NEUROANATOMY

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VOLUME 2 (2003)

SUPPLEMENT 1

2nd National Congress of Neuroscience

Bursa, Turkey, April 16-20, 2003

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ISSN 1303-1775 (electronic) 1303-1783 (printed)

2003 VOLUME 2

NEURONANATOMY

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Aims and Scope

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

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All material for publication should be sent to *Associate Professor M. Mustafa Aldur, MD, PhD, Department of Anatomy, Hacettepe University, Faculty of Medicine, 06100, Ankara, Turkey; e-mail: editor@neuroanatomy.org*. For detailed instructions concerning the submission of manuscripts, please refer to the Instructions to Authors at the back of the journal or visit the journal web site (*http://www.neuroanatomy.org*).

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Printed by ILERI

Neuroanatomy, 2003, Volume 2, Supplement 1, Pages 1-45.

Abstracts

Published online 21 April, 2003 © neuroanatomy.org

Presented at the 2nd National Congress of Neuroscience, 16th-20th April, 2003, Uludag University, Bursa, Turkey

ORAL COMMUNICATIONS

1

PHARMACOLOGICAL PROPERTIES OF THE LOW THRESHOLD POTASSIUM CURRENT IN OCTOPUS CELL OF THE MICE COCHLEAR NUCLEUS

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Octopus cells in the posterioventral cochlear nucleus (PVCN) are biophysically specialised to detect a coincidence in firing of auditory nerve fibers. They convey the synchrony to neurons in the ventral region of the ventral nucleus of the lateral lemniscus (VNLL) through calyceal endings and to the superior paraolivary nucleus with exceptionally precision. The precision in the timing of action potentials depends on the low input resistance and short time constant of octopus cells at rest. Two conductances contribute to the low input resistance in the physiological voltage range: hyperpolarisation-activated mixed cation current (Bal & Oertel, J. Neurophysiol 2001, 84:p806-817) and low threshold potassium outward current (Bal & Oertel, J. Neurophysiol 2001, 86:p2299-2311). Whole-cell and excised outside-out cell recordings were performed from visually identified octopus cells in coronal slices of the posterioventral cochlear nucleus from mice of between 17 and 20 postnatal days. The low threshold potassium current recorded using whole-cell configuration had varying extent of sensitivities to the toxins, alpha-dendrotoxin (alpha-DTX), dendrotoxin-K (DTX-K) and tityustoxin K-alpha, which are less selective blocker of Kv1.1, more selective of Kv1.1 and selective of Kv1.2 respectively. Alpha-dendrotoxin, DTX-K and tityustoxin K-alpha blocked ~91 %, 67 % and 58 % of the peak outward currents respectively.

2

CEREBELLAR CONNECTIONS TO THE ROSTRAL RETICULAR NUCLEUS OF THE THALAMUS IN THE RAT

Cavdar S (1), Onat F (2), Yananli HR (2), Sehirli US (1), Tulay C (1), Saka E (1), Gurdal E (1).

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This study demonstrates cerebellar connections to the reticular nucleus thalamus (RNT) by means of retrograde axonal transport of horseradish peroxidase (HRP) in the rat. Specific HRP pressure injections to the rostral RNT (1.6 -1.8 mm caudal to bregma) resulted in retrograde labelling of neurons in the cerebellar nuclei. The rostral RNT showed specific topographical organization concerning its cerebellar connections. Microinjections into the rostral RNT, 1.6 mm caudal to bregma, produced numerous HRP-labelled neurons within the anterior interposed (emboliform nucleus) and scarce HRP-labelled neurons within the lateral (dentate nucleus) cerebellar nuclei, whereas injections into the rostral RNT, 1.8 mm caudal to bregma, produced numerous HRP-labelled neurons within the posterior interposed (globose nucleus) and scarce lightly HRP-labelled neurons within the lateral (dentate nucleus) cerebellar nuclei. Cerebellar connections with the rostral RNT were exclusively ipsilateral to the injection site. No HRP-labelled cells were detected in the medial (fastigial nucleus) cerebellar nucleus. The cerebellar connections reach the RNT via the superior cerebellar peduncle. By contrast, HRP injections into the anterior, posterior interposed and lateral cerebellar nuclei produced no labelled cells within the RNT.

This study demonstrates the existence of direct cerebello-RNT but not RNT-cerebellar connections. The presence of the cerebello-RNT connections introduces a new route through which the cerebellum may influence RNT and thus cerebral cortical activity.

3

A SINGLE NUCLEOTIDE POLYMORPHISM OF HUMAN IFN-GAMMA GENE IN SUBACUTE SCLEROSING PANENCEPHALITIS PATIENTS

Isgor-Tilki E (1, 2), Yentur SP (2), Gurses C (3), Demirbilek V (5), Yilmaz G (6), Cokar O (7), Onal E (4), Gokyigit A (3), Saruhan-Direskeneli G (2).

I.U. (1) DETAE Department of Immunology, Istanbul Medical Faculty Departments of (2) Physiology, (3) Neurology and (4) Public Health, I.U. Cerrahpasa Medical Faculty Department of (5) Neurology and (6) Microbiology, and (7) Haseki Hospital, Istanbul.

Subacute sclerosing panencephalitis (SSPE), which is a rare, persistant infection of the central nervous system (CNS), is caused by measles virus (MV). Complications of measles are mainly attributed to generalized immunosupression caused by the virus. T helper-1 (Th1) like cytokine responses including IFN-gamma are reported to be diminished in measles infections. Although the pathogenesis of SSPE remains to be determined, viral but also host factors seem to be involved.

To identify host genetic factors involved in the development of SSPE we investigated the association of a single nucleotide polymorphism (SNP) in the first intron (+874 T/A) of IFN-gamma, which is a Th1 type cytokine. For this polymorphism, DNAs from 38 SSPE patients and 102 healthy controls are extracted by salting-out technique and screened by polymerase chain reaction amplification with sequence specific primers (PCR-SSP) for this SNP. Control primers are included in each reaction.

Although not reaching statistical significance, 34.2% of patients and 20.6% of controls were homozygote for IFN-gamma +874 AA, whereas IFN-gamma +874 TT distribution among patients and controls were 23.7% and 21.6% respectively. Similarly, 76.3% of patients and 78.4% of controls were carrying A allele, whereas T allele was present in 65.8% of patients and 79.4% of controls.

 ISSN 1303-1775 (electronic) 1303-1783 (printed)

Whether this SNP could have any significance in host response to measles infection or SSPE development, has to be evaluated in larger sample groups.

This study was supported by TUBITAK (SBAG-2456).

4

IL-12 AND IL-10 POLYMORPHISMS IN MYASTHENIA GRAVIS

Yilmaz V (1, 2), Parman YG (3), Serdaroglu P (3), Deymeer F (3), Saruhan-Direskeneli G (2).

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Myasthenia Gravis (MG) is characterized by T cell dependent autoantibodies to acetylcholine receptor (AchR) on the post-synaptic membrane of the neuromuscular junction. The production of these autoantibodies (Ab) is regulated by T cells via cytokines. Interleukin-12 (IL-12) is a key inducer of differentiation of uncommitted Th cells towards Th1, whereas IL-10 is mainly an anti-inflammatory cytokine which inhibits Th1 functions and potentiates Th2 regulated responses. The Th1 cytokines may be important in helping AChR Ab production and Th2 cytokines may be responsible for disease progression and persistence in MG. On the other hand, inter-individual differences in cytokine profiles appear related to allelic polymorphisms of cytokine genes and differences may have implications in disease susceptibility.

The aim of this study was to analyze the association between MG and polimorphisms in IL-10 and IL-12 genes in 62 patients and 101 healthy controls (HC). Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay was applied to two single nucleotide polymorphisms (SNP) of the IL-10 promoter region at positions -3575(A/T), -2763(A/C) and to one SNP of the IL-12p40 3'UTR at +16974 (A/C) region.

Comparison of IL-10 genotypes between MG and HC revealed that 45,9% of the patients and 39,6% of the controls were heterozygote for IL-10 -2763 and 48,4% of the patients and 44,6% of the controls had IL-10 -3575 TT. At the IL-12 p40 +16974 polymorphic site, 50% and 55,3% of the same groups had AA genotypes, respectively. Also, the carriage of any of these polymorphic alleles did not show a susceptibility effect to MG.

These results did not implicate any effect of these polymorphisms on susceptibility to MG in these relatively small patient groups.

This study is supported by the I.U. Research Fond (T-1125).

5

LATE EVENT-RELATED POTENTIALS RELATED TO FRONTAL-POSTERIOR SPATIAL ATTENTION PROCESSES

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The aim of the presented study is to investigate the dynamic nature of the cortical visuospatial attention processes. We recorded EEG of normal volunteers during a computerized line bisection test (LBT) administration. LBT is a simple visual spatial attention task in which subjects are required to mark the midline of the presented lines. EEG of 26 volunteers were recorded during 2 conditions with the use of both hands (total of 4 conditions): 1) LBT: Subjects marked the midline of the lines with a mouse in the LBT performance. 2) Control task: The same lines were presented as in LBT task but the subjects were just required to look at the lines and click the mouse button after a while. This condition was created to involve visual and motor processes that were also engaged in LBT performance. We obtained two event-related potentials subsequent and time locked to the line presentations namely P300 and a slow positive wave (SPW). P300 latency was shorter and P300 amplitude was greater significantly in the right hemisphere than left hemisphere and during LBT performance when it was compared to the control condition. P300 latency and P300 amplitude difference between the left and right hemisphere was significant in the parietal cortex. SPW amplitude was greater during task condition than control. SPW amplitude was significantly greater in the right hemisphere and especially in the frontal cortical sites. Results suggest that time course of the visual spatial processing after primary visual perception starts mainly in the right temporal parietal cortical sites and continues in the right prefrontal cortex. These findings may be helpful in clarifying the origins of attention deficits that were seen in neurological and psychiatric diseases.

6

QUANTITATIVE ANALYSIS OF MYELINATED AXONS OF ANTERIOR, POSTERIOR AND HABENULAR COMMISSURES IN THE CAT BRAIN

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The commissural fibres connecting the cortical regions of the two cerebral hemispheres with each other include the anterior, posterior and habenular commissures. Although these commissures have been investigated in some animals, there are no data about the number of their myelinated axons, except one study performed in the rat brain (Sargon et al., 2002). Therefore, in this study, the myelinated axons of anterior commissure, posterior commissure and habenular commissure were counted in the cat brain by using camera lucida. The numerical densities of these axons were compared with each other by means of quantitative analytical statistical methods. In the comparison of the number of myelinated axons of the anterior, posterior and habenular commissures; statistically significant differences were found between the anterior and habenular commissures, and between the posterior and habenular commissures. No statistically significant difference was found between the anterior and posterior commissures. Additionally, small sized myelinated axons were present in the anterior and posterior commissures. However, a heterogenous distribution of myelinated axons was present in the habenular commissure.

7

TIME LAPSE VIDEO VISUALIZATION OF PERIPHERAL NERVE REGENERATION IN VITRO

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Yuzuncu Yil University, Medical School, Neuroscience Research Unit (1) Department of Physiology, (2) Department of Histology, (3) Department of Pharmacology.

In order to observe and analyze cellular events taking place during peripheral nerve regeneration and to elucidate temporal and spatial relationships we use an in vitro model adapted for long term microscopic examination. Dorsal root ganglia with a piece of peripheral nerve were removed from the mice, explanted into extracellular matrix in a special petri dish and the peripheral nerve was cut in the middle to form a gap. The preparation was then covered with RPMI 1640 medium and transferred to a special inverted microscope which enables to keep the tissue at 37ºC and 5% CO2 for long periods. A CCD camera attached to the microscope captured images to a computer connected at predefined intervals for several days. The individual frames were then combined and used to form a video sequence. Experiments eloquently showed the migratory movements of Schwann cells across the gap to form a bridge

and elongation of neurites. We also made interesting observations about the relationship of migratory cells among themselves and with outgrowing axons, which included removal of a regenerating axon by its ensheathing Schwann cell, a novel observation.

8

FACTOR VII R353Q POLYMORPHISM IN TURKISH STROKE PATIENTS

Atac FB (1), Can U (2), Verdi H (1), Celiker G (2), Benli S (2), Kilinc M (2), Ozbek N (3).

Baskent University Faculty of Medicine, Departments of Molecular Biology and Genetics (1), Neurology (2) and Pediatrics (3).

The development of thrombotic disorders in human is one of the most common causes of morbidity and mortality. There is a growing research field in the genetics of blood coagulation factors, inhibitors, fibrinolytic factors and platelet membrane receptors. Recent findings suggested that high levels of Factor VII (F-VII) were independently associated with an increase in the risk of fatal myocardial infarction in middle-aged men. Polymorphisms in the F-VII gene contribute to variation in the level of this coagulation factor. Among these polymorphisms, R353Q reported to associate with F-VII levels. Patients with Q/Q genotype had lower levels of F-VII antigen and clothing activity. In this study 151 stroke cases and 98 healthy controls were examined. Restriction fragment size analysis was performed by visualisation of Msp I digested PCR products after separation by gel electrophoresis in a 2.5 % ethidium stained agarose gel. The genotype distribution of the polymorphism was; R/R: 65.6%, R/Q: 29.1%, Q/Q: 5.3% in stroke patients and R/R: 74.5 %, R/Q: 23.5% and Q/Q:2% in healthy controls. This is the preliminary study in stroke patients concerning F-VII polymorphisms. To better characterise the effect of polymorphisms in this gene, studies are in progress.

9

NEUROANATOMY

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It is our great pleasure and honor to introduce Neuroanatomy (ISSN 1303-1775, 1303-1783).

It is a fact that there are no neuroanatomy journals published in Turkey at present. Actually, the situation is not any different throughout the world. There are many 'neuroscience' journals dealing with neuroanatomy from the clinical sciences point of view. Neuroanatomical standpoints appear to be often omitted except in the anatomy journals containing neuroanatomical publications. The difference could be likened to looking through a window from the inside or the outside. This double reality or gap is the main core which led us to the idea of publishing Neuroanatomy.

Neuroanatomy is an annual, peer-reviewed journal, having a dynamic international Editorial and Scientific Advisory Board. Articles for the journal are chosen by the editors and published in English to make it easier for international use and more suitable for cataloging in the indexes.

The journal contains electronic and printed versions. Editors give special importance to the electronic version due to the fact that it can be updated easily and can reach a large mass of readers. The electronic version also aims any one paper to be able to be used by its author or international scientific members effectively and without delay. As soon as a paper is accepted for publication, it emerges as a PDF (Portable Document File) formatted style in the internet address. Collected papers throughout the year in the electronic version are put together in the printed version and published with the same page number and format. This is how our first volume came into being. Printouts pass as original copies until the end of the year. The same will apply for future volumes.

The electronic version of Neuroanatomy is free of charge and can be reached through the http://www.neuroanatomy.org in full text at PDF format.

As this journal came to life with an 'amateur' spirit, special care was taken to perform maximum professional quality to be cherished by all members of the scientific world.

The basic aim of the journal is to present a medium where all people concerned with neuroanatomy will have a chance to introduce their studies and hypotheses. From this point of view, it is clear that besides objective scientific observations, the journal also welcomes rational speculative scientific subjects. As in all scientific journals the only subject to which the journal's doors are barred, is scientific fraud.

We would especially like to thank our Editorial and Scientific Board members and all others who have worked for long days and given their unconditional support for the publishing of our journal. Our great many thanks also go to all the authors who have contributed with their works to the birth of Neuroanatomy.

10

CHARACTERIZATION OF A PUTATIVE G-COUPLED TRANSMEMBRANE PROTEIN USING BIOINFORMATIC TOOLS

Varisli L, Yildiz H, Cen O.

Harran University, Faculty of Art and Science, Sanliurfa, Turkey.

Background: The nervous and immun systems are functionally interconnected. One of the important common featurs of both is the high activity level of inter- and intra-cellular signaling. Several cDNA clones have been identified in the yeast two hybrid system as putative interacting molecules with IL-5 reseptor, a crucial component of the immun system. One of these clones - clone 38 harbors putative glycosylation, myristoylation, phosphorylation, and SH3 motifs, characteristics of some important signaling molecules.

Metods: The clones had been obtained in the yeast two-hybrid screening. Further characterization was performed using bioinformatic tools available through NCBI (National Center for Bioinformatic Instititute), EBI (European Bioinformatik Instititute), and KEGG (Kyoto Encyclopedia of Genes and Genomes) databases.

Results: Clone38 is localized on the chromosom 2. It has 8 exons. These exons may lead to different mRNAs by alternative splicing in different tissues or during different stages of development. It seems to encode for a 2.5 kilobase mRNA in fetal brain while another 1.5 kiobase mRNA in sciatic nerves. The protein product of clone38 is expected to be a G-coupled, five-span transmembrane portein.

Discussion: Our data needs be supported experimentally. Since it has alternatively spliced forms in fetal brain and adult sciatic nerves, it may have important functions during development.

Conclusion: Our data indicate that clone38 may be an important receptor regulating intracellular signals leading to different cellular functions.

11

TENASCIN IN MENINGIOMA: EXPRESSION IS CORRELATED WITH ANAPLASIA, VASCULAR ENDOTHELIAL GROWTH FACTOR EXPRESSION, AND PERITUMORAL EDEMA BUT NOT WITH TUMOR BORDER SHAPE

Kilic T, Bayri Y, Ozduman K, Acar M, Diren S, Kurtkaya O, Ekinci G, Bugra K, Sav A, Ozek MM, Pamir MN.

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Objective: Tenascin is an extracellular matrix glycoprotein that is expressed during embryogenesis, inflammation, angiogenesis, and carcinogenesis. The aim of this study was to investigate how tenascin expression relates to histological grade, angiogenesis, and radiological findings in meningiomas. Methods: Twenty typical, 20 atypical, and 5 malignant meningiomas were studied retrospectively. Tenascin expression and vascular endothelial growth factor (VEGF) expression in the tumor tissue were investigated by immunohistochemistry. Tenascin messenger ribonucleic acid expression was also studied by comparative reverse transcriptase-polymerase chain reaction. Magnetic resonance images from each case were assessed for peritumoral edema and tumor border shape. Results: The atypical and malignant meningiomas showed higher levels of tenascin expression than the typical meningiomas. The more sensitive messenger ribonucleic acid-based methods confirmed this finding. Tenascin expression was correlated with peritumoral edema and VEGF expression but not with tumor border shape. In the 13 tumors with marked tenascin expression, peritumoral edema was Grade 0 in one, Grade 1 in three, and Grade 2 in nine specimens. In the same 13 tumors, VEGF expression was Grade 1 in five and Grade 2 in eight specimens, and the findings for tumor border shape were Grade 0 in seven, Grade 1 in four, and Grade 2 in two specimens. Conclusion: In meningiomas, tenascin expression is correlated with anaplasia, tumor-associated edema, and VEGF expression but not with tumor border shape. This protein may play a role in the neoplastic and/or angiogenic processes in atypical and malignant meningiomas and may thus be a potential target for meningioma therapy.

12

EXPRESSION OF STRUCTURAL PROTEINS AND ANGIOGENIC FACTORS IN CEREBROVASCULAR ANOMALIES

Kilic T, Pamir MN, Kullu S, Eren F, Ozek MM, Black PM.

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Objective: The goal of this study was to describe the expression of matrix proteins and angiogenic factors in cerebrovascular malformations. Methods: Forty-six cerebrovascular malformations were immunohistochemically investigated with a battery of staining for five structural proteins (collagen IV, collagen III, smooth muscle actin, fibronectin, and laminin), and three angiogenic factors (vascular endothelial growth factor [VEGF], basic fibroblast growth factor [bFGF], and transforming growth factor alpha [TGFalpha]). The lesions consisted of 34 arteriovenous malformations (AVMs), 10 cavernous malformations (CMs), and 2 venous angiomas. Expression intensity for each histological layer in the abnormal vessel wall was graded and compared. Results: AVM endothelia and subendothelia expressed more laminin and collagen IV than the same layers of CMs. Conversely, CMs expressed more fibronectin than AVMs. CM endothelia exhibited more prominent staining for smooth muscle actin than AVM endothelia. AVMs and CMs expressed VEGF in the endothelium and subendothelium, and TGFalpha in endothelial and perivascular layers. However, unlike AVMs, CMs expressed bFGF in the endothelium as well. The brain tissue intermingled within AVMs also expressed growth factors. Modified glial cells in the brain tissue adjacent to CMs expressed bFGF and TGFalpha, but not VEGF. Venous angiomas did not express the studied growth factors and mainly consisted of structural proteins of angiogenically mature tissue. Conclusion: Expression characteristics of structural proteins reveal that AVMs and CMs have different immunohistological properties. This study provides strong confirmation of previous findings of VEGF and bFGF immunoexpression in AVMs and CMs. It adds new information on TGFalpha expression in these malformations and on expression of the angiogenic factors in venous angiomas.

13

EXPRESSION OF GROWTH FACTORS AND STRUCTURAL PROTEINS IN CHORDOMAS: BASIC FIBROBLAST GROWTH FACTOR, TRANSFORMING GROWTH FACTOR ALPHA, AND FIBRONECTIN ARE CORRELATED WITH RECURRENCE

Deniz ML, Kilic T, Almaata I, Kurtkaya O, Sav A, Pamir MN.

Department of Neurosurgery, Neurooncology Laboratories, Marmara University Institute of Neurosciences, Istanbul, Turkey.

Objective: To test the hypothesis that the expression of certain growth factors and/or structural proteins is correlated with the biological behavior of cranial base chordomas.

Methods: The study investigated 14 pathological specimens of cranial base chordomas from patients who were monitored for at least 2 years after their initial operations. Some cases involved multiple tumor recurrences and multiple operations. For those patients, the time to recurrence after each operation was recorded and a mean value was calculated. Nine patients with mean times to recurrence of 24 months or more or with 24 months of follow-up monitoring without recurrence after single operations were designated the ”good-prognosis” group. Five patients with mean times to recurrence of less than 24 months were designated the ”poor-prognosis” group. In each case, only the specimen from the initial operation was studied. Multiple sequential sections were cut from paraffin-embedded blocks of tissue and immunohistochemically prepared for detection of three growth factors and three structural proteins, i.e., basic fibroblast growth factor, transforming growth factor alpha, vascular endothelial growth factor, fibronectin, collagen III, and collagen IV. Intensity of expression was graded by using a four-tier system (Grades 0, 1, 2, and 3). Levels of expression of the molecules in the two groups were evaluated and compared.

Results: The mean transforming growth factor alpha expression intensity grades for the good- and poor-prognosis groups were 0.8 and 2.6, respectively, and the corresponding mean basic fibroblast growth factor grades were 1.4 and 2.6. For both groups, the mean grade for vascular endothelial growth factor expression was 0.6. For fibronectin, the mean staining grades for the good- and poor-prognosis groups were 2.2 and 3.0, respectively. The corresponding mean intensities for collagen III were 1.1 and 0.8, and those for collagen IV were 2.5 and 2.6.

Conclusion: Our descriptive data from immunohistochemical analyses of chordomas suggest that high levels of transforming growth factor alpha and basic fibroblast growth factor expression are linked to higher rates of recurrence. Strong fibronectin expression may also be a marker of aggressive biological behavior.

14

EFFECT OF SURGERY ON TUMOR PROGRESSION AND MALIGNANT DEGENERATION IN HEMISPHERIC DIFFUSE LOW-GRADE ASTROCYTOMAS

Kilic T, Ozduman K, Elmaci I, Sav A, Pamir MN.

Marmara University Institute of Neurological Sciences, Istanbul, Turkey.

The aim of this study is to determine the impact of surgery on tumor progression and malignant degeneration in hemispheric diffuse astrocytoma WHO grade II. Twenty-eight patients who were operated or underwent stereotactic biopsy for hemispheric diffuse astrocytoma WHO grade II at Marmara University between January 1987 and January 1996, were prospectively reviewed for the presence of recurrence and histopathological dedifferentiation at their fourth years after the initial treatment. Twenty-two patients underwent surgical resection. Of this group, 7 patients had a total, 11 had a subtotal and 4 patients had a partial resection. Six patients underwent

stereotactic biopsy. All patients, except for the ones in whom a radiological total surgical removal could be achieved, received postoperative radiotherapy. In the total surgical-removal group only one patient had recurrence, while no upgrade was noted. All of the patients in the partial resection and stereotactic biopsy groups recurred at a higher grade. Our results indicate that both tumor progression and histopathological dedifferentiation were less commonly seen when a total or subtotal resection could be achieved. So, surgery, as radical as possible, should be the choice of treatment in low-grade hemispheric astrocytomas.

15

GRADING ANGIOGENESIS OF CEREBROVASCULAR MALFORMATIONS WITH DYNAMIC EXPERIMENTAL MODEL

Konya D, Kilic T, Kurtkaya O, Yildirim O, Pamir MN.

Department of Neurosurgery, Marmara University Faculty of Medicine; Institute of Neurological Sciences, Marmara University, Istanbul.

Objective: In this study: we aimed to generate a dynamic experimental model in which normal brain , normal blood vessel wall, cavernous malformations and arteriovenous malformations were implanted on the non-vascular corneal-tissue. To compare the angiogenesis grades of normal and pathological tissues Material- Methods: Fifty Sprague-Dawley rat weighing 250-300 g were used. In all rats the upper layer of the cornea was excised 1 mm from the scleral union and an approximately 1mm3 micropocket was created. Human AVM, CM, mature vessel and brain tissues were impianted into the micropockets.

Results: In this experimental work which is implemented on the non-vascular corneal-tissue; both macroscopical and microscopical findings demonstrated that AVM, CM and vessel wall implantations generated angiogenesis. On the other hand angiogenesis was not optained in the brain tissue implanted in corneas. Angiogenesis started at the third day of implantation , enhanced at the fifth day and reached maximum at seventh to ninth days. Macroscopic observations of AVM implanted corneas angiogensis index were mostly Grade 3. In most of the macroscopic findings of CM implanted corneas showed Grade 1 angiogenesis. On light microscopical examination of hematoxylin and eosin stained prepareations angiogenesis was maximum in AVM's. This was followed by CMs. All corneas including brain tissue implanted ones showed VEGF expression on the basal membrane of multi-layered epithelium. AVM imlanted corneas also showed VEGF expression on endothelium of sproating new vessels.

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EXPRESSION OF INTEGRINS IN CEREBRAL VASCULAR MALFORMATIONS

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Objective: Integrins especially play critical roles in anjiogenesis. Cerebral vascular malformations are angigenically active and show different properties. No data are available on the expression of these integrins in cerebral vascular malformations. Methods: We analysed using immunhistochemical and (Western blot) analyses with polyclonal antibodies capable of recognizing each integrin heterodimer. The expression of VEGFR1 and VEGFR2 are also studied. We evaluated the expression of 5 i in a series of 6 AVM and 11 CCM's. Results: All 3,5 i and VEGFR1, VEGFR2 were expressed in AVM and CCM series. So it has shown that both AVM and CCM series angiogenetically active. 1 was strongly expressed both in AVM's and CCM's. 3 expressed in AVM and CCM but weaker corresponding to 5 expression. 5 integrin was more strongly expressed in CCM than AVM. Conclusion: This data demonstrates the expression of 5 i in AVM's and CCM's. Our data suggest that both malformations are angiogenically active and angiogenesis is mature in AVM's and immature in CCM's.

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CHARACTERIZATION OF A PUTATIVE NUCLEAR PROTEIN USING BIOINFORMATIC TOOLS

Varisli L, Yildiz H, Cen O.

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Background: The nervous and immun systems are functionally interconnected. One of the important common featurs of both is the high activity level of inter- and intra-cellular signaling. Several cDNA clones have been identified in the yeast two hybrid system as putative interacting molecules with IL-5 reseptor, a crucial component of the immun system. One of these clones - clone1 harbors putative myristoylation, phosphorylation, and SH3 motifs. It is predicted to have a nuclear localization signal. These features are characteristics of some important signaling molecules.

Metods: The clones were obtained in the yeast two-hybrid screening. Further characterization was performed using bioinformatic tools available through NCBI (National Center for Bioinformatic Instititute), EBI (European Bioinformatik Instititute), and KEGG (Kyoto Encyclopedia of Genes and Genomes) databases.

Results: Clone1 is localized on the chromosom 9. It spreads on 20 kilobase DNA containing 6 exons, which may lead to different mRNAs by alternative splicing. The protein product of clone1 has a putative zink finger domain, involving interactions with other proteins or DNA molecules, and c1Ig3a protein kinase-like motif. It is also predicted to harbor 2 transmembrane domains.

Discussion: The predicted features of clone1 should be confirmed experimentally. The fact that it can have a nuclear localization signal and two transmembrane segments may indicate that it may be embedded in nuclear membrane.

Conclusion: Clone1 seems be an important intracellular signaling molecule.

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POSTTREATMENT WITH MAGNESIUM SULFATE AND APOPTOSIS

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Our purpose was to study the neuroprotective effect of treatment magnesium sulfate with a bolus injection after the hypoxic-ischemic insult in newborn rats.

Twenty-eight each seven-day-old rats were enrolled into the study and control group. All subjects were exposed to unilateral carotid artery ligation and 1 hour hypoxia (8% oxygen in 92% nitrogen). The study group received a bolus injection of 300 mg/kg magnesium sulfate intraperitoneally. The control group received a bolus injection of saline in the same volume intraperitoneally as the study group. One, 2, 3, 4, 24 hours and 7, 21 days after the injury the four each rats were killed and their brains removed for histologic study with hematoxylin & eosin and the terminal deoxynucleotidyl transferase (tdt)-mediated deoxyuridine triphosphate (dutp)-biotin nick end labeling (TUNEL) staining. Cell counting was performed in the cerebral cortex and hippocampus. The hippocampus was divided in to the CA1, CA2 and CA3 subfields. The numbers of TUNEL- staining positive and necrosis cells were counted at X20 objective and X 10 eyes pieces (one visual field=0.1 mm2) in each right and left hemispheres. In each brain, the same area was counted in

adjacent section for all different staining. Positive cells were expressed as mean+SD values. The magnesium and control groups were compared by Mann Whitney U test.

Mean values of TUNEL positive cells per square milimeter of brain regions: CA1, CA2, CA3 and cerebral cortex for magnesium group were 449+132; 412+124; 423+102; 421+112 respectively. Although mean values of TUNEL positive cells for control group were 1059+549; 703+334; 644+272; 610+201 respectively. The decreasing of the number of TUNEL positive cells began at 3h post-hypoxia-ischemia peaked at 24h. The process appeared to occur at a faster rate in the CA1, compared with the others. The data demonstrate that magnesium sulfate treatment prevents apoptosis after hypoxia-ischemia (p=0.000) but no necrosis except at cerebral cortex.

In conclusion; posttreatment magnesium sulfate with a bolus injection has neuroprotective effects against apoptosis associated hypoxia-ischemia

Key words: Magnesium sulfate, posttreatment, hypoxia-ischemia, apoptosis, necrosis, bolus injection.

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ANTICONVULSANT EFFECTS OF NO IN EXPERIMENTAL EPILEPSY

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It is suggested that NO is involved in pathophysiology of epilepsy. In spite of contrary findings, our results show that NO may be an endogenous anticonvulsant molecule. The aim of this study was to investigate the effects of NO on penicilin induced epileptiform activity in anaesthetized Wistar rats. The epileptiform activity was produced by injection of penicillin G (3MIU/kg) i.p. or 500 IU i.c.v. The ECoG (Electrocorticogram) activity was displayed on a four channel recorder.

1. Epileptiform activity was significantly decreased by NO donor, sodium nitropurriside (SNP). Prior application of haemoglobin (5μl), a NO scavenger, prevented the anticonvulsant effect of SNP.

2. Injection of N±61527; -L-Arginine Methyl Ester (L-NAME, i.p.) 30 minutes before penicillin significantly reduced the latency of epileptiform activity. In addition L-NAME (300±61549; g/2±61549; l, i.c.v.) increased the frequency of epileptic spikes when applied 30 minutes after epileptiform activity onset. Saline and D-NAME (i.c.v.) were ineffective.

