Gene-by-Environment Expression and Calculation of the Frailty Index

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ABSTRACT 248 words

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Background

Frailty can be described as a phenotype (e.g., sarcopenia, reduced grip strength, decreased VO2 max) or as a ratio of deficits, i.e., a Frailty Index (FI). FI predicts survival, death, cognitive impairment, falls, and hospitalizations. Frailty is influenced by both genes and environment. We calculated the FI as the sum of measured deficits divided by the total number of items assessed in a pedigree-based sample of 1,029 Mexican Americans participants in the San Antonio Family Heart Study. We performed a novel search for genotype-by-environment interactions (GXE) influencing FI. Such interactions lead to heritable differences between individuals in their responses to the environment.

Methods

We investigated a panel of 34 measured environmental factors to look for GXE influencing frailty. We employed a powerful polygenic approach to genotype-by-environment modeling, allowing for both dichotomous and continuous environmental measures. We performed likelihood-based estimation of parameters and tests for the presence of GXE.

Results

GXE interactions influencing frailty were observed for the following environments: obesity (P=7.9E-10), hypertriglyceridemia (P=2.74E-09), low HDL (P=2.15E-06), impaired glucose status (P=.002), hypertension (P=0.01), and diabetes (P=0.02), Additionally, GXE interactions were detected for a number of quantitative dietary components: carbohydrates (P=5.73E-07), fats (P=2.01E-06), fiber (P=2.76E-05), dietary cholesterol (P=0.01), and protein (P=0.006). These results document substantial statistical evidence for the interactive effects of genes and environmental factors on frailty.

Conclusion

Our results support the presence of substantive gene-by-environmental interactions influencing frailty. This finding documents the presence of heritable differences between individuals that lead to differential response to environmental challenges.