A unique brain lipidome and metabolome biosignature in Alzheimer's Disease

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Alzheimer's disease (AD) is the most common cause of adult dementia, but the cause of this inexorable neurodegenerative disease remains still elusive. Alterations in both lipid and polar metabolites biochemical pathways have been associated with AD. Here we conducted an unbiased investigation of the underlying biochemical alterations in AD human tissues.

We used an integrated lipidomics and metabolomics approach to survey frozen brain tissue samples from clinically characterized AD patients and age-matched controls. Lipids and polar metabolites were extracted using a biphasic, liquid-liquid extraction procedure. Polar metabolites were separated using a hydrophobic interaction liquid chromatography (HILIC), whereas lipids using an integrated microfluidic device packed with reversed phase C18. Travelling-Wave ion mobility mass spectrometry was used to improve peak capacity and CID fragmentation specificity. Moreover, ion mobility-derived collision cross sections provided orthogonal physicochemical data that were used with retention time, accurate mass and MS/MS data to increase confidence of metabolite identification. Data was collected using both negative and positive ionization mode in the data-independent acquisition mode with an alternate low and elevated collision energy method to acquire both precursor and product ion information in a single analytical run. Lipidome and metabolome data were fused and mined using multivariate statistical and pattern-recognition tools. Initial observations were confirmed using more targeted approaches for quantification. Pathway analysis was then used to incorporate the novel molecular information into the known biochemical pathways. The results obtained were further integrated with clinical data to generate testable hypotheses on the functional significance of the abnormalities observed in AD.

Our preliminary results reveal novel molecular alterations in AD and a unique lipidome and metabolome biosignature that differentiates the brains from individuals with AD compared from those from control subjects.