3. 7-nitroindazole (7-NI, 60mg/kg i.p.) injection 30 minutes before penicillin significantly reduced the latency of epileptiform activity. Intracerebroventricular administration of L-arginine (300±61549; g/2±61549; l) and SNP (100±61549; g/2±61549; l) suppressed epileptiform discharges. D-arginine and saline were completely ineffective.

4. According to our preliminary results, NO precursor L-arginine has an inhibitory effect on audiogenic epilepsy in wistar rats.

These results suggest that NO might be an endogenous anticonvulsant substance under these experimental conditions.

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TUMOR NECROSIS FACTOR (TNF) AND INTERLEUKIN-8 (IL- 8) GENE POLYMORPHISMS IN NEURO-BEHÇET SYNDROME

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Behçet's disease (BD) is a chronic, inflammatory multisystemic condition of unknown etiology. It is clinically characterized by recurrent oral and genital ulceration, skin lesions, ocular manifestations, arthritis and vasculitis of all sizes and types of blood vessels. Central nervous system involvement in BD, namely neuro-Behçet (NB), occurs in 5% of patients and causes devastating complications.

Different genetic polymorphisms have been evaluated as disease susceptibility factors. Association of HLA-B51 with susceptibility to BD is well documented, and contribution of other genetic polymorphisms to different disease manifestations, such as neurological involvement is waiting to be explored. By using PCR-RFLP, the distribution of TNF gene -308 (G-A) and -376 (G-A), and IL-8 gene - 353 (A-T), +1530 (T-C), +3331 (A-G) single nucleotide polymorphisms were screened in 26 patients with NB, 87 BD patients without neurological involvement and in 100 healthy controls.

The results revealed relatively homogenous distribution of these polymorphisms in all groups. Comparison of NB with BD patients at TNF-308 (G-A) polymorphism showed that GA genotype was increased in NB group (38.5 vs 16.1%, p: 0.026, OR: 3.26). However, this increase was not statistically different from the healthy controls (29.9%).

These results may implicate a subtle but modifying role of TNF polymorphism in NB development on a susceptible genetic background shared by BD patients. A genetic heterogeneity in the pathogenesis of BD may also account for the observed difference.

This study was supported by I.U. Research Fund (T933).

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ANGIOTENSIN-CONVERTING ENZYME GENE INSERTION/DELETION POLYMORPHISMS AND SUSCEPTIBILITY TO MIGRAINE

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Angiotensin - converting enzyme plays an important role in blood pressure regulation and electrolyte balance by hydrolyzing angiotensin I into angiotensinII which is a potent vasopressor, and aldosterone stimulating peptide. After cloning the ACE gene, 50% of the interindividual variability of plasma ACE concentration is determined by an insertion (I) / deletion (D) polymorphism in the intron 16 of the ACE gene and known as the ACE/ID polymorphism. Previous reports have shown association between ace I/D polymorphism and coronary heart disease and related cardiovascular diseases. Paterna et al.(2000. Eur. Neurol 43 (3): 133-136) have shown an association between ACE -D allele polymorphism and migraine without aura.

We were interested to know whether ACE I/D polymorphism may cause susceptibility to migraine. To address this question, we evaluated 120 patients (70 migraine without aura,23 migraine with aura and 9 tension-type headache) with migraine type headache against 160 control subjects (Chi2=8.820; df:2; P=0.012). Genotypes were based on polymerase chain reaction amplification. The alleleic frequency of the I of ACE was 35.78% in total migraine type headache and 32.50% in the control subjects. In the present study, ID genotype alone in total migraine showed susceptibility to migraine (OR=2.111; 95% CI=1.274-3.499; Chi2=8.517; df:1; P=0.004). However DD genotype was protective against migraine (OR=0.598; 95% CI=0.360-0.995; Chi2=3.937; df:1; P=0.047). We also observed an association between ID of the ACE gene and patients with migraine without aura (OR=1.979; 95% CI=1.121-3.496; Chi2=5.611; df:1; P=0.018). The allelic frequency of the I allele of ACE was 32.28% in the patients with migraine without aura, and 32.50% in the control subjects. ACE I/D polymorphism of patients with migraine

without aura was statistically significant (Chi2=6.136; df:2; P=0.047). In patients with migraine with aura, we found that ID genotype was 2.593 - fold increased risk for migraine with aura (OR=2.593; 95% CI=1.058-6.354; chi2=4.560; df:1; P=0.033). Again DD genotype was protective towards migraine with aura (OR=0.371; 95% CI=0.139-0.990; Chi2=4.159; df:1; P=0.041). Although ID genotype was 2.593 - fold greater risk for tension type headache, it was statistically insignificant. In conclusion, the ID genotype of ACE gene may cause greater risk for migraine in patients with migraine without aura, migraine with aura and tension type headache.

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THE EFFECTS OF SYSTEMIC LEPTIN ADMINISTRATION ON NITRIC OXIDE METABOLITES OF SEVERAL BRAIN AREAS IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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Aim: It was known that serum leptin concentrations were decreased in rats with streptozotocin(STZ)-induced diabetes. Nitric oxide (NO) is also known to play an important role in the pathophysiology of insulin-dependent diabetes mellitus. The aim of this study was to investigate the effects of systemic leptin administration on nitric oxide metabolisma of the hypothalamus, hippocampal formation, cerebellum and pons in STZ induced rats.

Methods: Experiments were performed on 28 male Wistar Albino rats (250.6±6.06 g). The animals were divided to 2 main groups as nondiabetic (NDM; n=14) and STZ induced diabetic (STZ-DM; n=14). STZ was administrated (i.p.; 55mg/kg) in a single dose. Both of the main groups were divided as leptin and PBS (phosohate buffered saline) subgroups. Leptin was dissolved in PBS and injected daily (0.1mg/kg, i.p.) for 5 days in leptin groups. PBS groups were also received only PBS injections. On day 6, the animals were sacrificed by taken blood from their hearts. Total brain immediately removed and brain areas were dissected. Nitrite and nitrate levels (metabolits of NO) were measured by Griess Method.

Statistics: Experimental data were statistically analyzed by Mann Whitney U Test and $p<0.05$ values considered as significant.

Results: NOx levels were significantly high in the hypothalamus ($p<0.05$) and significantly low in the hippocampal formation ($p<0.05$) and cerebellum ($p<0.05$) of diabetic PBS group when compared to nondiabetic PBS group. Diabetic condition did not change the NOx levels in pons ($p>0.05$).

Administration of leptin did not significantly change NOx levels of brain areas in NDM group. However, in STZ-DM group, leptin administration decreased NOx levels significantly in hypothalamus ($p<0.05$), hippocampal formation ($p<0.05$) and cerebellum ($p<0.01$), but did not change these values in pons.

Conclusion: Data demonstrated that leptin may contribute some brain functions by mechanisms which are associated with nitric oxide in STZ-induced diabetes.

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EFFECTS OF CAFFEIC ACID PHENETHYL ESTER AGAINST DOXORUBICIN INDUCED NEURONAL OXIDANT INJURY

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Oxygen-derived free radicals have been implicated in the pathogenesis of doxorubicin induced toxicities. The aim of this study was to investigate the effects of caffeic acid phenethyl ester (CAPE), an antioxidant agent, on doxorubicin induced neuronal oxidative injury in rats. The rats were treated with CAPE (10 μmol/kg/day i.p.) or saline starting 2 days before a single dose of doxorubicin (20 mg/kg i.p.) or saline. Ten days later, the brain was excised to analysis. The doxorubicin alone resulted in higher malondialdehyde level than the other groups. The activity of catalase was higher in doxorubicin plus CAPE group than doxorubicin group. There was no significant difference in nitric oxide level, glutathione peroxidase and superoxide dismutase activities between the groups. There were negative correlations between glutathione peroxidase activity and malondialdehyde level in both doxorubicin and doxorubicin plus CAPE groups. It can be concluded that doxorubicin induced oxidant injury can be prevented by CAPE treatment with its antioxidant properties in rat brain.

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THREE-DIMENSIONAL COMPUTER RECONSTRUCTIONS OF VERTEBRAL CANAL AND SPINAL CORD BASED ON VISIBLE HUMAN PROJECT IMAGE DATASET

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Objectives: The spinal cord, spinal nerve roots, and their coverings, called meninges, are located within the vertebral canal, which is formed by the vertebral foramina in successive vertebrae. The aim of this study was to determine normal measurements of vertebral canal and spinal cord in anteroposterior and transverse planes from Visible Human Project Image Dataset and to compare these with previously published data.

Methods: Cross sectional images of fresh tissues from Visible Human Dataset were reviewed. Three-dimensional computer reconstructions of vertebral canal and spinal cord were generated from these data using a high speed operating system (Mac OS 9) and imaging software (Surfdriver 3.5).

Results: We measured the anteroposterior and transverse diameters of the vertebral canal and spinal cord at each vertebral level and investigated dorsal and ventral cerebrospinal fluid layer at each vertebral level. Obtained data at each vertebral level have been analyzed statistically.

Conclusions: Many variations were observed in the size and shape of the vertebral canal in different levels. These differences occur depending upon to the enlargement of spinal cord in the cervical and lumbosacral regions, for the innervation of the limbs. These morphological measurements will help to the neurosurgeons during the surgery of the spinal cord and vertebral canal.

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ec-NOS GENE POLYMORPHISMS IN STROKE PATIENTS

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The gene encoding endothelial nitric oxide synthase (ec-NOS) is aspirant for the mediation of initial endothelial cell damage seen in disease.ec-NOS is encoded by the ec-NOS gene located on chromosome 7q35-36 comprising 26 exons that span 21kb and expressed in endothelium. Recent studies improves the significant association between the ec-NOS gene polymorphisms and cardio vascular disease and hypertension. However the concerning role of ec-NOS gene polymorphism

as a risk factor in stroke is remained to be elucidated. Our aim was to investigete the frequency of ec-NOS intron 4 VNTR and intron 23(G10-T) polymorphisms in stroke patients and compare with that of healthy subjects by PCR -restriction fragment length polymorphism. The frequencies of ec-NOS4b/b, ec-NOSb/a and ec-NOSa/a for stroke patients and control group were 68.10%, 31.03%, 1.72% and 68.26%,29.34%,2.40% respectively. The distribution of the frequencies for ec-NOS intron 23 (G10-T) polymorphism were as fallows: g/g: 82.90%, g/t :17.05%, t/t: 0 for stroke group and g/g: 80.37% , g/t: 19.63%, t/t:0% for healthy individuals. To the best of our knowledge, this is the first and preliminary report showing an influence of ec-NOS gene polymorphisms in our ethnic group with stroke patients. Further studies involving E298D polymorphism of ec-NOS gene is under investigation.

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SERUM LEVELS OF MANNOSE-BINDING LECTIN IN MYASTHENIA GRAVIS, MULTIPLE SCLEROSIS AND HEALTHY CONTROLS

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The C-lectin pathway which is one of the three complement pathways is known to be activated by binding of mannose-binding lectin (MBL) to bacterial carbohydrates. Low serum MBL levels as well as MBL gene mutations are implicated in the pathogenesis of recurrent infections and some autoimmune disorders. Its plasma concentration is genetically determined by a series of allelic dimorphisms located within the structural gene and in the promoter region.

In this study, we investigated serum MBL levels in patients with autoimmune neurological diseases with possible role of infections. MBL levels were measured in the sera of 77 myasthenia gravis (MG) (F/M: 47/30, mean age: 49.1), 33 multiple sclerosis (MS) (F/M: 25/8 mean age: 34.4 years) and 105 healthy controls (HC) (F/M: 63/42, mean age: 34.8 years) with ELISA. Patient and control groups were divided into normal and below normal (low) MBL groups (the cut off value for low MBL levels was 500 ng/ml) and the ratios of low MBL producers were compared between groups.

A wide range of serum MBL levels were observed in all three groups of patients (range, MG: 3.2-8500 ng/ml, MS: 1.9-7020 ng/ml, HC: 0-5870.7 ng/ml) and no significant differences were observed in the median serum MBL levels among the three groups (MG: 3277 ng/ml, MS: 2398 ng/ml and HC: 3235 ng/ml). The numbers of low MBL producers (<500 ng/ml) were also not different between groups: 19% of MG compared to 6% of MS and 17% of HC had low serum levels of MBL.

These results do not suggest MBL deficiency as a contributary factor in the development of MG or MS by imparing innate immune responses against microorganisms.

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DOUBLE IMMUNOGOLD LABELING OF GABA AND GLUTAMATE IN HIPPOCAMPUS OF GENETIC ABSENCE EPILEPSY RATS FROM STRASBOURG (GAERS)

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Purpose: The understanding of the mechanisms underlying absence seizures in man and animal species has been studied by the use of a variety of animal models. A well known animal model of absence epilepsy is the use of a strain of Wistar rats with genetically determined seizures termed, genetic absence epilepsy rats from Strasbourg (GAERS). In the present study, we used double immunocytochemical technique at electron microscopic level in order to show the coexistence of glutamate and GABA in mossy fiber terminals in the hippocampus of GAERS and nonepileptic controls.

Materials and Methods: Adult GAERS and non-epileptic control rats were perfused through the aorta with a fixative solution containing 0.5% paraformaldehyde, 2.5% glutaraldehyde, 0.1% picric acid in 0.1 M HEPES buffer. Brains were removed and CA3 region of hippocampus was dissected under a stereomicroscope. Tissues were postfixed with osmium tetroxide and then dehydrated through graded series of ethanol. After clearing in propylene oxide and embedding in Epon, tissue blocks were obtained. Ultra-thin sections were first incubated in primary anti-GABA antibody and then in secondary goat anti-rabbit antibody conjugated to 20 nm gold particles. Grids were subjected to paraformaldehyde vapor in 60°C and then incubated with primary anti-glutamate antibody. Sections were then incubated with secondary goat anti-rabbit antibody conjugated to 10 nm gold particles. Sections were then viewed and photographed using a JEOL 1200 EX electron microscope.

Results: In the present study, GABA and glutamate immunoreactivity were found to coexist in mossy fiber terminals in CA3 region of both control and GAERS groups.

Conclusion: Although mossy fiber terminals are known to be excitatory, there is electrophysiologic evidence that GABAergic transmission occur and inhibitory postsynaptic currents can be elicited at mossy fiber synapses. An inhibitory input from dentate gyrus to CA3 was transiently activated in kindled rats [1]. It was also suggested that the physiologic role of the mossy fiber GABAergic signal might be of developmental importance and augmentation of this signal after seizures could have an inhibitory or disinhibitory effect [2]. Coexistence of GABA and glutamate in mossy fiber terminals and the mechanism of their effect on the physiological function of CA3 pyramidal neurons need further evaluation.

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CYTOGENETIC RESULTS IN TWO SIBLINGIS WHO WERE DETERMINED AS SPINA BIFIDA OCCULTA

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Neural tube defects (NTDs) are common congenital malformations that occur when the embryonic neural tube fails to close properly during early development. Although multifactorial in origin, NTDs appear to have a strong genetic component. Inductive interactive and genetic regulations during axis development may play a role in patterning of NTDs.

In this study,we have aimed to compare our cytogenetic results with the hystological and neurosurgical results in two siblings who were determined as spina bifida occulta a diagnosis based on the presence of a small truft of hair on their backs.

Chromosomes were prepared by conventional tecniques from lymphocyte cultures metaphase chromosomes were karyotyped by standart trypsin- giemsa banding methods.

The karyotype of the mother was determined 46, XX, del (17) (q25) in one field of 50 metaphase. The karyotype of her son was determined 46, XX, del (17) (q25) in three field of 50 metaphase and 46,XY, +m in one field of 50 metaphase. The karyotype of the daugther was determined 46, XX.

It is highly interesting that somatosensorial evoked potentials (SEP) examination and chromosome analysis were both revealed pathological results in brother who had thick, fatty filum and low lying conus medullaris. No deletion was detected in his mother. In addition,in his sister, SEP, chromosome analysis and macroscopical appearrance were all in normal limits.

As far as the correlation between histopathological appearance of the thick and fatty filum terminale and chromosome analysis is concerned, a strong correlation has been found between genetic, cystological and neurosurgical results regarding the deletion of chromosome 17 (q25).

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EFFECTS OF MELATONIN ON SYNAPTIC TRANSMISSION AND LONG-TERM POTENTIATION IN THE CA1 REGION OF MOUSE HIPPOCAMPUS

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The pineal hormone, melatonin has several biological and cellular effects that it is involved in the regulation of circadian rhythms and modulation of neuronal activity. It has been shown to inhibit [Ca2+]i in sensory neurons. Melatonin receptor is found in the dentate gyrus, CA3 and CA1 regions of the hippocampus. The aim of the present study was to investigate the effects of melatonin on synaptic transmission and long-term potentiation (LTP) in the CA1 field of mouse hippocampal slice. Transverse coronal slices (400um in thickness) were made using a vibrating slicer. A concentric bipolar stimulating electrode was placed schaffer colleteral afferents and an extracellular recording electrode placed near synaptic site in the CA1. A stimulation frequency of 0.066 Hz (50us duration) was used throughout the experiments except during tetanic stimulation. Extracellular field excitatory postsynaptic potential (fEPSPs) and LTP were recorded in all experiments to ensure response stability later. Melatonin (0.1-1mM) depressed fEPSPs in a concentration-dependent manner that mean fEPSPs amplitude was 92±6% (n=5) and 80±11% (n=5) ($p<0.05$) in the hippocompal area CA1, respectively. Additionally, melatonin (0.1-1mM) blocked the induction of tetanically induced LTP when recorded in the CA1. The LTP was 164±9% under control condition and 93±8% (n=5; $p<0.01$) after application of 0.1mM. Also 1 mM melatonin perfusion prevented LTP 87±12% (n=5; $p<0.01$). We conclude that melatonin inhibits synaptic excitability in a dose dependent manner in the hippocampal neurons and has the ability to prevent formation of LTP.

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ELECTROPHYSIOLOGICAL EVALUATION OF THE DOG; NORMAL VALUES OF NERVE CONDUCTION AND SOME REFLEX STUDIES

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Aim: The aim of the study was to assess the normal values of some electrophysiological tests in the normal dog.

Setting: Neurophysiology laboratory of our University Hospital and the Anatomy Laboratory of Faculty of Veterinary Medicine Animal Hospital.

Methods: Healthy mongrel dogs of twenty were included the study. After intravenous anesthesia of xylazine and ketamine combination, distal latencies of the median, ulnar, radial, suprascapular, tibial, peroneal nerves; repetitive stimulation test of the ulnar nerve; F wave latency of the ulnar nerve; bulbocavernosus reflex latency; facial nerve conduction and the blink reflex latencies were recorded with electrophysiological techniques. All of the studies were conducted with Nihon Kohden Neuropack II (Tokyo, Japan) diagnostic equipment. Later, whole of the anatomical landmarks and topographic points of surface anatomy related with electrophysiological study were shown with the classical anatomical dissection on two cadaver.

Results: Latencies of suprascapular nerve, bulbucavernosus and blink reflex were reported firstly in the literature by this study. These parameters were very similar to human values in general. Other parameters found in our study were similar to other dog studies in the literature. Topographic anatomy were also studied in relation with the electrophysiological work-up.

Conclusion: This study supported other nerve conduction studies in dogs and also added some new tests like bulbocavernosus relex, facial and suprascapular nerve latencies and blink reflex to the diagnostic work-up of the dog. Electrophsiological tests were assessed with the anatomical facts. The findings formed a basis for " dog model" studies and added some new "tools" to the evaluation of the diseased dog for the veterinary clinician

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THE EFFECTS OF EXTREMITY POSITION ON ELECTROPHYSIOLOGICAL AND ULTRASONOGRAPHIC PARAMETERS

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Aim: Assessment of the possible effects of the positional changings on nerve conduction studies and ultrasonographic findings in the entrapment regions.

Setting: A tertiary care university hospital, clinical neurophysiology laboratory.

Methods: Fifty healthy adult person recruited for the study. The motor and sensory distal nerve latencies, velocities and amplutudes of action potentials were recorded in median, ulnar and peroneal nerves in three different positions; neutral, hyperextension and hyperflexion. Also, ultrasonograhic evaluation of the median nerve in the carpal region with this three positions were performed and anteroposterior and mediolateral radius measurements recorded.

Results: Whole of the parameters in neutral position changed in other two positions in a statistical significance.Latencies were shorter in the hyperextension position and radius measurement of the median nerve was the biggest than the other two positions.

Conclusion: Hyperextension position is the most suitable position against the copressive effects. A reliable diagnosis of CTS could be made sonographically, mainly based on an increase in cross-sectional area of the median nerve at the level of the pisiform or hamate bone. But, most studies could not compare the diagnostic capabilities of sonography to those of electrodiagnostic studies, It is probable that sonography will not replace electrodiagnostic studies, but may serve as an additional investigation.

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INVESTIGATION OF ESTROGENIC AND ANTIESTROGENIC EFFECTS OF POLYCHLORINATED BIPHENYLS ON MCF-7 AND HYPOTHALAMIC GT1-7 CELLS

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Polychlorinated Biphenyls (PCBs) are persistent environmental pollutants and have potential endocrine disruptive properties. They can induce or inhibit estrogenic responses in vitro and in vivo. Antiestrogenic activity of the planar PCBs is thought to occur primarily through the aryl hydrocarbon receptor while estrogenic effect of the nonplanar, ortho-subsituted PCBs is primarily through the estrogen receptor. We have tested 14 PCB congeners in MCF-7 breast cancer cells using E2 Focus Assay. Seven PCBs (153, 170, 180, 187, 8, 28 and 118) were found to be estrogenic and two PCBs (126 and 156) antiestrogenic.

GT1-7 cells are immortalized hypothalamic neurons which can secrete gonadotrophin releasing hormone (GnRH) in culture media. These cells express estrogen receptor alpha and respond to physiological concentrations of 17beta-estradiol (E2). It has been reported that estrogens can inhibit Ca2+ influx in neurons. We investigated changes in [Ca2+]i concentrations and cell viabilitiy in cultured GT1-7 cells by Flow Cytometry. The cells were acutely exposed to various concentrations of PCBs, Aroclor and E2 and monitored for a period of 60 mins in test tubes. This experimental approach failed to provide insights on estrogen modulation of GT1-7 neurons. We plan to determine GnRH mRNA levels in this cell line by quantitative PCR. We also intend to examine the effects of these endocrine disruptors on hypothalamo-hypophyseal-gonadal axis in a rat model.

Supported by NIH ES049795-01A1 and TÜBİTAK-NATO.

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CORTICONUCLEAR INNERVATION TO FACIAL MUSCLES IN NORMAL CONTROLS AND IN PATIENTS WITH CENTRAL FACIAL PARESIS

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Purpose: The aims of this study are to evaluate the corticonuclear descending fibers to the perioral muscles; to discuss why the periorbital motor evoked potentials(MEP) are hardly elicited and how central facial palsy(CFP) could become mild and recovers often rapidly following stroke.

Methods: Eighteen healthy volunteers and 28 patients with stroke and CFP (mean ages: 51 and 61 years) were investigated by (transcranial magnetic stimulation)TMS with a figure of eight coil. Intracranial facial nerve and cortical MEPs were recorded from the perioral muscles. The periorbital MEPs were also studied.

Results: The absence of MEP in both oral muscles with affected hemisphere TMS was the most obvious and frequent abnormality. Central conduction time was significantly prolonged in the remaining patients. The mean amplitude of affected hemisphere MEP was about twice diminished. Meanwhile, the amplitudes of unaffected hemisphere MEPs to intact side were enhanced remarkable especially in the first week following stroke. During TMS, only the blink reflexes were elicited from the periorbital muscles due to stimulus spreading to trigeminal afferent nerve fibers.

Discussion and Conclusions: It is concluded that perioral muscles are innervated from the corticospinal tract bilaterally. The density of the ipsilateral corticonuclear fibers is less than contralateral fibers. Corticospinal fibers to lower facial muscles could be easily affected due to their larger representation in the cortex. CFP caused by stroke is generally incomplete and mild because of the ipsilateral cortical innervation and recovers fast related to the hemispheric disinhibition and cortical reorganisation. Upper facial muscles may be represented with a relatively smaller domain together with different cortical loci.

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EXPRESSION OF ESTROGEN RECEPTOR-α AND cFOS IN NOREPINEPHRINE AND EPINEPHRINE NEURONS OF YOUNG AND MIDDLE-AGED RATS DURING THE STEROID-INDUCED LUTEINIZING HORMONE SURGE

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In this study we assessed the mechanisms of the decreased chatecholamine release in the hypothalamus during reproductive aging in female rat. By using in situ hybridization and immunohistochemistry, we aimed to determine if, 1. norepinephrine (NE) and epinephrine neurons in the brain stem continue to express estrogen receptor (ER)-α in middle-aged rats; 2. ER-α or cFos expression in these neurons changes with the age during the steroid- induced LH surge and 3. tyrosine hydroxylase (TH), dopamine-β-hydroxylase (DBH), and phenylethanol-N-methyltransferase (PNMT) mRNA content change with aging during the surge. The results revealed no differences in TH mRNA content; however, DBH mRNA levels in areas A1, A2, and C1 of the middle-aged animals did not increase during the surge as opposed to the young animals. Although the percentage of NE and epinephrine neurons that express ER-α was unchanged during the surge in both groups, cFos expression was enhanced in areas A1 and A2 of the middle-aged animals but not in young animals. Together the results suggest that NE and epinephrine neurons in the middle-aged rat continue to express appropriate basal levels of TH, DBH, and PNMT mRNAs as well as ER-α and cFos. It is concluded that the reduced catecolamine release during the surge in middle-aged rats is caused, in part, by an altered sensitivity of the NE neurons to estradiol, which results in an aberrant cFos expression and probably not by major deficits in the expression of transmitter synthesizing enzymes or steroid receptors.

This work was supported by NIH Grants MH-59890, AG-17164, and RR-15592 to LJ.

Insitu hybridization and immunohistochemistry parts of this work was presented in poster format at the Endo 2001-Denver and Neuroscience 2001-San Diego, respectively.

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INTRACRANIAL INHIBITION OF PLATELET-DERIVED GROWTH FACTOR-MEDIATED GLIOBLASTOMA CELL GROWTH BY AN ORALLY ACTIVE KINASE INHIBITOR OF THE 2-PHENYLAMINOPYRIMIDINE CLASS

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Glioblastoma multiforme is the most common primary human brain tumor, and it is, for all practical purposes, incurable in adult patients. The high mortality rates reflect the fact that glioblastomas are resistant to adjuvant therapies (radiation and chemicals), the mode of action of which is cytotoxic. We show here that an p.o.-active small molecule kinase inhibitor of the 2-phenylaminopyrimidine class may have therapeutic potential for glioblastomas. STI571 inhibits the growth of U343 and U87 human glioblastoma cells that have been injected into the brains of nude mice, but it does not inhibit intracranial growth of ras-transformed cells. Studies on a broad panel of genetically validated human and animal cell lines show that

STI571 acts by disruption of the ligand:receptor autocrine loops for platelet-derived growth factor that are a pervasive feature of malignant astrocytoma. The cellular response of glioblastoma cells to STI571 does not appear to involve an apoptotic mechanism.

POSTER PRESENTATIONS

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COMPARISON OF THE EFFECTS OF ACETYLSALICYLATE ON SPINAL REFLEXES IN SPINALIZED AND NORMAL RATS

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The effects of nonsteroidal antiinflammatory drug acetylsalicylate, on spinal monosynaptic reflexes were investigated in spinalized and normal rats. Acetylsalicylate was administered orally (50 and 100 mg/kg for spinalized rats; 100 mg/kg for normal rats) via nasogastric tube. Adult rats (n=24) weighing 150-200 g were anaesthetized with ketamine (50 mg/kg, i.m) and artificially ventilated. Half of the rats were spinalized at C1 level. A laminectomy was performed in the lumbosacral region. The ventral roots of segment L5 were isolated and a pouch of skin formed at the site of the dissection to allow the exposed tissues to be covered with liquid paraffin. The temperature was kept at 36±0.5°C with a heating pad. After the dissection of left thigh region, sciatic nerve was isolated. Sciatic nerve was placed on a silver-silver chloride wire electrode for stimulation through an isolation unit. The reflex potentials were recorded from the ipsilateral L5 ventral root, mounted on a silver-silver chloride wire electrode. The systemic dosages of acetylsalicylicate significantly decreased the amplitude of reflex response in spinalized and normal rats. ($p<0.05$). These data verify that observed inhibition by acetylsalicylicate at the level of spinal cord. Also we suggested that the cyclooxygenase products of arachidonic acid may play an important role in regulating the reflex potential.

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THE EFFECT OF INTRACISTERNAL HIPEROSMALAR ALBUMIN IN EXPERIMENTAL BRAIN EDEMA

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Inefficiently treated traumatic brain edema gives rise to increased intracranial pressure which is a major cause of high mortality and morbidity in neurosurgery. This challenging fact is the main motivation for the search of more effective treatment modalities. Aim of the current study was to investigate the influence of intracisternal hyperosmalar human serum albumin on the resolution of brain edema following trauma.

36 male New Zealand rabbits each weighting 2.2-2.8 kg were randomized into six groups (control, trauma and four therapy group). Standart head traumas were performed by Feeney's method. Hyperosmolar human serum albumin was administered via the intracisternal route respectively 4, 24 and 72 hours after trauma. The efficacy of therapy was evaluated by cerebrospinal fluid (CSF) osmolality, cerebral tissue water content, and microscopy. Posttherapeutic values for CSF osmolality are obtained by cisterna magna puncture. Results have shown that hyperosmolar albumin administration has a positive therapeutic effect on the resolution of brain edema following trauma.

Keywords: Brain edema, human serum albumin, trauma,

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THE EFFECT OF NGF ADMINISTRATION ON SPATIAL WORKING MEMORY IN ADULT MEMORY DEFICIENT RATS

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The experiments on animals showed that NGF treatment ameliorates degeneration within the basal forebrain cholinergic system and associated cognitive impairment in both aged and lesioned subjects. Much less is known about NGF effects in the intact adult animals and the available data are rather conflicting. The aim of the present study was to investigate effect of chronic intra-cerebro-ventricular infusion of rat recombinant NGF on spatial working memory in adult. memory deficient rats.

Memory deficient rats were selected on the basis of their pre-operative performance in delayed matching-to-position (DMP) task carried out in a modified 8-arm radial maze. The delay between sample and test choices was prolonged stepwise from 10s, to 1, 5, and eventually 15 min with rats trained at each delay to an arbitrary performance criterion. Rats whose performance at the longest 15-min delay was at least 2 SEM above the group mean were classified as 'poor learners'. They were randomly assigned to either control or experimental group, and treated with either vehicle solution (artificial cerebrospinal fluid) or NGF at the total dose of 40 μg per rat. Intra-cerebro-ventricular drug infusions were made continuously over 14 days at the rate of 0.25 μl/hr using Alzet 2004 osmotic mini-pump. The post-operative training included the same stages as the pre-operative one.

NGF at the dose applied in the present study did not produce anorexia, and did not have a detrimental effect on the spatial learning and memory, as it has been earlier reported for the higher doses of this neurotrophin when applied to normal young rats. No significant between-group difference was noted at the shortest delay of 10s that could be bridged by the immediate memory. On the contrary, at all three longer delays, post-operative performance in experimental group was significantly better compared to control rats what indicates towards positive NGF effect on working memory in young but memory deficient rats.

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FIRING COINCIDENCES BETWEEN NEIGHBORING RETINAL GANGLION CELLS: INSIDE INFORMATION OR EPIPHENOMENON?

