P0010

Association Analysis of Bace1 C786g and Apolipoprotein E Polymorphisms in Alzheimer's Disease

A. Juhasz, A. Rimanoczy, A. Feher, M. Pakaski, J. Kalman, Z. Janka. *Department of Psychiatry, University of Szeged, Szeged, Hungary*

Amyloid β peptide (Aβ) is one of the hallmarks of Alzheimer's disease (AD). Aβ is a major constituent of extracellular plaques and is derived from the proteolytic processing of the β-amyloid precursor protein (APP). The β -site APP cleaving enzyme (BACE1) is a candidate risk factor for AD because of its involvement in generating Aβ. Its gene is located on chromosome 11q23.3.

The aim of this study was to investigate the BACE1 exon5 C786G polymorphism in AD and healthy control subjects and correlate it with the apolipoprotein E (ApoE) 4 allele status.

Blood was collected from 180 patients with AD and 102 healthy control subjects. The diagnosis of probable AD was based on NINCDS-ADRDA criteria. DNA was extracted by Roche kit. The ApoE and BACE1 polymorphisms were genotyped by RFLP-PCR. The results were analyzed by SPSS program.

There was a higher frequency of ApoE 3/4 genotype and ApoE 4 allele occurrence in AD patients (33%) than in the controls (10%). Regarding BACE1 C786G polymorphism there were no statistically significant differences between the investigated groups in the genotype and allele frequencies. In the presence of ApoE 4 allele the BACE1 GG and CG genotypes occurred in higher frequency in AD (10.2% and 22.2%) than in the control (2.0% and 5.1%) group.

These results suggest that BACE1 gene polymorphism itself is not associated with AD, but in the presence of ApoE 4 allele the GG and CG genotypes might be risk factors in the development of AD.

Supported by:ETT19804/2006, OTKA T046152/2004, K60589/2006.

P0011

Appearance of macromolecular form of Fibronectin in dementia patients

J.W. Leszek [1], A. Lemanska [2], A. Kiejna [1], I. Kątnik- Prastowska [2]. [1] *University of Wroclaw, Department of Psychiatry, Wroclaw, Poland* [2] *University of Wroclaw, Department of Chemistry and Immunochemistry, Wroclaw, Poland*

Background: Fibronectin(FN) is a multidomain adhesive glycoprotein present in connective tissue on cell surfaces in insoluble fibrilar form.

Objective: Because of reported experimental evidences for a very large elasticity of the FN molecule and in view of the hypothesis that conformational changes precede its function, we were interested in analyzing: 1)the eventual appearance of macromolecular form of fibronectin, 2) the expressions of the cellular, collagen, fibrin, and C-terminal fibronectin domains in the blood plasma of Alzheimer's(14 patients, mean age 70.2+/-6.5), vascular dementia patients(24 patients, mean age 73.1+/-5.3), and age-matched control(30 subjects, mean age 73.4+/-7.4).

Methods: The fibronectin domain concentrations were determined by ELISA using panel of domain-specific monoclonal antibodies. Western immunoblotting by the use a monoclonal antibody was performed to analyze the FN molecular forms.

Results: Immunoblotting pattern of plasma fibronectin of both dementia groups and age-matched group consisted of two FN bands(220-230 kDa), and some of them showed additionally of 2-3 macromolecular bands having molecular masses 260 and 350 kDa. However, the appearance of macromolecular fibronectin forms(260 and 350 kDa) happened more frequently in Alzheimer's dementia(85% of samples)than in samples with vascular dementia(50%) as well as in age-matched control(53%).Among the analysed domain expression on fibronectin, only the concentration of the C-terminal fibronectin domain(747.1+/-79 ug/ml)was significantly higher($p<0.004$)than that in age-matched control group(635.7+/-120ug/ml, whereas its level was negligible different in vascular dementia(659.2+/-137ug/ml).

Conclusions: The occurence of macromolecular forms of fibronectin seems to be associated more frequently with Alzheimer's dementia. Increased concentration of C-terminal domain suggests some conformational alterations of fibronectin present in Alzheimer's samples.

