Neurological/Neudegenerative diseases

Cod: 1182

SESAMIN ATTENUATES NEUROTOXICITY BY INHIBITING INFLAMMATORY AND MAPKINASE SIGNAL ACTIVATION IN MOUSE MODEL OF STROKE

S. Ahmad[1], K. Bhatia[1], A. Jamal[1], M. Al-Jahdali[1]
[1]*King Abdulaziz University, Rabigh, Saudi Arabia*

BACKGROUND: The present study was designed to evaluate the neuroprotective effect of sesamin, a natural antioxidant found mainly in sesame seed, in mouse model of stroke. Stroke is known as a leading neurological disorder worldwide and characterized by the sudden loss of blood circulation; and causes excess generation of reactive oxygen species (ROS), which activates MAPKinase and pro-inflammatory signaling pathway that leads to neuronal cell death in brain.

METHODS: Mice were pre and post treated with sesamin 30 mg/kg Body weight. Stroke was induced by middle cerebral artery occlusion (MCAO) for 2 h followed by the reperfusion for 22 h and then mice were sacrificed. Brain was collected for biochemical, cellular and histopathological studies.

RESULTS: Results demonstrated that sesamin treatment significantly reduced the, infarction volume, lipid per-oxidation and caspase-3 activation in treated group compared with lesioned group. DHE staining showed increased superoxide production in lesioned group as compared to sham and sesamin treatment significantly reversed this process. Western blot analysis showed low SODs, iNOS expression in lesioned group and sesamin treatment attenuated its expression. Furthermore, we investigated sesamin effect on inflammatory and oxidative stress markers and we found that immunohistochemical analysis of mice brain showed marked decrease of Iba1, Nox-2 Cox-2, iNOS and per-oxynitrite expression in treated group as compared to lesioned group. We also observed increased mRNA level of TNF-α, iNOS and IL-6 in lesioned group and sesamin treatment reduced the expression remarkably. Immunfloroscence study revealed that sesamin inhibits mitogen activated protein kinase pERK and p-p38 actiavtion in neurons. Results are expressed as mean ± standard error (± S.E.M) of six animals. Differences between the means of experimental and control groups were analyzed statistically by using student's t-test and one-way analysis of variance (ANOVA) followed by Tukey-Kramer test for multiple comparisons. A value $p>0.05$ and $p>0.01$ was considered significant.

CONCLUSIONS: Overall this study suggests that sesamin may protect stroke induced neurotoxicity by ameliorating oxidative, inflammatory and MAPKinase activation.

Neurological/Neudegenerative diseases

Cod: 1183

ISCHEMIC STROKE FREQUENCY IN A SAMPLE OF PATIENTS TREATED WITH ANTIPLATELET AGENTS

D. Al Kassam[1], J. Gonzalez [1], Y. Bravo[1], R. Saez de la Maleta[1]
[1]*Hospital Universitario de Burgos*

BACKGROUND: The failure in preventing stroke in patients receiving antiplatelet therapy may be due to lack of treatment adherence, due to pharmacological aspirin resistance, due to the presence of vascular risk factors like classic serological markers such as CRP ultrasensitive. Analyze the ischemic stroke frequency in a sample of patients treated with antiplatelet agents detecting drug resistance by PFA-100, AAS levels and ultrasensitive PCR and vascular risk factors, the characteristics of the event and the functional status at discharge and after three months.

METHODS: A prospective consecutive study with collection of the variables described involving Clinical Analysis and Neurology services. Results were analyzed by SPSS.

RESULTS: 94 patients were included with a mean age of 75.5 years and a slight predominance in males (61.1%). 75 patients had a stroke and 20 a transient ischemic accident. Lack of response to aspirin was found in 26 patients (27.4%), lack of detection of salicylates in blood (levels <3 mg / l) in 58 (61.1%) and average sensitivity CRP levels were found were 13 , 33 with a high variability (0.13 to 247.3). Association was found, but no statistical significance between aspirin resistance and the following variables: history of hypertension, dyslipidemia, and ischemic heart disease; admission glycemia (p = 0.83), lower cholesterol numbers, higher creatinine (p = 060), presence of salicylates in blood (p = 0.90) and lower levels of CRP, increased severity of neurological deficit at admission and discharge (as measured by the NIHSS scale) worse functional status at 3 months, recurrence at 6 months.

CONCLUSIONS: The frequency of aspirin resistance is consistent with that described in other studies. No statistically significant associations were found with factors described in other studies may be due to sample size. We found absence of blood salicylates detection in a high proportion of patients.

Neurological/Neudegenerative diseases

Cod: 1184

THE INTERACTION BETWEEN PERIPHERAL INFLAMMATORY MARKERS, COGNITIVE IMPAIRMENT AND HIPPOCAMPAL VOLUMES IN ALZHEIMER'S DISEASE

Ö. Yavuz[1], G. Avcı Aytav[1], A.D. Akçaer[1], M. Şahin[3], T. Yavuz[2], T. Karlıdere[3], B. Yanık Keyik[4], N. Özcan[1], A.A. Hişmioğulları[1]
[1]*Department of Medical Biochemistry, Balikesir University, School of Medicine, Balikesir, Turkey*
[2]*Department of Medical Microbiology, Balikesir University, School of Medicine, Balikesir, Turkey*
[3]*Department of Psychiatry, Balikesir University, School of Medicine, Balikesir, Turkey*
[4]*Department of Radiology, Balikesir University, School of Medicine, Balikesir, Turkey*

BACKGROUND: Results from previous studies have suggested that inflammation have a role in cognitive impairment observed in patients with Alzheimer's Disease (AD). Hippocampal volume loss is an early event in AD that triggers cognitive decline. The aim of this study was to investigate the relation between peripheral inflammatory markers and the severity of AD as assessed by cognitive function and hippocampal volumes.

METHODS: In this study, 24 patients with AD (mean age: 72, 63 ± 3, 60, male 46%) 24 age- and gender-matched healthy controls (mean age: 70, 75 ± 3, 52, male 50%) were evaluated. Global cognitive performance were assessed by the Mini-Mental State Examination (MMSE) test. The NINCDS-ADRDA and the DSM-IV- criteria for AD were used. Magnetic resonance imaging was used to measure volume of the hippocampus in AD cases and controls. Serum C-reactive protein (CRP) concentration was measured by spectrophotometric method on the clinical chemistry analyzer. α1 and α2 globulin levels were analyzed by capillay electrophoresis technique. In statistically analysis, the relationship between inflammation, cognitif disturbances and hippocampal volumes were explored by multivariable linear regression models that were initially adjusted for covariates (age, gender, education and illness duration)

RESULTS: MMSE scores, hippocampal volumes and CRP levels were significantly decreased among AD cases compared to controls ($p<0.001$). We found a significant inverse correlation between CRP level and MMSE score; α1 globulin level and MMSE score respectively ($r = -0.647$, $p=0.002$; $r = -0.788$, $p <0.001$) in patients with AD. A multiple regression analysis in AD patients showed that serum CRP was a significant predictor of MMSE score ($\beta= -0.869$, $p<0.01$).

CONCLUSIONS: The current results support previous findings of reduced serum CRP levels in patients with AD. Much larger sample sizes would be needed to ultimately asses the CRP as a biomarker for cognitive impairment.
Keywords: Alzheimer disease, İnflammatory markers, C-reactive protein, α1 globulin, α2 globulin, Imaging biomarkers, Hippocampal volume

Neurological/Neudegenerative diseases

Cod: 1185

ISCHEMIA MODIFIED ALBUMIN AND PLASMA OXIDATIVE STRESS MARKERS IN ALZHEIMER'S DISEASE

M. Can[1], F. Varlibas [2], B. Guven [1], O. Akhan [2], G.A. Yuksel [2]
[1]*Department of Biochemistry, Bulent Ecevit University, Faculty of Medicine, Zonguldak, Turkey*
[2]*Department of Neurology, Haydarpasa Numune Educational and Research Hospital, Istanbul, Turkey*

BACKGROUND: The objective of this study was to determine ischemia modified albumin (IMA) and oxidant status in Alzheimer's disease (AD). Therefore, we evaluated the IMA and oxidant status by measuring serum uric acid, albumin and gamma- glutamyltransferase (GGT) in AD.

METHODS: The plasma albumin, uric acid, GGT and IMA levels were measured by spectrophotometric methods in 32 AD patients and 32 healthy controls. The Mini Mental Status Examination and Clinical Dementia Rating Scale were used to evaluate the cognitive functions of AD patients.

RESULTS: AD patients had significantly higher IMA levels as compared to those of the controls respectively. Uric acid concentrations were significantly decreased and GGT values were significantly increased in AD when compared with control group. Albumin levels of the patients were also compared and no significant difference was detected.

CONCLUSIONS: Oxidative stress and IMA levels rise in AD. However, large prospective studies are required to understand the mechanisms leading to increased IMA levels during AD, whether preceded or not by AD.
Key Words: Alzheimer's disease, ischemia-modified albumin, gamma-glutamyltransferase , uric acid

Neurological/Neudegenerative diseases

Cod: 1186

NO EFFECT OF MTHFR C677T VARIANT ON HOMOCYSTEINE METABOLISM IN AMIOTROPHIC LATERAL SCLEROSIS

C. Bellia[2], G. Bivona[2], A. Pivetti[2], A. Caruso[2], B. Lo Sasso[2], V. La Bella[1], M. Ciaccio[2]
[1]*ALS Clinical Research Center, Bio.Ne.C, University of Palermo*
[2]*Section of Clinical Biochemistry and Clinical Molecular Medicine, Department of Biopathology and Forensic and Medical Biotechnologies, School of Medicine, University of Palermo, Italy*

BACKGROUND: Homocysteine (Hcy) has been associated to neurotoxicity through several mechanisms such as free radical and cytosolic calcium accumulation, mitochondrial dysfunction, activation of apoptotic pathways and excitotoxicity. However, the relationship between Hcy, motoneuron death and Amyotrophic Lateral Sclerosis (ALS) has not been elucidated yet. Aim of the present study was to analyze Hcy plasma and cerebrospinal fluid (CSF) levels in ALS patients and in neurological controls; we also evaluated whether MTHFR C677T variant can affect Hcy metabolism in this setting.