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Synchrony for impulses of nearby retinal ganglion cells in response to light stimulus represents a well established, consistent observation across different species. The question rather revolves around the possible functionality involved in the observed synchrony: Albeit its apparent pervasiveness, could it represent an unintended feature of the retinal processing? We addressed this question in our study through recordings by single extracellular electrodes from pairs of retinal ganglion cells of common gold fish (carrassius auratus). It turns out that the rate of synchronous activity is predictable

by the individual impulse trains as if it depends on rates of individual responses only, without itself presenting any additional containment of coding information. And the unexplained variance of synchronous spikes was found to be not contiguous to various stimulus dimensions considered. Hence we conclude that present data is indicative of the fact that a functionality can not be adhered to the synchronous activity of pairs of nearby retinal ganglion cells with the conditions of the present study.

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CELL RESCUE MECHANISM IN A MURINE MODEL OF PAKINSON'S DISEASE

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Parkinson's disease (PD) is characterized by progressive degeneration of the dopaminergic (DA) neurons in substantia nigra (SN). However the mechanism underlying DA cell death remains unclear. While apoptotic cell death has been implicated in DA cell death in PD, autophagy - a regulated cellular process for degradating intracellular proteins and organelles under stress - in PD is not known. Here, we reported evidence of autophagy, apoptosis and necrosis in DA neurons of SN in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) model of PD. Mice were treated with saline or MPTP (35 mg/kg, i.p.) and sacrificed after seven days, and brain tissue samples processed for immunohistochemistry using tyrosine hydroxylase (TH) antibody to reveal SN area. TH positive tissues were then processed for Transmission Electron Microscop and examined ultrastructural evidence of autophagy (double membrane, lysosome-like vacuoles of the cytoplasm), apoptosis (chromatin condensation) and necrosis (cell swelling and cytoplasmic membrane breakdown).

At ultrastructural level, features of apoptosis, autophagy and necrosis were occasionally observed in < 3% of DA neurons of saline-treated mice. MPTP treatment significantly induced morphological changes which closely resembled autophagic process. This autophagic degeneration was observed in ~35% of DA neurons of MPTP mice. In contrast, only 3-5% DA cells displaying features of apoptosis or necrosis were observed in this group.

We conclude that at ultrastructural level MPTP treatment produced a prominent autophagic process in DA neurons. The identification of autophagy in MPTP model of PD may provide insight into the mechanism of cell rescue and may lead to novel therapeutic strategy in PD.

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LESIONS OF THE BAZOLATERAL AMYGDALA DISRUPT FEAR BUT NOT ANXIETY DEPENDENT OF CONTEXTUAL CUES IN RATS

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The aim of the present study is to investigate the role of basolateral amygdala (BLA) in innate anxiety/fear behaviors and in learned cognitive and affective anxiety/fear behaviors. For that, we studied the effects of bilateral ibotenic acid lesions of the BLA on the innate anxiety behaviors by using open field and Black-White tests in rats. Using single-trail learning paradigms such as step-through passive avoidance (cognitive fear task) and unsignaled Pavlovian fear conditioning (affective fear task), the effects of BLA lesions on the acquisition, retention and retrieval of cognitive and affective fear conditioned behaviors were studied. Using One-Way- escape from unconditioned stimuli (US), the effects of BLA lesions on the sensory and motivational component of aversive US were assessed.

Experiment showed that Control and BLA lesioned rats exhibited similar behaviors in Open-Field and White-Black tests, indicating that lesions of the BLA did not alter innate behaviors related with anxiety. In the passive avoidance task, BLA-lesioned rats displayed dramatic decreases in freezing behavior and in step-through latency immediately or 48 h after the shock when compared to the control. In BLA lesioned rats, cumulative time to escape punishment context was also decreased. In unsignaled Pavlovian fear conditioning task, BLA rats exhibited deeper freezing deficits immediately and 48 h after the shock. Lesioned rats showed velocity of escape from aversive US, compared to control rats.

All together these results suggest that BLA is involved in processing of sensory aspects of fear and its associations with conditional context without impairing motivational aspect of US (anxiety) and its associations with the context

This study was supported by TUBİTAK-[101S255 (SBAG-AYD-379] and CU Research Fund (TF2002LTP63).

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TOPOGRAPHIES OF THE P3 EVENT RELATED POTENTIAL (ERP) LATENCIES SHOW SIGNIFICANT DIFFERENCES AMONG PROMOTER REGION POLYMORPHISMS OF THE MONOAMINE OXIDASE A (MAO A) GENE

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MAO A is a form of MAO (monoamine oxidase) enzyme which catalyzes the oxidative deamination of monoamines especially serotonin and norepinephrine. MAO A gene is encoded between Xp11.23-11.4 bands on X chromosome. In the promoter region of MAO-A gene a polymorphism was defined according to number of the 30-bp repeat sequence which affects the activity of MAO A. Although many polymorphic groups were defined related to this polymorphism called VNTR, allele 1 (3 repeats) and allele 3 (4 repeats) are widespread over the population. The results of in vitro studies revealed that allele 3 has 2-10 fold more transcription activity than allele 1. Considering its role in regulation of key neurotransmitter systems, this polymorphism was suggested to have relationship with several neuropsychiatric disorders. In our study, P3b potentials obtained by auditory oddball paradigm and P3a potentials obtained by auditory novelty paradigm were investigated for a relationship with VNTR polymorphism of MAO A polymorphism from 48 healthy male volunteers. The significance of the differences between amplitudes and latencies of P3a and P3b waves of the two groups defined according to the VNTR polymorphism is investigated by ANOVA test. Results: P3b latency of right and left hemispheres were symmetrically longer than that of central line in allele 3 group, while P3b latency on the right side of the scalp was close to the central and lower than the left side in allele 1 group. This result suggests that, the well known variability on transcriptional activity of MAO A enzyme which degrades norepinephrine and serotonin may partially explain the variability observed on P3b latencies of healthy population.

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EFFECTS OF LIPOPOLYSACCHARIDE ON THE RADIATION-INDUCED BLOOD-BRAIN BARRIER AND ASTROCYTIC CHANGES

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This study was conducted to investigate whether the permeability of blood-brain barrier (BBB) and glial fibrillar acidic protein (GFAP) in astrocytes were altered by lipopolysaccharide (LPS) treatment during the brain irradiation. Wistar albino male rats were irradiated by single dose of 18 Gy to the brain. LPS (3x5 mg/kg/day) was given to animals 12 days following the brain irradiation. On the day 13 after irradiation, the changes in the permeability of BBB were investigated by Evans blue (EB) dye, and immunohistochemical method was used to show the alterations in GFAP and in CD15 for polymorphonuclear (PMN) leukocytes. On the day 13 of irradiation, the permeability of BBB to EB dye significantly increased in the cerebral cortex, diencephalon and cerebellum ($p < 0.05$). In contrast, the BBB permeability was significantly reduced in rats exposed to irradiation by LPS ($p < 0.05$). TNF-±945; levels were increased following the LPS, irradiation and irradiation plus LPS treatment ($p < 0.01$). CD15 staining in the brain sections was not observed following the saline, irradiation and LPS treatment. GFAP staining was seen in very few astrocytes of irradiated brains. However, GFAP staining showed an increased positive intensity on the brain sections of LPS and also of irradiation plus LPS-treated animals. These results indicate that LPS reduces the passage of exogenous vascular tracer (EB)-binding albumin into the brain and increases the activity of GFAP in astrocytes, following the irradiation. LPS could have protective effects on the BBB and the astrocytes against irradiation damage, and TNF-±945; increased by LPS could play an important role in this protection, in addition to the other effects of LPS .

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MAGNESIUM SULFATE REDUCES BLOOD-BRAIN BARRIER DISRUPTION CAUSED BY INTRACAROTID INJECTION OF HYPEROSMOLAR MANNITOL IN RATS

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The study was performed to evaluate whether magnesium sulfate could alter the degree of disruption of the blood-brain barrier (BBB) caused by hyperosmolar mannitol. Under sodium pentotal anesthesia, Wistar adult female rats in a control group were infused with 25% mannitol into the internal carotid artery after i.v injecting the Evans blue tracer. Each animal received a 300 mg/kg i.p loading dose of magnesium sulfate followed by a 100 mg/kg dose with 20 min intervals in 40 min. In the control group, there was no significant increase in EB dye content in both hemisphere and also cerebellum. In the mannitol group, EB dye content of the ipsilateral hemisphere where mannitol was injected, increased compared with EB dye values in the controlateral cortex ($p < 0.01$). The EB dye content of the ipsilateral hemisphere of the magnesium sulfate plus mannitol-treated rats was decreased compared with EB dye content in the brain of mannitol-treated animals ($p < 0.05$). In the conclusion, magnesium sulfate attenuated BBB disruption induced by hyperosmolar solution. Our study suggests that magnesium sulfate may be effective in reducing the BBB disruption by hyperosmolar mannitol. This protection in the BBB by magnesium sulfate could indicate to be a strong advantage in the account of a transient osmotic opening of the BBB in order to provide

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ACUTE EFFECTS OF MELATONIN ON CEREBRAL AND CAROTID ARTERY BLOOD FLOWS IN RATS

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Melatonin is the most important pineale hormone; little is known about it's role in the regulation of cerebral blood flow. The aim of this study is to investigate the effect of 0.1 μg/kg (physiological dose) of melatonin on cerebral and carotid artery blood flow in rats.

Adult male Sprague-Dawley rats were randomized into three (n=6) groups. Dynamic scintigraphic measurement was performed to the control group following rapid intravenous injection of 99mTc HMPAO. Before scintigraphy, a solvent containing NaCl 0.9% plus 1% ethanol without melatonin was administrated to the vehicle group intraperitoneally. Another groups recieved 0.1 μg/kg melatonin together with infusion of solvent that contains NaCl 0.9% plus 1% ethanol before dynamic scintigraphic measurements.

Regions of interest (ROI's) were hand-drawn over the brain, left ventricule, right and left carotid arteries in rats; time activity curves of these ROI's were acquired. Brain retention indices (BRI), right carotid artery ratio (RCR), and left carotid artery ratio (LCR) values were determined.

In comparison with controls, BRI value was observed to be significantly lower in rats when melatonin was administrated at it's physiological dose (0.1 μg/kg) ($p=0.01$). RCR and LCR values did not significantly differ from control and vehicle groups.

The results suggested that the administration of melatonin at physiological dose reduces cerebral blood flow in rats.

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ACUTE EFFECTS OF MELATONIN ON REACTION TIME IN HEALTHY MEN

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Melatonin is thought to influence neurobehavioral functions and reduces alertness. Physiological significance of the hormone melatonin on reaction time is obscure. The aim of this study was to investigate the acut effects of single low dose of melatonin on visual and auditory reaction times given to healthy volunteers.

18 healthy male valunteers (age range 18-25 years, mean 20.0±1.4) paticipated in this study, after singing an informed consent form. The visual and auditory reaction times of subjects were measured with digital display response time apparatus. After the initial measurements, subjects received, in a double-blind fashion, placebo or 1.0 mg melatonin. Reaction time measurements were repeated 60 minutes after melatonin or placebo administration. Initial and final results compared with in the melatonin and plasebo groups. A Wilcoxon's signed-rank test for unpaired values was used to estimate the effect of melatonin and placebo.

There were no significant differences betwen initial and final reaction time measurements in the melatonin administration group. The results showed no objective acute effect on the visual and auditory reaction times after administration of melatonin. No differences in the visual and auditory reaction times were found after placebo administration.

The results suggest that single low dose of melatonin did not influence visual and auditory reaction times in healthy male subjects.

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NOVELTY PARADIGM IS SENSITIVE IN DETECTING EARLY STAGE ALZHEIMER'S DISEASE

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P3b is an event related potential (ERP) generated by the target detection task of Oddball and Novelty Paradigms. P3a is an ERP generated by novel stimuli of Novelty Paradigm. In this study, we investigated the relationship between ERPs and the cognitive defects in Alzheimer's Disease (AD). P3b and P3a amplitudes and latencies were measured from 20 healthy volunteers and 22 AD patients from Behavioural Neurology & Movement Disorders Unit, Department of Neurology, Istanbul Medical Faculty. All subjects were evaluated with Mini Mental State Examination. ERPs were compared with Global Deterioration Scale (GDS) and Clinical Dementia Rating Scale scores of patients and ERPs of controls. Comparisons of P3a and P3b according to the presence and the stage of AD were made with ANOVA. In Oddball Paradigm the differences in P3b between patients and controls were not statistically significant. In Novelty Paradigm the differences in P3a latency between early stage patients (determined by GDS) and controls were not statistically significant; however, there was a significant increase in medium stage patients compared to controls and early stage patients. In all patient groups the amplitude of P3b generated by target stimuli of Novelty Paradigm showed a significant decrease in the parietal lead. These findings, suggest that there is a delay in the processing of distractor stimuli in Novelty Paradigm and that this causes a difficulty in attention switching to target stimuli of the same paradigm. The P3b obtained by Novelty Paradigm is more sensitive in detecting early stage AD subjects than classical Oddball Paradigm.

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ULTRASTRUCTURAL EXAMINATION OF THE PINEAL GLAND IN RATS EXPOSED TO CONSTANT LIGHT AND CONSTANT DARKNESS

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Aim: The parenchyma of mammalian pineal gland contains pinealocytes and glial cells. Pinealocytes responsible for melatonin secretion in the pineal gland. Glial cells serve as supporting cells. It is generally accepted that light decreases the production of melatonin, whereas darkness increases it. Therefore, this study was aimed to examine the pineal gland of rats exposed to constant light and darkness at electron microscopic level.

Material and methods: For this purpose 18 male Wistar rats were used. Animals were divided into three groups. Rats in group I (Control) were kept under 12 hrs light: 12 hrs dark conditions. Rats in group II were exposed to constant darkness, while rats in group III were exposed to constant light for 6 weeks. At the end of the experiment, all animals were killed by decapitation. The pineal glands of rats were removed and processed for electron microscopy.

Results: It was observed that an increase in mitochondria and lipid droplets of the pinealocyte cell cytoplasm of the rats exposed to constant darkness. Furthermore, rough endoplasmic reticulum sacs were enlarged in the cell cytoplasm. Whereas, in rats exposed to constant light, mitochondria and lipid droplets were decreased in the cytoplasm of cells when compared to the control group. Additionally, rough endoplasmic reticulum sacs that we had observed in pinealocytes of rats exposed to constant darkness was seen less in this group.

Conclusion: It was concluded that the pinealocyte cell activity of rats exposed to constant darkness was increased but decreased in rats exposed to constant light.

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SEX DEPENDENT INVOLMENT OF NITRIC OXIDE IN SEIZURES ELICIDED BY PENTYLENETETRAZOL

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It has clearly been demonstrated that susceptibility to some type of epilepsy is affected by gender. In addition it has recently been suggested that nitric oxide(NO) may contribute to genesis of seizures activity. Animals were devided into four groups according to drug that was injected. The NO syntase inhibitor(L-NAME; 50mg/kgi.p) and a NO procursor sodium nitroprusside (SNP; 2.5mg/kg i.p) were used to determine the role endogeneous NO on convulsion induced by pentylenetetrazol (PTZ;80 mg/kg i.p) in relation to sex. We measured levels of the metabolites nitrit and nitrat as indices of NO generation in the brain. Furthermore alteration in convulsion latency, convulsion frequency and convulsion duration were observed to correlate them with NO. Both sex injected with PTZ only showed repetitive seizures causing an increase in NO concentration in brain. The increase in NO concentration and NOS activites and the severity of seizures was evident in female. The pretreatment with SNP in PTZ convulsion, prolonged the onset time of convulsion, diminished the frequency while significantly increased NO concentration and NOS activity in brain of female rat. Whereas in male the convulsion latency shortened and convulsion activity was severe. NO and NOS activity was also found increased. L-NAME pretreatment in PTZ convulsion in male prolonged the convulsion latency and decreased severity. It also decreased NO concentration and NOS activity in brain compere in those as control. In contrast the convulsive action and the number of convulsive episodes increased in female pretreated L-NAME. NO concentration and NOS activity was also found increased in brain of these animals. The results of the present study strongly indicated that the concentration of NO and NOS activity involve in the regulation of convulsive action depending on sex.

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EFFECTS OF NITRIC OXIDE AT CEREBRAL VASCULAR DEVELOPMENT OF CHICK EMBRYO

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Aim: At the beginning of research about nitric oxide (NO), this molecule was known as an enviromental toxin. However further studies depicted that, NO has different biological effects like development of vasculogenesis and angiogenesis. Despite so many studies about this issue, few evidence have been found. Our main goal is to investigate the possible roles of NO at vasculogenesis and angiogenesis in this study.

Material and Methods: In this study; we used spesific pathogen free (SPF), white Leghorin type fertilised eggs. These eggs were incubated at 37,8 ± 0,2 °C and 65- 75 % humidity to 24 hours. After 24 hours, we injected non- spesific nitric oxide synthase (NOS) inhibitor L- Nitro arginine methyl esther (L-NAME) at the dose of 100 micromol/l which was considered as a high dose, under embriyonal disc in ovo. Then the eggs were further incubated up to 48, 72 and 80 hours (n:10 per group). Same amount of saline was used in control group embryos (n:10 per group).

Eggs were opened at appropriate time points and embryos were dissected and inserted in formolin 10 % for 24 hour. Embryonal development was assesed regarding to Hamburger-Hamilton scale. 5 micron thick slices were obtained from embryos and stained with haemotoxilene-eosine. These slices were inspected under light microscope for developmental stages of vascular endothelium. Also these slices were stained with spesific anti- iNOS (inducible nitric oxide synthase) and anti- e- NOS (endothelial nitric oxide synthase) policlonal antibodies and with monoclonal mouse anti VEGF (vascular endothelial growth factor) antibody at 1/200 concentration.

Results: In 48 hour old embryos, anjioblasts were seen, but no mature endothelial structure were present. I- NOS activity was not present , and weak e- NOS and VEGF activities could be seen in control groups. At the L- NAME group, findings were similar. At 72 hours, endothelial maturation was begun , e-NOS and VEGF activities were significant and still no i- NOS activity was present. At 80 hours time point, endothelial maturation was in a high level. I- NOS activity was absent, e-NOS activity is lower than as it was present at 72 hours , and VEGF activity is high, especially around the endothelium. In groups of L-NAME at 72 and 80 hours, no significant difference were seen regarding to control groups.

Discussion: The results suggested that, VEGF is effective at early and late phases of vasculogenesis, while NO is effective in the early phases . Because, at the dose of as high as 100 micromol/ l , L- NAME could not able to block the effects of VEGF on vasculogenesis and angiogenesis, effects of VEGF may not be transmitted by nitric oxide system.

Conclusion: In conclusion; NO seems to be effective in early phases of vasculogenesis and angiogenesis, but its effect decreases with time. On the other hand, effects of VEGF on vasculogenesis and angiogenesis may not be transmitted by nitric oxide system.

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EFFECTS OF NITRENDIPINE ON SPECTRAL ANALYSIS OF SEIZURE EEG ACTIVITY IN PENICILLINE MODEL OF EPILEPSY

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Nitrendipine is a molecule blocking calcium ion channels and it has been subject for penicilline model of epilepsy for several studies. In this study we aimed to examine the effects of nitrendipine on seizure activity with a different tecnique by using spectral analysing of electroencephalography (EEG).

We seperated 6 adult Wistar rats in two groups.In first group nitrendipine and penicilline were given consequently and for the second group procedure was vice versa. Anesthetized rats were adapted to a stereotaxic instrument and after recording normal EEG by a polygraph the first group were given 500 IU penicilline G potassium intracortically by a hamilton microenjector. Epileptic activity in EEG was appeared in 15 min. After recording the epileptic activity, 2,5 mg/kg nitrendipine was executed intracortically to the same region. For the second group nitrendipine was given firstly, after 15 min we administrated penicilline G. Main differences for two groups' EEG records were changing amplitude, latency of epileptic seizures and frequency of cerebral EEG rhythms. We also analyzed seizure EEG activity by a spectral analysis programme.Results have shown that power spectrum of EEG activity decreased if we administrate nitrendipin before penicilline ($p<0.05$)(the results of spectral analysis were put on SPSS package programme and analyzed by ANOVA's) and it can be speculated as nitrendipine is a strong molecule for preventing and blocking seizures.

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ASSOCIATION OF THE C677T AND A1298C POLYMORPHISMS OF METHYLENETETRAHYDROFOLATE REDUCTASE GENE WITH SCHIZOPHRENIA

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Two polymorphisms C677T and A1298C of methylenetetrahydrofolate reductase (MTHFR) gene in humans have been shown to cause neurocardiovascular diseases. Although controversial, certain polymorphisms of MTHFR have also been involved in the pathogenesis of psychiatric conditions like schizophrenia and depression.There are studies showing association and lack of associations between MTHFR polymorphism and schizophrenia.

Since these studies are present in the literature, we examined whether the T allele of MTHFR677 and C allele of MTHFR1298 are associated with schizophrenia in a unrelated turkish population consisting of 63 schizophrenics (6.3% female, 93.7% male) and 226 controls. The T677T genotype was significantly greater among 63 schizophrenics 14.3%, when compared with 226 controls 7.5 %.(OR=2.049; 95% CI=0.866-4.850; Chi2= 2.753; df:1; P=0.097). The A1298C genotype was also significantly higher in 63 schizophrenics 54% in comparision with 226 controls 41.2% (OR=1.677; 95% CI=0.956-2.941; Chi2=3.286; df:1; P=0.070)

We next sudied the joint effects of the C677T and A1298C polymorphisms. The compound genotypes C677C/A1298C and T677T/A1298A were a risk factor for schizophrenia (OR=1.877;) %%CI=1.032-3.413; Chi2=4.333; df:1; P=0.037 and OR=2.383; 95% CI=0.941-6.036; Chi2=3.528; df:1; P=0.060). These results suggest that the MTHFR gene polymrphisms are implicated in schizophrenia.

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METHYLENETETRAHYDROFOLATE REDUCTASE GENE POLYMORPHISM IN PATIENTS WITH ISCHEMIC AND HEMORRHAGIC STROKE

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The mechanisms of ischemic and hemorrhagic stroke are not well understood. Although controversial, previous studies have shown evidence of causality of both stroke in patients with methylenetetrahydrofolate reductase gene polymorphism. Elevated plasma homocysteine levels are associated with an increased risk of atherosclerosis and endothelial dysfunction. Several studies have suggested that certain polymorphic variants of MTHFR gene may result in ischemic only, under low plasma folate concentrations. Therefore we have undertaken a study to show that C667T and A1298C polymorphisms of MTHFR gene may be a genetic risk factor for both ischemic and hemorrhagic stroke.

In 120 subjects, 92 of which is ischemic and 28 is hemorrhagic stroke who were ascertained through a neurological clinic, 67 of first degree relatives, together with 259 controls were genotyped for C677T and A1298C variants of MTHFR by using a PCR-RFLP based-method with HinfI and MboII restriction endonucleases respectively. Statistical analysis is based on SPSS.

In a case-control study,we determined the prevalence of two common MTHFR polymorphisms,C677T and A1298C, in 120 stroke patients (92 ischemic and 28 hemorrhagic) and 67 first degree relatives and compared them with that of 259 healthy controls.The frequency of T allele of MTHFR and the C allele of MTHFR1298 were significantly greater in the total stroke population (35.00%, 37.50%) than in controls (32.63%, 28.96%) respectively. Similarly the frequency of T allele and the C allele in ischemic stroke patients (32.06%, 40.76%) were higher than in controls (32.62%, 28.98%) respectively. Profound increase was obtained for hemorrhagic stroke (44.64% in patients, 32 in controls for the T allele and 26.78% in patients, 28.98% in controls for the C allele). Statistically significant results were observed for the total MTHFR1298 (Chi2=8.589, df: 2, P=0.014) and the C1298C genotype with a 2.544 fold inceased risk for stroke (OR=2.544; 95% CI=1.338-4.837); Chi2=8.524; df:1; P=0.004). The compound genotype, C677C/C1298C and T677T/A1298A showed a 3.020 and 1.943-fold increased risk for stroke respectively (OR=3.020; 95% CI=1.528-5.965; Chi2=10.872; df:1; P=0.001 and OR=1.943; 95% CI=0.961-3.928; Chi2=3.519; df:1; P=0.061). The individuals with T677T genotype were 3.120-fold increased risk for hemorrhagic stroke OR=3.120; 95% CI=1.207-8.064; Chi2= 6.008; df:1; P=0.014). In ischemic stroke patients, results were statistically significant for MTHFR1298 (Chi2= 11.166; df:2; P=0.004). The individuals with C1298C genotype and C677C/C1298C compound variant showed a 2.950 and 3.463-fold increased risk respectively. (OR=2.950; 95% CI=1.504-5.786; Chi2= 10.579; df:1; P=0.001) and (OR=3.463; 95% CI=1.699-7.058; Chi2=12.783; df:1; P=0.000). Moreover in the first degree relatives, C677C/C1298C and C677C/A1298C compound genotypes had a 2.209 and 1.852-fold increased risk (OR=2.209; 95% CI=0.937-5.206; Chi2=3.422; df:1; P=0.061) and (OR=1.852; 95% CI=1.033-3.321; Chi2= 4.363, df:1, P=0.037) respectively.

Therefore, MTHFR genotypes, T677T,T677T/A1298A are significantly associated with hemorrhagic stroke, similarly, C1298C, C677C/C1298C are significantly associated with ischemic stroke. In first degree relatives, C677C/C1298C genotype are a risk factor for stroke.

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PROLIFERATIVE RESPONSES TO MYELIN ANTIGENS IN SUBACUTE SCLEROSING PANENCEPHALITIS PATIENTS

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Subacute sclerosing panencephalitis (SSPE) is a rare, persistant infection of the central nervous system (CNS) caused by measles virus (MV). The cause of MV persistence in this disease is not known and defective host immune response to MV has been proposed as a possible mechanism. Proliferation of peripheral blood mononuclear cells (PBMC) from patients to both T and B cell mitogens is reduced.

To investigate possible “bystander” T cell responses to myelin antigens, we analyzed the proliferative responses from 35 SSPE patients and from 33 healthy controls (HC) to myelin basic protein (MBP), myelin oligodendrocyte glycoprotein (MOG), aB-crystallin, live attenuated measles vaccine, PPD and PHA. T cell proliferation was measured at the 6.th day by 3H-Thymidine uptake. Stimulation indices (SI) were calculated and analyzed by non-parametric tests (Mann-Whitney).

The mean SI values to MBP and MOG did not differ between patients and controls (SI: 1.2 vs 1.1, 1.3 vs 1.2, respectively). As a small heat shock protein, aB-crystallin did also not stimulate a higher response in SSPE patients compared to controls (1.3 vs 1.2). As described previously, proliferative responses to PPD were significantly lower in SSPE patients than HCs (7.1 vs 52.8, $p<0.0001$). In vitro proliferative responses to live attenuated measles vaccine were not statistically different among the SSPE patients and HCs.

The results did not demonstrate enhanced cellular responses against myelin antigens or against aB-crystallin in SSPE patients, implicating that the central nervous system as well as stress antigens are not primary targets of an autoimmune response in SSPE.

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AN ANAGLYPHIC THREE DIMENSIONAL (3D) INVESTIGATION OF SEM IMAGES TAKEN FROM THE CIRCUMVENTRICULAR ORGANS OF RATS THAT HYDROCEPHALUS AND SUBARACHNOIDAL HEMORRHAGE PERFORMED EXPERIMENTALLY

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It’s known that circumventricular organs are lack of blood-brain barrier around the ventricular system in the brain and support body water-salt balance, effecting physiological events such as neuroendocrine and reproduction. It’s unknown that circumventricular organs affecting in the different pathological conditions are affected which phase and what results occured. Although circumventricular organs are not contain blood-brain barrier they are not completely shown same charecteristics.

In the pathological conditions they show their own effects by means of mediators. It is necessary to make research structural changes in addition to changes in the neurotransmitters that affected by circumventricular organs. The one of main aims of this study is to investigate changes in this organs as a ultrastructural by scannig electron microscope after hydrocephalus and subarachnoidal bleeding. In our study we examine slices of subfornicial organ, organum vasculosum lamina terminalis, area postrema and median eminence. In rats hydrocephalus was occurred by injecting kaolin into subarachnoidal space at the cranial convexity; subarachnoidal bleeding was realized with puncture of basillar artery through transclival route.

The aspect of this study as methodological and as originally will be reported is to investigate by a tecnique which is able to watch scanning electron microscopic image of the circumventricular organs that named anaglyph, first recorded as three dimensional stereopairs then converted as a red-blue image in three dimensional by special glasses.

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TIME-DEPENDENT MORPHOLOGICAL CHANGES IN YOUNG AND ADULT RAT HIPPOCAMPUS AFTER KAINIC ACID INJECTION

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Introduction: Kainic acid (KA) treated rats have been widely used as an animal model of human mesial temporal lobe epilepsy with hippocampal sclerosis. The aim of this study is to investigate time- and age-dependent differences in the neuronal damage in rat hippocampus after KA injection.

Material-Method: Five day-old and adult Wistar albino rats were injected KA intraperitoneally. Fifteen, 30, and 90 days after the injection, animals were perfused through the aorta with 3% paraformaldehyde and 0.2% glutaraldehyde in PBS. After decapitation, the entire brain was removed, left overnight in the same fixative and 40μm thick coronal sections were obtained. The sections were stained with cresyl violet to demonstrate morphological changes under light microscope.

Results: In 5 day-old rats, widespread gliosis and disorganization in CA4 mossy cells were observed 15 days after KA injection. 30 days after the injection, we observed loss of CA1 pyramidal neurons and disorganization in CA1 pyramidal layer. Widespread neuron loss in CA1, disorganization in CA3 pyramidal layer and loss of mossy cells and irregularity in CA4 region were seen 90 days after the injection. There were no morphological changes in dentate regions of 5 day-old groups.

In adult rats, widespread gliosis and pyramidal neuron loss in CA1, CA3 regions were observed 15 days after KA injection. 30 days after the injection, pyramidal neuron loss in CA1 and CA3 regions, mossy cell loss and disorganization in CA4 region and enlargement and irregularity in dentate granular layer were observed. Neuronal loss and irregularity in CA1, CA3, and CA4 pyramidal cell layers and widespread enlargement and irregularity in dentate granular layer were observed 90 days after the injection.

Conclusion: In the present study, young rats showed less morphological alterations in early period than adults. In addition both groups showed similar morphological changes in late period after KA injection. The results of the present study suggest that young rats might be more resistant to the effects of KA in early period after the injection.

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SYNAPTIC TRANSMISSION: A STUDY FOR MODELLING AND SIMULATION OF END PLATE ACTION POTENTIAL

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In this study, generation of postsynaptic action potentials are investigated by using simulation study, which is depended on statistical model of Acetylcholine (Ach) quantal release theory at motor end plate,

It is supposed that, end plate potentials (EPP) are sum of miniature end plate potentials (MEPP) which are release as quantal and random in number (N). By the hypothesis that N number has a Poisson and MEPP has a Gaussian distribution, EPP are obtained by simulating distributions parameters.

Our study suggest that, simulation of EPPs are a convenient tool in understanding both physiological process of synaptic transmission and pathological process of neuro-muscular junction.

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EFFECT of ACETYLCHOLINE RECEPTOR GENE MUTATIONS on ACETYLCHOLINE RECEPTOR EXPRESSION IN THYMUS AND PERIPHERAL LYMPHOCYTES

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Aim: Nicotinic acetylcholine receptors (nACR) are expressed in various cells including muscle, peripheral blood lymphocytes (PBL), thymic myoid and medullary epithelial cells. nACR gene mutations often diminish muscular nACR expression, causing congenital myasthenic syndromes (CMS). We examined whether they also reduced expression on lymphoid cells.

Material: PBL of patients with CMS (n=7), autoimmune myasthenia (AM) (n=8), and healthy controls (n=5), and thymus tissue from thymectomy material (CMS, n=3, AM, n=6).

Method: Fluorescent microscopy using FITC-conjugated alpha-bungarotoxin on acetone-fixed PBL and paraffin-embedded thymectomy specimens by blinded examiner.

