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

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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.

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Appearance of macromolecular form of Fibronectin in dementia patients

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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.

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Mixed dementia: A cohort study

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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.

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Compression of Risperidone and Olanzapine in behavioral disturbances of Alzheimer

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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

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