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Abstracts

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ORAL COMMUNICATIONS

S1

Intelligence: is there a sex difference?

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It is known that women are better than men in verbal and men are better than women in spatial intelligence; this difference depends upon sex hormones. The most prominent sex difference is the mental rotation ability. Since the sex difference may be related to the body size, we restudied the sex differences in verbal and spatial abilities, considering the weight and height of the subjects.

In adults (N=89) the perceptual-verbal ability was tested using the "As Test"; the spatial ability was tested using the "Mental Rotation Test". Handedness, eye and foot preference, height and weight of the participants were also recorded. According to the results of MANOVA, only sex was found to be a significant factor, influencing the dependent variables (verbal and spatial test scores, height, and weight) ($F=33.18$, $df=4$, $p<0.001$, eta sq=.62).

That is, as expected, women (140.5, sd=6.27, N=53) outperformed men (135.34, sd=12.36, N=38) in verbal ability; men (16.14, sd=4.90, N=36) outperformed women (12.85, sd=4.43, N=53) in spatial ability; the mean height and weight were significantly greater in men than women. Correlation analysis showed that the mental rotation scores significantly correlated with height in women ($r=0.41$, $p<0.005$); there was a significant negative correlation between these variables in men ($r=-0.48$, $p<0.05$). Verbal IQ did not show any significant correlations with height and weight.

Since the spatial intelligence depended upon height, the sex difference in verbal and spatial abilities were reanalyzed using ANCOVA. As height was taken as a covariant, the mean mental rotation test scores were found to be 13.83 in women and 14.69 in men. There was no significant difference between these marginal means ($F=0.35$, $p>0.55$). Verbal intelligence was not changed during this procedure.

The results showed that there is a definite sex difference in verbal intelligence, the sex difference in spatial ability depending upon height is not a real sex difference opposite to the viewes reported till now, if considered at the population level the relation between spatial ability and height may be a quadratic relation (inverse U), i.e., subjects with short and high stature may have lower scores in mental rotation test than those with moderate height.

Key Words: *intelligence, sex difference, height, weight, laterality*

S2

Hand preference in normal and neurologically disabled children

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In children with no neurological and psychiatric signs and symptoms, and in children with neurological disorders (epilepsy, mental retardation, attention deficiency and hyperexcitability, language disorders, cerebral palsy, ataxi, and traumatic delivery with hypoxy), we studied the possible differences in hand preference, since it is claimed that the left-handededness is associated with brain injuries.

We used a 10-item questionaire to assess the hand preference: writing, ball throwing, scissors holding, thread a bead, paper tearing, putting cubes, book opening, forming dough, buttoning, opening a jar).

Consistent right-handers signed every item as "always right", consistent left-handers signed every item as "always left", mixed right-handers with weak left tendencies wrote yes for thread, mixed left-handers with weak right tendencies put "right" except for two left-hand actions.

In normal children (N=194), 65.5% was consistently right-handed, 5.2% consistent left-handers, 21.6% right-handers with weak left tendencies, and 7.7% left-handers with weak right tendencies, i.e., 65.5% was consistent right-handers, and 34.5% non-right-handers. In children with neurological disorders, the percentage of the consistent right-handers (46.7%).

Was much lower than that of the non-consistent right-handers (53.3%). The differences between the numbers of the subjects in different handedness classes were significantly different in normals and neurologically disabled children ($\gamma^2=11.55$, $df=3$, $p<0.01$).

In light of the above results, it was concluded that the percentage of left-handedness may be higher in children with neurological disorders than those without neurological signs and symptoms, and the percentage of the right-handedness may be lower in children with neurological disorders than normals; this can be a result of the different vulnerabilities of the cerebral hemisphers to brain injuries.

Key Words: *cerebral lateralization, right-handedness, left-handedness, pediatric neurology, brain*

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S3

Asymmetric motor learning and handedness in rats

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Approximately 90% of the human population shows a right hand preference. There is a considerable debate about uniqueness of man in population-level right handedness. Until recently there was a general consensus that among primates, only men have population-level biases in the distribution of hand preference. There was no bias to either side in other animals. Many studies of rats and cats exhibit equal proportions of right- and left-handedness. From the evolutionary standpoint, however, population-level right-handedness should also exist in other animals. Many studies of handedness suggest the existence of population-level handedness biases in primates. Tan and his co-workers supported this opinion using cats and dogs. In rats, there is hand preference, but only in individual-level. In the present study, we designed a new method to test the hand preference in rats. The results suggested that practice can enhance the paw skill in rats, especially the right-paw skill. We used the traditional food reaching test to asses the pawedness in ratso but the animals were in quadrupedal position insetad of the classical bipedal position in the studies of the other authors. The opening in the testing cage was large enough to allow the animals to reach the food easily. Animals were given water and food ad lib except for 2 days prior to and during the food-reaching test. On the day of testing, animals were put in the testing cage. The test finished when the sum of the paw reaches was 50 (right paw+left paw=50). Of 68 rats, 56 (82.4%) were right-handed (right-handed reaching score was equal to or greater than 29), 7 (10.3%) were left-handed (left-handed reaching score was equal to or smaller than 21) and 5 (7.4%) were mixed-handed (right-handed reaching score was between 22 and 28). The distribution of the right minus left paw reaches was not U-shaped as hitheto claimed by others, it was J-shaped like in humans. Estrus cycle was a significant factor influencing the paw preference: most of the right-handed animals were in estrus, most of the left-handers were in proestrus, and most of mixed-handers were in postestrus. In right-handers, frequency of right-paw usage (right-hand skill) increased linearly with testing days, but the frequency of left-paw usage (left-hand skill) did not show any significant changes with the successive testing days. The results suggested that (i) man is not unique in population-level right handedness, (ii) female sex hormones may play a role in the degree of right-handedness, and (iii) handedness may be learnt using the left hemispheric motor strategies. The asymmetric cognitive-motor control in an animal model may have a major impact in many aspects of biology with regard to normal functioning, superior talents, and disease.

Key Words: *Cerebral laterality, handedness, pawedness, learning, motor system, rats, brain*

S4

The effects of different hormon replacement therapy regimes and tamoxifen on affect and locomotion in female rats

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Hormone replacement therapy (HRT) aims to improve life quality during the postmenopausal period and within this context, estrogen replacement therapy is suggested to enhance cognitive processes. During this period, depression is also a major problem that interacts with cognitive processes. The aim of this study is to elucidate the effect of HRT (in ovariectomised-OVX- rats) and tamoxifen, an estrogen receptor antagonist, on depression in a rat model: Porsolt forced swim test. Adult female Spraque Dawley rats were used (n=14 in each group). In HRT groups 4-5 weeks following OVX rats received i.p. peanut oil (16:00-17:00 h), 17-β Estradiol (E, 50 µg/kg, 16:00-17:00 h) and progesterone (P, 2.5 mg/kg, 08:30-09:00 h) for two weeks. The protocol for different group was as fallows: OVX (peanut oil, daily), OVX+E (E, daily), OVX+EP (E and P, daily), OVX+EintP (daily E and intermittent P). To study the effect of E receptor blockade, saline and tamoxifen (5mg/kg) were administered i.p. for 14 days. In Porsolt test rats swam 15 min. on the first and 6 min. on the second day between 09:00-11:00 h. Locomotor activity of the rats were also monitored before and after the Porsolt forced swim test photo-activity cages automatically. The results were analyzed, using the SPSS program, with multivariate ANOVAs followed by post-hoc tests; HRT and tamoxifen groups were analyzed separately. Regarding the behavior of HRT groups during Porsolt tests, freeze duration was different between the groups ($p=0.018$) and post-hoc tests revealed that OVX+E groups displayed freeze behavior significantly less than the OVX ($p<0.05$). Although there was a difference between swim and struggle durations when the two days of testing were compared ($p=0.022$ and $p=0.001$, respectively), the difference between groups was not significant. Tamoxifen treated groups (saline as control) also displayed significant differences in freeze and struggle duration between day 1 and day 2 ($p=0.032$ and $p=0.001$ respectively). Although there was a tendency in tamoxifen treated rats to increase freeze duration, the difference did not reach significance ($p=0.068$). These results suggest that estrogen prevents behavioral despair or may act as an antidepressant.

The evaluation of locomotor activity parameters ("repetead moves" and "cage cross") in the HRT groups depict a significant difference between two test sessions ($p=0.006$ and $p=0.001$, respectively), and also between groups ($p=0.001$ and $p=0.001$, respectively). Post-hoc tests indicated that the OVX+E group was the most and the OVX+EintP group was the least active group. Similarly, tamoxifen treatment resulted in significant differences between the two sessions regarding both parameters ($p=0.001$ and $p=0.001$ for repeated moves and cage crosses, respectively); post hoc tests depicted an increase by tamoxifen of repeated moves during the first session compared to saline ($p=0.022$).

Our results in the rat imply that progesterone is not effective in preventing depression when included in a HRT protocol; however estrogen apparently has an antidepressant effect.

Key Words: *hormone replacement therapy, forced swimming test, locomotor activity, tamoxifen, menopause*

Support: *Menopause Research Project Award, Wyeth 2003*

S5

Sex differences in the conditioning effect of nicotine in rats

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Nicotine has rewarding, conditioning (state dependency), cognitive and emotional effects which involve related as well as distinct mechanisms that mediate in addiction. Contextual cues may play a significant role in the maintenance of the smoking habit. Female

smokers are less successful in smoking cessation programs which employ pharmacotherapeutic approaches, and this has been attributed to a greater impact of state-dependency in women than men. The present study aimed to study sex differences in conditioned place preference (CPP). The CPP apparatus consisted of black and white chambers (associated with nicotine or saline), and a third neutral chamber. Adult Sprague Dawley 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, nicotine (0.2, 0.4, and 0.6 mg/kg, s.c.) or saline were administered alternatively and rats were placed in appropriate chambers (nicotine was paired with the unpreferred chamber) for 15 minutes. Control animals received only saline. 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. Our results show that: (1) Nicotine treatment induces CPP in male and female Sprague Dawley rats; the ffect is stronger in males than females. (2) In males the lower (0.2 mg/kg), and in females the higher (0.6 mg/kg) dose of nicotine is more effective in inducing CPP (3) The behaviour of rats is not uniform throughout the final exploration session. Females spend less time in the non-preferred/nicotine chamber as time progresses whereas males do not.

Our results show that nicotine induces CPP, that this effect is dose dependent and displays a variable time-course with sex differences. These findings can be employed in developing useful strategies in smoking cessation programs.

Key Words: *nicotine, addiction, conditioned place preference, sex differences*

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S6

The effects of different hormon replacement therapy regimes and tamoxifen on spatial learning in the Morris Water Maze in female rats

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Hormone replacement therapy (HRT) is frequently practiced clinically with the aim of improving life quality during the postmenopausal period and within this context, estrogen replacement therapy is suggested to enhance cognitive processes. Spatial learning is an accepted model to test cognitive performance in experimental animals; place learning in the Morris Water Maze (MWM) is one of the most frequently employed tests for spatial learning in rodents. The aim of this study is to elucidate the effect of HRT (in ovariectomised-OVX-rats) and tamoxifen, an estrogen receptor antagonist, on spatial learning in the MWM in rats.

Adult female Spraque Dawley rats were used (n=10 in each group). The effects of HRT and estrogen receptor antagonism were studied in two different but parallel experiments. In HRT groups 3 weeks following OVX rats received i.p. peanut oil (16:00-17:00 h), 17-β Estradiol (E, 50 µg/kg, 16:00-17:00 h) and progesterone (P, 2.5 mg/kg, 08:30-09:00 h) for 12 days before the MWM experiments and continued throughout the MWM testing. The protocol for different groups was as fallows: OVX-V (peanut oil, daily), OVX+E (E, daily), OVX+EP (E and P, daily), OVX+EintP (daily E and intermittent P). To study the effect of E receptor blockade, vehicle (%10 DMSO in saline) and tamoxifen (5 mg/kg) were administered i.p. for 12 days before the MWM experiments and continued as described above. Spatial learning in the MWM was performed with a platform (visible on day 1 and hidden during the following 11 days) always in the same position. Each day, rats were released from four different quadrants of the MWM on four different trials and were allowed 30 seconds to find the platform; time and path length to reach the platform as well as swimming speed were evaluated. On the final probe trial, the platform was removed and the rats were allowed to search for the platform for 60 seconds. During this memory task, the %time spent in the quadrant where the platform had been during acquisition was evaluated. Statistical analyses (MANOVAs) show that, in the HRT groups, during acquisition the time to reach the platform [$F_{(3,40)}$=28.032, $p<0.001$] and the path length to the platform [$F_{(3,40)}$=33.733, $p<0.001$] decreased significantly through days, indicating that rats were learning the place of the platform using spatial cues. However no differences between the groups or interactions were observed. Similar results were obtained for the E receptor antagonist experiments ($p<0.001$ for both measures). During the probe trial for testing memory, similar to acquisition results, all groups spent more than 40% of the total time in the quadrant where the platform had been, indicating that the target quadrant was significantly different compared to other quadrants, but no significant difference was found between the groups. The results of the present study indicate that HRT in OVX rats or estrogen receptor blockade (tamoxifen) in intact female rats do not result in a significant difference regarding cognitive performance in water maze place learning in female rats.

Key Words: *Hormone replacement, Morris Water Maze, spatial learning, tamoxifen, menopause*

Support: *Menopause Research Project Award, Wyeth 2003*

S7

The effect of chronic olanzapine, fluoxetine and combined application on behavioral despair precipitated by stress

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Although the reduction of monoamine neurotransmitters in the synaptic cleft is implicated in depression, some findings indicate that the change in monoamine levels alone cannnot satisfactorily explain the pathophysiology of depression. There are reports that the atypical antipsychotic drug, olanzepin, can be successfully used in the treatment bipolar depression or depression resistant to therapy, in combination with an antidepressant. The aim of the present study was to asses the effects of fluoxetine and olanzepine (separately or combined) in a rat model of depression precipitated by chronic stress.

Male and female adult Sprague Dawley rats (total n=160) were used in the experiments. Half of the rats underwent chronic stress. The protocol for drug treatments was as follows: Fluoxetine (FLX, 5 mg/kg/day), Olanzepine (OLZ, 3 mg/kg/day), Fluoksetine+Olanzepin, Saline. Stress was in the form of restraint in ventilated glass cylinders for 60 min/day and was applied 30 days. Drug treatments began on the 8th day of stress and continued for 23 days. During the last 2 days of drug treatment

restraint stress was discontinued, the rats were tested in the Porsolt Forced Swim Test (FST) and their performance was recorded. Additionally locomotor activity was monitored 3 times: before the experiment, after restraint stress and 24 hours after FST.

Separate multifactorial ANOVAs were performed for FST performance (freeze, swim and struggle) and locomotor activity measures (repeated moves and cage crosses) followed by Post-hoc Bonferroni tests using the SPSS program. Pearson's correlation analyses were performed to see the relations between FST and locomotor activity measures.

In FST, days emerged as a significant effect in all three measures: Freeze duration increased ($p=0.001$), swimming decreased ($p=0.007$) and struggling decreased ($p=0.001$) on the second day compared to the first. Treatment (saline, FLX, OLZ and FLX+OLZ) was also a significant main effect regarding freeze and struggling ($p=0.001$ for both); while FLX prevented despair, FLX+OLZ and OLZ augmented it. Stress increased struggling ($p=0.019$) and decreased swimming durations ($p=0.016$).

Locomotor activity was measured three times: before testing, after stress and after the FSTs were over; hence, sessions was a within-subjects factor. Both repeated moves ($p=0.001$) and cage crosses ($p=0.001$) decreased through sessions implying reduced activity by stress and despair. Repeated moves decreased ($p=0.006$), but cage crosses increased ($p=0.002$) with stress. Drug treatments resulted in reduced activity in both measures in the following direction: saline>FLX > OLZ>FLX+OLZ ($p=0.001$ for both). Sex emerged as a significant effect in cage crosses with females showing greater activity than males ($p=0.001$). Significant interactions between these main effects were observed for both FST performance and locomotor activity, suggesting complex relations. Furthermore, there were weak but significant correlations between locomotor activity and FST performance measures indicating that the more active the animals, the less freeze behavior and the more swimming and struggling they exhibit.

Overall, our results indicate that fluoxetine has a positive effect in preventing behavioral despair precipitated by previous stress exposure; however olanzepine is not effective as an antidepressant and furthermore combined use with fluoxetine augments behavioral despair.

Key Words: *Depression, olanzepine, fluoxetine, stress, sex differences, locomotor activity, forced swim test*

Supported by Ege University Research Fund grant 2002/ TIP/ 019

S8

Potential role of connexin36 in neuronal differentiation: a functional genomic approach

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Gap junctions are the ultra-structural hallmark of electrical synapses, mediating direct electrical coupling in the mammalian brain by bridging the plasma membrane of adjacent neurons. These interneuronal connections are formed by members of a heterogeneous multigene family termed connexins. Besides the function of connexins (Cx) as electrical synapses involved in the synchronization of neuronal networks, gap junctional communication is thought to play an important role in differentiation and development of the mammalian brain.

We used novel functional genomic approaches to unveil the potential role and function of gap junctional communication in differentiation and development of the mammalian nervous system. Transfection of murine neuronal connexin Cx36 into the multipotent neuronal crest stem cell line RT4-AC led to specific alterations of cell morphology characterized by process formation and changes in expression of molecular markers indicative of early neuronal differentiation. The genetic basis of these alterations was investigated by cDNA microarray analysis, RT-PCR and side directed mutagenesis.

The transfection of Cx36 into the stem cells led to the differential expression of 504 distinct annotated genes. Analysis of these differentially regulated genes revealed that some gene subpopulations can be functionally linked to neuronal differentiation and development. We were further able to show for the first time that connexin gene expression can affect a distinct development and differentiation associated signaling pathway in neuronal crest stem cells.

Key Words: *electrical synapse, neuronal stem cell, cDNA microarray, RT-PCR*

S9

Detection of myeloperoxidase activity in various brain regions in 3-nitropropionic acid induced Huntington's disease rat model

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3-nitropropionic acid (3-NPA) is a fungal toxin and inhibits the succinate dehydrogenase activity of both Krebs cycle and electron transport chain. Systemic administration of 3-NPA to rats and primates results in selective striatal lesions. Our previous studies have shown that reactive oxygen and nitrogen species, especially hypochloric acid (HOCl) and nitric oxide, have an important role in the pathogenesis of 3-NPA toxicity. The aim of this study is to measure the activity of myeloperoxidase (MPO) enzyme in various brain regions after systemic administration of 3-NPA in order to determine inflammation.

In this model, 3-NPA (20 mg/kg/day) was administered to 12 weeks old female Sprague-Dawley rats. We injected 0.9% NaCl to the control groups at the same dose. After 10 days rats were sacrificed and the brain regions were removed. Isolated cortex, striatum, hippocampus and cerebellum were homogenized and centrifuged. Pellets were suspended in HETAB buffer, aliquots were added to a reaction mixture containing o-dianisidine and H_2O_2 and the absorbances were measured at 460 nm.

MPO activity was increased in striatum and hippocampus after 3-NPA injection with respect to the control group ($p<0.01$). But in cortex and cerebellum, MPO activity change was not significant ($p>0.05$).

In conclusion, our results have shown that polymorphonuclear neutrophils (PMNs) infiltrate the striatal and hippocampal brain regions after 3-NPA administration. PMNs have the capacity to produce reactive oxygen species via MPO activity. Therefore, 3-NPA administration to rats may cause neutrophil infiltration and an inflammatory response with concomittant free radical generation.

Key Words: *3-nitropropionic acid, Huntington's disease, rat, myeloperoxidase activity, free radicals*

S10

A sample application of a user-friendly event related potential (ERP) analysis software: wavelet analysis of ERPs of mild and moderate Alzheimer patients

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An efficient processing of event related brain potential (ERP) waveforms should involve the decomposition of the signal into basic functional components reflecting different cognitive subprocesses using their time, frequency and space features. Such a decomposition may facilitate to understand the connections among the functions, the anatomical structures and neurophysiological mechanisms of the brain. Wavelet transform (WT) is a powerful tool for extracting ERP components occuring at different time and frequency regions. The studies in our laboratory since 1993 showed that WT can be very useful in identifying the subcomponents of ERPs that are more specifically related to distinct subprocesses of the main cognitive operation in an ERP paradigm. Based on this experience, we developed a software with a graphical user interface that can handle both continuous and epoched data file formats using conventional analysis techniques and WT based decomposition methods, as well as advanced statistical analysis tools. The facilities of the software will be presented by using recent clinical data obtained from patients with Alzheimer's disease (AD). Analysis of the ERPs of AD patients in time domain showed that neither the P3b to classical oddball targets, nor P3a to nontargets of the novelty paradigm can discriminate the early AD cases from age matched controls, which could only be differentiated by the P3b to target stimuli of the novelty paradigm. After WT analysis of the data set, however, specific time-frequency regions in the target P3b potentials of the simple classical oddball paradigm showed highly significant differences between early AD patients and healthy controls, and others differentiated the stage of the disease. The early and fast signal components in alpha (8-16 Hz) band between 60-180 ms after stimulus presentation were correlated with the stage of disease, whereas slow and late components observed in delta (0-4 Hz) and theta (4-8 Hz) bands between 250-1000 ms after stimulus presentation could distinguish healty controls from early AD patients.

Key Words: *Wavelet Decomposition, Alzheimer Disease, Event Related Potentials, P300*

S11

P3a and P3b responses in first-episode schizophrenia and chronic schizophrenia

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Auditory P3a and P3b event-related potentials (ERPs) that were suggested to reflect the automatic and selective attention processes respectively, were evaluated in first-episode and chronic schizophrenia patients compared to two different control groups. Subject groups comprised patients with first-episode schizophrenia (n=31) and younger control subjects (n=36), and patients with chronic schizophrenia (n=26) and older control subjects (n=34). All patients were evaluated during the acute phase of schizophrenia. P3b component was assessed by applying an active oddball paradigm consisting of standard (1000 Hz, 80%) and target (1500 Hz, 20%) stimuli. For the P3a component, a novelty paradigm consisting of standard (60%), deviant (20%) and novel (20%) stimuli was applied. ERPs were recorded from 9 electrodes placed at F3, Fz, F4, C3, Cz, C4, P3, Pz, P4 regions according to the 10-20 system. P3b and P3a were identified as the largest positive peaks occurring within 250-400 ms of the poststimulus period of target and novel stimuli respectively.

P3b amplitude was decreased in first-episode patients compared to younger controls ($p<0.038$). A decrease in P3b ($p<0.0001$) and P3a amplitude ($p<0.001$) was observed in the chronic schizophrenia group compared to controls. In first-episode schizophrenia, P3a amplitude did not differ from that of controls. No group differences for P3a and P3b latency were obtained. These results suggest that in the first-episode of schizophrenia, selective attention processes are impaired, although not as prominent as in chronic schizophrenia, but the automatic attention processes, which are deteriorated in chronic schizophrenia, are preserved.

Key Words: *first-episode schizophrenia, event-related potentials, P3a, P3b, P300*

S12

Wavelet analysis of event-related brain potentials discriminates sub-processes of stimulus evaluation

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Event related potentials (ERPs) are generated by parallel and sequential activation of different neuronal groups in the brain during cognitive processes. Time-frequency analysis is an ideal method to isolate both consecutive and/or temporally overlapping ERP components with distinct frequency characteristics. In this study, assuming that distinct neuronal structures responsible for specific subprocesses of a cognitive operation may operate in different frequency bands, we aimed to decompose auditory ERPs into specific time-frequency components that reflect signal discrimination, motor response, response inhibition, and context updating. Data obtained from 16 healthy volunteers using auditory single-stimulus, oddball, go/no-go, and three-stimulus paradigms were decomposed by a quadratic spline-wavelet transform of 5 octaves. Alpha, theta, and delta coefficients in the post-stimulus period were evaluated in parallel with the conventional P200 and P300 peak analysis. Time-domain analyses revealed that discrimination process decreases the P200 amplitude, and that motor response, response inhibition and context updating processes increase the P300 amplitudes. Time-frequency analysis detailed these results by showing that a prominent alpha oscillation between 0 and 500 ms with a central maximum occurred in non-discrimination condition, whereas it was strongly suppressed and only bitemporal alpha foci remained between 125 and 312 ms in signal discrimination condition. Furthermore, in 250-375 ms interval a right temporal theta component in relation with signal discrimination and context updating, and a parietal delta component that was diminished by signal discrimination and motor response were distinguished. In conclusion, time-frequency components and topographies related more specifically to different subprocesses of stimulus processing could be obtained by decomposing ERPs using wavelet transform.

Key Words: *Event related potential (ERP), P300, P200, time-frequency analysis, wavelet transform*

S13

Automatic classification of Alzheimer patients using wavelet feature extraction of event related brain potentials

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The most consistent electrophysiological findings in Alzheimer's Disease (AD) include a prolonged latency and decreased amplitude of the P3b ERP of the classical oddball paradigm. However, these findings remain relatively undetectable in the early stages of the disease. Novelty paradigm, where unexpected novel stimuli are inserted in the series of target and non-target stimuli of the oddball paradigm, is less studied in AD.

The Wavelet Transform (WT) can partition the Event Related Potentials (ERP) between several independent frequency components with parallel time courses, thus respecting the overlapping component composition of the ERPs. Earlier studies have shown that the analysis of these overlapping components may reveal more detailed information about the ERP changes in pathological conditions. The aim of this study is to find a more sensitive sign of the early AD by wavelet based pattern classification. For this purpose ERP recordings of 37 subjects, divided into 3 classes (11 early stage AD patients, 11 moderate stage AD patients and 15 control subjects) were studied. All patients were referred from the Department of Behavioral Neurology and Movement Disorders, and P3b and P3a potentials in auditory oddball and novelty paradigms were measured in the Department of Physiology of Istanbul Faculty of Medicine. The class and stage information was derived from CDR (Clinical Dementia Rating) and GDS (Global Deterioration Scale) scores.

Based on the results of an earlier study that showed that the mild AD can cause more prominent changes especially in the target P3bs of the novelty paradigm, we focused on this ERP component.

A bayesian classifier was used to discriminate different subject groups. For evaluation, 90% of the total data is selected randomly for training set and the remaining data is used as validation set. We have implemented a search algorithm which explores the wavelet approximation coefficients for best possible features that minimize the classification error.

The level 5 approximation coefficients of the Daubechies 12 wavelet decomposition enabled the most efficient classification of the subjects. Best error rates for the discrimination between AD patients and control group was between 4%, and for classification of the disease stages was 20%.

The results of this study show that the use of the target P3b potentials of the novelty paradigm, preprocessing of these ERPs by using wavelet decomposition, and classification of the resulting feature vectors by means of a Bayesian classifier may lead to a high correct discrimination of the AD patients.

Considering the very mild to moderate levels of the AD patients studied, such a metric might lead to the development of a useful clinical tool that supports the diagnosis of early AD cases based on objective electrophysiological measures.

Key Words: *Pattern classifier, Alzheimer Disease, ERP, Wavelet Transform*

S14

The effects of paclitaxel on nerve conduction velocity and motor unit action potentials in Spraque-Dawley rats.