Results: All control and AM but only 5/7 CMS cases showed bungarotoxin binding on PBL. In thymus of AM cases, fluorescent-positive cells were observed around blood vessels (2/6 cases), or around Hassall corpuscules and in some parenchymal cells (3/6); no binding was observed in CMS thymuses (0/3).

Discussion: No previous data exist on thymic nACR expression in CMS, mainly because thymectomy is not performed in CMS. The presented CMS cases had thymectomy in a period where serological and genetic tests were unavailable for differentiating CMS from AM. Previous studies of our CMS patients showed nACR (subunit mutations resulting in low nACR expression in HEK cells and 125I-alpha-bungarotoxin binding in lymphocytes (4/5 cases). Current results indicate thymic nACR expression is also diminished in CMS. Thymic expression is important for self-antigen recognition by immune cells: it therefore is of interest to examine immune response to nACR or to tumors of muscle origin in CMS, and the prognosis of such tumors compared to the general population.

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ANTIBODIES AGAINST MUSCLE-SPECIFIC KINASE (muSK) IN JUVENILE MYASTHENIA GRAVIS

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Aim: Muscle-specific receptor tyrosine kinase (MuSK) is an enzyme of the neuromuscular junction involved in the development and maintenance of the postsynaptic membrane as an agrin receptor. Recently, antibodies against MuSK have been shown in 70% of myasthenia patients with no acetylcholine receptor antibodies (ACR-Ab). MuSK antibodies inhibit the function of the molecule in cultured myotubes and may play a role in the pathogenesis of ACR-Ab-negative myasthenia. Because a higher proportion of juvenile myasthenia cases are ACR-Ab-negative, we investigated the presence of MuSK antibodies in this age group.

Material: Sera from patients who were ACRAb-negative on at least two occasions (n=8).

Method: ACRAb were tested with a commercial RIP kit (IRB, Germany). Antibodies to MuSK were tested by immunoprecipitation of 125I-labelled human and rat MuSK.

Results: All sera were negative for MuSK antibodies.

Discussion: The absence of MuSK antibodies in our patients may be due to their mild or restricted disease, or to their treatment with steroids. A previous muSK antibody-positive case series included two childhood-onset cases. On the other hand 29% of all myasthenia cases are negative for ACRAb and muSK antibodies, and might carry antibodies against other yet undefined antigens of the neuromuscular junction. Our results indicate that children with ocular or mild generalized myasthenia are less likely to have MuSK antibodies.

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ADENOSINE DECREASES THE CHANGES IN BLOOD-BRAIN BARRIER PERMEABILITY FOLLOWING PTZ-INDUCED SEIZURES IN RATS

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Adenosine is a major regulator of neuronal activity in central nervous system and has been shown to possess protective effect in epileptic seizure. This study aimed to investigate the effect of systemic adenosine administrations on the blood-brain barrier permeability in pentylenetetrazole-induced (PTZ) generalise tonic-clonic seizures.

Animals divided into two groups: 1) 100 mg kg-1 PTZ-induced convulsions group (n=7), 2) PTZ 100 mg kg-1 + 500 mg kg-1 adenosine-treated group (n=7),. The rats were injected adenosine 15 min prior to administration of PTZ. Administration of PTZ caused tonic-clonic convulsions all animals. Total duration of seizure didn't shown any differences between groups. On the other hand, adenosine caused a significant delay onset latency to seizures (53±61617; 5 sec versus 79±61617; 8 sec, $p< 0.05$).

PTZ treatment induced an increase in mean arterial blood pressure (MABP) (165 ±61617; 2 mmHg), however adenosine administration prior to PTZ treatment prevented the abrupt rise seen in MABP (112 ±61617; 7mmHg). In PTZ group, there was bilateral Evans blue leakage in the olfactory bulb, caudate-putamen, thalamus, hypothalamus, inf. colliculus, midbrain, brain stem and cerebellum in all animals, whereas the group given adenosine before PTZ administration showed slight staining at the olfactory bulb, thalamus, hipocampus, inf. colliculus, brain stem, and cerebellum in 2 out of 7 rats.

These results indicate that treatment with adenosine may increase convulsive threshold and restrict the opening of blood-brain barrier against PTZ- induced seizures. Preventing effect of adenosine in blood-pressure increment appear to be contributed to the protection of blood-brain barrier permeability.

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MULTIPLE OSCILLATORY PROCESSES DURING RECOGNITION OF FACES

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We performed experiments with 10 subjects for recognition of complex percepts in the shape of anonymous faces in order to test our recently developed concept of "superbinding" relying on the existence of multiple oscillatory processes that are selectively distributed and selectively coherent in the brain .

As control we used simple light stimulations, the complex signal being the face of an anonymous elder woman. We have analysed event- related oscillations in frontal, central, parietal and occipital locations. Event Related Oscillations in the range of delta (0.5-3.5), theta (4-7), alpha (8-13), beta (15-28), and gamma (28-48) frequency ranges were analysed with adequate digital filtering. The results show reliable distinct 'Face' potentials in comparison to simple 'Light' EPs. The changes in event (face) related oscillations are selectively distributed in all cortical positions. The differentiation consists mainly increased delta responses, increase of gamma response in central positions, increase of frontal alpha and theta responses and reduced occipital alpha response to face stimulation in comparison to simple light. The recognition of faces is with increase of ERP amplitudes and prolongation of oscillations. Moreover, the response oscillations show significant differentiations depending on topology of recording sites. These results confirm our earlier hypothesis that integrative brain functions are manifested with oscillatory responses in the whole cortex, and most probably in the whole brain as the comparison of data with related animal experiments revealed.

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MORPHOMETRIC EVALUATION OF THE CORPUS CALLOSUM IN TOTALLY DEAF PERSONS BY USING MAGNETIC RESONANCE IMAGING

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Auditory association cortices are interconnected to each other by fibers passing through the dorsal part of corpus callosum. In totally deaf persons no auditory impulses are conveyed to the auditory cortices. Hence the auditory pathways become nonfunctional. It is thought that this could cause a decrease in the amount of fibers passing through the corpus callosum and in turn a decrease in the dimensions of dorsal part of the corpus callosum in sagittal plane. The aim of this study was to determine and compare the differences in the dimensions of certain parts of corpus callosum in deaf persons and normal subjects.

18 deaf and 18 healthy male volunteers, ages varying between 28 and 56 years, were examined. Only male volunteers were selected for this study to prevent possible sex differences. Audiometrical tests were applied to both groups at the department of otorhinolaryngology of our faculty. Then T1-weighted midsagittal MR images were obtained by a 1,5 Tesla Siemens Magnetom MR unit. Certain dimensions and areas were measured on these images. Results were analysed by Kolmogorov-Smirnov test and Student's t test.

As a result, there was no statistically significant difference between deaf and healty persons in the dimensions of the corpus callosum except the thickness from the splenium.

Key words: Corpus callosum, auditory pathways, magnetic resonance imaging, deafness

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THE EFFECTS OF MELATONIN, 7-NITROINDOSOLE, AND RILUZOLE ON GLUTAMATE TOXICITY IN PRIMARY MIXED GLIAL CELL CULTURES

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We have previously reported moderate to dramatic functional recovery by systemic administration of melatonin, 7-nitroindosole, and Riluzole in surgical rat models of spinal injury and cerebral ischemia. In this study, we aimed to simulate the acute neurodegeneration by addition of 20mM glutamate in cultures of primary mixed glial cells derived from 1-2 days old rat brains. Following addition of 100uM melatonin, 100uM Riluzole, and 500uM 7-nitroindosole, we determined the LDH and total nitrite levels in supernatants by spectrophotometry at 1, 6, 24 and 48 hours. To verify the cultured cells as glia, GFAP immunocytochemistry was performed on culture days 1-2. Data evaluation was done by

multivariate ANOVA and post-hoc LSD on SPSS, and by Student T test for some paired analysis. We found that melatonin and 7-nitroindosole decreased cell death significantly at all time points ($p<0.01$), melatonin was more protective at 1, 6, and 48 hours ($p<0.01$), and that Riluzole was ineffective. Nitrite levels which peaked in the glutamate toxicity group were lowered significantly by addition of melatonin and 7-nitroindosole at 24 and 48 hours ($p<0.05$), and also by Riluzole at 48 hours ($p<0.05$). We conclude that the protection of glia in parallel with or even prior to neuronal populations may contribute very significantly to the ultimate functional restoration process obtained following administration of melatonin, 7-nitroindosole and Riluzole to our spinal cord and cerebral injured rats in our in-vivo studies.

Supported by Ege University Science and Technology Reserach and Application Center and Research Fund

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FURTHER EVIDENCE FOR ENHANCING EFFECTS OF NO ON MONOSYNAPTIC AND POLYSYNAPTIC SPINAL REFLEXES IN CATS

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There are a number of studies on the effects of different NO donors and inhibitors on spinal cord with quite contradictory results. The aim of this study was to investigate the effects of Sodium nitroprusside (SNP), a NO donor, and NG-nitro-L-arginine methyl ester (L-NAME), a nonselective NOS inhibitor, on monosynaptic and polysynaptic spinal reflexes in anaesthetized and spinalized cats. After a dorsal laminectomy between L5 and S1, monosynaptic and polysynaptic spinal reflexes were evoked by stimulation of gastrocnemius nerves. Following

control recordings, administration of L-NAME in 100, 200, 500 μM (local) and 10, 20, 50 mg/kg (i.v.) doses decreased significantly the monosynaptic and polysynaptic reflex amplitudes in a dose dependent manner.

Administration of SNP in 100, 200, 500 μM (local) and 100, 200, 500 μg/kg (i.v.) doses enhanced significantly the both reflex amplitudes in a dose dependent manner. In another series of experiments it has been observed that the maximal decrease in reflex amplitudes caused by 500 μM local L-NAME administration in 15th minute was reversed by locally administered SNP (500 μM). Our results support the hypothesis stating that NO may play a role in the modulation of mono- and polysynaptic spinal reflexes and the NO appears to have an enhancing role on these responses.

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PLASMA 3-NITROTYROSINE: AN IN VIVO MARKER OF PEROXYNITRITE FORMATION AFTER THROMBOLYSIS

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Background-purpose: Reperfusion of ischemic tissues, especially the myocardium and brain induces a cascade of hazardous biochemical events known as reperfusion injury. Concomitant surges of superoxide and nitric oxide during reperfusion lead to formation of peroxynitrite which plays an important role in reperfusion injury. The detection of 3-nitrotyrosine (3-NT), a stable marker of peroxynitrite generation, in the plasma is a potential candidate as an in vivo marker of reperfusion injury. Due to the accesibility to a large number of patients in a short time, patients undergoing coronary thrombolysis were included in this study to verify the validity of plasma 3-NT detection as a surrogate marker of peroxynitrite generation.

Methods: Streptokinase (n=11) or tPA (n=6) was administered to 17 acute myocardial infarction patients for thrombolysis. Plasma samples were collected before the initiation of therapy and 90,180 and 360 minutes thereafter. 3-NT levels were determined by ELISA.

Results: The mean plasma 3-NT level 90 minutes after thrombolysis was significantly elevated compared to the baseline value by 21% ($p<0.01$). The increase was prominent (16-52%) in 10 of 16 patients in whom reperfusion had been attained. No significant elevations were detected 180 and 360 minutes after thrombolytics.

Conclusion: Plasma 3-NT levels, a marker of nitrosative/oxidative stress, increase in patients after coronary thrombolysis. Assessment of plasma 3-NT levels by ELISA is an appropriate method in detecting a surrogate marker of peroxynitirite formation. Future studies will delineate the role of 3-NT as an in vivo marker of reperfusion injury, not only after coronary thrombolysis but also after cerebral thrombolysis.

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ISCHEMIC NEURONAL DEATH IS NECROAPOTOTIC

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It is well known that both necrotic and apoptotic cell death pathways are activated after focal cerebral ischemia. However, no study has been reported demonstrating that these two pathways are activated in the same cell, at the same time.

Caspase-3, a cysteine protease involved in dismantling of cells undergoing apoptosis, has been shown to be activated after cerebral ischemia. Cathepsin-B, a lysosomal protease considered as a marker of necrotic cell death, has also been shown to be activated within ischemic neurons. Colocalization of caspase-3 activation along with cathepsin-B may provide an answer to the question whether necrotic and apoptotic pathways are concomitantly activated after cerebral ischemia.

To evaluate this, we used a transient middle cerebral artery (MCA) occlusion model in adult Swiss Albino mice. Mice were sacrificed after 1 hour of occlusion followed by 5 minutes, 1, 3, 6, 12 and 24 hours of reperfusion. Antibodies against caspase-3p20 and to cathepsin-B were used to immunolabel slices. Anti-caspase-3p20 antibody detects the active form of caspase-3 whereas anti-cathepsin-B antibody detects the mature and precursor forms of the enzyme.

We observed prominent caspase-3p20 immunoreactivity in neurons within the MCA territory soon after reperfusion, which partially decreased by 24 hours. In most of these neurons, first the size and immunoreactivity of cathepsin-B granules were increased, and later diffuse cytoplasmic cathepsin-B reactivity, reflecting degranulation of lysosomes were detected.

These data, demonstrating a concomitant increase in caspase-3 and cathepsin B activities after transient focal cerebral ischemia, suggest that ischemic neuronal death has a mixed (necroapopitotic) phenotype.

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NECROAPOPTOTIC CELL DEATH IN NMDA INDUCED TOXICITY

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Necrosis and apoptosis are two mechanistically distinct, but related forms of cell death. Both forms have been reported to

mediate N-methyl-D-aspartate (NMDA) toxicity in the brain. Caspase-3, a cysteine protease involved in dismantling of cells undergoing apoptosis, has been shown to be activated after NMDA toxicity.

Colocalization of caspase-3 activation along with cathepsin-B, a lysosomal proteases considered as a marker of necrotic cell death, may demonstrate whether both necrotic and apoptotic pathways are concomitantly activated in the same cell after NMDA toxicity.

To evaluate this, we produced excitotoxic lesions by intrastriatal/cortical NMDA microinjections stereotactically. Antibodies against caspase-3p20 and to cathepsin-B were used for immunolabeling of brain slices. Anti-caspase-3p20 antibody detects the active form of caspase-3 whereas anti-cathepsin-B antibody detects the mature and precursor forms of cathepsin-B.

Microinjections of NMDA consistently produced well-delineated lesions. The lesions were confined to the striatum along with the adjacent cortex. NMDA-induced pallor was visible at 1 hour, and pyknotic neurons could be detected as early as 2 hours. In most of the neurons, first the size and immunoreactivity of cathepsin-B granules increased, and later diffuse cytoplasmic cathepsin-B reactivity, reflecting degranulation of lysosomes were detected. Prominent caspase-3p20 immunoreactivity concomitant with cathepsin-B activation was also found within these neurons. However, caspase3p20 positive cells were more prominent in the periphery, while cathepsin-B activation was more robust in the center of the lesion.

These data demonstrate that excitotoxic cell death has a mixed (necroapoptotic) phenotype, necrosis prevailing in severely injured neurons and apoptosis more prominent in moderately damaged cells.

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MELATONIN PREVENTS GLIAL REACTIVITY IN HIPPOCAMPUS, CORTEX AND CEREBELLUM OF STZ-INDUCED DIABETIC RATS

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Hyperglicaemia plays a critical role in the development and progression of diabetic neouropathy. One of the mechanisms by which hyperglicaemia results in the development of neuropathy is the increased oxidative stress in diabetes mellitus. Supplementation with antioxidants in animal models of diabetes have been shown to attenuate the development of diabetic neuropathy. Metabolic and oxidative insults cause rapid changes in the glial cells and this phenomenon is called reactive gliosis. The key indicator of the reactive gliosis is the increased synthesis of glial fibrillary acidic protein (GFAP) and S100B. In the present study we aimed to investigate glial reactivity in hippocampus, cortex and cerebellum of streptozotocin-induced diabetic rats by determining the expression of GFAP and S-100B and to evaluate possible effects of melatonin against reactive gliosis.

Western blot measurement of GFAP contents in brain regions after 6 weeks of STZ-induced diabetes showed significant increases compared with non-diabetic controls. Administration of melatonin prevented the up regulation of GFAP in all stadied brain regions of diabetic rats. By GFAP immunohistochemistry, we observed an increase in GFAP immunostaining in hippocampus of STZ-diabetic rats compared to the control rats. Treatment with melatonin resulted in distinct alteration of GFAP-immunoreactive astrocytes in hippocampus. These results suggest that diabetes causes reactive gliosis possibly due to elevated oxidative stress and administration with melatonin represents an achievable adjunct therapy by preventing gliosis.

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A NOVEL SYSTEMATIC FIELD SAMPLING APPROACH FOR RELATIVELY LARGE REFERENCE SPACES USED IN NEUROSTEREOLOGICAL STUDIES

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Systematic uniformly random sampling throughout a reference space is a standard practice in neurostereological studies. Performing this procedure, especially at the level of sampling section fields, without the usage of certain electronic equipment (e.g. computer-controlled motorized stage) is often viewed as prohibitively time-consuming. Here, we describe a simple, cost-effective and yet efficient method for sampling section fields of relatively large reference spaces. Its practical application is demonstrated for certain central nervous system structures and is based on the idea of scanning the structure of interest directly from the glass slide using a high-resolution scanner. After importing the acquired digital images into a standard graphics program (PowerPoint(r)), application of a sampling lattice and field sampling on these images is performed. Details of this later stage and the remaining practice are already described in the literature. The proposed approach is quite simple to implement and requires no special-purpose hardware. It will be satisfactory to fulfil the needs of many stereological studies. Encouraging potential users who do not have access to such tools in this way therefore makes stereological methods practically more feasible.

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VENTRICLE VOLUMES IN SCHIZOPHRENIA (A STEREOLOGICAL STUDY)

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The purpose in this study was to assess neuroanatomic morphology of the ventricles in schizophrenic patients (n=17; 10 women and 7 men) and healthy volunteers (n=14, women 7, men 7) by a different morphometric technique, the method of Cavalieri.

A detailed systematic series of the third and lateral ventricles were obtained in the coronal MRIs of the entire brain (3mm thickness, T1-Weighted, TR/TE 400/10 msec).

The mean volumes of lateral ventricles were 10818,3 mm3 and 7718,3 mm3 in the female schizophrenics and controls, respectively ($p<0,05$). Their corresponding coefficients of errors were 0,06 and 0,05 respectively. The mean volumes of lateral ventricles were 9942,6 mm3 and 8003,9 mm3 in the male schizophrenics and controls, respectively ($p<0,05$). Their corresponding coefficients of errors were 0,05 and, 0,07 respectively.

The mean third ventricles volumes in the female schizophrenics and control subjects were 1237,8 mm3 and 844,4 mm3, respectively ($p<0,05$). Their corresponding coefficients of errors were 0,06 and, 0,07 respectively. The mean third ventricles volumes in the male schizophrenics and control subjects were 1272 mm3 and 910,9 mm3, respectively ($p<0,05$). Their corresponding coefficients of errors were 0,05 and, 0,07 respectively.

In conclusion, the morphometric features of the patients with schizophrenia are different than the healthy subjects as far as the volumes of the third and lateral ventricles are concerned. Quantitative morphometric evaluation of MRI in conjunction with stereologic method can be used for clinical evaluation of patients with schizophrenia in the further studies.

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THE EFFECT OF CAFFEIC ACID PHENETHYL ESTER ON TOTAL RNA LEVELS IN THE HYPOTHALAMUS DURING CISPLATIN-INDUCED NEPHROTOXICITY MODEL OF RATS

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Cisplatin is one of the most active cytotoxic agents in the treatment of various solid tumors, but its clinical use is associated with side-effects such as neurotoxicity, ototoxicity and nephrotoxicity.We studied the effect of cisplatin on the total RNA levels in the hypothalamus of rats during cisplatin-induced acute renal failure model of rats. The second aim of this study was to investigate the protective role of caffeic acid phenethyl ester (CAPE) on cisplatin-induced changes of total RNA levels in the hypothalamus.

The intraperitoneal injection of cisplatin (7 mg/kg for five days) induced a significant increase in the total RNA levels when compared to the control rats ($p<0.0001$). Co-treatment with intraperitenal CAPE at a dose of 10 mg/kg attenuated the increase in the total RNA levels in the hypotalamus of rats ($p<0.0001$).

In conclusion, our results demonstrate that CAPE protects the increase of total RNA levels in hypothalamus of rats treated with cisplatin and suggest that CAPE may be a promising agent to prevent cisplatin-induced neurotoxicity.

Key words: Cisplatin, caffeic acid phenethyl ester, hypothalamus, total RNA, rat

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THE EFFECTS OF AGMATINE AND L-NAME ON NO PRODUCTION IN NUCLEUS ACCUMBENS CORE REGION IN MORPHINE-DEPENDENT RATS DURING MORPHINE ABSTINENCE

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Purpose: In this study, the effects of L-NAME (a nitric oxide synthase inhibitor) and agmatine (carboxylated L-arginine) on NO production in nucleus accumbens core region (NAcc) of morphine dependent rats (MDR) were examined during morphine-withdrawal syndrome. The change in L-citrulline levels was used as an indirect measure of NO production. The behavioral changes were also evaluated simultaneously.

Materials and Methods: Vehicle or morphine pellets (75 mg/kg) were implanted subcutaneously into the Sprague-Dawley rats. Following a resting period of 5 days, stereotaxic surgery was performed to implant a concentric microdialysis probe into the NAcc of the each animals. Microdialysis samples were collected at 20 min intervals. After collection basal samples, the rats were treated either with intraperitoneal saline or L-NAME (100 mg/kg) or Agmatin (40 mg/kg). 40 min later the rats were injected with naloxan (2 mg/kg) to elicit the signs of abstinence syndrome. L-citrulline concentration in the microdialysis samples were analyzed using HPLC with fluorescent detection.

Results: The L-citrulline levels in MDR treated with saline increased significantly during abstinence ($p<0,01$) but no change was observed in the agmatin- and L-NAME-treated rats. However, L-NAME and agmatine significantly suppressed the sings of withdrawal syndrome being more prominent in agmatine-treated rats.

Discussion: These results imply that agmatine exerts its favorable effects during abstinence through some other mechanisms rather than its NO synthase inhibition effect.

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MICROWAVE-ASSISTED ANTIGEN RETRIEVAL (MW-AR) AND PRIMARY ANTIBODY INCUBATION OF COX-2 IN ARCHIVAL PARAFFIN EMBEDDED HUMAN OLIGODENDROGLIOMAS

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MW-AR often reverses loss of antigenicity and often improves the quality and sensitivity of conventional immunohistochemical staining. MW irradiation has been widely used to enhance histopathological staining for light and electron microscopy and more recently to enhance immunohistochemical staining quality. Cyclooxygenases (cox) are potent mediators of inflammation. Two cox-isoenzymes are described: cox-1, cox-2. Cox-2 is cytokine inducible and enhanced cox-2 expression has been attributed a key role in the development of edema and immunomodulation in pathologically altered brain tissues. The aim of the present study was to assess the effects of MW irradiation on the primary antibody incubation (PAI) stage of cox-2 immunohistochemistry. For this aim we used archival formalin-fixed, paraffin embedded human tissue; diagnosed as oligodendroglioma. Initially antigen retrieval was performed by microwave heating in Citra Plus, 5 cycles of 3 min. While one group of sections was treated by conventional immunohistochemistry(1h-12h PAI),the other group was heated at 360W for 5 min during the primary antibody incubation.

The data showed that there was no significant difference in the quality of immunostaining between the conventional and MW-assisted immunohistochemistry. It was suggested that, following the MW-AR, using MW-irradiation for primary antibody incubation would produce equal staining quality compared to the room temperature incubation with the advantage of significant time gain, especially important for the rapid diagnosis of pathological specimens.

This work was supported by TUBITAK SBAG-2112.

This work was presented as a poster in Neuroscience-2002, Orlando.

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THE EFFECT OF PENTYLENETETRAZOLE ON ISOMETRIC MUSCLE CONTRACTIONS OF RAT PHRENIC NERVE-HEMIDIAPHRAGM PREPARATIONS

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Pentylentetrazole (PTZ), central nervous system convulsant, acts on Cl±61485; channel of GABAA receptor and reduces GABAergic inhibition. Besides the contribution of glutamate on the generation of nerve stimulated muscle contractions, the inhibitory effect of GABA on hemidiaphragm contractions has been recently reported. In order to investigate whether GABA acts through GABAA receptors on mammalian neuromuscular junction we examined the alterations of rat hemidiaphragm twitches following the administration of pentylentetrazole (PTZ).

The phrenic nerve-hemidiaphragm preparations were isolated from Wistar albino rats killed by a sharp blow to the neck. Whereas organ baths were aerated with a mixture of 95 % O2 and 5 % CO2 at 37ºC the preparations were mounted with a resting tension of 2 g for 30 minutes to reach equilibrium in

Krebs solution. Phrenic nerve and hemidiaphragm were stimulated separately with rectangular pulse at 0.1 Hz 0,3 ms and 3 ms of duration respectively. The tension, expressed as grams, was recorded isometrically via a force displacement transducer (Grass FT03 and May FDT10-A) on a polygraph (GRASS 7400). Following the optimum concentrations (20 mM) of PTZ administration (n=4) the difference between the baseline and the final response of muscle twitches was expressed as percentage.

Supramaximal contractions, elicited by phrenic nerve stimulation, increased 10 %, however in the meantime contractions of directly stimulated hemidiaphragm are decreased 11 % . The effect of PTZ on neuromuscular junction reveals the excess release of excitatory neurotransmitters due to the suppression of a possible inhibitory system.

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HISTOCHEMICAL EVALUATION OF NOS ACTIVITY IN TOXOCARA CANIS INFECTED BALB/C MICE

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Toxocara canis is a nematod found in dog intestine.Second stage larvae of this parasite can migrate in various organs and tissues of humans and other paratenic hosts. Migrating larvae cause pathological disorders in liver, lungs, brain, eyes and other organs and are known as Visceral Larva Migrans (VLM). Recently, histological changes caused by T.canis larvae were inspected in tissues of infected hosts in some studies.

The aim of this study is to evaluate NOS activity histochemically in brain tissue of mice infected with T.canis. Mice were infected with 2000 larvated eggs of T.canis by oral inoculation in VLM groups. In order to cancel inducible NOS (iNOS) sythesis due to VLM, a specific iNOS inhibitor, Aminoguanidine (AG) was injected intraperitonally to the mice at 100 mg/kg dose for 2 days at 4 hours intervals. Control and experimental groups were sacrificed 48 hours after infection. Brain tissues fixed in 20% parafolmaldehyd and NADPH-d histochemistry was applied to the cryostat sections. Stained areas with NADPH-d activity were found as 12.75±1.87 in control animals, 100.50±7.31 in T.canis infected animals, 15.30±1.42 in animals received only AG and 21.11±2.42 in animals infected and received AG respectively (magnification:10x15). According to these results, NOS activity was found higher in the T.canis infected animals in comparison with the controls ($p<0.001$). In the group of infected animals received AG, NOS activity was affected by AG and a decrease of NOS activity was seen when compared with T.canis infected group ($p<0.001$). As a result of this study, VLM infection was detected to lead to an increase not only in iNOS but also in eNOS and nNOS activities and affects NO metabolism like other pathologic agents do.

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THE ROLE OF L-TYPE CALCIUM CHANNELS IN SPINAL REFLEX RESPONSES IN CATS

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We have investigated the effects of verapamil, which blocks L-type calcium channels on spinal monosynaptic reflexes in spinalized cats. Adult cats (n=10) weighing 1.5-3 kg were anaesthetized with ketamine (50 mg/kg, IM), artificially ventilated and spinalized at the Cl level. A laminectomy was performed in the lumbosacral region. The ventral and dorsal roots of segment L5 were isolated and a pouch of skin formed at the site of the dissection to allow the exposed tissues to be covered with liquid paraffin. The body temperature was kept at 37 oC with a homoethermic blanket. A polyethylene cannula was introduced into the left carotid artery to monitor blood pressure, which was kept between 90-110 mmHg. The lateral and medial gastrocnemius nerves were placed on an Ag-AgCl wire electrode for stimulation through an isolation unit. The reflex potentials were recorded from the ipsilateral L7 ventral root, mounted on a silver-silver chloride wire electrode. The intraperitoneal administration of verapamil significantly decreased the amplitude of the reflex response ($P<0.05$). This finding suggests that L-type calcium channels in the spinal cord may play an important role in regulating the reflex response.

Keywords: calcium channel blocker, verapamil, spinal reflex and cat.

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EFFECT OF L-CITRULLINE ON PENICILLIN INDUCED EPILEPSY

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L-Citrulline is the main product of the L-arginine reactions catalyzed by nitric oxide synthase which to produce NO. Some previous reports suggest a provacative role for L-citrulline on epilepsy and these findings present some questions on the role of NO on experimental epilepsy models. In the present study we investigated the effects of intracortical L-citrulline injection on penicillin induced epileptiform activity. 5 male wistar rats were anaesthetized with urethane (1,2g/kg) and connected to a digital data acquisition system after removal of the skull covering the somatomotor cortex. ECoG recordings were recorded from somatomotor cortex via two Ag-AgCl ball electrodes. Epileptiform activity was induced by i.p. penicillin injection (3 MIU/kg). L-citrulline (250μM) administered intracortically after epileptiform aktivity reached its maximal level. Spike numbers (/min), spike amplitudes and power spectra of recorded signals were analyzed offline. ECoG recordings before and after cortical L-citrulline administration were compared to see whether L-citrulline has any effect on ongoing epileptiform activity. According to our results, intracortical L-citrulline injection did not produced a significant effect on ongoing epileptiform activity ($p>0,05$ for all parameters; Student's t-test). This finding suggest that, L-citrulline may not provoke epileptiform discharges at least in these experimental conditions and reported outcomes partly or completely attributed to NO in previous experimental epilepsy studies are unlikely to be affected by increased production of L-citrulline. More studies with different doses and different routes are needed to clarify the role of L-citrulline on penicillin-induced epilepsy.

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UNILATERAL NYSTAGMUS IN AN INFANT WITH ACROCALLOSAL SYNDROME

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Purpose: To report on the first known Turkish girl with Acrocallosal Syndrome (ACS) who had nystagmus, external hydrocephaly, triventricular hydrocephaly, midline brain abnormalities including partial agenesis of the CC, cavum septi pellucidi, cavum vergae, absence of the adhesio interthalamica.

Methods: Case report.

Results: The patient had intermittent nystagmus only on the left eye. Amplitude was small, but frequency was fast. No head shake or abnormal head posture was observed. The remaining eye examination results were normal except for a myelinated nerve fibre only at the half of the quarter of the superior temporal border of the optic nerve head.

Conclusion: In conclusion, additionally to neuroimaging, systemic research is also needed in all patients presenting with asymmetric nystagmus since such nystagmus may be associated with various external developmental abnormalities in addition to CNS involvement. On the other hand, our case indicate that asymmetric nystagmus and midline brain abnormalities should also be taken into account in the cases with ACS.

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THE EFFECT OF CAFFEIC ACID PHENETHYL ESTER ON TOTAL RNA LEVELS IN THE HYPOTHALAMUS DURING CISPLATIN-INDUCED NEPHROTOXICITY MODEL OF RATS

Yilmaz HR (1), Sogut S (2), Ozyurt H (3), Selamoglu Z (4), Uz E (1), Yildirim Z (5).

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Cisplatin is one of the most active cytotoxic agents in the treatment of various solid tumors, but its clinical use is associated with side-effects such as neurotoxicity, ototoxicity and nephrotoxicity.We studied the effect of cisplatin on the total RNA levels in the hypothalamus of rats during cisplatin-induced acute renal failure model of rats. The second aim of this study was to investigate the protective role of caffeic acid phenethyl ester (CAPE) on cisplatin-induced changes of total RNA levels in the hypothalamus.

