

Altered phosphatidylcholine metabolism in Alzheimer's disease found using UPLC-Q-ToF and NMR based metabolomics

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Aberrant lipid metabolism is implicated in Alzheimer's disease (AD) pathophysiology, but the connections between AD and lipid metabolic pathways are not fully understood. To investigate plasma lipids in AD, a multiplatform screen (N=35 by LC-MS and N=35 by NMR) was developed which enabled the comprehensive analysis of plasma from three groups (AD, MCI and age matched control). This Metabolomics screen identified three phosphatidylcholine (PC) molecules that were significantly diminished in AD cases. In a subsequent validation study (N=141), PC variation in a bigger sample set was investigated. These three PCs were again significantly lower in AD cases: PC 16:0/20:5 ($p<0.001$), 16:0/22:6 ($p<0.05$) and 18:0/22:6 ($p<0.01$). A receiver operated characteristic (ROC) analysis of the PCs combined with ApoE data produced an area under the curve predictive value of 0.828. Confirmatory investigations into the background biochemistry indicated no significant plasma change in three further PCs of similar structure, total choline containing compounds or three fatty acid side chains, adding to the evidence that specific PCs play a role in AD pathology.

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