METHODS: Sixty-nine sporadic ALS patients and 79 aged- and sex-matched controls (tension headache, cervical spondylotic myelopathy, hereditary motor-sensory polyneuropathy, idiopatic polyneuropathy, conversion disorder or neurosis and myositis) were enrolled. Homocysteine was measured in plasma and CSF by HPLC with fluorimetric detection. MTHFR C677T genotyping was conducted by PCR-Real Time with melting curves analysis (Light Cycler, Roche). Statistical analysis was conducted by SPSS 15.0 software.

RESULTS: Hcy plasma levels were higher in ALS than in controls (9.9 [7.45-14.56] vs 7.23 [6.6-8.3] micromol/L, P<0.001); similarly, also Hcy CSF levels were higher in patients than in controls (0.46 [0.37-0.68] vs 0.23 [0.19-0.26], P<0.001). In order to investigate if the increased Hcy in ALS was associated to MTHFR C677T status, we compare the distribution of this variant in cases and controls but no significant differences were found (CC 35%, CT 33%, TT 32% in ALS; CC 44%, CT 26%, TT 30%; P=0.47). We further compared Hcy plasma levels among CC, CT and TT MTHFR C677T ALS individuals: plasma homocysteine was 11.3 (8.5-15.0) in CC, 9.8 (7.1-16.9) in CT and 8.9 (7.0-12.0) micromol/L in TT (P=0.36); CSF homocysteine in CC, CT and TT individuals was 0.4 (0.3-0.6), 0.5 (0.4-0.8) and 0.5 (0.4-0.6) micromol/L, respectively (P=0.18).

CONCLUSIONS: ALS patients presented increased homocysteine plasma and CSF levels, suggesting the involvement of this aminoacid in the pathogenesis of the disease and its potential use as diagnostic marker. The mechanism underlying increased homocysteine is independent from MTHFR C677T in ALS.

Neurological/Neudegenerative diseases

Cod: 1187

CEREBROSPINAL FLUID ARYLESTERASE ACTIVITIES IN CENTRAL NERVOUS SYSTEM DISEASES

M. Ergin[1], Ö. Erel[1], F.M. Yılmaz [2], R. Dündaröz[4], U. Erenberk[4], H. Bayındır[3]
[1]*Department of Biochemistry, Ankara Atatürk Training and Research Hospital, Ankara, Turkey*
[2]*Department of Biochemistry, Ankara Numune Education and Research Hospital, Ankara, Turkey*
[3]*Department of Neurology, Ankara Atatürk Training and Reseach Hospital, Ankara, Turkey*
[4]*Department of Pediatrics, Bezmialem Vakif University, Faculty of Medicine, Istanbul, Turkey*

BACKGROUND: Oxidative status has a significant role in the pathogenesis of central nervous system diseases. Paraoxonase enzyme is an ester hydrolase that has both paraoxonase (PON1) and arylesterase (ARES) activities. It is known that PON-ARES have antioxidant and antiinflammatory characteristics. There is no available data researching cerebrospinal fluid (CSF) ARES activities in human. Therefore we investigated the cerebrospinal fluid ARES activities in subjects with central nervous system diseases.

METHODS: In our study 54 patients (20 patients with cerebreovascular disease, 17 patients with meningitis,10 patients with multiple sclerosis and 7 with epilepsy) were examined for cerebrospinal fluid ARES activities. Arylesterase activity was measured using commercially kits (Relassay, Gaziantep, Turkey). Since the data were not normally distrubted the Kruskal-Wallis tests were managed to compare ARES activity among groups.

RESULTS: ARES activities were expressed as median (IQR); in cerebreovascular disease subjects 42.30 (64.85) U/L; in meningitis 37.80 (73.35) U/L; in multiple sclerosis 31.55 (30.57) U/L; in epilepsy 28.70 (24.70) U/L. There was no significant difference between cerebrospinal fluid ARES activities in patients among groups ($p > 0.05$).

CONCLUSIONS: As PON-ARES enzyme is a small, lipophilic glycoprotein (43-45 kDa), we thought that arylesterase enzyme may diffuse through the blood-CSF barrier and blood-brain barrier. Cerebrospinal fluid ARES activities may be a potential biomarker for revealing the pathogenesis of central nervous system diseases. Consequently further experimental studies are necessary to understand the role of cerebrospinal fluid ARES activities.

Neurological/Neudegenerative diseases

Cod: 1188

SIMULTANEOUS BIOCHIP BASED IMMUNOASSAYS FOR APOLIPOPROTEIN E4 GENOTYPING

E. Healy[2], C. Richardson[2], M. Veitenger[1], E. Umlauf[1], M. Zellner [1], J. Lamont [2], R. McConnell[2], S. FitzGerald[2]
[1]*Institute of Physiology, Medical University of Vienna, Austria*
[2]*Randox Laboratories Limited, Crumlin, United Kingdom*

BACKGROUND: Apolipoprotein E (ApoE) is a polyvariant protein with three common isoforms: ApoE2, ApoE3, and ApoE4. The presence of the APOE4 allele is a risk factor for Alzheimer's disease (AD) development. ApoE4 genotype is not diagnostic, but it may improve the power of other diagnostic tests to estimate the likelihood of developing AD. Since most other potential AD biomarkers are quantified at the protein level, it will be advantageous to multiplex biomarkers with a protein-based genotyping test. This study reports the development of novel biochip based immunoassays for the simultaneous detection of total ApoE and ApoE4 isoforms on a single sample.

METHODS: Sandwich chemiluminescent immunoassays defining discrete test sites on a biochip surface were employed for the detection.The Evidence Investigator analyser was used. Plasma samples from 42 ApoE genotyped patients were studied [25 patients carried the ApoE4 allele, (18 heterozygotes, 7 homozygotes) and 17 were ApoE4 negative]. Relative light units (RLU) were determined for total ApoE and ApoE4, relative levels of ApoE4 were expressed as a proportion of total ApoE (ApoE4:totalApoE ratio). Receiver Operating Characteristics Curves (ROC) were also constructed.

RESULTS: The ratio of these two assays demonstrated normal Mendelian protein expression patterns. The mean (95% CI) of the ApoE4:totalApoE ratio for ApoE4 null, heterozygous and homozygous patients were 0.01 (0.008-0.01), 0.652 (0.535-0.769) and 1.184 (0.921-1.447) respectively. Using the ApoE4:total ApoE ratio above 0.022 as a cut-off, this assay was able to accurately discriminate between ApoE4$^{(+/-,+/+)}$ and ApoE4$^{(-/-)}$ patients: ROC area under the curve (AUC) 1.00 (CI=0.916 to 1.000, Sensitivity=100%, Specificity=100%). Furthermore, methodology was able to discriminate between heterozygotes and homozygotes. Using a ApoE4:totalApoE cut-off ratio of 0.726, 24 of 25 ApoE4 positive patients were correctly classified (94.44%).

CONCLUSIONS: This study demonstrates applicability of biochip based immunoassays for the ApoE4 genotyping through the simultaneous determination of total ApoE and ApoE4. This is of interest for application to clinical settings to aid the diagnosis of patients suspected of having or at risk of developing AD.

Neurological/Neudegenerative diseases

Cod: 1189

EVALUATION OF SIEMENS N LATEX FLC KAPPA INDEX TO SUPPORT THE DIAGNOSIS OF MULTIPLE SCLEROSIS

E. Georg[1], M. Dejan[1], H. Wolfgang[1], B. Thomas[2], P. Stefan [2]
[1]*Wilhelminenspital Central Lab*
[2]*Wilhelminenspital Dept. of Neurology*

BACKGROUND: The detection of oligoclonal bands (OCB) in cerebrospinal fluid (CSF) indicating intrathecal immunoglobulin synthesis is an important marker for multiple sclerosis (MS). However, OCB detection by isoelectric focusing electrophoresis (IFE) is technically demanding and results sometimes difficult to read. Recently, kappa free light chain (KFLC) index was shown to be an excellent predictor of positive OCB in CSF. The purpose of the present study was to evaluate the new N Latex FLC assay (Siemens Healthcare Diagnostics, Marburg, Germany).

METHODS: A total of 303 CSF and serum samples from patients with various neurologic diseases were investigated, including 28 cases of MS and 30 cases of clinical isolated syndrome (CIS). FLC kappa in serum and CSF were measured by N Latex FLC and Freelite (The Binding Site, Birmingham, UK) assays on a Siemens BN ProSpec. The KFLC index was calculated: (CSF KFLC/serum KFLC)/(CSF albumin/serum albumin).

