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Genetic and Environmental Moderation Among Plasma-Based Biological Markers of Alzheimer's Disease

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ABSTRACT:

The current research framework for Alzheimer's disease (AD) defines the condition in terms of the progressive accumulation of beta-amyloid (Aβ) and tau, as well as progressive neurodegeneration. This framework represents a biological definition of AD, and shifts AD research toward examining younger cohorts where the progression of biological markers can be examined prior to dementia onset. The genetic analysis of these biomarkers is still in its infancy, as little is known regarding their genetic and environmental determinants, or if the magnitude of genetic and environmental influences change over disease progression. The goal of the present study was to determine whether plasma-based Aβ, tau, and neurodegeneration – assessed by neurofilament light (NFL) – moderated the genetic and environmental determinants of one another. Data were from the Vietnam Era Twin Study of Aging. The average age at assessment was 67.1 years (SD=2.6). Using a bivariate model for the analysis of gene-environment interaction, we found evidence for significant genetic and environmental moderation across multiple biomarkers. All variance components of $A\beta_{42}$, for example, significantly increased as a function of NFL level, resulting in a change in heritability from .26 to .47. A similar pattern of moderation was observed between tau and $A\beta_{42}$. The heritability of $A\beta_{42}$ also increased as a function of $A\beta_{40}$, a more abundant form of the peptide, while the genetic correlation between them decreased. These results suggest that the degree to which AD biomarkers are influenced by genetic and environmental factors is in part dependent on disease staging as indexed by biomarker accumulation.

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