplitude of 18-30 Hz frequency bands increased significantly compared to basal values. In animals which drank enoant after ischemia, the amplitude of 0.5-2 Hz frequency bands decreased, while the amplitude of and 10-35 Hz frequency bands increased significantly compared to basal values. In animals which drank enoant before and after ischemia the amplitude of 0.2-2, 2-4, 7-10 Hz frequency bands increased significantly compared to basal values. This study showed that ischemia/reperfusion induced to increased the amplitude of 18-30 Hz frequency bands and administration of enoant before to the rats subjected to ischemia/reperfusion prevented this effect.

**Keywords:** Rat, cerebral ischemia, EEG, Enoant, polyphenol.

### P52

The change of nitric oxide concentration in men exposed to 1.5 Tesla magnetic fields

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This study was carried out on voluntary and healthy young men from 20 to 25 years old to determine nitric oxide production immediately after 1.5 Tesla magnetic field exposure. The men were exposed to 1.5 T static magnetic field by using Magnetic field by using Magnetic resonan imaging apparatus 30 minutes. 5 ml blood was taken intravascularly from all the subjects one minute before and after exposure immediately. Nitrit and nitrate concentration was determined by UV-VIS spectrophotometer. The obtained results related to the parameters under investigation were compared between pre and post exposure groups. The results related to the parameters measured in this study were analyzed by paired student t-test. Finally, total nitric oxide concentration post exposure samples was higher than pre exposure samples. In conclusion, 30 minutes of 1.5 T static magnetic field affected nitric oxide concentration.

**Keywords:** Magnetic Field, Nitric Oxide

### P53

The effects of intrahippocampal beta amyloid peptide injection in rats on spatial learning and memory and hippocampal nitric oxide levels

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Deposition of amyloid beta peptides is thought to play a central role in the development of cognitive impairments and Alzheimer’s disease. In some animal models cognitive impairment and neurodegenerative disorders that mimicks Alzheimer’s disease can be reproduced by intracerebral or intracerebroventricular administration of beta amyloid peptide (A-beta). It has been demonstrated that inflammatory responses develops after administration of A-beta. A-beta and activated microglia stimulates cytokines and nitric oxide. Besides its putative role in learning and memory nitric oxide has significant physiological roles in the central nervous system. Nitric oxide can also be neurotoxic primarily to its free radical properties and it has been implicated in neurodegenerative diseases. At low concentrations, beta amyloid is not toxic and even has beneficial effects on neuronal survival, axonal length, and neurite outgrowth. These activities may be related to antioxidative properties of the peptide. At low–nanomolar concentrations (i.e., those circulating in CSF and plasma) beta amyloid involves as an antioxidant. The aim of this study is to study the effects of intrahippocampal beta amyloid (1-42) peptide injection on spatial learning and memory and hippocampal nitric oxide levels in rats. In the study, 24 male adult Wistar albino rats were used. Sham (n=6) and the group which had administered intrahippocampal bidistilled water (n=6) were the control groups. The group which had administrated A-beta was the experimental group. A-beta(1-42) peptide 20 microgram/4 microliters was injected bilaterally into the hippocampal fissure of rats (stereotaxic coordinates: AP=-4.8mm, L=-3.5mm from the bregma, H=-4.9mm. from the dura). 14 days after the surgery spatial learning and memory was tested in Morris water maze for seven repetitive days. Half of the subjects (n=6) in the experimental group performed the learning task 75 days after the surgery. After learning and memory tasks rats were sacrificed by decapitation, brains rapidly removed and hippocampus dissected. NOx levels in hippocampus were determined spectrophotometrically based on Griess reaction. There was a statistical significance between experimental and control groups of escape latencies during acquisition of place learning on 1st, 4th and 6th days but no statistical significance was found on 7th day that retention was tested. A-beta administered groups showed significantly decreased hippocampal NOx levels than the controls. Finally, the results of this study demonstrated that intrahippocampal injections of beta amyloid (1-42) peptide at nanomolar concentrations has beneficial effects on spatial learning and memory in rats by preventing the production of excess amounts of nitric oxide in hippocampus and possibly prevents the oxidative stress.

**Keywords:** Beta amyloid peptide, Morris water maze, spatial learning and memory, nitric oxide, hippocampus.

### P54

Neuronal nitric oxide synthase inhibitor 7-nitroindazole prevents zinc sulphate induced hippocampal cell loss in rats

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The effect of neuronal nitric oxide synthase (nNOS) inhibitor 7-nitroindazole (7-NI) on hippocampal neurotoxicity and neuronal cell death induced by zinc hemisulphate salt (ZnSO4.7H2O) was studied in rats. Lab animals were classified into three groups as control, zinc and zinc + 7-NI (treated animals). The loss of the cells in the left and the right hippocampi were calculated with new stereological counting method which is more unbiased and reliable. At the end of the experiments, when compared with the control group, the loss of the cells in zinc and treatment groups has been 43.5 % and 16.2 % on the left hippocampi, and 46.1 % and 18.5 % on the right hippocampi, respectively. A neuroprotective effect was observed.
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in rat group pretreated with 7-NI according to only zinc administration group significantly (p<0.05). These results indicate that neuronal nitric oxide (nNO) may be accepted as a neurotoxic substance in relation to hippocampal chemical neurotransitivity by administration ZnSO4.7H2O in rats.

Keywords: Zinc, cell death, hippocampus, 7-Nitroindazole, rat

P55
Antioxidant effects of beta-estradiol and phytoestrogens on colchicine induced changes in rat organotypic hippocampal slice cultures
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Epidemiological studies have indicated that estrogen replacement therapy can reduce the risk of developing Alzheimer’s disease. Phytosterogens are plant-derived molecules that structurally resemble endogenous estrogens and can directly bind to estrogen receptors. Addition of colchicine to organotypic hippocampal slice cultures leads to inhibition of axonal transport and therefore it is used in an ex vivo Alzheimer’s disease model. The aim of this study was to determine the antioxidant effects of beta-estradiol, 2-methoxyestradiol (a phytoestrogen with estrogenic effect) and formononetin (a phytoestrogen with estrogenic effect) on colchicine induced changes in rat organotypic hippocampal slice cultures. Sprague-Dawley rats (12 days old) were decapitated and transversal hippocampal slices were obtained using a vibroslicer. Slices were placed on semipermeable membranes and incubated for 15 days. After this, cultures were incubated with either 10 micromolar colchicine or lumicolchicine (control group) for 24 h. Additionally, cultures were incubated with beta-estradiol, 2-methoxyestradiol and formononetin at the same time and dose. Chemiluminescence measurements were made with lucigenin, a probe selective for superoxide radical. Results were given as AUC for rlu/mg slice. Our results have shown that colchicine treatment increased superoxide radical generation with respect to the lumicolchicine group (34.9 +/- 6.6 vs 14.9 +/- 1.7; p<0.001). Addition of beta estradiol to colchicine group reduced superoxide radical generation (22.9 +/- 2.7; p<0.001). A similar effect was observed with formononetin (24.6 +/- 4.9; p<0.001) but addition of 2-methoxyestradiol had no significant effect (29.8 +/- 1.9; p>0.05) on colchicine-induced changes. In conclusion, our results have shown that not all phytosterogens have similar antioxidant effects in organotypic hippocampal slice cultures thus further studies are required for suggesting treatment of Alzheimer’s disease patients with estrogens and phytoestrogens. This work was supported by TUBITAK-BAD Brain Research Project Support Programme.

Keywords: beta-estradiol, formononetin, methoxyestradiol, colchicine, organotypic slice culture, chemiluminescence, superoxide radical, Alzheimer’s disease

P56
The effect of cadmium on the antioxidant enzymes in brain of ovariectomized rats
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In this study the chronic effect of cadmium on the levels of antioxidant enzyme in brain of ovariectomized female rats was investigated. 29 female Wistar albino rats were included to this study. These rats were divided into four groups: Control (n=6), II.cadmium (n=8), III.lovatoxicated (n=6) and IV.lovatoxicated+cadmium (n=9). Ten weeks: after ovariectomy, cadmium chloride (CdCl2, 0.5mg/kg) was given ip three times a week for 18 weeks to the cadmium (II. group) and ovariectomized-cadmium group (IV.group). At the end of treatment period (18 weeks), rats were decapitated and then brain tissues were removed. Superoxide dismutase (SOD), catalase (CAT) and myeloperoxidase activities and the levels of malondialdehyde (MDA) in the brain rats were measured by using the biochemical methods. When the ovariectomy group was compared with the controls, SOD activity and MDA concentration were significantly decreased (p<0.05). MPO activity was decreased (p<0.05). Although CAT activity did not show any significant difference between the groups. Similar results obtained at the group IV but MDA concentration and SOD activities were determined to be higher in this group than those of the other groups. Based on the data, it can be stated that cadmium induce the oxidative stress.

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Keywords: Cadmium, ovariectomy, antioxidant, MDA, SOD

P57
The effect of restraint stress and lipoid acid on brain antioxidant status and lipid peroxidation
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Stress is defined as a state of threatened homeostasis and induces physiological and behavioral changes. Intensive stress has detrimental effects on organism by causing tissue injuries The exact mechanism of stress has not yet been clearly defined. However, there have been many reports suggesting that free radicals play an aberrant role in the mechanism of stress As previously shown, there is accumulating evidence to indicate that stress can stimulate numerous pathways leading to an increased production of free radicals. Therefore, the present study was undertaken to investigate the effects of stress and/or antioxidant lipoid acid on lipid peroxidation and antioxidant status. Forty male albino rats, aged three months, were equally divided into four groups: Control (C), the group exposed to restraint stress (R), the group treated with lipoid acid (L) and the group exposed to stress and treated with lipoid acid (RL). Rats were exposed to 1 hour of restraint stress daily for 21 days by placing the animals in a 25x7 cm plastic bottle . Lipoid acid (100 mg/kg/day) and physiologic serum were injected intraperitoneally to the L, RL and C, R groups, respectively. After the end of the experimental period, animals were sacrificed by cardiac puncture and brain tissues were removed for biochemical analysis. Cu, Zn-superoxide dismutase (Cu, Zn-SOD), glutathione peroxidase (GSH-Px), catalase (CAT) and thiobarbituric acid-reactive substances (TBARS) levels of brain were measured. The stress group exhibited an increased levels of TBARS with decreased levels of antioxidant enzymes compared with the C group. Lipoid acid, markedly decreasing TBARS levels, increased Cu, Zn-SOD, GSH-Px CAT activities in the brain of stress group compared with the R group. Our findings clearly indicated that lipoid acid treatment was found effective in preventing both stress-induced decrease of the activities of antioxidant enzymes and formation of thiobarbituric acid reactive substances. The protective effect of it, due to decreased lipid peroxidation and increased GSH-Px activity, contributes significantly to tissue protection against oxidative injury in the brain subjected to restraint stress. Lipoid acid, restraint stress, lipid peroxidation, antioxidant enzymes