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In this study the toxic effects of paclitaxel, a chemotherapeutic agent used for the therapy of certain solid tumors, on sensory and motor nerve conduction velocities (SNCV and MNCV) and motor unite action potentials were studied in Spraque-Dawley rats.

Then adult male rats were diveded into two equile groups. Controls were injected 0.5 ml physiological saline, while experimental animals were given paclitaxel (6 mg/kg in physiological saline) for three days i.p. On days 4,7,10 and 13 of experiment animals were weighed, and SNCV-, MNCV- and MUAP-values were recorded by Biopac® MP30 under sedation with pentothal sodium (35 mg/kg). Data were analysed by using unpaired and paired t-Tests and Mann Whitney-U test.

Body weights, MUAP and MUAP-time values were not affected by paclitaxel. The most affected variable by paclitaxel application was SNCV and MNCV, respectively. SNCV- and MNCV-values of the experimental group were 41% and 20% less than those of controls on day 4 ($p<0.001$ and $p<0.05$, respectively). On days 7, 10 and 13 of the experiment mean SNCV values of the experimental group were 35%, 20% and 33% less than that of cotrols, respectively ($p<0.001$, $p<0.05$ and $p<0.01$). In contrary to this, the differences of mean MNCV values were not confirmed. Results of the Mann Whitney-U test confirmed only the differences of the mean values of SNCV between twoo groups for all measurement times ($p<0.01$, $p<0.01$, $p<0.01$ and $p<0.05$, respectively). The results of t-Test for unpaired groups suggested that in experimental group means for SNCV on day 10 ($p<0.01$), for MNCV on days 10 and 13 ($p<0.05$ and $p<0.01$), and for MUAP on day 10 ($p<0.05$) were significantly less when compared with the mean value on day 4 of experiment. Furthermore, the differences for mean body weights of animals between different measuring poits were statistically confirmed.

In control group the difference of the mean MNCV values between days 7 and 10 of experiment was statistically confirmed ($p<0.05$). Furthermore, the mean body weights of controls underwent also to significant changes.

Results indicate that a two-weeks breaktime between chemoterapy sections is insufficient for the recovery of the neuro-musculer toxic effects of paclitaxel.

Key Words: *Paclitaxel, SNCV, MNCV, MUAP, rats*

S15

Event related brain potential correlates of aggression subtypes and the anger traits of healthy young adults with aggression tendency

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There are different modalities to understand the etiology and definition of aggression. The emotional, behavioral and cognitive

processes regarding aggression has not been extensively researched. It becomes more acceptable that aggression is not a uniqe behavior but it has different subtypes. Recently the scales and tests developed to measure human aggression have focused on these subtypes of aggression. In this study our aim is to investigate the neurocognitive processes related with the aggression subtypes and the trait of the anger which is an emotion prior to the aggression by using event related potentials.

140 right handed medicine students without a psychiatric history and drug use were incorporated to the study. Aggression Questionary (AQ) and State Trait Anger Scale (STAS) applied to the students. 127 valid tests were evaluated and aggression and anger scores were documented. Event Related Brain Potentials of 15 students with high general aggression scores and 15 students with low scores have been investigated by using auditory Go/NoGo and Contingent Negative Variation (CNV) paradigms. The amplitudes and latencies of the N100, P200 and P300 waves of the Go- and NoGo responses and mean amplitudes of the early and late phases of the CNV wave were evaluated. Statistical means of general aggression, physical aggression, verbal aggression, anger-aggression, hostility and indirect aggression according to AQ and means of general expression of anger, implicit and explicit expressions and anger control according to subscales of STAS were determined. The students were divided into two groups for each parameter as a result of these subscale measurements. Statistical significance of the differences of event related potential parameters between these two groups were tested by repeated measures ANOVA.

In general aggression group, statistically significant results were obtained only in Go-P200 latancies. In the groups formed according to physical aggressivity scores, both Go- and NoGo-P300 amplitudes of the subjects with high scores were smaller than those of the low score group, and NoGo-P300 latencies were longer. Compared with the low anger control group, subjects with high anger control showed smaller NoGo-N100 amplitudes, and there were significant differences in the fronto-parietal distrubitions of NoGo-N100 amplitudes and NoGo-P300 latancies. In the groups with both high anger-aggression and high explicit-anger scores, the NoGo-N100 amplitudes were smaller. Subjects with indirect aggression had significantly smaller late CNV amplitudes.

These findings support that subtypes of aggression as a behavior show different electrophysiological characteristics, which point to variations in different cognitive processes among the aggression subtypes.

Key Words: *Aggression, aggression subtypes, anger, event related potential*

S16

The effects of MAO A gene polymorphism on ERP potentials

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The interindividual variability in ERP (event related potential) waveforms and heritability of the waveform characteristics is an unclear subject that needs to be studied. There are a number of recent studies in the literature searching for the effects of neurotransmission related genotypes on event related potentials. MAO A enzyme, a form of MAO (monoamine oxidase), plays a critical role in the regulation of catecholamine and indolamine (especially norepinephrine and serotonin) neurotransmission. A variable number of tandem repeats (VNTR) polymorphism was found in the promoter region of the gene associated with MAO A transcriptional activity. In our study, we investigated the effects of MAO A gene polymorphism on N100, P200, P3a and P3b waves of event-related potentials obtained by auditory oddball and auditory novelty paradigms. The amplitude and latency differences of these waves between these allelic groups were analyzed by an ANOVA design with the between-subject factor, genotype, and within-subject factor, topographic distribution. Allele 1 and allele 3 were most common alleles for this gene in our population (98%). There was a significant overall difference between the two allelic groups in N100 latency, which was statistically significant in N100 potentials evoked by the target stimuli of the oddball and the standard stimuli of the novelty paradigm ($p=0.035$ and $p=0.01$, respectively). In both conditions, the N100 latencies of allele 3 group were longer than those of allele 1 group.

No genotypic association was found for the MAO A polymorphism with the overall amplitudes and latencies of P200, P3a, and P3b potentials. However, there was a statistically significant interaction effect of MAO A polymorphism x antero-posterior distribution x lateral distribution of P3b latencies in the oddball paradigm.

Because of the high serotonergic innervation of the primary auditory cortex, MAO A gene might have its strongest effects on N100 potential via serotonin level regulation. These results suggests that, MAO A gene could be a neurobiological substrate for the interindividual variance of auditory N100 potential in several conditions.

Key Words: *event related potentials (ERP), MAO A, N100, P200, P3a, P3b*

S17

Localized effects of neurotrophins on central trigeminal axons in wholemount cultures

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Nerve growth factor (NGF) family of neurotrophins plays an important role in differentiation of axonal processes of sensory neurons. In wholemount explant cultures, exogenous application of NGF promotes exuberant elongation of trigeminal axons, whereas neurotrophin-3 (NT-3) leads to precocious arborization. The aim of present study was to investigate whether local neurotrophin applications affect the growth patterns of central trigeminal axons.

The brainstem explants were prepared from embryonic day 15 rats by leaving trigeminal ganglia (TG) intact on both sides. These wholemounts are laid on to microporous membranes and small sepharose beads loaded with either NGF or NT-3 were placed along the lateral edge of the central trigeminal tract. They were cultured in the serum-free culture medium and fixed by 24-hour intervals to examine the initial behavior and progression of axonal responses.

Labeling of the TG with carbocyanine dye, DiI, revealed that trigeminal axons defasciculated, took abrupt turns from their normal course, and extended towards the bead soaked with NGF. In these cultures, some axons left the central tract and grew in a direction opposite to the bead. NT-3 soaked beads, on the other

hand, induced localized interstitial branching and formation of neuritic tangles in the vicinity of the neurotrophin source.

Double immunolabeling of cultures showed that in both cases, different populations of TG cells express TrkA and TrkC. However, axons responding to NGF beads were predominantly TrkA-positive, while both TrkA and TrkC-positive axons showed similar responses to NT-3 beads.

These results show that localized neurotrophin sources along the routes of embryonic sensory axons in the central nervous system, far away from their parent cell bodies, can alter restricted axonal pathways and induce elongation, arborization responses.

Key Words: *neurotrophic factors, trigeminal ganglion, Trk receptors, axon elongation, axon arborization, development*

S18

The effect of multifonctional scaffold for sustained delivery of neuronal progenitor cells and growth factors in recovery of spinal cord injury

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One limitation of most implant strategies is the development of an inflammatory response and fibrous encapsulation of the implant. To overcome this problem, we can use polymeric microspheres. They can be prepared from poly (lactic acid), poly (lactic-co-glycolic acid) or poly (ethylene glycol-b-lactic acid). In this study, we will use an anti-adherent hydrogel called poly (2-hydroxyethyl methacrylate) (pHEMA). Hydrogel delivers different therapeutic agents as neurotrophic factors (BDNF or NT-3), vascular endothelial growth factor (VEGF), Nogo receptor antagonist peptides (NEP1-40) and neuronal restricted precursor cells (NRPs). In vivo, hydrogels can be easily extracted, their soft, flexible nature mimics natural tissue, and their hydrophilic character minimizes interfacial tension.

Adult female Fischer SD rats will be deeply anesthetized, the C3/C4 spinal segment exposed by a laminectomy, the right side of the C3/C4 segment removed by gentle aspiration and microscissors, the cavity filled with pHEMA and combined with therapeutic agents. Control animals (group 1) receive collagen gel (vitrogen) only. Group II receives pHEMA. Group III receives pHEMA+ BDNF, and group IV receives pHEMA +VEGF. All groups consist of six animals.

At 1 week, 2 weeks and 4 weeks after implantation surgery rats for each time point will be euthanized and perfused for evaluation of the host reaction to different types of grafts.

The C3/C4 and adjacent spinal segments will be removed and serially 20µm thick sagittal sections cut in a cryostat. Sections are analyzed with initial Nissls staining followed by immunohistochemical analyses using the following antibodies: RT97, anti-Laminin, GFAP. Scaffold was well integrated into spinal cord injury site as observed by Nissl stain. Especially at the 1 week time point, significantly, angiogenesis increased in pHEMA and pHEMA+BDNF groups (respectively p=0.02 ve p=0.01). Also at the same time point, number of axons penetrating into the pHEMA+BDNF group enhanced (p=0.01). We did not find significantly increased both angiogenesis and axons penetrating in groups at 2nd and 4th weeks.

Key Words: *scaffold, BDNF, pHEMA, VEGF, spinal cord injury*

S19

Cathepsin B is concomitantly activated with instrinsic and extrinsic apoptotic pathways in the same neuron after cerebral ischemia

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Brain infarction was once considered as an example of coagulation necrosis, but challenging this concept, inhibition of protein synthesis has been shown to decrease ischemic neuronal damage. Although considerable amount of data gathered supporting the role of apoptosis in ischemic neuronal death; electron microscopic studies show that ischemic neurons display apoptotic and necrotic ultrastructural changes together. However, whether or not these mechanisms are actived simultaneously in the same cell, have not been studied yet, in vivo. In this study, caspase activation (caspase 3p20 immunreactivity), a marker of apoptosis, and lysosomal protease activation (cathepsin B degranulation), a marker of necrotic cell death, were evaluated together, in vivo in a mouse model of transient focal cerebral ischemia. Co-activation of these processes with the extrinsic (appearance of truncated Bid), and intrinsic (release of cytochrom c from mitochondria) pathways of apoptosis were also studied. We found that cathepsin B release from lysosomes was colocalized in neurons with caspase-3 activity as well as with appearance of truncated Bid and cytocrome c release, soon after reperfusion. These findings suggest that apoptosis and necrosis are simultaneously activated in the same cell starting from the early stages of ischemia. The coexistence of these processes after NMDA-induced excitotoxic injury was also evaluated. We found that NMDA also induced cathepsin B degranulation along with caspase-3 activation. In conclusion, we have demonstrated that, under in vivo conditions, the biochemical features of apoptosis and necrosis are activated in the same neuron, at the same time, after ischemic or excitotoxic injury.

Key Words: *cerebral ischemia, apoptosis, caspase-3, cathepsin B, truncated Bid, cytocrome c*

S20

The effects of hyperosmolarity on pathogenesis of diabetic neuropathy

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In this study, we investigated how the hyperosmolar condition due to high glucose concentration in diabetic neuropathy affects peripheral neural cells in the mixed cell culture.

Six days old Swiss Albino mice were killed by cervical transaction and dorsal root ganglions (DRGs) with a long pair of peripheral nerve were bilaterally removed under a stereomicroscope and kept in culture medium. The DRGs and their attached nerves were digested with enzymatic procedure. The final suspensions contained both neuronal and nonneuronal (glia) cells. Then, they were transferred to petri dishes which were covered with Type I

collagen gels. For this purpose; media with 1500 mg/dl (G1500) and 3000 mg/dl glucose (G3000) concentrations were used. Same osmolarity levels were assured with glucose and mannitol at equal proportions (G1500+M200) and with mannitol (M3500) only. Preparations which were divided into 5 groups were incubated for 24 hours. Then, each preparation was imaged with a special microscope system (Zeiss Axiovert 200M Cell Observer System) for 2 hours and images were captured at certain time intervals. Migration speeds and mitotic activities of Schwann cells (SCs) and fibroblasts (FBs) were calculated from these captured images.

Migration rates of both cell types were lower with any higher concentrations of glucose and mannitol; being more affected by equamolar amounts of glucose than mannitol. This suggested that, hyperglycemia exerts both metabolic and hyperosmolar toxic effects. In general, FBs were affected more than SCs from hyperosmolarity and earlier than SCs from metabolic toxicity of high glucose. While mitotic activities of SCs were affected earlier than FB in hyperglycemic conditions. FB seemed to be affected from hyperosmolarity, but not from hyperglycemic metabolic toxicity. On the other hand, hyperosmolarity contributed to the decreased mitotic activity of SCs.

In conclusion, hyperosmolarity had equally negative effects migratory activities of both SCs and FBs. Mitotic activities of FBs were affected from only hyperosmolarity, whereas, SCs were affected from both hyperosmolarity and hyperglycemic metabolic toxicity.

Key Words: *diabetic neuropathy, hyperosmolarity, pathogenesis, Schwann cell, fibroblast*

S21

The use of confocal laser scanning microscopy in nervous tissue preparations

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Confocal laser scanning microscopy enables to visualize the three dimensional structure of the inspected preparations. This makes it an ideal technique to study organization of nervous tissue. Fixed or living tissue samples can be visualized with the system provided that they were labelled with fluorescent dyes. In this study, optical sections of several preparations including cultured mouse dorsal root ganglia with regenerating axons and cultured brain slices were obtained using Zeiss LSM 510 Meta Confocal laser scanning microscope. With various antibody combinations, neurons and their processes, glial cells and connective tissue components were succesfully visualized and three dimensional reconstructions were produced from the collected data. The presentation includes the basic principles of the technique and several samples in the form of still and moving images.

Key Words: *Confocal Laser Scanning Microscopy, Three dimensional reconstruction, Nervous Tissue*

S22

The peculiarity of cat cerebellar Purkinje cells to form various autonomous systems in the conditions of narcosis and decerebration.

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In the brain Purkinje cells (PC) are remarkable because of known electrophysiological parameters of simple and complex spikes (SS) and (CS), taking place in their bioelectric activities. The third electrophysiological parameter is known as “inhibitory pause” (IP) set in the SS activity, generated immediately after CS firing, as a rule. In the time of analysis of PC activity the interspike intervals (II) exceeded the average II corresponding to the maximum of the irregular II histogram, at least, as much as 3 times, have been accepted as the 4th of the parameter and was called “Large Intervals” (LI).

Our experiments have been carried out on two groups (anesthetized and decerebrated) of adult cats. The PC with their irregular impulse activities, known to be, exceptionally, characteristic to adult animals, were subjected to statistic analysis. PC were subdivided into three classicaly accepted distinguished groups of “slow” (to 10 imp/s), “intermediate” (10-20 imp/s) and “fast” (20 imp/s and over) cells. The ratio of all registered PC turned out to be distributed on the slow, intermediate and fast cell groups, accordingly, 35.0% (73 PC), 52.0% (108 PC), and 13.0% (27 PC) in the intact, and 9.9% (9 PC), 26.4% (24 PC) and 63.7% (58 PC) decerebrated animals, respectively. These PC activities, 116 PC and 78 PC being in the intact and decerebrated animals, respectively, have been undergone a statistic analysis..

The rise in SS frequency of 16 accidently selected PC from 14.7±2.3 imp/s to 38.2±2.6 imp/s with slowing down of CS frequency from 1.87±0.82 imp/s to 0.05±0.02 imp/s, displaying certain functional relationship between mossy and climbing fibre entrances of PC, point out the existance of a certain autonomous system consisted of a PC and its entrances, being characteristic to an intact animal. In the anesthetized and decerebrated animals the values of average II (35.0±4.8 and 18.0±2.2 ms) corresponding to the maximum of irregular II histogram, SS (28.6±3.8 and 54.2±6.7 imp/s) and KS (0.13±0.04 and 0.63±0.08 imp/s) frequencies, and IP (413.0±40.0 and 89.0±17.0 ms) and LI (427.0±49.0 and 337.0±56.0 ms) durations appeared to be very different**.**

As it is seen from the distribution of PC on the groups, and the data given above, PC activity is distinguished by a greater ratio of fast cells and rather low dimensions of IP and LI in decerebrated animals compaered to that in the condition of narkosis. The variabilities of the electrophysiological parameters of PC activities for intact and decerebrated animals, according to the data obtained**,** display the ability of a PC with its entrances to form a new unit of an autonomous system making it capable of working in a new physiological condition.

Key Words: *cerebellum, Purkinje cell, decerebration, autonomous system, mossy fiber, climbing fiber*

S23

The evolution of cat cerebellar Purkinje cell bioelectric activity as the consecutive changes in its electrophysiological parameters under the action of microwave irradiation

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Our experiments have been carried out on 126 adult cats exposed to MW radiation (460 MHz) (10min.) directed to the head of an animal in the projection of cerebellum by the help of contact applicators, cerebellar PC biopotentials being registered

extracellularly. Animals were anesthetized or decerebrated. MW intensities were selected within the physiotherapeutic norms: 400mW/cm^2 (SAR=28.0±5.7mW/gr) and 1200mW/cm^2 (SAR=81.6±11.5mW/gr).

PC bioelectric activity estimated by the average value of interspike intervals (II), is known to be a certain combination of irregularly appeared electrophysiological parameters: the simple spike (SS) and complex spike (CS) frequencies, durations of "inhibitory pause" (IP) and large intervals (LI). The analysis of the parameter changes under MW irradiation revealed an evolution in PC activity reaction to MW as a consistant succession in starting of the parameters to change.

In the intact animals the increase in MW intensity from 400mW/cm^2 to 1200mW/cm^2 was accompanied by the decrease in the average II from its background value of 35.0±4.8ms to 23.1±2.2ms and 19.5±1.2ms, respectively, but, in the decerebrated animals, to 8.0±2.0ms and 5.0±1.0ms, beginning from 18.5±2.2ms. It appeared that the first factor contributed to this change with the MW intensity enhancement was SS frequency increase (from 28.6±3.8imp/s to 43.2±2.6imp/s and 51.3±3.0imp/s in anesthetized, and from 54.2±6.7imp/s to 120.0±20.0imp/s and 180.0±30.0imp/s in decerebrated animals), and the second that turned out to be IP with its shortening from 413.0±40.0ms to 213.0±46.0ms and 40.0±10.0ms in the case of narcosis, and practical disappearance, beginnig from 89.0±17.0ms for decerebration, at both of MW intensities. It was found out that CS frequency change had been the third, beginning to function in formation of the reaction of PC to MW irradiation (from 0.13±0.04imp/s to 0.12±0.03imp/s (P>0.05) and 0.20±0.04imp/s in the intact animals with the increase of SAR, whereas the increase in CS frequency, biginning from 0.63±0.08imp/s, promoted the formation of burst type of firing for both of MW intensities in the cats decerebrated). In the evolution of the PC bioelectric activity changes, LI has come to light as the last parametric factor. The rise in MW intensity led LI to gain the values of 676.0±54.0ms and 813.0±37.0ms, beginnig from 427.0±49.0ms in the condition of narcosis, and to pack up the spikes into bundles, not only by the increase in the value from 337.0±56.0ms, but also becoming more frequent in its appearance in that of decerebration

The data obtained point out the existence of an evolution in the consecutive changes of the PC bioelectric activity parameters in the course of MW irradiation.

Key Words: *cerebellum, Purkinje cell, decerebration, biopotentials, microwave radiation.*

S24

Lipopolysaccharide reduces blood-brain barrier disruption during L-NAME hypertension followed by angiotensin II in rats

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We investigated the effects of lipopolysaccharide (LPS) on the functional and structural properties of the blood-brain barrier (BBB) and the activity of astrocytes in the N$^{\omega}$-nitro-L-arginine methyl ester (L-NAME) and L-NAME plus angiotensin (ANG) II-induced hypertensive rats. We measured the changes in the BBB permeability using the Evans blue dye and concomitantly in the levels of TNF-α, IL-1β and IL-6 in serum and nitric oxide in plasma. We performed two tight junction-specific proteins, zonula occludens-1 and occludin, and glial fibrillary acidic protein, by using immunohistochemical method. The serum levels of TNF-α, IL-1β, IL-6, and the plasma level of nitric oxide significantly increased in LPS-treated rats (P<0.01). The content of Evans blue dye dramatically increased in cerebellum (P<0.001) and slightly increased in diencephalon (P<0.05) in L-NAME plus ANG II-treated animals compared with control values. However, LPS reduced the increased BBB permeability to Evans blue dye in the brain regions of L-NAME-induced hypertensive rats treated with ANG II (P<0.001). In L-NAME, there was a considerable loss of staining in both zonula occludens-1 and occludin. Staining for zonula occludens-1 and occludin was highly intensive in animals treated with LPS. Glial fibrillary acidic protein staining was seen in a few astrocytes in brains of L-NAME-treated animals. However, this staining showed an increased intensity in the brain sections of animals treated with LPS. This study indicates that, in hypertensive rats, ANG II leads to an increase in microvascular-Evans blue dye-albumin efflux to brain as a result of decreased activity of tight junction proteins and astrocytes following the L-NAME. Consequently, LPS could significantly attenuate this protein's transport to the brain through the increased activity of tight junction proteins and astrocytes, which may be mediated by an increased level of TNF-α, IL-1β, IL-6 and nitric oxide.

Key Words: *Nitric oxide, Evans blue, occludin, zonula occludens-1, glial fibrillary acidic protein.*

S25

Ependymal tumors: correlation of proliferative (mib-1), tumor supressor (blc-2) and anti-apoptotic (p53) indices with histologic types and grading

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Tumor growth depends on cell division and cell death. Cell cycle investigations are of major importance in human neuro-oncology. The objectives of this study are to correlate both proliferative activity of ependymomas as determined by MIB-1 (also known as Ki-67) immunohistochemical analysis and additional p53 and bcl-2 proteins as to assess whether expressivity are correlated with ependymoma subtypes and tumor grade. We investigated routinely formalin-fixed, paraffin-embedded brain and spinal cord biopsy tissues from 33 patients with ependymal neoplasms retrieved from the files of the Neuropathology division, Institute of Neurological Sciences, Marmara University. This study included 2 subependymomas, 3 myxopapillary ependymomas (WHO Grade I), 13 ependymomas (WHO Grade II), 15 anaplastic ependymomas (WHO Grade III). The MIB-1 proliferative index was significantly higher in anaplastic ependymomas (non-parametric Kruskal-Wallis test; p=0.064) with a mild level of correlation. Grade I and Grade II ependymomas showed low proliferative activity in all of ependymoma subtypes and grade specially prominent in myxopapillary ependymoma. Seven tumors (%21.2) showed nuclear p53 positivity with different percentages with staining of nuclei. Positivity was significant

in anaplastic ependymomas (%33.4). We found LI values with significant correlation between supratentorial and infratentorial ependymomas [(Mann-Whitney-U test p=0.0222 (p<0.05)]. These data suggest that high MIB-1 and p53 immunolabeling might be objective indicators of high grade in ependymomas. Additional experiments involving larger numbers of cases with complete and long term clinical follow-up are needed to determine the clinical relevance of bcl-2 and p53 expression and MIB-1 cell kinetic studies in ependymomas.

Key Words: *ependymoma, MIB-1, p53, bcl-2, histologic type, grade.*

This study was presented in the Second Meeting of Asian Society of the Neuro-Oncology (ASNO) in December, 4-7, 2003, Sheraton Grande Walkerhill, Seoul, South Korea, by Sav A

S26

Grouping of oligodendrogliomas: correlation of mib-1, p53 and bcl-2 indices and s-phase fraction. a new mib-1 "cut-off" value (*)

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Oligodendroglioma is a type of infiltrating glioma composed of oligodendrocytes. This spectacular tumor consists 1-4% of all primary intracranial tumors as well as only 4-8% of all glial tumors. A variety of classifications are used for classifying the oligodendrogliomas. The is no

consensus about the definition of pathologic prameters associated with survival rates. Also, to our knowledge no well defined prognosticators are in use for the oligodendrogliomas with a potential for recurrence and progression. The objectives of this study are to correlate both proliferative activity of oligodendroglial tumors as determined by MIB-1 (also known as Ki-67) immunohistochemical analysis and additional p53 and bcl-2 proteins and S phase fraction as to assess whether expressivity are correlated with different histologic types and tumor grades and to define a MIB-1 "cut-off" value.

In order to analyse biologic behaviour of oligodendrogliomas a group of different markers and labeling indices (MIB-1: proliferave), p53 (tumor suppressor gene protein) and bcl-2 (anti-apoptotik gene protein) and DNA flow cytometry are used. Two groups consisted of oligodendroglioma, grade 2 (n=15) and grade III (n=15) are selected. The results of MIB-1, p53, bcl-2 and DNA flow cytometry findings are correlated with histologic types. Also, "cut-off" value for MIB-1 is determined by comparing a set of above mentioned parameters. It has been established that there is a well defined difference between the groups with MIB-1 index higher than 10% from the group with MIB-1 less than 10%. Correlation between histologic type and p53, bcl-2 labeling indices and S-phase fraction are evident. It has been proposed while for grading the oligodendroglial tumors, and analysing their biological behaviour, a cut-off value of 10% could be used for grouping high versus low grade oligodendrogliomas. Also, p53 and bcl-2 labeling indices are used for the understanding of cell kinetics of these tumors.

Key Words: *oligodendrogliomas, MIB-1, p53, bcl-2, S-phase fraction, histologic type, grade.*

This study was presented in the Second Meeting of Asian Society of the Neuro-Oncology (ASNO) in December, 4-7, 2003, Sheraton Grande Walkerhill, Seoul, South Korea, by Sav A.

S27

Superior and inferior main ven oclusion in rat brain: a new model

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Arterial system occlusion in rat brain is a commonly using model in the producing of arterial ischemia and infarct. This can not be said in the issue of venous ischemia. In the medial literature, venous sinus occlusion models and bridging venous sacrifice were used in the producing of venous infarction. We developed a new experimental model for venous occlusion by using superior and inferior anastomotic vein occlusion in rat brain. These venous structures are similarly found in human brains. In here the operation technique and results will be presented.