P0012

Mixed dementia: A cohort study

N.M. Mikhailova. *Alzheimer's Disease Department, Mental Health Research Center RAMS, Moscow, Russia*

Alzheimer's disease associated with cerebrovascular disease is now considered as the most frequent type of dementia. The aim is to study psychopathological features and clinical evolution of mixed cases of dementia with alzheimer's and vascular brain affection. 94 patients with mixed dementia were admitted to day-clinic of Moscow Alzheimer's disease center in 2005-2006. Two control groups made up 38 patients with vascular dementia and 40 patients with Alzheimer's disease without vascular risk factors. MRI, neuropsychological examination, EEG-mapping, ultrasonography of intracranial vessels and APO E genotyping are used. The cases of mild and moderate dementia are included. Mixed dementia is four times more frequent in females since m/f ratio in VaD and AD is 1:2. Mean age for the moment of the first examination is 74,9 years for mixed cases, 71,4 years is for patients with VaD and 70,1 years for patients with AD. Mixed dementia had more frequent late onset than VaD and AD. Mild dementia is more common in patients with VaD. Non-cognitive neuropsychiatric disorders are presented in 64,8% of mixed dementia, in 57,5% of AD and in 73,6% of VaD. Transient ischemic brain attacks were in history of 71,1% VaD cases and in 13,8% of mixed dementia since were absent in AD cases. MRI picture is very different in three groups of patients. Ventricular and subarachnoidal space enlargement was common, but signs of leukoaraiosis as well as number and localization of vascular focal changes are very various. A longitudinal (5-years follow-up) prospective study is proposed.

P0013

Compression of Risperidone and Olanzapine in behavioral disturbances of Alzheimer

N. Mokhber [1], M.R. Azarpazhooh [2]. [1] *Psychiatry Department, Mashad University, Avicenna Hospital, Mashad, Iran* [2] *Neurology Department, Mashad University, Ghaem Hospital, Mashad, Iran*

Introduction: There are some doubts about therapeutic effects of olanzapine and risperidone two antipsychotic drugs on behavioral disturbances in patients with Alzheimer's disease and concerns about safety have emerged. We assessed the effectiveness of these two atypical antipsychotic drugs in outpatients with Alzheimer's disease.

Methods & Materials: In this double-blind trial, 69 outpatients with Alzheimer's disease and psychosis, aggression, or agitation

https://doi.org/10.1016/j.eurpsy.2008.01.303 Published online by Cambridge University Press

were randomly assigned to receive olanzapine (dose, 2.5- 7.5 mg per day) or risperidone (dose, 0.5-4.5 mg per day). Patients were followed for up to 10 weeks. The main outcomes were the scores of the Clinical Global Impression of Change (CGIC) scale and Brief Psychiatric Rating Scale (BPRS).

Results: There were no significant differences among treatments with regard to improvement in risperidone and olanzapine group on the CGIC (3.2±4.3 vs. 3.5±5.8 & P Value=0.564) and BPRS scale (8.2±9.2.vs. 8.8±9.2 & P Value = 0.522) .Furthermore, although the number of patients who had left the study cause of side effects, was greater in risperidone group , sedation and headache are more common with olanzapine than risperidone.

Conclusion: Both risperidone and olanzapine might be useful and reasonable treatment for patients who suffering from behavioral disturbances due to psychosis in Alzheimer disease

P0014

The outcome of dementia in Clinical County Hospital of Arad

D.M. Podea, R.M. Chenderes. *Department of Psychiatry, West University Vasile Goldis, Arad, Romania*

Objective: The aim of this study is to appreciate the outcome of patients diagnosed with dementia in the Psychiatric Clinic of Arad, Romania.

Material and Methods: The study was conducted on 40 patients admitted in the Clinic during January2006-July2007. They were diagnosed with Alzheimer and mixed dementia. The diagnosis was established according to ICD-10 and DSM-IV-TR operational criteria.

The patients were evaluated three times, at the admission, at discharge and after 6months of clinical evolution and treatment through psychiatric exam and psychological assessment (MMSE-Mini Mental State Evaluation and QI-Quotient of Intelligence).

The patients were treated with acetylcholinesterase inhibitors(donepezil) and NMDA(N-metil-D-aspartat)inhibitors(memantine). Some patients(n=20) were treated with occupational psychotherapy also.