RESULTS: Correlation of KFLC: Spearman rank correlation showed high correlations of N Latex FLC and Freelite KFLC concentrations both in serum and CSF (r= 0.922 and 0.957, resp.). In serum and CSF N Latex FLC yielded slightly lower KFLC results than Freelite, especially in the upper KFLC range. Consequently, KFLC indices differed, with lower N Latex FLC indices with increasing KFLC results. Prediction of OCB: OCB were detected in 62 CSF samples by IFE. In OCB positive CSF samples KFLC concentration and index were significantly higher with both methods ($p<0.0001$) when compared to OCB negative samples. ROC analysis evaluating the clinical efficiency of the KFLC index to predict OCB in CSF showed virtually identical results for both methods with AUCs of 0.959 and 0.958, respectively. Both assays detected OCB with 95% sensitivity and 91% specificity applying a KFLC index decision limit of 5.0 for N Latex FLC and 4.1 for Freelite.

CONCLUSIONS: While showing an excellent correlation the two tests yielded slightly different results regarding absolute levels of CSF KFLC, serum KFLC as well as KFLC index. Nevertheless, both tests proved equally well suited to predict OCB in CSF and can thus support current MS diagnostic criteria. Decision limits will to some extent vary between the two assays.

Neurological/Neudegenerative diseases

Cod: 1190

INVESTIGATION OF THE ROLE OF OXIDATIVE STRESS, FACTORS AFFECTING VASCULAR PATHOPHYSIOLOGY AND INFLAMMATION IN MIGRAINE PATHOGENESIS

E.M. Guler[1], U.A. Kelleci[2], H.G. Polat[2], A.D. Yalcin[2], A.S. Yalcin[1]
[1]*Marmara University, School of Medicine, Department of Biochemistry, Istanbul, Turkey*
[2]*Umraniye Training and Research Hospital, Neurology Clinic, Istanbul, Turkey*

BACKGROUND: We have compared oxidative stress, vascular pathophysiology and inflammation markers of migraine patients with healthy volunteers.

METHODS: Blood and urine samples were obtained from 27 healthy individuals and 27 patients with a diagnosis of migraine who had applied to Neurology Outpatient Clinics of Umraniye Research and Training Hospital. Participants were between ages 18 – 49. All patients had their diagnosis established prior to the study and the volunteers in the control group had no systemic disease or relevant disorders. Urine samples were tested for malondialdehyde while erythrocytes were investigated for glutathione, glutathione related enzymes, superoxide dismutase, catalase, malondialdehyde and protein carbonyls. Plasma samples were analyzed for malondialdehyde, bilirubin, uric acid and albumin as oxidative stress parameters. Thrombocyte count and fibrinogen levels were measured for vascular pathophysiology and IL 1β, IL 6, IL 10, TNF α, adenosine deaminase, CRP and ferritin were used as inflammation markers.

RESULTS: Antioxidant levels were significantly lower in the patient group. Glutathione, glutathione related enzymes, superoxide dismutase and catalase levels were also significantly lower. Albumin levels were similar in both groups whereas uric acid and bilirubin levels were significantly higher in the patient group. Similarly, protein carbonyls, which are oxidative damage markers as well as urine, plasma and erythrocyte malondialdehyde levels were higher in the patient group. Thrombocyte count and fibrinogen levels, both of which are vascular pathophysiology markers, were found to increase in patient group. The participants in the patient group had higher levels of adenosine deaminase, IL 1β, IL 6, IL 10 and TNF α as inflammation markers. On the other hand, their CRP and ferritin levels were lower.

CONCLUSIONS: Considering oxidative stress, vascular pathophysiology and inflammation markers as a whole, we suggest that patients with migraine had increased oxidative stress due to suppressed and decreased levels of antioxidants and consequently had inflammatory and vascular changes.

Neurological/Neudegenerative diseases

Cod: 1191

CEREBROSPINAL FLUID BIOMARKERS IN THE DIAGNOSIS OF ALZHEIMER'S DISEASE

M. Martínez-Villanueva[1], F. Avilés-Plaza[1], C. Ruiz-González[1], J. Marín-Isla[2], F. Noguera-Perea[2], C. Antúnez-Almagro[2], J.A. Noguera-Velasco[1]

[1]*Clinical Laboratory Service. Clinical Universitary Hospital Virgen de la Arrixaca, Murcia, Spain*
[2]*Dementia Unit Clinical Universitary Hospital Virgen de la Arrixaca, Murcia, Spain*

BACKGROUND: Alzheimer's disease (AD) is the main cause of dementia around the world. The main changes in AD are the accumulation of amyloid plaques and neurofibrilary tangles, composed by hyperphosphorilated tau. Although knonwledges, a gold standar for AD diagnosis hasn't been found yet, therefore the diagnosis is still based on clinical criteria. However, some studies say that amyloid peptide, tau protein (tau) and hyperphosphorilated tau (p-tau) measurement, in cerebrospinal fluid (CSF), are very useful for the diagnosis of Alzheimer's disease. Objective: The aim of our study is to correlate CSF biomarkers with neuropsychological tests used to diagnose dementia as well as evaluate its diagnostic efficacy and establish possible cutoffs for the diagnosis of AD.

METHODS: In our study, with 74 patients from the Dementia Unit, we compare the available tools for the diagnosis of AD (hippocampus atrophy, clinical criteria and the neuropsychological tests Reisberg Global Deterioration Scale-GDS and Mini-Mental) with the concentrations of β-amy, tau and p-tau measured in CSF (solid-phase enzyme immunoassay, Innotest®β-amy(1-42), Innotest®hTAU Ag and Innotest®p-tau(181P), Innogenetics) and IATI index, calculated from the concentrations of β-amy and tau. Statistical analysis was performed with spss19.0 and MedCalc programs.

RESULTS: All biomarkers and IATI index have significant correlations with mini-mental test ($p<0.001$) and the suspected diagnosis of AD ($p <0.001$) and also β-amy and IATI with GDS ($p<0.05$) and hippocampus atrophy ($p<0.05$). We found a high diagnostic efficiency of all CSF biomarkers for the identification of patients with AD versus other dementias (AUC: β-amy=0.836, tau=0.769 p-tau=0.767; IATI =0.844). The cutoffs obtained for the diagnosis of AD in our patients group were: β-amy=608 pg/ml, tau=340 pg/ml p-tau=65 pg/ml; IATI =0.9, with the following values of Sensitivity (S, %) and Specificity (Sp,%): β-amy: S=80.8, Sp=81.8, tau: S=84.6, Sp=75; p-tau: S=76.9, Sp=79.5; IATI: S=88.5, Sp=72.7

CONCLUSIONS: The use of CSF biomarkers provides additional and useful information for the diagnosis and early identification of patients with Alzheimer's disease compared with mild cognitive impairment and other dementias.

Neurological/Neudegenerative diseases

Cod: 1192

CLINICAL AND LABORATORY PERFORMANCE OF CSF STUDIES IN MULTIPLE SCLEROSIS

A. Mendes[1], I. Batista-Fernandes[1], A. Matoso Ferreira[1], A. Torrinha[1], J. Faro-Viana[1]
[1]*Centro Hospitalar De Lisboa Ocidental*

BACKGROUND: Multiple Sclerosis (MS) is the most common primary demyelinating disease of the central nervous system, with a prevalence of 50 per 100000 in Portugal. With the improvement of imaging techniques, the importance of lumbar puncture to assess intrathecal IgG synthesis for the diagnosis of multiple sclerosis (MS) has diminished, also because of differences in the clinical performances reported between studies. Our aim in this study was to assess the clinical performance of our laboratory's CSF investigations, in patients with MS and other inflammatory diseases.

METHODS: Retrospective study of all the 781 CSF samples received in the Immunology Laboratory, from July 2008 to February 2014, for which the immunological study of CSF had been requested. CSF IgG Index (nephelometric quantification, BN ProSpec, Siemens) and CSF oligoclonal band detection (OCB) by isoelectric focusing (Hydrasis, Sebia) results were analyzed. In the Sensitivity (Se), Specificity (Sp), Likelihood Ratios (LR) and ROC curve calculations, only patients with definitely confirmed (87) or excluded (424) diagnosis of MS in their clinical records were considered. The laboratory agreement between the two tests was also investigated.

RESULTS: The IgG Index ROC curve study showed an exclusion cutoff point (LR-=0.1) of 0.45 (Se=97%, Sp=29%) and a confirmation cutoff point (LR+=10) of 0.71 (Se=71%, Sp=93%). OCB Se and Sp were 95% and 91% respectively (LR +=10.4 and LR-=0.05). For the same Se, the IgG index Sp was only 53%. All OCB negative samples had IgG Indexes lower than 1.06 and 97.5% of them were lower than 0.73.

CONCLUSIONS: Our ROC curve derived confirmation cutoff compares well with the one we are using in the Laboratory (0.7) that was also obtained from other studies. OCB studies are superior to IgG Indexes in terms of MS investigation. With IgG Indexes higher than 1.06, there is no need to perform OCB (it will be positive).

Neurological/Neudegenerative diseases

Cod: 1193

EVALUATION OF DIHYDROFOLATE REDUCTASE ENZYME ACTIVITY AND ONE CARBON METABOLISM IN PATIENTS WITH BIPOLAR DISORDER

R.A. Gürkan[1], T. Muftuoglu[1], A. Cosar[3], S. Hira[1], O. Ozcan[1], O.M. Ipcioglu[1], H. Balıbey[2], C. Basoglu[2], M. Gultepe[1]
[1]*GATA Haydarpasa Training Hospital, Biochemistry Department*
[2]*GATA Haydarpasa Training Hospital, Psychiatry Department*
[3]*Girne Military Hospital, Biochemistry Laboratory*

BACKGROUND: Dihydrofolate reductase (DHFR) is the enzyme converting dihydrofolate and folic acid to tetrahydrofolate as their reduced and active form. Reduced folate cofactors have biological significance, carrying 'methyl groups' in various oxidation levels. Loss of intracellular folate cofactors is required to prevent and this is possible by creating glutamate chain connected to them. In order to bind glutamate to the folate cofactors, they must be the reduced form i.e. tetrahydrofolate. If not, dihydrofolate and folic acid can not act as a substrate. Therefore, DHFR is essential for intracellular production of THF. Also, DHFR may affect neurotransmitter synthesis and stability by accepting dihydrobiopterin as substrate tries to ensure the levels of tetrahydrobiopterin (BH4).