The intraperitoneal injection of cisplatin (7 mg/kg for five days) induced a significant increase in the total RNA levels when compared to the control rats ($p<0.0001$). Co-treatment with intraperitenal CAPE at a dose of 10 mg/kg attenuated the increase in the total RNA levels in the hypotalamus of rats ($p<0.0001$).

In conclusion, our results demonstrate that CAPE protects the increase of total RNA levels in hypothalamus of rats treated with cisplatin and suggest that CAPE may be a promising agent to prevent cisplatin-induced neurotoxicity.

Key words: Cisplatin, caffeic acid phenethyl ester, hypothalamus, total RNA, rat

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EFFECTS OF TREATMENT WİTH ERYTHROPOIETIN ON NEUROPATHY DEVELOPMENT IN EXPERIMENTAL RAT DIABETES MODEL

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The aim in this study was investigation into the protection of erythropoietin in diabetic neuropathy in the diabetic rat model established by streptozotocin. Sixty male winstar rats were included in this study. Forty five of these was made diabetic with a single i.p. injection of streptozotocin at a dose of 50 mg/kg. Fifteen of these diabetic rats were placed in the therapy group (diabetes+EPO), applying 1000 U/kg erythropoietin once per five days and a placebo group (diabetes+placebo) was established including 15 rats, by intraperitoneal administration 0.4 cc physiological serum in same time. No application was carried out on 15 rats (diabetes). The rats that were not rendered diabetics established the healthy control group (control). Before as well as 4 and 8 weeks after induction of diabetes compound muscle action potentials evoked by electrical stimulation were repeatedly recorded from gastrocnemius muscles of the same 60 animals. Distal motor latency, compound muscle action potential peak to peak amplitude (CMAP) and nerve conduction velocity were measured. CMAP was significantly lower in the placebo (diabetes+placebo) and diabetic groups (diabetes) compared to the control group. A significant difference was not observed in the group treated with erythropoietin (diabetes+EPO) compared to the control group. Similarly, distal latency was found to be longer in the placebo and diabetic groups compared to the control group and the group treated with erythropoietin. In the 8th week, in all the rats in the placebo and diabetic groups, neuropathy development was observed. However, in the erythropoietin group, in 4 rats out of 12, neuropathy development was observed. Our findings demonstrate the existence of the protective effect of erythropoietin in neuropathy development in rat diabetics model induced by streptozotocin.

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LIGHT AND ELECTRON MICROSCOPICAL STUDY OF NEWBORN RATS CEREBELLUM WHICH HAD EPILEPTIC SEIZURE DURING PREGNANCY

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Today, the studies about showing the effect of mothers epileptic seizure on newborns during pregnancy were insufficient so that its hard to learn the exact clinical cares and take precautions about it. This kind of experiments are important to form healty new generations according to world standarts.

In this study; rats were separated into three groups. The first group was; (n= 6) rats which had acute grand mal epileptic seizure after 400 IU penicilin-G administration into their intrahippocampal CA3 region with stereotaxic device during the 13th day of their pregnancy. The second group was; intrahippocampal saline-injected Sham group(n=6) and the third group was the control (n=6) group. After lethal dose anesthesia were administered to neonatal 1 st day rats, newborn cerebellums were perfused with intracardiac perfusion, and dissected surgically for light and electron microscopic studies

In control and sham groups; normal migration and cerebellar maturation were determined. In cerebellar cortex; external granular layer which was seen in the late embryonal period, was compatible with medial zone and internal granular layers. Cerebellar cortex of newborn epileptic rats were evaluated by observing structural findings which belong to early embryonal period cerebellar cortex, such as dendrits and axonal filopodia, intercelular gap density and settlements of purkinje cell body in medial zone. Some of the purkinje cell body were found in the internal granular layer near the substantia alba that made us think that it was because of the migration delay.

As a result it is necessary to investigate epileptic pregnant phenomenons to search the possible relation between epilepsy and congenital malformations and mental retardation.

Keywords; Epilepsy, Pregnancy, Newborns, rat,cerebellum

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SHELL-LESS CULTURE OF THE CHICK EMBRYO AS A MODEL SYSTEM IN THE STUDY OF DEVELOPMENTAL NEUROBIOLOGY

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Experimental studies on animal models play essential roles in the development of preventive, diagnostic and therapeutic procedures for diseases in a wide spectrum of fields including neurological sciences. The goal of this study was to demonstrate the shell-less culture system of the chick embryo as a potential experimental model in the field of developmental neurobiology.

Shell-less culture of the chick embryo is an embryo culture model, where the intact in ovo relationship between the embryo and the yolk sac/albumen is preserved outside the eggshell and shell membranes, i.e., in an artificial experimental culture container. In this study, fertilized chick eggs (the "Cock of Denizli" strain) were pre-incubated for 30-33 h in a standard egg incubator at 37,5 Co and humidified environment. Then these eggs were cragged and the embryos were transferred into the specially designed artificial culture containers pre-sterilized under UV light and cultures were covered with sterile petri-dish lids. These embryo cultures were kept in a humidified, 37,5 Co incubator for the desired amount of time.

In this chick embryo model system we were able to observe and record the central nervous system development of a vertebrate embryo in an artificial experimental culture container starting from an early, three-vesicle brain stage, i.e., Hamburger-Hamilton (HH) stage 9 (Figure-1A), up to a well developed five-vesicle brain stage, i.e., HH stage 24 (Figure-1F), with an embryo survival rate of 100 %.

This model system recently started at Pamukkale University Research Center for Genetic Engineering and Biotechnology and Department of Anatomy laboratories has the potential to enhance our knowledge on molecular and developmental neurobiology at both basic and clinical science level.

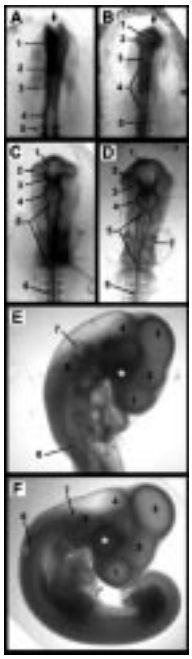

Figure 1: Developing structures of the chick central nervous system. (A) HH stage 9 chick embryo (30-33 h of incubation); arrow, anterior neuropore; 1, prosencephalon; 2, mesencephalon; 3, rhombencephalon; 4, notochord; 5, somites. (B) HH stage 10 chick embryo (33-38 h of incubation) arrow, anterior neuropore; 1, prosencephalon; 2, optic vesicle; 3, mesencephalon; 4, rhombencephalon; 5, spinal cord. (C) HH stage 11 chick embryo (40-45 h of incubation). (D) HH stage 12 chick embryo (45-49 h of incubation). For both (C) and (D); 1, prosencephalon; 2, optic vesicle; 3, infundibulum; 4, mesencephalon; 5, rhombencephalon; 6, spinal cord; 7, auditory pit. (E) HH stage 17/18 chick embryo (60-69 h of incubation). (F) HH stage 24 chick embryo (96 h of incubation). For both (E) and (F); 1, telencephalon; 2, diencephalon; 3, mesencephalon; 4, metencephalon; 5, myelencephalon; 6, spinal cord; 7, otic capsule; *, optic cup and lens.

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THE EFFECTS OF CATECHOL-O-METHYLTRANSFERASE (COMT) GENE POLYMORPHISM ON EEG AND EVENT RELATED POTENTIALS (ERPs)

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Catechol-O-methyltransferase (COMT) enzyme, responsible of catecholamine degradation is encoded by 22q11.1- q11.2 band region. A functional polymorphism was defined on the coding region of this gene (i.e. G‡A transition codon 158 of the membrane-bound and codon 108 of the cytoplasmic form). This variation causes a valin to methionine substitution in the enzyme structure and produces two different variants, H and L with 3 to 4-fold difference in enzymatic activity. Because of the huge differences in enzyme activity, it is thought that this polymorphism may be involved in the pathogenesis of several neuropsychiatric disorders. In this study, the relationship between the functional gene polymorphism of COMT and P3a and P3b ERPs which are obtained by auditory novelty and oddball paradigms, was investigated in 48 healthy male volunteers. Power spectrum of the spontaneous EEG was analyzed and relative band power of delta, theta, alpha, beta and gamma frequency bands of the polymorphic groups were compared. The significance of group differences of the amplitudes and latencies of P3a and P3b waves and spectral band powers were assessed by ANOVA test. Results: three genotype groups HH, HL and LL were defined for the COMT polymorphism. The P3a latency distribution of HH group was found to be significantly different from other two groups. Spectral analysis of EEG showed that HH genotype group's alpha band power was relatively lower on the posterior scalp region with respect to the others. In addition, delta band power of HL group was considerably more dominant on fronto-central electrode sites. In conclusion, COMT activity variance due to functional polymorphism in the enzyme gene affects EEG and ERP.

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TOPOGRAPHIES OF THE P3 EVENT RELATED POTENTIAL (ERP) LATENCIES SHOW SIGNIFICANT DIFFERENCES AMONG PROMOTER REGION POLYMORPHISMS OF THE MONOAMINE OXIDASE A (MAO A) GENE

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MAO A is a form of MAO (monoamine oxidase) enzyme which catalyzes the oxidative deamination of monoamines especially serotonin and norepinephrine. MAO A gene is encoded between Xp11.23-11.4 bands on X chromosome. In the promoter region of MAO-A gene a polymorphism was defined according to number of the 30-bp repeat sequence which affects the activity of MAO A. Although many polymorphic groups were defined related to this polymorphism called VNTR, allele 1 (3 repeats) and allele 3 (4 repeats) are widespread over the population. The results of in vitro studies revealed that allele 3 has 2-10 fold more transcription activity than allele 1. Considering its role in regulation of key neurotransmitter systems, this polymorphism was suggested to have relationship with several neuropsychiatric disorders. In

our study, P3b potentials obtained by auditory oddball paradigm and P3a potentials obtained by auditory novelty paradigm were investigated for a relationship with VNTR polymorphism of MAO A polymorphism from 48 healthy male volunteers. The significance of the differences between amplitudes and latencies of P3a and P3b waves of the two groups defined according to the VNTR polymorphism is investigated by ANOVA test. Results: P3b latency of right and left hemispheres were symmetrically longer than that of central line in allele 3 group, while P3b latency on the right side of the scalp was close to the central and lower than the left side in allele 1 group. This result suggests that, the well known variability on transcriptional activity of MAO A enzyme which degrades norepinephrine and serotonin may partially explain the variability observed on P3b latencies of healthy population.

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MAPPING LONG THORACIC NERVE COURSE

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Long thoracic nerve (LTN) injury has been reported after radiotherapy, trauma, patient's position, transaxillary breast augmentation, implantation of transvenous leads, anesthetic nerve block and transaxillary incision. Denervation of the serratus anterior muscle to LTN injury results in loss of scapular stabilization or winged scapula. LTN injury results in prolonged disability and impact on quality of life for patient and potential medicolegal concerns for the physician.

The purposes of this study was to map the course of LTN relative to the scapula, thereby developing guidelines to aid in the prevention of LTN injuries.

The course and arterial supply of the long thoracic nerve were investigated in 15 adult Turkish cadavers. Each cadaver was placed in the transaxillary thoracotomy positions. The LTN was exposed bilaterally in its course from axilla to its penetration into serratus anterior m.

The nerve courses vertically, gets progressively closer to the anterior scapular border. The length of the LTN was measured 180-220 mm. The largest branches leading to the serratus anterior m. had length of 15-41 mm and an average diameter of 0.5 mm on entering the muscle. Around the courses of the LTN, it gave off six to ten branches to the upper, middle and lower segments of the serratus anterior muscle. The LTN is gave off two or three terminal branches in 96 % of the cases to the middle and lower segments of the serratus anterior m.

Our data shows that the LTN is located at the greatest distance from the scapula at its tip. Distances from the scapular tip to the LTN are listed as mean/outer range: transaxillary line, 4.9/7.0 cm left, 5.2/7.5 cm right. The LTN was constantly found within 1.5 cm lateral to the axillary line on the fascia of the serratus anterior m.

There were no statistically significant differences in our measurements by gender or side.

Before the proliferation of open thoracotomy techniques, most LTN injuries resulted from nerve pinching between the coracoid process and the first or second rib as a result of patient positioning, trauma or lifting heavy objects. Current studies indicate that LTN injury results in both significant and chronic disabilities.

Surgical intervention using a thoracodorsal to long thoracic nerve transfer in order to reconstruct then nerve and restore neural continuity will allow reinnervation of the serratus anterior muscle providing good muscle strength and shoulder function.

On the other hand vascularized LTN transplants can lead to satisfactory functional reconstruction for nerve defect.

By using these anatomic guidelines, we believe that the incidence of iatrogenic long thoracic nerve injury can be minimized.

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SCREENING MICRODELETION BY FLUORESCENCE IN SITU HYBRIDIZATION (FISH) METHOD IN PATIENTS WITH MILLER-DIEKER SYNDROME (MDS)

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MDS is a multiple malformation syndrome characterized by type I lissencephaly and characteristic facial appearance. In addition to the lissencephaly, a severe mental retardation, prominent forehead, bitemporal narrowness, a short nose with upturned nares, protuberant upper lip, and a small jaw is present the findings in MDS. Microdeletions of chromosome 17p13.3 also known as the MDS artical region, have been associated whith both MDS and isolated lissencephaly syndrome. Normal chromosomes are present in %90 but others are associated with chromosomal abnormalities which include deletion of the short arm in association with the duplication of long arm of chromosome 17, ring chromosome 17, and 12q:17p translocation. Here, we performed screening for microdeletions in 13 patients suspected of having MDS , by means of FISH and have compared the results with data from a typical routine cytogenetic laboratory. MDS/ILS and SMS probs for 17p13.3 region in MDS cases were used by FISH technique. The results of FISH in 13 cases with MDS and lissencephaly who were diagnosed according to the clinical assessment; were compared with the cytogenetic findings of those cases. No microdeletion or cytogenetic anomaly was detected in all patients.

In 13 patients no microdeletion was detected FISH method has been reported that is the first choice to investigate the microdeletion in MDS patient. In this study having no patient with microdeletion generated a thought of being more cautious in clinical diagnosis.

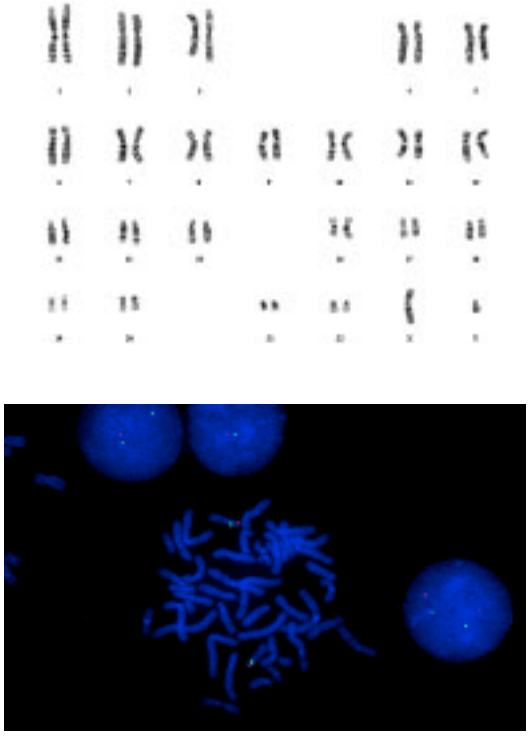

Fig. Metaphase spread from non-deleted patient.

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THE EFFECT OF DEXFENFLURAMINE ON THE MEMORY AND BRAIN LIPID PEROXIDATION

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Introductıon : Dexfenfluramine (dF) which is serotonin (5-HT) releaser and reuptake inhibitor, is widely used as anorectic drug. 5-HT is effective on memory. The use of anorectic drugs can cause damage in membranes by lipid peroxidation. We planned to investigate the effects of 5-HT on the memory and the brain oxidative systems induced by dF treatment.

Material and Methods : Two equal groups of 16 adult male albino Wistar mice (40±5g) were used in the experiments 1.controls (saline solution 0.9 %, 0.2 ml ,ip, 7 days) 2. dF treated (0.2 x 2 mg/kg 0.2 ml, ip, 7 days). For the memory trials all mice were trained for 7 days by learning time in ''Hansen Rapid Assembly Maze'' which is a kind of labyrinth. Brain malondialdehyde (MDA) and glutathione (GSH) levels were assayed with spectrophotometrical methods. Brain tissue 5-HT level was observed by immunohistochemical method.

Results: Learning time decreased significantly in two groups both at the 5 th and 8 th days, but was more significant in the dF treated group. Brain 5-HT levels increased in dF group compared to control. The brain MDA levels increased in dF groups, meanwhile GSH levels decreased.

Conclusions: dF treatment decreased learning time by enhancing 5-HT levels in the brain. Our previous data indicated that also tryptophan (TRP) increased 5-HT levels in the brain and decreased learning time. But learning time in the dF treatment was longer than the learning time in TRP administration. Also dF groups' MDA levels were higher than TRP administration group. These observations suggest that there is a relation between brain 5-HT, MDA, GSH levels and learning.

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EXPRESSION OF MATRIX METALLOPROTEINASES IN VASCULITIC NEUROPATHY

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Matrix metalloproteinases (MMP) are endopeptidases degrading components of extracellular matrix proteins and they have been implicated in the pathogenesis of inflammatory demyelination. They are induced by cytokines, secreted by inflammatory cells and enhance T-cell migration. Vasculitic neuropathy occurs as a component of systemic vasculitis or as an isolated angiitis of the peripheral nervous system. T-cell-mediated inflammation is detected in its pathogenesis. The aim of this study is to investigate the expression pattern and cellular source of matrix metalloproteinases (MMP) in vasculitic neuropathy. Nerve biopsy sections of eight patients with nonsystemic vasculitic neuropathy (NSVN) and four patients with systemic vasculitic neuropathy were examined for the presence of CD4+, CD8+, CD68+ cells and for MMP-2 and MMP-9 expression immunohistochemically. Nerve biopsies of eight patients with non-inflammatory neuropathy were used as a control group. Semiquantitative polymerase chain reaction (PCR) analysis was performed to detect MMP-2 and MMP-9 mRNA. Predominant cells were CD8+ and CD68+ T cells. Expression of MMP-9, but not MMP-2, was increased in perivascular inflammatory infiltrate in nerve tissues of vasculitic neuropathy patients. MMP-9 expression was positively correlated with immunostaining of CD8+ T cells. No difference was detected between immunostaining patterns of nonsystemic and systemic vasculitic neuropathies with the antibodies used, except MMP-9 immunostaining, which was found to be enhanced in NSVN group. PCR analysis revealed elevated mRNA levels of MMP-9 and MMP-2 compared with controls but this elevation did not reach statistical significance. Our results imply a pathogenic role for MMP-9 secreted from CD8+ cells in vasculitic neuropathy.

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NOVELTY PARADIGM IS SENSITIVE IN DETECTING EARLY STAGE ALZHEIMER'S DISEASE

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P3b is an event related potential (ERP) generated by the target detection task of Oddball and Novelty Paradigms. P3a is an ERP generated by novel stimuli of Novelty Paradigm. In this study, we investigated the relationship between ERPs and the cognitive defects in Alzheimer's Disease (AD). P3b and P3a amplitudes and latencies were measured from 20 healthy volunteers and 22 AD patients from Behavioural Neurology & Movement Disorders Unit, Department of Neurology, Istanbul Medical Faculty. All subjects were evaluated with Mini Mental State Examination. ERPs were compared with Global Deterioration Scale (GDS) and Clinical Dementia Rating Scale scores of patients and ERPs of controls. Comparisons of P3a and P3b according to the presence and the stage of AD were made with ANOVA. In Oddball Paradigm the differences in P3b between patients and controls were not statistically significant. In Novelty Paradigm the differences in P3a latency between early stage patients (determined by GDS) and controls were not statistically significant; however, there was a significant increase in medium stage patients compared to controls and early stage patients. In all patient groups the amplitude of P3b generated by target stimuli of Novelty Paradigm showed a significant decrease in the parietal lead. These findings, suggest that there is a delay in the processing of distractor stimuli in Novelty Paradigm and that this causes a difficulty in attention switching to target stimuli of the same paradigm. The P3b obtained by Novelty Paradigm is more sensitive in detecting early stage AD subjects than classical Oddball Paradigm.

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A REVIEW ON COMPUTERIZED THREE DIMENSIONAL (3D) RECONSTRUCTION OF NEUROLOGICAL STRUCTURES IN TURKEY: THE PAST, PRESENT AND FUTURE

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Computerized modeling of anatomical and histological morphologies has become very useful for visualizing complex 3D forms. 3D reconstructions from routine anatomical/ histological sections are being performed since the last quarter of the 19th century. The first 3D reconstruction, by using serial sections was reported by Born in the cranium of an embryo. Following Born, many researchers performed the 3D reconstructions of many structures.

In Turkey, similar practices appear in 1990s, with a hundred years of delay. Human internal capsule was reconstructed from cadaveric serial sections. In this leading study, computer programs like Adobe Photoshop 3.0 and Adobe Dimensions 2.0 that we can class them primitive reconstruction programs now, were used. Human coccygeal body's 3D reconstruction

was made with the same computer programs above, using semi-thin serial sections. This study was the first one reporting the 3D reconstruction of the contours of the human coccygeal body. Another study which has been the cover of Folia Morphologica 2002, 61, was on lentiform nucleus of man. This study has special clinical importance when applying pallidotomy. Also computer aided reconstruction of lentiform nucleus regarding its dimensions was firstly being reported.

Human claustrum, external capsule and capsula extrema have been reconstructed with similar computer aided models on serial parallel sections. Purkinje cell's reconstruction was an importance that was made up from ultrathin serial sections (60 nm in thickness) and micrographed using a transmission electron microscope. Also human lateral, third and fourth ventricules were reconstructed using magnetic resonance images, so an in-vivo 3D reconstruction was under consideration.

Nowadays computer based reconstruction and simulation programs are rapidly improving. On the other hand, with radiological techniques like computerized tomography and magnetic resonance imaging, highly thin and sensitive sections can be hold. Studies on 3D reconstruction from these data with comparing them with the National Library of Medicine's Visible Human Dataset, have a great importance as a pure knowledge source for the use of clinicians.

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ANTINOCICEPTIVE EFFECTS OF INTRATHECALLY ADMINISTERED MELATONIN IN RATS

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It has been shown that there is an interaction between pain sensitivity, melatonin and opioid system. Peripheral and central administration of melatonin has analgesic effects in rats. This study was planned to determine whether melatonin has an analgesic effect when it is administered intrathecally (i.t.). To determine the mechanism by which i.t. melatonin exerts its effects on nociception, naloxone, an opioid antagonist, and luzindole, a melatonin antagonist, were also used.

Twelve male Wistar rats weighing 200-250 g were used. They were kept at a 12h light/dark cycle, with food and water available ad libitum. The animals were exposed to intrathecal catheterization and injected with either vehicle or one of these treatments; melatonin (MT), melatonin plus luzindole and melatonin plus naloxone. Mechanical nociception threshold was assessed using electrovonfrey. The results were tested using the Wilcoxon signed rank test.

I.t. melatonin injection produced a significant increase in withdrawal threshold compared with vehicle treatment, thus indicating a reduced pain sensitivity to mechanical stimulation. Both luzindole and naloxone administration antagonized this effect.

In conclusion, i.t. melatonin utilization may have a therapeutic possibility in painful situations in humans.

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THE EFFECTS OF THE NITROANALOG TETRAPEPTIDAMID ON THE SYNTHESES OF THE (-ENDORFIN AND CORTICOTROPIN

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Objectives: By recent studies, the importance of the opioids, has been shown in the regulatıon of the blood circulatıon.

In this study, the purpose is to study the effect of the nitroanalog terapeptidamid on the levels of (-endorfin and corticotropin in blood plazma and spino-cerebellar fluid.

Methods:The studies were performed on the cats weight from 3.5-4.0 kg under general anesthesia by sodium pentobarbital (Nembutal, 40 mg/kg, intravenously i.v.)

The blood taken from jugular vein and from spinal fluids were withdraved from a part of the thoraxic region of the vertebral column by steriotaxis devices. Blood and spinal fluid were withdrawed at the 3 and 20 minutes before and after the application of the tested substances. Nitroanalog tetrapeptidamid was applied in 1 mg/kg of dose intravenously.The level of the (-endorfin and corticotropin were assessed by the radioimmunological methods (Tracor Europa, France)

Results: 3 minutes after the application of the nitroanalog tetrapeptidamid in 1 mg/kg of dose, the level of the (- endorfin, did asses any changing, but 20 minutes after the application of the tested substance, in blood plasma, the level of the (-endorfin decreased significantly. 20 minute after application of the test substance in average of %61(6.4 the value of the control in blood was 39(9.5 pkmol/l. The intensity of the (-endorfin were 33(9.5 and 11(2.9 at 3 and 20 minutes after the application of the tested substance

Similar changes seem to be in the spinal fluid. Nitroanalog tetrapeptidamid did not effect on the intensity of the plasma corticotropin at 3 and 20 minutes after the application of the tested substance in plasma and spinal fluid.

Conclutions: The decreasing in plasma and spinal fluid of the (-endorfin can explain by the effect of the nitroanalog tetrapeptidamid to the opioids synthesis in hypothalamus, hypophysis and other related regions of the brain. We can say that nitroanalog tetrapeptidamid inhibited the synthese of the (-endorfin by the negative feedback as a result of the stimulation of the opioid receptors.

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THE EFFECT OF TAURINE ADMINISTRATION ON PLASMA, BRAIN, LIVER AND KIDNEY VITAMIN C LEVELS IN MICE

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Objective: Taurine (2-aminoethane sulfonic acid), a sulphur-containing beta amino acid, is the most prevalent free intracellular amino acid in many human and animal tissues. In humans, taurine is synthesized mainly in the liver and brain, and is formed from the sulfur-containing amino acids. There is relationship between vitamin C and sulfur-containing amino acids. The aim of this study is to investigate the effect of taurine administration on the vitamin C levels of plasma and several tissues in mice.

Methods: Male Swiss Albino mice (n= 12) weighing 32.2±1.0 g were divided into two groups as control (C) and taurine (T). Taurine was freshly dissolved in sterile saline (50 mM aqueous solution) and administered daily (60±956;L, i.p.) for five days in the group T mice. The group C mice were also received just saline injections. At the end of the 5 day, the animals were killed by decapitation and blood was collected from the cervical wound. The brain, liver and kidneys were immediately removed. Vitamin C levels were measured by method of Roe and Kuether in plasma and by method of Berger in tissues.

The data were statistically analyzed by ANOVA and $p<0.05$ considered as significant.

Results: The administration of taurine had no effect on the levels of vitamin C in plasma ($p>0.05$) and brain ($p>0.05$) but significantly increased in liver ($P<0.001$) and kidney ($P<0.001$).

Conclusion: Taurine may have affected the vitamin C metabolism in tissues by different mechanism.

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7-NITROINDAZOLE DEPRESSES POLYSYNAPTIC SPINAL REFLEXES IN THE CAT SPINAL CORD

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The aim of this study was to investigate the effects of 7-NI, a relatively selective neuronal nitric oxide synthase (nNOS) inhibitor, on polysynaptic reflexes in different i.v. and local doses and draw conclusions about the function of nitric oxide (NO) in the polysynaptic reflexes in the cat spinal cord.

Cats were anaesthetized with pentobarbital sodium (40 mg/kg i.p.) and a spinalization was done at the level of T1. A dorsal laminectomy was performed between L5 and S1. Monosynaptic and polysynaptic spinal reflexes were produced by electrical stimulation of gastrocnemius nerves and recorded from ipsilateral ventral spinal roots. After control recordings, the effects of 7-NI administration in 500 μM, 1, 5 mM (local) and 10, 20, 50 mg/kg (i.v.) doses were observed on polysynaptic reflexes. The recorded reflexes were evaluated according to their latencies and amplitudes.

Our results suggest that intravenous and local administration of 7-NI decreases the amplitude of the polysynaptic reflexes significantly in a dose dependent manner. There was no significant difference between the reflex latencies.

Our findings suggest that NO may contribute in the modulation of polysynaptic spinal reflexes and these reflexes can be attenuated by nNOS inhibitors such as 7-NI.

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EFFECTS OF THEOPHYLLINE ON CONVULSIVE ACTIVITY AND BLOOD-BRAIN BARRIER PERMEABILITY FOLLOWING PTZ- INDUCED SEIZURES IN RATS

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Theophylline is known as a non specific adenosine receptor antagonist. It behave as proconvulsive agent in convulsive seizures. This study aimed to evaluate the effects of theophylline treatment on seizure activity, blood pressure and blood-brain barrier permeability in pentylenetetrazole (PTZ)-induced generalise tonic-clonic seizures.

Animals divided into two groups: Group I: 100 mg kg-1 PTZ-induced convulsions group (n=7), Group II: 40 mg kg-1 theophylline + 100 mg kg-1 PTZ-induced convulsions group (n=7), Theophylline was given 40 min before PTZ injections in theophylline-treated group.

Administration of PTZ induced tonic-clonic convulsions together with simultaneously increase in mean arterial blood pressure and caused cerebrovascular permeability changes in PTZ group. Theophylline pretreatment caused significant increase in seizure activity. Onset latency to seizures was shortened in theophylline group compared with PTZ-induced seizure group (33±61617; 4 sec versus 53±61617; 5 sec, $p< 0.05$). All rats experienced stage 4 seizures after PTZ injection alone, however pretreatment with theophylline induced stage 5 seizures and also caused 100 % mortality of rats. There were minimal Evans blue staining in the brain regions in theophylline -treated rats and also pretreatment of theophylline did not caused significant differences in mean arterial blood pressure (161±61617; 4 mmHg) compared with PTZ -treated group (165±61617; 2 mmHg).

Our results supported the data which explain the proconvulsive action of theophylline in PTZ -induced convulsions. On the other hand, while theophylline potentiated the convulsive activity of PTZ, it did not increase cerebrovascular permeability.

This result show that the changes in convulsive threshold, increase in blood pressure and duration of increase may contribute to cerebrovascular permeability changes.

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THE EFFECTS OF PRENATAL STRESS ON THE GRANULE-TO-PURKINJE CELL RATIO IN THE RAT CEREBELLUM

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In this study, a model of restraint stress was used to investigate the effects of prenatal stress on the cerebellar neuronal development. In the rat cerebellum, macroneurons like the Purkinje cells are generated prenatally; whereas microneurons like granule cells are generated postnatally. Therefore, by applying stereological procedures, the granule-to-Purkinje cell ratio was compared in prenatally stressed animals with their age-matched controls.

In the experimental group, rat embryos were exposed to stress on their embryonic day (E) 7 and 14, by keeping the dam in close-fitting wire mesh cylinders for six hours. Six animals from each group were fixed by intracardiac perfusion at postnatal day (P)30. Their cerebella were removed and semi-thin sections (0,5 μm) from lobes IV, V and VI were stained with toluidine blue. Quantitative analyses were performed on the camera lucida drawings and the estimates of numerical density for both granule (NVG) and Purkinje (NVP) were made on the basis of the number of cells per unit volume of whole cortex.

The granule-to-Purkinje cell ratios (estimated by dividing NVG by that of NVP) were found significantly different in the stressed (306.85 ± 25.21) and control (419.68 ± 16.95) groups. However, neither volume fraction (Vv) of granular cell layer to whole cortex nor the proportion of white matter to whole cortex did show a significant change in the stressed group. Therefore, as it is expected, prenatal stress caused a dramatic change in the granule-to-Purkinje cell ratios by increasing the number of Purkinje cells, but not affecting the number of granule cells.

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SECONDARY BILATERAL SYNCHRONY: CASE REPORT

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Introduction; Absence seizures are characterized with 3Hz spike and slow wave complexes. Clinical features of some partial epilepsies look like absence epilepsies. In order to produce 3Hz spike and slow wave discharges, partial epilepsies must stimulate certain regions.