Keywords: Lipoid acid, restraint stress, lipid peroxidation, antioxidant enzymes

P58
Restraint stress induced changes of antioxidant enzymes and enhancement of lipid peroxidation on brain: effect of aminoguanidine
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Stress is common in everyday life and is known to induce alterations in various physiological responses leading to pathological stress. Restraint stress, as used in the present study, is a well known model to study chronic physical and emotional stress. Previous studies have shown increased lipid peroxidation and nitric oxide levels in various tissues of rats exposed to stress. Many reports have suggested that L-NAME (non-selective nitric oxide synthase inhibitor) decreased lipid peroxidation in the group exposed to stress. Nitric oxide synthase (NOS) enzyme exists as three distinct isoforms; the endothelial NOS (eNOS), the neuronal NOS (nNOS) and the inducible NOS (iNOS). Many studies determined the relation of iNOS activity in the brain injury in rats exposed to stress. Therefore, in this study, we examined the effect of aminoguanidine, a specific iNOS inhibitor, on stress induced brain antioxidant enzymes activities and TBARS level changes. In our study, forty healthy male Wistar rats, aged three months were equally divided into four groups: Control group (C), the group exposed to restraint stress (S), the group treated with aminoguanidine (A), the group exposed to restraint stress and treated with aminoguanidine (AS). For the duration of 21 experiment days, one hour of restraint stress administered per day. Aminoguanidine (50 mg/kg/day) and physiologic serum were injected intraperitoneally to the A, AS and C, S groups, respectively. At the end of the experiments, animals were sacrificed by cardiac puncture and brain tissues were removed for biochemical analysis. Superoxide dismutase, catalase, glutathione peroxidase, nitrite, nitrate and thiobarbituric acid-reactive substances (TBARS) levels of brain were measured. The present study revealed that restraint stress caused a significant increase TBARS, nitrite and nitrate levels, while decreasing the activities of enzymes SOD, catalase and GSH-Px in comparison with control rats. Aminoguanidine treatment of stressed rats significantly prevented the increase in lipid peroxidation, nitrate and nitrite levels. Additionally, aminoguanidine treatment increased the SOD, catalase and
GSH-Px activities of restraint stress exposed rats. Thus, this study indicates that iNOS plays an important role in lipid peroxidation under pathological conditions like stress and aminoguanidine may act as an effective antioxidant for protection against stress induced enhancement of brain free radical.

Keywords: Stress, lipid peroxidation, antioxidant enzymes, aminoguanidine, nitric oxide

P59

Neuroprotective activity of vitamin E on formaldehyde induced hippocampal tissue injury

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Formaldehyde is a very reactive one carbon compound which is widely used in industry and medicine. Everyday exposure to formaldehyde includes building materials, cosmetics, cigarette smoke, and even various fruits, vegetables. Formaldehyde causes central nervous system disorders, which include headache, insomnia, anorexia and dizziness. Vitamin E is a free radical scavenger and tissue antioxidant which plays an important role in preventing lipid peroxidation and cell destruction. The aim of the study was to investigate the possible protective effects of vitamin E pretreatment against to formaldehyde induced oxidative damage in hippocampal tissue. In this study, 24 Wistar albino rats (250-300 g), were randomly divided into three groups, each containing 8 animals. Formaldehyde treated and formaldehyde+vitamin E treated groups were received 10 mg/kg (i.p) formaldehyde. In addition, formaldehyde+vitamin E treated group was given 300 mg/kg (i.m) vitamin E and control group was received only distilled water (i.p). All injections continued for 30 days. On 31st day, the hippocampal tissues harvested for biochemical and histological investigations. Biochemical analysis indicated that formaldehyde significantly increased tissue malondialdehyde (MDA) level and decreased superoxide dismutase (SOD) enzyme activity in hippocampal tissue compared to the control. Vitamin E treatment decreased MDA level and also increased SOD enzyme activation. In the control group, the morphology of the neurons in CA1, CA2, CA3 and CA4 regions were normal. The most consistent findings in neurons of CA4 region in formaldehyde group were the severe degenerative changes, including shrunken cytoplasm and extensively dark picnotic nucleus. The number of neurons in hippocampal tissue of formaldehyde group were also significantly less than formaldehyde + vitamin E and control groups. We concluded that vitamin E pretreatment causes morphological and biochemical improvement on hippocampal tissue which has been exposed to formaldehyde.

Keywords: Formaldehyde, vitamin E, free radicals, antioxidant, oxidized low density lipoprotein, frontal cortex.

P60

Protective effects of vitamin E on formaldehyde induced oxidized low density lipoprotein accumulation in frontal cortex tissue

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Formaldehyde is a very reactive compound which reacts with different macromolecules such as proteins and nucleic acids. Formaldehyde exposure causes central nervous system disorders. Free radicals not only induce oxidative stress, but also initiate and maintain oxidation of low density lipoprotein (oxLDL). oxLDL leads to foam cell formation and cellular hyperplasia. The aim of the study was to investigate the protective effect of vitamin E pretreatment against to formaldehyde induced oxidative damage and histopathologic consequences of oxLDL accumulation in the rat frontal cortex. For this experiment, 24 male Wistar albino rats (200-250g) were allotted into three groups, each containing 8 animals. Formaldehyde treated and formaldehyde+vitamin E treated groups were received 10 mg/kg i.p. formaldehyde. In addition, formaldehyde+vitamin E treated group was given 300 mg/kg i.m. vitamin E. Control group was received i.p. distilled water. All injections continued for 30 days. After treatments, frontal cortex tissues harvested for biochemical, light microscopic and immune-fluorescent investigations. Formaldehyde significantly increased tissue malondialdehyde (MDA) level and decreased superoxide dismutase enzyme (SOD) activity compared to the control. Vitamin E decreased MDA level and also increased SOD enzyme activation. In control group, the morphology of the neuronal cells was normal. In formaldehyde treated group, neuronal cells became extremely dark and degenerated with picnotic nucleus. The morphology of neuronal cells in formaldehyde+vitamin E treated group was nearly similar to that of the control group. In Immune-fluorescent investigations, while there was no staining in the control group, formaldehyde exposure resulted in positive oxLDL staining in the frontal cortex tissue. In formaldehyde+vitamin E group, positive oxLDL staining was less than formaldehyde group. In conclusion, this study indicated that vitamin E might be effective in preventing formaldehyde induced oxidative damage, and reducing the accumulation of oxLDL in formaldehyde toxicity in frontal cortex.

Keywords: Formaldehyde, vitamin E, free radicals, antioxidant, oxidized low density lipoprotein, frontal cortex.

P61

Neuroprotective effects of preischemia L-Carnitine and vitamin E in transient cerebral ischemia in rats

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Objective: Neurological injury due to transient cerebral ischemia is a potential complication of cardiovascular surgery. In this study, the neuroprotective effects of L-carnitine and vitamin E on ischemic injury were tested in a rat model of transient global cerebral ischemia. Methods: Thirty-five Wistar albino rats were used for the study. The animals in group 1 (Sham group, n=7) were anesthetized and subjected to operative dissections without vascular occlusion. Animals in group 2 (Ischemia –Reperfusion, n=7), cerebral ischemia was induced with a four vessel occlusion technique with the duration of 15 minutes. Group 3 animals (n=7) received L-carnitine (100 mg/kg, i.v) before cerebral ischemia. In group 4 (n=7) vitamin E was given 50 mg/kg intravenously before the procedure. Group 5 animals (n=7) received combined treatment of L-carnitine and vitamin E. At the end of the experiment, malondialdehyde (MDA), superoxide dismutase (SOD), myeloperoxidase (MPO) and glutathione (GSH) levels were measured in cerebral tissues. Histopathologically, intact hippocampal CA1 and CA2 pyramidal neurons were semiquantitatively counted on three consecutive 789 micron square areas outlined with a counting frame on X40 magnification and three consecutive hippocampus sections. Results: In group 2, MDA and MPO levels were high, SOD and GSH were low when compare with group 1, group 3, group 4, and group 5 (p<0.05). Between group 3, group 4, and group 5, there were no difference in MDA, MPO and SOD levels (p>0.05). However in group 5, GSH levels were high when compare with group 3 and group 4 (p<0.05). The mean of CA1 pyramidal neuronal variable values indicate statistically significant difference in five groups (F=32.729, P=0.0001). In order to find out which groups cause that difference, post hoc comparisons were used. The mean of Isch-Rep group was significantly different from Carnitine, Vit – E and Carnit-Vit-E groups. Similarly, Sham group was different from Carnitine, Vit – E and Carnit-Vit-E groups. The mean of CA3 pyramidal neuron variable values indicate statistically significant difference in five groups (F=15.113, P=0.0001). In order to find out which groups cause that difference, post hoc comparisons were used. The mean of Isch-Rep group was significantly different from Carnitine, Vit – E and Carnit-Vit-E groups. Similarly, Sham group was different from Isch-Rep, and Carnit-Vit-E groups. Analytic results have been evaluated using SPSS 11.5 statistical package program. In data analysis, One Way ANOVA and Tukey (Post hoc comparison test) tests were used. Significance was set at 5% level (P<0.05). Conclusion: The results suggest that L-carnitine and vitamin E reduces cerebral injury due to lipid peroxidation and enflamation. But there is no difference between combined and individual treatment of L-carnitine and vitamin E on these effects. However combined treatment of L-carnitine and vitamin E provided better biochemical protection against oxidative damage in cerebral ischemia.

Keywords: ischemia - reperfusion, oxidative damage, carnitine, vit-E, hippocampus

P62

Comparison of the changes in blood and spinal cord no levels after direct peripheral nerve injury

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Nitric oxide, axonal transport, crush injury, spinal cord, sciatic nerve, five times a week.

Brain, morphometry, Stereology, long term centrifugation, 5 min -1 and a slope of 0 min -1 and a slope of 0.

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P65 The effects of regular aerobic exercise in adolescent period on hippocampal neuron density, apoptosis and spatial memory

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It’s known that regular aerobic exercise positive effects of cognitive functions in humans and also animals; but adolescent period that continues brain development exercises effects is unknown. The aim of this study, effects of regular aerobic exercise on hippocampus in adolescent rats. Wistar Albino male rats at 22 days of age (n=8 for each group) were used. Rats were divided into two groups: 1) Exercised; 2) Control. Rats were run on a treadmill for 5 min-session 1 at a speed of 5 m/min-1 and a slope of 0°. Five times a day for 1 week to adapt them to running before the experiment. Then, exercised group were run on a treadmill for 30 min-session 1 at a speed of 8 m/min-1 and a slope of 0°, five times a week for 8 weeks. 2 days later the exercise period (thirteen weeks old) performed spatial learning test with using Morris water maze. Then, the brains were scored sectioned and stained with cresyl violet, and evaluated under light microscope by stereological techniques. For comparison between groups, Mann Whitney-U test was used. Daily differences in learning experiments have been evaluated using repeated measures post hoc Bonferroni and T-test. The present study showed that exercise induced significant cognitive improvement throughout brain maturation in rats. Exercised rats had shorter escape latencies (second day, F = 2.566, p = 0.023; third day, F = 1.025, p = 0.045) and In probe trials (quadrant time), and had spend significantly more time than control group (F = 0.632; p = 0.007). The density of hippocampal CA1 and CA3 neurons, and gyrus dentatus neurons were significantly more in the exercised rats in comparison control rats (CA1; 65.8 ± 1.1; 65.8 ± 1.8, CA3; 40.2 ± 1.6 and 34.0 ± 0.8, gyrus dentatus; 89.7 ± 1.4 and 76.3 ± 1.7, respectively). There was no significant difference of CA2 neuron density between exercise and control groups. There was no significantly differences in any groups according to the results of apoptosis that account of TUNEL positive cells (exercise; 17.1 ± 4.09, control; 20.00 ± 2.38). These results indicate the regular moderate aerobic treadmill exercise benefit in cognitive functions. This result derived from treadmill exercise-induced increase cell proliferation without altering of apoptosis in the hippocampus and dentate gyrus of the hippocampus in adolescent rats.