METHODS: In our study, in bipolar disorder patients group, DHFR activity, the basic one- carbon metabolism markers of homocysteine, methylmalonic acid, vitamin B12, folate, erythrocyte (RBC) folate, erythrocyte folate sub-groups, serum and urine levels of amino acids were measured. 30 patients with bipolar disorder and 31 healthy persons were participated.

RESULTS: While mean DHFR enzyme activity in patients was 86,1 mol/min/g protein whereas it was 124,9 mol/min/g protein in the controls, p = 0,046. Also patients' RBC- folate level 139,6 ng/ml, while the control group 215,4 ng/ml, p = 0,001. Higher urine MMA levels were found in patients group. Among subgroups of folate, total 5-MTHF% and 5-MTHF-Glu6% were significantly reduced in patients, p = 0,001, p = 0,000. These results were considered as important evidences for methylation imbalance and consequently corrupted neurotransmitter synthesis. Glycine and serine among the amino acids as one-carbon sources were found significantly higher, p = 0,000. Normal homocysteine levels achieved by transsulfuration pathway were concluded. As an indicator of the defective neurotransmitter synthesis, we found high levels of serum phenylalanine, p = 0,005.

CONCLUSIONS: We have detected that DHFR activity is reduced, the metabolism of one-carbon carriers and folate cofactors changed in bipolar disorder. All of these changes could affect neurotransmitter synthesis and kinetics.Further studies on causes should be planned.

Neurological/Neudegenerative diseases

Cod: 1194

THE EFFECT OF PRENATAL EXPOSURE TO RESTRAINT STRESS AND MORPHINE ON POSTNATAL PENTYLENTETRAZOL-INDUCED EPILEPTIC BEHAVIORS AND BODY WEIGHT IN RAT

E. Nakhjiri[3], E. Saboory[2], S. Roshan-Milani[1]
[1]*Department of Physiology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran*
[2]*Neurophysiology Research Center, Urmia University of Medical Sciences, Urmia, Iran*
[3]*Student of Physiology (Master Degree), Studental Research Committee, Urmia University of Medical Sciences, Urmia, Iran*

BACKGROUND: Stressful events during gestation have important effects on the later physical and mental health of the offspring. Prenatal exposure to opiates can have devastating effects on the development of human fetuses, and may induce long-term physical and neurobehavioral changes during postnatal maturation. The present study aimed to identify effects of prenatal restraint stress and morphine exposure on PTZ-induced seizure and body weight in rats.

METHODS: Twenty pregnant rats divided into 4 groups (n=5, each), namely control, stress, saline, and morphine. The rats in stress group exposed to restraint stress on gestational days 15, 16, and 17. The rats in saline and morphine groups received saline and morphine (0.5 ml) subcutaneously in the same days. The control rats were used intact. The pups were weighed at days 1, 15 and 22 after birth (P1, P15, and P22, respectively). On P22, pups were injected with PTZ 60 mg/kg, and epileptic behaviors of each rat were observed for 60 min.

RESULTS: Our data indicated that Prenatal stress and morphine led to low birth weight ($p<0.001$). Also, PTZ-induced seizure was more sever in stressed and morphine treated rats than control and saline treated ones ($p<0.001$). Prenatal stress and morphine exposure affected the male pups more severely than female ones.

CONCLUSIONS: These data emphasize the inhibitory impact of prenatal stress on fetal growth, and neural development. Meanwhile, the effect of prenatal stress and morphine is sex- and age- specific.
KEYWORDS: restraint stress, morphine, seizure, rat

Neurological/Neudegenerative diseases

Cod: 1195

LONGITUDINAL PLASMA LIPID PROFILE IN MULTIPLE SCLEROSIS PATIENTS DURING TWO YEARS OF TREATMENT WITH INTERFERON-BETA

R. Obrenovic[1], I. Vujosevic[1], E. Colak[1], S. Stankovic[1], I. Dujmovic[2], S. Mesaros[2], E. Savic[3], J. Drulovic[2], M. Mostarica Stojkovic[3]

[1]*Center for Medical Biochemistry, Clinical Center of Serbia, Belgrade, Serbia*
[2]*Clinic of Neurology, Clinical Centre of Serbia & Faculty of Medicine, University of Belgrade, Belgrade, Serbia*
[3]*Institute of Microbiology and Immunology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia*

BACKGROUND: Interferon-beta (IFNβ) has been widely used as the first-line disease-modifying therapy for multiple sclerosis (MS). It has been recently suggested that IFNβ might alter plasma lipid profile in treated patients. However, data on longitudinal plasma lipid profile in MS patients treated with IFNβ are scarce and with conflicting results. The aim of our study was to evaluate longitudinal plasma levels of total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglyceride in MS patients treated with IFNβ-1a or IFNβ-1b (both subcutaneously) over two years.

METHODS: The study comprised 43 patients (12 male, 11 female; mean age 35.5±7.6 years; age range 24-51 years) in whom lipid profile analysis has been performed before (baseline,BL) and after 6, 12 and 24 months of treatment with IFNβ. Laboratory investigations were performed in the Center for Medical Biochemistry at the Clinical Center of Serbia. Plasma levels of total cholesterol, LDL, HDL and triglyceride were analyzed by commercial tests on Dimension Xpand, SIEMENS.

RESULTS: Total plasma cholesterol levels at treatment month 6 (median 5.12; range 2.69-8.59 mmol/L) were significantly higher (p=0.0187) than at BL (median 4.31; range 2.95-6.79 mmol/L). Similarly, plasma LDL levels at treatment month 6 (median 3.69; range 1.44-6.73 mmol/L) were significantly higher (p=0.0002) compared with LDL levels at BL (median 3.01; range 1.72-5.23 mmol/L). Plasma levels of HDL at treatment month 6 (median 0.71; range 0,51-1,24 mmol/L) were found to be significantly lower (p<0.0001) than at BL (median 0.91; range 0.48-1.29 mmol/L). Plasma levels of total cholesterol, LDL and HDL either at treatment month 12 or month 24 did not differ significantly from BL levels. Plasma triglyceride levels were found to be significantly increased (p=0.0438) compared with BL values (median 0.87; range 0.34-1.92 mmol/L) only at treatment month 24 (median 1.22; range 0.46-5.70 mmol/L).

CONCLUSIONS: Our results further support a notion that IFNβ treatment in MS patients might originate changes in plasma lipid profile. Further research is needed to investigate whether those changes might reflect changes in disease activity in patients with MS treated with IFNβ.

Neurological/Neudegenerative diseases

Cod: 1196

ALTERED OXIDATIVE STRESS MARKERS' LEVELS, NOT NEUROTROPHIN 4 LEVELS IN PATIENTS WITH BIPOLAR DISORDER AND SCHIZOPHRENIA

S. Erdin[5], E. Onur[3], Ö. Aydemir [2], A.E. Esen Danacı[2], Z. Çubukçuoğlu[1], A. Var [3], Y. Güvenç[3], C. Kabaroğlu[4]
[1]*Bedburg-Hau Psikiyatri Hastanesi, LVR-Klinik, Bedburg, Almanya*
[2]*Celal Bayar Üniversitesi, Tıp Fakültesi, Psikiyatri Anabilim Dalı, Manisa*
[3]*Celal Bayar Üniversitesi, Tıp Fakültesi, Tıbbi Biyokimya Anabilim Dalı, Manisa*
[4]*Ege Üniversitesi, Tıp Fakültesi, Klinik Biyokimya Bilim Dalı, İzmir*
[5]*Van Bölge Eğitim ve Araştırma Hastanesi Biyokimya Laboratuvarı, Van*

BACKGROUND: Schizophrenia is a chronic clinical syndrome giving rise to impairments both in cognitive and emotional functions. Bipolar disorder (BD) is characterised by relapsing manic and depressive episodes. The neurochemical mechanisms underlying the pathophysiology of these diseases are not fully understood. Oxidative stress is the potential damage resulting from prooxidant-antioxidant balance. If the reactive oxygen molecules can not be eliminated effectively, they may lead to peroxidation of proteins, DNA and lipids. Malondialdehyde (MDA) is an end product of lipid peroxidation and a reliable marker for oxidative stress. Glutathione (GSH) and superoxide dismutase (SOD), which are major antioxidants, protect cells against superoxide anion radicals. Neurotrophins are involved in neuroplasticity and continuity of the cell life in the central nervous system. In this study, we investigated total GSH, SOD, NO and MDA levels together with Neurotrophin-4 (NT-4) levels in patients with schizophrenia and bipolar disorders and in healthy controls to establish a possible relationship.

METHODS: 50 euthymic patients with bipolar disorder and 50 schizophrenic patients and 50 healthy subjects were included. NT-4, SOD and NO levels were measured in serum samples, MDA leves were determined in plasma samples, GSH analyses were completed in whole blood samples. For group comparisons ANOVA and Tukey's test (as post hoc test) were used.

RESULTS: Oxidative stress parameters (GSH, MDA, NO, SOD) showed statistically significant differences between the three groups (p= 0.000). The lowest GSH and SOD concentrations were obtained in schizophrenic patients. NT-4 levels were not different between the three groups (p= 0.385). No statistically significant correlation between NT-4 levels and oxidative stress parameters in schizophrenia and BD disorder patients were obtained.