Key Words: *Rat veins, venous occlusion, experimental model.*

S28

The ultrasound-neurographic demonstration and clinical importance of proximal stump and/or segment swelling in the patients with median nerve entrapment neuropaty, radial and ulnary nerve sectioning

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The aim of this prospective study is to demonstrate the changes of the cross-sectional diameter of proximal segment and/or proximal stump in the patients with median nerve entrapment neuropathy, radial and ulnary nerve sectioning. The secondary aim is to describe the clinical importance of this situation. Cross-sectional diameter was estimated in affected and unaffected nerves by using ultrasonography. In the patients with median nerve entrapment neuropathy, the diameter of proximal segment increased in comparison with those of unaffected individuals. The degree of this swelling was correlated with the severity of clinical symptoms. The proximal stump swelling was clear in the patients with peripheral nerve sectioning.

We speculated that the cause of this swelling, the accumulation of chemical substance during the slowing of neuronal flow and transportation. In here, cases, methods and results will be presented.

Key Words: *Ultrasonographic neurography, peripheral nerves, and proximal stump.*

S29

Changes in whole brain volumetry in Alzheimer's Disease and normal controls: an analysis using voxel-based morphometry

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Morphological investigation of brain anatomy is an important tool for understanding the extent and location of pathological changes that take place with degenerative brain diseases. Studies of morphological change in Alzheimer's disease have demonstrated,

at a macroscopic anatomical level, involvement of medial temporal lobe (MTL) structures consistent with the microscopic pathology of the disorder.

Gross changes in the MTL have also been shown to correlate with cognitive decline. However, current morphological techniques are typically time and labor intensive, and require possibly biased, user-dependent delineation of regions of interest (ROIs) focused on particular areas of the brain. Voxel-based morphometry (VBM) is a non-operator dependent morphological method that has the advantages of being able to assess the entire brain at once for anatomical changes, while at the same time avoiding operator bias in selecting or delineating ROIs.

Eleven patients with a diagnosis of mild to moderate, probable Alzheimer's Disease (PRAD) and 19 healthy elderly control subjects matched for age and years of education took part in the study. High resolution, structural T1 weighted MRI scans were acquired (slice thickness=1 mm). Normalization, segmentation and smoothing of images were performed on using SPM99 (Statistical Parametric Mapping- Welcome Department of Cognitive Neurology) running under MATLAB (Mathworks, Natick, MA).

Group differences were analyzed using a two sample t-test. Significance was defined as $p<0.05$ corrected for multiple comparisons across the entire volume.

VBM analysis displayed decreased gray matter in bilateral hippocampus, parahippocampal gyrus, and superior and middle temporal gyri. Reduced gray matter was also seen in the right amygdala, left basal forebrain (substantia innominata), left prefrontal cortex, and left temporal pole.

In our sample of AD patients and controls, VBM demonstrated reduced gray matter in patients with AD in the temporal lobes, amygdala, hippocampus, and substantia inominata. These regions have all been shown to have severe pathologic involvement in AD. Two previous studies have also used VBM to study AD, but were unable to show anatomical changes at levels that were clearly significant. The face validity of our VBM technique is demonstrated by the finding in our AD subjects of significant anatomical changes in regions previously shown to have high loads of neurofibrillary tangles. VBM could thus serve as a technique for following disease progression in the entire brain, and for making more accurate clinicopathological correlations in the living patient.

Key Words: *Alzheimer's Disease, Voxel-Based Morphometry, Volumetry*

S30

Production of stereological "Unbiased Counting Frame" and "Uniform Point Grid" by visual basic programming in the use of neural morphometric image analysis and research.

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It is clear that the most current, and only unbiased group of methods for morphometry is "Design Based Stereological Methods" in Biomedical Research. "Design Based Stereological Methods" provide the most efficient and accurate estimations for tissue volume, cell number, surface area and cell volume parameters. In stereological neural research, Cavalieri's volume estimation method, more than 600 years old, has been used with the help of uniform point grids. In 1980s, leading outstanding figure in neuro - stereology Viking stereologist Hans J. Gundersen invented and implemented "The Unbiased Counting Frame" for cell number estimation. This frame is the base of several number estimation methods and it can also be used for both vessel and nerve fibre length estimations.

Although some of the "Design Based Stereological Methods" can be implemented with the help of a system consisting of a conventional microscope, a digital or LCD camera and a higer-resolution- monitor, nowadays the stereological estimations are being made by image analysis programmes on computer monitor screens. We produced both "Unbiased Counting Frame" and "Uniform Point Grid" for the use on computer monitor, because the available programmes in the market are too expensive and sufficient resources exist to produce here.

The programme produced is the product of "Visual Basic.NET Programming". The most basic feature of this programme is that the frame is transparent. Thus, the image of the tissue on the computer monitor screen can easily be seen and processed. During the enlargement and the reduction of the frame, x and y edge lengths can be seen in the boxes placed above the frame. In order to estimate the volume of the tissue under investigation more accurately, the frame was divided into squares whose corners are marked with "+" and whose sizes can also be changed. Thus, the volume estimation of the tissue can be made.

Our next aim in production is to have "uniform curves on vertical direction" for surface area estimation, "Isotropic Uniform Random Lines" for cell volume estimation by Nucleator method and to reach the level where we would be able to make some estimations in second order stereology in three-dimension.

Key Words: *design based, unbiased stereology, number estimation, volume estimation, uniform point grid, unbiased counting frame*

S31

Oksoxcarbazepine offers superior pain relief to gabapentin in the treatment of painful diabetic neuropathy

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This is the first prospective, randomised, open-label study comparing the effectiveness of oxcarbazepine with gabapentin, a widely used treatment for neuropathic pain, in treating painful diabetic neuropathy (PDN). Patients with PDN (graded using Dyck's criteria) for >1 year were recruited. No adjuvant analgesics or other antiepileptic drugs were permitted. Patients received oxcarbazepine or gabapentin for 12 weeks: 4-week periods for titration, dose adjustment (tolerability-based) and stable dose. Assessments included relief of pain severity (global VAS), neurological and electroneurographical examinations, and tolerability. Of 44 patients recruited, 41 completed the study: Baseline VAS scores were similar between the groups ($p>0.05$). Oxcarbazepine was significantly more effective in relieving pain than gabapentin ($p<0.01$ at week 12) . Oxcarbazepine provided significant pain relief over time (mean±SD VAS: 6.43±1.54 [baseline] vs 5.29±1.76 [week 4], 3.76±1.64 [week 8], and 2.52±1.57 [week 12, $p<0.001$ vs baseline]). Gabapentin also relieved pain over time (mean±SD VAS: 5.65±1.14 [baseline] vs 4.20±1.40 [week 12], $p<0.001$). Eleven patients taking gabapentin were switched to oxcarbazepine at the end of the study One oxcarbazepine-treated patient and 2 gabapentin-treated patients withdrew due to adverse events (mainly somnolence and/or dizziness) . Thus in patients with PDN, oxcarbazepine monotherapy provides fast and effective pain relief that is superior in efficacy to gabapentin. These data indicate that oxcarbazepine may be a valuable first-line therapy for PDN and should be confirmed in large controlled studies.

Key Words: *Oksoxcarbazepine, pain, gabapentin, diabetic neuropathy*

P1

Mutational analysis of cerebral cavernous patients

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Cerebral Cavernous Malformation (CCM) is one of the most common causes of intracerebral hemorrhage. These vascular malformations are characterized by abnormally enlarged capillary cavities without intervening brain parenchyma and blood brain barrier (BBB).

Mutations in KRIT1, a gene located on chromosome 7q21 cause Cerebral Cavernous Malformation 1 (CCM1) that mainly affect brain vasculature. We recently reported that KRIT1 is expressed in cerebral vascular malformations and hypothesized that mutations in KRIT1 protein alter its expression pattern in CCM tissues. To test this hypothesis, we performed immunohistochemistry using polyclonal KRIT1 antibodies and correlated results of this study with KRIT1 mutational analysis. Using a series of 40 CCM tissues from Yale and Marmara Universities, we show that KRIT1 is expressed by the endothelial cells of CCMs and that KRIT1 staining is variable and inconsistent within the CCM lesions. To correlate these results with KRIT1 mutations, we collected blood samples from 19 CCM patients and tested the DNA extracted from these samples for KRIT1 mutations by using DHPLC analysis and direct sequencing.

As a result, we demonstrate that in patients with KRIT1 mutations, there is weak or absent KRIT1 expression within the CCM lesions. This result supports the hypothesis that the genetic mechanism underlying this vascular malformation is a two-hit model. Consistent with molecular genetic studies, lesions that show strong KRIT1 staining are presumably due to CCM2 or CCM3 mutations. These findings also support the hypothesis that mutations either in KRIT1 or the newly identified CCM2 gene, malcavernin, or the CCM 3 gene contribute to the CCM pathophysiology by interfering with endothelial cell physiology.

Key Words: *cerebral vascular malformations, cerebral cavernous malformatios, KRIT1, mutational analyses*

P2

Involvement in the formation of the blood-retina barrier during early angiogenesis

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Cerebral Cavernous Malformation (CCM) is the second most common cerebral vascular malformation that causes cerebral hemorrhage. The pathogenesis of cerebral cavernous malformations (CCM) is unknown. Structural and ultrastructural studies of lesions which consist of aberrant, dilated capillary cavities and exhibit leaky channels suggest abnormalities of the blood-brain barrier.

The KRIT1 protein is the known product of CCM1, one of three genetic loci that have been implicated in CCM. While the function of KRIT1 is unknown, we have previously demonstrated its localization to endothelial cells and astrocytes suggesting its involvement in the formation and/or maintenance of the blood brain barrier (BBB). To study the potential role of KRIT1 in BBB, we used a well-established retina model in which astrocyte-endothelial cell interactions resemble the BBB.

Newborn rat retinas were harvested each day of the 21-day period of vascularization of the retina. RT-PCR and western blot procedures were utilized to determine mRNA and protein expression levels. Immunohistochemistry with KRIT1, GFAP, and Factor VIII (to show endothelial cells) was also utilized to reveal expression patterns in the tissue.

KRIT1 expression was demonstrated within structures important in formation of the blood-retina barrier including astrocytes and endothelial cells in the developing rat retina. Expression increased during angiogenesis, with mRNA expression peaking at Day 7 and protein expression as vascularization of retina occurs and peaking at 21.

KRIT1 is expressed by the blood-retina barrier on astrocytic foot processes and endothelial cells. These findings suggest that KRIT1 may be important in mediating the interaction between brain parenchymal cells such as astrocytes and endothelial cells. Mutations in KRIT1 seen in CCM may perturb this interaction leading to classical CCM phenotype.

Key Words: *Cerebral Vasculer Malformations, Cerebral Cavernous Malformations, Anjiogensis, Blood-Retina Barier, KRIT1*

P3

Relationship of the antidepressant and anxiolytic effects induced by REM sleep deprivation with nitrergic system

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Although the information about the antidepressant and anxiolytic effects of Rapid Eye Movement (REM) sleep deprivation increase in recent years, the mechanism is still unclear. On the other hand, according to nitric oxide (NO) studies, this mediator might have a role in depression and anxiety. In this respect, antidepressant and dose dependent anxiolytic/anxiogenic effects of nitric oxide synthase (NOS) inhibitors have been shown in some experimental studies. Also there are some studies showing the inhibitor effect of NO on REM sleep period.

The aim of this study is to investigate a possible role of NO on the antidepressant and anxiolytic effects induced by REM sleep deprivation.

Three day platform method has been used in order to induce REM sleep deprivation in rats. Antidepressant effect has been evaluated with "forced swimming" and the anxiolytic effect with "elevated plus maze" tests. To investigate the role of NO on these effects, specific neuronal NOS (nNOS) inhibitor 7-Nitroindazol (7-NI) (50 mg/kg i.p.) was used and nNOS expression analysis was done in the hippocampus at the end of the experiments.

REM sleep deprivation showed antidepressant and anxiolytic effects in rats. 7-NI has antidepressant but not anxiolytic effect

when used alone. It also enhanced the antidepressant activity of REM sleep deprivation groups. Hippocampal nNOS expression decreased significantly in all groups except the group that 7-NI was administrated alone. Consequently, NO might have a role in antidepressant and anxiolytic effects induced by REM sleep deprivation and this interaction may lead the generation of new antidepressant and anxiolytic drugs.

***Key Words**: REM sleep deprivation, depression, anxiety, nitric oxide, neuronal nitric oxide synthase, hippocampus*

P4

The effect of the tryptophan hydroxylase A218C gene polymorphism on event related potentials

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Serotonin (5-HT) which is synthesed from tryptophan with tryptophan hydroxylase enzyme is an important neurotransmitter in the central nervous system. Tryptophan hydroxylase is the initial step and rate-limiting enzyme in the synthesis of serotonin. With studies on TPH gene, 12 polymorphisms have been detected in this gene. It is suggested that TPH gene polymorphism has an association with major depression, schizophrenia, suicide attempts, aggression and anger-related traits. In this study, it is investigated whether A218C polymorphism on the seventh intron with 785 bp that is caused by adenin-cytosine transition of TPH gene has an effect on event-related potentials. For this purpose, ERPs were recorded from forty-eight healthy male volunteers by using the auditory oddball and novelty paradigms. The amplitudes and latencies of the ERP waves from subjects that were grouped according to the A218C polymorphism of TPH gene identified by PCR method were measured, and statistical significance of the differences between the polymorphism groups were tested with ANOVA. The latency of the P200 wave of the C/C genotype group was longer than those of the A/C genotype group ($p=0.007$). There was also a trend for longer P200 latencies obtained with the novel stimuli of the novelty paradigm for the C/C group ($p=0.079$). A significant P200 latency lateralization difference was observed between the two groups for the novel stimulus in the novelty paradigm ($p=0.054$). In the A/A and C/C genotype groups, P200 latency on the right hemisphere was shorter in comparison to those obtained in the midline and the left hemisphere, while in the A/C group P200 latency on the right hemisphere was slightly longer ($p=0.027$). Serotonin activity differentiations have an effect on the ERPs, and beneficial for pathologic situations to explain variabilities at ERPs.

***Key Words:** serotonin, tryptophan hydroxylase, A218C, gene polymorphism, event related potentials*

P5

The N2 wave but not the P3a wave of event-related potentials (ERPs) indexes the novelty of the eliciting stimuli

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The typical novelty paradigm in cognitive electrophysiology is an experimental design, in which the effects of novel stimuli on brain electrical activity are measured using unexpected and ever-changing novel non-target stimuli interspersed in the set of standards and targets in the classical oddball paradigm. The typical event-related potential (ERP) component obtained during the novelty paradigm is an N2-P3a complex occurring in response to novel non-targets, where the P3a is a positivity around 300 ms after the stimulus and has a more centro-frontal topography in contrast to the parietal P3b of the target responses. This N2-P3a complex has been attributed to the novelty effect of non-targets, which shift the focus of the attention reflexively on themselves and induce an orienting response. However, recent studies of Polich et al. have shown that a P3a potential can also be obtained using the three-stimulus paradigm, where instead of the novel stimuli a single third stimulus is used, as long as one of the physical characteristics of this third stimulus is enough far from the general context generated by standard and target stimuli. Therefore, Polich concluded that the P3a does not index the novelty of the stimulus, but rather the disruption of the task context generated by standard and target stimuli by infrequently occurring non-target event.

In the present study, we aimed to test both hypotheses on the genesis of the N2-P3a complex. Therefore, we applied a new experimental paradigm, in which novel stimuli were placed as task-relevant targets instead of being distracting non-targets; and we compared the ERPs elicited with the novel targets in this paradigm both with those elicited by novel non-targets in the novelty paradigm and by constant targets in the standard oddball paradigm. The results show that the P3 potentials obtained with the novel targets have the same parietal maximum as those elicited by the typical targets of the classical oddball paradigm. However, the N2 potential generated by the novel targets is bigger in amplitude compared with the N2 wave in typical target response, and is almost similar to those generated by the novel non-targets of the novelty paradigm. These results support the hypothesis of Polich et al., in that not the novelty effect of the ever-changing stimuli but their role in interrupting the general task context in the "novelty" paradigm elicits the P3a wave, whereas the bigger N2 wave observed both in responses to novel targets and novel non-targets is the real index of the novelty of inducing stimuli.

***Key Words:** event related potentials, novelty, N2, P3a, P3b, task context*

P6

The effect of fasting on event related potentials in mice

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Neurobiological properties of learning and memory have been investigated not only in molecular level but also electrophysiologically by Event Related Potentials. In many experimental learning and memory studies, fasting was used as an impulse. In this study, we aimed to examine the effects of fasting on Event Related Potentials in mice. We placed symmetrically three pairs of cortical electrodes to the frontal, pre and post parietal regions of Balb/C mice's hemispheres. Eight days after operation, we recorded the Event Related Potentials by using

Oddball paradigm with 3500 Hz standard and 3000 Hz deviant stimuli. We recorded early and P300 similar responses from bilateral three localizations.

The early responses were clearer in the rostral and the P300 similar responses in caudal regions. 24 h after fasting (approximately 11% body weight lost), the amplitudes of early responses in frontal loci were increased. After 48 h fasting (approximately 18% body weight lost), the amplitudes of early responses increased compared to basal values, while decreasing compared to 24 h values.

This study showed us that recording from mice are quite easy and safe compared to monkey and rats. It was thought that restriction in calorie can change the neuronal excitability threshold and can increase the amplitude of early responses in 24 h fasting. As it was shown in molecular studies, the change in the excitability threshold can change learning and therefore may increase attention and learning in fasting.

Key Words: *Mice, Fasted, Event Related Potential.*

P7

The effect of antimuscarinic drugs on oddball paradigms in mice

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Is it possible that antimuscarinic drugs can destroy learning by decreasing attention? Improvements in living standards have caused an increase in average human life time in industrial society. General attention to diseases involving learning and memory lost due to extended human life has increased in last decades. New molecular investigation methods and increasing attention to learning and memory resulted in increased information.

Acetylcholine saved its currency by the use of acetylcholine esterase inhibitor in clinical treatment recently and after its established role in learning in experimental studies. There are a lot of studies showing the effects of cholinergic and muscarinergic mechanisms in learning by different ways. In this study we aimed to investigate the effect of scopolamine (muscarinic antagonist, M1-5 nonselective) with Oddball paradigm in fasted mice.

We placed symmetrically three pairs of cortical electrodes to the frontal, pre and post parietal regions of Balb/C mice's hemispheres. Eight days after operation, we recorded the Event Related Potentials by using Oddball paradigm with 3500 Hz standard and 3000 Hz deviant stimuli.

Ten minutes after administration of scopolamine (3 mg/kg i.p) to full and 48 h fasted mice, Oddball paradigm was applied. Scopolamine caused a gradual decrease in the amplitudes from frontal to post parietal loci in response to standard stimuli. But caused a decrease in the amplitudes to deviants without any spatial effect.

The decrease in attention seen in frontal locations with scopolamine was not observed in post parietal regions (sensory process region). Consequently, it was thought that muscarinic antagonists can affect neurobiology of learning with attention suppression mechanism.

Key Words: *Mice, antimuscarinic drug, Scopolamine, Oddball Paradigm.*

P8

Source Localization of EEG and Event Related Potentials with Realistic Head Models

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A 3D head model was constructed using the average MR images from human brain issued by the Montreal Neurological Institute and the locations of the dipole sources of the brain electrical activity were estimated. The EEG signals were prefiltered by integer spline wavelet functions to facilitate the visual inspection of waveforms in multichannel data. The forward problem and the inverse problem were solved by the Boundary Element Method and the MUSIC alogorithm, respectively. The algorithms were tried on epileptic EEG data to localize the focus. The locations of the estimated sources of the interictal epileptic waveforms associated with the Mesial Temporal sclerosis were in agreement with the lesions on the MR images. Research is ongoing to improve the method so that it can be used in the localization of the sources of the Event Related Potentials as well.

Key Words: *source localization, boundary element method, MUSIC algorithm, wavelet transform*

P9

The effects of 900 MHz electromagnetic field on serum TSH and T_3 -T_4 hormones in rats

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It has been discussing for the last twenty years, if the electromagnetic fields (EMF) are harmfull or not for human health. Pulsed radio frequency electromagnetic waves spread out from cellular phones and base stations interests more and more people. Using cellular phones increases day by day. With the inspired thought of the articles that reports the harmfull 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 harmfull effects too and it is believed that they may have side effects on neuroendocrine system. The aim of this study was to investigate the effects of continous 900 MHz EMF on hormonal alterations of the rat organism. Twenty Sprague Dawley male rats were included in the study. The rats were seperated into two groups as control (C) and magnetic field (MF) group. There were 10 rats at each group. MF group was exposed to the carrier frequency of 900 MHz with average power flux density 1±04 mW/cm^2, 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. In this study; serum TSH, total T_3 and total T_4 levels were measured by RIA. The findings we have got in this study are; TSH values at the MF group was significantly lower than the C group. But there were no statistically significant difference between T_3-T_4 values of the MF and C groups.

In conclusions, TSH levels may be affected by thermal effects of EMF. No changes were observed in T_3-T_4 levels. Further investigations were needed on this subject.

Key Words: *electromagnetic field, TSH, T_3, T_4, rat.*

P10

Estimation of head tissue resistivity distribution by using in vivo EEG and MEG data

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Knowledge of tissue resistivities is needed to construct reliable volume conductor models that are used in many areas such as forward/inverse problem solutions, source reconstruction in functional brain imaging, calculation and experimental estimation of electromagnetic field energy caused by the use of RF energy source, spatial temperature estimation of subsurface skin compartments under hyperthermia treatment, detection of ischaemic states or lesions. The data were measured by EEG and MEG sensors during SEP/SEF experiments involving one volunteer in the Biomagnetic Center of Friedrich-Schiller University (Jena, Germany). In the experiment, the median nerve has been stimulated. The MEG data have been obtained by using a 31-channel magnetometer over the somatosensory cortex. Simultaneously, electric scalp potentials were recorded over the contralateral somatosensory cortex using 32 electrodes.

The geometry information has been incorporated into the model by using anatomical boundary information which has been extracted from 256 T1-weighted MRI images separated by 1 mm. The human head is modelled with three regions, namely scalp, skull and the brain. The numerical head model has been constructed and regional resistivities are estimated by using two different estimation algoritms, namely Minimum Mean Squared Error Estimator (MiMSEE) and Bayesian MAP estimator by using MATLAB software. The MiMSEE has been developed and tested in previous studies (Baysal and Eyuboglu 1998, 1999, 2000) and shown to be significantly more accurate and robust compared to conventional least squares algorithm.

In this study, the estimations are obtained by using three different data subsets: (a) only EEG, (b)only MEG (c)combinned EEG-MEG data By using the two estimation algorithms, scalp, skull and brain resistivities have been estimated and estimation variances have been calculated. When all the data are used, the MiMSEE estimator yields 3.197, 66.667, 2.748 ohm.m that belongs to scalp, skull and brain regions, respectively.

The estimation uncertainties are 12.5%, 13.7%, 20.4% respectively normalized to their estimations. The Bayesian MAP estimator yielded higher (20.5%, 27.8%, 20.8%) uncertainty values. From one patient data set, it has been observed that MiMSEE can be used to estimate in vivo head tissue resistivities and observed to be slightly more robust than the Bayesian MAP estimator. Nevertheless, the study is planned to be continued to include more patient data and the effects of utilizing how many EEG / MEG data to be used, has to be investigated.

Key Words: *Resistivity, estimation, EEG, MEG, conductivity, MiMSEE, Bayesian MAP, estimator, SEF, SEP.*

P11

The effect of gabapentin on isometric muscle contractions of rat phrenic nerve-hemidiaphragm preparations

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The effect of anti-epileptic drugs on central nervous system has been elucidated however their action on peripheral system has not been well investigated. Several anti-epileptic drugs such as lamotrigine and ethosuximide have been already studied according to the stimulation-contraction coupling of phrenic nerve-hemidiaphragm preparations yet the effect of gabapentin on neuromuscular junction remains unclear. Gabapentin, developed as a GABA-mimetic agent is a novel anticonvulsant. Besides the treatment of partial seizures it has been used in the management of neuropathic pain. In this study we aimed to investigate whether gabapentin affects muscle contractions elicited by indirect and direct stimulations. Muscle preparations, isolated from Wistar albino rats, were mounted with a resting tension of 2 g for 30 min to reach equilibrium in Krebs solution (133 mM NaCl; 4.9 mM KCl; 1.8 mM $CaCl_2$; 11.9 mM $NaHCO_3$; 0.7 mM NaH_2PO_4; 11 mM Glucose) which was aerated with a mixture of 95% O_2 and 5% CO_2 at 37¼C. Phrenic nerve and muscle were stimulated (indirect and direct stimulation) separately with rectangular pulses at 0.1 Hz, with durations of 0.3 ms and 3 ms respectively. Isometric contractions were recorded via a force displacement transducer on a polygraph (GRASS 7400). Gabapentin incubated preparations were stimulated continuously for 30 min. The difference of tension between the baseline and the final response of muscle twitches was expressed as percentage.

The effect of gabapentin was a slight reduction of tension of direct and indirect contractions at concentrations of 75 µM, 100 µM, 500 µM, 1mM and 5 mM. The most prevailing effect is observed at 100 µM (n=4) that caused 20% of reduction for both contractions.

Key Words: *Gabapentin, isometric muscle contractions*

P12

The effects of gender in model of visceral pain

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Experimental pain models have been used to investigate the effect of analgesic substances, the mechanism of analgesic systems and the neurobiology of pain. Visceral pain models are performed on experimental animals by applying mechanical or chemical stimuli. In this study, female (n=10) and male (n=10) mice were given acetic acid (0.3%,0.2 ml, ip.) as a chemical stimulant, and their behavioural responses were observed. The mice were placed individually in transparent observation chambers and the number of writhes per animal between 5 and 15 minutes following the injection was counted. In addition to recording the number of writhing during the observation period, the number of stretching, rearing and licking behaviours were observed as additional behaviour parameters. The data were statistically analysed with the Mann-Whitney U-test and the Student's t-test. It was observed that the number of writhes increased in female mice ($p<0.01$) compared to the male ones. However, the number of stretching, rearing and licking behaviours did not differ between the gender.

Interestingly, the onset of writhing, stretching and licking behaviours were observed earlier in female mice than in male mice. The first durations of writhing were 208sec, 320sec ($p<0.05$), stretching 245sec, 362sec ($p<0.04$) and licking 126sec, 273sec ($p<0.03$) in female and male mice, respectively. Thus, there are differences in response to inflammation, receptor dispersion, neuromodulator and neurotransmitter dispersion - and the effect of gonadal hormones on these systems in female and male mice. The results of the present study suggest that chronic nociceptive processing differs as a function of gender and gonadal hormones.

Key Words: *model of visceral pain, rat, gender, behaviour parameter*

P13

Modelling and simulation of spreading cortical depression (SCD) wavefront on the surface of human brain

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Spreading Cortical Depression is a biological phenomenon that has been known since 1944 and believed to be related with migrain. It is firstly described by Brazilian physiologist A.A.P. Leao (1944) on the cortex of the rabbit brain. Spreading depression (SCD) is a slowly moving suppression of neuronal activity which propagates circularly through affected regions at a slow rate of 2-5 mm/min. Then the depression continues for about 1-2 minutes through the affected regions and the depressed area is recovered back after several minutes.

