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The genetic and environmental etiology of weighted gene co-expression network module eigengenes in middle age sample of male twins.

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KEYWORDS: Weighted gene co-expression network analysis, module eigengene, twin gene

ABSTRACT:

Weighted gene co-expression network analysis (WGCNA) is a well-validated multivariate network-based analytic method for identifying genes driving complex traits. Despite their increasing application, the sources of individual differences in network module eigengenes have never been empirically established. WGCNA works by classifying gene sets into 'network modules' based on their particular patterns of gene expression (GExp) and connectivity. These patterns are typically summarized with a single quantitative metric or module eigengene (ME), which is a quantitative summary of the correlated expression and connectedness across all genes in a module. Using a sample of 646 early old age male twins from the Vietnam Era Twin Study of Aging with GExp data based on blood lymphocytes, our aim was to explore the genetic and environmental etiology of WGCNA-derived MEs. GExp data were filtered to have >1 CPM expression in at least 50% of the sample, adjusted for batch effects, and log-transformed before running WGCNA. Full Informative Maximum Likelihood biometric genetic models were then fitted to the first 30 MEs. Results were adjusted for covariates including age, ethnicity, site, storage time and comorbid disease. Across all MEs, familial aggregation was significant and was explained by varying proportions of additive genetic (ranging 37%-63%) and shared environmental (ranging 26%-52%) risks. Detailed results and implications along with exploratory associations with mild cognitive impairment will be presented.

GRANT SUPPORT: This work was assisted through funding from the National Institute on Aging [R01 AG054002, R01 AG060470, R01 AG022381, R01 AG050595].