CLUSTERIN AND APOLIPOPROTEIN E PLASMA LEVELS AS EARLY RISK FACTOR FOR AD

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Introduction: APOE epsilon4 is the major genetic risk factor for late onset Alzheimer's disease (AD). Recently, different genome-wide associations (GWAS) studies found polymorphisms in APOJ, also named clusterin (CLU), to be a risk factor for AD. Clusterin as well as ApoE co-localize with cerebral amyloid deposits. Clusterin possibly transports amyloid beta, and its expression level is increased in AD brain.

Methods: Offspring (N=203; mean-age 49.8) of patients with AD and (N=197; mean-age 51.6) of parents with good cognitive functioning (non-AD) were compared. APOE and APOJ genotyping were performed by real time PCR. ApoE and ApoJ levels were measured by ELISA, either commercially available (ApoE) or in house developed (ApoJ).

Results: No significant difference in clusterin plasma levels was found between the two populations. Whereas SNPs (rs11136000, rs9331888), described in many GWAS studies, did not, SNP (rs9314349) in the promoter region showed different distribution in AD and non-AD offspring, the A allele being over represented in AD offspring. No association between CLU SNPs and clusterin levels was found. However, there was a relation between plasma ApoE levels and either rs9314349(p=0.030) and rs9331888(p=0.031) CLU polymorphism in the non-AD offspring, or rs11136000(p=0.031) polymorphisms in AD offspring. Interestingly, increased ApoE plasma levels were associated with decreased levels of ApoJ in AD offspring, whereas in non-AD offspring high ApoE levels correlated with high ApoJ levels.

Conclusion: High plasma apoE levels and low apoJ levels in middle age may be a risk factor for Alzheimer's disease in old age, independent of APOE genotype.