By this work, it is aimed to improve a work for human brain similar to the one that is tried before by Baysal and Haueisen (2002) for cavy brain. If the improved model gives successful results, it is expected to obtain some important advances in the characterization of the relation between SCD and migrain.

In this work, the numerical model of the cortex surface is obtained with the help of segmentation from 256 cross-sectioned, T1 weighted, 1mm spaced MRI images, in the Friedrich Schiller University. Then this data is set to three dimensional coordinate data, by converting to discrete finite elements. After obtaining the brain surface data, the surface data is processed by using visual C++ or C++ program, and then the SCD movement on the human brain is started in an arbitrary position. In order to simulate SCD movement, we used some complex trigonometric equations.

After performing SCD simulation, some results in a small area on the brain surface are obtained.

Key Words: *SCD, migrain, brain, modelling, simulation, SCD wavefront, discrete element.*

P14

Electrophysiological changes and wallerian degerenation in the crushing type lesions: an in-vitro study of rat sciatic nerves

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Peripheral nerves are constituted of connective tissue and nerve fibers that lead to the target organ. In the nerve fibers due to different causes, in the neuropathies that affect nerve system, according to the type and intensity of the lesion, there develops first degeneration and then regeneration. In a crushing type of lesion that is the mildest type of all lesions, Wallerian degeneration develops beginning from the lesion site. In this process, electrophysiological changes that can not be found in normal conditions can be seen. After functional recovery and building up the connections with the peripheral targets, regenerated nerve fibers preserve their abnormal morphological and physiological properties. In our study electrophysiological changes in the Wallerian degeneration was observed.

Unilateral crush type lesion of sciatic nerves were performed in the Wistar adult rats. 5, 15, 25 and 38 days after the lesion, sciatic nerves were removed and examined with histological and electrophysiological methods. Electrophysiological changes in the rat sciatic nerves were recorded via sucrose-gap techniques.

In all the crushed nerves, Wallerian degeneration was found. In the 5th day fo the regeneration, resting membrane and compound action potentials were recorded lower than the normal values. The parameters approach to normal levels in the following days that proceed with recovery. The duration of the compound action potentials (depolarization time, half duration) were recorded also longer at the beginning of the degeneration, this duration also approached to normal levels in the following days.

In the beginning of the Wallerian degeneration, the membrane and action potential can not be occurred because of the destruction of the Na^+ channels that are responsible from both of them. In the conditions in which the axon membrane remains intact, K^+ channels that come out because of the destruction of the Schwann cells, stop the conduction via hyperpolarizing the membrane. In the couple of days after the crushing cellular debris, intracellular fluids and widespread edema changes the normal electrophysiological activity. Also insufficient myelination and low density of Na^+ channels in the node of Ranvier, may negative affect the development and the conduction of the action potential.

Key Words: *Wallerian degeneration, nerve regeneration, sucrose gap, electrophysiology*

P15

Conduction blocks with conduction frequency in the crushing type lesions of rat sciatic nerves

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In the neuropathies that occur with crushing in the peripheral nervous system, all the structure of the myelinated and unmyelinated nerves, axon membrane and ion channel are degenerated. In the pathological conditions like these, normal electrophysiolgical properties of the nerves are also deteriorated. Abnormal electrophysiolgical changes continue during the regeneration period. In this study, conduction blocks depending on the frequency were observed in the crushed sciatic nerves.

In our study, sciatic nerves of the female Wistar rats weighing 250-300 g were used. Electrophysiological properties were investigated with the sucrose gap technique 5, 15, 25 and 38 days after the crushing lesion. Sciatic nerves were stimulated with 20 pulses with a frequency of 10, 40 and 100 Hz and compound action potential recordings were evaluated.

The results of the study showed that the nerves can transmit low frequency stimulation but not the high frequency ones 2 weeks after the lesion. Depending on the regeneration in the consequent weeks high frequency stimulation transmission returned to normal levels.

In the regenerating axon membranes, the density of the Na^+ channels that are responsible for the onset of the action potential, are less than the other parts. Myelination is not well developed and diameters of the nerves are thinner than the normal. In this situation, the number of the Na^+ channels that become active in the high frequencies become relatively high. Also small axon diameter with insufficient myelination decreases the conduction velocity and increases the refractory period. These conditions may block the high frequency conduction in the regenerating rat sciatic nerve.

Key Words: *Axon, nerve regeneration, sucrose gap, electrophysiology*

P16

ERD/ERS in continuous movement

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Rolandic mu rhythm, which originates in Rolandic fissure, is recorded from central EEG electrodes as 7-8 waves per second during no-movemet (idle) periods and is suppressed for a few seconds starting before the onset of muscular activity. Suppression of this activity with movement onset and its enhancement following movement offset were called ERD (event-related desynchronization) and ERS (event-related synchronization), respectively. Correlation of the ERD/ERS with movement-related cortical processes has been repeatedly reported. Most of the ERD/ERS literature is about discrete movements, however. It was reported recently that the mu desynchronization due to sustained wrist extension did not last very long and mu activity recovered to its idle level within 5 seconds after the onset of movement. This study showed that, even with continuous muscular activity, motor cortical activity may resume its idle state. And, this would suggest disengagement of motor cortex during sustained movement. In the present study, we examined if mu rhythm of the motor cortex remains suppressed as long as the movement continues.

Subjects performed self-paced extensions and flexions of the four fingers (excluding thumb) of their either hand continuously for at least 30 seconds, at a pace of about one extension-flexion pair per two seconds. At the end of this period, the subjects rested for at least 30 seconds (idle period). No start/stop signal was presented. EEG was recorded bilaterally from 32 central and frontal electrodes.

It was observed that, in the 60 sec-epochs centered by movement onset, ERD lasted as long as the movement continued, but with a gradual recovery of mu activity towards its idle state reference level. In the 60 sec-epochs centered by movement offset, however, we noted an extra desynchronization in addition to that already present just prior to the offset. Shortly after this additional ERD, which was probably related to the decision of stopping the movement, mu activity fully recovered, as expected. Our study yielded two important results: a) ERD is present as long as the movement continues (at least for periods up to 30 seconds); b) ERD may display a sort of adaptation for constantly repeated movements. These results suggest that, contrary to the case of sustained movement, maintenance of even simple periodic movements requires long lasting cortical involvement, though this involvement loosens with time.

Key Words: *ERD, ERS, continuous hand movement, Rolandic mu rhythm.*

P17

The effects of dexamethasone on frog *(Rana Ridibunda)* sciatic nerve action potentials, during oxidative injury

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Nitric oxide (NO) not only acts in different physiological processes, but also shows neurotoxic affects when produced in high concentration by associated species. It is known that the electrophysiological properties of nerve tissues can change in oxidative injury but the effects of glucocorticoids upon these changings are not clear. In this study, we want to see if Dexamethasone (Dex.) that is one of glucocorticoids can recover the action potentials of damaged nerve by oxidative injury. For this purpose, isolated sciatic nerves from frogs were divided in 4 groups, and made following procedure. Isolated sciatic nerves were incubated in frog ringer lactate solution (Group I=Control group). Group II (=Oxidative injury group) was composed by exposure of isolated nerves in 10^{-2} M Sodium nitroprusside (SNP=NO donor). Group III (=Dex. Group), isolated nerves were exposed to 10^{-3} M Dex. solution after 10^{-2} M SNP incubation. Group IV (=Control Dex. group), nerve tissues were incubated in 10^{-3} M Dex. solution. Action potential conduction velocity, maximum amplitude, slope of increasing phase of action potential and areas under signals were measured electrophysiologically, then in order to examine oxidative injury, superoxide dismutase (SOD) activity and thiobarbituric acid reacting substances (TBARS) levels were measured for all groups. Conduction velocity, maximum amplitude, slope of increasing phase of action potential and areas under signals were decrased to 11%, 13%, 16%, 22% respectively with Oxidative injury group compare to Control group but the Dex. group values were even higher than Control group, we measured these values quantitavely as 8%, 40%, 3%, 75% for conduction velocity, maximum amplitude, slope of increasing phase of action potential and areas under signals respectively. Biochemical results also supported with electrophsiological changing. TBARS levels were measured as 34.3, 61.4, 44.10, 39.05 (nmol/g.wet tissue) for Group I, II, III, IV respectively, and SOD activity were measured as 85.09, 64.70, 73.49, 83.52 (U/g.wet tissue) respectively. It is concluded that oxidative stress directly effects nerve action potentials and Na^+ ion current can also be changed and Dexamethasone can recover all these malfunctions, especially electrphysiological parameters.

Key Words: *oxidative injury, nerve action potential, dexamethasone.*

P18

Effects of piracetam on spectral analysis of EEG in Alzheimer and minimal cognitive impairment

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Piracetam increases the fluidity of the neuronal membran and it is effective on the microcirculation. Influence of piracetam in post-stroke aphasia and myoclonic epilepsia have been shown with EEG spectral power analysis. Particularly piracetam is involved in restitution of alpha topography in these patients. On the other hand electrophysiologic effects of piracetam in Alzheimer or minimal cognitive impairment (MCI) patients have not been determined so far. In this study we evaluated spectral EEG analysis of 13 (MCI) and 18 mild or less severe Alzheimer dementia patient after receiving piracetam 2400 mg and 4800 mg respectively for 4 weeks . EEG power spectral values before and after 2400 or 4800 mg piracetam were compared with each other. EEG was recorded using a digital 19-channel EEG system (Medelec/Profile U.K.). Under vigilance control EEG was recorded and at least 3 artefact-free 10-second periods were selected for analysis.

In Alzheimer group 2400 mg piracetam enhances delta band power spectrum significantly ($p<0.019$) but it does not show any significant change after increasing dose to 4800 mg and minimal changes in theta and alpha power spectrum values were not statistically significant. There was no change in beta band spectral

power. Spectral analysis of in MCI patients' delta band power were similar with Alzheimer patients but enhance of delta power was dose dependent. We observed non-significant attenuation in theta band power and there was no difference in alpha and beta band spectral powers .

We emphasize that piracetam enhances slow-wave band powers in Alzheimer and MCI patients and this effect is dose dependent in MCI patients. Although effects of piracetam on cognitive functions is well-known, electrophysiologic correlation has to be evaluated.

Key Words: *Piracetam, EEG, spectral analysis, cognitive, Alzheimer*

P19

Behavioral effects of electrolytic lesioning of the medial septal area

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The medial septal area is an important source of cholinergic projection to the hippocampus. Damage to the septohippocampal projections results in behavioral losses, that are considered to be part of the symptamatology of dementia of the Alzheimer's type. The present study investigated the effect of electrolytic lesion of the medial septal area on behavioral despair, an animal model of depression, elevated plus maze often used to assess anxiety in animals and open field test used to measure exploratory behavior. Loss of septohippocampal projection in the lesioned animals was determined by histological staining for AchE. Compared to controls, an aggravation of behavioral despair in lesioned animals was observed. Septal lesioned animals also were significantly less active in the open field test and spent more time in the open arm of the elevated plus maze before entering the safe closed arm on two consecutive 5 min tests separated by 24 hr. The fact that controls learned to enter the closed arm earlier on the second day whereas septal animals could not points to impaired learning after septal damage. The results indicate lowered anxiety in the lesioned animals. Caution, however, should be taken in such interpretations in that septal lesions also lower exploratory behavior as measured by the open field test. (This research was supported by BAP grant OOR103 to RC).

Key Words: *Behavioral despair, elevated plus maze, open field test, septal lesions*

P20

Effects of melatonin on oxidative stress and spatial memory impairment induced by acute ethanol in rats

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Recently, melatonin has been suggested as an antioxidant that may protect neurons from oxidative stress. Acute ethanol administration produces both lipid peroxidation, as indicator of oxidative stress, in the brain and impair water-maze performance on spatial learning and memory tasks. The present study investigated the effect of melatonin against ethanol induced oxidative stress and spatial memory impairment. Morris water maze used to evaluate the cognitive function of the rats. Thiobarbituric acid reactive substances, which are indicator of lipid peroxidation, and antioxidative enzymes (Glutathione peroxidase and superoxide dismutase) activities were measured in the rat hippocampus and the prefrontal cortex which are form interconnected neural circuits for spatial memory. Acute administration of ethanol significantly increased in thiobarbituric acid reactive substances levels in the hippocampus. Combined melatonin-ethanol treatment caused a significant increase in Glutathione peroxidase activities and a significant decrease in thiobarbituric acid reactive substances levels in the rat the hippocampus. In the prefrontal cortex, there was only a significant decrease in thiobarbituric acid reactive substances levels in the combined melatonin- ethanol receiving group as compared to the ethanol group. Melatonin did not effect the impairment of spatial memory due to acute ethanol exposure, while melatonin was used alone had positive effect on water maze performances. This study demonstrated that melatonin prevent acute dose ethanol-induced lipid peroxidation by increasing Glutathione peroxidase activities in the rat the hippocampus.

Key Words: *Melatonin, oxidative stress, spatial memory, acute ethanol, hippocampus*

P21

Investigation of the relation between memory, learning, success with electrophysiologic and neuropysichological test on primary school students

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In this study, we investigated the importance of electrophysiologic records and neurophysichological test on learning, memory and success in healthy primary school students.

Studies were performed 20 successfull male/female and 20 unsuccessfull male/female 12-15 years old students of Aydinlikevler Burhan Dincbal primary school. EEG-UP records were taken in Fz and Cz regions accondingto the international 10-20 systemswith using Ag-AgCl electrodes.Classic oddball paradigm is performed as stimulation model. The latencies and amplitudes of P300 component of ERP were measured and statistically evaluatedas a function of gender and school success with Student-t test. Neurophysichological assesment was conducted using Visual Aural Digit Span (VADS) test selected evaluated short term memory. The results analyzed with Mann Whitney U test.

P300 latency is significantly different only in male succesfull and unsuccessfull grups at Fz regions. P300 amlitude is significant shorter in unsuccesfull male and female students (Cz record region). There were no differences between gender in VADS test, but there were significant correlation between school success and short term memory performances.

P300 latency longed, amplitude decreased in unsuccess male and female. There was a pozitive correlation between their cognitive function and their school performance. The male group showed reduced P300 amplitude and prolonged P300 latency. These results suggest that the development and the maturation of brain are later in male than female. Short term memory is not different in male and female but it is considerable at school success.

Key Words: *P300 potential, neurophysiologic test, learning, memory*

P22

The evaluation of anxiety in diazepam withdrawal syndrome in rats by measuring changes in grooming behaviour

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Animals exhibit increased grooming behaviour in novel environments. This response, which is decreased by pre-treatment of diazepam, has been suggested to reflect anxiety in animals. Anxiety, a major symptom in diazepam withdrawal syndrome is generally determined by using plus-maze, open field and social interaction tests. In this study, the contribution of changes in grooming behaviour for the evaluation of anxiety in diazepam withdrawal syndrome was investigated.

Wistar albino rats were divided into two groups as control (n=9) and diazepam (n=11). They were treated subcutaneous olive oil (0.4 ml/100 g) or diazepam (15 mg/kg) once daily for 28 days. On day 10 and 48 hours after the last administration, anxiolytic effect of diazepam and withdrawal-induced anxiety were determined, respectively. Novelty induced grooming was evaluated in an observation cage. Total time spent by scratching body and face and licking of body fur, tail, limbs and genital area was determined for 20 min. Exploratory activity was evaluated in an exploration cage by counting number of square crossing, head dipping, rearing and defecation for 5 min. Time spent on open arms and number of open arm entries were determined in an elevated plus-maze for 5 min. Results were evaluated statistically using Mann Whitney U test.

On day 10, diazepam caused anxiolytic activity and thus time spent in open arms increased ($p<0.02$) and grooming decreased ($p<0.05$). Forty-eight hours after the last administrations, due to withdrawal-induced anxiety, number of open arm entries and time spent in open arms decreased ($p<0.01$) and grooming increased ($p<0.05$). No significant differences were obtained in exploratory behaviour on both days.

These results indicate that changes in grooming during administration and withdrawal of diazepam are parallel to changes observed in plus-maze behaviour. Thus, evaluating novelty-induced grooming may contribute to better assessment of anxiety in diazepam withdrawal syndrome.

Key Words: *diazepam, withdrawal syndrome, grooming, anxiety, rat*

P23

Differential effect of pre- and post-session administration of low-to-moderate doses of amphetamine on avoidance learning in rats.

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A number of lines of evidence, mainly from the primate studies, suggest that dopamine agonists, among them psychostimulants such as amphetamine, affect not only motor and emotional aspects of behavior but also cognitive processes, such as attention, learning, and memory. The data concerning the role of dopamine and its agonists in mnemonic processes in non-primate animals are scarce and rather conflicting.

The objective of this study was to evaluate the effects of chronic d-amphetamine administration on avoidance learning in rats.

Four groups of male Moll-Wistar rats were trained in the two-way shuttle box, each group receiving different dose of d-amphetamine sulphate (0.0, 0.5, 1.0, and 2.0 mg/kg) administered i.p.30 min prior the daily session. In the fifth group, a single dose of d-amphetamine (1 mg/kg) was administered after the daily session. The 9-day avoidance training was followed by the 10-day rest period, and the retention test carried out under drug-free conditions.

With pre-session administration, d-amphetamine had mild effect on avoidance frequency but highly increased emission of short-latency responses and thus impaired development of inhibition of delay. On the first retention day, in the control group, Kolmogorov-Smirnov test and two-way ANOVA revealed significant increase in the frequency of short-latency avoidances (disinhibition of the inhibition of delay) associated with the significant increase in response accuracy. Conversely, in the pre-session medicated groups, a dose-dependent decrease in the frequency of fast avoidances and also a significant decrease in overall responding were found. Post-session medicated group, during both, the initial avoidance training and the retraining, did not differ from the control.

In summary, in the present study, the facilitating effect of prior-to-training amphetamine administration on the avoidance execution was observed. However, no positive effect of the drug on response retention and thus on learning was noted in the medicated groups, regardless of the drug's dose and the way of administration: prior to, or after the session. Conversely, administration of a psychostimulant such as d-amphetamine prior to learning had adverse effect on response retention that partially can be related to the drug dissociation.

Key Words: *rat, amphetamine, avoidance response, learning, memory*

P24

The effects of tianeptine pre-treatment on emotional activity and spatial memory in the conditions of acute and chronic immobilization stress

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In this study we investigated the probable protective effects of intraperitoneal (i.p.) tianeptine administration on the rats that were exposed to acute and chronic immobilization stress by using open field, holeboard and Morris water maze tests. 250-300 g. weighted, Wistar-albino male adult rats were divided into 5 groups:

1. Control group: (n=8).
2. Acute immobilization group: the group that was given 1 ml. i.p. normal saline (NS) and then was exposed to acute immobilization stress for 20 minutes (n=9).
3. Acute immobilization tianeptine group: the group that was given 1 ml. i.p. tianeptine (10mg/kg) and then was exposed to acute immobilization stress for 20 minutes (n=9).
4. Chronic immobilization group: the group that was exposed to 6 hours daily immobilization stress for 21 days and was given i.p. 1 ml. NS twice a day (n=7).
5. Chronic immobilization tianeptine group: the group that was exposed to 6 hours daily immobilization stress for 21 days and was given i.p. 1 ml. tianeptine (10 mg/kg) twice a day (n=6).

Results were statistically analysed by using one way ANOVA Tukey test and Student's t test.

When acute immobilization stress and the efficacy of tianeptine is evaluated; in open field and holeboard tests, the number of squares crossed, holes explored and rears were significantly decreased ($p<0.05$) in acute immobile group compared to control group. In tianeptine+acute immobile group the values of these parameters were found to be close to those of the control group. In Morris test, the latency to find the platform was getting shorter in control and tianeptine+acute immobile group, whereas in acute immobile group no significant shortening was found. When chronic immobilization stress and the efficacy of tianeptine is evaluated; in open field and holeboard tests, as in the acute immobilization, the number of squares crossed, holes explored and rears were significantly decreased ($p<0.05$) in chronic immobile group compared to control group. In tianeptine+chronic immobile group the values of these parameters came closer to the values of control group. However, in Morris test no significant shortening was found in both groups. These findings suggest that pre-stress tianeptine administration has protective effect against the anxiety that is developed with acute and chronic immobilization. Futhermore, it is observed that in the acute immobilization conditions tianeptine can preserve spatial memory functions, but it cannot reverse the spatial memory deficits caused by chronic immobilization.

Key Words: *tianeptine, stress, holeboard, open field, Morris test, rat*

P25

Effects of neurotoxic median raphe lesions on scopolamine-induced cognitive impairment in the passive avoidance

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The present experiment investigated the effects of interactions between median raphe nucleus (MRN) serotonergic and septo-hippocampal muscarinic cholinergic systems in attention, nonmnemonic processes such as environmental stimulus discrimination and working (episodic) memory.

The rats with ibotenic acid (Sigma I2765, 2 µl / 2 µg) or sham lesions of MRN received either systemic (1 mg/kg, i.p.) or intrahippocampal scopolamine hydrobromid (2-4 µg / each side) administration prior to training and the conditioned immediate fear memory was tested in the single trial passive avoidance task.

Scopolamin infusion either systemic or intrahippocampal produced a decrease in nonmnemonic escape latencies in sham lesioned rats ($P<0.05$). MRN lesions prevented the effects of intrahipocampal and systemic scopolamine on nonmnemonic escape latency. MRN lesions prolonged avoidance latency immediately after the shock in rats with systemic and intrahipocampal scopolamine treatment ($p<0.01$).

These results suggest that the antagonistic interactive processes between serotonergic projections of the MRN and muscarinic cholinergic system modulate non-mnemonic processess (attention and environmental stimuli discrimination) dependent on the working memory in the inhibitory avoidance.

Key Words: *Working memory, Serotonin, Median raphe nucleus, Muscarinic cholinergic, Passive avoidance, Rats.*

P26

Gender dependent effects of vertical exploratory movement isolation on acquired and innate fear responses in the rats

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In the present study, without deprivation of social contact and horizontal movements, the effects of isolation rearing during developmental period (from 21 day to 3 months), a vertical type's of exploratory behavior, on acquired and inbred fear expression were examined. The experiments were performed on adult male and female Wistar rats. Control rats were embody in the standard conditions. The animals were tested on the passive avoidance task and in the White/Black apparatus after finishing the isolation regimen. Experiment showed that in male rats, isolation of vertical movement resulted in a significant decrease in conditioned freezing (immediate testing, control group 47±5%; experimental group 15±7%, $p<0.01$ and long term testing, control group 31±5%; experimental group 13±5%, $p<0.05$ ANOVA) without changing response latencies in test immediately after the shock and 48 h later. In female rats, the isolation of vertical movement did not affect the acquisition, storage and retrieval of avoidance conditioning. Test in White /Black apparatus showed that rearing isolated male rats exhibited much less unconditioned fear to lighted space when compared to the control male rats. The time spent in the Black box was decreased (control group 195.2±10 s; experimental group 129.8±8 s, $P<0.05$) and latency to entry from White to Black box prolonged (control group 9.3±1.3 s; experimental group 21.8±4 s; $P<0.001$) In female rats, compared to control rats, isolation rearing did not alter behavior in the White/Black test. These findings suggest that when compared to female rats, male rats with vertical movement isolation during developmental period have much more deficit in correct perception of the information related with fear/anxiety.

Key Words: *Rearing behavior, Development, Fear-anxiety behavior, Rat*

P27

Changes in responsiveness to environmental novelty and motor activity in young and adult rats

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It has been reported that when young and old rats are placed in novel environments, old rats exhibit less response to novelty. They show less exploration, less motor activity and more grooming. In addition, old animals do not develop habituation to these behaviours. The numbers of studies, which examine these behavioural changes in adult animals, are very few. Thus in this study, age related changes in response to novel environment, motor activity and behavioural habituation were investigated in adult rats.

Wistar albino male rats were assigned in two groups as young (2.5 months) and adults (11.5 months). Novelty induced grooming was determined in an observation cage. Total time spent by scratching body and face and licking of body fur, tail, limbs and genital area was determined for 20 min. Exploratory activity was evaluated in an exploration cage by counting number of square crossing, head dipping, rearing and defecation for 5 min. Locomotor activity was determined in a motor activity cage for 10 min. These tests were repeated 24 h and 30 days later. Results were evaluated statistically using Mann Whitney U test.

Compared with young rats, adult rats had higher grooming time and lower locomotion ($p<0.01$), square crossing ($p<0.01$) and head dipping ($p<0.05$) scores. Age related differences in grooming ($p<0.01$) and locomotor activity ($p<0.02$) were also present when the tests were repeated 1 and 30 days later. Compared with the initial scores, adult rats had lower square crossing 30 days later ($p<0.01$). Young rats had lower square crossing and lower square crossing and head dipping ($p<0.01$) 1 and 30 days later, respectively.

Adult rats have increased grooming and reduced exploratory and locomotor activities. This pattern of activity shows similarities with that observed in old rats. However, age related changes in habituation to novel environment do not confirm previous findings observed in both old and young animals.

Key Words: *novelty, grooming, exploration, motor activity, rat*

P28

The effects of magnetic field on paw preference in rats

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The purpose of this study is to examine the effects of 50 Hz, 1000 mT static magnetic fields on the paw preference in rats.

In this study 30 male and 20 female, a total of 50 Wistar rats were used. Their paw preferences were determined by the application of the "food obtaining from the tube test". Only the head of rats were exposed to magnetic field. After the exposure of the rats to magnetic field, their paw preference were determined again.

As a result, a statistically significant difference between paw preferences which were determined before and after the exposure of rats to magnetic field couldn't be found.

However, the preference of right paw was a greater in female rats whilst the preference of left paw was a greater in male rats. But there was not a correlation in the between male and female rats, either.

Furthermore the using their right paw of right pawed rats and the using their left paw of left pawed rats increased more and more after they exposed to magnetic field. In other words, the right pawed was more right pawed, the left pawed had been more left pawed.

In conclusion, it is thought that the magnetic field has been effective on paw preference. Numbers of rats should be enhanced to observe these effects more clearly.

Key Words: *static magnetic field, paw preference, cerebral asymmetry, rat.*

P29

The rhythmicity of drinking behavior might be the indicator of the course of cognitive decline in aging

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The suprachiasmatic nucleus (SCN) is the major brain structure in charge of regulating biological rhythms in mammals. Aging and stress are two identified factors that are known to disrupt rhythmicity. Especially, in severe cases of age related neurodegenerative disorders, such as Alzheimer's disease (AD) and dementia, the degree of deterioration in circadian rhythms is even more evident. In relevant literature, there is support for an association between the level of impairment and circadian rhythms and decline in cognitive functioning. The current experiment utilized the pattern of drinking behavior as a measure of circadian rhythmicity. Animals showing disrupted circadian rhythmicity were expected to show poorer performance in Morris Water Maze (MWM) task, a widely used test to measure the spatial ability and memory in rodents. Poor MWM performance is proposed to mimic the complications involving dysfunction of the hippocampus encountered in AD. Additionally, the putative debilitating effect of disrupted circadian rhythms on behavioral despair, an animal model of depression, was investigated using forced swimming tests (FST).

