

BIOMARKERS (NON-NEUROIMAGING)

Evolution of circulating metabolites through lifespan according to gender and APOE

Bruno Bonnechère^{1,2} | Jun Liu² | Najaf Amin² | Rima F. Kaddurah-Daouk³ |
Cornelia M Van Duijn²¹Hasselt University, Hasselt, Belgium²University of Oxford, Oxford, United Kingdom³Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC, USA

Correspondence

Bruno Bonnechère, Hasselt University, Hasselt, Belgium.

Email: bruno.bonnechere@uhasselt.be

Abstract

Background: There is increasing interest in blood-based metabolic biomarkers for Alzheimer's disease (AD). Studies show consistently that branched chain amino acids (BCAAs) and a large scale of lipids are changed in patients with AD. Little is known of how these metabolites associate to age, genes and apolipoprotein E (APOE). This study aims to study these metabolites over the lifespan and determine the influence of age, sex and APOE.

Method: We conducted this study in UK Biobank, a large prospective cohort of 459,227 subjects with extensive genotypic and phenotypic data. Using the Nightingale nuclear magnetic resonance technology, 249 metabolites (165 directly measured metabolites and 84 derived measures) have been determined in the blood of 118,071 participants. We used mixed-effect models to study the effect of age, sex and APOE on metabolite levels and adjust for lifestyle factors and medication.

Results: APOE*4 is the major determinant of total of 216 metabolites of the Nightingale platform using a FDR < 0.05. We find that 41 were also associated to dementia in the population 60+ years old. Also, APOE*2 is associated with 226 metabolites (FDR<0.05) including 41 dementia associated metabolites. Concerning gender differences, significant differences were found for the metabolites at the FDR 0.05. Overall, we find a significant interaction between age² and APOE*4 for valine and BCAA. When stratifying for gender, for most of the metabolites concentrations in blood remain stable over age in men. For amino acids, we observed a decreased concentration level with age in men. For females, we find that the metabolite levels increase over age, reaching a plateau around 55 years old.

Conclusion: This study shows that AD associated metabolite levels in blood are determined by sex and APOE. In women, the levels of metabolites in women are also associated to age up until menopause.