Analysis of TOMM40 rs2075650 polymorphism frequency in polish Alzheimer's disease patients

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Alzheimer's disease (AD) is a progressive demented disorder with poorly understood pathogenesis. Currently, the variants in TOMM40 gene were shown to play an important role in developing AD. The poly-T variants (rs10524523) may influence age at onset of AD, while rs2075650 polymorphism is an AD risk factor. Both loci may be co-inherited with pathogenic APOE E4 allele. The aim of the study was the frequency analysis of TOMM40 rs2075650 polymorphism in Polish AD patients. The peripheral blood of 69 subjects with AD, 54 control volunteers (UC) and 48 control persons with family history of AD (RC) was collected for plasma and DNA isolation. The APOE and TOMM40 genotypes were determined by qPCR, HRM and capillary electrophoresis. The G allele of TOMM40 rs2075650 was significantly overrepresented in Polish AD patients as compared to UC and RC (OR=6.94, 95%CI: 2.82-17.1, p0.0001 and OR=2.86, 95%CI: 1.41-5.80, p=0.0037 respectively), and was more specific than APOE E4 (OR=5.15, 95%CI: 2.38-11.1, p0.0001; and OR=1.90, 95%CI: 1.02-3.51, p=0.05) as compared to UC and RC, respectively. Moreover, G/G genotype was accompanied with slightly earlier age at onset (69.8 vs 72.5 years, p=0.508) and faster disease progression (5.06 vs 4.78 MMSE/year, p=0.821), as compared to A/A variant. Subsequently, 24.6% of AD patients were carriers of both rs2075650 G and APOE E4 alleles, as compared to 3.70% of UC (OR=8.83, 95%CI: 1.94-40.1, p=0.0009). It seems that G allele of TOMM40 rs2075650 polymorphism is a significant risk factor for developing AD in Polish population, providing additional information to APOE genetic status.