CONCLUSIONS: In schizophrenic patients, while GSH and SOD levels were increased and NO levels were decreased, in bipolar patients there were increased levels of MDA and NO and decreased SOD levels compared to the controls. Observed changes in the oxidant-antioxidant systems in both schizophrenia and bipolar disorders indicate that the oxidative stress may play a role in their pathogenesis.

Neurological/Neudegenerative diseases

Cod: 1197

THE RELATIONSHIP BETWEEN THYROID HORMONE PROFILE AND COGNITIVE DECLINE IN PATIENTS WITH DEMENTIA

Ö. Yavuz[1], A.D. Akçaer[1], N. Özcan[1], T. Karlıdere[2], G. Avcı Aytav[1], M. Şahin[2], A.A. Hişmioğulları[1]
[1]*Department of Medical Biochemistry, Balikesir University, School of Medicine, Balikesir, Turkey*
[2]*Department of Psychiatry, Balikesir University, School of Medicine, Balikesir, Turkey*

BACKGROUND: There is increasing evidence relating alterations of the thyroid function to the pathogenesis of Alzheimer's disease (AD) and other dementias. It has been shown that thyroid hormones play a major role in cognition and thyroid dysfunction increases with age. However, previous studies evaluate the associations thyroid hormone levels and cognitive performance in patients with dementia have yielded inconsistent results. This study aimed to investigate the relationship between thyroid hormone levels and cognitive decline in euthyroid patients with dementia.

METHODS: 24 patients with AD, 9 patients with vascular dementias (VD) and 24 age and gender-matched without dementia controls were included in this study. All of them underwent structural MRI brain scans. Cognitive performance was assessed by the Mini-Mental State Examination (MMSE) test. A MMSE value <24 points was considered as cognitive impairment. The diagnosis of probable AD was made according to the NINCDS-ADRDA criteria. VD was diagnosed according to the NINDS-AIREN criteria for probable VD. Serum Free T3, were measured by competitive immunoenzymatic assay, Free T4, TSH, thyroperoxidase antibody (TPOAb) and thyroglobulin antibody (TgAb) levels by using sandwich enzyme immunoassay technique on chemiluminescence immunoassay analyzer. In statistically analysis, the unique relationship between thyroid status and cognitive function was examined by multivariate linear regression models that were initially adjusted for covariates.

RESULTS: Patients with AD and VD have lower FT3 levels than those controls ($p<0.05$; $p<0.001$). Patients with VD have significatly higher TSH levels than those patients with AD ($p= 0.014$). In AD group, MMSE score is significatly associated with the FT4 levels ($\beta= 0.554$, $p= 0.018$).

CONCLUSIONS: The current results suggested that FT4 levels within reference range were independently associated with the cognitive impairment in the euthyroid patients with AD. It may be concluded that patients with demantia should always be assessed for subclinical hypothyroidism.
Keywords: Alzheimer disease, cognition, thyroid hormone

Neurological/Neudegenerative diseases

Cod: 1198

THERE ARE NO DIFFERENCES IN IL-6, CRP AND HOMOCYSTEINE CONCENTRATIONS BETWEEN FEMALE DESCENDANTS WITH OR WITHOUT A FAMILY HISTORY OF AD

S. Devcic[1], N. Ruljancic[1], L. Glamuzina[1], M. Mihanovic[1]
[1]*Psychiatric Hospital Sveti Ivan, Jankomir 11, 10 000 Zagreb, Croatia*

BACKGROUND: Alzheimer disease (AD) is most present among dementias. A wide range of recent studies have detected inflammation as one of the most influent factors in the appearance and spreading of neurodegenerative brain diseases.

METHODS: We aimed to understand the influence of IL-6, CRP and homocysteine on patients suffering from AD and on their descendants. Three groups of subjects were analyzed, namely: 55 patients suffering from AD, 51 daughters of the diseased patients, and 53 subjects without positive family anamneses on AD.

RESULTS: The results of the conducted research are in accordance with the present scientific knowledge, thus a statistically significant difference for examined parameters has been determined between women suffering from AD and their daughters and control group examinees. There were no significant difference in hsCRP (p=0.601), IL-6 (p=0.582) and Hcy (p=0.188) concentrations between female descendants with or without a family history of AD.

CONCLUSIONS: Obtained results indicate that the increased concentration of inflammatory factors and Hcy in AD patients is a symptomatic rather that causal factor. This is supported by the obtained positive correlation between IL-6 and hsCrp and IL-6 and Hcy in AD patients while there is no such correlation between female subjects with or without a family history of AD.

Neurological/Neudegenerative diseases

Cod: 1199

EFFECTS OF LEPTIN, GHRELIN AND NEUROPEPTIDEY (NPY) ON SWD ACTIVITY AND SOME BIOCHEMICAL PARAMETERS IN WAG/RIJ RATS WITH GENETIC ABSENCE EPILEPSY

D. Sahin[2], B. Oztas[3], H. Kir[1], S. Kuskay[1], N. Ates[2]
[1]*Kocaeli University, Faculty of Medicine, Department of Biochemistry, Kocaeli, Turkey*
[2]*Kocaeli University, Faculty of Medicine, Department of Physiology, Kocaeli, Turkey*
[3]*Sisli Hamidiye Etfal Research and Training Hospital, Department of Biochemistry, Istanbul, Turkey*

BACKGROUND: Some cytokines and oxidative stress with the endogenous peptides are proposed to have significant interactions which are suggestive of a critical role on the spread of epileptic seizures in the brain and the formation of subsequent seizure. We evaluated the effects of endogen peptides; Ghr, Lep and NPY, on the development of nonconvulsive seizure activity, their peripheral antioxidant effects, its role on combatting oxidative stress and effects on cytokines which are the result of systemic immune response in the WAG/Rij rat model for nonconvulsive absence epilepsy.

METHODS: Experiment groups; Group 1 (SF), Group 2 (Lep, 4 mg/kg, i.p.), Group 3 (Ghr, 80 µg/kg i.p.) and Group 4 (NPY, 60 µg/kg i.p.). In all groups, simultaneously monitored EEG recordings were taken during the experiments. Also, in order to evaluate the roles of these endogen peptides on some biochemical parameters thought to have important roles in epileptogenesis, serum sitokines (TNFα, IL1β, IL6), $NO^{\cdot}$, MDA, GSH levels of each group were measured.

RESULTS: Peripheral injection of these peptides administration facilitated spike-wave discharges (SWD) characterizing absence epilepsy in WAG/Rij rats. Leptin administered group than control group; significant increase in serum IL1β and FGF2 levels, significant decrease in serum $NO^{\cdot}$ levels were found. MDA levels were found significantly decreased in ghrelin administered group than the control group. The group administered NPY as opposed to the control group; detected significant increase in serum FGF2 levels and significant decrease in serum MDA levels. On the other hand except Leptin, Ghrelin and NPY do not create a significant change on IL1β, IL-6 and TNF-α levels, suggesting that these peptides might contribute to the development of absence seizures without affecting proinflammatory cytokine parameters.

CONCLUSIONS: This study demonstrates the multidimensional nature of epileptic seizures. Evaluation of the complicated relationship between cytokines, immune system and epilepsy will illuminate future studies by contributing to reveal the role of endogen ligands in the modulation of these relationships.
Key Word: Epilepsy, WAG/Rij, leptin, ghrelin, NPY, TNF-α, IL-1β, IL- 6, FGF-2, galanin, NO, MDA, GSH

Neurological/Neudegenerative diseases

Cod: 1200

DISCRIMINATION OF PSEUDODEMENTIA FROM ALZHEIMER'S DISEASE USING CSF BIOMARKERS

G.M. Sancesario[1], C. Liguori[2], M. Nuccetelli[1], A. Martorana[2], G. Sancesario[2], S. Bernardini[1]
[1]*Dept. of Experimental Medicine and Surgery, University of Rome "Tor Vergata"*
[2]*Dept. of Neuroscience, University of Rome Tor Vergata*

BACKGROUND: Depression and dementia, often in the form of Alzheimer's disease (AD), can occur together in the elderly and may be confused each other. In the depressed elderly, depression itself can affect cognitive performances, diagnosed as pseudodementia secondary to depression, which is an independent process from cognitive impairment caused by dementia. However, depression could be an early symptom or a risk factor of AD, complicating the early and correct diagnosis. Biomarkers can help to identify possibly treatable patients to reverse underlying causes of mood disorder.

METHODS: We evaluate the level of baseline CSF biomarkers β-amyloid42 (Aβ42), total Tau (T-Tau) and Phospo-tau181(P-Tau) in individuals that were admitted to the Neurological Centre of the Tor Vergata General Hospital between 2009-2011 and retrospectively divided in three groups: patients suffering of pseudodementia (n=9), AD (n=12) and other neurological disorder (n=14). Interestingly, after one-two years follow-up the cognitive functions further deteriorated in AD patients, but were stable or improved in the patients with the pseudodementia.

RESULTS: Interestingly, the level of Aβ42 in pseudodementia patients was significantly higher than in AD group (749.10±199.30 vs 322.50±87.51 pg/ml, respectively), and similar to control group (862.90±230.40 pg/ml); moreover, both T-Tau and P-Tau were lower in pseudodementia patients than in AD (185.10±59.49 vs 712.70±327.20 pg/ml for Total-Tau and 32.56±8.09 vs 76.83±24.01 pg/ml for P-Tau, respectively) and similar to control (231.10±78.42 pg/ml for T-Tau and 40.50±11.81 pg/ml for P-Tau).