Case 1: Forty-six year-old female was admitted to our emergency department with confusion. Her examination revealed that she was disoriented for time, place and person. On inspection, subtle myoclonias were seen. At admission, we performed EEG. EEG revealed generalized 3Hz spike and slow wave complexes. During her out patient clinic follow-up, her EEG's revealed frontal foci either right or left and secondary bilateral synchrony (SBS).

Case 2: Twenty-one year old girl started with seizures by the age of 11 years. At age 16 months, she experienced tuberculous meningitis. She developed mild left hemiparesis because of the right middle cerebral artery infarction due to tuberculous vasculitis as a complication. Her seizures were started with bending of the body to left and rapidly spreading to other parts of the body. Seizure frequency ranged from 1-2 per week. EEG showed left frontotemporal spiking and intense SBS.

Discussion; Generalized 3Hz spike and slow wave discharges appeared in lesions of the paramedian area, frontoparasaggital, mesifrontal and mesiotemporal area was first reported by Jasper and Tükel. They used the term secondary bilateral synchrony to describe the spike-wave complex that had a focus in local lesions and became generalized secondarily. We present and discuss two of our patients with SBS, with lesional and nonlesional frontal lobe epilepsy.

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NERVE GROWTH FACTOR DECREASES REACTIVE OXYGEN SPECIES FORMATION INDUCED BY COLCHICINE IN RAT HIPPOCAMPAL SLICE CULTURES

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Organotypic hippocampal slice culture (OHSC) technique is a specific method with the characteristics of synaptic organization. Colchicine is a plant alkaloid which blocks axonal transport by microtubule depolymerization. Incubation with colchicine induces a neurodegenerative injury model in OHSC's. On the other hand, Nerve Growth Factor (NGF) is a mammalian and human neurotrophin, which is required on central and periferic neuronal survival and protection. Studies have shown, that NGF has a protective effect on cholinergic uninjured neurons and has a neurotransmitter like effect on cholinergic neurotransmission and neuronal exitability. In this study, we have determined the effect of NGF reactive oxygen species (ROS) formation in an axonal degeneration model which was induced by adding colchicine to OHSC's. For this purpose, freshly isolated hippocampal slices from 9-12 days old Sprague-Dawley rats were incubated in a culture flask for 20 days. At the end of this time, colchicine (10±61549;M) or lumicochicine (for control group) was added to the culture medium for inducing axonal degeneration. ROS are quantitated with luminol or lucigenin chemiluminescence probes after NGF (250 ng/mL) treatment. Our results have showed that colchicine significantly increased ROS (.OH, H2O2 ve HOCl- ile O2.-) in this axonal degeneration model. Additionally, NGF decreased ROS formation which has an important role on neurodegeneration.This effect is probably related to the structure of NGF which has a cysteine knot containing three disulfide bonds.

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GLUTATHIONE DEPENDENT ENZYME ACTIVITIES IN VARIOUS BRAIN REGIONS IN EXPERIMENTAL HUNTINGTON'S DISEASE MODEL

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Huntington's disease is a neurodegenerative disorder associated with degeneration of basal ganglia neurons and is characterized by progressive dementia and involuntary abnormal choreiform movements. 3-Nitropropionic acid (3-NPA) is a fungal toxin that effects primarily striatum and secondarily hippocampus. It irreversibly inhibits succinate dehydrogenase, which is a component of both the Krebs cycle and complex II of mitochondrial electron transport chain. Systemic administration of 3-NPA to rats or primates results in selective striatal lesions. In the present study, we have examined the effect of 3-NPA administration on glutathione peroxidase (GSH-Px), glutathione-S-transferase (GSH-Tr) and glutathione reductase (GSH-Red) in various brain sites. Female Sprague-Dawley rats (12 weeks old) weighing 180-250 g were injected 3-NPA or 0.9 % NaCl (control group) was intraperitoneally at a dose of 20 mg/kg for 10 days. One day after the last injection rats were decapitated and brain was removed. Homogenates of isolated cortex, striatum, hippocampus and cerebellum were prepared in sucrose buffer. After centrifugation the supernatants were used for enzyme activity assays. GSH-Px, GSH-Tr and GSH-Red activities were measured by standard methods. GSH-Px activity was significantly increased in hippocampus and cerebellum but decreased in cortex. Increasing in striatum was not significant. GSH-Tr activity increased significantly in striatum and hippocampus, but not in cortex and cerebellum. GSH-Red activity was significantly decreased in cortex, striatum and hippocampus. In conclusion, our results show that in striatum GSH-Red activity is decreased and GSH-Tr activity is increased whereas increase in GSH-Px was not significant. Since GSH-Px catalyses the reaction of GSH and H2O2 to GSSG and H2O, our results imply that H2O2 has an important role in 3-NPA toxicity.

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DOXORUBICIN-INDUCED OXIDANT STRESS ON BRAIN TISSUE AND EFFECTS OF ERDOSTEINE

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Doxorubicin, which is one of the widely used drugs in the treatment of various human neoplasms, has limited usage due to its toxicity. The aim of this study was to investigate effects of erdosteine that has antioxidant property with its metabolites, on the doxorubicin induced oxidant stress. Three groups of male Sprague-Dawley rats were used for this experiment. The first animal group without any treatment was used as controls; the other groups were treated with doxorubicin (single i.p. dosage of 20 mg/kg b.wt.) or doxorubicin plus erdosteine (10 mg/kg/day, orally), respectively. The study was finished at tenth day of doxorubicin injection. The level of malondialdehyde was significantly increased in doxorubicin group compared to control group. The activity of glutathione peroxidase was higher in doxorubicin plus erdosteine group than doxorubicin group. There was a negative correlation between malondialdehyde and glutathione peroxidase activity in both doxorubicin and doxorubicin plus erdosteine groups. In conclusion, treatment with doxorubicin resulted in lipid peroxidation in the brain tissue, but erdosteine could not prevent this oxidative stress although glutathione peroxidase activity was found to be increased.

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NEURONAL EXPRESSION OF THE MULTIDRUG RESISTANCE PROTEIN MDR1 IN THE HIPPOCAMPUS AND TEMPORAL NEOCORTEX OF PATIENTS OPERATED FOR MESIAL TEMPORAL LOBE EPILEPSY SYNDROME

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Purpose: MDR1 is an efflux pump which is normally expressed in endothelial cells of the human brain. Few studies performed in epileptic brains have reported its presence in reactive astrocytes and dysplastic neurons as well. We aimed to investigate the presence and pattern of expression of MDR1 in the hippocampus and temporal neocortex of patients who were operated for drug resistant mesial temporal lobe epilepsy syndrome (MTLES) and had hippocampal sclerosis.

Methods: The expression of MDR1 protein was investigated in hippocampal and temporal neocortical tissues of selected MTLES patients by immunohistochemistry.

Results: Nine (7 F, 2 M) patients (age: 15-49, mean: 27.8) were included in the study. They had been experiencing seizures for 8 to 31 years. Microscopic investigations revealed dense immune reactivity in endothelial cells and reactive astrocytes of all the tissues examined. Spared neurons in the dentate gyrus and CA sectors of the hippocampus also exhibited positive staining for MDR1. Strong immune reactivity was also observed in ectopic neurons and neurons in layer VI of the neocortex whereas neurons in the superficial layers were not stained.

Conclusion: In this study we have observed positive immune reactivity for MDR1 not only in endothelial cells and reactive astrocytes, but also in ectopic neurons and neurons in layer VI of the neocortex. This finding has not been reported previously. Further investigations are needed to clarify the significance of this finding in drug resistant epilepsies.

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CENTRAL THROMBOXANE A2 MEDIATES HEMORRHAGIC HYPOTENSION IN RATS

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Objective: In the present study, we aimed to determine the involvement of brain thromboxane A2 (TxA2) in hemorrhagic shock conditions. Methods: Male Sprague-Dawley rats were used throughout the study. The surgical and experimental protocols were approved by the Animal Care and Use Committee of Uludag University and are in accordance with the National Institute of Health Guide for the Care and Use of Laboratory Animals. Acute hypotensive hemorrhage was performed by withdrawing a total volume of 2.1 ml of blood per 100g body weight over a period of 10 min. In graded hemorrhage, a blood sample (0.55 ml per 100g body weight) withdrawn over 10s and arterial pressure monitored for the following 5 min. This procedure was repeated three times at 5 min intervals. Furegrelate, a TxA2 synthesis inhibitor, (250 μg) and U-46619, a synthetic analog of TxA2, (1 μg) were injected intracerebroventricularly (i.c.v.) 60 min and 5 min before haemorrhage, respectively. Results: Furegrelate pretreatment (250 μg; i.c.v.) partially attenuated the fall in arterial pressure evoked by acute or graded hemorrhage. However, pretreatment of rats with U-46619 (1 μg; i.c.v.) caused greater decrease in blood pressure during haemorrhage than that observed in saline pretreated animals. Heart rates of control rats increased during haemorrhage. Furegrelate did not affect the changes in heart rate which observed in control group while U-46619 abolished the increase in heart rate during haemorrhage. Plasma vasopressin and adrenalin levels of rats pretreated with furegrelate were significantly higher than saline treated controls. Conclusion: Our data show that endogenously synthesized brain TxA2 is involved in the fall in arterial pressure induced by hemorrhage. Blockade of brain TxA2 synthesis with furegrelate prevents the fall in the arterial pressure induced hemorrhage. Increase in plasma vasopressin and adrenaline mediates this effect.

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CARDIOVASCULAR EFFECTS OF CENTRALLY INJECTED U-46619, A THROMBOXANE A2 ANALOG, IN HAEMORRHAGIC SHOCK: INVESTIGATION OF DIFFERENT BRAIN AREAS

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Objective: In the present study, we investigated the cardiovascular effects of centrally injected U-46619, a thromboxane A2 (TxA2) analog, and the central and peripheral mechanisms of these effects in haemorrhagic shock conditions. Methods: Male Sprague-Dawley rats were used throughout the study. The surgical and experimental protocols were approved by the Animal Care and Use Committee of Uludag University and are in accordance with the National Institute of Health Guide for the Care and Use of Laboratory Animals.. Haemorrhage was performed by withdrawing a total volume of 2.0 ml of blood per 100 g body wt over a period of 10 min. Injections were made into lateral cerebral ventricle (LCV), paraventricular nucleus of hypothalamus (PVN), rostral ventrolateral medulla (RVLM) and nucleus of tractus solitarius (NTS) in a volume of 10 μl (for i.c.v.) and 1 μl (for PVN, RVLM and NTS) over 60 s period. Results: U-46619 (0.1, 1 and 2 μg) increased blood pressure and reversed hypotension in haemorrhagic shock. Pressor effect was dose- and time-dependent in all investigated brain areas. Heart rate changes were not significantly different in all groups. Pretreatment of rats with SQ29548 (4 or 8 μg), a TxA2 receptor antagonist, completely blocked the pressor effect of U-46619. Haemorrhage, itself, increased plasma adrenaline, noradrenaline, vasopressin levels and renin activity. U46619 (1 μg) injected into LCV, PVN, RVLM and NTS produced additional increases in these hormone levels and in renin activity. Pretreatments of rats intravenously with prazosin (0.5 mg/kg), an alpha1-adrenoceptor antagonist, [beta-mercapto-beta, beta-cyclopentamethylenepropionly1, O-Me-Tyr2, Arg8] vasopressin (10 μg/kg), a vasopressin V1 receptor antagonist, or saralasin (250 μg/kg), an angiotensin II receptor antagonist, in hemorrhaged rats partially blocked the pressor response to U46619 (1 μg) injected into LCV, PVN, RVLM and NTS. Conclusion: Results show that centrally administered U-46619, a TxA2 analog, increases blood pressure and reverses hypotension in hemorrhagic shock. Central TxA2 receptors mediate the pressor effect. Furthermore, the increase in plasma adrenaline, noradrenaline, vasopressin levels and renin activity are involved in these effects.

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IMMUNOHISTOCHEMICAL LOCALIZATION OF KAINATE RECEPTOR SUBUNITS GLUR6 AND KA2 IN RAT HYPOTHALAMUS

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Glutamate is a major excitatory regulator of mammalian central nervous system (CNS) function, and is important in the control of various neuroendocrine systems. Two groups of glutamate receptors (ionotropic and metabotropic) participate in mediating glutamatergic effects. Ionotropic receptors are further subdivided into alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionate (AMPA), kainate (KA) and N-methyl-D-aspartate (NMDA) receptor subfamilies. Previously we described the distribution of KA receptor subunit (KA2, GluR5-7) mRNAs in the hypothalamus with in situ hybridization histochemistry, which revealed diverse distribution patterns for each subunit. To follow up that study, we conducted immunohistochemical experiments to assess the distribution pattern of GluR6 and KA2 subunit protein in the hypothalamus of the rat using specific antibodies that recognize GluR6 or KA2 protein. KA2-expressing cells were detected in the median preoptic nucleus, anteroventral periventricular nucleus (AVPv), medial preoptic nucleus, supraoptic nucleus (SON), suprachiasmatic nucleus, posterior magnocellular and medial parvocellular parts of paraventricular nucleus (PVN), arcuat nucleus (ARC), ventromedial nucleus (VMH) retrochiasmatic area and to a limited extend, in the dorsomedial nucleus. GluR6-expressing cells were localized in anterior hypothalamic nucleus, PVN, SON, ARC, and lateral hypothalamic area. In addition, a few GluR6-immunoreactive neurons were observed in anterodorsal preoptic nucleus, AVPv and VMH. The results of the present

study are in agreement with our previous data on the distribution of KA2 and GluR6 mRNA in rat hypothalamus. In conclusion, it is suggested that the KA2 and GluR6 receptor proteins are expressed in hypothalamus and that these subunits can participate in conveying the glutamatergic signals to select neuroendocrine systems.

Supported by grants from Uludag University (2001/56) and NIH (MH 59890)

Keywords: KA2, GluR6, hypothalamus, immunohistochemistry.

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C-FOS EXPRESSION IN OXYTOCIN NEURONS FOLLOWING KAINIC ACID ADMINISTRATION

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Oxytocin is synthesized and secreted by a subset of magnocellular neurons (MCNs) which are localized in the paraventricular (PVN) and supraoptic nuclei (SON) of the rat hypothalamus. Previous immunohistochemical and electrophysiological studies has shown that glutamate is present in the presynaptic terminals contacting MCNs in both PVN and SON. In addition, recent studies indicate that select glutamate receptor subunits were expressed in PVN and SON. The present study was designed: 1. to assess if the oxytocinergic neurons in PVN and SON express c-Fos, following the injection of a kainate receptor agonist (kainic acid,) and 2. to investigate whether this effect of kainic acid in oxytocin neurons can be blocked by a specific non-NMDA glutamate receptor antagonist (CNQX). Three groups of animals (n=5/each) received saline (ip, control group), kainic acid (2.5 mg/kg, ip) or CNQX (1 mg/kg, ip, 15 min prior to kainic acid injection) and were sacrificed by perfusion fixation 90 min after the last treatment. The results of dual immunohistochemistry for oxytocin and c-Fos showed that 49.8±3.7 % of the oxytocin neurons in SON and 43.6±2.7 % in PVN express c-Fos following kainic acid administration, a significant increase in number of neurons when compared to the control group (1±0.4 % in SON and 0.8±0.4 % in PVN). Administration of CNQX prior to kainic acid injection caused a significant reduction in the number of double-labeled neurons (11.5±4.3 in SON and 11.2± 1.8 in PVN). The results of the present study suggested that oxytocin neurons contain functional glutamate receptor channels and that these channels are probably formed by kainate receptor subunits, since the administration of kainate receptor analog kainic acid activates these neurons and this activation is blocked by CNQX administration.

Supported by TUBITAK (SBAG-2459), Turkey.

Key words: c-Fos, oxytocin, kainic acid, CNQX, immunohistochemistry

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EXPRESSION OF KAINATE RECEPTOR SUBUNITS IN OXYTOCIN NEURONS

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Glutamate, the principle excitatory amino acid in the hypothalamus, participates in the regulation of oxytocin synthesis and secretion. The effects of glutamate are mediated by ionotropic and metabotropic glutamate receptors. As one of the non-NMDA glutamate receptor families, kainate receptors are composed of five subunits including GluR5-GluR7, KA1 and KA2 which can form homomeric and/or heteromeric functional receptor channels. Since different compositions of the subunits have different functional properties, it is important to identify individual subunits which are expressed in oxytocin neurons. In the present study we used dual immunohistochemistry to assess the expression of the kainate receptor subunits GluR6 and KA2 in oxytocin neurons. When analyzed with laser scanning confocal microscope, oxytocin-immunoreactive neurons were detected in the paraventricular (PVN) and supraoptic nuclei (SON) of the hypothalamus. Of these neurons, 41.2 % in SON and 43.2 % in PVN were also immunoreactive for GluR6 receptor protein. KA2 subunit protein expression was detected in almost all oxytocin-positive neurons in the SON and PVN. In order to determine which subset of these neurons were activated following kainic acid injection (2.5 mg/kg, 90 min prior to sacrifice), we used the transient expression of immediate early gene c-Fos protein as a marker of neuronal activation. Triple-labeling immunohistochemistry revealed that 68.6 ± 2.9 % of KA2-expressing oxytocin neurons in SON and 42.4 ± 4.9 % of KA2-expressing oxytocin neurons in PVN also express c-Fos protein, hence, are activated. The results of these studies suggest that GluR6 and KA2 kainate receptor subunits are expressed in oxcitocin neurons and these subunits can form functional receptor channels through which the neurons can be activated by the glutamate analog kainic acid.

Supported by TUBITAK (SBAG-2459), Turkey.

Key words: oxytocin, kainate receptors, KA2, GluR6, immunohistochemistry

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AMIGDALOID KINDLING IN GENETIC ABSENCE EPILEPTIC RATS PRETREATED WITH ETHOSUXIMIDE

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Coexistence of idiopathic generalized epilepsy in patients with partial epilepsy is only exceptionally reported. In our previous study, we evaluated whether process of kindling as a model of complex partial seizures with secondary generalization is altered in Genetic Absence Epileptic Rats from Strasbourg (GAERS). All control Wistar rats were became fully kindled after 12th-15 th stimulus. GAERS had only Grade 1 or 2 limbic seizures without motor seizures development although the number of stimulations had reached to 30. In this study, we aimed to evaluate kindling process in GAERS pretreated with ethosuximide which supresses absence seizures.

Non-epileptic control Wistar rats and GAERS were used in the experiments. One week before the experiments, we implanted a stimulation electrod into the basolateral amygdala and four cortical electrods for EEG recording. Animals were stimulated with their afterdischarge threshold current twice daily for the kindling process and accepted as fully kindled after the occurence of five times Grade 5 seizures according to the Racine's seizure scale. Bilateral EEG's from cortex were recorded continuously during the experiments: 20 minutes before i.p. injections of ethosuximide (100 mg/kg) or saline, 60 minutes after injections and 20 minutes after each stimulation. Stimulations were given 60 minutes after ethosuximide or saline injections.

Five animals with electrod placement in basolateral amigdala reached Grade 3-5. Others with incorrect placement had only Grade 1 or 2 limbic seizures without motor seizures.

These results indicate that the supression of absence seizures may result in development of kindling in GAERS.

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THE COMPARISON OF THE VIDEO ASSISTED FOOTPRINT ANALYSIS AND COMPOUND ACTION POTENTIAL TO EVALUATE THE RAT SCIATIC NERVE REGENERATION

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Rat sciatic nerve crush is a frequently used model of experimental peripheral nerve injury. This model is used with footprint analysis to observe the nerve regeneration. On the other hand, this method can give indirect information about the regeneration process, but is insufficient to inform about the action potential that occur in the nerve. In this study, the relation between the data obtained from footprint analysis and the compound action potentials that were recorded with the sucrose-gap technique was examined.

In our study, female Wistar rats weighing 250-300 g were used. After crushing their right sciatic nerve, the functional recovery was observed for 35 days with 5 days intervals by video assisted footprint analysis and evaluated with sciatic function index (SFI). Besides, at the days of 5, 15, 25, 38 the action potentials were recorded with the sucrose-gap method from the rat sciatic nerves. The amplitude of the action potential and the SFI was compared for the days.

The results show a similarity between the SFI and the amplitude of the action potentials except the day 15.

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THE EFFECT OF PULSED ELECTROMAGNETIC FIELD WITH VARIABLE FREQUENCY

On Rat Sciatic Nerve Functional Regeneration

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A number of experimental studies report that biological systems can be affected and the regeneration of peripheral injuries can be accelerated by pulsed magnetic fields. The aim of this study was to evaluate the effect of variable frequency pulsed magnetic field on the functional recovery of the peripheral siatic nerve injury.

In our study, variable frequency pulsed magnetic field (1, 10, 40,100 Hz) was used with a magnetic density of 1.5 mT generated by a pair of Helmholtz coils 60 cm in diameter. Female Wistar rats weighting 250-300 g were used. Their right sciatic nerve was crushed and the animals exposed to magnetic field 90 min everyday. Functional recovery of the sciatic nerve was observed with a video assisted footprint test for 35 days with 5 days intervals and evaluated with sciatic function index (SFI).

The results show no significant effect of the variable frequency pulsed magnetic field on the functional recovery of the sciatic nerve injury.

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COMPARATIVE ANALYSIS IN LEARNING AND MEMORY ABILITY, RELATED WITH FEAR IN C57BL/6J AND BALB/C STRAINS OF MOUSE

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In the present study we examined the difference in escape and freezing memory storage and retrieval on the partial and whole conditioned context in C57BL/6J and Balb/c strains of mouse. The difference between C57BL/6J and Balb/c strains of mice in step-through passive avoidance task was examined. Experiments showed that both strains of mice had a similar ability to store and retrieve a long-term passive avoidance task on the partial and whole conditioned context except a non-mnemonic behavior assessed with entry latency in which Balb/c mice performed shorter compared to C57BL/6J.

The difference of unsignaled Pavlovian fear conditioning acquisition, storage and recognition-retrieval was examined between C57BL/6J and Balb/c strains of mice through measuring freezing responses on the context paired with foot-shock. Experiments showed that in immediate test (short-term memory) the Balb/c mice exhibited trend in enhance conditional freezing compared to C57BL/6J mice whereas in long-term memory test the time spent in freezing in C57BL/6J mice was significantly longer than Balb/c mice($P<0.05$).

These finding indicate that both fear conditioning task ability of storing and /or retrieving a freezing conditioning in Balb/c mice was weak compared to C57BL/6J and suggest an innate deficit in sensorial processing related with fear, make Balb/c strain less able to retrieve memory on partial presentation on conditioned context.

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c-FOS AND NADPH-d REACTIVITY IN PERIAQUEDUCTAL GRAY NEURONS PROJECTING TO THALAMUS FOLLOWING NOXIOUS PERIPHERAL STIMULATION IN THE RAT

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Electrophysiological studies have shown that PAG (periaqueductal grey) neurons projecting to thalamus are involved in pain modulation. Gaseous neurotransmitter nitric oxide (NO) is involved in pain transmission. NADPH-d reaction shows nitric oxide synthase activity. Fos is a nuclear-phosphoprotein-product of mammalian c-fos proto-oncogene. Fos immuno-histochemistry is used in revealing neurons responding to noxious stimulation and pain pathways. In this study, we aimed to show NO using NADPH-d histochemical reaction, and c-fos immunohistochemistry, to reveal if PAG neurons projecting to thalamus contained NO and c-fos and by this way to show the involvement of PAG-thalamus connection in pain modulation, previously shown by electrophysiologic studies. 6 Sprague-Dawley rats were stereotaxically injected Fluoro-Gold into thalamus. After 4-6 days survival time, rats were subjected to formalin test. Sections were processed for NADPH-d histochemical and c-fos immunohistochemical reaction. No PAG neurons projecting to PAG contained NADPH-d and/or c-fos. About 15% of NADPH-d/c-fos co-localization was observed. There was a close relationship or opposition of NADPH-d (+) neurons with c-fos immunoreactive neurons. This situation proposes PAG-thalamus relation is not via NO, but possibly a different mediator. It is suggested that the relationship between other supraspinal centers and the involvement of NO in this relation should be investigated in further studies.

(This study was supported by a grant from Ege University Faculty of Medicine Research Fund -2000TIP014- and performed at the laboratories of Ege University Center for Brain Research)

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COMPARATIVE ANALYSIS OF ANXIETY-FEAR BEHAVIORS IN INBRED C57BL/6J AND BALB/C STRAINS OF MICE IN THE ELEVATED PLUS MAZE, LIGHT/DARK EXPLORATION AND ONE-WAY ESCAPE TESTS

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For investigating genetic determination in behavior like emotional and cognitive functions and disorders of brain, in present we examined anxiety/fear related behaviors in inbred C57BL/6J and Balb/c strains.

Using Elevated Plus Maze (EPM) for evaluating anxiety we found that C57BL/6J mice exhibits more fear compared to Balb/c. For instance, escape latency defined as the time spent for the first entry into an open arm was significantly shorter in Balb/c than C57BL/6J ($P<0.05$), and total time spent in the middle section was longer in C57BL/6J than Balb/c ($P<0.05$), and also the number of lines crossed in the open arm was significantly higher in Balb/c than C57BL/6J ($P<0.05$)

Light / Dark Exploration Test evaluates innate fear of illuminated places and we found that C57BL/6J strain mice prefer dark compartment more than the Balb/c mice. For instance, escape latency; time taken to enter the dark compartment for the first time is significantly longer in Balb/c mice ($P<0.05$) and also total time spent in the light compartment is longer in Balb/c ($P<005$)

Using One-Way Escape Test delivered by foot-shock to assess the unconditioned / conditioned sensory and motivational component of fear on pain stimulus showed that escape latency of C57BL/6J mice was sorter than Balb/c ($P< 005$).

The results are debated in a view that Balb/c mice has deficit in sensory processes related with anxiety/fear.

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THE ROLE OF NITRIC OXIDE IN THE CARDIOVASCULAR RESPONSES ELICITED BY CENTRAL NUCLEUS OF AMYGDALA

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Purpose: Previously it was shown that amygdala is involved in central cardiovascular regulation. In this study, the role of nitrergic system in the cardiovascular responses were evaluated using electrical stimulation of central nucleus of amygdala (CeA).

Materials and Methods: Stereotaxic surgery was performed to implant a bipolar electrode into the CeA of Sprague-Dawley rats. After a resting period of 4 days, iliac artery was cannulated to record pulsatile blood pressures on a polygraph via a pressure transducer. The heart rate values were also recorded via a tachograph connected to the system. All experiments were performed on conscious rats. After recording the basal blood pressure and heart rate values, rats were treated with saline (0.1 ml/100 g, i.p.; n = 5) or L-NAME (100 mg/kg; n = 5), and CeA was stimulated with a current of 300 mA intensity for 30 seconds.

Results: Electrical stimulation of CeA increased mean arterial pressure (MAP). The percent increase in MAP was found to be 24 ± 4 and 11.5 ± 2, in saline - and L-NAME - treated rats, respectively. The difference in pressor effect in saline and L-NAME treated rats was statistically significant ($p < 0.05$). No significant effect on heart rate was observed.

Discussion: The pressor response induced by electrical stimulation of CeA was suppressed by L-NAME. Therefore these results imply that nitric oxide might have a role in the central regulation of cardiovascular system.

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MELATONIN PROTECTS CENTRAL NERVOUS SYSTEM AGAINST THINNER INTOXICATION BY PREVENTING REACTIVE GLIOSIS IN RATS

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Neuroprotective effects of melatonin against free radical damage have been studied extensively. Thinner containing 60-70% toluene is a neurotoxic chemical and it is widely used as an aromatic solvent in industrial works. Thinner has been shown to cause functional and structural changes in the central nervous system.

Neurotoxic toluene generates the production of reactive oxygen species (ROS) and its toxic effects are caused by formation of ROS. In the present study we aimed to investigate glial reactivity in hippocampus, cortex and cerebellum of toluene-exposed rats by determining the expression of glial fibrillary acidic protein (GFAP) and also to examine the protective effects of melatonin against gliosis.

Western blotting experiment demonstrated a marked elevation in total and degraded GFAP, a specific marker for astrocytes, content by thinner inhalation in the hippocampus, cortex and cerebellum of rats. Melatonin administration prevents both the increase of total GFAP and its degradation products induced by thinner inhalation. Thinner exposure caused a significant increase of lipid peroxidation (MDA + 4 HDA) levels and this elevation also was inhibited by melatonin administration. Furthermore, melatonin augmented glutathione levels in all studied brain parts. In conclusion, melatonin treatment may provide neuroprotection against toluene neurotoxicity through surviving of glial cells possible by scavenging ROS and augmenting their antioxidant capacity.

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INCREASE OF GLIAL FIBRILLARY ACIDIC PROTEIN AND S-100B IN HIPPOCAMPUS AND CORTEX OF DIABETIC RATS: EFFECTS OF VITAMIN E

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Glial interactions with neurones play vital roles during the ontogeny of the nervous system and in the adult brain. Physical and metabolic insults cause rapid changes in the glial cells and this phenomenon is called reactive gliosis. One of the important events during astrocyte differentiation is the increased expression of glial markers, glial fibrillary acidic protein (GFAP) and S-100B protein. Diabetes mellitus is the most common serious metabolic disorder which is characterised by functional and structural changes in the peripheral as well as in the central nervous system. In the present study we aimed to investigate glial reactivity in hippocampus, cortex and cerebellum of streptozotocin-induced diabetic rats by determining the expression of GFAP and S-100B and also to examine the protective effects of vitamin E against gliosis. Western blotting showed increases in total and degraded GFAP content and S-100B protein expression in brain tissues of diabetic rats compared with those of controls. In addition, there was a significant increase in lipid peroxidation in these brain regions of diabetic rats. Both glial markers and lipid peroxidation levels were reversed by vitamin E administration. These findings indicate that streptozotocin-induced diabetes alters degradation and production of GFAP and S-100B which are markers of reactive astrocytosis. Thus, determination of GFAP and S-100B may provide a relevant marker in the central nervous system for studying neurodegenerative changes in experimental diabetes mellitus. This study also suggests that the gliosis that occurs in diabetes mellitus is mediated, at least indirectly, by free radical formation and antioxidants may prevent reactive gliosis possibly by reducing damaging effects of reactive oxygen species in the central nervous system.

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EFFECT OF MEDIAL SEPTAL LESION ON BEHAVIORAL DESPAIR AND LEARNING IN FEMALE WISTAR RATS

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As part of our ongoing investigation of the impact of stress and depression on learning in female rats, we have found a significant correlation between severity of behavioral despair, an animal model of depression, and impairment in navigational learning as tested in the Morris water maze. The medial septal area may be involved in the effect of depression on navigational learning in that its destruction in the rat results in impairment of navigational learning. The septal area is also implicated in learned helplessness, an animal model of depression related to behavioral despair. The present study therefore investigated the impact of the destruction of the medial septal area on performance in behavioral despair. Ten days after medial septal (n=8) or sham (n=7) lesions, female Wistar rats underwent two forced swim tests separated by 24 hr. Increased immobility in te second swim compared to the first is a sign of behavioral despair. Compared to controls, the septal lesion group showed significantly less struggling behavior (in the form of jumping) and in general displayed longer immobility, less swimming, diving and headshakes. A week later, animals were tested in the Morris Water Maze (MWM) for ten days (5 trials/day). The septal animals were impaired in learning the maze compared to controls: those that exhibited long immobility in the second forced swim test of the behavioral despair treatment were more impaired than the ones with shorter duration of immobility. The results indicate that the medial septal region has the capability of modulating different manifestations of behavioral despair and may play a critical role in the debilitating effect of stress on learning. (Supported by Bogazici University ARFON/BAP Grant 00R103 to RC).