Keywords: Nitric oxide, axonal transport, crush injury, spinal cord, sciatic nerve.

P64 Morphology of brain cortex and medulla in adult mice following long term centrifugation

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In order to determine the potential effects of rotation and long-term gravitational changes, we have investigated the structural changes of brain tissue under hypergravity conditions. Mice subjected to one gravity (IG) long-term centrifugation or 2G long-term centrifugation were compared with a separate control group. After 4 weeks of centrifugation, the mice were sacrificed and their brains were perfused through the ascending aorta with 10% formaldehyde. After removal of the brains, paraffin embedding and the cutting of serial (10 micron) sections, systematic uniform random samples were analysed and stereologic cortex and medulla volume measurements were made. In addition, immunohistochemical distribution of glial fibrillary acidic protein was investigated to analyse neurodegenerative effect of different gravity. Our results demonstrated that there were no long-term hypergravitational effects upon brain volume, and that the cellular morphology of the brains in the three groups were normal, without any degenerative areas being seen.

Keywords: Brain, morphometry, Stereology, long term centrifugation, hypergravity

P66 A simple technique for localizing consecutive fields for disector pairs in light microscopy: application to neuron counting in rabbit spinal cord following spinal cord injury

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Locating the same microscopic fields in consecutive sections is important in stereological analysis. The tools for achieving this requirement have limited number in practice. This paper presents a simple and inexpensive technique for localizing the same fields on disector pairs in conventional light microscopes equipped with widely available dial indicators. It is partly a modification of equipment previously described. The presented procedure requires two light microscopes equipped with dial indicators and modified slide clips. An application of the present system was shown at the model of spinal cord injury. A midthoracic laminectomy was performed leaving the dura intact. A 300-gm/cm2 contusion injury of the midthoracic (T7-T9) spinal cord segment was inflicted by dropping a 10-gm mass from a height of 30 cm using a modified weight-drop technique. After a traumatic event, the assessment of changes in neuron number in spinal cord over time may be used as an indicator of therapeutic effectiveness. The subjects were randomly divided into three groups (10 animals in each): hypothermia group, methylprednisolone group, and traumatic spinal cord injury (SCI) alone group. Treatment with hypothermia after spinal cord trauma has a neuroprotective effect on cell damage but not in the methylprednisolone treatment group.

Keywords: Spinal Cord, Neuron Damage, Light Microscopy, Stereology, Disector, Neuron Counting
cerebrum and the cerebellum the difference between the groups was statistically significant (p<0.000). The factorial variance analysis was also applied to analyze the effects of sex and group (experiment-control) on the cerebral and cerebellar weights. While the difference between the cerebral weights of male and female rats was statistically significant (p=0.028), the difference between cerebellar weights was not statistically significant. For all these statistical analyses, SPSS 11.5 statistical software was used.

Keywords: lead, cerebrum, cerebellum, nevre, rat

P67
The effects of chronic cadmium exposure on the EEG power spectrum
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Cadmium which is one of the widely studied environmental contaminant, causes functional disturbances in both the peripheral nervous system and central nervous system due to its toxic effects on various tissues. Amongst the various hazardous effects of cadmium, inhibition of bioamine uptake, Na+–K+ ATPase and voltage-dependent Ca++ channels are important. In our study it was aimed to investigate the effects of cadmium on the EEG power spectrum. Fourteen healthy Sprague Dawley, male rats (weight of 257±43 g, the average age of 4 months) were used. They were divided into two groups (n=7 for each group): Control and Cadmium. Control group animals received tap water and the rats of cadmium group received cadmium as in form of cadmium chloride (10 mg/kg) diluted in their drinking water during the experimental period. At the end of the 60 days experimental period, rats which were anaesthetized with urethane (1 g/kg) were placed in stereotaxi apparatus. EEG recording was made with polygraph (with data acquisition system) (PowerLap/SSP, Avustralya). Bipolar EEG recordings were made for 30 minutes. Elected EEG traces were transferred into the spectral analyse programme of polygraph. Differences between groups were analysed with Mann Whitney U test. According to control group, cadmium group significantly increased the spectral power values. This study was supported by the grant of Pamukkale University Research Fund.

Keywords: cadmium, exposure, EEG, power spectrum

P68
The effects of chronic cadmium exposure on the spinal reflexes
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Cadmium is environmental contaminant to which exposure of the human was increased with the development of modern industries. Cadmium is a potent inhibitor of voltage-dependent calcium channels (L-type). It has been shown that it causes functional disturbances in both the peripheral nervous system and central nervous system via moderation of several events in the cell. But information about the effects of cadmium exposure on monosynaptic reflexes in medulla spinalis remains unclear. In the present research we investigated the effects of cadmium on the spinal reflexes. Fourteen healthy Sprague Dawley, male rats (the average weight of 257±43 g, the average age of four months) were used. They were divided into two groups (n=7 for each group): Control and Cadmium. Control group animals received tap water and the rats of cadmium group received cadmium as in form of cadmium chloride (10 mg/kg) diluted in their drinking water during the experimental period. At the end of the 60 days experimental period, rats were anaesthetized with urethane (1 g/kg). 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. After recordings were performed for every 15 min from 5. min to the 30. min. Statistical analysis were made with Mann Whitney U test; p<0.05 was considered significant. When the cadmium group compared with control group, in the cadmium group the amplitudes of reflex responses were significantly increased. This study was supported by the grant of Pamukkale University Research Fund.

Keywords: cadmium, exposure, reflex, medulla spinalis, rat

P69
The informative and thermal approaches to the estimation of the reaction of cerebellar Purkinje cells to microwave radiation
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In the base of understanding of the biological mechanisms of microwaves (MW) and living system interactions two approaches, one being related with the MW energy absorption by living tissue and known as a thermal effect, other known as an informative effect and concerned to the biological effects of magnetic and electric vectors of the physical factor, have been placed. The estimation of the effects based on the two principle approaches on one and the same object and at the same time, is known to be one of the up-to-date problems of bioelectromagnetics. The most important stage in evaluation of MW biological effects from the points of the approaches is the determination of appropriate objects. Our experiments found out that cerebellar Purkinje cell (PC) could be considered as a proper biological object to appreciate the effects of MW. Experiments have been carried out on the anesthetised cat cerebellum, using glass microelectrode technique. MW has been applied to the brain in the projection of cerebellum by the help of widely used in the practice of physiotherapy contact applicator. In order to imitate the thermal effect, besides the known standard methods, the method found more important from the standpoint of us and based on controlled body temperature regulation by the help of which the temperature of cerebellum could be changed within the range that was in the case of MW irradiation, has been used. In these experiments MW irradiation of 460 MHz frequency and 400+40 mW/cm2 (SAR = 28.0±5 mW/g, SAR – Specific Absorption Rate) intensity with 10 min, exposition period has been used. The minimal difference between the rectal (body) temperature (35-360 C) and that of the cerebellum opened for PC registration maid up at least 0.5, C and turned out to be dependent on the value of body temperature. For example, the temperature of cerebellum opened was measured in the range of 34-350 C, while that in the rectum was 37-380 C. Taking into consideration that under MW irradiation of the parameters given above the temperature growths in cerebellum of intact animal maid in average up 1,470±300 C, and 4,360±600 C for the cerebellum of a dead body, it was concluded that approximately 66% of MW energy absorbed has been carried away from the cerebellum by its blood circulation. According these data, the temperature rise in cerebellum by 1,500 C, the entire body being heated, led to great increases in PC impulse activity standard deviations (dispersion) which raised irregularity in the activity that turned out to be proportional to the temperature increase in cerebellum. Under these conditions MW application caused amplifications in both PC bioelectric activity and its regularity, cutting down the increased dispersion 10’s of times as large, in spite of temperature increase in cerebellum. The results obtained testify to the thermal effects causing possible cell membrane ion concentration redistribution, and informative effects lain in the base of synaptic current regulation to be the origin of PC bioelectric activity changes caused by MW.

Keywords: microwaves, cerebellum, Purkinje cell, thermal effect, informative effect, magnetic field, electric field

P70 [NOT PRESENTED]
Study of multiple sclerosis cases followed up in a state hospital neurology clinic
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Multiple sclerosis (MS) is a demyelinating inflammatory disease involving the areas of the white matter of the central nervous system with an unknown etiology. In this descriptive study we aimed to evaluate the MS cases, which were diagnosed according to Poser's diagnostic criteria, followed in Neurology Clinic of Elazig State Hospital between 01.01.2004 and 31.12.2004. Of the total 19 cases, 12 (63.2%) were female and 7 (36.8%) were male. The mean age of the cases was 39.6 y; the mean duration of illness was 51.4 months and mean attack frequency was 3.3. Of the cases, 5.7% had onset before 18 years of age while 2.6% of the cases had onset after 50 years of age. When the cases were evaluated with regard to the Poser's diagnostic criteria; 68.4% of the cases were relapsing-remitting, 18.7% were secondary progressive, 4.9% primary progressive while 3.8% had stable condition. The most frequently initial symptoms were motor symptoms (43.5%), sensory deficit (56.9%), psychiatric problems (53.2%), brain stem involvement (34.5%), bladder symptoms (21.4%) and cerebellar involvement (11.1%), respectively. Typical MRI lesions were detected in 95.6% of the cases. In conclusion in agreement with the literature our findings indicate that there is a significant correlation with the age of onset of the disease and the clinical progression (P<0.05). For a better and conclusive comment on the prognosis of the disease there is a need for studies involving larger patient populations.

Keywords: sensory deficit, magnetic resonance imaging, motor deficit, multiple sclerosis, Poser's criteria

P71
The examination of morphometric changes in blood vessels in jejunum of vagotomised and sympathectomised rats

Keywords: sensory deficit, magnetic resonance imaging, motor deficit, multiple sclerosis, Poser's criteria
In this study, 28 Sprague-Dawley rats were used in order to investigate the morphological changes in muscular layer thickness in blood vessels in jejunum of vagotomised and sympatheticated rats. Rats were divided into four groups (control, vagotomy, sympatheticotomy, vagotomy+sympathetomy) and each group has 7 rats. Rats in control group did not perform any treatment. Rats in vagotomy group were performed surgical vagotomy, sympatheticotomy group were performed chemical sympatheticotomy (ip, 120 mg/kg 6-Hydroxydopamine;6-OHDA), vagotomy+sympathetomy group were performed both surgical vagotomy and chemical sympatheticotomy. After 6 days vagotomised rats, chemical sympatheticotomy was carried out. After one day control group, 6 days vagotomised group, one day chemical sympatheticotomised group and vagotomised+sympathetomised group were killed, the both values of mean arterial pressure (MAP) and of heart rate (HR) were measured in a time period of 1 hour. The blood pressure and heart rate of vagotomised rats, weighting 250-280 g, are anaesthetized using Penthobarbital Sodium. Under spontaneous breathing, tracheostomy, femoral vein and artery catheterizations were performed. An electrofile solution (4 ml/h) is via femoral vein administered, as the physiological need of animal. Following that procedure, four groups are designed. First group (control) has received 1 ml bolus injection of saline via femoral artery. In second group, 15 ml/kg DBcAMP in 1 ml saline is similarly administered. In third group, left vagal nerve is cutted. In the last group (4th) the administration of DBcAMP as well as left vagal DBcAMP are applied. For each animal, the both values of mean arterial pressure (MAP) and of heart rate (HR) are measured in a time period of 1 hour. The blood pressure and heart rate signals are numerically recorded by a personal computer (Power Lab). In saline group, the MAP and the HR were stable, during the record period of one hour. The dropping effects of DBcAMP on HR and MAP were not seen, rapidly; after 3 min, statistically significant drops were determined and this effect was maximum at the 10th minute. The mentioned effects were temporary; the return of HR and MAP values to initial values was seen within 30 min. and thereafter, they were fixed. In left vagotomised animals, the HR as well as MAP values decrease rapidly; the time interval from initial to drops of parameter was shorter. In the group with DBcAMP administration and vagotomism, the decrease in HR was slightly but the decrease in MAP was more remarkable and significant. In a previous study of ours(*), the depressive effects of DBcAMP on HR and MAP were not dose-dependent. For this reason, it was considered that a complex reflex mechanism may be involved. According to the results of present study; administration of DBcAMP with vagotomism, causes slight decrease in HR particularly, namely a potamalization is not considerable. In contrast, vagotomism may neutralize the effect of DBcAMP. In conclusion, we consider the cardiovascular depressive effect of DBcAMP to be complexity interacted with vagal reflexes. ‘Ekerbiser N, Taralçı F, Özbek M, Özel H.F. ’Time and dose dependent effect of intraarteral enjeksion of DBcAMP on blood pressure and heart rate in rats’. 30. National Physiology Kongress, Konya.

