Alzheimer’s Disease May be Predicted by a Panel of Plasma Lipids
Do Bile Acids also Play a Role?

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Dr. Allison Abbott, European correspondent of Nature, commented on the landmark publication by Mapstone et al. (Mapstone et al., 2014) as follows (Abbott, 2014):

“A simple blood test has the potential to predict whether a healthy person will develop symptoms of dementia within two or three years. If larger studies uphold the results, the test could fill a major gap in strategies to combat brain degeneration, which is thought to show symptoms only at a stage when it is too late to treat effectively. The test was identified in a preliminary study involving 525 people aged over 70. The work identified a set of ten lipid metabolites in blood plasma that distinguished with 90% accuracy between people who would remain cognitively healthy from those who would go on to show signs of cognitive impairment.”

A panel of 10 lipids were tested by performing a targeted metabolomic analysis of plasma samples using the Biocrates AbsoluteIDQ® p180 Kit (BIOCRATES Life Sciences AG, Innsbruck, Austria). In addition to the lipids, a few putative biomarkers (including some amino acids) could possibly increase the predictive value of the test. Interestingly, glycoursodeoxycholic acid (GUDCA) levels were consistently “higher” in subjects who later developed Alzheimer’s disease (AD), but no absolute concentrations were measured in the study.

Ursodeoxycholic acid (UDCA) is a primary bile acid in bear and nutria (Hofmann, Hagey, & Krasowski, 2010), but a secondary bile acid in humans, formed by the gut microbiome (mainly in the colon) from chenodesoxycholic acid (CDCA) via 7-oxo-litocholic acid (7-oxo-LCA) (Dawson & Karpen, 2014), (Ridlon, Kang, & Hylemon, 2006). 7-oxo-LCA, which is a minor component of the human bile acid pool, can be “rescued” by human liver 11β-hydroxysteroid dehydrogenase 1 and converted back to CDCA or UDCA (Odermatt & Klusonova, 2014).

In an early cross-sectional metabolomic investigation in plasma (employing ultraperformance liquid chromatography - MS), in which healthy controls were compared to those with a medical history of mild cognitive impairment (mMCI) and full blown AD, three bile acids - glycocholic acid (GCA), glycochenodexoycholic acid (GCDC) and glycodeoxycholic acid (GDCA) - tended to be higher, albeit with high inter-individual variations in AD patients (Greenberg, Grassano, Thambisetty, Lovestone, & Legido-Quigley, 2009).

A blood-based 7-metabolite signature for “early diagnosis” of AD was reported recently (Olazaran et al., 2015). In a cross-sectional study comprising 93 normal controls, 58 patients with mMCI and 100 AD patients,
44 plasma metabolites were significantly “altered” in aMCI and AD patients, including three bile acids which were increased: deoxycholic acid (DCA), lithocholic acid (LCA) and glycodeoxycholic acid (GDCA). The authors largely confirmed the data of the 10-lipid metabolite panel obtained with the Biocrates AbsoluteIDQ p180 Kit by Mapstone et al. (2014), but selected glutamic acid, alanine, aspartic acid, and three lipids - nonesterified fatty acid (22:6n-3), phosphatidylethanolamine (36:4), sphingomyelin (39:1) - and deoxycholic acid in their final diagnostic algorithm, which distinguished AD patients from controls with an accuracy of more than 80 %, and aMCI patients with somewhat less accuracy. Notably, metabolite levels in the three groups were expressed relative to “batch-averaged quality-control plasma”.

Analogous to the targeted lipidomics approach, these preliminary findings in cross-sectional studies may be reproduced by accurate and targeted phenotyping of the serum or plasma bile acid metabolome in controlled prospective studies, as performed by Mapstone et al. (2014).

References