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THE EFFECT OF HYPOGLYCEMİA IN SCOP0LAMINE-INDUCED CONVULSIONS IN FASTED MICE AFTER FOOD INTAKE

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We have recently reported that mice treated with scopolamine after fasting for 48 h develop clonic convulsions soon after allowed to eat ad lib. Forty eight h of fasting in mice produces a moderate degree of hypoglycemia. This study was performed to evaluate the role of hypoglycemia in the occurrence of these convulsions. Mice, weighing 25-30 g, were divided into two groups and were deprived of food for 48 h. One group had free access to water, the other group had free access to % 5 glucose solution. On the day of testing, groups were divided into two subgroups for the biochemical and behavioral analysis. Blood glucose levels were determined by glucose oxidation method. For the evaluation of convulsions, mice were administered saline or 3 mg/kg scopolamine. After twenty minutes, animals were allowed to eat ad lib and were observed for 30 min for the incidence of convulsions. The frequency of the incidence of convulsions was evaluated using Fisher's Exact test. Student's t test was used for the evaluation blood glucose levels. After fasting for 48 h, animals fell to approximately 80-85% and 88-90% of the starting body weights in water consumed and glucose consumed groups, respectively. In glucose consumed group, blood glucose levels were significantly higer than those in the water consumed group ($p<0.001$). Scopolamine administration caused convulsions in both glucose ($p<0.02$) and water consumed ($p<0.002$) groups. Although consuming glucose during fasting prevented the occurrence of hypoglycemia and provided a normoglycemic blood level, it was unable to prevent the occurrence of convulsions. Thus, the present results indicate that hypoglycemia does not seem to be a possible factor contributing to these convulsive activities.

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THE EFFECTS OF FOOD DEPRIVATION AND SCOPOLAMINE ON CORTICAL ELECTROENCEPHALOGRAPHY IN RATS PRELIMINARY RESULTS

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Food deprivation have been used as a impulse in some of learning and memory studies. Also, in these studies, anticholinergic scopolamine that destroy cognitive functions have been used as a reference drug. In present study, we aimed to investigate the effects of food deprivation and scopolamine on cortical electroencephalogram (EEG) in rats. Wistar albino male rats, weight 200-220 g, were used. Under phenobarbital anesthesia, ten electrodes were surgically implanted in symmetrical areas of cortex. One week after the operation, continuous EEG records were taken with Neuroscan for 1 h in freely moving rats. Then rats were divided to two groups, while the first group of rats were deprived from food, the others were fed ad lib. EEG records were taken in the 24th and 48th hours their food deprivation. Later all animals were treated with saline or scopolamine 3 mg/kg and again EEG records were taken. Continuous EEG records were divided into 2 second epochs and analysed by averaged frequency spectra (0.5-30 Hz). In the 24th and 48th h of food deprivation it was found that there were no changes in cortical bioelectrical activities. The peak point of theta frequency was shifted from 6 Hz to 7.5 Hz in rats which were treatment with scopolamine fed or deprived from food. Scopolamine induced an increase in the amplitude of theta frequency from 10.11 ±61549; V±61617; 0.69 to 15.6 ±61549; V±61617; 1.55 and from 11.7 ±61549; V±61617; 0.82 to 19.3 ±61549; V±61617; 1.4 in fed rats and in food deprived rats, respectively.

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EFFECT OF MEDIAL SEPTAL COLCHICINE INFUSION ON NAVIGATIONAL LEARNING PERFORMANCE

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Adult male Wistar rats injected in the medial septal area with colchicine (2 microgram in 1 microliter saline, n=8) or saline (n=8) were trained approximately 2 weeks later in Morris water maze (5 trials per day for 6 days) followed a week later by a one-day retraining session (5 trials). Intraseptal colchicine slowed but did not significantly alter water maze performance in the 6-day training period but impaired retraining a week later.

Results indicate that the dose of colchicine used has a slow impact, possibly on hippocampal function that impairs learning 3 to 4 weeks after intraseptal colchicine injection. (Supported by Bogazici University ARFON Grant 00R103 to RC).

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MODELLING STROOP EFFECT BY A CONNECTIONIST MODEL

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Introduction: A connectionist model given in Fig. 1 to simulate the processes of prefrontal circuits during the Stroop test [1] is proposed.

Method: The aCG component of the model is composed of two sub-systems: novelty detector and conflict-detector. A winner-take-all network [2] with two neurons, each for one task is used as novelty-detector. The conflict-detector, takes turn when the subject generates an improper response and it is composed of three perceptrons [2]. The function of OF cortex is realized by a Hopfield [2] network. The role of the Hopfield network is to generate sufficiently large output in order to let OF to inhibit the output of the preferred word reading neuron. The BG component of the model is a maxnet network [2] with two neurons. In the model two neurons compete to activate related sensory motor networks which are simulated by two Hopfield networks; one for word reading and the other for color naming.

The aim of simulation is to demonstrate how the activations of components i.e., OF, BG etc., affect each other during Stroop task. The results in Table 1 represent the means and standard deviations of 20 virtual subjects' color naming scores for different parameter values. The time duration of word reading task is 11.4 ± 0.6 sec.

Conclusion: Unlikely from the earlier models [3,4], the proposed model is based on the frontal circuits taking action during the Stroop task. So this modelling paradigm leads to generate every aspect of Stroop performance such as elapsed time, number of errors and spontaneous corrections and impulsive errors. In simulation results, observing the change of performance indices obtained by tempering the parameter values, confirm the validity of the model.

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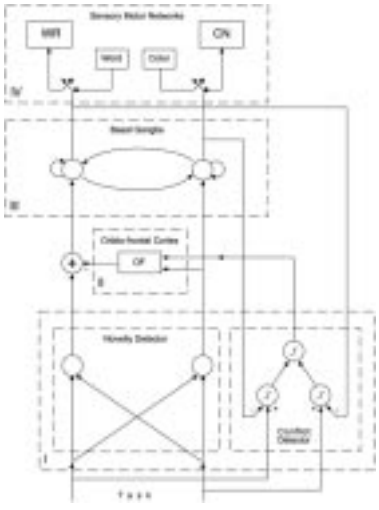

Figure 1. The proposed model

OF	Pr.	Time(sec)	#Error	#Corrections
0.01	0.1	44.4 ± 3.5	1.6 ± 1.15	10.5 ± 3.2
0.01	0.9	40.1 ± 1.9	11 ± 2.6	0.8 ± 1.02
0.4	0.1	28.1 ± 2.5	0.16 ± 0.39	0.41 ± 0.6

Table 1. The results of color naming task.

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EFFECT OF BEHAVIORAL DESPAIR ON NAVIGATIONAL LEARNING

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The study assessed the impact of behavioral despair on navigational learning as tested in the Morris Water Maze with a hidden platform at a fixed location. In the first phase of the experiment, adult female Wistar rats (n=14) first underwent two forced swim tests separated by 24 hr and a week later were tested in the Morris Water Maze (MWM) for 12 days (6 trials per day) together with a control group (n=7) that was not subjected to forced swim tests earlier. A day later, all subjects were tested for 2 min in MWM with the platform removed. A week later, in the second phase, the control group from Phase I and a MWM-naïve group of animals (n=7) underwent two forced swim tests separated by 24 hr. In the first phase, the results indicated no difference between the controls and the experimental subjects that had previously undergone forced swimming in navigational learning in the MWM as measured by decrease in the latency to locate the fixed platform. However, when MWM performance was evaluated according to whether the experimental subjects displayed short (n=7) or long duration (n=7) of immobility in the second swim test, the latter subjects showed a significant impairment in the acquisition of the MWM compared to the former (short-dauration) group and the controls. In the second phase, the two groups displayed similar durations of immobility in both swim tests. These results indicate that in female Wistar rats the degree of behavioral despair has an impact on subsequent navigational learning in the MWM but acquaintance with navigational learning and swimming does not affect induction of behavioral despair. (Supported by Bogazici University ARFON/BAP Grant 00R103 to RC).

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EFFECTS OF MOBILE PHONES ON NUMBER OF HIPPOCAMPAL NEURONS IN MICE AT THE FETAL PERIOD: A STEREOLOGICAL STUDY

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For the last decade the mobile phones have been increasingly used. Aim of this study was to investigate the effects of mobile phones on total number of hippocampal neurons by using optical fractionator technique.

Ten Swiss albino mice were used as both control and groups in this study. The mobile phones were placed just beneath the animal cages. Thus, animals were exposed to the electromagnetic field phones create. This procedure was performed with a mobile phone at 890-915 MHz carrier frequency, 217 Mhz modulation frequency and 2W maximal power, for 11 h. 45 min. standby and 15 min. talking mode, twice a day. At the postnatal period, new pups were kept under this condition for another 21 days. At the end of application, cervical dislocation was performed to the animals. Brains were separated from cerebellum and brain stem. Two hemispheres were separated through cutting corpus callosum. Frozen

sections were cut and systematically randomized sections were selected and stained with H.E. The profiles of neuron counting was performed in this sections according to optical fractionators technique.

Mean pyramidal neuron profiles count was estimated as 439.401 in control group. 441.722 in experimental group. There was no statically significant difference between two groups ($p<0.05$)

As a result, mobile phones do not affect the number of pyramidal neurons of hippocampus at indicated duration, dose and frequency in mice at the fetal period.

Key words: Hippocampus, mice, neuron number, optical fractionator, stereology.

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A REVIEW OF THE LATEST LITERATURE IN NEURONAL REGENERATION

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One of the latest aims of neural sciences is regenerating a neuron, accomplishment of which will provide extremely valuable information for medicine in treatment of patients with peripheral nerve injuries, strokes, etc., as an option amongst the aproaches of biomedical engineering in this area. In this study, the review of the latest approaches towards accomplishment of this task, with a rather precilinical point of view is summarized .

Scientists hope that by understanding more about the life and death of neurons, they can develop new treatments, and possibly even cures, for brain diseases and disorders that affect the lives of millions of people. The most current research suggests that neural stem cells can generate many, if not all, of the different types of neurons found in the brain and the nervous system. Learning how to manipulate these stem cells in the laboratory into specific types of neurons could produce a fresh supply of brain cells to replace those that have died or been damaged.

Therapies could also be created to take advantage of growth factors and other signaling mechanisms inside the brain that tell precursor cells to make new neurons. This would make it possible to repair, reshape, and renew the brain from within.

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A MODEL FOR PERSEVERATION AND DISTRACTIBILITY IN WISCONSIN CARD SORTING TEST BY USING A COMPOSITE NEURAL NETWORK SYSTEM

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Introduction: A composite artificial neural network model is proposed for the simulation of Wisconsin Card Sorting Test [1] performance of healthy subjects and prefrontal lesioned patients.

Method: In the model, it is assumed that the subject's behavior is completed in two phases for each test step: rule determination and card selection according to this rule. These two phases are realized by "selection" and "rule determination" modules as shown in Figure 1. The card selection process is modeled by a Winner-Take-All network [2]. Maintenance of the valid rule is accomplished by a Hopfield network [2]. The other network (Hamming network [2]), offers to the Hopfield network a set of alternatives when the experimenter's response is "wrong". This mechanism has been shown in Figure 1 via switches.

In order to spot the statistical validation of the model 10 computer experiments, for each 18 condition (different Hamming distance values and threshold vectors of Hopfield network); on the total 180 experiments are done.

Conclusion: The results in Table 1 show that the proposed relatively simple model is capable of simulating the wide range of the performance of both normal subjects and prefrontal patients as intended. While the lowering of the Hamming distance in the Hamming network allowed us to obtain the performance of the subjects on a mentally flexible to rigid continuum, changing the threshold vector of the Hopfield network prevented perseverance and gave rise to distractibility. The earlier models deal with only perseveration and while two of them [3,4] simulate only one healthy and one prefrontal lesioned subject, the other one [5] offers a theoratical analysis and it is a complex model.

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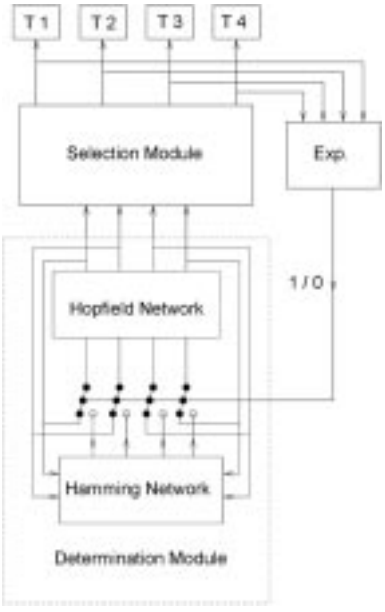

Figure 1. Proposed composite neural network model.

Cond	Harun Dist.	Hap Thresh	#Correct Responses	#Categories	Pers. error %	PMS score
1	3	T	64.6 ± 3.5	6.0 ± 0	9.9 ± 2.8	0 ± 0
2	3	T1	73.7 ± 6.1	1.1 ± 0.5	19.7 ± 2.9	3.2 ± 1.6
3	3	T2	66.2 ± 8.4	0.3 ± 0.5	26.5 ± 6.4	2.4 ± 1.8
4	2	T	67.6 ± 3.7	6.0 ± 0	14.2 ± 4.6	0 ± 0
5	2	T1	66.3 ± 9.1	0.4 ± 0.5	24.6 ± 4.9	2.6 ± 2.1
6	2	T2	66.7 ± 9.9	0.3 ± 0.7	27.9 ± 8.6	2.0 ± 1.5
7	1	T	39.4 ± 0.5	1.0 ± 0	67.8 ± 0.5	0 ± 0
8	1	T1	58.8 ± 6.9	1.1 ± 0.4	32.4 ± 6.2	1.1 ± 0.6
9	1	T2	61.9 ± 8.3	0 ± 0	27.7 ± 6.8	2.4 ± 1.2
10	0	T	32.8 ± 2.5	0.1 ± 0.3	75.0 ± 1.5	0 ± 0
11	0	T1	31.5 ± 4.7	0 ± 0	38.6 ± 4.8	0 ± 0
12	0	T2	30.4 ± 4.1	0 ± 0	39.4 ± 3.5	0 ± 0
13	3-2	T	64 ± 1.8	6.0 ± 0	9.5 ± 2.1	0 ± 0
14	3-2	T1	75.9 ± 6.1	1.6 ± 1.0	17.7 ± 3.4	2.7 ± 1.3
15	3-2	T2	72.6 ± 7.9	0.8 ± 0.8	25.9 ± 6.2	3.1 ± 1.7
16	2-1	T	70.7 ± 3.5	6.0 ± 0	17.9 ± 3.7	0 ± 0
17	2-1	T1	73.2 ± 6.3	1.3 ± 0.5	21.2 ± 5.0	2.4 ± 1.2
18	2-1	T2	59.8 ± 6.3	0.1 ± 0.3	29.1 ± 6.9	2.0 ± 0.9

Table 1. Results for each condition.

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AN MRI STUDY: THE DIMENSIONS OF CORPUS CALLOSUM IN PROFFESSIONAL ARTISTS

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The several previous studies suggested that the differences of callosal size shows the connection of inter emispheric degree and interhemisferic symetry or asymetry. We aimed in this study to investigate the effects of special manuel activities such as drawing and painting on the size of corpus callosum. The callosal dimensions were measured in 13 professional artists and 13 non artists by using magnetic resonance imaging (MRI) technique.The induviduals in both group were right handed.Their age were 30-45 year. Seven regions were measured from the midsagittal MRI slice of corpus callosum.

N: 13 BX AX BP PR DC EF MN

Group I 76 14 15 12 6 8 8

Group II 76 12 12 10 7 7 8

P <0.05 ,336 ,039 ,005 ,039 ,448 1,0 ,687

There were statistically significant differences between two groups. AX, BP, PR values were larger in artists than those of non artists.According to our study, visual sensivity and creativeness may increase inter hemispheric connectivity. We thought that corpus callosum have an important role on high and complex activities of brain. It may be also possible that corpus callosum is related with high entellectual activities

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THE USE OF MICROWAVE IRRADIATION IN THE LIGHT AND ELECTRON MICROSCOPICAL EXAMINATION OF DEGENERATED MYELIN

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Classical methods for histologic preparation of degenerated myelin is time consuming and difficult applications. The use of microwave in the light and electron microscopic fixation and staining is suggested to increase the quality, perform standardisation and economic use of time and chemicals.

The purpose of this study is to achieve a time gaining procedure, which includes the fixation for both light and electron microscopy and staining for light microscopy, by the use of microwave irradiation for light and electron microscopical examination of degenerated myelin in the central and periferal nervous system. While shortening the preparation time we aimed to get a better or at least an equal quality results that can be used in pathology laboratories for the diagnosis of demyelinated diseases.

Middle cerebral artery occlusion and full thichness schiatic nerve cutting were performed in rat to produce myelin degeneration. Tissues were fixed with conventional methods and with microwave irradiation for light and electron microscopical evaluation. Marchi method was used for the staining of degenerated myelin. This method was applied to both fixation groups as in the conventional procedure and by using microwave irradiation. Light microscopic fixation time, taking 2 days in conventional procedure, was completed in 16.5-18.5 minutes with microwave irradiation. Electron microscopical double fixation took 19 minutes in the microwave oven. While degenerated myelin staining time was taking 10 days in conventional Marchi method, it was decreased to 7 hours for brain tissue and 1 hour for schiatic nerve. Besides the quality of the slides were equal to the conventionally prepared ones.

With these findings we concluded that microwave irradiation can be used for the light and electron microscopical examination of degenerated myelin.

Key words: Myelin degeneration, histologic preparation, microwave irradiation.

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EFFECTS OF ADRENALECTOMY ON CART EXPRESSION IN THE RAT ARCUATE NUCLEUS

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In order to test for glucocorticoid regulation of CART (cocaine and amphetamine regulated transcript) in the arcuate nucleus, adrenalectomies (ADX) and corticosterone replacements (HR) were carried out in groups of rats. CART mRNA levels were determined by in situ hybridization and CART peptide levels by immunocytochemistry. ADX caused a lowering of CART mRNA and peptides levels in the arcuate and this was reversed by HR. These results indicate a glucocorticoid regulation of CART in the arcuate. The regulation could be direct through an action of glucocorticoid receptors or indirectly through ADX-induced changes in leptin levels.

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EFFECTS OF ACUTE AND CHRONIC STRESS AND CHRONIC NICOTINE TREATMENT ON SPATIAL LEARNING IN THE WATER MAZE

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Stress has substantial impact on cognitive processes and some of the reported effects involve sex differences. The aim of the present study was to study the effect of acute or chronic stress on acquisition and memory performance in a water maze place learning task. The classical water maze procedure of R.G. Morris (1981) was employed with 6 days of acquisition followed by a probe trial on day 7, where the rat searches for the platform which was removed. Stress was in the form of restraint, in ventilated glass cylinders for one hour, and the subjects were male and female adult Sprague Dawley rats (n=10 in each group). In experiment 1, rats were subjected to stress immediately before water maze testing for 7 days in a 2 x 2 factorial design with sex (male, female) and stress (control, stressed) as factors. In experiment 2, rats were chronically

stressed for 15 days (one hour/day) followed by water maze testing; no stress was applied during water maze testing. Additionally, in experiment 2, nicotine treatment (0.4 mg/kg) was also included resulting in a 2 x 2 x 2 factorial design with sex, stress, and nicotine tratment (NIC and saline) as factors. Performance measures (HVS Image, UK) were analyzed by multifactorial ANOVA followed by post-hoc tests. In both experiments, the distance the rats swam to locate the platform decreased ($p<0.001$) during acquisition and all groups reached asymptotic levels by the 6th day; however in the 2nd experiment there were interactions because females reached asymptote earlier than males (0.001) and nicotine treated groups reached asymptotic levels later than controls ($p<0.01$); furthermore nicotine effect was stronger in females ($p<0.05$). Experiment 1 revealed a significant effect of stress ($p<0.05$) during the probe trial [rats spent less time searching for the platform in the respective quadrant (%T)] suggesting impaired spatial learning following acute restraint. In experiment 2, nicotine decreased %T ($p<0.05$) with no interaction or effect of sex or stress. In conclusion, the present study suggests that while acute stress impairs spatial learning, long term effects of chronic stress on learning are not significant. On the other hand, chronic nicotine, with or without acompanying stress, has detrimental effects on memory in a place learning task in rats.

*O.E. is an undergraduate Psychology student (4th year). This study is part of Ö.E.'s graduation thesis.

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RESPONSE VERSUS VISUAL-CUED LEARNING IN A WATER MAZE PLACE LEARNING TASK: EFFECTS OF LATERALITY, SEX, NICOTINE AND NO INHIBITION

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Males and females use different strategies for solving some problems and pharmacological interventions may modify these strategies. The aim of the present study was to see if there are sex differences in cognitive strategy employed in a water maze place learning task where rats can locate the platform either using visual cues or response learning (i.e. turning to one side). Initialy naive male and female Sprague Dawley rats were trained to locate the platform, visible or hidden, by turning either to the right or left. After rats reached asymptotic performance levels, the platform was placed in the opposite direction and made visible, thereby presenting the rats wih a choice. The % time rats spent in the quadrant where the platform used to be during aqquisition (%T) and the length of the swim path to the new platform were performance measures (HVS Image, UK). After establishing the procedure in naive animals, male and female rats treated with saline (S), nicotine (NIC) or NG-L-nitro arginine (L-NA) were tested (N=10 for all groups). Data were analyzed with multifactorial analyses of variance followed by post-hoc tests. Swimming speeds were different throughout all stages with females swimming faster than males, and learning to locate the platform was faster when the platform was visible. Overall, there were minimal group differences during acquisition, with the exception of L-NA treated groups: NOS inhibition impaired acquisition and more prominently in females. During the choice trial of the 13th day, laterality was a significant effect in most of the groups: rats trained to turn right had difficulty with reversal learning (unlearning) to go to the newly positioned visible platform on the left; this effect was more pronounced in males. Laterality emerged as a significant main effect ($p<0.001$) with regard to %T and interacted with drug treatment ($p<0.005$). In summary, NIC and L-NA had a more pronounced effect in facilitating reversal learning in rats trained to turn left, furthermore NIC effect was stronger in males. Our results point to a significant laterality effect in reversal learning and provide evidence for the mediation of cholinergic and nitrergic systems in this effect with minor sex differences.

*O.E. is an undergraduate Psychology student (4th year).

Supported by grants from Ege University Research fund: 98-BAM-001 and 98-TIP-011

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ANALYZING BEHAVIOR DURING PORSOLT SWIM TEST IN MALE AND FEMALE RATS

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Since stress response and depression involve sex differences and modulation by gonadal hormones, we wanted to asses possible behavioral sex differences in the Porsolt Swim Test in Sprague Dawley rats. Adult rats were handled for 2 days (n=14 for both groups) and exposed to forced swimming: 15 minutes first day and 6 minutes second day. We developed a computer program for recording the behavior of rats during the Porsolt Swimming Test. This program allows the observer to record the duration and number of "freeze" and "struggling" behaviour and the number of "head moves" and "diving". These behaviors are recorded at 1, 5, 6, 10, and 15 minutes (1-6 for day 1 and 1-15 for day2). The period between 1-6 minutes were compared using ANOVA with days (1 and 2) and sex (male,female) as factors The results are summarized in the table (mean+sem) below.

Since freezing and struggling are the major components reflecting affective states, these two behaviors received the most attention. There was a significant difference between freeze [$F(1,26)=67.92$, $p=0.001$] and struggling duration [$F(1,26)=17.97$, $p=0.001$] between day one and day two: freeze increasing and struggling decreasing. Diving also decreased significantly. Our results indicate that sexes do not differ significantly in behavioural responses to forced swim stress.

*S.Y. is an undergraduate Psychology student (4th year). This study is part of S.Y.'s graduation thesis.

		Freeze (dur. ; sec.)	Struggling (dur. ; sec.)	Head m.	Diving
Day	Male	66.4±10.8; 170±16	111.9±12.2; 83±10	25.5±2.4	4.2±0.8
1	Female	14.2±8.8; 17.3±16	109.4±13.2; 53±6.6	35.3±3.4	4.3±1.0
Day	Male	158.1±16.3; 210±23	72.1±14.6; 6.8±1.4	31.5±3.2	0.8±0.3
2	Female	149.5±14.4; 22.9±2.1	66.3±10.6; 7.0±0.8	31.2±3.7	0.5±0.3

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CHRONIC NICOTINE TREATMENT REDUCES DEPRESSIVE BEHAVIOR FOLLOWING STRESS IN RATS

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Nicotine ineracts with stress and some of the proposed effects involve sex differences. Depression is a significant health problem with a higher incidence in females. The smoking rate among depressed patients is significantly higher than in the general popolation. Behavior of rats following stress is analogous to depression. The present study was undertaken to study the effect of chronic stress and nicotine on Porsolt Swim test performance in male and female rats. 40 adult Sprague Dawley rats were treated with nicotine (0.4 mg/kg) or saline injections for 30 days and were stressed for 15 days starting the 16th day of injections. Stress was in the form of restraint, in ventilated glass cylinders for one hour/day. The weights of the animals were monitored throughout the experiment (5 times). Behavioral analyses involved freeze and struggling during the period between 1-6 minutes and were compared using multifactorial ANOVA with days (1 and 2), sex (male,female) and nicotine treatment (saline, nicotine) as factors. Our results show that nicotine treatment prevents behavioral despair induced by stress as freeze duration was decreased ($p<0.001$) and struggling was increased ($p<0.001$) significantly in nicotine treated groups compared to controls. Post hoc tests revealed a significant behavioral sex difference in these

responses: Nicotine reduced freeze duration significantly in males ($p<0.005$) and struggling was significantly lower ($p<0.05$) in saline treated females on day 2 compared to day 1. Nicotine also emerged as a significant factor in reducing weight gain ($p<0.01$), and there was a significant sex interaction since saline treated females gained less weight than saline treated males ($p<0.01$). Our results suggest that nicotine may have an antidepressant effect on rats subjected to chronic stress.

* E.A.B is a 4th year Biology student, E.Y. is a 5th year medical student and H.E is a senior high scholl student. This study is part of E.A.B.'s graduation thesis.

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THE EFFECT OF LONG-TERM THERAPY WITH SODIUM VALPROATE ON NAIL AND SERUM TRACE ELEMENT STATUS IN EPILEPTIC CHILDREN

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Antiepileptic drugs may cause changes in the trace element status of the body. Nail trace element content is a reliable index of trace element nutritional status of the body. To determine whether some of the side effects of antiepileptic drugs could be due to zinc (Zn) depletion within tissues, Zn concentrations as well as copper (Cu) concentrations in nail and serum in 59 various types of epileptic patients receiving valproate (VPA) and 31 controls were assessed. Fasting blood samples obtained from subjects in the morning were taken into normal tubes to prepare serum. Routine laboratory tests were performed at the same time with serum and nail sampling. The drug (VPA) received by the patients was prescribed at the normal dosage and all plasma levels of VPA were within the therapeutic range during the time of study. Control subjects were not treated with any antiepileptic drugs.

Although serum Zn level in epileptic patients was found to be decreased, there was no difference in nail samples when compared to controls. There was a statistically significant increase in nail Cu level in epileptic patients when compared to controls. On the other hand serum Cu levels were not different between the groups. Although none of our patients showed any symptoms of Cu elevation and Zn depletion, we should pay attention to potential body trace element changes in patients with epilepsy under VPA treatment. In conclusion, our results indicate that serum trace metal homeostasis may be affected by VPA therapy, but not by the convulsive disorder itself.

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A NITRIC OXIDE RELEASING DERIVATIVE OF FLURBIPROFEN INHIBITS EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS IN C57BL/6 MICE

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Nitric oxide (NO)- releasing derivatives of non-steroidal anti-inflammatory drugs(NSAID) represent a new class of anti-inflammmatory compounds which are more efficacious in blocking ongoing inflammation compared to conventional NSAID. We tested their therapeutic efficacy in experimental autoimmune encephalomyelitis(EAE), the elective model of multiple sclerosis. NO-releasing derivative of flurbiprofen (HCT 1026) were per os administered to C57BL/6 mice immunized with 50 mikrogram of MOG 35-55 in CFA and 500 nanogram of pertussis toxin. Mice eating a normal diet or with flurbiprofen only were used as controls. Administration of HCT-1026 beginning on the day of immunization significantly delayed the EAE onset (27.8+/- 2.9 days postimmunization vs. in flurbiprofen treated mice vs. 20.3+/- 3.7 days and 11.0+/- 0.5 days postimmunization in controls; $p<0.01$ logrank test) and reduced the severity of symptoms (mean maximum score 0.9+/- 0.3 vs. 1.6+/- 0.2 in flurbiprofen treated mice vs. 2.4+/- 0.2 in control mice; $p=0.0033$ and $p=0.0191$ Mann-Whitney, respectively). In 2 out of 7 mice (28%) HCT 1026 prevented the development of the disease. Therapeutic efficacy of HCT 1026 was not associated to decreased T cell proliferation ability or decreased IFN gamma release in response to in vitro MOG 35-55 re-stimulation. However MOG 35-55 specific T cells from HCT 1026 treated mice released increased levels of IL-10 as compared to T cells from sham-treated control mice. We conclude that oral administration of the NO-releasing derivative of flurbiprofen HCT 1026 is able to inhibit EAE development in MOG 35-55- immunized C57BL/6 mice without overt side effects.

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CYTOGENETIC RESULTS IN TWO SIBLINGIS WHO WERE DETERMINED AS SPINA BIFIDA OCCULTA

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Neural tube defects (NTDs) are common congenital malformations that occur when the embryonic neural tube fails to close properly during early development.

In this study,we have aimed to compare our cytogenetic results with the hystological and neurosurgical results in two siblings who were determined as spina bifida occulta a diagnosis based on the presence of a small truft of hair on their backs.

Chromosomes were prepared by conventional tecniques from lymphocyte cultures metaphase chromosomes were karyotyped by standart trypsin- giemsa banding methods.

The karyotype of the mother was determined 46,XX,del(17)(q25) in one field of 50 metaphase. The karyotype of her son was determined 46,XX,del(17)(q25) in three field of 50 metaphase and 46,XY,+m in one field of 50 metaphase. The karyotype of the daugther was determined 46,XX. It is highly interesting that somatosensorial evoked potentials (SEP) examination and chromosome analysis were both revealed pathological results in brother who had thick, fatty filum and low lying conus medullaris. No deletion was detected in his mother. In addition,in his sister, SEP, chromosome analysis and macroscopical appearrance were all in normal limits.

As far as the correlation between histopathological appearance of the thick and fatty filum terminale and chromosome analysis is concerned, a strong correlation has been found between genetic, cystological and neurosurgical results regarding the deletion of chromosome 17 (q25).

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REPETITIVE SILENT PERIOD

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Background-purpose: Silent period (SP) is the electrical silence elicited by peripheric, cortical or cutenous stimulation in a contracting muscle.Although SP is reported to appear only once in the literature,our personal observations were consistent with repetitions in some people.This study was performed to test the objectivity of repetitive SP and describe the circumstances under which the repetitions are observed.

Methods:SP was recorded in 11 healthy volunteers from abductor pollicis brevis muscle following median nerve and transcortical magnetic stimulation (TMS).The median nerve SP study was performed during application of 25%,50% and 100% of the maximum strength, determined by dynamometer.For TMS-SP study,the threshold of transcortical stimulation was detected and stimuli were applied at the stimulation threshold,50% over the stimulation threshold and 100% over the stimulation threshold.Each stimuli were applied during 25%,50% and 100% contraction. Each study was performed four times and only the reproducible results were taken into analysis.

Results: Repetitive SP was elicited in 4 of the volunteers following median nerve stimulation; two during 25%,one during %50 and one during 100% contraction.In the TMS-SP study, the repetitions were as follows:threshold stimulation 3 in 25%,3 in 50% and 4 in 100% contraction; 50% over threshold stimulation 8 in 25%,6 in 50% and 4 in 100% contraction;100% over threshold stimulation 7 in 25%, 7 in 50% and 4 in 100% contraction.

Conclusion:Repetitive SP is an objective finding that can be elicited more easily during TMS. The frequent observation of repetitions during moderate intensity contractions during 50% over threshold stimulations should be evaluated in large series of controls in future studies to identify the pathophysiological role and organization of cortical inhibitory circuits.