Keywords: Vagotomy, sympatheticotomy, rat, jejunum, blood vessels

P73
Leptin receptors
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Leptin was discovered in 1994 by Zhang and co workers. It is a protein type hormone made of 167 amino acid residues. If resembles cytokines and is produced mainly by adipose tissue. The main role of leptin in the body, is to protect the body from obesity by the regulation of food intake and energy metabolism, by means of negative feed back effect upon hypotalamus via leptin receptors (LEPR).

The first leptin receptor db/db has been described in mouse coroid plexus as a db gene product. This leptin receptor is from the class I cytokin receptor family and 6 other different isoforms of leptin receptor (LEPPr, LEPRb, LEPRd, LEPRa, LEPRd, LEPRf) have also been described up to date. Long receptors (LEPRb) are mainly found in hypotalamus. The intraceller side of this receptor has a role in activating JAK-STAT, the signal conducting pathway in hypotalamus.

The short receptor LEPRa does not have all the segments needed for signal conduction, but it may have an important role in carrying the leptin into the central nervous system. LEPRa is a soluble receptor within the circulatory system.

The binding of leptin receptor with leptin, triggers the JAK-STAT cascade, finally regulating specific gene expression. The mice with db/db mutation in DB gene, have a leptin receptor insufficiency and leptin resistence. These animals are hyperphagic, morbidly obese, sexually immature and have cold intolerance. In humans, leptin receptor mutations are rare.

To understand the effect of leptin and its usage within the medical field, studies concerning leptin and leptin receptors are increasingly becoming of greater interest to scietists.

Keywords: leptin, leptin receptors, appetite, energy expenditure, obesity

P74
XRC1 399 gene polymorphism in Parkinson’s disease
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The etiology of Parkinson’s Disease (PD), a neurodegenerative disorder, is still unknown and the role of genetic factors have been implicated. XRC1 (X-Ray Repair Cross-Complimenting) gene is required for DNA single-strand break repair and interacts with poly-ADP-ribose-polymerase (PARP), DNA-ligase III and DNA polymerase beta. It has been shown by mouse models that PARP deficiency may have a role in the pathogenesis of various diseases including PD. The aim of the study is to investigate the association of PD with XRC1 399 gene polymorphism. Seventy-one unrelated PD patients (50 male, 21 female) and 96 healthy age and sex matched volunteers (53 male, 43 female) have been included in the study. Molecular analyses have been performed with polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) methods. The relationship between the XRC1 399 gene polymorphism and the PD has been investigated with the binary logistic regression analysis, and no statistically significant relation has been determined (p=0.364). As a result, although this study did not reveal significant association, similar studies should be performed in different populations to clarify whether DNA repair genes have a role in the etiopathogenesis of PD.

Keywords: Parkinson’s disease, DNA repair gene, XRC1

P75
Central role of RHO/ROH-kinase pathway in the neurogenic contractile activity of the sheep gallbladder smooth muscle
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Rho kinase (ROK) has been reported to be ubiquitously expressed in different types of smooth muscle, and mediates in Ca2+ sensitization, which enhances contraction. Therefore, in this study we aimed to investigate this novel signalling pathway in the sheep gallbladder smooth muscle contraction induced by electrical field stimulation (EFS, 40 V, 0.5 ms, 2, 4, 8, 16, 32 Hz, 15 s.). Longitudinal strips (2-3 mmx3-4 cm) of the gallbladder were mounted in organ chambers filled with Krebs solution under an initial tension of 1g between two platinum ring electrodes. Isometric responses of the tissue were transferred to a data acquisition system.
The modulation of cocaine and amphetamine regulated transcript (Cart) expression in the arcuate and paraventricular nuclei of the rat following restraint and forced swim stress

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Our previous studies showed the modulation of CART positive neurons and CART mRNA expression by adrenalectomy (ADX) and corticosterone (CORT) replacement in hypothalamic nuclei of male rat brain. ADX lowered CART mRNA levels only in arcuate (ARC), but not in paraventricular nucleus (PVN). However CART peptide expression was reduced in both nuclei. CORT replacement restored CART mRNA levels in ARC. This study aimed to evaluate the effects of different stress procedures on CART expression in ARC and PVN in male and female Sprague Dawley rats. In restraint stress (RS), rats were exposed to one hour restraint stress either once (acute) or for 15 days (chronic). In forced swim test (FST), rats were forced to swim on two consecutive days, in a glass cylinder for 15 and 6 minutes, respectively. Trunk blood was collected for ACTH and CORT level determinations or rats were perfused for immunohistochemistry to assess CART peptide expression. ACTH and CORT levels were different between different treatment groups. In the acute RS and FST, stress increased CORT more prominently in females while chronic RS lowered the elevated hormone levels in both sexes. Basal levels of CART expression were similar in males and females. In males, acute RS did not change CART expression in either nuclei while chronic RS lowered CART expression relative to acute treatment in ARC. In females, acute stress lowered CART expression in PVN but increased it in ARC. Chronic stress lowered CART positive cells in ARC while PVN was not affected. On the other hand, FST increased CART + cells significantly in PVN of females. Our results suggest differential and sexually dimorphic modulation of CART expression in PVN and ARC by different stress procedures. Since both chronic stress and ADX lowers CORT levels, it seems probable that CART expression is modulated by CORT more profoundly in ARC following RS in females. FST is an acute form of stress where CART expression increases in PVN and only in females. Future studies will elucidate the mechanisms underlying the involvement of CART peptide in stress response. Supported by NIH Grant No. 3 R01 DA010732-05S1

**Keywords:** Quadriceps, muscle metabolism, fNIRS, isometric exercise, Fatigue

P76

The involvement of central cholinergic system in the pressor effect of intracerebroventricularly injected U-46619, a thromboxane A2 analog, in conscious normotensive rats

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Thromboxane A2 (TXA2) is one of the biologically active metabolites of prostaglandin synthase metabolism. It exerts and promotes many actions in various tissues including platelet aggregation and vasoconstriction. Considerable evidence suggests that TXA2 may act as a neuromediator and/or neuromodulator in the central regulation of a variety of functions including cardiovascular and neuroendocrine activities. Recent studies demonstrate that centrally injected U-46619, a synthetic TXA2 analog increases blood pressure in normal conditions and reverses hypotension in haemorrhagic shock conditions. Considering the previous studies suggested that eicosanoids may play a role in maintaining the sensitivity of cholinergic signaling mechanisms in the central nervous system and the importance of central cholinergic activation in the cardiovascular regulation, we aimed to determine the involvement of central cholinergic system in the pressor effect of centrally injected U-46619, a TXA2 analog, in normal and various stress conditions. Intracerebroventricular (i.c.v.) injection of U-46619 (0.5, 1.0 and 2.0 µg; i.c.v.) produced dose- and time-related increases in blood pressure and decreased heart rate. I.c.v. pretreatment of SQ-29548 (8 µg; i.c.v.), selective TXA2 receptor antagonist, completely inhibited cardiovascular responses to subsequent injection of U-46619 (1 µg; i.c.v.). The mecamylamine, a cholinergic nonspecific nicotinic receptor antagonist, (50 µg; i.c.v.) pretreatment attenuated the pressor effect of U-46619 (1 µg; i.c.v.). Atropine, a cholinergic nonspecific muscarinic receptor antagonist, (10 µg; i.c.v.) pretreatment did not influence the pressor response observed after i.c.v. injection of U-46619 (1 µg). Neither atropine nor mecamylamine pretreatments affected the decrease in heart rate induced by U-46619. Intracerebroventricular administration of U-46619 (1 µg) caused an approximately 28% increase in extracellular hypothalamic choline levels but it did not change hypothalamic acetylcholine levels. Interestingly, pretreatment of rats with β-hungarotoxin (10 µg; i.c.v.), selecetivemethyllycaconitine (10 µg; i.c.v.) or 7-nicotinic receptor antagonist, α7 subtype of nicotinic acetylcholine receptors (α7 antagonists of significantly inhibited the pressor and heart rate responses to subsequent injection of U-46619 (1 µg; i.c.v.). The present results show that U-46619 can increase hypothalamic choline levels and the cardiovascular response to i.c.v. injection of U-46619 was mediated at least in part through central nicotinic 7-nAChRs. This study was supported by thecholinergic activation, predominantly grand from the Scientific Research Foundation of Uludag University, 2003/31.

**Keywords:** Thromboxane A2, Choline, Blood Pressure, Cholinergic Receptors, Hypothalamus

P77

The effect of diazepam on performance of mice in forced swimming test

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Forced swimming test is the most frequently used animal model to screen psychotropic drugs. The rat or mouse is put in a water tank and the duration until it becomes immobile or the total duration of immobility in a specified time period is recorded. In this model, immobility and decrease in the effort to escape are interpreted as ‘behavioral despair’. Antidepressants are reported to increase the active coping response against the stress induced by swimming. Benzodiazepines are reported to reverse the effect of antidepressants in decreasing the total duration of immobility. Benzodiazepines increase the immobility in a dose-dependent manner and independent of their muscle relaxing effect. It is suggested that the increase in immobility of mice was correlated with the anxiolytic activity of benzodiazepines. The excessive activity at the beginning of forced swimming...
test may be due to the anxiety provoked by the contact of mice with water and when the anxiety decreases, the movements may also decrease. Therefore, less anxious mice can be expected to become immobile at a shorter time. In order to test this hypothesis, 8 mice were assessed with forced swimming test. The control and study groups consisted of 4 mice each. All mice were male and the mice in the study and control groups were matched according to age and weight. In the study group, diazepam was injected intraperitoneally at an anxiolytic dose (0.250mg/kg) that would not cause muscle relaxation. The mean weight of mice was 32.2 ± 6.7g in the control and 31.0 ± 5.6g in the diazepam groups. There was no significant difference between the two groups with regard to weight with Mann-Whitney U test. The mean duration of immobility was 91.4± 68.5 sec in the control and 187.3±45.3 sec in the diazepam groups. When the two groups were compared for duration of immobility with Mann-Whitney U test, the difference was found to be significant (p=0.043). The results of this study show that diazepam, when given at an anti-anxiety but not muscle relaxing dose, increased the total duration of immobility significantly compared to controls. Therefore, the mice whose anxiety were relieved by the drug continued to float with less movement. These results suggest that forced swimming test is not a reliable model of depression. Many confounding factors may affect the results of this test. Immobility can be considered as an adaptive symptom instead of an indicator of depression.

