P3-236 ASSOCIATION OF THE CHOLINE ACETYLTRANSFERASE G+A POLYMORPHISM WITH ALZHEIMER'S DISEASE AND MILD COGNITIVE IMPAIRMENT

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Background: It has been reported that the choline actetyltransferase (ChAT) was associated with pathogenesis of Alzheimer's disease (AD). However, the association of the ChAT 2384G>A polymorphism with AD has been conflicting and its' association with mild cognitive impairment (MCI) has never been studied. We investigated the association of the ChAT 2384G>A polymorphism with AD and MCI and its' interaction with the presence of apolipoprotein E (APOE) e4 allele in a Korean elderly population. **Methods:** A total of 277 AD patients, 181 MCI, and 1189 normal elderly subjects were participated. MCI was diagnosed according to the criteria proposed by the International Working Group on MCI, and AD was diagnosed according to the NINCDS-ADRDA criteria. Multinominal logistic regression analyses were performed to examine the impact of the ChAT AA, APOE e4 allele and their interaction on the risk of MCI and AD. **Results:** The distributions of the ChAT and APOE polymorphisms were in Hardy-Weinberg equilibrium in each diagnostic group ($P>0.05$ in each group by Pearson chi square tests). The frequency of the ChAT AA genotype in the AD group was significantly higher than that of the control group ($\chi 2 = 15.87$ df=4, $P=0.003$). The frequencies of APOE e4 allele carrier for AD, MCI and normal controls were 41.9%, 21.0% and 17.7% ($\chi 2 = 76.00$, df=2, $P<0.001$). The ChAT AA genotype conferred the risk of AD (OR=3.86, 95% C.I.=1.77-8.43) but not the risk for MCI (OR=0.394, 95% C.I.=0.051-3.021). The interaction between the APOE e4 allele and the ChAT AA genotype was not significant either in the development of AD and MCI ($\chi 2=2.413$ df=4, $P=0.660$). **Conclusions:** The ChAT AA allele was found to confer the risk for AD in Korean elderly individuals. Although the risk of MCI conferred to the ChAT AA was not statistically significant, further studies with the larger samples are warranted.

P3-237 EXPERIENCES FROM GENETIC TESTING IN FAMILIAL ALZHEIMER'S DISEASE AND FRONTOTEMPORAL DEMENTIA: MUTATION AND PHENOTYPE SPECTRUM IN A DANISH COHORT

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Background: Autosomal dominantly transmitted AD and FTD are genetically heterogeneous disorders. To date, three genes have been identified in which mutations cause early-onset autosomal dominant inherited AD: *APP*, *PSEN1* and *PSEN2*. Mutations in two genes on chromosome 17, the *MAPT* and the *PGRN* genes, are associated with autosomal dominant inherited FTD. As a common feature, the pathogenic mutations cause abnormal aggregation and deposition of proteins, which leads to formation of the neuropathological features characteristic of the disorders. **Methods:** Clinical and genetic investigations in families with inherited dementia have not been undertaken previously in a Danish memory clinic population. This study from the Copenhagen Memory Clinic is based on clinical and molecular genetic investigations in 90 cases of familial dementia. The overarching aim of the present study was to characterize the mutation spectrum and describe genotype-phenotype correlations in families with inherited dementia. The identification of novel mutations and/or atypical genotype-phenotype correlations contributes to further characterising the disorders.DNA-samples from the 90 index cases representing families with presumed inherited AD or FTD were screened for causative mutations in the known genes with sequencing, DHPLC and MLPA techniques. **Results:** Seven presumed pathogenic mutations (2 *PSEN1*, 1 *PSEN2,* 1 *APP*, 1 *MAPT* and 2 *PGRN*) were identified, including a novel *PSEN2* mutation (V393M). **Conclusions:** We describe distinct genotype-phenotype relations with reference to previously reported families.

P3-238 A NOVEL MISSENSE MUTATION IN PSEN2 GENE ASSOCIATED WITH A CLINICAL PHENOTYPE OF FRONTOTEMPORAL DEMENTIA

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Background: In Familial Alzheimer's disease defects in three genes - the amyloid precursors protein (APP) gene on chromosome 21, the presenilin 1 (PSEN1) gene on chromosome 14 and the presenilin 2 (PSEN2) on chromosome 1- have been identified. More than 160 pathogenic missense mutations have been described in PSEN1, with wide clinic phenotypic variability. In PSEN2 only 11 missense mutations are known, in two of which (M239V and T122R) the clinical phenotype may be frontotemporal dementia-like. **Methods:** We present a novel PSEN2 mutation (**Y231C**) in an Italian patient who seven years ago, at age 55, manifested mood and behavioural disorders characterized by apathia, delusions, physical aggressive behaviour and psychomotor agitation. Language disturbances appeared one year later and mild memory loss three years later. The neuropsychological pattern suggested a main dysfunction in posterior temporal and parietal cortex. MRI showed diffuse atrophy, especially in posterior regions. **Results:** The genetic study showed an A-to-G mutation in exon seven of PSEN2 gene, resulting in tyrosine to cysteine substitution at residue 231. **Conclusions:** This new mutation confirms the variability of the phenotypes associated with PSEN2 mutations and justified the analysis of this gene in behavioural disturbances associated with degenerative dementia, at least in Italy in which PSEN2 mutations seems more frequent than in other countries.

P3-239 CAN THE APOE AND ACT GENES MODIFY THE CONVERSION FROM AMNESTIC MILD COGNITIVE IMPAIRMENT TO ALZHEIMER'S DISEASE?

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Background: We have investigated the signal peptide polymorphism of the alpha1-antichymotripsin (ACT) gene or the APOE genotype with the purpose to find early genetic markers which predict an increased risk of developing Mild Cognitive Impairment (MCI) or affect the risk of evolution to Alzheimer's Disease (AD). **Methods:** We have followed up for 49 months 89 patients with initial diagnosis of amnestic MCI fulfilling Petersen criteria. Clinical assessment was supported on the Mini Mental State Examination (Folstein et al., 1975), GDS, cognitive subscale (CAMCOG) of the CAMDEX, Rivermead Barrage Memory Test, Benton visual memory test, Wechsler Adult Intelligence Scale, Blessed Dementia Scale, Law-