The drinking behaviors of 12 old (25 months of age) and 2 young (17 months of age) male Wistar rats were monitored to determine the level of impairment in circadian rhythmicity for one week. Subsequently, animals were subjected to MWM hidden platform paradigm for 7 days which was then followed by a visible platform task that lasted for 3 days. In the last phase of the experiment, the performance of animals was further observed in FST. Analyses revealed that the old and dysrhythmic animals performed significantly worse than the young and rhythmic animals in MWM hidden platform task. However, old and rhythmic rats did not differ significantly from young and rhythmic animals in the same task. Furthermore, the rhythmicity of drinking behavior was not significantly related to the visible platform performance and durations of immobility in the FST.

The results of the current experiment raise questions about the nature of task demands. It must be considered that the present model has several limitations such as the relatively small size of control group and separation of animals from group housing to single cages for screening the drinking behavior. Monitoring of drinking behavior appears to be a feasible and efficient way for circadian rhythmicity and deserves further consideration.

Key Words: *suprachiasmatic nucleus, circadian rhythms, Morris Water Maze, forced swimming test*

This research was supported by BAP grant 00R103 to RC.

P30

The influence of cerebral lateralization on impairment and performance based balance tests in patients with left and right side hemiplegia

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The aim of this study was to investigate the influence of hemispheric differences on impairment and performance based balance functions in patients with right and left side hemiplegia.

Sixteen ambulatory chronic hemiplegic patients (10 right, 6 left heimplegia) aged between 39-78 years (mean 62±13 years) were recruited into the study. Patients were evaluated as follows;

- Clinical test of sensory integration and balance (CTSIB)
- Functional reach test (FRT)
- Berg Balance Scale (BBS)
- Timed up&go test (TUG)
- Fall Impact Scale (FIS)

Minor disability status was standardized according to Orpington Prognostic Scale Score (1.97±0.37). This prework with limited number of patients showed that although the FRT and FIS scores were higher in the right sided hemiplegic patients, there difference was not significant (p>0.05). Also the BBS and TUG showed no significant difference (p>0.05)

There was no strike difference between the balance functions of patients with right and left hemiplegia. However great number of patients are needed in order to make more reliable conclusion.

Key Words: *Hemiplegia, balance, cerebral lateralization*

P31

The relationships between testosteron (T), progesteron (P), estradiol (E2) and nonverbal intelligence, hand skill and cerebral lateralization in right or left handed females and males

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The associations between T, P, E_2 levels and Nonverbal Intelligence (IQ), Hand Preference (HP), Hand Skill (HS) in relation to cerebral motor lateralization (CL) and sexual dismorfism in right and left handed subjects were studied.

In 180 volunteered C.B.U Medical Faculty Students (between 18-22 age) IQ determined by 'Cattels Culture Free Intelligence Test'. HP was assessed by 'Edinburgh Handedness Questionnaire'. HS was evaluated by 'Peg Moving Test' for both hands separately and difference between them was calculated. The blood had been taken from subjects simultaneously and then P, T, E_2 levels were measured. The results were evaluated by SPSS programme.

There was positive linear correlation between HS and IQ in males. In females it was seen negative significant correlation. But in right handed females it was positive.

In total subjects; there was significantly positive linear correlation between CL and HS. In males it was seen more significantly positive linear correlation between CL and HS than in females. This situation was also seen in right handed males. In right handed subjects there was positive correlation between CL and HS.

In total subjects; there was negative correlation between IQ and E_2 levels. In males, it was seen positive correlation between IQ and P but with E_2 it was negative. In females, there was negative correlation between IQ and T, but it was positive with P.

In right handed males, there was significant negative correlation between IQ and E_2. In right handed females there was significant positive correlation between IQ and P. But with T it was negative. In left handed subjects there was negative correlation between IQ and T.

In total subjects; there was negative significant correlation between HS and T. But with E_2 it was positive. In males there was significant negative correlation between HS and E_2, P. In females there was negative correlation between HS and T, E_2. In right handed males, there was significant negative correlation between HS and E_2, P. In right handed females there was negative correlation between HS and T, E_2.

In right handed subjects it was seen negative correlation between HS and T. But with E_2 it was positive.

It was concluded that there are significantly assosications between T, P, E_2 levels and IQ, HS and CL.

Key Words: *testosteron, progesteron, estradiol, nonverbal intelligence, hand skill, lateralization, females, males*

P32

Comparison of the proliferative index (Ki-67) and the angiogenic factors-vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF) immunexpression with the histopathological grades in the meningiomas

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Grading has major importance in determining the prognosis and the treatment of meningiomas which is the most frequently seen among primary nonglial tumors.

Recently, finding obtained concerning that there is a relation between tumor's grade and tumor angiogenesis and angiogenic growth factors in the meningiomas. In addition, the correlation between the proliferative index with the grade and angiogenesis is a well known fact. With this purpose in our study; in meningiomas of different grades the two angiogenic growth factors VEGF and bFGF immunexpression with Ki-67 (MIB-1) the

proliferative index have been examined;their relations with eachother and with the meningiomas' grades have been investigated. For this, 20 grade I (typical, benign), 11 grade II (atypical), 6 grade III (4 malignant and 2 papillary) meningiomas, in all told 37 intracranial meningioma cases the Ki-67 (MIB-1) Labelling index, VEGF and bFGF expression have been evaluated with the immunohistochemical method.

According to our findings, as grade rises, Ki-67 (MIB-1) Labelling index value also rises. A statistically meaningful relation has been found between the tumor Ki-67 (MIB-1) Labelling index and the grade I, grade II meningioma cases with tumor inside vascular wall bFGF immunoreactivity. However such a relation in VEGF immunoreactivity hasn't been determined.

As a result, in the meningiomas with high proliferative index, the finding that more bFGF immunexpression were determined within the tumor's microvascular structure's endothelial cells demonstrates that this angiogenic growth factor plays an important role in the angiogenesis and malignancy of the meningiomas.

Key Words: *meningioma, grade, angiogenesis, bFGF, Ki-67, malignancy*

P33

Cyclooxygenase-2 expression in astrocytes and microglia in human oligodendrogliomas

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Cyclooxygenases (cox) are potent mediators of inflamation and two cox-izoenzymes, cox-1, cox-2, are described to date. Cox-2 is cytokine-inducible in inflammatory cells and enhanced cox-2 expression has been attributed a key role in the development of edema and immunomodulation in pathologically altered brain tissues. In normal cerebral cortex Cox-2 is present only in neurons, but not in the glial or vascular endothelial cells. The function of microglia in gliomas is unclear. Microglia have both neurotrophic and neurotoxic functions and have been shown to release a variety of cytokines. Our preliminary results showed that the expression pattern of cox-2 is predominantly neuronal

although glial expression was observed with the correlation of high malignancy. In this study we aimed to assess the phenotypes (astrocyte, microglia) of the cox-2-expressing glial cells in various types of human oligodendrogliomas and to compare their expression patterns. For this purpose we employed dual immunohistochemistry for cox-2 and GFAP (astrocyte) or LCA (microglia) in archival formalin-fixed, paraffin embedded human tissue diagnosed as oligodendroglioma. The results showed that cox-2 immunoreactivity is up-regulated in the neurons according to the tumor grade. Most of the cox-2 immunoreactive glia were GFAP-positive in anaplastic oligodendrogliomas and at lesser extend in glioblastomas. Cox-2 and LCA co-localization was detected in more glial cells in glioblastomas.

It may be speculated that the induction of cox-2 in microglia may contribute to the deleterious effects of prostanoids in cerebral edema formation during the progression of oligodendrogliomas. The detection of cox-2 in astrocytes surrounding the necrotic areas might be important to develop new strategies, such as the usage of cox-2 inhibitors in the treatment of oligodendroglioma patients.

Key Words: *cox-2, microglia, astrocyte, oligodendroglioma*

* This study was presented as a poster format at Neuroscience 2004 in New Orleans.

P34

The expression of PDGF ligands and their receptors in cerebrovascular malformations

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Arteriovenous malformations (AVMs) and cavernous malformations (CMs) are two subgroups of cerebrovascular malformations (CVM) and defined as non-neoplastic lesions consisting of abnormal blood vessels of central nervous system. Both AVMs and CMs are dynamic lesions and both are thought to be angiogenically active. Platelet Derived Growth Factor (PDGF) is one of these angiogenic growth factors, it has important roles in processes, which have close relations with physiological and pathological angiogenesis; like embryonic development, wound healing, atherosclerosis and cancer. In this manner showing the expression profile of PDGF in CVM pathogenesis will support the idea of CVM - angiogenesis relation. In this work we aimed to investigate the expression pattern of PDGF ligands and receptors in AVM and CM pathogenesis. Paraffin embedded tissues of 15 AVM and 15 CM lesions were used for immunohistochemical analysis. We support our immunohistochemical data with western blot analysis of total protein extract isolated from fresh tissues of 5 AVM and 5 CM lesions.

Our results showed that, PDGF-AA homo-dimer is expressed strongly in both lesions compared with control group. When two lesions are compared, AVMs express PDGF-AA stronger than CMs, (endothelium $p=0.026$; vesselwall $p=0.009$; adventisya=0.014), ($p<0.05$). PDGF receptor-α specifically expressed more in AVM endothelium than CM endothelium ($p=0.036$). PDGF-BB homo-dimer expression is stronger in CMs when two lesion types are compared, (endothelium $p=0.015$, vesselwall $p=0.011$). PDGF receptor-β, which binds only PDGF-B ligand, is specifically expressed more in CM endothelium than AVM endothelium, ($p=0.008$.)

In conclusion, our data revealed that cerebrovascular malformations have a relation with PDGF signaling. And the expression pattern of different isoforms of PDGF ligands and receptors in two different subgroups of cerebrovascular malformations indicate that these isoforms may have a role in representing the different pathological characteristics of these two subgroups.

Key Words: *cerebrovascular malformations, angiogenesis, PDGF*

P35

Investigation of KRIT1/cerebral cavernous malformation 1 protein localization in diverse human tissues

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Cerebral cavernous malformation (CCM) is a sporadic or inherited disease of the microvasculature mainly affecting the central nervous system (CNS). Structural and ultra-structural studies of CCM lesions which consist of aberrant endothelial cells with disturbed cell to cell contact and dilated capillary cavities and exhibit leaky channels demonstrated presence of abnormalities of the blood-brain barrier. Three genetic loci (Cerebral Cavernous Malformation 1-3) associated with CCM was identified using molecular genetics methods, but only KRIT1 gene, localized on CCM1 locus, was cloned.. The function of KRIT1 protein is still unknown thus pathogenesis of the disease could not be explained. In order to understand Krit1 protein functions and its role in pathogenesis of CCM. We used RT-PCR, Western blotting to investigate KRIT1 mRNA and protein expression in fetal and adult human tissues, respectively, and immunohistochemistry to verify the localization in adult tissues. We have found that KRIT1 expressed not only in CNS but also in many other tissues with different expression patterns. And our immunohistochemical results shows that in all tissues examined KRIT1 protein localizes in vascular formations especially in capillaries and arterioles. Interestingly, KRIT1 expression is significantly increased in tissues that contains blood-tissue barrier such as thymus and CNS. KRIT1 is strongly expressed in cell types that form blood-brain barrier (BBB) like astrocytes, astrocyte feet and endothelial cells as well as pyramidal neurons. This might provide an answer for why CCM is mainly affecting brain and also shows BBB formations involved in the pathogenesis of CCM. As a result, in cerebral cortex expression of KRIT1 by astrocytes and astrocyte feet and endothelial cells and pyramidal neurons shows that KRIT1 plays a key role in cerebral angiogenesis and formation or regulation of blood-brain barrier.

Key Words: *Cerebral cavernous malformation (CCM), of KRIT1/ cerebral cavernous malformation 1 protein, blood-brain barrier, immunohistochemistry, Western blot, RT-PCR*

P36

The effect of vitamin E on the superoxidase dismutase activity and malondealdehyde levels on frontal lobe tissue of rats in formaldehyde intoxication.

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Formaldehyde is widely used in a variety of applications, especially in medicine and industry. It has deterious effects on the respiratory tract, skin, eyes and central nervous system. But, there are only a few studies about biochemical and histopathological changes of frontal lobe caused by formaldehyde toxicity. Vitamin E, a lipid-soluble vitamin, is a chain-breaking tissue antioxidant that is present in all cell membranes in low concentrations, and to acts as a scavenger of highly reactive oxygen radicals. The aim of the present study was to investigate a possible protective influence of Vit E pretreatment on superoxide dismutase (SOD) enzyme activity and malondialdehyde (MDA) levels in the frontal lob tissue of rats treated with formaldehyde. We used male 3-month-old Wistar albino rats weighing 280 g in this experiment. The animals were randomly divided into one of three experimental groups: Control, formaldehyde treated, and formaldehyde+vitamin E treated groups. Each group consisted 6 animals. Formaldehyde treated, and formaldehyde+vitamin E treated groups received intraperitoneal injection of 10 mg/kg formaldehyde for 10 days. In addition, formaldehyde+vitamin E treated group received intramuscular injection of 300 mg/kg vitmin E for 10 days. After the treatment, the animals were sacrificed and frontal lobe tissues were removed for biochemical and histological investigation. Formaldehyde group had significantly increased tissue MDA levels and decreased SOD enzyme activity in frontal lobe tissue compared to controls. Vitamin E treatment decreased MDA levels and prevented SOD enzyme inhibition. In control group, the morphology of the frontal lobe neuronal cells was normal. In formaldehyde group, the number of neuronal cells was significantly less than both control and vitamin E groups. In this group, shrunken cytoplasma of neuronal cells was observed and they had picnotic or large hiperchromatic nuclei . The morphology of neuronal cells in the vitamin E group was similar to that of the control group. In conclusion, vit E brought disturbed oxidant and antioxidant balance in the formaldehyde groups close to control values. Our findings clearly indicated that vitamin E has the potential to prevent neuronal damage caused by formaldehyde toxicity.

Key Words: *formaldehyde, frontal lobe, malondialdehyde, superoxidase dismutase, histology, rat.*

P37

Hippocampus glutamic acid decarboxylase activity in acute toxicity of lithium in rats

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Central nervous system is mainly affected in acute toxicity of lithium. Severe memory impairment and a permanent seizure disorder have been reported as sequelae of this toxicity. The mechanism behind this toxicity has not been clarified yet. Our previous studies showed that glutamatergic system may be involved in the effects of lithium on behaviour of rats. Present study was designed to investigate the role of this system in acute toxicity of lithium. Acute lithium toxicity in rats was done administering lithium chloride (LiCl) at the dose of 18 meq/kg intraperitoneally. At this dose 55.5% of rats die within 24 hour. The activity of glutamic acid decarboxylase (GAD) enzyme which is responsible to metabolise glutamate was determined by fluorimetric method in hippocampi of rats received saline (0.9% NaCl) or LiCl. Hippocampi were taken one hour after the injections. The hippocampus GAD activity in LiCl group was not different from saline group. This result suggests that glutamate metabolism does not change in hippocampus in the early period of acute lithium toxicity. Our studies will continue to investigate the possible change of GAD activity in hippocampus and other brain regions in the late period of this toxicity.

Key Words: *lithium, toxicity, glutamic-acid-decarboxylase, hipocampus, rat*

P38

FGF-2, fibronectin and VEGF expression in craniopharyngiomas

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Craniopharyngiomas are histologically benign epithelial neoplasms of the sellar region that often exhibit aggressive and invasive growth. Tumor proliferation, spread and recurrence are angiogenesis dependent and investigated the significance of vascularization relative to biologic behavior. Fibroblast Growth Factor-2 (FGF-2), Fibronectin and Vascular Endothelial Growth Factor (VEGF) are the factors assessed by immunohistochemical analysis in paraffin embedded tissues of 10 craniopharyngiomas, which is separated into two groups. One is no recurrence after the total excision of tumors in 2 years and the other is tumors that recurred after to the total removal. We aimed to analyze the cellular distribution and the expression pattern of these factors in recurrent and non - recurrent craniopharyngiomas. There has been only one trial reported in the literature for the angionesis of craniopharyngiomas and just VEGF was published. Our data include FGF-2, Fibronectin with VEGF. Our results revealed that FGF-2 is expressed 75% of patients strongly just in recurrent craniopharyngiomas. No expression was seen in non-recurrent group. This is the first data reported as a comparision of angiogenic factors in recurred craniopharyngiomas and non-recurred craniopharyngiomas. Fibronectin expression pattern is similar in both craniopharyngiomas. VEGF expression was seen in macrophages and stroma of the tumors. All stromas of recurrent group expressed VEGF, but just in 50% of non recurrent group showed expression of VEGF. Our data implied that angiogenic activity is correlated with the recurrence of craniopharyngiomas. Both VEGF and FGF-2, which are potent angiogenic factors, may affect the recurrency as their expression levels significantly high in recurrent craniopharyngiomas.

Key Words: *craniopharyngiomas, angiogenesis, angiogenic factors.*

P39

The effects of Ca^{2+} and EDTA on glucose-6-phosphate dehydrogenase activity inhibited by Zn^{2+}

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Glucose-6-phosphate dehydrogenase (D-Glucose-6-phosphate: $NADP^+$ oxidoreductase (E.C 1.1.1.49) has been purified from six-month old lamb kidney cortex by two-step purification procedure, 2', 5'-ADP Sepharose 4B affinity and DEAE Sepharose Fast Flow anion exchange chromatography. The enzyme was stable at 4¼C for a week. Zinc is a known inhibitor of the enzymes.

The purified enzyme was completely inhibited by Zn^{2+} ion at 3 mM concentration. Inhibition kinetics of glucose-6-phosphate dehydrogenase was studied in detail. On the other hand Ca^{2+} and EDTA reversed partially glucose-6-phosphate dehydrogenase inhibition by Zn^{2+}. This observation suggests that EDTA may act via a chelating mechanism. And Ca^{2+} may compete with Zn^{2+} for the same binding site on the enzyme. In addition Ca^{2+} inhibited the enzyme activity above 8 mM concentration. This is the first report for inhibition of glucose-6-phosphate dehydrogenase from any source by Zn^{2+} and reactivation by Ca^{2+} or EDTA.

Key Words: *Glucose-6-phosphate dehydrogenase, lamb kidney cortex, inhibition, Ca^{2+}, and Zn^{2+}.*

P40

The effect of Ca^{2+} and EDTA on glucose-6-phosphate dehydrogenase activity inhibited by Cd^{2+}

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Glucose-6-phosphate dehydrogenase (D-Glucose-6-phosphate: $NADP^+$ oxidoreductase (E.C. 1.1.1.49) catalyses the first and rate limiting step in the pentose phosphate pathway. The aim of this study was to evaluate inhibitory effect of Cd^{2+} on glucose-6-phospahte dehydrogenase and the effect of Ca^{2+} or EDTA on this inhibition. We used 2', 5'-ADP Sepharose 4B affinity and DEAE Sepharose Fast Flow anion exchange chromatography for purification. The enzyme was purified from lamb kidney cortex, about 3640 fold with an overall yield 26.32%. Cadmium is one of the toxic heavy metal that can cause enzyme inhibition. We have found that Cd^{2+} ions inhibited lamb kidney cortex glucose-6-phosphate dehydrogenase activity completely at 3.5 mM concentration at described conditions. Adding Ca^{2+} or EDTA to the assay mixtures, the inhibition was reversed only at low Ca^{2+} or EDTA concentrations.

Key Words: *Glucose-6-phosphate dehydrogenase, lamb kidney cortex inhibition, Ca^{2+}, and Cd^{2+}.*

P41

Modulation of nitric oxide synthase by stress in rat brain

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Nitric oxide (NO) modulates the secretion of stress hormones (adrenocorticotrophic hormone and corticosteron) and exposure to various stressors increases the activity of NO synthetase (NOS) in the limbic-hypotalamo-hypophiseal-adrenal (HPA) axis. Besides, following activation of the stress axis, glucocorticoids have been shown to decrease the transcription and activity of NOS by means of a biofeed back mechanism. However, somatic and behavioral reflections of acute and chronic stress are considerably different. It is well known that stress responses and cerebral NO levels are effected by sex differences. Amygdala plays a key role in central evaluation of stress. The aim of this study is to determine the impact of acute and chronic stress on NOS expression in the HPA axis and to evaluate the possible effects of sex differences.

42 Sprague Dawley rats (3-4 months-old, F/M:21/21) were used. Stress was administered by restricting motor activity in ventilated glass sylinders under light exposure for 60 minutes during the day. The effectiveness of this method, in acute (once) and chronic (15 days) stress conditions was confirmed by determining ACTH and corticosteron hormone levels. In this study, 42 rats were divided into 3 groups: acute stress, chronic stress and control. Each of these groups consisted of equal numbers of male and female rats, thus forming 6 groups altogether. 10 minutes after acute stress exposure and 24 hours after chronic stress exposure, rats were decapitated. Trunk blood was collected to determine hormone levels (RIA); brains were dissected on ice and brain regions of interest (amygdala and hypothalamus) were stored at -80°C. NOS expression was determined with Western Blotting. Beta-actin was used as the internal protein control. Tissue protein concentrations were determined using the Lowry technique. The bands obtained, were evaluated with Image J program of NIH (density and area). In Western blotting, one sample from each group was run on a single gel and the results were expressed for each group as the percentage of respective controls. Data was analyzed using the SPSS program by two-way ANOVA (stress: acute-chronic and sex: male:female) followed by post-hoc tests, and t-tests to determine the difference from 100%.

ACTH and corticosterone levels were significantly different between the groups ($p=0.001$ for both). Corticosterone levels were also found to be significantly higher in female rats ($p=0.018$) indicating a sex difference. Post-hoc Bonferroni test confirmed that the increase in corticosterone levels following acute stress were significantly higher than following chronic stress, both in males ($p=0.010$) and in females ($p=0.016$). These results confirmed that stress application was effective. With regard to nNOS expression in amygdala, near-significant decreases were observed only in female rats exposed to acute stress expression ($p=0.06$). On the other hand, no significant diference was observed in hypothalamus.

Our results suggest that stress does not have an important modulatory effect on nNOS expression in amygdalas and hypothalamus. However, based on the results of our previous studies, a change in NO activity is plausible without a a significant difference in nNOS expression. With respect to this assumption, further studies to determine NO metabolites following the same procedures are planned.

Key Words: *Nitric oxide synthase, amygdala, stress, Western blot, sex differences*

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Sex differences in the modulation of cart expression in the arcuate and paraventricular nuclei of the rat by stress

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Recent work from our laboratories has suggested the modulation of CART positive neurons and CART mRNA by adrenalectomy and corticosterone (CORT) replacement in hypothalamic nuclei of male rat brain. Adrenalectomy lowered CART expression in the arcuate (ARC) and paraventricular (PVN) nuclei. On the other hand, CART mRNA levels were reduced only in the ARC, but not in the PVN; CORT replacement, restored CART mRNA levels in the ARC. The current study aimed to evaluate the effects of

acute and chronic restraint stress on CART positive neurons in the ARC and paraventricular (PVN) nuclei; sex was included as a factor since significant sex differences are observed in stress responses. Male and female rats were exposed to one hour restraint stress in ventilated glass cylinders either once (acute) or for 15 days (chronic); control animals were only handled. In one group of rats trunk blood was collected at the termination of treatments for hormone level determinations (ACTH and CORT). The second group of rats was perfused, brains were removed and serial coronal sections were prepared. Immunohistochemistry was used to assess CART peptide expression in cells of the PVN and ARC nuclei. ACTH [$F(2, 38)=4.188$, $p=0.024$] and CORT [$F(2, 38)=13.483$, $p=0.001$] levels were different between different treatment groups and sex was a significant main effect with regard to CORT levels [$F(1, 38)=6.243$, $p=0.018$]. Acute stress increased CORT more prominently in females and chronic stress lowered the elevated hormone levels in both sexes. Basal levels of CART expression (average number of cells per section) were not different in males and females (68.26±7.31 and 71.96±4.40 in ARC and PVN, respectively). In males, acute stress did not change CART expression in either nuclei while chronic stress lowered CART-positive cells relative to acute treatment in the ARC nucleus ($p<0.05$). On the other hand, in females the effect of stress was opposite in the two nuclei studied: Acute stress lowered CART expression in the PVN ($p<0.005$) but increased it in the ARC ($p<0.005$). Female PVN was not affected by chronic stress but CART positive cells were lowered in the ARC following chronic stress ($p<0.05$). Since following chronic stress, CORT levels are lowered, comparable to the ADX application in previous studies, it seems probable that CORT modulates CART expression more profoundly in the ARC. However, in females only, elevated CORT levels have an early effect (acute treatment) on CART expression in both nuclei, but in the opposite directions. Our results suggest differential and sexually dimorphic modulation of CART expression in the PVN and ARC by stress.

***Key Words**: CART, Stress, Paraventricular nucleus, Arcuate nucleus, glucocorticoids*

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P43

Glial surface glycoconjugate anionic regions disappear significantly bytunicamycin in culture

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N-glycosylation in eukaryotic cellular and ultrastructural membranes is essential for signalling, inter- and intra-cellular communication, and eventually for various vital events from developmental processes to defense mechanisms. Tunicamycin (T), an aminoglycoside that inhibits N- glycosylation by blocking the transfer of GlcNAc-1-P from UDP-GlycNAc to dolichyl-P is used for studying the role of N-glycans during glycoprotein maturation, secretion and function. In the brain, T is reported to downregulate GABAa-R expression, eventuallly causing apoptotic death. There is controversial data regarding T's attenuating and worsening effects on neurons and glia, especially in case of ischemia and excitotoxicity. This preliminary study aimed to detect by electron microscopy (EM) and compare qualitatively the surface anionic regions of control and T treated glial cells. Primary mixed glia cell cultures obtained from 1-3 d.o. Sprague Dawley rat brains and verified by GFAP i-s, were administered 10 mg/ml T on c.d. 16. After 24 h, treated with Karnovsky fixative and embedded in Epon 812, the unstained thin sections were investigated by EM. E-d reaction fibrils in various length were observed on the surfaces of the control cells. They were absent or evidently decreased in the T treated cells, however. Our observation supports those reporting significant abundance of N-glycosilated products on glial membranes and that T inhibits their existence and thrive. We speculate implications for in-vivo glial and/or glial-neural damage due to long term/high dose aminoglycoside treatments, and foresee future studies targeting the underlying mechanism.

***Key Words:** Tunicamycine, glial cell culture*

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P44

Protective effects of omega-3 fatty acids against formaldehyde-induced neuronal damage in prefrontal cortex of rats

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In this study, neurotoxicity of formaldehyde on prefrontal cortex and protective effects of omega-3 fatty acids against this toxicity were investigated. For this purpose, 21 male Wistar rats were divided into three groups. Rats in group I were used as control. Rats in group II were injected every other day with formaldehyde. Whereas, rats in group III daily received omega-3 fatty acids with exposure of formaldehyde. At the end of 14-days experimental period, all rats were killed by decapitation. The brains of animals were removed. Following routine histological procedures, sections of prefrontal cortex were examined by light microscopy and immunohistochemistry. In formaldehyde injected rats, apoptotic cell numbers were increased compared to those in control group. In light microscopic examination of this group, it was observed that apoptotic cells including nuclear fragmentation and membrane budding, picnotic cells and apoptotic bodies. Whereas, in rats received omega-3 fatty acids with exposure of formaldehyde, number of apoptotic cells and cellular damage were decreased. Furthermore, these histological findings were confirmed by immunohistochemical evalution. In conclusion, it was determined that formaldehyde-induced neuronal damage in prefrontal cortex was prevented by administration of omega-3 fatty acids.