Keywords: Anxiety, Benzodiazepines, Depression, Forced swimming test, Immobility

P80
Differential effects of short light pulses given at different hours in the night on forced swim tests
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Circadian rhythms in mammals are regulated by the suprachiasmatic nuclei (SCN). The major entraining factor of SCN is light. Recent studies have emphasized the role of SCN in affective functions. We have previously shown that disruption of circadian rhythms by electrolytic SCN-lesions or exposure to constant light destroys the rhythm and reduces the amplitude of the circadian rhythms. In the present study, we report the effects of short light pulses given at different hours in the night on forced swimming test. Subjects in one of the two experimental groups received a 3 minute light pulse of 60 watts three hours after the light offset (ZT-15), a time where light is known to induce phase delays. Subjects belonging to the other experimental group received the same light stimulus 3 hours before the light onset (ZT-21), a time where light is known to induce phase advances. A control group was not exposed to any light stimulus during the night. Forced swimming tests were performed after 3:00 pm, for two days in a Plexiglas cylinder filled with water of 25 °C up to a height of 15 cm. On the first day, each animal was immersed into the water for 15 minutes followed by a 5-minute test in the same cylinder 24 hours later. Animals receiving a light pulse 3 hours before the light offset exhibited less immobility compared to the animals from other groups whereas the control group exhibited the longest immobility duration. The results of the present study show that light pulses given at different times may have different effects on FST. These results make circadian rhythms a stronger candidate in affective functions since different modulations of circadian rhythms resulted in different FST performances. (This research is supported by the Bosphorus University 00R103 grant to RC).

Keywords: Suprachiasmatic Nucleus, Circadian Rhythms, Light, Forced Swim Test, Depresion, Wistar rats

P81
Effect of long-term exercise on electrophysiological parameters in diabetic rats
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We used the present study was the evaluation of effect of long-term exercise on compound muscle action potential (CMAP) parameters in diabetic rats. Wistar-Albino male rats, 3-months of age, with a mean body weight of 189-306 g were used in this study. Animals were randomly divided in eight groups of 15: Control (C), exercise (E), sedentary diabetic (SD), diabetic-exercise (DE), diabetic after exercise (DAXE), sedentary diabetic-insulin (SDI), diabetic-exercise-insulin (DEI), diabetic after exercise-insulin (DAEI). Diabetes was induced by a single intraperitoneal injection of streptozotocin (STZ) at a dose of 45 mg/kg of body weight, freshly dissolved in 20 mmol.1 sodium citrate buffer, pH 4.5. Control group was injected with the same volume of isotonic NaCl as the diabetic groups received. Insulin treatment began immediately after the onset of diabetes. A single subcutaneous injection of 0.75 U of insulin was given daily to all insulin groups. Animals in the exercise groups were applied swimming once for one hour once a day in a plastic tank (60x100x60 cm). These applications were continued daily until the end of the study for 5 days/week (for 8 weeks). Four weeks prior to induction of diabetes, DAES and DAEL groups were applied swimming for same protocol. CMAP were recorded using a BIOPAC MP 100 Acquisition System Version 3.5.7 (Santa Barbara, USA). CMAP parameters (peak-to-peak amplitude, area, duration and distal latency) were measured by software and motor conduction velocity between the proximal and distal sites of stimulation was calculated by dividing the distance between these sites by the difference in latency of the responses. Eight weeks after beginning of the study, the rats were sacrificed and the sciatic nerves were harvested. Histology was performed blindly. Tissues were stained with haematoxylin and eosin to evaluate the degenerative and possible regenerative areas. Then all data were analysed statistically. Exercise applying attenuated the increase (p<0.05) in distal motor latency in diabetic rats. This study suggests that long-term exercise may be useful in the treatment of diabetic neuropathy.

Keywords: Exercise, diabetes, streptozotocin, diabetic neuropathy, action potential, conduction velocity

P82
Spontaneous locomotor activity and stress in immobilized rats
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Immobilization stress activates hypothalamo hypophyseal axis. The effect of stress on hormone levels in blood causes weight changes of various organs. In this study, we aimed to determine the effects of immobilization, a stress factor, on spontaneous locomotor activity and adrenal glands. For this study, 24 Wistar albino male rats (12 control and 12 immobilized) were used. The right hindlimbs of the rats in experimental group were immobilized by a new method for 4 weeks. The rats in both control and experimental groups were weighed at the beginning of the experiment and 4 weeks later. At the end of the immobilization period, the rats in both groups were taken to activity cage and spontaneous locomotor activity scores were evaluated in 5th, 10th, 15th minutes. And then, left and right adrenal glands of the rats were extracted and weighed by a sensitive scale. At the end of the immobilization period, the decrease in the final body weight in immobilized group when compared with the initial values was statistically significant (p<0,02). The decrease in the scores obtained for spontaneous locomotor activity of immobilized rats was statistically significant (p<0,001). However, there was a statistically significant increase in the weight of both adrenal glands of immobilized rats in comparison with the control group (p<0,02 and p<0,003, respectively). In the light of these findings, it was determined that immobilization caused stress on rats. Because of the stress, the body weight and locomotor activities decreased, whereas the weight of adrenal glands increased.

Keywords: adrenal glands, body weight, immobilization, spontaneous locomotor activity, stress

P83
The effects of 7-nitroindazole on anxiety and spatial memory of rats exposed to chronic immobilization stress
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Nitric oxide (NO) is proposed to modulate stress, further has anti-stress and adaptogenic effects. In this study, we aimed to investigate the effects of 7-Nitroindazole (7-NI), selective inhibitor of neuronal nitric oxide synthase, on anxiety and memory of the chronically immobilized rats by using open field, holeboard and Morris water maze tests. We used Wistar albino strain mature male rats weighing between 250-300g. Animals were divided into three groups: 1- Control group:The rats without any intervention, injection or immobilization (n=9). 2- peanut oil + chronic immobilization group: the group that was exposed to 30 minutes daily immobilization stress for 15 days and was given intraperitoneal (i.p). 0.5 ml peanut oil 30 minutes before immobilization (n=9). 3- 7-NI + Chronic immobilization
Effects of tianeptine pretreatment on trace elements levels in brain, liver and spleen in chronically immobilized rats

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In the present study, we aimed to determine the effects of intraperitoneal tianeptine administration on trace element disturbances in brain tissues (frontal and temporal lobes and brain stem), liver, and spleen (Zn, Cu, and Fe rich-tissues) in chronically immobilized rats. The animals were divided into three groups: control group (n=9), chronic restraint group (n=7), chronic restraint+tianeptine group (n=9). Restraint stress was applied by keeping the rats in plexiglass cages that does not let the rats to move inside. In the rats in chronic restraint group and chronic restraint+tianeptine group had 6 hours daily restraint stress for 21 consecutive days and had either intraperitoneal 1 ml saline injection or 10 mg/kg tianeptine twice a day within an interval of 8 hours, respectively. First injections were applied one hour before the beginning of the stress procedure. Controls and immobilized rats were decapitated 30 minutes after last restraint period was over, and tissue samples were taken. Zn, Cu and Fe levels of the frontal lobe, temporal lobe, brain stem, liver and spleen were determined by flame atomic absorption spectrophotometer. Cu and Fe levels were significantly increased in the frontal lobe, temporal lobe and brain stem in response to chronic restraint stress. Tianeptine administration prevented the elevation of Cu and Fe in these brain samples. On the other hand, while tianeptine administration led to an increase in Zn levels of all tissues in this study, it caused a decrease in Cu levels. Increased levels of Cu and Fe in frontal, temporal lobes and brain stem may be related to induction of metallothionein-1 (MT-I) and iron transfer protein synthesis in the brain areas. Tianeptine showed its effect probably by suppressing these syntheses.

Keywords: Tianeptine, restraint stress, rat, trace elements, tissues

Electrophysiological and histological changes in peripheral nerves in ovariectomized rats

Cemeralpoglu U [1], Yalın S [2], Hatanli R [3], Bagis S [4], Ogenler O [5], Coskun B [5], Bakır L [5].


In this study, the cerebellar interneuronal connectivity was taken into account to determine the effects of prenatal stress exposure on the cerebellar development at postnatal day (P) 30, the expression of a synaptic vesicle-associated protein, synaptophysin, was quantitatively analyzed in the neuropil area of the granule cell layer. Although the volume fraction of the granular layer to whole cortex and the numerical density of granule cells per unit volume of granular layer were not affected by exposure to stress, synaptophysin immunoreactivity showed a significant decrease (41%) in the granular layer of the cerebellum. Since synaptophysin is ubiquitously distributed as a presynapse-specific component in the brain, decrease in the staining intensity of coarse synaptophysin immunoreactive granule neurons indicates a decrease in the density of presynaptic terminals. Collectively, these results demonstrate that exposure to gestational stress causes a profound and long-lasting deficit in the sensory input to the cerebellar granule cells of offspring.

Keywords: Hemispheric preferences, Mental Work Load, Differential aptitudes, Left preference, Right Preference

Effects of prenatal stress on stress response of adult rats

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Prenatal stress is thought to be important, besides genetic vulnerability, in the expression of many psychiatric disorders. Prenatal stress is supposed to decrease the ability to cope with the stressors in adult life. This study aimed to investigate the role of prenatal stress exposure on stress responses during adulthood. It is hypothesized that the adult rats that were subjected to prenatal stress would show increased immobility in Porsolt's forced swimming test. Female rats were housed with males during the dark phase of their cycle. Presence of spermatozoa in the vaginal smear indicated the first day of pregnancy. Beginning from the 10th day of the pregnancy half of the pregnant rats were forced to swim in water maintained at 22 centigrad degrees for 10 minutes till the end of the pregnancy. Male rats born from both stress subjected mothers (n: 18) and control groups (n:16) were subjected to Porsolt's test between 56-60 days of age after their weights being recorded. There was no difference regarding the immobility times between the offspring of the two groups. However weight of the offspring subjected to prenatal stress was significantly less than that of the control group. These results suggest that the type and severity of prenatal stress exposure used in this study has no effect on the stress responses during adulthood measured by Porsolt's forced swimming test, but may cause growth retardation.

Keywords: Prenatal stress, rat, Porsolt's forced swimming test, stress response, growth retardation

Prenatal stress reduces sympathetic expression in the rat cerebellar granular layer

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The cerebellum receives sensory, motor, perceptual and cognitive information from all parts of the nervous system and can be severely affected from the environmental adversity during the development of the central nervous system. In this study, the cerebellar interneuronal connectivity was taken into account to examine the effects of prenatal restraint stress. Rat embryos are exposed to stress on their embryonic day (E) 7 and 14, by keeping the dam in close-fitting wire mesh cylinders, for six hours. After completion of the cerebellar development at postnatal day (P) 30, the expression of a synaptic vesicle-associated protein, synaptophysin, was quantitatively analyzed in the neuropil area of the granule cell layer. Although the volume fraction of the granular layer to whole cortex and the numerical density of granule cells per unit volume of granular layer were not affected by exposure to stress, synaptophysin immunoreactivity showed a significant decrease (41%) in the granular layer of the cerebellum. Since synaptophysin is ubiquitously distributed as a presynapse-specific component in the brain, decrease in the staining intensity of coarse synaptophysin immunoreactive granule neurons indicates a decrease in the density of presynaptic terminals. Collectively, these results demonstrate that exposure to gestational stress causes a profound and long-lasting deficit in the sensory input to the cerebellar granule cells of offspring.

