Alzheimer’s Disease may be predicted by a Panel of Plasma Lipids. Do Bile Acids also have a Role?*

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Dr. Allison Abbott, the 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.”

The result of a panel of 10 lipids was obtained by targeted metabolomic analysis of plasma samples using the Biocrates AbsoluteIDQ p180 Kit (BIOCRATES, Life Science AG, Innsbruck, Austria). However, in addition to the lipids there were other putative biomarkers (among them amino acids) discovered that could possibly increase the predictive value. Quite surprising was the observation that glycoursodeoxycholic acid (GUDCA) was consistently “higher” in subjects who later converted to Alzheimer disease (AD) but no absolute concentrations were measured in this 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 one of the early cross-sectional metabolomic studies in plasma (employing ultraperformance liquid chromatography-MS) which compared healthy controls, to those with amnestic mild cognitive impairment (aMCI) and full blown AD, three bile acids e.g. glycocholic acid (GCA), glycochenodexoycholic acid (GCDCA) and glycodeoxycholic acid (GDCA) were identified that tended to be higher, albeit with high inter-individual variation in AD patients (Greenberg, Grassano, Thambisetty, Lovestone, & Legido-Quigley, 2009).

Recently a blood-based, 7 metabolite signature for "early diagnosis" of AD was reported (Olazaran et al., 2015). In this cross-sectional study with 93 normal controls, 58 patients with aMCI and 100 AD patients, 44 plasma metabolites were identified which were significantly “altered” in aMCI and AD patients, including three bile acids: deoxycholic acid (DCA), lithocholic acid (LCA) and glycodeoxycholic acid (GDCA), which were increased. The authors confirmed to large extent the data of the 10-lipid metabolite panel obtained with the Biocrates AbsoluteDQ p180 Kit (Mapstone et al., 2014), but chose to select glutamic acid, alanine, aspartic acid, three lipids e.g. 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 over 80 % and aMCI patients with somewhat less accuracy. Of note is that metabolite levels in the three groups were expressed relative to “batch-averaged quality–control plasma”.

In analogy 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 in (Mapstone et al., 2014).

* Views and Opinions expressed in this commentary do not necessarily coincide with those of Biocrates AG.