***Key Words:** Formaldehyde, prefrontal cortex, omega-3 fatty acids, apoptosis, rat*

P45

The investigation of apoptotic changes and macromoleculer oxidation in prefrontal cortex of rat brain in an experimental psychosis model and the protective effects of omega-3 fatty acids

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Evidence has become increasingly available to support the view that some of the neuropathological changes in schizophrenia may be the result of increased free radical-mediated or reactive oxygen species mediated neuronal injury. n-3 fatty acids is an essential fatty acid found in large amount in fish oil.. Primary objective of this study is to indicate the contribution effect of lipid peroxidation to the neuropathophysiology of schizophrenia, and that prevention of lipid peroxidation may improve prognosis, probably by producing improvements in the structure, and thereby also in the functions, of neuronal membranes.

Healthy adult and male Wistar Albino rats were obtained Firat University Biomedical Research Unit and 30 rats divided into three groups. MK-801 was given intraperitoneally at the dose of 0.5mg/kg/day for 5 days in experimental psychosis group. n-3 fatty acid (800 mg/kg/day, Marincap® capsule) was given to treatment group for 6 days by peroral. In control group, saline was given in the same way. In 7 days the beginning of the experiments rats were killed by decapitation. Brain were removed and prefrontal part of the brain was divided for histological and biochemical analyses. Histological preparats were stained with HE and analyzed. Malondialdehyde (MDA) and protein carbonyl (PC) analyses were made by spectrophotometric methods.

The histological examination demonstrated that MK-801 induced prefrontal apoptosis. A similar series of experiments has shown that n-3 fatty acids supplementation to the diet of rats decreased the apoptotic cell account in the prefrontal cortex after MK-801 injection. Malondialdehyde, as an indicator of lipid peroxidation, as well as protein carbonyl, as an indicator of protein oxidation, levels were found to be increased significantly in prefrontal cortex of MK-801 group ($p<0.0001$) compared to the control group. In n-3 treated rats, prefrontal tissue malondialdehyde and protein carbonyl levels were decreased significantly when compared to MK-801 group ($p<0.0001$).

MK-801 at the dose of 0.5 mg/kg/day may induce apoptotic changes and oxidative stress in prefrontal cortex of rats. This experimental study also provides some evidences for the protective effects of n-3 fatty acids on MK-801-induced changes in prefrontal rat cortex.

Key Words: *MK-801, prefrontal cortex, apoptosis, omega-3 fatty acids, malondialdehyde, protein carbonyl.*

P46

Effect of exogenous and endogenous melatonin on hyperbaric oxygen induced oxidative stress in rat brain tissue

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Hyperbaric oxygen (HBO) is a widely used treatment modality in many diseases. A known side effect of HBO is the production of reactive oxygen species. This oxidative stress appears especially in brain and lung tissue. Many antioxidants have been used successfully to scavenge the reactive oxygen species caused by HBO administration. In this study, we aimed to see if melatonin, a newly discovered antioxidant, has a protective effect against the overproduction of reactive oxygen species produced by HBO in rat brain tissue. In this study, it was investigated that the effect of exogenously administered (10 mg/kg, i.p.) and endogenously secreted melatonin on 3 Atmosphere Absolute (ATA), 2 hours HBO - a HBO treatment procedure used for human disease and also oxidative stress potency of this procedure was shown in brain previously- induced oxidative stress in rat brain.

Sixty male Sprague-Dawley rats were divided into 7 groups as follows: (A1) daytime control, (A2) nighttime control, (B) daytime HBO, (C) nighttime HBO, (D) daytime melatonin, (E) daytime HBO plus melatonin (10 mg/kg), and (F) nighttime HBO (under light exposure). Brain MDA levels were measured as oxidative stress marker. Daytime groups (B,D,E) according to daytime control (A1), nighttime groups (C,F) according to nighttime control (A2) were measured.

The MDA level of daytime HBO (group B) (4.57±0.60 nmol/g tissue) and nighttime HBO (group F) (6.67±0.87 nmol/g tissue) increased significantly according to control groups (A1: 2.52±0.29 nmol/g tissue- A2: 2.29±0.37 nmol/g tissue). This significance was not found in the group C (3.44±0.55 nmol/g tissue) and group E (2.12±0.07 nmol/g tissue). Group D MDA levels (2.72±0.44 nmol/g tissue) was not different from control group (2.52±0.29 nmol/g tissue).

In this study, 3 ATA, 2 hours HBO caused significant oxidative stress in rat brain. Both endogenously secreted and exogenously administered melatonin blocked oxidative stress.

Key Words: *Hyperbaric oxygen, brain, oxidative stress, melatonin, antioxidant*

P47

Intracerebroventricularly administered VEGF protects brain against transient focal ischemia with a long therapeutic window

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Vascular endothelial growth factor (VEGF) exerts a late protective effect by promoting angiogenesis in focal ischemia. However, early intravenous administration of VEGF is reported to increase blood brain barrier (BBB) leakage, hemorrhagic transformation, and infarct volume whereas topical administration of VEGF to cortical surface is neuroprotective. We have investigated whether or not intracerebroventricularly administration of VEGF could replicate the neuroprotective effect observed with topical application and the mechanism of action of this protection.

Mice were subjected to 90-minute middle cerebral artery occlusion and 24 hours of reperfusion. VEGF (8 ng) was administered intracerebroventricularly 1 or 3 hours after reperfusion. The infarct volume, neurological disability score, number of TUNEL-positive apoptotic nuclei and tissue phospo-Akt levels were determined. BBB permeability was assessed by measuring albumin extravasating tissue volume (immunostaining).

Compared to the vehicle-treated group, VEGF significantly decreased the infarct volume by 35% (29±4 vs. 44±1 mm^3) and by 46% (27±3 vs. 49±3 mm^3) in 1 and 3-hour groups, respectively. Mean neurological disability scores paralleled the changes in infarct volume. Independently to the decrease in infarct size, VEGF significantly reduced the number of TUNEL-positive neurons by 52% in 3-hour treatment group. Phospo-Akt levels were also higher in these mice compared to vehicle-treated animals (0.56±0.08 vs 0.27±0.04 densitometric units).

In conclusion, in agreement with studies using topical administration, ICV injection of VEGF protects brain against ischemic injury with a relatively long therapeutic time window. This action is independent of its angiogenic properties and possibly involves activation of the PI-3-AKT pathway.

Key Words: *VEGF, Neuroprotection, Apoptosis, Akt, Focal cerebral ischemia, Blood-brain barrier*

P48

Statin treatment protects brain against focal cerebral ischemia

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Cerebrovascular disease and vascular complications are common and cause considerable mortality and morbidity in diabetes. Statins reduce the risk of stroke by 30% independently of their lipid-lowering effect and are proven to be protective against focal cerebral ischemia. In this study, we used a mouse diabetes model and investigated the effect of pre-ischemic statin treatment on focal cerebral ischemia.

Swiss mice, weighing 20-22g were randomized into two groups. Diabetes was induced in the first group by streptozotosin injection (225mg/kg, i.v.). The second group served as the control. After 4 weeks, half of the mice in diabetes and control groups were randomized to receive simvastatin treatment (1mg/kg/day, i.p.) for 14 days. After statin, mice were divided into four groups as control (n=7), statin-treated (n=8), diabetic (n=6), statin-treated diabetic (n=6) and were subjected to 90 minutes of proximal middle cerebral artery occlusion and 24 hours of reperfusion. For each group, 7 mice were sham-operated (n=28). The brain infarct volume was measured.

Infarct volume (mean±SE) was significantly increased in the diabetic group (60±4mm^3) compared to controls (54±4mm^3). Fourteen days of statin treatment reduced infarct volume significantly in diabetics as well as controls (40±3mm^3, 35±3mm^3, respectively).

These data suggest that, diabetes increases the ischemic damage after focal cerebral ischemia and statin treatment protects the brain in both diabetics and healthy animals. Statins may be used in patients with cerebrovascular risk factors for protection against stroke.

Key Words: *Focal cerebral ischemia, DM, Statin, Neuroprotection*

P49

Evaluation of astrocyte glycogen metabolism and viability at cellular level after focal cerebral ischemia/ reperfusion

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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 develop methods to investigate the progression of astrocytic cell death after focal cerebral ischemia/reperfusion.

Since, unlike neurons, astrocytes can metabolize glycogen, detection of glycogen may be used as a selective viability marker for astrocytes. Therefore, we developed a novel PAS staining technique to evaluate brain glycogen metabolism at cellular level. Additionally, two florescent in vitro cellular viability markers; calcein, which is used to monitor cell viability, and propidium iodide (PI), which is used to detect necrotic cells, were adapted to in vivo conditions. Glial fibrillary acidic protein (GFAP) and neuron-specific nuclear protein (NeuN) were used as astrocyte and neuron markers, respectively.

After focal cerebral ischemia (MCA occlusion) / reperfusion in mice (n=6), a decrease in PAS staining intensity was detected in core ischemic regions on coronal brain sections (n=18).

In contrast, there was an increased PAS staining in the penumbra area. In serial sections, glycogen-rich cells corresponded to GFAP-positive astrocytes whereas neurons (NeuN positive cells) and apical dendrites appeared as PAS-negative spaces. Astrocytic end-feet around microvessels were also intensely PAS-positive.

These data demonstrate that PAS staining provides a specific marker for detecting the metabolic activity, hence, viability of astrocytes. After intracerebroventricular injection, several cells were stained with either calcein or PI in the ischemic MCA territory. The triple staining experiments with calcein, PI and GFAP to determine the phenotype of these cells are in progress.

Key Words: *focal cerebral ischemia, reperfusion, astrocyte, glycogen*

P50

Searching the possible role of nitrergic and glutamergic systems in hippocampal injury caused by glucocorticoids in rats

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Hippocampal atrophy has been observed in human subjects with post-traumatic stress disorder, recurrent depressive disorder, Cushing Syndrome, schizophrenia and older age. Glucocorticoids have been claimed to be responsible for this atrophy. Similar structural changes have been observed in rats and primates in relation to stress. In the studies about stress, either changes in the organisms, that are exposed to immobilization, cold, noise and similar stimuli, are investigated or high doses of corticosteroids are administered for a long time in order to determine the effects of glucocorticoids at stress levels more specifically.

The purpose of this study was to explore the expression of neuronal nitric oxide in hippocampus. The synthesis of neuronal nitric oxide is induced by glutamate through the stimulation of NMDA receptors. The data about the dysfunction of memory and learning in stress related disorders, the role of hippocampus as a target tissue where these functions are located, the structural changes in hippocampus as a result of hypersecretion of stress hormone glucocorticoids and the relation of these changes with glutamate, an excitatory amino acid will be taken into consideration.

We administered corticosteron (20 mg/kg, i.p.); 7-Nitroindazol (7-NI), a specific nNOS inhibitor (20 mg/kg, i.p.) and MK-801 which is a non-competitive NMDA receptor antagonist (0.1mg/kg, i.p.) for 2 weeks at non-severe stress levels and we studied hippocampal nNOS expression.

When corticosteron, 7-NI and MK-801 were administered alone, there was not a statistically significant impact on nNOS expression compared with the control group. On the other hand, in the groups where corticosteron+7-NI and corticosteron+MK-801 were administered together, nNOS expression was significantly decreased compared to control and corticosteron groups ($p<0.001$).

As a result, there was no change in nNOS expression when corticosteron, 7-NI and MK-801 were administered alone. However, nNOS expression was significantly decreased when corticosteron+7-NI and corticosteron+MK-801 were administered together. That specific nNOS inhibitor 7-NI and non-competitive NMDA receptor antagonist MK-801 decrease nNOS expression significantly in hippocampus when they are administered concomitant with corticosteron implies that nNOS and NMDA receptors have a role in "hippocampal dendritic remodeling" dependent on stress/glucocorticoids

Key Words: *hippocampus, glucocorticoids, 7-NI, MK-801, nNOS expression*

P51

Investigation of matrix metalloproteinases in cerebrovascular malformations by immunohistochemical methods

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Angiogenesis, which is necessary for reproduction, development and wound healing, is a highly regulated biologic process. But if angiogenesis is not well regulated or incorrectly regulated much pathology can be seen. After angiogenic signal transport, angiogenesis consists of four steps, degradation of extra cellular matrix, migration, proliferation, and tube formation. In this study matrix metalloproteinases are investigated in cerebrovascular malformations by immunohistochemical methods and they are compared with other structural proteins.

In this study 86 AVMs and 80 cavernoma patients, which were operated in Marmara University Neurosurgery Department or Marmara University Neurological Sciences Institute from January 1987 to November 2003 and diagnosed pathologically, were investigated. Paraffin blocks of 14 AVMs and 15 cavernomas patients were found in archives of Pathology Department of Marmara University Neurological sciences institute and were included in this study after looking at their size and hemotoksilen-eosin staining. These preparations were stained immunohistochemicaly for five structural proteins (laminin, tenascin, fibronectin, MMP-2, MMP-9). AVMs were categorized into five histological layers: endothelium, subendothelium, tunica media, adventitia and perivascular area, cavernomas were categorized into three histological layers: endothelium, subendothelium and perivascular area. Immunohistochemical staining were evaluated and graded as 0, 1, 2 or 3 by looking at grading degree.

After evaluation of immunohistochemical staining, cavernomas expressed more fibronectin in subendothelial layer, AVMs expressed more laminin in subendothelial layer, and cavernomas expressed more tenascin, MMP-2 and MMP-9 in all layers.

After immunohistochemical staining for structural proteins, it is determined that AVMs and cavernomas had different immunohistochemical features. Cavernomas had more immature proteins than AVMs. Cavernomas expressed more metalloproteinases than AVMs; this finding supports the hypothesis that cavernomas were being formed in early phases of angiogenesis.

Key Words: *serebrovascular malformation, angiogenesis, MMPs.*

P52

Scanning electron microscopic examination of the hair in giant axonal neuropathy

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GAN was originally described as a unique syndrome involving the peripheral nerve but subsequent reports have indicated that it is a multisystem disorder involving the central and peripheral nervous systems and other organs such as the heart, muscle, skin and hair. Structural changes in the hair of patients with GAN have not been demonstrated in detail using scanning electron microscopy (SEM) techniques before.

This study presents the results of SEM examimation of hair of patients with GAN. The biopsy specimens were obtained from 2 patients age of 11 and 13 years respectively. 20 hair specimens were taken from 2 patients. Routine SEM procedure was performed to the tissue specimens and then, they were examined on SEM.

Most of the specimens showed normal hair shafts with a delicate and squamous surface. Longitudinal and opposing grooves which indicate severe keratinization anomalies were observed. Literature survey revealed that, structural changes in the hair of patients with GAN were not demonstrated in detail before using SEM techniques. Thus, having detected the pathology in 20 hair specimens taken from 2 patients with GAN, a notable contribution is made to the literature by completing the gap about this syndrome.

Key Words: *Giant axonal neuropathy, ultrastructure, SEM*

P53

Effects of estrogen hormone on the pineal gland in rat: an electron microscopic study

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This study was aimed to examine the effects of ovariectomy and ovariectomy followed by estrogen administration on the pineal gland at electron microscopic level. For this purpose, 15 female Wistar rats were used. Animals were divided into three groups. Grup I and Grup II were designated as control (sham-ovariectomized) and ovariectomized, respectively.

Tha rats in Group III were ovariectomized and injected daily with estradiol benzoate for one month. At the end of the experiment, all animals were killed by vascular perfusion. The pineal glands of rats were removed, then processed for electron microscopic examination. In our study, it was seen that increase of mitochondria, ribosomes and lipid droplets in the cytoplasm of pinealocytes after ovariectomy.

Additionally, extensiveness of rough endoplasmic reticulum sacs was noticed in the cell cytoplasm. Whereas, in rats injected with estrogen following ovariectomy, it was determined that a decrease in the amount of mitochondria and lipid droplets in the cytoplasm of pinealocytes. In conclusion, increased of cell activity was observed in the pinealocytes after ovariectomy and this increase was suppressed following administration of estrogen.

Key Words: *rat, pineal gland, ovariectomy, estrogen, electron microscopy*

P54

The oxidative and morphological effects of chronic thinner exposure on rat hippocampus.

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Thinners are abused substances and well known as neurotoxic agents. Thinner abuse results in structural and functional impairment of a variety of organs. But, no more study have been reported on hippocampus tissue. This study was designed to investigate the effects of chronic thinner inhalation on lipid peroxidation, antioxidant enzyme activities and morphological changes in hippocampus of rats.

The male Wistar albino rats (150-250 g) were divided in two experimental groups: the control and the thinner treated group (n=10 for both). Thinner treatment was performed by inhalation of 2000 ppm thinner, in 6 day/week order for 12 weeks. Blood and tissue samples were obtained for biochemical and histopathological investigation. Morphometry was carried out with the aid of an image analyzer.

Thinner significantly increased both blood and tissue MDA, and decreased tissue SOD and GSH-Px, but not tissue CAT levels when compared with controls. There were significant decrease in neuron number in thinner group than control group. The morphology of neuronal cells were mostly shown that axonal and pericarional degeneration, picnotic or hyperchromatic nucleus in thinner group.

As conclusion, increased lipid peroxidation, reduced antioxidant enzyme activities, and histopathological changes found in this study indicate that chronic thinner inhalation might be involved free radical processes. Further studies are required to evaluate the possible molecular mechanisms of chronic thinner exposure toxicity on hippocampus.

Key Words: *toluene, lipid peroxidation, antioxidant enzymes, ultrastructural, hippocampus, rat*

P55

Characterization of miniature excitatory postsynaptic currents (mEPSCs) in the visual cortex of the heterozygous knock-out mice for brain-derived neurotrophic factor

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Brain derived neurotrophic factor (BDNF), is expressed in the developing and mature mammalian central nervous system, and it controls neuronal survival and differentiation. BDNF binds to TrkB receptors and triggers a signaling pathway, which leads to activation of Phospholipase C (PLC), Mitogen Activated Kinase (MAPK), and Phospho Inositol 3 Kinase (PI3K). BDNF is involved in axonal and dentritic growth and synapse formation. BDNF is also reported to mediate fast synaptic transmission and plasticity. The effects of BDNF on glutamatergic neurotransmission vary between different regions of the mammalian brain and needs to be further clarified in visual cortex.

In this study we characterized the effect of BDNF on the excitatory synaptic transmission in the visual cortex of 21-27 days old mice, which partially lack the BDNF coding gene (Heterozygous mice, HT) (n=8). Age matched wild type littermates were used as controls (n=10). After preparation of acute visual cortex slices, miniature excitatory postsynaptic currents m (EPSCs) were acquired from layer II/III pyramidal neurons of the visual cortex by using the whole-cell patch clamp method.

We analyzed the frequency and amplitude of miniature postsynaptic excitatory currents. According to our findings, the frequency of mEPSCs ($p=0.019$) is found to reduce in the visual cortex of HT mice when compared to wild type tissues. The amplitude of mEPSCs did not differ between HT and wild mice. These results imply that the reduced level of BDNF impairs glutamatergic system. In the same experimental model, the regulation of the excitatory receptors is also tested. The ratio of the currents mediated by N-methyl-d-aspartate (NMDA) receptors and alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors are analyzed.

Key Words: *Bdnf, visual cortex, glutamate, mEPSCs, whole cell patch-clamp*

This study was supported by the IGSN and DFG (SBF 509, C4)

P56

Effects of CDP-choline and its endogenous metabolites on plasma cathecholamines response to graded hemorrhage in rats.

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CDP-choline is a drug used to treat several cerebral ischemic situations and neurodegenerative diseases. Exogenously given CDP-choline rapidly metabolized to cytidine monophosphate, phosphocholine, cytidine and choline. The roles of these metabolites in the pharmacological actions of exogenous CDP-choline are not known.

Recently we have demonstrated that centrally given choline (Savci, Goktalay, Ulus. Brain Res, 942; 58,2002) or CDP-choline (Cavun, Savci, Ulus: Fund&Clin Pharmacol, 17, 1,2003) increases plasma vasopressin. In the present study we tested whether peripheral administration of CDP-choline or its metabolites (choline, cytidine, cytidine monophosphate and phosphocholine) alter the plasma vasopressin response to graded hemorrhage in rats.

Wistar rats (female, 250-300 g) were injected intraperitoneally saline (1 ml/kg), CDP-choline (0.6 mmole/kg), choline (0.6 mmole/kg), phosphocholine (0.6 mmole/kg), cytidine monophosphate (0.6 mmole/kg) or cytidine (0.6 mmole/kg) and then 5 minutes after they were subjected to graded hemorrhage as described previously (Ulus, Arslan, Savci, Kiran. Br J Pharmacol, 116;1911,1995). Briefly, a blood sample (0.6 ml per 100 g of body weight) was withdrawn over 10 s from the carotid artery catheter into a chilled plastid syringe containing 0.1 ml of EDTA solution (5 mg/ml). This procedure repeated four times at 5-min interval. The cumulative blood loss in each animal consisted of volumes equal to 0.6, 1.2, 1.8 and 2.4 ml per 100 g of body weight. Blood samples were designed for S1 through S4 and were assayed for plasma vasopressin by radioimmunoassay.

The graded hemorrhage resulted in a significant rise in plasma vasopressin levels. In saline treated control rats plasma vasopressin levels in the fourth blood sample (S4) were about 4-fold higher than those observed in the first (S1) samples. The effect of graded hemorrhage on plasma vasopressin was enhanced by CDP-choline at S3, by choline at S1, S2 and S3 or by phosphocholine at S2, S3

and S4. Plasma vasopressin response to graded hemorrhage was not influenced either by cytidine or cytidine monophosphate pretreatment.

These data show that CDP-choline and its metabolites phosphocholine and choline, but not cytidine or cytidine monophosphate, enhance plasma vasopressin response to graded hemorrhage. The increase in central cholinergic neurotransmission to vasopressin secreting neurons after CDP-choline may involve in this action of CDP-choline on plasma vasopressin.

Key Words: *CDP-choline, choline, phosphocholine, graded hemorrhage, vasopressin*

P57

Effects of doxycycline on lymphocyte functions in autoimmune central nervous system disorders

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Antibiotics of the tetracycline family have neuroprotective and antiinflammatory properties. The latter are mediated through the inhibition of cytokine, matrix metalloproteinase, and iNOS production, and also decreased microglial activation. They prevent experimental allergic encephalomyelitis, an autoimmune disease of the brain and spinal cord. Minocycline is the most well-studied derivative among this group of drugs. We investigated the effect of doxycycline, a more widely used antibiotic in humans, in childhood autoimmune neurological disorders by *in vitro* experiments. Peripheral blood lymphocytes from patients with acute disseminated encephalomyelitis (ADEM, n=12), multiple sclerosis (MS, n=10) and control cases (epilepsy, n=10), all aged 5-16, were examined for proliferative response against concanavalin A and myelin basic protein (MBP) assessed by the MTT assay, matrix metalloproteinase activity assessed by penetration through gelatin-coated filter, and apoptosis assayed by acridine orange staining and DNA laddering.

Proliferative response against conA in ADEM and MS was decreased compared to controls ($p=0.04$). Doxycycline increased proliferation in controls but not in ADEM or MS ($p=0.03$). Doxycycline increased apoptosis in the MS group. Matrix metalloproteinase activity was unaffected.

The inhibition of proliferation and increase in apoptosis in the MS group might be associated with the suppression of inflammatory responses, a potentially beneficial effect in ADEM and MS. This study contained patients in various stages of the disease, some under treatment. Although no consistent difference was found between treated vs. untreated, or acute vs. chronic patients, future studies including homogeneous patient groups are worthwhile, given the safety and potential efficacy of doxycycline.

Key Words: *autoimmune, doxycycline, lymphocyte, multiple sclerosis*

P58

Effect of Dehydroepiandrosterone sulfate on the nitric oxide system in the rat brain

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Obesity can be induced by high fat diet. Dehydroepiandrosterone sulfate decreases body fat mass and have an antiatherogenic effect**.** The objective of our study was to investigate the high fat diet changes and the effect of DHEAS on the nitrite/nitrate (NOx) system in the rat cerebrum.

Thirty-eight female rats were divided into 4 groups. Group 1 (control) (n=12) were fed with standard rat chow, Group 2, 3, and 4 with high fat diet for five months. DHEAS was administered as 1 mg/kg for group 3 (n=9) and as 10mg/kg for group 4 (n=9) for seven days. The same amount of saline was used in group 1 and 2 (n=9). After decapitation, brain tissues were collected and, nitrite and nitrate (NOx) concentrations, were determined by Griess method in the cerebral tissues. Possible histological changes due to high fat diet were examined in the cerebral tissue specimens. Mann Whitney U test was used for statistical comparisons.

NOx levels were found statistically lower in group 4 than group 1 ($p=0.037$). The highest level of NOx was found in the control group (23.62±3.45 ng/gr protein). High fat diet although not significant had a decreasing effect in tissue NOx levels in the cerebral tissues. However NOx levels in DHEAS or saline applied groups were not statistically different. There was not any endothelium damage or lipid deposit on cerebellum and cortex areas. The groups were not statistically different histologically

As a conclusion DHEAS in 10 mg/kg dose significantly decreases tissue NOx levels in the cerebral tissue of the rats on high fat diet. These findings question the role of NOx system on the antiatherogenic effect of DHEAS.

Key Words: *dehydroepiandrosterone sulfate, NOx system, rat, high fat diet*

P59

$GABA_A$-mediated transmission in different regions of reticular thalamic nucleus of genetic absence epilepsy rats

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Genetic Absence Epilepsy Rats from Strasbourg (GAERS), that serve as a genetic model of absence epilepsy, display spike and wave discharges (SWDs) spontaneously. The increased gamma-aminobutyric acid (GABA)-mediated transmission in thalamo-cortico-thalamic pathway has been shown to be the most accepted theory in the pathogenesis of absence epilepsy. In GAERS, GABAergic inhibitory neurotransmission in the thalamus, particularly in the reticular nucleus of the thalamus (nRt) plays a crucial role in the pathogenesis of the synchronization of the oscillatory activities.

This study was planned to demonstrate the effect of administration of $GABA_A$ receptor antagonist, bicuculline, into the anterior and intermediate parts of the (nRt) and to clarify the role of $GABA_A$ receptors on the generation of SWDs in the nRt of GAERS.

GAERS were stereotaxically instrumented with guide cannulae for drug microinjections and extradural electrodes for electroencephalogram (EEG) recordings. After a one-week recovery period, bicuculline at different doses (40 pmol, 80 pmol and 150 pmol) or artificial cerebrospinal fluid were given to GAERS within a volume of 100 nl into the anterior or intermediate regions of nRt. Simultaneous EEG recordings were also analyzed and compared to the basal EEG parameters.

Administration of bicuculline into the intermediate part of the nRt produced statistically significant increases ($p<0.05$) in the

cumulative duration of SWDs in a dose-dependent manner; conversely there were significant decreases ($p<0.05$) in the cumulated duration of spontaneous SWDs after microinjections into the anterior part of nRt. Injections of artificial cerebrospinal fluid produced no significant change on EEG.

