ASSOCIATION STUDY OF GENES INVOLVED IN AMYLOID-BETA DEGRADATION AND CLEARANCE IN ALZHEIMER'S DISEASE

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Introduction: Alzheimer’s disease (AD) is a genetically heterogeneous disorder and it is characterised by the progressive accumulation of amyloid β-peptide (Aβ) in the brain. It is a well-established fact that the accumulation of Aβ in the AD brain is partially caused by defects in its degradation and clearance.

Aims: Here we have selected 12 genes encoding enzymes or proteases involved in Aβ degradation or clearance to study their genetic association with AD among a Finnish case-control cohort.

Methods: Thirty one SNPs in 12 genes were selected for genotyping using the Sequenom platform. Case-control cohort consisted of altogether ~1300 Finnish AD patients and controls. Cerebrospinal fluid (CSF) levels of Aβ42, total-tau and phospho-tau (p-tau) were correlated with the genetic data.

Results: APOE, gender and age-adjusted logistic regression analysis revealed a protective effect for the C allele carriers of rs7120118 in the liver X receptor-alpha (NR1H3) gene (p=0.014; OR=0.70, 95% CI 0.53-0.93). Interestingly, we also detected a significant decrease in CSF p-tau levels among AD patients carrying the C allele of rs7120118 and the A allele of rs2279238 in the NR1H3 gene. Furthermore, there was a significant increase in the CSF p-tau levels among AD patients carrying the G allele of rs1080093 in transthyretin (TTR) gene. We also observed a significant decrease at the age of onset among AD patients carrying the A allele of rs723744 and C allele of rs3794884 in the TTR gene.

Conclusions: These results suggest that genetic alterations in NR1H3 and TTR may play a role in AD.