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PRESENCE OF HERPESVIRUSES' GENOMES IN THE SURGICAL SPECIMENS OF ADULT PATIENTS WITH CORTICAL DEVELOPMENTAL ABNORMALITIES

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In order to investigate viral etiology for cortical developmental abnormalities, we aimed to study the presence of HSV-1, HSV-2, CMV, HHV-6 and HHV-8 genomes by PCR method in surgical brain tissue specimens of patients with cortical developmental abnormalities.

Eighteen pathologically different cortical developmental lesions obtained from 17 adult patients were included in the study. In an attempt to elucidate the presence of HSV-1, HSV-2, CMV, HHV-6 and HHV-8 genomes, real time PCR method and light-cycler system were used.

HHV-8 DNA was detected in three lesions (16.6 %), whereas HHV-6 and HSV-1 DNA were identified in five lesions (27.7%) and three lesions (16.6 %) consecutively. None of our specimens revealed positivity for HSV-2 and CMV genomes, however. Nine of 17 patients were pathologically diagnosed as dysembryoblastic neuroepithelial tumor (DNET). HHV-6 and HSV-1 genomes were detected in 3 out of 9 DNET cases, and genome of HHV-8 was found in one out of 9 cases as well.

The presence of HHV-6 and HSV-1 genomes detected in our study was within the reported range of the normal brain tissues. Despite 20 and 35 % positivity rates in the brain tissues of the normal population in the literature, none of our specimens revealed of HSV-2 and CMV DNA positivity. However, HHV-8 genome was higher than normal range reported as 0-2.3 % and was investigated for the first time in epilepsy patients selectively. This preliminary study provides molecular evidence of higher persistency or latency rates of HHV-8 in epilepsy patients with cortical developmental abnormalities that needs to be supported by further studies.

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CONNECTIONS OF THE FACIAL, VESTIBULAR AND COCHLEAR NERVES WITHIN THE INTERNAL AUDITORY CANAL

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The internal auditory canal (IAC) contains the facial, vestibular and cochlear nerve, surrounding blood vessels and a common dural sheath. Connections between these nerves within the IAC are functionally important. The aim of the present study, is to show the connections and topographical relationship between the facial, cochlear and vestibular nerves within the IAC in 5 human cadavers. Series histological sections were obtained from 3 region (brainstem end, mid point and inner ear end of the of the IAC) of the nerves within the IAC.

The vestibulocochlear nerve was situated posterior to the facial, and the cochlear nerve was below the vestibular nerve. The average number of fibers forming the vestibular, cochlear and facial nerves were counted as 13968, 13824 and 35034 sequently.

Scanning electron microscopic evaluations showed communications between the vestibular and facial nerves and communication between the inferior portion of the vestibular and the cochlear nerves were observed within the IAC.

Presence of connections between the vestibular, cochlear and facial nerves contributed to the vestibular disturbance in facial paralysis cases. The anatomical knowledge of the topography of the nerves in the IAC will help in the success of the surgical procedure.

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MORPHOLOGICAL STUDY OF THE PERIRETICULAR NUCLEUS IN HUMAN FOETAL BRAINS

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The perireticular nucleus (PRN) is a newly described neurons group which are scattered within the internal capsule. Studies have shown that during early development the perireticular nuclei are very large, susequent to maturity the PRN reduce dramatically. Little is known about the human foetal PRN. This preliminary study aims to investigate the morphology, number of perireticular neurons within the anterior and posterior crus of the internal capsule and the relations of the number of perireticular neurons compared to gestations of the human foetal brain.

Three human foetal brains were obtained from legel elective abortions or routine autopsies. The ages were 26 (750gr), 26.5 (915gr) and 37 (2870gr) weeks of gestation. The internal capsule's were removed from the brain. Sections (30-50 μm) were cut using a cryostat (Microtom, FRG) and were laied on jelatiated lam and Nissel staining were applied. Morphological observations showed that the PRN is composed of small and large neurons. The small neurons were more abundant compared to the large ones. The perireticular neurons were bipolar, multipolar and triangular neurons. The large neurons were mainly localized arround the vessels. The number of perineticular neurons were calculated in each anterior and posterior crus in the feutus with 26 , 26.5 and 37 weeks of gestation. The number of neurons within the PRN decreased according to the increasing gestations in the human foetus brains. The existance of the perireticular nucleus in the internal

capsule and the large size in early development stage , have lead to the suggestion that the perireticular nucleus might play a role in the reorganization of thalamocortical and corticothalamic connections.

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BAROREFLEX SENSITIVITY IN THE KINDLED RATS

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Purpose: The purpose of this study was to investigate baroreflex sensitivity in the kindled rats.

Method: Male Wistar rats were randomized into two groups: Kindled (n=8) and sham operated (SO) (n=8). Unilateral stimulation and recording electrods were implanted stereotaxically into the basolateral amydala and cortex, respectively. Animals were stimulated at their after discharge threshold current twice daily for kindling process, and accepted as fully kindled after the occurence of ten grade 5 seizures. After 4-6 weeks, arterial pressure and barorereceptor reflex responses (BRR) were assessed in both groups. BRR was defined as the heart rate (HR) response to acute blood pressure changes caused by i.v nitroprusside (10, 25 ±956; g/kg) or i.v phenylephrine (10, 25 ±956; g/kg). To verify the BRR, atenolol (0,5 ±956;g/kg) and atropine (0,5 ±956; g/kg) were given.

Results: Basal mean arterial pressure (MAP) and heart rate were similar in SO and kindled groups. Increase in the MAP and decrease in the HR with two doses of phenylephrine were same in both groups (p>0,05). Decrease in the MAP with administration of i.v nitroprusside 10 ±956; g/kg was significantly lesser in the kindled group (p=0,01) than that observed in SO group. Increase in the HR was higher in the kindled group (p=0,03) than SO animals. With nitroprusside 25 ±956;g/kg there were no istatistical differences in the changes MAP and HR (p=0,06, p=0,06). Nitroprusside decreased the gain of BRR (Dbeats-1. DmmHg-1) significantly in both doses (p=0,13, p=0,004 respectivly). Atenolol and atropin completely abolished all BRR.

Conclusions: These results indicate that amygdaloid kindling affects baroreflex sensitivity in chronic and seizure free period.

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EVALUATION OF EFFECT OF HYPERGLYSEMIA ON ELECTRODERMAL RESPONSIBILITY IN STREPTOZOTOCIN-DIABETIC RATS

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In this study, it was aimed to examine the effect of hyperglycemia on Elektrodermal Activity (EDA) in streptozocin-induced diabetic rats. Three groups of Spraque Dawley rats were used: two diabetic groups (D1, n=15 and D2, n=15) and non-diabetic control group (n=15). Diabetes was induced by a single intraperitoneal injection of streptozotocin (STZ) in diabetic groups (D1, 60 mg/kg STZ and D2, 80 mg/kg STZ). The control group was injected i.p. physiological saline-0.9 % NaCl .

In all groups body weight, urine glucose, blood glucose and EDA were measured. These measurements were realized before STZ injection (Day 0), and 1 and 10 days after STZ injection.

EDA was recorded from rat's planter surface of posterior extremities using 0.8 cm diameter Ag/AgCl electrodes. Agar-agar jelly was placed between skin and electrodes. Skin conductance level taken from skin was recorded with Skin Conductance Unit. The analog signals taken from Skin Conductance Unit were transferred to PC computer. Phasic parameters were recorded by applying 15 auditory stimuli. If there was no response to the stimulus in skin conductance 0.5-5 sec, it was accepted as non-responding.

Blood glucose levels, urine glucose levels and body weight were significantly different among the groups ($p<0.05$). When we compared non-responding rat numbers according to days, there were no statistically significant difference, but the numbers of non-responding rats in control group (%46.6) and D1 group (%46), were lower than in D2 group (%80) in the 1. day.

We think that the non-response of EDA stems form the fact that hyperglycemia changes sweat gland activity by affecting sympathetic skin response. The results we obtained reveals that hyperglycemia affects peripheral nervous system and EDA parameters are influenced by blood glucose level.

This study was supported by TUBITAK (SBAG-AYD-364 "101S181").

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THE EFFECT OF ERYTHROPOIETIN ON SPATIAL MEMORY IN HYPOXIC-ISCHEMIC BRAIN INJURY MODEL IN NEONATAL RATS

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It is well known that neonatal hypoxic-ischemic encephalopathy (HIE) leads mental retardation and deficits in cognitive abilities such as learning and memory in human beings. Erythropoietin (EPO) is a neuroprotective factor. The ameilorative effect of this agent on brain injury in HIE has been reported. However, the effect of EPO on cognitive abilities in hypoxic-ischemic brain injury model is unknown. The aim of this study is to investigate the effects of EPO on learning-memory and neurodegeneration induced by hypoxia-ischemia. Seven days old Wistar Albino rat pups have been used in the study (n=28). The experimental groups in the study were; 1) Saline-treated HIE group, 2) EPO-treated (i.p., 1000 U/kg) HIE group, 3) Sham group, 4) Control group. In HIE groups, right common carotid artery has been ligated permanently in postnatal seventh days. Two hours after operation, hypoxia (92% nitrogen and 8% oxygen) has been performed for 2.5 h. When pups were 22 days old, learning experiments were performed using Morris water maze. Learning experiments have been repeated in adult period in which brain development has been completed (20th weeks). Then, rats were perfused and brains were removed for microscopic evaluation. The brains were scored macroscopically, sectioned and stained with cresyl violet, and evaluated under light microscop by stereological techniques. For comparison between groups, ANOVA post hoc Tukey HSD test was used. Daily differences in learning experiments have been evaluated using repeated measures.

It was demonstrated that HIE disabled spatial memory. and as compared with control and sham groups, first study group have longer time taken to find the platform ($p<0.001$) and reduced time spent in the target quadrant ($p<0.001$). It was observed that EPO decreased memory impairment. In macroscopic evaluation, it was determined that right hemispheres are significantly smaller than left hemispheres in the first and second study groups. The volumes of right hemispheres in the first group were significantly smaller than that of the second group. There was no significantly differences in any groups according to the results of learning experiments performed postnatal 22 days. These results indicate that EPO decreases spatial memory impairment and cerebral injury in HIE model.

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FINGERPRINTS ABNORMALITIES IN SCHIZOPHRENIA

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This study was planned to determine the dermatoglyphical abnormalities and their frequency in the schizophrenia. Abnormal dermatoglyphic patterns have been observed in which not only chromosome aberations but also gene disorders will be found.

We studied the fingerprints dermatoglyphic of 45 subjects with schizophrenia and 45 comparison healthy controls.The prints were obtained with the classical method of printing with a special black dye on paper. Dermatoglyphic patterns as fingertip patterns, total ridge count were evaluated. In the findings of dermatoglyphic samples of 45 schizophrenia subjects, we obsreved ulnar loops decreased, while archs and whorl increased significantly in schizophrenia. On the other hand, TRC decreased significantly.

The presence of abnormalities in the fingerprints may constitute indelible evidence of a prenatal insult in the 4th or 5th month of pregnancy. The brain and skin develop from the same ectoderm. It is thought, therefore, that dermatoglyphics may be informative for early disturbances in brain development in schizophrenia.

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INHIBITION OF ENDOTHELIAL NITRIC OXIDE OR SUPEROXIDE FORMATION DURING REPERFUSION PREVENTS BLOOD BRAIN BARRIER DAMAGE AFTER TRANSIENT FOCAL CEREBRAL ISCHEMIA

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Reperfusion injury affects stroke outcome unfavorably and shortens the window for thrombolytic agents in acute serebral ischemia. Concomitant generation of nitric oxide (NO) and superoxide is thought to play a significant role in reperfusion injury. We previously showed that peroxynitrite formation on recirculation might be one of the major mediators of reperfusion-induced blood brain barrier (BBB) damage and proposed that high throughput NO synthesis in the vascular endothelium along with superoxide formation might lead to peroxinitrite generation (Stroke, 2000; 31:1974-1981). We now provide supporting evidence by showing that partial inhibition of endothelial NO synthesis or suppresion of superoxide formation does prevent BBB damage and reduce infarct volume.

Twenty-six mice were subjected to proximal middle cerebral artery occlusion (2 hours) and reperfusion (6 hours). Fifteen minutes before reperfusion, mice were injected(ip) either with the non-selective NOS inhibitor N(-nitro-L-arginine (L-NA) (1mg/kg, n=6) or with free radical scavenger N-tert-butyl-(-phenylnitrone (PBN) (100mg/kg, n=6) or with the putative selective eNOS inhibitor L-N5-(I-iminoethyl) ornithine (L-NIO) (10mg/kg, n=6) or saline(n=8). Additionally, all mice received Evans blue (iv) before reperfusion to assess the BBB permeability. The infarct volume was evaluated by Nissl staining.

L-NIO, L-NA and PBN reduced infarct volume (mean(SE) (26.3(7; 44.7(5; 32.0(5mm3, respectively) compared to the saline-treated control group (62(6). Evans blue extravasation were significantly decreased in animals treated with L-NIO, L-NA and PBN (2.7(1; 3.1(1; 3.4(1mm2, respectively) compared to controls (6.4(1).

These data support the hypothesis that suppression of peroxynitrite formation during reperfusion by partially inhibiting endothelial NO synthesis or scavenging superoxide may prevent BBB damage and reduce infarct volume after transient focal cerebral ischemia.

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MORPHOLOGICAL AND BIOPHYSICAL PROPERTIES OF THE CELLS OF CORTICES OF INFERIOR COLLICULUS

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The cortices are the shell of the inferior colliculus (IC) encapsulating the central nucleus of the inferior colliculus (CNIC). In this study, it was aimed to characterize the 3-D morphology of neurons and physiological firing patterns of the neurons in the cortices of IC. The intrinsic membrane properties of the cortices of the inferior colliculus neurons were studied in 300-mikrometre transversal cochlear nucleus slices from rat IC. Membrane properties of the neurons were determined by intracellular stimulation with current pulsee the shell of the inferior colliculus (IC) encapsulating the central nucleus of the inferior colliculus (CNIC). In this study, it was aimed to characterize the 3-D morphology of neurons and physiological firing patterns of the neurons in the cortices of IC. The intrinsic membrane properties of the cortices of the inferior colliculus neurons were studied in 300-mikrometre transversal cochlear nucleus slices from rat IC. Membrane properties of the neurons were determined by intracellular stimulation with current pulses. Of 49 intracellularly recorded neurons, 21 were successfully stained intracellularly with biocytin. Three-dimentional reconstructions of biocytin labelled cells were made using the Neurolucida. Morphologically all of the 21 neurons were identified as multipolar. These cells had resting potential around -60 ±61617; 3.3 mV and the input resistance was 71.4 ±61617; 6 megaohm (n=28). The mean membrane capacitance and time constant of the neurons were 86.4 ±61617; 9.3 pF (n=25) and 5.4 ±61617; 0.8 ms (n=20) respes. Of 49 ntracellularly recorded neurons, 21 were successfully stained intracellularly with biocytin. Three-dimentional reconstructions of biocytin labelled cells were made using the Neurolucida. Morphologically all of the 21 neurons were identified as multipolar. These cells had resting potential around -60 ±61617; 3.3 mV and the input resistance was 71.4 ±61617; 6 megaohm (n=28). The mean membrane capacitance and time constant of the neurons were 86.4 ±61617; 9.3 pF (n=25) and 5.4 ±61617; 0.8 ms (n=20) respectively. Three firing patterns, onset (4/49), regular (28/49) and adapting (17/49) were identified on the basis of response patterns to depolarizing current injections.

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EVIDENCE THAT THE VENTRO MEDIAL HYPOTHALAMUS REGION MEDIATES THE HYPOTENSION AND BRADYCARDIA EVOKED BY SEVERE HEMORRHAGE.

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Severe hemorrhage lower arterial pressure through a central mechanism. This study tested hypothesis that the ventro medial hypothalamus (VMH) region mediates the hypotension and bradicardia evoked by severe hemorrhage. To test this,

neuronal activity was inhibited in the VMH by injecting lidocaine (0.5 μl, 2 %) bilaterally immediately before hemorrhage (2.5 ml/ 100 gr body weight over 20 min). Hemorrhage lowered mean arterial pressure (- 62.5 mm Hg) and heart rate (-103.5 bpm) in halothane-anesthetized rats. Inhibition of neuronal activity in the VMH with lidocaine reduced the fall in mean arterial pressure (-38.0 mm Hg) and heart rate (-68.9 bpm) significantly. In control experiments with non-hemorrhaged animals, VMH lidocaine administration did not change mean arterial pressure and heart rate.

Next, we examined the distribution of Fos protein immunoreactivite neurons in the VMH evoked by severe hemorrhage in the anesthetized rats. Immunohistochemical visualization of Fos protein, the nuclear phosphoprotein product of the early-immediate gene c-fos, permits identification of populations of neurons that are activated in response to a variety of stimuli. We have showed that in hemorrhaged rats there was a heavy concentration of Fos-positive cell nuclei in the ventro medial hypothalamus (184 (65). In the non-hemorrhaged rats there were a few Fos-positive cell nuclei present in the VMH (15 (15).

These data support the hypothesis that VMH plays an important role in response to severe hemorrhage.

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ANOXIA INDUCED DOPAMINE RELEASE IN RAT CORPUS STRIATUM SLICES: ROLE OF CA+2 IONS AND GLUTAMATE

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Excitotoxicity is the most important hypothesis proposed about neuronal degeneration caused by ischemia and similar conditions. In spite of excitator amino acids, it has been revealed that dopamine (DA) released during ischemia and ischemia-like conditions contributes to degeneration. The present study investigates anoxic DA release, the contribution of extracellular and intracellular Ca+2 ions and the role of endogenoeus glutamate in this process.

Striatal slices (0.3 mm thickness) prepared from male Sprague-Dawley rats were placed into incubation tubes containing 2 ml oxygenized medium. After 90 min. of preincubation period, the slices were moved into control or anoxic incubation lasting for 60 min. During this period, incubation medium (2 ml) was replaced with fresh congener at every 10 min and the samples collected were used for the measurement of DA and DOPAC released from the slices. At the end of the assay slices were homogenized in 2 ml 0.4 N HClO4 and the homogenates were processed for tissue protein and DA measurements. The incubation of slices in anoxic conditions caused a substantial increase in DA release whereas DOPAC release was reduced. Neither the omission of extracellular Ca+2 ions from the medium, nor the inactivation of the intracellular Ca+2 ions with BAPTA affected anoxia induced DA release. Similar findings were obtained with Ca+2 channel blockers nifedipine and amlodipine (100 μM each). However verapamil, used at the same concentration caused a substantial reduction in anoxia induced release. The role of endogenoeus glutamate in the anoxic induction was tested by measurement of glutamate release from the slices and blocking the glutamate receptors by MK-801. MK-801 reduced the anoxia induced dopamine release in a dose-dependent manner, whereas glutamate release did not significantly increase under anoxic conditions. These findings suggest that DA release induced by anoxia exists with a mechanism independent of Ca+2 ions and this mechanism seems to be relevant with an increase in glutamate receptor responses.

This study was supported by a grand from Uludag University Research Council (2002/65)

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EFFECTS OF CDP-CHOLINE AND ITS HYDROLYSIS PRODUCTS ON BLOOD PRESSURE AND THE ROLE OF SYMPATHOADRENAL SYSTEM IN THE EFFECT

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Cytidine-5'-diphosphate choline (CDP-choline, citicoline), is an endogenous molecule which is an intermediate product in phosphatidylcholine synthesis. It was reported that CDP-choline is effective in some neurodegenerative diseases and ischemic events but there are only a few studies about its pharmacological effects. In our study, the effects of intraperitoneally (i.p.) injected CDP-choline and its hydrolysis products choline, phosphocholine and cytidine on blood pressure and the role of the sympathoadrenal system in these effects were investigated.

After the control values were obtained, CDP-choline at the doses of 105, 210 and 315 mg/kg or choline (30, 60 and 90 mg/kg), phosphocholine (56, 111 and 167 mg/kg) and cytidine (53, 105 and 158 mg/kg) at equimolar doses were administered intraperitoneally to rats. Then the changes in blood pressure at 5, 10, 20, 30, 45 and 60 minutes were observed. CDP-choline, phosphocholine and cytidine caused significant increases in blood pressure which peaked at 5 minute. Choline caused a decrease in blood pressure dose-dependently. This decrease was maximum at 5 minute.

Then the changes in plasma catecholamine levels in the blood sample which was obtained in the 5th minute for 315 mg/kg and its hydrolysis products at equimolar doses were investigated. Plasma catecholamine levels increased significantly in CDP-choline, choline and phosphocholine given rats. But cytidine did not alter catecholamine levels significantly.

After these observations, 315 mg/kg CDP-choline and its hydrolysis products at equimolar doses were administered i.p. to adrenalectomized or sham operated rats. No significant changes were observed in blood pressure in adrenalectomized rats compared to those of sham operated group.

These findings suggest that intraperitoneally administered CDP-choline or its hydrolysis products cause significant effects on blood pressure which are mediated by the sympathetic system but not the adrenal medulla.

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EFFECTS OF CDP-CHOLINE AND ITS HYDROLYSIS PRODUCTS ON SERUM GLUCOSE LEVELS: THE ROLE OF SYMPATHOADRENAL SYSTEM

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Cytidine-5'-diphosphate choline (CDP-choline, citicoline), is an endogenous molecule which is an intermediate product in phosphatidylcholine synthesis. It was reported that CDP-choline is effective in some neurodegenerative diseases and ischemic events but there are only a few studies about its pharmacological effects. In our study, the effects of various doses of intraperitoneally (i.p.) injected CDP-choline and its hydrolysis products choline, phosphocholine, cytidine monophosphate and cytidine on serum glucose levels were investigated.

After the control values were obtained, CDP-choline at the doses of 105, 210 and 315 mg/kg or choline (30, 60 and 90 mg/kg), phosphocholine (56, 111 and 167 mg/kg), cytidine monophosphate (79, 158 and 237 mg/kg) and cytidine (53, 105 and 158 mg/kg) at equimolar doses were administered i.p. to rats. Then the changes in serum glucose levels at 5, 10, 20, 30, 45 and 60 minutes were observed. CDP-choline, phosphocholine, cytidine monophosphate and cytidine caused

increases in serum glucose levels. These increases peaked at 10 minute.

After these observations 315 mg/kg CDP-choline and its hydrolysis products at equimolar doses were administered i.p. to adrenalectomized or sham operated rats. Serum glucose responses decreased significantly in adrenalectomized rats compared to those of sham operated group.

These findings suggest that intraperitoneally administered CDP-choline or its hydrolysis products cause significant effects on serum glucose levels which are mediated by the sympathoadrenal system.

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VALPROIC ACID INCREASES HISTONE H3 ACETYLATION AND 5-LIPOXYGENASE (5-LOX) CONTENT IN THE MOUSE HIPPOCAMPUS IN-VIVO

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Gene expression can be regulated by chromatin remodeling induced by the opposing actions of histone acetyltransferases (HAT) and histone deacetylases (HDAC). In the central nervous system (CNS), neuronal activity (e.g., during status epilepticus) modulates histone acetylation in a promoter-specific manner and may participate in pathobiologic mechanisms, suggesting that histone acetylation and deacetylation are dynamic processes even in postmitotic neurons. Thus, although HDAC inhibitors are considered putative anti-cancer drugs, they may also be important for the regulation of gene expression in the CNS. Valproic acid (VPA), a drug used for treatment of bipolar disorder, has recently been characterized as an HDAC inhibitor. Studies in neuronal cultures demonstrate that VPA increases the expression of 5-lipoxygenase (5-LOX), a gene susceptible to regulation by chromatin remodeling. Currently, no data are available on whether such an action of VPA occurs in-vivo. Here we show that in vivo treatment of mice with intraperitoneal VPA injections increases the acetylation of histone H3 and the content of 5-LOX protein in the hippocampus. Since the extent of 5-LOX expression may alter mouse behavior, our data suggest that VPA-altered chromatin remodeling and 5- LOX expression may participate in the CNS activity of this drug.

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LIPOMATOUS MEDULLOBLASTOMA / CEREBELLAR LIPONEUROCYTOMA

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A case report: Lipomatous medulloblastoma is a rare cerebellar neoplasia of adult age that has focal lipomatous differentiated regions and low proliferative index with a good clinical prognosis. According to WHO 2000 CNS tumor classification lipomatous medulloblastoma/lipidized medulloblastoma is classified as a different clinical entity as WHO Grade I or II. İn this case report, histopatological, immunhistochemical and flow cytometric analysis of a 49 years old patient who applied to Haydarpasa Numune Hospital Neurosurgery department with localized obstructive hydrocephaly and cerebellar tonsiller herniation and had microscopic total tumor exsicion are presented and findings of case reports published till this day reviewed.

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NEUROENDOCRINE EFFECTS OF CDP-CHOLINE AND ITS HYDROLYSIS PRODUCTS: CHANGES IN PLASMA INSULIN, GLUCAGON AND CATECHOLAMINE LEVELS

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Cytidine-5'-diphosphate choline (CDP-choline, citicoline), is an endogenous molecule which is an intermediate product in phosphatidylcholine synthesis. It was reported that CDP-choline is effective in some neurodegenerative diseases and ischemic events but there are only a few studies about its pharmacological effects. In our study, neuroendocrine effects of intraperitoneally (i.p.) injected CDP-choline and its hydrolysis products choline, phosphocholine and cytidine were investigated.

After the control values were obtained, CDP-choline at the dose of 315 mg/kg or choline (90 mg/kg), phosphocholine (167 mg/kg) and cytidine (158 mg/kg) at equimolar doses were administered i.p. to rats. Then the changes in plasma insulin, glucagon and catecholamine levels were observed.

In the blood samples which were collected during 60 minutes, CDP-choline and choline caused increases in plasma catecholamine levels. These increases were more significant in choline injected group and peaked within 10 and 20 minutes using choline and CDP-choline,respectively. Both returned back to basal levels around 45 minutes. Phosphocholine increased catecholamine levels in the samples collected at 10th minute, whereas, cytidine, did not alter plasma catecholamine levels in the same samples significantly.

CDP-choline and its hydrolysis product choline increased insulin and glucagon levels in the 10th minute samples significantly.

These findings suggest that intraperitoneally administered CDP-choline or its hydrolysis products cause significant neuroendocrine effects.

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THE EFFECT OF LONG-TERM PHYSICAL EXERCISE ON THE PHYSIOLOGY AND COGNITIVE SYSTEMS

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Introduction and aim: In the recent years the effect of long term exercise on the physiological systems has been investigated vastly. On the other hand; Its impact on the cognitive behaviour is little known. The aim of this paper is to investigate the correlations of maximum oxygen uptake capasity , mental reaction time and P 300 (electrophysiological cognitive value).

Methods: Master athletes exercising regularity (n=11)and control group who live sedentarily (n=11) are included in the study. Maximum oxygen uptake capasity assessed by Astrand test.Astrand test is given to these groups but before the test, groups is hold not to exercise heavily. P300 and mental reaction time are recorded at the same time and at the same environment. A through, neurological, physical and mental examination is applied for each person. Every person has been questioned for a history of migraine, psychological disorder, diabetes, hypertension, epilepsy, cancer, alcohol and smoking habits.

Results: The maximal oxygen uptake capasities in master athlete group is mean: 31.4±5.9 ml/min/kg, in sedantary group

it is 18.8±5.0 ml/min/kg in maters. The reaction time is 105.5±22.30 s, in masters and 148.27±39.30 s. İn control group. The statistical analysis indicated that the difference between the groups is found significant ($p<0.05$). The latency of P300 was mean:. 330.30±33.54 ms. in masters group and mean:345.58±22.73 ms. sedantary group ($p=0.433$). The amplitude of P300 mean:. 12.42 ±9.74 mV and mean:10.86 ±5.30 mV sedantary group ($p=0.05$).

Conslusion: This study indicates that long-term exercise increased the mental reaction time and maximal oxygen uptake capasity. Theelectrophysiological data is the less affected aspect of this study. Although there is no marked difference , we can say that the latency of the P300 decreased and amplitude of the wave increased.

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INFLUENCE OF SURGICAL PAIN STRESS ON THE BLOOD-BRAIN BARRIER PERMEABILITY

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The blood-brain barrier minimizes the entry of molecules into central nervous system. The unique characteristics of this barrier include tight junctions between adjacent endothelial cells, a paucty of pinocytotic vesicles, and an absence of fenestra. Breakdown of the blood-brain barrier in humans and experimental animals in various pathological conditions, such as acute hypertension, convulsions, ischemia have been shown by many investigations. The aim of the present study was to investigate the direct effect of surgical acute pain stress on the blood-brain barrier permeability in rats. The experiments were performed on Wistar albino rats. The rats were divided into three groups: group 1: control (n=8) ; group 2: immobilization stress (n=8); group 3: immobilization plus surgical pain stress (n=8). All animals were immobilized under diethyl-ether anesthesia. Pain stress was produced by bilateral hind paw surgical wound. In all animals, Evans-blue which binds to serum albumin was used as a blood-brain barrier tracer , and was given intravenously. At the end of experiments, i.e. approximately 20 min after Evans-blue injection, under diethyl ether anaesthesia, all rats were killed by perfusion through the heart with saline solution to avoid artificial staining of the brain during removal. The brains were removed and examined for Evans-blue albumin extravasation. A quantitative estimation with spectrophotometer using homogenized brain to release the dye was also performed to evaluate the macroscopical findings.

There is no significant blood-brain barrier breakdown after short-time immobilization stress, but surgical pain stress increased blood-brain barrier permeability in comparison to both control, and immobilization stress groups. ($P<0.0l$). In surgical pain stress induced animals distinct Evans-blue leakage was observed in occipital, frontal parieto-temporal cortices. Our results suggest that surgical pain-stress significantly increases blood-brain barrier permeability in rats.

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INFLUENCE OF HYPOGLYCEMIC COMA AND ALCOHOLIC COMA ON THE BLOOD-BRAIN BARRIER PERMEABILITY IN RATS

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The endothelial cells of cerebral blood vessels are joined together by tight junctions and contain few pinocytotic vesicles. The entry of macromolecules into the brain is therefore severely restricted . The aim of the present study was to investigate blood-brain barrier permeability in alcoholic coma and in hypoglycemic coma.

The experiments were performed on adult Wistar albino rats . In hypoglycemic group, the animals were fasted for 15 hours before the experiment but were allowed free access to water.The rats were divided into three groups. Group 1:normoglycemic control animals (n=8); Group 2: hypoglycemic coma (n=10) Group3: Alcoholic coma(n=18). To induce hypoglycemic coma in group 2, 100 IU/kg body weight crystallin zinc insulin was administered intraperitoneally under light diethyl-ether anesthesia. Approximately 3-4 hours after insulin administration, the animals became comatose. Alcoholic coma was induced intraperitoneal alcohol injection (4g/kg i.p.). Approximately 3-5 min after alcohol administration, the animals became comatose. Evans-blue, which binds to serum albumin, was used as a blood-brain barrier tracer and given intravenously at a dose of 4ml of 2% solution per kg body weight. At the end of experiments, approximately 20 min after Evans-blue injections, all rats were killed by perfusion through the heart with saline solution to avoid artificial staining of the brain during removal. The brains were removed and examined for Evans-blue albumin extravasation. A quantitative estimation with spectrophotometer using homogenized brain to release the dye was also performed to evaluate the marcoscopical findings. No Evans blue albuming extravasation was seen in the brains of control rats. In the second group, which underwent hypoglycemic coma, Evans-blue albumin extravasation was most pronounced in the occipital, frontal, and parieto-temporal cortices. Evans blue albumin complex was observed in the brain in 7 out of 10 rats. Hypoglycemic coma increases blood-brain barrier permeability in comparison to control rats ($P<0.01$). In Alcoholic animals , Evans-blue albumin complex was observed in the brain in 4 out of 18 animals. In conclusion, hypoglycemic coma increases blood-brain barrier permeability much more than alcoholic coma .

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