These data may reveal the existence of regional differences of $GABA_A$-mediated effects within the nRt in the occurrence of SWDs in GAERS.

Key Words: *bicuculline; absence epilepsy; spike and wave discharges; reticular nucleus*

This project is supported by Marmara University Scientific Research Council (SAÚ-047/131102

P60

Investigation of protective effect of vitamin E on oxidative damage of rat hippocampal tissue in formaldehyde intoxication

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Formaldehyde is a highly reactive one-carbon compound. It is widely used in medicine and industry. It was shown in clinical investigations and experimentally that formaldehyde could cause severe respiratory system impairment. But, there are only a few studies about biochemical and histopathological changes of hippocampus caused by formaldehyde toxicity. Vitamin E (vit E) is the primary liposoluble antioxidant, which may have an important role in scavenging free oxygen radicals and in stabilizing the cell membranes, thus maintaining its permeability. The aim of our study was to investigate a possible protective influence of vit E pretreatment on superoxide dismutase (SOD) and malondialdehyde (MDA) concentrations in the hippocampal tissue of rats acutely treated with formaldehyde. We used male 3-month-old Wistar albino rats weighing 280 g in our experiment,. The animals were kept at 21±1 ¼C and exposed to a 12 h light - 12 h dark cycle. The animals were randomly allotted into one of three experimental groups: Control, formaldehyde treated, and formaldehyde+vitamin E treated groups. Each group consisted 6 animals. Formaldehyde treated, and formaldehyde+vit E treated groups received intraperitoneal injection of 10 mg/kg formaldehyde for 10 days. In addition, formaldehyde+vit E treated group received intramuscular injection of 300 mg/kg vit E for 10 days. All rats were housed in individual cages and given a standard diet and water *ad libitum*. After the treatment, the animals were sacrificed and hippocampal tissues were removed for biochemical and histological investigation. Formaldehyde significantly increased tissue MDA levels and also decreased SOD enzyme activity in hippocampal tissue compared to controls. Vit E treatment decreased MDA levels, prevented SOD enzyme inhibition. In control group the morphology of the hippocampal neuronal cells was normal. In formaldehyde group, the number of neuronal cells was significantly less than both control and vit E groups. In formaldehyde group, neuronal cells became extensively dark and degenerated with picnotic nuclei. The morphology of neuronal cells in vit E group was similar to that of the control group. It was concluded that vit E might be beneficial in preventing formaldehyde-induced oxidative hippocampal tissue damage, therefore, shows potential for clinical use.

Key Words: *formaldehyde, lipid peroxidation, superoxidase dismutase, hippocampus, histology, rat.*

P61

Effect of immobilization on axonal regeneration after sciatic nerve crush injury.

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Peripheral nerve trauma has been a challenge to surgeons, with significant advances in the surgery of repair. Immobilization of the injured limb after repair has been the traditional method of treatment. Although peripheral nerve regeneration has been studied extensively, effect of the duration of immobilization on axonal regeneration has been studied by a few authors. In the present study, we aimed to study the effect of immobilization after sciatic nerve injury by a standardized compression device. We found a detrimental effect of the immobilization on axonal regeneration after sciatic crush injury. We think that such detrimental effect should be considered by scientist who dealing with peripheral nerve regeneration.

Key Words: *immobilization, crush injury, sciatic nerve.*

P62

Detection of viral DNA of HSV-1, HSV-2, CMV, HHV-8, HHV-6 using PCR method in surgical resection materials of epilepsy patients with mesial temporal lob sclerosis

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There are a few numbers of hereditary factors that related to mesial temporal lobe epilepsy (MTLE) and it is accepted that the primary causes of the disease are external factors. Fever, convulsions and coma are not rare in the clinical history of patients with MTLE. In most of the cases, meningitis or encephalitis cannot be diagnosed as a cause of the attacks. Moreover, the mental and motor development of these patients is usually normal. It is known that herpes simplex virus type1 (HSV-1) and type2 (HSV-2), human herpes virus-6 (HHV-6) are related to symptomatic epilepsies. HHV-6 was found to be the cause of febrile convulsions. HHV-8 must kept in mind in differential diagnosis of encephalitis with unknown etiology.

The aim of this study is to investigate the role of environmental factors like HSV-1, HSV-2, CMV, HHV-6 and HHV-8 in etiopathogenesis of MTLE.

Thirty-three patients, who had temporal lobe seizure with mesial temporal lobe sclerosis in their surgical resection materials, were included the study. Real time PCR method and light-cycler system were used for detection of DNA of these viruses from paraffin embedded hippocampal tissues. Patient's medical history for febrile convulsion, meningoencephalitis, consanguinity, and family history was investigated.

Mean age was 30 (16-46) years old. The rate of febrile convulsions was 72%, consanguinity was 18%, and family history for epilepsy was 42%. HHV-6 was detected in 3 patients (9%); HHV-8 was identified in 1 patient (3%) and HSV-1 in 2 patients (%6). None of our specimens revealed positivity for HSV-2 and CMV viral DNAs.

Incidence of HSV-1 and HHV-6 seems to be very low compared with incidence of autopsy series published before. No difference was detected between patients who had febrile convulsion history and who did not, in terms of having viral DNA in their surgical resection materials. None of the patients with HSV-1, HHV-6 and HHV-8 positivity had meningoencephalitis.

We conclude that no relation was detected between viral infections and MTLE in our series.

Acknowledgment: *This study was supported by the Turkish League Against Epilepsy.*

Key Words: *epilepsy, PCR, HHV-6, HHV-8, CMV, HSV-1, HSV-2.*

P63

Intra cytoplasmic sperm injection and neurodegenerative disease risk: a medical hypothesis

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Nowadays, neurodegenerative disease (ND) reasons is getting clear by emerging the new improvement of our knowledge on genomic basis of the diseases. Human genome project provides some benefits for molecular studies about the gene changes that might be responsible for many ND such as Alzheimer's and Huntington's Diseases.

Although not having precise results on genomic basis of Parkinson's disease, some clues obtained from new studies made the subject lightened a little. In these studies, it has been proposed that there might be a relation between ND and mitochondrial DNA (mtDNA) mutations.

The mutation in mtDNA makes trouble for energy system, and leads the cell to death. The studies on Parkinson's patient brains revealed the cell loss and autophagic granules in the neurons of Substantia Nigra (SN) area. In experimental model of PD with MPTP (1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine), it has been also shown cell loss and autophagic granules in Substantia Nigra (SN) area.

Autophagic granules are a kind of cell defense mechanism to remove the harmful cytosolic structures, and usually contain bulk of mitochondrial structures. MPTP disrupts cellular respiration by inhibiting mitochondrial pathways. Observing the autophagic structure in PD patients provides that mitochondrial defects may play a role in the ND survey.

Mitochondria defects might be resulted by the mutations in mtDNA. Other hand, Intra Cytoplasmic Sperm Injection (ICSI) is a common method of In Vitro Fertilization (IVF). In this method, a sperm and its tale are injected into an ovum. In normal way of fertilization, it has been known that paternal mitochondrion in sperm tale, which provides sperm motility, do not enter the ovum, and sperm nuclear materials are only transferred into ovum cytoplasm.

After fertilization, fetus contains only maternal mitochondrion and its mtDNAs. It has been shown in wide epidemiologic studies that NDs mostly are seen in men. In this medical hypothesis, it has been proposed that ICSI method makes the possibility of NDs, such as PD, high in children produced by transferring the paternal mtDNAs, which might be more suspicious for NDs.

Key Words: *Neurodegenerative diseases, mtDNA, ICSI*

P64

A neuronal migration disorder: Walker-Warburg syndrome (case report)

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Neuronal migration disorders, a group of malformations of the brain by the abnormal migration of neurons in the developing brain and nervous system. Neurons must migrate from the ventricular zone to their final position at cerebral cotex during embryogenesis. Deficiency of this process result in structurally abnormal brain including schizencephaly, porencephaly, lissencephaly, agyria, macrogyria, pachygyria, microgyria, neuronal heterotopias, agenesis of the corpus callosum, and agenesis of the cranial nerves. The most severe and most common of these is lissencephaly (smooth brain). Cobblestone lissencephaly or lissencephaly type II is consist of cobblestone cortex, abnormal white matter, enlarged ventricles, small brain stem, and small cerebellum especially vermis with cerebellar polymicrogyria. Several syndromes with lissencephaly have been described. One of these syndromes is Walker-Warburg syndrome which is a lethal autosomal recessive disorder characterized by brain, eye and muscle abnormalities.

In this study a case of Walker-Warburg syndrome with of hypotonia, microphthalmia, bilateral cataract, immature anterior chamber, congenital muscular dystrophy on muscle biopsy, hydrocephaly, cobblestone lissensencephaly, hypoplasia of cerebellar hemispheres and extremly high serum creatinine phosphokinase, is presented. A careful physical examination is emphasized in the diagnosis of associated malformations in newborn infants who have hydrocephalus and the early diagnosis is essential for genetic counseling.

Key Words: *Neuronal Migration Disorders, Lissencephaly, Walker-Warburg Syndrome, Hydrocephalus, Congenital Muscular Dystrophy.*

P65

Apolipoprotein e (ApoE) and angiotensin-converting enzyme (ace) gene polymorphisms in patients with alzheimer disease in the aegean region

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Alzheimer's disease (AD) is a progressive multifactorial neurodegenerative disorder which is the major cause of dementia in the elderly. To date, the only recognized risk factor for the most common forms of AD-defined as sporadic or complex is the APOE gene on the long arm of chromosome 19 (19q13.2). ApoE is the major lipoprotein in CNS, where it is synthesized by astrocytes. Previous reports have suggested that additional factors within the APOE locus itself might also modulate this risk. Genetic studies

of markers in the vicinity of the APOE locus have demonstrated that a combination of several polymorphisms increases the APOE-associated risk for AD, compared with the APOE polymorphism alone. Based on these evidence, the angiotensin converting-enzyme (ACE) gene has been investigated as genetic risk factors for AD. ACE is a dipeptidyl carboxypeptidase mainly involved in blood pressure regulations, body fluid and sodium homeostasis.

However, the contribution of these promoter polymorphisms to AD susceptibility is controversial. Discrepancies between studies may result from several biases including ethnic heterogenety, weak effects not detected in small populations, or some specific effects that are not restricted to a particular age group. To address these concerns, we performed an analysis on patients with AD and control subjects from Aegean region in Turkey.

Blood was collected and analyzed for the ACE and ApoE genotypes from 45 healthy and 45 patients. The frequencies of ApoE allele among the patients with AD were 3.33% for ε2ε2; 9.99% for ε2ε3; 3.33% for ε2ε4; 49.95% for ε3ε3; 26.64% for ε3ε4; 6.66% for ε4ε4. We found frequencies distribution for ACE genotype in AD were 38.88% for DD; 27.77% for II; and 33.33 for ID.

Key Words: *ApoE, angiotensin-converting enzyme, polymorphisms, alzheimer disease*

P66

Effects of excessive dietary vitamin B6 (pyridoxine-Hcl) intake on cerebral cortex neuron in rats

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Vitamin B6 is a cofactor in different reactions of metabolism during development. Ultrastructural changes in developing brain regions associated with maternal vitamin B6 deficits were carried out, but there is not information for dietary excess of vitamin B6 effects on ultrastructure of cerebral neuron. The purpose of this study is to investigate whether dietary excess of vitamin B6 affects the ultrastructure of the brain cortex neurons, and to examine some blood parameters and compare the cholesterol level in experiment groups.

In this study, three different experiment groups (EG) of 36 rats (Swiss Albino rats, for each group n=12) were treated 5mg/kg intraperitonally (IP) vitamin B6 daily for 10, 15, and 20 days (EG-I, II, III). Control group (totally n=36, for each EG n=12) was injected saline. Fresh tissue samples of cerebral cortex were taken from all of the experiment groups, prepared for routine conventional methods.

Blood samples were obtained from all experiments through cardiac punction. The levels of total cholesterol, HDL cholesterol and total lipid index in serum were determined. Ultrastructural observation revealed some degeneration in cellular region of the cerebral motor cortex in experiment group treated with high dose of vitamin B6 for long period. Degeneration in mitochondria, increased lipofuscin pigment granules in pericaryons, increased vacuoles and edema in neuropil, and decreased synaptic density were found. Results showed that in vitamin B6 treated rats total cholesterol level was significantly lower than those in the control group ($P<0.05$). Moreover, HDL cholesterol levels were significantly higher in vitamin B6 treated ($P<0.01$) groups.

In conclusion, the findings of the present study suggest that when high dosage treatment of vitamin B6 should be used for its beneficial effects on blood total HDL cholesterol, the treatment period should not be longer than one week.

Key Words: *vitamin B_6, cerebral cortex, cholesterol, rat, ultrastructure*

P67

Distribution of RS (reticulospinal neurons) by using vital dye during chicken embryonic development

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The brain stem contains reticulospinal (RS) neurons that are located at various levels of the hindbrain and project the earliest axons to the spinal cord. The majority of these neurons must be RS because they are ventral to the vestibular region.

A few methods have been used to study axonal morphology. In recent years, several studies have followed the development and morphology of axons and neural processes using modern tracing techniques. The tracers are typically different dextran-amines or DiI.

The difference between the two tracers is that DiI, being lipophilic, diffuses along the cell membrane in the fixed tissue. On the other hand, dextran-amines are used in living preparations in vitro where they are taken up by cut axons (Glover et al. 1986, Glover 1995.).

We used rhodamine-conjugated dextran-amines in the chicken embryo hindbrain at specific stages determined according to the Hamburger-Hamilton staging system. After applying the dextran-amines the preparations were incubated at room temperature in chicken ringer solution for 6-8 hours, depending on the transport of the dye. Experiments were performed on in vitro preparations of the brain stem to allow for precisely localized tracer injections combined with selective lesions of axon tracts. We observed both axon processes and retrogradely labeled cell bodies under the fluorescence microscope.

It is well known that is difficult to label the embryonic brain stem in vivo with the precision necessary to selectively trace specific axon populations, especially because cytoarchitectonic landmarks are not well established at early embyronic stages. Our experiments were designed to provide a developmental profile for comparison to the mature state.

We charted ipsilaterally and contralaterally projecting RS neurons as a function of developmental stage, and showed that RS neuronal differentiation proceeds in a rhombomere-specific pattern.

The results obtained with this technique represent only a small drop in the ocean of knowledge about brain stem and spinal cord organization, but illustrate the potential for comprehensive mapping of axonal projection systems in the developing brain.

Key Words: *chick, embryo, brain stem, vital dye, reticulospinal neuron*

P68

Anatomical properties and clinical importance of sural nerve

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The sural nerve supplies the lateral and posterior sides of the distal third of the leg and ankle. It continues its course on the lateral side of the foot to the lateral aspect of the little toe classicaly. The aim of this study was to define the constitution of the sural nerve and its variations. The clinical importance of the results

were discussed. Thirty lower limbs from formalin fixed cadavers were used for this study. In two specimens (6.7%), there were communications between the medial cutaneous nerve from the tibial nerve and the lateral cutaneous nerve from the common peroneal nerve. The medial cutaneous nerve was absent in two specimens (6.7%). On the other hand, in five specimens the lateral cutaneous nerve was missing (16.7%).

The sural nerve was passing 12.76±8,79 mm behind the posterior edge of the lateral malleolus and then 13.15±6.88 mm below its tip. After that, the sural nerve was directed on the lateral side of the foot. The presence and the course of the communicating branches between the sural nerve and intermediate dorsal cutaneus nerve were observed. The communicating branches between these two nerves were determined in 50% of the specimens.

This knowledge about the variations and course of the sural nerve allows one to avoid nerve injury during the surgical approaches to this region. Beside this, the development of the loco-regional anesthetic techniques and nerve grafts are led to increasing the interest to the anatomy of this nerve.

Key Words: *Sural nerve, lateral malleolus, nerve injury.*

P69

Severe crush injury performed by a Yasargil aneurysm clip.

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Various devices have been used to make a peripheral nerve injury. However, in the literature, there is few study on the standardization of these devices. Standardization problems effect to the intergroups and interlaboratories' results. Yasargil aneurysm clips are commercially available and stardarized devices. We reported previously 5, 10, and 20 minutes siatic nerve compression by that kind of devices. In the present study, we performed 30, 45, and 60 minutes siatic nerve compresssion and found that there was a cross correlation between the increase of the compression force and axonal regeneration. Additionally, we found that Yasargil aneurysm clip is an appropriate device to perform a severe sciatic crush injury. We think that it is necessary to consider the relationship between compression force and compression time in surgical and diagnostic procedures.

Key Words: *sciatic nevre, crush injury, Yasargil aneurysm clip*

P70

The examination of morphological changes in duodenum of vagotomised and sympathectomised rats

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In this study, 35 Spraque-Dawley rats were used in order to investigate the morphological changes in duodenum of vagotomised and sympathectomised rats. Rats were divided into 3 group; five rats were for control group, 10 rats were for surgical vagotomy and other 10 rats were for chemical sympathectomy (ip. 120mg/kg 6-Hidroxidopamine).

Vagotomised rats were sacrificed after 6 days and sempatectomised rats were sacrificed after 24 hours. After decapitation, duedonum's of control and experimental groups rats duodenum's were taken so as to routine histological techniques. After taken 6µm sections and stain with H+E and PAS, the slides were examined.

In the vagotomised group, while there were decreased mucosal secretion and destroyed Brunner's glands ($p<0.05$), there were no differences in muscular thickness and vascular dilatations between control and the experimental group.

After chemical sypathectomy, there were dilatation in submucosal vessels and decrease in the number goblet cells of crypta and villi ($p<0.05$). There was also lenfoid cell infiltration in the submucosal layer.

In conclision, autonomic nervous system could play important role in the duedonum via sympathetic and parasympathetic fibers. It could be concluded that while the sympathetic system has effect on blood vessel, numbers of goblet cells and structure of epithelia; the parasympathetic system effects blood vessels, numbers of goblet cells in villus as well as fluid of mucoid and musculer layer. It is concluded that the pharmalogical, biochemical and pathological studies could give more detailed information in this subject.

Key Words: *Vagotomy, sympathectomy, rat, duodenum*

P71

The effect of ethanol exposure on optic nerve in a chick embryo model system

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Fetal Alcohol Syndrome (FAS) due to maternal misuse of alcohol during pregnancy is characterized with pre- and postnatal growth retardation, central nervous system anomalies and a variety of other malformations craniofacial anomalies being the most common. The eye is known as a sensitive organ to toxic agents and teratogens. Ocular anomalies seen in children with FAS suggest that ocular structures are also sensitive to alcohol exposure during their development. This study was designed to investigate the effect of in ovo ethanol (EtOH) exposure on myelinization of optic nerve fibers in a chick embryo model system.

Fertilized "Cock of Denizli" strain chicken eggs were collected and divided into 5 groups with 20 eggs in each group. The first group was incubated as the non-treated group. The rest were injected with 100 µl of either 0.9% NaCl (vehicle control), or 10% EtOH, or 30% EtOH, or 50% EtOH solution (all EtOH solutions were v:v in 0.9% NaCl) into their air sacs. Injection holes were taped and all the eggs were placed into the egg-incubator at 37.5°C and saturation humidity. On days 13, 16, and 19 of incubation 5 eggs from each group were cragged and the embryos were analyzed in terms of their morphology and growth. In addition, on day 19 of incubation 5 additional eggs from each group were cragged and the optic cups including the optic nerves were dissected out. Specimens were processed for routine histology, sectioned, stained with toluidine blue, analyzed under a light microscope and photographed.

Results showed that, EtOH caused prenatal growth retardation in a dose-dependant manner. Prenatal exposure to EtOH also resulted in optic nerve hypoplasia in a dose-dependant manner. Myelinated nerve fibers ranging from small to big in diameter as well as glial cells, i.e. astrocytes and oligodendrocytes, were observed in controls. The tissue in between the cells and nerve fibers was intact in controls. On the other hand, a dose-dependant decrease in the number of myelinated nerve fibers was found in groups exposed to EtOH. Furthermore, the tissue in between the cells and nerve fibers lost its intact appearance in these groups.

In conclusion, this study showed that myelinization of optic nerve fibers is suppressed by EtOH in a dose-dependant manner. FAS can easily be mimicked in chick embryo model system. Thus, as a cheap and easy system chick embryo model is important in the study of FAS.

Key Words: *EtOH, fetal alcohol syndrome, optic nerve, chick, embryo*

P72

Three dimensional (3D) reconstruction of the rat hippocampus proper

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Hippocampus is a brain area that is effected by the kinds of disorders like epilepsy and Alzheimer. Furthermore, it has been sighted changes during the biologic course of aging. So, in nowadays, many studies have been done about the hippocampus. In these studies, the most preferable animal is rat, because the histological structure of the rat's hippocampus is similar to that of human. Especially, the pyramidal layer of the hippocampus proper is one of them. It is important to determine the exact border of this area pertinent to basic science and clinical science.

To improve the understanding of the hippocampus anatomy, we created three dimensional (3D) images of rat hippocampus. Hippocampus was reconstructed to 3D by a computer-aided program. The images produced as 3D supplies the understanding of the complex anatomic structure with ease. At the same time, 3D images may be used as a tool for virtual reality modeling of the hippocampus at the planning of the stereotaxic trial formerly. We are of opinion that this study will be useful for the neuroscientist on studies of rat hippocampus morphology and quantitative analysis.

Key Words: *Hippocampus proper, pyramidal layer, rat, 3D, computer-assisted, anatomy*

P73

A review of magnetic resonance imaging (MRI) studies of hippocampus volume in mood disorders

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The hippocampus plays an essential role in cognition and emotion and may be implicated in the pathophysiology of mood disorders. Most magnetic resonance imaging (MRI) studies have used a region of interest approach, where the borders are: superiorly temporal horn and alveus, inferiorly white matter of parahippocampal gyrus, medially ambiens cistern and laterally temporal stem. Hippocampal volume reduction in patients with recurrent major depression has been reported in the majority of MRI studies, particularly on the left side. This volume loss was reported to be related to anxiety, sexual abuse history, memory problems, and longer durations with depressive episodes went untreated, and it was particularly evident in treatment resistant unipolar depression and aged depressive patients. Elevated cortisol levels, decreased neurotrophic factors, glutamate neurotoxicity and inhibition of neurogenesis are some of the proposed mechanisms for hippocampal volume loss in major depression. Most studies with bipolar patients reported no hippocampus volume change compared to healthy controls. Therefore, current MRI literature suggests that hippocampus plays a key role in the pathophysiology of recurrent major depression, but not of bipolar disorder.

Furthermore, hippocampus is highly sensitive to neurotoxic effects of stress (i.e. elevated levels of cortisol and glutamate) and has also been found to be reduced in size in post-traumatic stress disorder and borderline personality disorder, as a possible result of stressors associated with these disorders. Therefore, hippocampal atrophy may cut across psychiatric diagnoses and may be a feature of psychiatric disorders characterized by repeated stressful events.

Key Words: *hippocampus, depression, bipolar disorder, magnetic resonance imaging, mood disorders*

P74

Three dimensional reconstruction and anaglyph of limbic system related structures

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The basal ganglia are a set of large structures toward the center of the brain that surround the deep limbic system. The basal ganglia are involved with integrating feelings, thoughts and movement, along with helping to shift and smooth motor behavior. The thalamus is the gateway to the cerebral cortex. The thalamus is a major sensory correlation center -all sensory signals except olfactory (smell) reach the thalamus before they are transmitted to the cerebral cortex where they are consciously perceived. The hippocampus is involved in converting short term memory to long-term memory. It is critical to learning. The fornix connects the hippocampi to each other and to other areas of the brain. it has a special relationship with the basal ganglia. The aim of this study is to demonstrate these neurologic structures using anaglyph technique and three dimensional (3D) imaging

Cross sectional images of fresh tissues from Visible Human Dataset were reviewed. Three-dimensional computer reconstructions of diencephalon, basal ganglia and fornix were generated from these dataset using a high speed operating system (Mac Os 9.2) and imaging software (Surfdriver 3.5).

The results of this study can be used to demonstrate the 3D relationships of the examined structures and explain the clinical pictures in their lesions.

Key Words: *basal ganglia, diencephalon, fornix, 3D reconstruction*

P75

The effect of the tarsal joint positions on the tibial nerve motor action potential latency in dog: electrophysiological and anatomical studies

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This study has been carried out to determine on the tibial nerve motor action potential latency and tarsal canal (tunnel) compartment pressure depending on the neutral, hyperextension and hyperflexion positions of the tarsal joint in dog by using electrophysiological and anatomical studies. For the electrophysiological study a total of twenty healthy mongrel dogs were used and latency of motor nerve action potential studies (MNAPL) of tibial nerve was performed in right hind limb of all dogs, the compartment pressures of the tarsal canal were determined both hind limbs in ten of these dogs. Nerve conduction studies showed that hyperflexion position of the tarsal joint caused prolongation of the MNAP latency of the tibial nerve as well as the highest pressure value of tarsal canal. For the anatomical study, in one dog, tarsal regions of left and right hind limbs were imaged by using magnetic resonance imaging (MRI) and two dogs were euthanatized for correlative anatomy. It was seen that the tibial nerve was located between flexor hallicus longus and superficial digital flexor muscles and the distance between these two muscles was the shortest in hyperflexion positions. In addition to this the plantar branch of saphenous artery, lateral and medial plantar nerves located more laterally in cadaver and MR imaging sections in hyperflexion as compared to neutral and hyperextension positions. As a result of this study, we thought that tarsal region diseases which cause the increased compartmental pressure and stretching nerve can provoke tarsal tunnel syndrome in dog and this syndrome may be aggravated in long time hyperflexion position of tarsal joint.

Key Words: *Tarsal canal (tunnel)-motor nerve latency-compartment pressure-anatomy-dog*

P76

Arcuate foramen and its clinical significance

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The ossification of ligamentous structures in various part of the body is frequently observed. This may result in a clinical problem such as compression to neighbouring structures and complications in the regional surgery. The posterior atlantooccipital membrane can sometimes partly or wholly ossify and forms a bony bridge over the vertebral groove, and forms the so-called arcuate foramen. The bony foramen may limit the normal mobility of the vessels during flexion and extension of the neck and may cause disturbances of arterial flow and of the peri-arterial sympathetic plexus giving rise to symptomps similar to those found in the Barre-Lieou syndrome. The aim of the present study is to determine the ossification state of the posterior atlantooccipital membrane in dry bone, in plane lateral X-ray films and CT. Further, correlate the clinical symptoms of the patients with the presence of bony foramen arcuale. Among the 60 dry atlases examined 7 had complete bony bridge formation, one was bilateral and 6 were unilateral. Incomplete unilateral bony bridge formation were observed in two atlases. The average data of length and width of foramen arcuale were measured on dry atlases as 8.0±0.2, 6.3±0.2mm on the left and 8.3±0.2, 6.4±0.1mm on the right side. Of the 100 plane lateral X-ray graphies examined 9% had complete and 3% had incomplete bony bridge formation. The patients with complete ossifications were voluntarialy invited for a CT scan. The avarage data of the length and width of the unilateral arcuate foramen were measured on 9 CT scan as 6.5±0.3, 4.8±0.2mm on the left and 6.4±0.1, 5.4±0.3mm on the right side. The results of the patients with foramen arcuale discussed with the correlation of symptoms, age and sex.

