

5th World Congress on

Diabetes & Metabolism

November 03-05, 2014 Embassy Suites Las Vegas, USA

The cholesterol-ceramide connection as a possible link between diabetes and Alzheimer's disease

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Molecular mechanisms involved with neuroendocrine diseases such as obesity and diabetes are closely linked to insulin resistance and require attention since metabolic dysfunction has also been associated with neurodegeneration. The global increase in these chronic diseases supports a role for lipids, such as ceramide and its metabolites in the pathogenesis of these diseases. The link between the ceramide and its pathogenesis of diabetes has been an important discovery that may assist with the role of ceramide in the pathogenesis of Alzheimer's disease (AD) also referred to as Type 3 diabetes. Lipids such as cholesterol and ceramide have been connected to processing of the amyloid precursor protein with generation or regulation of beta-amyloid production that is central to the amyloid hypothesis in AD. The cholesterol-ceramide connection has been previously linked with aging and AD. Lipidomic analysis using mass spectrometry of fasting plasma from an ageing cohort (AIBL) that includes mild cognitively impaired individuals, cognitively healthy controls and AD patients at baseline have been provided in this study. The plasma lipid ceramide was elevated in AD patients and this study provides potential for early therapeutic targets that reduce ceramide levels to manage hypercholesterolemia and insulin resistance in both diabetes and AD.

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