Results and Conclusions: The diagnosis of mixed dementia is more frequent than Alzheimer dementia(26vs.14). Almost all the patients were professionally inactive(n=34). The QIis in direct relationship with the MMSEscores at the admission and in inverse relationship with the hospitalization period. The hospitalization period is in inverse relationship with the MMSEscores. Almost all the patients present a moderate cognitive impairment, according to MMSE score (n=24). Temporal and spatial orientation, registration and recall were affected to all patients. The improvement of cognitive impairment, evaluated at discharge, was minimal. 14 patients presented no improvement at all and the others 26 recorded a 1 or 2 points improvement. After 6 months of treatment, the average of MMSE scores increased with 0,9 points versus 0,4 points after discharge. Those patients who were treated with ooccupational psychotherapy have had a favorable improvement of average MMSE scores(1,4points versus 0,3points).

P0015

Reduction in brain atrophy associated with Ethyl-Eicosapentaenoic Acid in Patients with Huntington's disease

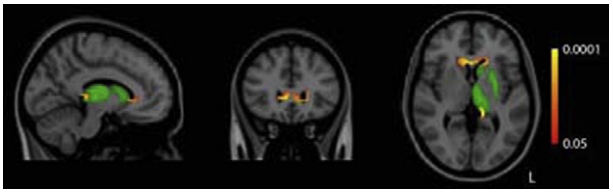
B.K. Puri [1], G.M. Bydder [2], A. Clarke [3], M.S. Manku [3], C.F. Beckmann [4]. [1] *MRI Unit, Imaging Sciences Department, MRC CSC, Imperial College London, Hammersmith Hospital, London, UK* [2] *Department of Radiology, University of California, San Diego, School of Medicine, San Diego, CA, USA* [3] *Amarin Neuroscience Limited, The Oxford Science Park, Oxford, UK* [4] *Clinical Neuroscience Department, Imperial College London and FMRIB Centre, University of Oxford, Oxford, UK*

Background and Aims: Ultra-pure ethyl-EPA, a semi-synthetic, ethyl ester of eicosapentaenoic acid, is associated with clinical improvement in motor functioning in Huntington's disease. The aim was to determine the extent to which it might reduce the rate of progress of cerebral atrophy.

Methods: High-resolution MRIs were acquired at baseline, six months and one year in 30 patients with stage I or II Huntington's disease who took part in a randomized, double-blind, placebo-controlled trial of 2 g daily ethyl-EPA. For each subject and each pair of T1 images, the two-timepoint percentage brain volume change was estimated in a double-blind fashion using SIENA (Structural Image Evaluation, using Normalisation, of Atrophy), Version 2.5, part of FSL (version 4.0, http://www.fmrib.ox.ac.uk/fsl).

Results: Figure 1 shows areas of significant group-level reduction in brain atrophy between patients receiving ethyl-EPA and those receiving placebo (red-yellow: the colour bar shows the p-value under the null hypothesis of no change). Significant changes are observed at the head of the caudate and the posterior section of the thalamus.

Conclusion: Treatment with ethyl-EPA is associated with significant reduction in brain atrophy in Huntington's disease, particularly in the caudate and thalamus. No other drug tested in Huntington's disease has shown this effect (fx).



P0016

Alzheimer's disease – type 3 diabetes?

M. Flirski, T. Sobow, I. Kloszewska. *Department of Old Age Psychiatry and Psychotic Disorders, Medical University of Lodz, Lodz, Poland*

The negative influence of diabetes mellitus (DM), both insulin-dependent and non-insulin dependent on the level of cognitive functions has been proven in multiple studies. DM is considered one of the primary risk factors for vascular dementia. The results of epidemiological studies suggest that DM increases the risk of Alzheimer's disease (AD) by 50-100% as well. The effect is largely independent of other, so-called vascular risk factors. The association could be explained by chronic brain hypoperfusion, the toxic effects of hyperglycaemia itself (damage to the blood-brain barrier), and the mediating role of insulin. Since the discovery of insulin and its receptors in the central nervous system, brain has no longer been considered an insulin-independent organ. Physiologic concentrations of insulin exert a beneficial effect on cognition. Too low a concentration of insulin in the periphery as well as hyperinsulinaemia, usually as a result of insulin resistance, both can significantly increase the risk of AD (even in people not suffering from DM!). There are several mechanisms through which central hypoinsulinaemia can accelarate the generation of

https://doi.org/10.1016/j.eurpsy.2008.01.303 Published online by Cambridge University Press