Keywords: Hemispheric preferences, Mental Work Load, Differential aptitudes, Left preference, Right Preference

Electrophysiological and histochemical changes in peripheral nerves in ovariectomized rats

Cemeralpoglu U [1], Yalın S [2], Hatanli R [3], Bagis S [4], Ogenler O [5], Coskun B [5], Bakır L [5].


In this study, we investigated the effect of ovariectomy on the rat sciatic nerve using electrophysiological and histological techniques and observed electrophysiological and morphological changes in ovariectomized rats. Twelve female Wistar albino rats were divided into two groups as control and ovariectomized (OVX) (n=6 each). The OVX rats were operated underwent bilateral ovariectomy after being anesthetized with ketamine. Ventral incision was made and ovaries were removed after ligation of the uterine horn. 30 weeks after ovariectomy compound motor action potentials (CMAP) were recorded by using standardized nerve conduction study techniques, progesterone and estrogen levels in the serum were measured employing the biochemical methods and sciatic nerve samples were examined using the light microscope for two groups. Progesterone and estrogen were significantly decreased in OVX group compared with the control group. But distal latency was significantly increased in OVX group. No statistically significant difference was found regarding the amplitude and area in OVX group compared with the control group. Ovariectomy affects electrophysiological and morphological parameters of rat periferal nerves.

This work was supported by the grant from Mersin University, Scientific Research Projects Fund (BAP ECZ. F.BBSY(5) 2002).

Keywords: Ovariectomy, nerve conduction, action potential, myelin, progesterone

Quantitative EEG analysis in patients with severe COPD: some clues of chronic hypoxic degeneration
This prospective clinical and electrophysiological study was performed in order to determine the electroencephalographic correlates of cognitive disturbances in patients with severe chronic obstructive pulmonary disease (COPD), using quantitative electroencephalographic (QEEG) measurements. Electroencephalograms (12 channels) were obtained from 33 patients with severe or very severe COPD and from 20 age and sex matched controls. Patients showed mild cognitive impairment (mean MMSE score was 24.6±3.7), unrelated to depression, especially in the construction, language and memory areas. Electroencephalograms revealed fronto-temporal slow waves especially in the left hemispheres. QEEGs revealed higher frequency slow wave-bands and lower frequency beta activity, predominantly in the bilaterally fronto-temporal localizations, in addition to decreased global relative beta power in patients with COPD. Analysis of variance of QEEG parameters and clinical characteristics showed that age, PaO2, PaCO2 and FEVI had significant correlation with QEEG variables in different cerebral localizations. Supported with the first detailed QEEG findings, it was concluded that cognitive impairment in COPD patients was far from being a coincidence and some important clues about its degenerative basis, especially in data processing areas, existed.

Keywords: Chronic obstructive pulmonary disease, cognitive impairment, quantitative EEG, slow wave asymmetry, chronic hypoxemia.

P89
Effect of electromagnetic fields emitted by cellular phones on the latency of evoked electrodermal activity
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The widespread use of cellular phones raises the question of their possible adverse biological effects on the central nervous system (CNS). Therefore, we were interested in studying the effects of electromagnetic fields emitted by cellular phones (CPEMFs) on brain activity related to generation and representation of EDA. EDA, which is the accepted common term for all electrical phenomena in skin, result from eccrine sweat glands activity driven by sympathetic cholinergic neurons. It has been suggested that there are two different neural substrate of EDA in CNS. In this study, we have concentrated primarily change in EDA that are controlled by the substrate named EDA-2, a neural pathway originating in the premotor area of contralateral cortex and projects down by way of the basal ganglia. Patellar tendon (PT) stimulation was used to activate this pathway during three different exposure conditions to CPEMFs: sham exposure, ipsilateral or contralateral exposure with respect to the EDA site exposed to CPEMFs. Hemispheric asymmetry of EDA-2 pathway, which is represented by shorter SRR latency in the right hand (rapid information processing in left hemisphere) of the right hand responders, was also distorted with CPEMFs. Since the CNS regions including EDA-2 are also involved in tasks of motor timing and time estimation, delayed response in this neuronal network due to CPEMFs may increase the response time of the mobile phone users. Therefore, our findings points to the potential risks of mobile phones on the function of CNS and consequently, possible increase in the risk of phone-related driving hazards.

Keywords: electrodermal activity, cellular phone, reaction time, brain

P90
Effect of 900 MHz electromagnetic field emitted from cellular phone on serum cortisol and testosterone levels
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Using cellular phones increases day by day with the inspired thought of the articles that reports the harmful effects of cellular phones on human health. This is a growing health problem for human being. These vehicles are in the service of mankind and they are useful for man but at the same time they have harmful effects too and it is believed that they may have side effects on neuroendocrine system. In the present study, our aim was to investigate the effects of pulsed 900 MHz electromagnetic field (EMF) on cortisol and testosterone levels of the rat organism. In this study, we have used 20 Spraque Dawley male rats. The rats were separated into two groups as control (C) and EMF group. EMF group was exposed to the carrier frequency of 900 MHz with average power flux density 1±0+4 mW/cm², 30 minutes a day and 5 days a week for 4 weeks. C group was kept at the experiment environment but they didn’t exposed to magnetic field. Cortisol and testosterone levels were evaluated in serum rats. The findings we have got in this study are; cortisol values at the EMF group was significantly higher than the C group, however, testosterone values were lower at the EMF group when it is compared with the C group. In conclusion, the effect of the EMF waves that is spread out by the cellular phones on neuroendocrine system may be originated from thermal and stress processes. However, physiological and morphological advanced studies has to be done about this subject.

Keywords: 900 MHz, electromagnetic field, cortisol, testosterone, rat

P91
Neocuproine, a copper (I) chelator, potentiates purinergic component of vas deferens contractions elicited by electrical field stimulation
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Effects of the specific copper (I) chelator, neocuproine, on the purinergic and adrenergic components of nerve-evoked contractions were investigated in the prostatic rat vas deferens. Electrical field stimulation (EFS; 4 Hz) induced bimodal contractions of vas deferens tissue in the presence of alpha[1]-adrenoceptor antagonist prazosin (to isolate the purinergic component) or prulineceptor antagonist suramin (to isolate the adrenergic component). Neocuproine significantly potentiated the purinergic component of the contractile responses to EFS. However, the same agent failed to elicit any significant effect on the adrenergic component of nerve-evoked contractions. The copper (II) chelator cuprizone could not affect the purinergic component of contractions. The potentiating effect of neocuproine or ATP suppressed the EFS-induced contractions. In conclusion, our results suggest that neocuproine potentiates purinergic component of rat vas deferens contractions elicited by EFS, presumably by facilitating purinergic neurotransmission and that copper(I)-sensitive mechanisms can modulate purinergic transmission in this tissue. Also, it can be suggested that selective copper (I) chelators which potentiate the actions of ATP at P2X1 receptors may be useful in the treatment of male infertility.

Keywords: Neocuproine, copper, rat vas deferens, purinergic activity, electrical field stimulation

P92
Morphological alterations produced by zinc-deficiency in rat sciatic nerve: a histological, electron microscopic and stereological study
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Zinc (Zn) is an essential trace element for humans and animals. It is required for normal growth, gene expression, wound healing, protein metabolism, immune function and membrane integrity. In this study, unbiased stereological methods have been used to quantify the effects of Zn-deficiency on the sectioned surface area and number of myelinated axons in the sciatic nerve of rats. Animals were fed a Zn-deficient or Zn-sufficient diet containing 0.007 mg Zn per 100 g and 3 mg Zn per 100 g, respectively, for a period of 4 weeks. At the end of this time, animals were anesthetized via a short inhalation of ether; intracardial fixation was carried out by rinsing for 30 min with 0.9% saline solution followed by a mixture of 2% paraformaldehyde+2% glutaraldehyde in 0.1 M phosphate buffer, pH 7.4 at room temperature. The samples of sciatic nerves were removed from the animals, processed for electron microscopy and embedded in Epon resin. The Zn-deficient group of rats was found to have a lower body weight compared to rats in the control group (p< 0.001). The sectioned surface area of nerve cross-
section and myelinated axon number in Zn-deficient rats decreased by 8.696% and 20.15% respectively, compared to the control group. A significant correlation between sectioned surface area and myelinated axon number was also determined. Morphological findings were as follows: on light microscopy, it was determined that certain abnormalities occur specifically in the experimental group, such as collapsed nerve fascicles, irregular profiles in myelin sheaths, and on electron microscopy, extensive myelin damage was seen in Zn-deficient groups compared with control groups. This study suggests that peripheral nerves require Zn for development and preservation of their structure.

Keywords: Sciatic nerve, axon number, zinc-deficiency, stereology, rat

P93
Effect of L-Dopa on dimensional complexity of EEG in patients with Parkinson's disease with dementia
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Objective: To investigate the effect of L-DOPA on the intrinsic complexity of resting EEG in demented patients with Parkinson disease (PD). Background: Spatial-temporal complexity of EEG reflects the degrees of freedom of the underlying brain dynamics. Some measures of dimensional complexity were found to be normal in non-demented PD patients in resting conditions, but, in contrast to normal subjects, not reduced while performing mental imagination and complex motor tasks. The sustained level of complexity during motor and cognitive tasks in PD is in accordance with the notion that the basal ganglia have a role of inhibiting lateral -competing- motor and cognitive neuronal populations, thus reducing complexity. Presuming that demented PD patients have uninhibited cognitive neuronal assemblies, we hypothesized that their background -idling- EEG has a dimensional complexity that could be reduced by L-DOPA. Methods: Eight demented patients with PD were studied. 21-channel EEGs of 20 minutes length were recorded in a resting/eyes-closed condition in the morning before the first daily dose of L-DOPA, and 1-3 hours after the first dose when the patient became clinically “on”. Independent component analysis was used to remove the eye movement, blink, EKG, and EMG artifacts. Complexity Index (CI) was computed following the algorithm described by Lo and Chung (IEEE Trans Biomed Eng 2001;48[3]:394-7). Averaged power spectrums were computed, and summed across the channels to obtain the “collapsed spectra”. Individual alpha frequency (IAF, the frequency of the highest peak between 5 to 15 Hz), and the relative power of delta, theta, alpha, and beta bands of the collapsed spectra were calculated. CI, IAF, and logarithmic transformation of power variables were evaluated using ANOVA for repeated measures. Results: CI dropped from 5.19 ± 0.06 (CI=5.044 ± 0.0161) after the L-DOPA dose. A border left-shift was noted for IAF (from 7.76 ± 0.43 Hz for off, to 7.47 ± 0.54 Hz for on, p=0.0740). CI was not correlated with IAF, and none of the power variables differed significantly between on- and off-conditions, together suggesting that the observed drop in CI were not due to the changes in the underlying linear -spectral- dynamics. Conclusion: In accordance with the above hypothesis, L-DOPA decreases the intrinsic complexity of idling electrocortical activity of PD patients with dementia.