CONCLUSIONS: These new findings demonstrate that the CSF biomarkers can clearly discriminate patients suffering of pseudodementia from AD patients. A timely diagnosis of dementia or pseudodementia is crucial to the choice of treatment strategy.

Neurological/Neudegenerative diseases

Cod: 1201

VITAMIN B6, B12 AND FOLIC ACID DEFICIENCY IN MIGRAINE AND TENSION TYPE HEADACHE

M. Şeneş[2], A.B.Ç. Sivri[1], Ö. Coşkun[3], S. Üçler[3], S. Yüksel[1], D. Yücel[2]
[1]*Gazi University, Dept. of Medical Biochemistry, Ankara, Turkey*
[2]*Ministry of Health Ankara Training and Research Hospital, Dept. of Medical Biochemistry, Ankara, Turkey*
[3]*Ministry of Health Ankara Training and Research Hospital, Dept. of Neurology, Ankara, Turkey*

BACKGROUND: Migraine and tension type headaches are common and important public health problems having socio-economical aspects. In this study we aimed to investigate the deficiency of vitamin B6, B12 and folic acid and the deficiency markers of these vitamins (Methylmalonic acid, Homocysteine, and Holotranscobalamin) whether they are important in the patogenesis of both diseases and to evaluate clinical performance of markers used to diagnose functional vitamin B12 deficiency.

METHODS: The study included 51 patients with migraine [30 patients without aura (age=39±9 years) and 21 patients with aura (age=34±9 years)] and 15 patients with tension type headache (age=34±9 years).The patients were diagnosed with IHS's ICHD-2 criterias. A control group was formed by 25 healthy persons (age=34±9 years). Serum vitamin B12, holotranscobalamin, folic acid and erythrocyte folic acid were analyzed with immunochemical methods, plasma vitamin B6 and homocysteine with HPLC and serum methylmalonic acid with ESI LC-MS/MS.

RESULTS: Serum vitamin B12, holotranscobalamin, serum and erythrocyte folic acid and homocysteine results were not significantly different between patients and control groups. However vitamin B6 and methylmalonic acid concentrations were significantly different in migraine (p=0.005 and p=0.014, respectively) and in tension type headache groups (p= 0.013 and p=0.006, respectively) than the control group. ROC analysis showed that methylmalonic acid was the most effective marker for diagnosing of functional vitamin B12 deficiency in both patient groups.

CONCLUSIONS: Our results indicate the presence of vitamin B6 and vitamin B12 deficiency in patients with migraine and tension type headache. In migraine and tension type headache, methylmalonic acid is the most effective marker in the diagnosis of functional vitamin B12 deficiency. Methylmalonic acid accumulation in the nervous system may play a role in the pathogenesis of migraine and tension type headache because of its neurotoxic effects.

Neurological/Neudegenerative diseases

Cod: 1202

THE EFFECT OF MALIGNANCY ON THE EXPRESSION OF NEUROTROPHIC FACTORS IN PERIPHERAL BLOOD MONONUCLEAR CELLS

M. Slawomir[4], J. Rybacka – Mossakowska[4], D. Swiniuch [1], J. Gazdulska[2], M. Litwiniuk [1], R. Ramlau [3], W. Kozubski [5]

[1]*Chemoterapy Clinic Greater Poland Cancer Centre*

[2]*Clinical Oncology with The Sub-department of Diurnal Chemotherapy Wielkopolska Center of Pulmonology and Thoracosurgery of Eugenia and Janusz Zeyland*

[3]*Department of Cardio-Thoracicsurgery, Poznan University of Medical Sciences, Poznan, Poland*

[4]*Department of Neurochemistry and Neuropathology Poznan University of Medical Sciences, Poland*

[5]*Department of Neurology Poznan University of Medical Sciences, Poland*

BACKGROUND: Neurological complications in oncological patients include direct effects of malignancy, paraneoplastic neurological syndromes (PNS) and side effects of chemotherapy. Detection of onconeural antibodies satisfies the definitive diagnostic criteria of PNS. However, biological markers and the role of neurotrophic factors in the development of neurological deficit and cognitive impairment await elucidation. The aim of the study was to evaluate the expression of neurotrophic factors in peripheral blood mononuclear cells (PBMC) in relation to neurological and cognitive status of cancer patients.

METHODS: Consecutive 60 patients were included in the study (9 colon cancer, 33 breast cancer, 18 lung cancer patients). Neurological examination, MiniMental State Examination, Trail Making Test (TMT) and Hamilton depression scale were performed. PBMC were isolated by density gradient centrifugation. Nerve growth factor (NGF) and neurotrophin 4 (NT4) in PBMC was evaluated by means of ELISA and expressed in pg per mg of protein.

RESULTS: Neurological deficit was observed in 8,8% of patients. Autoantibodies were detected in 33% of patients: 17% antibodies against nucleosom antigens (ANA), 7% anti-neuroendothelium, 3% – anti-MAG (myelin-associated glycoprotein), 3% anti-myelin, 3% coexisting ANA with anti-GFAP (glial fibrillary acidic protein). Worsening in TMT B were observed in lung cancer (143.00; 112.65-165.88 s) compared to breast (86.00; 45.22-104.62 s; P=0.0006) and colon cancer (77.00; 49.88-174.06s; P=0.0484). The expression of NGF in PBMC in breast cancer (0.00; 0.00-23.88pg/mg protein) was decreased compared to colon (18.43; 0.00-44.66pg/mg protein, P=0.0126) and lung cancer (16.39; 0.00-43.70pg/mg protein, P=0.0386). Multivariate analysis in the model including the expression of NGF, NT4, autoantibodies, TMT B showed significant (P=0.045) correlation with NGF expression in PBMC (B=1.4228; r=0.4037).

CONCLUSIONS: NGF expression in PBMC is affected independently from cognitive dysfunction in cancer patients and is downregulated during the course of breast cancer. Trail Making Test B was the most useful tool for the evaluation of cognition, which is particularly impaired in lung cancer patients.

Neurological/Neudegenerative diseases

Cod: 1203

BRAIN CATALASE AND SUPEROXIDE DISMUTASE IN THE STREPTOZOTOCIN- RAT MODEL OF SPORADIC ALZHEIMER'S DISEASE TREATED WITH THE IRON- CHELATOR M 30

E. Sofic[2], A. Sapcanin[2], I. Tahirovic[2], M. Youdim[3], P. Riederer[1]

[1]*Clinical Neurochemistry, Clinic and Polyclinic for Psychiatry, Psychosomatics and Psychotherapy; University - Hospital Wuerzburg, and NPF – Center of Excellence Laboratories for Neurodegenerative Disorders – Wuerzburg, Germany*

[2]*Department of Chemistry, Faculty of Science, University of Sarajevo, Sarajevo, Bosnia and Herzegovina*

[3]*Eve Topf Center for Neurodegenerative Diseases Research and Department of Molecular Pharmacology, Faculty of Medicine, Technion, Haifa, Israel*

BACKGROUND: Low doses of streptozotocin (STZ) in rats produces regionally specific brain neurochemical changes that are similar to those found in the brain of patients with sporadic Alzheimer's disease (sAD). The overall peroxidation activity in regional brain tissue from animals treated with STZ and M-30 [5-(N-methyl-N-propargylaminomethyl)-8-hydroxyquinoline] was estimated by determination of the activities of Cu/Zn superoxide dismutase (SOD) and catalase (CAT)- which detoxicate reactive oxygen species - superoxide and hydrogen peroxide, in brain regions where the STZ pathophysiological changes radical are most severe.

METHODS: Male Wistar, 3 to 4 month old rats, were used in the study. Peroral pre-treatment of adult male Wistar rats with a daily M-30 5 or 10 mg/kg dosis was done for 5 days followed by a a single injection of STZ 1 mg/kg icv. CAT and SOD were measured in five different brain regions: hippocampus (HPC), brain stem (BS), cerebellum (CB), striatum (S) and frontal cortex (FC) from the controls (C) and STZ treated rats. CAT and SOD activity was measured by using commercial colorimetric assay kits.

RESULTS: The results showed that the CAT activity in BS, CB and HPC of the STZ treated rats is significantly lower than in C ($p<0.05$ for BS and CB groups, and $p<0.01$ for HPC). However, CAT activity in BS of rats treated with M-30 was statistically higher than in C ($p<0.05$).

CONCLUSIONS: This data demonstrates a beneficial effect of the iron chelator M-30. SOD activity is statistically different among the various brain regions studied. M-30 (10 mg/kg) significantly increases SOD activity of STZ treated rats in the HPC and FC ($p < 0,001$). Our findings are in line with the assumption that reactive oxygen species contribute to the pathogenesis of STZ in a rat model of sAD.

Neurological/Neudegenerative diseases

Cod: 1204

EVALUATION OF COMBINATION OF S100B PROTEIN, GFAP, MMP-9, AND CRP TO PREDICT NIHSS DETERIORATION IN ISCHEMIC STROKE

Y. Surjawan[2], S. As'ad[2], T. Ranakusuma[1], A. Wijaya[2]
[1]*Department of Neurology, Medical Faculty of Indonesia University*
[2]*Medical Faculty of Hasanuddin University*

BACKGROUND: Early prediction of stroke evolution is important to give an aggressive treatment for patient with a worsening tendency. The presence of the blood brain barrier hampers the early detection of brain cell markers in the blood. Inflammation process, that is induced by the presence of brain cell damage, is important in stroke progression. This study aimed to evaluate the combination of S100B protein and glial fibrillary acidic protein (GFAP) as brain cell markers, with matrix metalloproteinase-9 (MMP-9) and C-reactive protein (CRP) as inflammatory markers to predict National Institute of Health Stroke Scale (NIHSS) deterioration in ischemic stroke patients.

