Mitochondial function in Alzheimer's disease

Anne-Mette Hejl[1], Scott Maynard[2], Tran Thuan Son Dihn[2], Gunhild Waldemar[1], Niels A Bohr[2], *[1]Memory Clinic, Copenhagen, Denmark; [2]Center for Healthy Aging, Copenhagen, Denmark.*

Background: Mitochondrial DNA damage and mitochondrial dysfunction are associated with aging. In this study the aim was to investigate the potential correlation between Alzheimer's disease (AD) and mitochondrial-related molecular parameters in peripheral mononuclear blood cells (PBMCs), such as mitochondrial/glycolytic bioenergetics (oxygen consumption rate and extracellular acidification rate), Reactive Oxygen Species (ROS) production, and whole-cell levels of Deoxyribonucleotide Triphosphates (dNTPs including dATP, dGGT, dCTP and dGTP). **Methods:** We included 54 patients with AD in mild to moderate degree with a mean age of 68.7 years (50-83) and 27 age-matched healthy controls with a mean age of 65.7 years (53-87). The NINDS-ARDRA criteria were used for the diagnosis of AD. In freshly isolated PBMCs we investigated mitochondrial bioenergetic parameters with the Seahorse XF24 Analyzer. Measurement of mitochondrial ROS production using FACS analyses was performed on PBMCs from 30 AD patients and from 24 age-matched healthy controls. In a subgroup (12 AD patients and 12 age-matched healthy controls) whole-cell levels of dNTP were performed from frozen samples. **Results:** There was no significant difference between AD patients and healthy elderly in the mitochondrial bioenergetic parameters of oxygen consumption rate and extracellular acidification rate except for the level of proton leak which was significantly lower in the AD group then the healthy elderly ($p = 0.02$). Also we did not find any significant difference between the two groups in the mitochondrial production of ROS. The whole-cell levels of dATP were significantly higher in AD patients ($p = 0.002$) compared to healthy elderly but not for dTTP, dCTP and dGTP. **Conclusions:** We could not confirm that mitochondrial oxygen consumption and ROS production is affected in patients with AD. However, the proton leak in AD may be an indication of mitochondrial dysfunction. We found an imbalance in the whole-cell level of dATP in patients with AD compared to healthy elderly. It has previous been suggested that imbalance in dNTPs induces changes in the genomic stability leading to cell death. The nucleotide imbalance will be further explored as a biomarker.