Keywords: Parkinson's disease, dementia, EEG, dimensional complexity

P94
Subconjunctival nodular lesions, glaucoma and intracranial mass in a patient with polyarteritis nodosa and familial mediterranean fever
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We report a case of familial Mediterranean fever (FMF) and polyarteritis nodosa (PAN) with glaucoma, subconjunctival nodules, and cerebral lesions. A 19-year-old male patient underwent a detailed ophthalmological examination. Innschial biopsy of his ocular lesions were performed and examined under light microscope. Cerebral Magnetic Resonans Imaging (MRI) was performed. The visual acuities were 20/20 in both eyes. He had bilateral subconjunctival nodular lesions. Incisional biopsy of these lesions showed lypocytes, vascular structures and plasma cell infiltration in fibrous tissue samples. He was diagnosed as open-angle glaucoma depending on the high intraocular pressures and high cup to disc ratios in both eyes. His perimetric examination showed generalized visual field depression in both eyes. MRI revealed a supraclcular mass invading optic chiasm, multiple cystic lesions in thalamus, globus pallidus and anterior fossa, and lipomas in the pontocerebellar system. FMF and PAN coexistence may be accompanied by various ocular and cerebral lesions. A careful ophthalmological examination and MRI are mandatory to detect those pathologies in such patients.

Keywords: FMF, PAN, glaucoma, subconjetival nodular lesions, MRI, cerebral mass, cerebral cyst.

P95
Topographic relation of the lingual nerve to the infratemporal fossa and paralingual area
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The lingual nerve (LN) passes through the infratemporal fossa and paraligual space, LN occurs damage during surgical procedures, such as local anesthesia, orthognathic surgery, preprosthetic surgery, tumor excision, or third molar extraction. The aims of this study were clarify the comprehensive courses and topography of the LN and to determine its positional relationship and communication patterns with other mandibular nerve branches in infratemporal fossa and paraligual space. Forty-two hemisectioned head specimens from 21 adult cadavers perfused with formaldehyde fixative were used in this study. Preceding dissection was performed from medial and lateral aspect, origin and diameter of the lingual nerve, anatomic relationships maxillary artery and pterygoid muscles are investigated. In addition, the horizontal distance between the lingual nerve and inferior alveolar nerve; vertical distance from oral foramen and bifurcation spot of the LN from the mandibular nerve. In the present study, the furcation patterns of the LN and inferior alveolar nerve (IAN) were classified into four categories based on their relative positions. Type I was seen cases in which the LN and IAN bifurcated above the level of the mandibular notch. Type II cases in which the LN and IAN bifurcated in the upper half between the mandibular notch and the mandibular lingula. Type III cases in which the LN and IAN bifurcated in the lower half between the mandibular notch. Type IV cases in which the mandibular nerve branches in a plexiform. Type I is the most frequency. The distance between retromolar portion and LN was minimum 3 mm to maximum 14 mm. The average distance from the medial and distal portion of the mandibular third molar area to the LN was minimum 5.2 to maximum 16.2 mm. Therefore, anatomical variations are assumed a possible cause of complications or incomplete performance during surgical procedures, such as local anesthesia or third molar extraction. We believe that the topographic relation of the LN, as clarified by this study, will provide a useful reference for clinical applications and surgical procedures.

Keywords: lingual nerve, infratemporal fossa and paralingual area, surgical procedure

P96
Molecular and biochemical procedures for the diagnosis of mitochondrial disorders
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Mitochondrial disorders are a wide group of pathologies affecting particularly the nervous and muscular systems with involvement of mitochondrial DNA (mtDNA) or respiratory chain complexes. Laboratory investigations are complimentary to the clinical data of these disorders. In this study, 16 patients with a preliminary diagnosis of mitochondrial disorder were investigated. The suspected clinical picture determined the laboratory investigation due. Depending on the clinician’s decision, blood, urine, or muscle tissue was used, if possible in combinations. Two patients had MELAS, one MERRF, three Leigh syndromes, seven mitochondrial myopathy, three mitochondrial encephalopathy as the preliminary diagnoses. Respiratory complexes were analyzed on frozen muscle samples with spectrophotometric assays. The biochemical components for electron transfer were NADH, Coenzym-Q, succinate, dichlorofenol-indophenol, cytochrome c electron donors of the complex. Any abnormality of mitochondrial proliferation was normalized with citrate synthase activity. The four cases investigated did not reveal any pathology. Genetically, three common point mutations (MELAS A3243G, MERRF A8344G, NARP T8993G) were investigated with PCR amplification and RFLP analysis. In appropriate cases a screening for deletions were performed with long-PCR. The primer pair for long-PCR was located on mtDNA. No deletions were found. Further phylogenetic analysis of the patients were performed with MWG Biotech program. The result of this control was that patients with mitochondrial DNA mutations was having no significant influence in the clinical course.
investigated for SURF1 mutation. A new mutation on the sixth exon (A527C) was detected through sequencing of the exons. This has changed a preserved valine into a glycine. The application of biochemical and molecular genetic assays for the diagnosis of mitochondrial disorders enables identification of a small number of cases. The choice of the tissue where the assays are applied is critical. The variability of the biochemical assays and the fact that none are very specific renders the laboratory diagnosis more difficult. This group of disorder warrants use of all clinical, genetic, radiological, pathological, and biochemical data to reach the diagnosis.

Keywords: Mitochondria, respiratory chain complexes, MELAS, MERFF, NARP, Leigh syndrome, deletion

P97
Effects of toluene on pentose phosphate pathway enzymes in the brain of rats
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Toluene is neurotoxic, which is widely used as an aromatic industrial solvent. This has long been suspected to be ototoxic agents and generates reactive oxygen species. Glucose-6-phosphate dehydrogenase catalyses the oxidation of glucose-6-phosphate in the presence of NADP+ and is the first enzyme in the pentose phosphate pathway. 6-phosphogluconate dehydrogenase, is the second control enzyme of pentose phosphate pathway, is responsible for the regeneration of glutathione, the main cellular reductant. These enzymes are essential to control intracellular reductive potential and might be considered as an antioxidant defence system components. Reactive oxygen species levels are regulated by the supply of reducing equivalents, glutathione and thioredoxin, as well as NADPH generated in the pentose phosphate pathway. Glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase activity, may have an important role in detoxification in toluene toxicity, since reducing power is necessary for reduction of glutathione. Toluene, is extremely volatile compound, is used widely as a solvent of paint and as raw material for the production of various petrochemicals. Because of toluene have some complications on some of the workers that are studying toluene industry; this study investigated the effects of 5 days treatment with toluene (1.3 ml/ kg/ day) and combination with each another on the rat brains. Vitamin treatment may provide neuroprotection against toluene neurotoxicity by directly scavenging reactive oxygen species and by indirectly augmenting their antioxidant capacity.

Keywords: Glucose-6-phosphate dehydrogenase, 6-phosphogluconate dehydrogenase, toluene, brain, and toxicity

P98
Effects of toluene on rat brain glutathione-S-transferase and catalase
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Induction of detoxification enzymes is a major mechanism whereby a wide variety of chemical agents protect organisms against xenobiotics. Some of the chemicals alter the metabolic rate of the xenobiotics by modulating the activities of phase I and phase II drug metabolising enzymes. Induction of enzymes that detoxify xenobiotic metabolites of toxic chemicals may interrupt the neoplastic process. Some complications on some of the workers that are studying toluene industry; this study investigated for SURF1 mutation. A new mutation on the sixth exon (A527C) was detected through sequencing of the exons. This has changed a preserved valine into a glycine. The application of biochemical and molecular genetic assays for the diagnosis of mitochondrial disorders enables identification of a small number of cases. The choice of the tissue where the assays are applied is critical. The variability of the biochemical assays and the fact that none are very specific renders the laboratory diagnosis more difficult. This group of disorder warrants use of all clinical, genetic, radiological, pathological, and biochemical data to reach the diagnosis.

Keywords: Mitochondria, respiratory chain complexes, MELAS, MERFF, NARP, Leigh syndrome, deletion

P99
Effects of toluene on rat brain glutathione peroxidase and glutathione reductase
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The defence of brain cells against peroxide-mediated oxidative damage is essential for maintaining functionality of brain cells. Peroxides are generated continuously in cells that consume oxygen. Among the different peroxides, hydrogen peroxide is the molecule that is formed in highest quantities. Also, organic hydroperoxides are synthesized as products of cellular metabolism. Generation and disposal of peroxides is a very important process in the human brain, because cells of this organ consume 20% of the oxygen used by the body. Peroxides are removed predominantly in cells by glutathione peroxidase. In the reaction catalysed by glutathione peroxidase, the tripeptide glutathione (-glutamyl-cysteinyl-glycine) serves as electron donor to reduce H2O2 to water. The cytosolic isofom of glutathione peroxidase (GPx1) seems to be very important for antioxidative defence of the brain. Oxidized glutathione (GSSG) is reduced to GSH by glutathione reductase that uses NADPH as the electron source. The ratio of GSH/GSSG in most cells is greater than 500. Glutathione plays a very important role in detoxification. In this study we have investigated the effect of toluene on rat brain cytosolic glutathione peroxidase and glutathione reductase. Wistar albino rats were sacrificed after 5 days toluene (1.3 ml/ kg/ day) treatment. The brain removed and after washing with ice-cold sterile physiological saline solution, brain samples were placed in −85°C, where they remain until the procedures for determining enzyme activities. Then each brain was homogenised with ultra turax homogeniser with S18N-10G probe at 22 000 ×g for an hour at 4°C by Beckman ultracentrifuge, and supernatants were used for the measurements of glutathione peroxidase and glutathione reductase activities. Enzyme activities determined spectrophotometrically.

Keywords: Glutathione reductase, glutathione peroxidase, toluene, brain, detoxification

P100
Organotypic spinal cord culture: a model for amyotrophic lateral sclerosis
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Amyotrophic lateral sclerosis (ALS) is a late onset, progressive disease characterized by upper and lower motor neuron degeneration. 90-95% of ALS patients consist of sporadic cases while 5-10% comprises the familial form. 20% of familial ALS patients carry a mutation in the superoxide dismutase 1 (SOD1) enzyme gene. Mice with SOD1 mutation are used as a model for ALS but the results do not satisfy sporadic cases. The involvement of glutamate excitotoxicity in sporadic ALS is widely accepted. In ALS patients, glutamate levels in the CSF are higher than controls. Glutamate is rapidly cleared from the synaptic cleft by a high affinity/high-capacity transporter, the excitatory amino acid transporter 2 (EAAT2) located on astrocytes. A selective loss of EAAT2 has been identified in the spinal cord and selected brain regions of ALS patients. In organotypic spinal cord culture model for ALS, threohydroxyaspartate (THA) which selectively inhibits glutamate transport is used to alter glutamate levels. Chronic exposure to high levels of glutamate results in a gradually progressive neuronal loss. The organotypic spinal cord cultures combine the following advantages: opportunity to use postnatal motor neurons (F2-P16), long-term survival and well-preserved organotypic morphology. For each animal, preparing the culture takes 30 minutes. Sprague Dawley litters at P8 are sacrificed. The contents of thoracic and abdominal cavities are removed. Vertebral column is exposed. Under laminar flow, spinal cord is dissected and meninges are removed. Spinal cord is transferred into sterile Petri dishes containing GBSS (Gey’s Balanced Saline Solution). 350 Micron sections are obtained using Millwain tissue chopper and the sections are collected in GBSS filled Petri dishes. Only the lumbar sections are used to prepare the cultures. Organotypic media containing MEM (Minimum Essential Medium), Hepes, Hanks, horse serum and glutamine is prepared. Six-well plates with inserts are filled with organotypic media. In each insert (Millipore CM)
five sections are placed. Media is changed twice a week. During the first week, since there is abundant astrogliosis, only the media is changed. Starting from the second week, THA (3-25 micromolar) is added into the media to induce the ALS model. Note: This training is supported by 2004 TUBITAK/BAD Travel and Training Scholarship awarded to OG. Keywords: ALS, Organotypic culture

