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Genetics/genetics of cognitive aging

Trans-ethnic meta-analysis of interactions between genetics and early life socioeconomic status on memory performance and decline in older Americans

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Abstract

Background: Later life cognitive function is influenced both by genetics as well as early- and later-life socioeconomic context, and these factors may also interact with each other. Previous research has demonstrated interactions between adult socioeconomic status and several gene regions that influence memory performance and decline in older adulthood, but few studies have examined whether genetics also interacts with childhood socioeconomic factors.

Methods: We used growth curve modeling to estimate episodic memory performance at age 65 (trajectory intercept) and decline thereafter (trajectory slope) in European ancestry (EA, N = 10,468) and African ancestry (AA, N = 2,252) participants from the Health and Retirement Study. Early-life socioeconomic context included measures of parental education and financial strain. We selected 39 gene regions previously associated with cognitive performance, dementia, and related traits from GWAS. We tested whether all variants (1000 Genomes imputed data) and/or rare exomic variants (exome chip data) in these gene regions interacted with childhood socioeconomic context to influence memory using gene-based tests (Interaction Sequence Kernel Association Test (iSKAT) or iSKAT Optimal Unified Test (iSKAT-O)). For iSKAT analyses, we conducted a trans-ethnic meta-analysis.

Results: Of the 39 genes, 22 in EA and 19 in AA had nominally significant interactions ($p < 0.05$) with at least one childhood socioeconomic measure on memory performance and/or decline; however, all but one (father's education by *SLC24A4* gene region in AA) were not significant after multiple testing correction (FDR <0.1). In trans-ethnic meta-analysis, two gene regions interacted with childhood socioeconomic context (FDR <0.05). Both interactions were robust to adjustment for respondent's own educational attainment and *APOE* ε4. For both interactions (mother's education by *MS4A4A* on memory performance (meta-analysis $p = 0.0005$), and father's education by *SLC24A4* on memory decline (meta-analysis $p = 0.0009$)) in both EA and AA, the genetic effect was stronger in participants with low parental education.

Conclusions: Examination of common and rare variants in genes discovered through GWAS shows that childhood socioeconomic context may interact with a few key gene regions to jointly impact memory function and decline in later life. Genetic effects may be more salient for those with lower childhood socioeconomic status.