NEUTRAL LIPIDS ACCUMULATION IN PERIPHERAL BLOOD MONONUCLEAR CELLS: HALLMARK OF ALZHEIMER'S DISEASE?

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Purpose: Alzheimer's disease (AD) is the most common progressive neurodegenerative disease. Recently, numerous progresses have been made on investigating novel AD biomarkers in brain and biological fluids. Among them, lipid metabolism is emerging as candidate. Infact, we found neutral lipids (NL) accumulation in skin fibroblasts from AD patients. Therefore, to assess whether peripheral alterations in cholesterol homeostasis might be relevant in AD development and progression, in this study we analyzed lipid metabolism in peripheral-blood-mononuclear-cells (PBMCs) and plasma from AD patients and from their first-degree relatives (FDR).
Methods: PBMCs and plasma were obtained from 93 probable AD patients and from 91 of their FDR. As controls we utilized 57 cognitively normal over-65 volunteers and 113 blood donors aged 21-66 years. NL were evaluated by Oil Red O (ORO) staining; plasma total-cholesterol and HDL by enzymatic methods; ACAT-1 by western-blotting.
Results: Data show high NL-levels and increased ACAT-1 in 85% of PBMCs from AD patients compared to 7% of controls. A significant reduction in AD plasma HDL levels was also observed. Additionally, correlation analyses reveal a negative correlation between HDL and MMSE, as between HDL and NL. We observed great variability in the NL-PBMCs data and in plasma lipid analysis of AD-FDR subjects. However, about 30% of them display a peripheral metabolic cholesterol pattern similar to that of AD patients.
Conclusion: We suggest that NL-PBMCs and plasma HDL determinations might be of interest to outline a distinctive metabolic profile applying to both AD patients and asymptomatic subjects at higher risk of disease.