P101

Relative changes in striatal striosome/matrix activation in a rodent model of levodopa-induced dyskinesia

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Objective: Relative changes in neuronal activation, assessed by c-Fos mapping, in relation to behavioural changes were evaluated after administration of two dopamine agonists with different dyskinesia potential in unilaterally dopamine denervated rats, to investigate the possible role of striatal circuit level mechanisms underlying levodopa-induced dyskinesia (DD). Methods: Apomorphine (5 mg/kg, s.k., n=4), lisuride (0.1 mg/kg, s.k., n=7) or isotonic saline (n=4) was administered for 14 days to rats with unilateral nigrostriatal lesion formed by 6-hydroxydopamine. Following a 3-day withdrawal period, a challenge dose of apomorphine was administered and c-Fos expression was analysed by double-immunohistochemistry (anti c-Fos and as a striosomal marker anti m-opioid receptor antibodies) in a visual image analysis programme. Fos expression was analysed seperately for striosomes; matrix and 80 mm matrix area around the striosomes in lateral medio-in area of striatum and relative activation indices were obtained. Additionally the correlation between these indices and behavioral changes were calculated. Results: Behavioral sensitization developed in both treatment groups, being more prominent in the apomorphine group. As shown previously, chronic agonist treatment lead to a change in c-Fos expression from the diffuse patern induced by acute treatment to striosome predominant pattern, significantly in medial striatum. Quantitative analysis demonstrated decreased c-Fos expression in both compartments, but more prominently in matrix, therefore leading relative striosomal predominance. Relative activation indices calculated by ratios of striosomal expression to different matrix areas (striosome/peristriosomal matrix activation index, PSMAI, and striosome/matrix activation index, SMAI) were significantly different for PSMAI in lateral striatum. Despite the presence of more severe behavioral sensitization in apomorphine group, no statistically significant difference was evident among the two treatment groups, possibly due to low number of test subjects. Probably for the same reason, no significant correlation was present between the activation indices and behaviour; but, although not significant, the r-value was highest in the lateral striatum for PSMAI. Conclusion: The differential down regulation of c-Fos expression in striatal compartments following chronic dopaminergic treatment in denervated striatum, implicates the importance of obtaining relative activation indices from a methodological point of view. The relative activity loss in the matrix area just around the striosomes in lateral (motor) striatum would be meaningful if considered in terms of "lateral inhibition"concept and would be important in understanding the compartment level changes of striatal circuits in relation to DD.

Keywords: C-Fos, striatum, striosome, matrix, apomorphine, lisuride

P102

Investigating toxic effects of the potential HIV-RT inhibitor 2-phenoxymethyl-5-chlorobenzimidazole on rat brain


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2-Phenoxymethyl-5-chlorobenzimidazole is a substituted benzimidazole newly synthesized by our team. Some of the benzimidazole root derivatives have previously been shown by our team in screening studies to be inhibitors of HIV-RT and Adenosine Deaminase (ADA) enzymes. This study was designed to test in vitro toxic effects of this compound in rat tissues. Previous evidence has been collected regarding the fact that the compound is likely to be metabolized in or secreted from the liver as well as being excreted from the kidney. The experimental groups consist of the acutely compound injected group, acute solvent injected controls, chronic compound injected group and chronic solvent injected controls as well as a non-injected control. The results were as follows; 48 hours solvent group: Occasionally, neuron cytoplasms display vacuoles. Some neuron nuclei are indented. Some nuclei are vacuolated. Findings suggest occasional axonal and neurilemmal degeneration. Sometimes only axonal degeneration is seen. Some axons are discontinuous with only some remnants of it left. Some vessel walls display oedemulations suggesting contraction. Endothelium resembles that of HEV (high endothelial venules) in such vessels. HEV-like vessels are seen often. Capillaries are usually normal but larger vessels occasionally display convolutions. There are microglia in their close vicinity. Rarely, neighboring the HEV-like vessels the cytoplasmic contour of neurons seem distorted. 15 days solvent group: This group was similar to 48 hours solvent group. 48 hours solvent+drug group: This group was similar to both solvent groups. 15 days solvent+drug group: Some neurons display distorted cytoplasmic contours. Some neuron cytoplasms are vacuolated. Nuclei of considerable amount of neurons are over-indented. Totally, considerable number of cells had gone through nuclear and cytoplasmic degeneration. Oligodendrocytes are in close vicinity of degenerated cells. When compared to previous groups, suggested axonal degeneration display an increase. But mostly, neurilemma display findings suggesting degeneration whereas axons seem to be saved. Sometimes neurilemma is saved but findings suggesting axonal degeneration is seen. (374 words)

Keywords: Brain, Rats, Light Microscopy, 2-Phenoxymethyl-5-Chloro-Benzimidazole

P103

Changes in blood-brain barrier permeability in rats with reduced renal mass-saline hypertension

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The behaviour of brain capillary endothelium to the passage of macro-molecules in a model known as volume expanded, reduced renal mass-saline hypertension (RRM-S) was investigated. For this, initially normotension was documented in all Wistar rats (250-300g) by measurement of systolic blood-pressures (BP) (tail plethysmography) and then underwent subtotal nephrectomy (%70-80). Under ether anesthesia, the right kidney and approximately 50 percent of the left (both poles) were removed. Afterwards all rats offered to consume a low sodium chow. While the control rats drank water, the experimental animals were drank a 1 % NaCl solution. At 3th weeks, after subtotal nephrectomy plus 1 % saline solution drinking, BP of rats with reduced renal mass was significantly higher than baseline level (120±4, 146±6 mmHg, respectively, P<0.03). Three weeks later 3 ml/kg of 3% Evans blue (EB) solution, as a marker blood-brain barrier permeability, was administered intravenously for macroscopic evaluation. With concomitant increase in blood pressure, RRM-S hypertension caused bilateral, widespread EB extravasation in the cortical and deep brain areas. Several studies have demonstrated that an increase in extracellular fluid volume after renal mass reduction and excess sodium intake stimulates the release of ouabain like factors in the plasma which block Na+K+-ATPase. Therefore, it can be assumed that suppressing Na+K+-ATPase in cerebral capillary leads to an increase in blood-brain barrier permeability in rats with reduced renal mass-saline hypertension. Keywords: Blood-brain barrier, hypertension, EB

P104

Neonatal pinealectomy induces morphological alterations in the cerebellum of chick: a stereological study

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Melatonin has an important role in some physiological functions and morphological features of various structures. The effects of pinealectomy on morphological features of developing cerebellum in the chick were investigated using stereological methods. Twelve Hybro Broiler new-hatched chicks were divided into two groups: pinealectomized group (n=6) and non-pinealectomized control group (n=6). Surgical pinealectomy procedure was performed at the age of 3 days. At 8 weeks, all animals were sacrificed for histopathological evaluation and subsequent stereological analysis. It was found that there was no significant difference between non-pinealectomized control and pinealectomized groups for the volumes of each layers of the cerebellum, while the volume fraction of cerebellar layers from pinealectomized animals were lower than from the non-pinealectomized control animals. It was also observed that pinealectomy
reduced significantly the Purkinje cell number in cortex of cerebellum (P<0.01). In conclusion, the results of the current study demonstrated for the first time a pinealectomy-induced histomorphometric changes in chick cerebellum using stereological methods, suggesting that pineal gland/melatonin may play an important role on morphological features of developing cerebellum in the chick.

**Keywords**: Cerebellum, purkinje cell, pinealectomy, melatonin, chick, volume, stereology

**P105**

In silico northern expression profile of an uncharacterized probable GPCR

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Bioinformatics, as a new interdisiplinary study, has an improtant role in in data-mining from the fast growing public biomedical databases. Knowing the expression of a new gene is important to identify its function. Because, the activation period and the and tissue it is present can be observed from the expression profile of a gene. It is possible to predict the expression profile of known or unknown gene with the bioinformatics tools. We have defined the expression profile of a gene previously we have characterized with bioinformatics. The expression profile of the gene was curated from public databases Using NCBI's EST Profile Viewer. 154 ESTs corresponding to the Flj90024 gene was defined in the databank. These ESTs were present in many tissues. However, its expression was found to be very high in spleen and nervous sistem. It was also observed to be highly expressed in during early development.

**Keywords**: EST, In silico expression profile
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**INSTRUCTIONS TO AUTHORS**

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The manuscript which is submitted to the journal must not contain previously published material or material under consideration for publication elsewhere. Accepted manuscripts become the property of NEUROANATOMY and may not be republished.

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**The authors should:**

Submit the one original copy of all elements. Please also submit an electronic version (as a MS word document) and unlabeled image files (as JPEG files) on a PC or MAC compatible CD. The manuscript should be typed double-spaced throughout on one side of A4 paper with at least a 2.5 cm margin on all sides. Number all pages consecutively, beginning with the title page. Prepare a cover letter and a copyright transfer form signed by all authors. Attach a portrait picture of the corresponding author to the cover letter. Organize the manuscript as follows: title page, abstract, introduction, material and methods, results, discussion, conclusion, acknowledgments, references, figure legends, and tables. Keep acronyms and abbreviations to a minimum. When an abbreviation is used, define it at first mention and follow with the abbreviation in parentheses.

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The author(s) is absolutely free to design the paper. There is no limitation in the page count in this category. References, figures, and legends follow the guidelines described below under ‘Original Articles.’ The Abstract section is needed.

**Original Articles**

**Title Page.** The following information should appear: title of article; authors’ name, and last name; affiliations, grant support, and presentation in part or whole at any meeting. Identify the corresponding author and provide full mailing address, phone and fax numbers, and e-mail address.

**Abstract.** The abstract is limited to 250 words, and should describe the essential aspects of the investigation. In the first sentence state the background; in the second sentence state your specific purpose or hypothesis; in the third, fourth and fifth sentences summarize methods, results and conclusion. No references should be cited.

**Introduction.** Include brief background information on what has been done in the past in this area and the importance of your investigation. End with a statement of the purpose or hypothesis of the study.

**Material and Methods.** This section may be divided into subsections if it facilitates reading the paper. The research design, subjects, material used, and statistical methods should be included. Do not mix results and discussion into this section. Do not include manufacturer’s names unless the specific product is important to the procedures performed, in which case the city and state or country of the manufacturer should also be given. Indicate that informed consent has been obtained from patients who participated in clinical investigations. In animal experimentation, acknowledge that ethical guidelines were followed. When appropriate, indicate that approval was obtained from the institution’s review board.

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**Conclusion.** In a separate section, summarize the major findings of the study and their clinical usefulness. This paragraph should address the hypothesis or purpose stated earlier in the paper.

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**References.** Section must be double spaced and begin on a separate page. References are numbered consecutively in the order in which they appear in the text. All references must be cited in the text, where numbers are enclosed in square brackets (not superscript). Papers submitted but not yet accepted for publication should also be cited in the text (Koran A, unpublished data, 2004). Inclusive page numbers (e.g., 491–492) must be provided for all references. Journal names should be abbreviated according to the Current Medicinal Index. All authors should be listed in references.

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While the journal encourages the submission of full-length original articles, it will consider the publication of concise case reports. These should be unusually educational and medically important. In addition to a title page (formatted as described above), include a summary (150 word) describing the essence of the report, an introduction (two or three sentences of background information); a case report (written in the past tense) or a description of the technique, and a discussion highlighting the educational value of the case or the technique. References should be limited (no more than 10 preferred) to only those that give essential background material. References, figures, and legends follow the guidelines described above in ‘Original Articles.’

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