MITOCHONDRIAL HAPLOGROUPS AND ALZHEIMER’S DISEASE

A. Maruszak¹, K. Gąweda-Walerych¹, J.A. Canter², M. Styczynska¹, M. Kobryś¹, M. Barcikowska¹, C. Żekanowski¹

¹Department of Neurodegenerative Disorders, Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw, Poland, ²Center for Human Genetics Research, Vanderbilt University Medical Center, Nashville, TN, USA

Introduction: Mitochondrial dysfunction is an early event in Alzheimer's disease (AD). Data from PET studies, autopsy, transgenic animals and cell culture models support this notion. Moreover, there is a higher incidence of AD in children of AD affected mothers in comparison to children of AD affected fathers and persons without family history of AD. Therefore we decided to perform an analysis of mitochondrial DNA (mtDNA), in particular mitochondrial control region and mitochondrial haplogroups characteristic for the Caucasians.

Aims: The aim of the study was to assess the role of mtDNA variability in AD risk.

Methods: A group of 422 AD patients and 318 controls were employed in the study. Sequencing of mtDNA control region (CR) and genotyping of 9 polymorphisms (m.7028C>T, m.10398A>G, m.13708G>A, m.1719G>A, m.4580G>A, m.8251G>A, m.12308A>G, m.9055G>A, m.13368G>A) in the coding region of mtDNA was performed. This allowed assignment of mitochondrial haplogroups and subhaplogroups. Patients and controls were stratified according to the APOE4 status.

Statistical analysis was based on univariate analysis, multivariate logistic regression and metaanalysis.

Results: Haplogroup H (p=0.049) and cluster HV (p=0.018) are significant risk factors for AD. Haplogroup K has a neutralizing effect on APOE4+ status (p=0.014). A synergistic interaction between subhaplogroup H5 and APOE4 status was detected (OR=33.13). Haplogroups and subhaplogroups (U4, U5a1, K, J1c, J2, T) previously proposed to take part in partial uncoupling of oxidative phosphorylation decrease AD risk (OR< 1).

Conclusions: MtDNA variability could constitute an important genetic modifier in AD risk.