METHODS: This was an observational prospective study that involved 143 ischemic stroke patients who were admitted to hospital not more than 72 hours after the onset. Blood for biomarkers examination was collected between 48 to 72 hours after the onset. The presence of NIHSS deterioration was determined if there was a worsening NIHSS classification/ score.

RESULTS: This study showed that the concentration of all biomarkers was significantly higher in subjects whose outcome were worse after hospitalization ($p < 0.05$). Subjects with high level of biomarker had a greater risk to get NIHSS deterioration (S100B: OR = 18.1, p = 0.006; GFAP: OR = 23.6, p = 0.003; MMP-9: OR = 18.1, p = 0.006; CRP: OR = 17.2, p = 0.007). Logistic regression analysis showed that combination of 3 markers, GFAP, MMP-9, and CRP, could predict the occurence of NIHSS deterioration (R2 = 52.4 %, p = 0.000). However, the best true prediction was yield with the combination of GFAP and CRP (AUC = 92.5 %, p = 0.001). Subject with high level of both markers have the highest probability (36.6 %) to get NIHSS deterioration.

CONCLUSIONS: Examination of GFAP and CRP at 48 to 72 hours after stroke onset could predict the presence of NIHSS deterioration in ischemic stroke patient.

Neurological/Neudegenerative diseases

Cod: 1205

OXIDATIVELY INDUCED MACROMOLECULAR DAMAGE AND EXPRESSION OF DNA REPAIR ENZYMES IN ALZHEIMER'S DISEASE

G. Tuna[2], G.H. Islekel[2], F. Ozkaya[3], G.G. Yener[4], F.G. Kirkali[1]

[1]*12505 Viewside Drive, North Potomac, 20878, Maryland, USA*

[2]*Department of Medical Biochemistry, School of Medicine, Dokuz Eylul University, Izmir, Turkey*

[3]*Department of Molecular Medicine, School of Medicine, Dokuz Eylul University, Izmir, Turkey*

[4]*Department of Neurology, School of Medicine, Dokuz Eylul University, Izmir, Turkey and Brain Dynamics, Cognition and Complex Systems Research Center, Istanbul Kültür University, Istanbul, Turkey*

BACKGROUND: Alzheimer's disease (AD) is the most common neurodegenerative disorder of the elderly. Free radical-mediated oxidatively induced macromolecular damage plays a role in basic neurodegenerative mechanisms in AD. In living organisms, DNA repair mechanisms exist to repair oxidatively induced DNA damage.

METHODS: In this study, oxidatively induced DNA, lipid, protein, carbohydrate damage and the mRNA expressions of OGG1 and NEIL1 DNA glycosylases were studied in peripheral blood of AD patients and healthy volunteers. DNA base lesions in 33 AD and 37 control subjects were determined by isotope dilution gas chromatography/tandem mass spectrometry. The mRNA expression levels of OGG1 and NEIL1 were measured by RT-PCR in AD (n=15) and control individuals (n=20). The levels of protein oxidation marker 3-nitrotyrosine was measured with ELISA, malondialdehyde (MDA), one of the lipid peroxidation products and $N\varepsilon$-carboxymethyllysine (CML) -an advanced glycation end product- levels were investigated with HPLC in 44 AD and 45 control subjects.

RESULTS: The level of 4,6-diamino-5-formamidopyrimidine (FapyAde), a lesion of base damage, were significantly higher in AD patients compared to those in control subjects ($p<0.05$). There were no statistically significant differences between AD and the control groups in 8-hydroxyguanine, 2,6-diamino-4-hydroxy-5-formamidopyrimidine, 5-hydroxy-5-methyl-hydantoin and 5-hydroxycytosine DNA bases. The thymineglycol, 5-hydroxymethyl-uracil, 5-hydroxyuracil, 5,6-dihydroxyuracil damages were not detected neither in AD patients nor in the control group. The mRNA expression levels of NEIL1 and OGG1 showed no significant difference between the two groups. The levels of MDA were significantly higher in AD patients compared to those in control subjects ($p<0.05$) whereas no statistically significant difference were found between AD and control groups in 3-nitrotyrosine and CML levels.

CONCLUSIONS: This study is noteworthy since markers of oxidative macromolecular damage and expressions of DNA repair enzymes have been studied extensively in AD. Oxidative macromolecular damage plays an important role in pathogenesis of AD. It is important to be able to detect which molecule is involved at which level of this process, in understanding the etiology and selection of treatment strategies for this disease.

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Cod: 1206

CIRCULATING LEVELS OF Aß1-40, Aß1-42, Aß OLIGOMERS, SRAGE, ESRAGE, SLRP1 AND NEPRILYSIN IN ALZHEIMER'S DISEASE

F. Uysal[3], M. Örmen[1], M. Uysal[2], B. Onvural[1]
[1]*Dokuz Eylul University, Medical Biochemistry Department, Izmir*
[2]*Gaziosmanpasa University, Anatomy Department, Tokat*
[3]*Tunceli State Hospital, Laboratory of Biochemistry, Tunceli*

BACKGROUND: Beta-amyloid (Aß), the key component of the amyloid plaque, has been shown to be central to Alzheimer's disease (AD) pathogenesis. Over production of Aß is observed in the familial type AD, but there is no evidence if this situation is also observed in the sporadic type AD. According to a widely accepted view, Aß oligomers are responsible for the formation of the disease. The aim of the study is to determine the plasma levels of Aß1-40, Aß1-42 and Aß oligomers and the serum levels of neprilysin and sLRP. We also determined the serum levels of sRAGE and esRAGE which are the secreted forms of RAGE.

METHODS: A total of 100 participants (50 patients with AD and 50 healthy controls) were enrolled in the study. Circulating levels of Aß1-40, Aß1-42, Aß oligomer, sRAGE, esRAGE, sLRP and neprilysin were determined by the ELISA method. Simultaneously, routine biochemical and hematologic parameters were measured by the autoanalyzer.

RESULTS: Aß oligomer levels in patients after staging a severe stage were significantly lower than mild stage and control. Serum sRAGE was significantly decreased in the severe stage when compared with the moderate stage. Also, serum esRAGE was significantly lower in the severe stage than the mild stage. Serum esRAGE was significantly higher in the AD patients treated with galantamin than patients treated with donepezil and rivastigmine. A correlation was found between the Aß1-42 and sRAGE in AD and control groups. In both groups, the esRAGE/sRAGE ratio was determined as 1:3. A correlation was found between the age and Aß1-42 in AD patients. Additionally, in AD patients, MMSE correlated with Aß oligomer, sRAGE and esRAGE.

CONCLUSIONS: We think that the blood levels of Aß1-40, Aß1-42, sRAGE, esRAGE, sLRP and neprilysin could not be used as a diagnostic marker in AD patients. However, plasma Aß oligomers could be used for this purpose in patients in the severe stage. We report, for the first time, serum levels of esRAGE and neprilysin in AD patients. In addition there is only one report, besides our study, for the measure mean of blood levels Aß oligomers in AD patients. For these reasons, additional studies are greatly needed to determine whether these parameters possess the capacito to aid in the clinical diagnosis of AD.

Neurological/Neudegenerative diseases

Cod: 1207

INTRATHECAL IMMUNOGLOBULIN G AND MRZ REACTION IN DEMYELINATING DISEASES OF CENTRAL NERVOUS SYSTEM

I. Vukasović[1], A. Tešija Kuna[1], V. Bašić Kes[2], M. Lisak[2], N. Vrkić[1]
[1]*Clinical Institute of Chemistry, Medical School University Hospital Sestre Milosrdnice, Zagreb, Croatia*
[2]*University Department of Neurology, Medical School University Hospital Sestre Milosrdnice, Zagreb, Croatia*

BACKGROUND: We aimed to assess the MRZ reactivity (MRZR) in comparison with oligoclonal IgG bands (OIgG) and positive intrathecal IgG fraction (IgG IF) in demyelinating diseases of central nervous system (DD) because of its higher specificity for chronic autoimmune inflammation.

METHODS: 48 inpatient subjects with multiple sclerosis (MS) and 43 with other demyelinating diseases (ODD) were enrolled in the study. Paired samples of serum and cerebrospinal fluid (CSF) were analyzed. OIgG bands were detected by semi-automated method of isoelectric focusing with immunofixation (SEBIA, France). IgG and albumin were determined by immunonephelometry (Siemens, Germany) and IgG IF were calculated from CSF/serum quotients using Reiber's formula. Measles (M), rubella (R), varicella zoster (Z) and herpes simplex (H) virus-specific IgG antibodies were detected both in serum and CSF by enzyme immunoassay (Euroimmun,Germany). The specific antibody index (AI) was calculated, values ≥1.5 were considered indicative for intrathecal IgG synthesis against the respective pathogen. MRZR was considered positive if two or more AI values were ≥1.5.

RESULTS: OIgG were positive more frequently than IgG IF both in MS (85% vs 52%, P=0.049) and in ODD cohorts (40% vs 12%, P=0.0105). Comparing MS and ODD, both IgGIF and OIgG was found more frequently in MS (85% vs. 40%, p=0.0062 and 52% vs. 12%, p=0.0008, respectively). OIgG was found in 74% of MS and in 32% of ODD subjects who were IgG IF negative (p=0.0201). Positive MRZR was found in 31% MS and 5% ODD subjects (p=0.0034). Along with OIgG in 39% MS and 12% ODD patients (p=0.0898); along with IgG IF in 57% MS and 40% ODD (p=0.6473). Positive MRZR was found in 9% MS and 3% ODD without IgG IF (p=0.3006), but in none of OIgG negative MS or ODD patients.

