Lipid Measurements: Noninvasive Biomarkers for Alzheimer Disease?

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The study covered in this summary was published on medRxiv.org as a preprint and has not yet been peer reviewed.

Key Takeaways

- Higher expression and upregulation of fatty acid pathways and the phospholipids phosphatidylethanolamine (PE) and diacylglycerol (DAG) were associated with smaller whole-brain volumes and may be linked with neurodegeneration and Alzheimer's disease (AD).
- Overall, three clusters of co-expressed lipids (PE and DAG, fatty acids, and sphingolipids) were found to be associated with whole-brain or hippocampal volume. In addition, the researchers identified 22 metabolites that could serve as potential study markers. No significant metabolic associations for amyloid-beta (Aβ) status or for AD polygenic risk were found, suggesting that these findings are nonspecific to AD but may be relevant to brain structure in advancing age.

Why This Matters

- These findings help identify potential blood-based markers for further research and therapeutic use in the diagnosis and treatment of AD.
- Noninvasive and scalable markers are particularly valuable for research and for clinical trials of brain health and pathology.

Study Design

- Participants of Insight 46 — the neuroscience substudy of the UK National Survey of Health and Development (NSHD) — underwent comprehensive clinical and cognitive tests, MRI, and ^{18}F-florbetapir positron-emission tomography (PET) imaging.
- Concentrations of 1401 metabolites were detected and measured among NSHD participants. Metabolites were assigned to nine families: lipids, amino acids, xenobiotics, peptides, nucleotides, cofactors and vitamins, carbohydrates, energy and partially characterized molecules. They were further organized into pathways on the basis of their proposed biological function.
- Associations between blood metabolites and whole-brain volume, hippocampal volume, and Aβ status, plus the association of key metabolites with polygenic risk of AD among participants, were assessed using data from Aβ-PET and MRI scans, ultra-high-performance liquid chromatography–tandem mass spectrometry, and statistical analysis.

Key Results

- Although no definitive association between lipids, their metabolites, and AD was found, relationships between groups of lipids and structural brain measures suggest possible driving mechanisms for the pathology of AD.
- The association of these metabolites with longitudinal changes in brain volumes could elucidate understanding of brain health and neurodegeneration and lead to possible therapeutic targets.

Limitations

- Study participants were on average in better self-rated health, had higher cognitive ability, and had higher socioeconomic status than the full NSHD cohort. In addition, all were White persons, so findings may not extend to

the general population.

- Further study is needed to determine causal relationships.

Study Disclosures

- One author has received research funding from Avid Radiopharmaceuticals, has consulted for Roche Pharmaceuticals, Biogen, Merck, and Eli Lilly, and has given educational lectures sponsored by GE Healthcare, Eli Lilly, and Biogen.
- The study was principally funded by grants from Alzheimer's Research UK, the Medical Research Council Dementias Platform UK, the Wolfson Foundation, and the Alzheimer's Association. The genetic analyses were funded by the Brain Research Trust. Florbetapir amyloid tracer was provided by Avid Radiopharmaceuticals.
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This is a summary of a preprint research study, "Investigating Associations Between Blood Metabolites, Later Life Brain Imaging Measures, and Genetic Risk for Alzheimer's Disease," written by Rebecca Green from King's College London, London, UK, and colleagues. It was publihsed on medRxiv.org and is provided to you by Medscape. This study has not yet been peer reviewed. The full text of the study can be found on medRxiv.org.

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