Key Words: *Arcuate foramen, atlas, atlantooccipital membrane, vertebral groove*

P77

Recombinant human erythropoietin protects peripheral nerves against acrylamide-induced neurotoxicity

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Acrylamide, a water soluble toxic chemical agent, causes dose-dependent loss of myelinated axons in peripheral nervous system of animals and humans. Animals given acrylamide exhibit behavioral deficits such as hind limb weakness and ataxia and show degeneration of axons distally. Thus, this distal axonopathy has been used as a model of human peripheral polyneuropathies. Recently, we have shown that erythropoietin (EPO), an erythrogenic hematopoietic factor widely distributed in the nervous system, protects dorsal root sensory neurons against a variety of cytotoxic insults. In this study, we examined the potential neuroprotective role of EPO in acrylamide-induced peripheral neuropathy in rats.

Acrylamide was administered to adult Sprague-Dawley rats in drinking water for 2 weeks. At the onset of acrylamide administration, animals were given daily intraperitoneal injection of EPO (2500 IU/kg/d; n=10) or vehicle (n=10) for a total of 3 weeks. Behavioral sensory (paw withdrawal latency) and motor (rotorod and grip strength) tests were done at baseline, 1, 2 and 3 weeks. Plantar footpads, intrinsic foot muscles and sciatic nerves were harvested for histological analysis of preservation of target innervation and axonal preservation.

Acrylamide treated animals developed mechanical hyperalgesia which was prevented by EPO administration. Similarly, compared with controls, EPO treated animals had less reduction in their grip strength at 2 weeks. Acrylamide induced a significant reduction in rotorod performance in rats and there were no differences between EPO or vehicle treated animals. These behavioral studies were reflected in morphological analysis of target innervation. Plantar footpads were almost devoid of any intraepidermal unmyelinated axons in acrylamide treated animals (as measured by PGP 9.5 staining), but there were many axons in EPO treated animals. Similarly, innervation in intrinsic foot muscles (as studied by alpha-bungaratoxin binding) were better preserved in EPO treated animals.

These results indicate that EPO has a neuroprotective effect on acrylamide-induced distal axonopathy. Although this neuroprotective effect is seen in both motor and sensory axons, it is more prominent for sensory neurons. The results of this study may provide a proof-of-concept rationale for human trials of recombinant human EPO in sensory neuropathies.

Key Words: *erythropoietin, acrylamide, neuropathy, neuroprotective, degeneration*

P78

An ultrastructural study of degenerating unmyelinated axons in the rat sciatic nerve

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Wallerian degeneration (WD) is a series of changes that occur in distal portion of a transected axon. Structural changes that occur during WD of myelinated axons are well described and molecular mechanisms underlying these changes are being sorted out. However, the sequence of structural changes in unmyelinated axons after axotomy is not well described. In this study, we examined the ultrastructural changes that occur in transected unmyelinated axons in rat sciatic nerve.

The left sciatic nerves of adult Sprague-Dawley rats were transected at mid thigh and the distal segments were collected at 12, 24, 48, 72 hrs and 5 and 7 days (n=5/group). The nerves were processed for both electron microscopy and immunohistochemistry for isolectin B-4 (IB-4), a marker of a subpopulation of unmyelinated axons.

Earliest changes that we observed in sciatic nerves were aggregation of organelles and swollen mitochondria. These changes were first seen occasionally at 12 hrs, but most prominent at 24 hrs. Following these changes, a brief stage of axonal swelling was observed prior to dissolution of the axoplasm. Axonal swellings were first seen at 24 hrs, but most prominent between 48-72 hrs. By 5 days post axotomy, most of the unmyelinated axons had disappeared and empty Schwann cell pockets within the intact basal lamina could be seen. At 7 days post axotomy, there were no unmyelinated axons left. These ultrastructural findings correlated with the disappearance of IB-4 staining from the axoplasm.

Our study describes the early structural changes that occur in unmyelinated axons following axotomy. These studies will form the basis for future studies aimed at understanding the molecular mechanisms underlying WD in unmyelinated axons. In many peripheral neuropathies, unmyelinated axons are affected first, prior to involvement of the large myelinated axons. Rational design of future neuroprotection studies in peripheral nerves will need to rely on better understanding of molecular mechanisms of WD in unmyelinated axons.

Key Words: *unmyelinated, sciatic nerve, axotomy, wallerian degeneration, neuroprotection*

P79

Identifying the effects of gamma knife on arteriovenous malformations by a dynamic angiogenesis modal

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We aimed to investigate the effects of Gamma Knife on the angiogenic activity of AVMs.

40 Sprague-Dawley, 250-300 gr weight rats were used. AVM samples, which were obtained from the operations performed at Marmara University Neurosurgery Department, implanted in rat corneas. One day after the implantation experimental group were applied 1.5 Gy, 3 Gy, 15 Gy and 30 Gy Gamma Knife. Control group were not applied Gamma Knife despite the AVM implantation. Angiogenic activity of implantation observed at days 2, 5, 10, 14 and 20 by surgical microscope. Surgical microscope data saved as video record. Rats that had purulent infection were excluded from the experiment. Corneal angiogenesis was graded macroscopically.

The initial effects of Gamma Knife application is endothelial destruction, after months, intimal proliferation and additional activities lead obliteration of vessel lumen. In addition to this knowledge, our data showed that Gamma Knife slows down the angiogenic activity induced by AVM. Intensity of angiogenesis induced by AVM tissue in the nonvascular cornea showed differences when control and experimental group compared.

These data implied that Gamma Knife slows down the angiogenic activity of Arteriovenous Malformations.

Key Words: *arteriovenous malformations, gamma knife, angiogenesis*

P80

Role of serotonergic activity in the antidepressant-like effects of L-Arginine and L-NAME

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Recent findings have indicated that nitric oxide (NO) modulators have dual effects in experimental depression studies. It has also been shown that serotonergic system plays an important role in these effects.

In the present study, we investigated the effects of selective serotonin re-uptake inhibitor sertraline, NO precursor L-arginine and NO synthase inhibitor L-NAME in the mouse forced swimming test (Porsolt's test). p-Chlorophenylalanine (p-PCA), an endogenous serotonin depletor was used for investigating serotonergic mediation on the dual effects of NO modulators. Sertraline, L-arginine and L-NAME reduced the immobility time in the mouse forced swimming test (antidepressant-like effect). p-PCA reversed the antidepressant-like effects of these drugs. In conclusion, our results suggest that NO modulators elicit their antidepressant-like activity in the mouse forced swimming test through a serotonin dependent mechanism.

Key Words: *nitric oxide, depression, p-PCA, mouse*

P81

Effects of pinealectomy and melatonin on brain ischemia-reperfusion induced morphologic changes in rats

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Over production of free radicals is important in the pathogenesis of the cerebral damage induced by ischemia-reperfusion. Melatonin the chief indoleamine produced by the pineal gland, and a well-known antioxidant and free radical scavenger. The purpose of the present study was to evaluate the effects of melatonin and pinealectomy on histopathological changes resulting from brain ischemia-reperfusion method, which intraluminal suture occlusion of the middle cerebral arter. Rats divided into three groups: sham-operated (control), Pinealectomized with melatonin, Pinealectomized. Rats were pinealectomized or sham-operated (control) 6 months before the ischemia-reperfusion studies.

Melatonin (5 mg kg/kg, i.p) was given to pinealectomized rats for last 30 days. To produce brain damage, middle cerebral arter was occluded for 60 min, followed by 24 h reperfusion, in anesthetized rats. At the end of each in vivo study the rats were sacrified and the brains were quickly removed, and were placed in

formaldehyde solution for routine histopathological examination. Sections from the blocks were stained with Hematoxylen-Eozin and Toluidine blue.

Depending on ischemia-reperfusion, widespread necrotic areas, vacuolization, eozinophilic degeneration and vascular congestion were observed in the brain slices. Pinealectomy leads to markedly increasing this damage. Melatonin given to pinealectomzied rats reduced brain damage resulted from middle cerebral arter ischemia-reperfusion.

These data suggest that physiologic melatonin release as well as exogenously given melatonin has a neuroprotective effect in focal cerebral ischemia.

Key Words: *Pinealectomy, melatonin, brain, focal, ischemia*

P82

No effects of 900 and 1800 MHz electromagnetic field emitted from cellular phone on nocturnal serum melatonin levels in rats

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There is growing public concern that radio frequency electromagnetic fields (EMF) may have adverse biological effects. Furthermore, there is accumulating evidence that exposure to the radiofrequency fields from mobile telephones or their base station could affect people's health

In this study, the effects of exposure 900 and 1800 MHz GSM-like electromagnetic field upon serum melatonin levels of adult male Sprague Dawley rats were studied. Thirty rats were randomly divided into three groups. First, control (sham operated) group (n=10), second 900 MHz EMF group (n=10) and third 1800 MHz EMF group (n=10). Rats were exposed 30 min/day, for 5 days/wk for 4 weeks to 900 MHz EMF or 1800 MHz EMF and compared to control rats. Control animals were sham-exposed under the same environmental conditions as the exposure groups. The concentration of nocturnal melatonin in the rat serum was measured by RIA.

In conclusion, statistically significant changes in nocturnal serum melatonin levels of 900 MHz exposed and 1800 MHz exposed rats compared to control group were not found either at 900 or 1800 MHz EMF exposure.

Key Words: *Electromagnetic field, serum melatonin, rat*

P83

Vitamin C levels of several tissues in guinea pigs in limited diet

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Vitamin C has numerous biologic functions such as, catecholamines synthesis, antioxidation, glucoregulation neuromodulation, and myelin formation in the schwann cells, etc. In the present study, we investigated the effect of the high doses of vitamin C administration with limited diet in the several tissues of guinea pigs. The objective of the present research was to determine the effect of vitamin C application (a single dose, 500 mg/ kg, ip) following acute and chronic limited diet periods (acute limited diet periods such as, 24 h, 48 h and chronic limited diet period such as, 120 h) in the vitamin C levels of tissues such as blood, liver, brain, kidneys and heart. Adult male guinea pigs (Cavia aperea porsellus) weighing 421± 25 g were caged in a temperature-controlled room (20-22 ¡C) and water was given ad libitum and they were maintained on a 12-hr light dark cycle. Guinea pigs of control group were fed with guinea pigs pellets. Vitamin C (L-Ascorbic acid) administration was given just prior to limited diet periods. Animals had free access to water and guinea-pig chow during feeding period and only limited lettuce (10 g/daily) during limited diet periods. The chronic limited diet period is chosen as 120 hrs, because half life of vitamin C is 96 hrs in the guinea pigs. The results of this study showed that blood vitamin C levels decreased by limited diet but increased by vitamin C administration. The brain vitamin C levels increased (except the 120 h), depending on the length of limited diet period in the limited diet groups. The liver vitamin C levels decreased depending on the length of limited diet period in the vitamin C administration following limited diet in the period groups. Vitamin C levels of heart and kidneys did not change significantly. The weight loss was regularly induced by increasing the the length of limited diet period together with vitamin C administration.

We suggest that vitamin C may be used for homeostasis of organism in limited diet situation.

Key Words: *Vitamin C administration, limited diet*

P84

Effects of CDP-choline and its endogenous metabolites on plasma catecholamine response to graded hemorrhage in rats.

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CDP-choline, an endogenous intermediate in membrane phosphatidylcholine synthesis, is a drug used to treat several cerebral ischemic situations and neurodegenerative diseases. Exogenously given CDP-choline rapidly metabolized to cytidine monophosphate, phosphocholine, cytidine and choline. The roles of these metabolites in the pharmacological actions of exogenous CDP-choline are not known. In the present study we tested whether peripheral administration of CDP-choline or its metabolites alter the plasma catecholamines response to graded hemorrhage in rats. Wistar rats (female, 250-300 g) were injected intraperitoneally saline (1 ml/kg), CDP-choline (0.6 mmole/kg), choline (0.6 mmole/kg), phosphocholine (0.6 mmole/kg), cytidine monophosphate (0.6 mmole/kg) or cytidine (0.6 mmole/kg) and then 5 minutes after they were subjected to graded hemorrhage as described previously (Ulus, Arslan, Savci, Kiran. Br J Pharmacol, 116;1911,1995). Briefly, a blood sample (0.6 ml per 100 g of body weight) was withdrawn over 10 s from the carotid artery catheter into a chilled plastid syringe containing 0.1 ml of EDTA solution (5 mg/ml). This procedure repeated four times at 5-min interval. The cumulative blood loss in each animal consisted of volumes equal to 0.6, 1.2, 1.8 and 2.4 ml per 100 g of body weight. Blood samples were designed for S1 through S4 and were assayed for plasma catecholamine (as adrenaline and noradrenaline) by radioimmunoassay. In saline treated control rats, the graded hemorrhage resulted in a significant rise in plasma adrenaline

levels; plasma noradrenaline was also increased slightly, but not significantly. In saline treated control rats plasma adrenaline levels in the fourth blood sample (S4) were about 12-fold higher than those observed in the first (S1) samples. The effect of graded hemorrhage on plasma adrenaline was enhanced by choline at S1 and S2 or by phosphocholine at S1 S2 and S3. Plasma noradrenaline response to graded hemorrhage was enhanced by choline, phoscholine and CDP-choline at S1 to S4. Cytidine or cytidine monophosphate failed to alter plasma adrenaline and noradrenaline responses to graded hemorrhage.

These data show that CDP-choline and its metabolites phosphocholine and choline, but not cytidine or cytidine monophosphate, enhance plasma catecholamine response to graded hemorrhage. The increase in ganglionic cholinergic neurotransmission in the sympathoadrenal system may involve in this action of CDP-choline on plasma catecholamine.

Key Words: *CDP-Choline, choline, adrenaline, noradrenaline, graded hemorrhage*

P85

Light and electron microscopic investigation of chronic thinner exposure on rat sciatic nerve tissues.

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Thinner is an organic solvent heavily used in industry. Thinner is inexpensive and readily available, and its use has continued to increase. It can cause severe central nervous system impairment as well as in experimental investigations. But, no more histopathological changes of sciatic nerve caused by chronic thinner addiction have been reported. In the present study, it was evaluated to light and electron microscopic investigations of chronic thinner exposure on rat sciatic nerves. It was aimed that the results may be helpful to contribute of understanding the histopathologic damage of periferic nervous system

The male Wistar albino rats (150-250 g) were divided in two experimental groups: the control and the thinner treated group (n=10 for both). Thinner treatment was performed by inhalation of 2000 ppm thinner, in 6 day/week order for 12 weeks. Tissue samples were obtained for histopathological investigation.

Sciatic nerves in thinner group indicated that endoneurial edema, axonal degeneration and myelin sheath vacuolisation. The area of injury on the myelin sheath were measured by Image-Pro Plus. Mean of the injury area was estimated 18% per myelin. In our study, morphological findings showed that chronic thinner inhalation caused degenerative changes on the sciatic nerves of rats. Further studies will be required to evaluate the possible mechanism of chronic thinner exposure toxicity on the sciatic nerves.

Key Words: *thinner, electron microscopy, morphological changes, sciatic nerve, rat*

P86

Effects of copper on the axon reflex induced vasodilation in the human forearm microcirculation

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Dietary copper is known to be essential for the normal functioning of the cardiovascular system and also contributes to the acetylcholine (ACh) induced vasodilation. Several studies have demonstrated that the microvascular vasodilation in response to ACh is the sum of direct stimulation of the endothelium by ACh and of the vasodilation that is related to the axon reflex. However, neuro-modulatory role (s) of copper in skin microcirculation is not defined. Therefore the aim of this study was to test whether there are neural pathways of this transition metal in the control of skin blood flow and was to determine the its contribution to the total response.

The study was performed in a quiet room with the subjects lying in the supine position. All subjects were nonsmokers and had no history of cardiovascular disorder. Laser Doppler flowmetry (LDF) in combination with iontophoresis was used for assessing forearm skin microvascular function. The responses to the iontophoresis of ACh (%1), and to the iontophoresis of $CuSO_4$ (0.1μM) solutions containing ACh (%1) or not were compared to determine the effect of Cu^{2+} on acetylcholine induced vasodilation. Individual trials were performed after an aclimatization period of 30 min between trials. To clarifying the role played by axon reflex, cutaneous sensory nerve blockade with topical anesthesia (EMLA cream) was applied before each study and, blood flow responses to the iontophoresis of above mentioned agents were measured at this EMLA-treated site again. In addition, theoretical curve analysis was also used to determine the involved mechanisms.

The major finding in our study is that copper significantly increases ACh-induced vasodilation. This integrated response have three components and two of them was inhibited in the presence of topical anesthesia.

Theoretical analysis and experimental results suggest at least one of the mechanisms by which copper augments vasodilation is that of axon reflex. This vasodilator action of Cu^{2+} seems to be independent of ACh-provoked axon reflex. As a second possibility Cu^{2+} may activate vascular endothelial synthase or may prolong the half-life of NO by mechanisms that mimic the action of superoxide dismutase, ultimately resulting in the potentiation of NO activity in vascular tissue. Although we did not perform NO/NOS- inhibitor studies theoretical analysis in light of literature suggest that the vasodilatory pathways of Cu^{2+} and ACh was additive.

Key Words: *Axon reflex, microcirculation, copper, acetycholine.*

P87

Analgesic activity of *Foeniculum vulgare* Miller fruits in mice

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In this study Gas-chromatographic analysis, analgesic effect and median lethal dose (LD_{50}) of *Foeniculum vulgare* Miller essential oil (FEO) extract were investigated in Swiss albino mice. Thirty min before drug administration in the baseline latency determinated and 30, 90 and 150 min after drug administration by tail-flick device. Aspirin (150 mg/kg, per oral) was used as a reference standard. Only isotonic saline solution (0.2 ml, intraperitoneal) was given to the control group. 0.25 ml/kg and 0.50 ml/kg FEO extract were given intraperitoneally to FEO groups. At the 150. minute of the study it was determined that all of the study groups had significantly analgesic effect when

compared with control group and there was no difference between Aspirin and FEO groups. It was concluded that FEO has statistically significant and same analgesic effect with Aspirin at the 150th minute of the study. LD_{50} of the FEO was determined as 1.038 ml/kg.

Key Words: *mice, Foeniculum vulgare Miller, analgesic activity*

P88

Anticonvulsive effect of alpha-terpineol on mice

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Alpha terpineol is a volatile oxygenated monoterpene, found in various animals and plants and plant juices consumed in daily life. In this study, activities on the experimentally induced convulsions were studied as one of the steps of our studies on alpha-terpineol. Albino mice of either sex were subject to 1, 10 and 100 mg/kg i.p alpha-terpineol. Anticonvulsive actions were tested using pentylenetetrazol (80 mg/kg) induced convulsions. As a result, alpha-terpineol inhibited convulsive effects of pentylenetetrazol only at 100 mg/kg but not at other tested doses, and to the best of our knowledge, this is the first report on the anticonvulsive effect of alpha-terpineol.

Key Words: *monoterpene, essential oil, alpha-terpineol, neuropharmacology, anticonvulsive*

P89

Return to work after peripheral nerve injuries at upper extremity

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The aim of this study was to determine whether any improvements return to work potential of patients with peripheral nerve injuries after a carefully designed vocational rehabilitation program. This study covered 56 patients received a vocational rehabilitation program for 6 weeks. Patients were evaluated with at before and after vocational rehabilitation program by grip strength, valpar upper extremity range of motion test and purdue pegboard test. At the end of study grip strength ($p<0.01$) and functional dexterity regarding to endurance and coordination ($p<0.05$) increased and time of return to work ($p<0.05$) decreased. This study shows that vocational rehabilitation program has very important role in improvement of return to work potential of patients with peripheral nerve injuries at upper extremity.

Key Words: *upper extremity injuries, peripheral nerve injuries, physiotherapy, hand rehabilitation, vocational rehabilitation.*

P90

The effectivines of physiotherapy in patients with carpal tunnel sendrom

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Different physiotherapy methods use for the treatment of carpal tunel sendrom (CTS). The use of manual therapy to treat somatic pain sendrom and associated disabilities is widespread. The purpose of this study was to determine whether manual therapy as a new and popular approach in physiotherapy, heat and home exercise program could decrease the pain in patients with CTS. 13 wrist treated in 8 female and 1 male patients with CTS aged 42.85±11.43 years. Mean treatment seans was 13.38±2.53. 20 minutes hot pack as heat application, traction and gliding of radiocarpal and intercarpal joints as manual therapy and home exercise program were used in treatment. Amount of pain by recording on a visual analog scale was measured in milimeter (mm.) before and after treatment. The amount of the pain at before and after treatment respectively were 67.21±15.89 mm. and 36.85±12.32 mm. The decrease of pain amount after treatment was statisticaly significant ($p<0.05$).

This finding suggests that combine physiotherapy treatment program which includes manual therapy, heat and home exercise is effective approaches for decreasing pain in patients with CTS.

Key Words: *Carpal tunnel syndrome, physiotherapy, manuel therapy, therapeutic heat, therapeutic exercise.*

P91

Effects of gabapentin in acute pain combined with tramadol

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In oncology patients, gabapentin (Neuroentin®) used for neuropathic pain can be combined with tramadol (Contramal®). In this experiment, we aimed to examine affects of antiepileptic gabapentin and/or tramadol in acute pain.We used tail- flick and hot-plate tests to determine the effects of these drugs in mice. After having approval from Animal Ethics Comite; 32 Swiss albino mice (30-40 grams) divided into four groups, each containing 8 mice. First group (Group K) received distiled water, second group (Group N) received gabapentin (Neuroentin) (30mg/kg), third group (Group T) received tramadol (Contramal) (30mg/kg) and finally fourth group (Group NT) received 30mg/kg gabapentin+30mg/kg tramadol. All injections were intraperitoneal and mice received 0.1ml solution per 10g of their weights. Thirty minutes after drug application tail-flick and hot-plate tests were done. Tail-flick (May Ltd. Ankara) equipment was set for 50% power and hot-plate (May Ltd. Ankara) was set for 56°C. All results were tested with ANOVA. Tail-flick test for Group one (mean 7.2 sec) and Group two (mean 7.9 sec) were significantly shorter ($p=0.01$) then Group three (mean 20.9 sec). Foot drawing and foot licking tests in Group one were 9.0 and 10.2 sec; in Group two 73.6 and 77.3 sec; in Group three 110.3 and 112.7 sec, respectively ($p=0.000$ and $p=0.000$). Tail-flick test that determine acute pain was longer with tramadol treatment. Also in hot-plate tests tramadol and neuroentin+tramadol treatment groups were longer than control and neuroentin groups. With 30mg/kg dose; neuroentin found non-effective while tramadol was effective. Effect of tramadol in acute pain might have decreased by adding neuroentin. In conclusion, dose regulation may be important for these drugs and this subject should be explored extensively in the future.

Key Words: *gabapentin, pain, tramadol*

P92

Effects of second generation tetracyclines on hippocampal neuron number in the rat model of penicillin-induced epilepsy

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Minocycline and doxycycline are second generation tetracyclines which have high lipophilic properties. Recently, it has been found that these drugs have neuroprotective action on the animal models of global and focal ischemia, Huntington's disease, amyotrophic lateral sclerosis, Parkinson's disease and traumatic brain injury. In this study, we examined the effects of minocycline and doxycycline on the decreased hipocampal neurons caused by intracortical penicillin 500 IU-induced epilepsy in rats.

The epileptic rats were divided into 3 groups received either minocycline, doxycycline or saline. A fourth group operated intracortically but without application of penicillin was regarded as sham group.

Minocycline and doxycycline (90 mg/kg i.p.) were injected one minutes after the epilepsy induction. Beginning 12 hours after operation, the animals received minocycline and doxycycline 90 mg/kg every 12 hours for the first 24 hours and then 45 mg/kg every 12 hours for further 3 days. Animal brains were removed and frozen at -50°C in a cryostat.

The brains were sectioned horizontally and the sectiones were selected according to the Randomised Systemic Sample Strategy. The selected sectiones were stained with H&E. The total pyramidal neuron numbers were estimated in CA1, CA2, CA3 fields using optical fraction method.

The total pyramidal neurons in the control group (105.153±6.898) were lesser ($p=0.002$) than the sham (150.082±9.479). In the minocycline group, the total pyramidal neurons (130.538±3.034) were higher ($p=0.015$) than the the control group.

On the other hand, doxycycline also increased the total pyramidal neurons (125.230±8.206) but the effect did not reach significant level ($p=0.086$). Moreover, the number of hippocampal neurons in the sham group was not different from those determined in either minocycline ($p=0.11$) or doxycycline ($p=0.8$) groups.

In conclusion, the second generation tetracycline minocycline decreased the loss of hippocampal neurons caused by penicillin-induced epilepsy in rat.

Key Words: *epilepsy, penicilline, minocycline, doxycycline, hippocampus, cell count*

P93

Potential role of some oxidant/antioxidant parameters in prefrontal cortex of rat brain in an experimental psychosis model and the protective effects of omega-3 fatty acids

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Schizophrenia is a major mental disorder with unknown etiology and its pathophysiology is complex. Evidences support the hypothesis that schizophrenia may be the result of increased reactive oxygen species mediated neuronal injury. Omega-3 (n-3) fatty acids is an essential fatty acid found in large amount in fish oil. The aims of this study are to demonstrate the contribution effect of oxidative stress to the neuropathophysiology of schizophrenia and that prevention of oxidative stress may improve prognosis and thereby also in the functions of neuronal membranes. It has been known for several decades that noncompetitive NMDA antagonists such as phencyclidine (PCP) and MK-801 induce psychomimetic reactions. MK-801 induced selective neurotoxicity has been proposed as an animal model for psychosis.

Healthy adult and male Wistar Albino rats were obtained Firat University Biomedical research Unit and 30 rats divided randomly into three groups. MK-801 was given intraperitoneally at a dose of 0.5 mg/kg/day for 5 days in the experimental psychosis group. n-3 fatty acids (800 mg/kg/day) was given to the treatment group for 6 days by per oral rout. In control group, saline was given in the same way. In 7^{th} day from the beginning of the experiments, rats were killed by decapitation and prefrontal cortex was removed immediately. Nitric oxide (NO) levels as well as total superoxide dismutase (t-SOD), xanthine oxidase (XO), catalase (CAT), adenosine deaminase (ADA), and glutathione peroxidase (GSH-Px) activities in prefrontal cortex were measured.

MK-801 group had significantly higher values of XO ($p<0.0001$), NO ($p<0.0001$), GSH-Px ($p<0.0001$), and ADA ($p<0.0001$), t- SOD ($p<0.0001$) than those of the control group and n-3 treated group. There were no significant changes in CAT enzyme activities in MK-801 group compared to control group and n-3 FA group. These results indicate that MK-801 can increase reactive oxygen species (ROS) and antioxidant ezymes activities in prefrontal cortex. On the other hand, n-3 EFA may reduce the oxidative damaged. This animal study also may provide some evidences for a therapeutic effect of n-3 supplementation to neuroleptic regimen in the treatment of schizophrenic symptoms.

Key Words: *MK-801, prefrontal cortex, omega-3, oxidants, antioxidants, schizophrenia.*

Author Index

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