CONCLUSIONS: OIgG reveals more subjects with positive intrathecal synthesis than IgG IF in patient with DD. Although MRZR was significantly more prevalent in MS than ODD our results couldn't confirm its additional value in differential diagnosis. However, this conclusion should be tested in a larger cohort.

Neurological/Neudegenerative diseases

Cod: 1208

ASSOCIATION OF VEGF SNPS (-2578C>A,-1154G>A AND +936C>T) AND LIPID PROFILE WITH AORTIC CALCIFICATION

B.K.Y. Yadav[1], B.S. Shin[2]

[1]*Department of Biochemistry, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal & 2. Research Institute of Clinical Medicine of Chonbuk National University-Biomedical Research Institute of Chonbuk National University*

[2]*Department of Neurology, Chonbuk National University Medical School,Jeonju, Republic of South Korea*

BACKGROUND: Aortic calcification (AC), a disorder in the aorta of the heart, is principally caused due to abnormal metabolism of calcium that leads to deposition of large amounts of calcium in blood vessels.AC is one of the leading cause of aortic valve replacement and third leading cause of cardiovascular disease. The objective of this study was to find the association between aortic calcification and VEGF SNPs (-2578C>A,-1154G>A and +936C>T) and to evaluate the association of these SNPs with biochemical parameter in relation to aortic calcification.

METHODS: Aortic calcification was diagnosed by examining the posteroanterior chest X-rays by radiologist and graded into four groups. The real-time polymerase chain reaction with melting curve analysis in LightCycler was used to genotype the VEGF SNPs.

RESULTS: A significant genetic difference was found only between the aortic calcification and control group with VEGF SNP -2578C>A but haplotypes C-G-A and T-A-C of +936/-1154/-2578 were significantly difference in control and aortic calcification and could enhance the aortic calcification development with the odd ration 1.50 and 2.79 ,respectively. By regression analysis, it was found that age, hypertension, Diabetes, dyslipidemia, hyperhomocysteinemia were found significantly different with the different genotypes of VEGF SNPs which may induce aortic calcification development.

CONCLUSIONS: Age, hypertension, diabetes, dyslipidemia, and hyperhomocystenemia were established as aggravating factors for the aortic calcification in association with different VEGF genotypes.

Neurological/Neudegenerative diseases

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ASSOCIATION OF SOD2 (RS4880) GENE POLYMORPHISM, PLASMA LIPID AND LIPOPROTEIN WITH STROKE

R.K. Yadav[2], R. Yadav[1]
[1]*Center for Public Health Laboratory, Kathmandu, Nepal*
[2]*Gandaki Medical College and Teaching Hospital, Pokhara, Nepal*

BACKGROUND: Reactive oxygen species (ROS), by-product of oxygen metabolism, are small molecules which are unstable, highly reactive and short-lived. ROS play an important role in the development of vascular disease, including hypertension, atherosclerosis, diabetes, cardiac hypertrophy, heart failure, ischemia-reperfusion injury, and stroke. ROS are usually produced at very low concentration which is controlled by endogenous antioxidant system that include superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT) and antioxidant vitamins (E and C). ROS can accelerate oxidation of LDL, forming ox-LDL, which is not recognized by the LDL receptor leading to foam cell formation, a major cause of atherosclerosis which ultimately may cause stroke. Superoxide is dismutated to H_2O_2 by SOD which is further converted to H_2O and O_2 by glutathione peroxidase or catalase in the mitochondria and the lysosomes. The functional polymorphism SOD2 (rs4880) affects its localization and ability to scavenge superoxide radicals. The present study was aimed to investigate the association of SOD2 polymorphism in the development of stroke.

METHODS: DNA was amplified and the single nucleotide polymorphism (SNP) in SOD2 was investigated by melting curve analysis using real-time PCR. Plasma lipid and lipoprotein were measured in automated clinical chemistry analyzer, Hitachi, Japan.

RESULTS: Significant differences in the T-allele and CT/TT genotype frequency of SOD2 (p=0.005 and 0.016, respectively) between the control and stroke patients were observed. Significant differences were observed for HDL–cholesterol, LDL/HDL and Cholesterol/HDL, lipoprotein-a, apoprotein-B and glucose level between the controls and cases.Interestengly, Cholesterol, non HDl-choleterol and glucose were significantly different with different genotypes of SOD2 genotypes.

CONCLUSIONS: Our result indicates that SOD2 genetic polymorphism is involved in the development of strokes and thus warrants further investigation.

Neurological/Neudegenerative diseases

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CILOSTAZOL AND PIOGLITAZONE ATTENUATES ISCHEMIA/REPERFUSION-INDUCED ADAMTS16 IN RABBIT SPINAL CORD

Y. Yaral[1]
[1]*Turgut Ozal University, Medical School*

BACKGROUND: The aim of this work was to investigate the ADAMTS16 protein levels and the effect of cilostazol (CL) and pioglitazone (CL) in ischemia/reperfusion (I/R) model in rabbit spinal cord. CL is a compound for effective treatment of peripheral ischemia. CL is a selective phosphodiesterase-3 and has vasodilator and anti-thrombotic properties. PG a potent synthetic agonist of PPARγ, was shown to ameliorate I/R injury in different diseases. PG was shown to control neuroinflammation in many nervous system-related disorders. ADAMTS16 is a member of ADAMTS (A disintegrin and metalloproteinase with thrombospondin motifs) family and is expressed many in human tissues (Brain, kidney and lung) but little is known about its function in disease pathogenesis. Recently, ADAMTS16 reported as candidate gene in controlling blood pressure. Therefore, we carried out this experiments to check whether CL or PG has an effect on I/R induced ADAMTS16 protein level.

METHODS: New Zealand rabbits weighing 3–3.5 kg were used. Rabbits were subjected to standard I/R to perform SCI at L4-L6 levels through occluding aorta distally and proximally by clamping renal and common iliac arteries, respectively, for 30 minutes, followed 3-day reperfusion. Experiment was comprised of four groups. In the sham-operated group (n=4), abdominal aorta was exposed without I/R procedure. In I/R group (n=8), abdominal aorta was clamped without drug treatment. Drug-given groups were treated with 30 mg/kg/day CL (n=9) or 10 mg/kg/day PG (n=9) 3 days before I/R procedure. Spinal cord tissues were studied with polymerase chain reaction (PCR) and Westen Blotting.

RESULTS: ADAMTS16 cDNA was detected in all groups. The ADAMTS16 protein level was determined using Western Blot. ADAMTS16 protein level was significantly increased in I/R group compared to the sham-operated group ($P<0.01$;1.8 fold). CL or PG effectively reduced ADAMTS16 protein levels compared to the I/R group, and this attenuation was significant ($p<0.01$).

CONCLUSIONS: To the best of our knowledge, we found for the first time, that ADAMTS16 protein level was higher in I/R group. CL or PG reversed this effect. Our preliminary report demonstrates that ADAMTS16 might have a role in I/R pathogenesis, and ADAMTS16 might be a CL and PG regulated gene.

Neurological/Neudegenerative diseases

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THE EFFECTS OF BOGMA RAKI AND WALNUT CONSUMPTION ON EXPRESSION OF NR2A AND NR2B IN RAT HIPPOCAMPUS

Z. Yönden[1], O. Özcan[1], H.M. Okuyan[4], E. Geyik[5], C. Zeren[2], G. Açıkgöz[4], H. Kokaçya[3], B. Hamamcı[4], Y.Z. İğci[5]
[1]*Mustafa Kemal University, Faculty of Medicine, Department of Biochemistry*
[2]*Mustafa Kemal University, Faculty of Medicine, Department of Forensic Medicine*
[3]*Mustafa Kemal University, Faculty of Medicine, Department of Psychiatry*
[4]*Mustafa Kemal University, Hatay Vocational School of Health Services*
[5]*University of Gaziantep, Faculty of Medicine, Department of Medical Biology*

BACKGROUND: Illegal alcohol consumption is an important public health problem in Turkey, same as in Europe. Earlier we have reported that Bogma Raki (Homemade illegal alcohol) has a lot of toxic compounds such as metanol, acetic acid as compared with commercial Raki. N-Methyl-D-aspartate (NMDA) is an iontropic glutamate receptor, which is involved in many CNS functions, including synaptic plasticity, learning, and memory. In this study, we aimed to investigate that effect of Bogma raki and walnut consumption on expression of NR2A and NR2B in rat hippocampus.

METHODS: In the experiments, 36 Wistar albino adult male rats weighing 250±20 g were used. The rats were randomly divided into four groups; A : Control group (n=9), B: Walnut group (n=9), C: Bogma Raki group (n=9) and D: Bogma Raki-Walnut group (n=9). Saline, Bogma Raki (9.2 ml/kg/day) and Walnut (10g/kg/day) were given orally for 30 days. At the end of the experiments, hippocampus tissues were removed for analysis. RNA isolated from tissues samples and used for gene expression analysis. Expression levels of NR2A and NR2B genes were examined using Real-Time PCR method.

RESULTS: compared with control group, NR2A mRNA level of bogma Raki group C were significantly decreased ($p<0.05$) but no significant difference were found in expression of NR2B mRNA levels in groups.

CONCLUSIONS: In this study it has been shown that illegal alcohol consumption may alters expressions of NR2A and NR2B in hippocampus and this may also plays important role in NMDA receptor-associated diseases such as Alzheimer's Disease.
Key words: NR2A, NR2B, Bogma Raki, Walnut
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