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Genetic Variation Linked to Neuroticism Is Associated with Amygdala Function

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Neuroticism is a heritable personality trait characterized by emotional instability and psychological stress that places individuals at risk for psychopathology. The amygdala is a brain region that plays a critical role in behavioral vigilance and assigning emotional significance to stimuli that may contribute to the expression of neuroticism. A recent GWAS of 180,911 individuals identified common genetic variation associated with neuroticism. Here, we explored whether single nucleotide polymorphisms (SNPs) that were associated with neuroticism at genomewide levels of significance are associated with threat-related amygdala function.

Genomic, neuroimaging, and self-report data were available for 448 non-Hispanic European-American participants who completed the ongoing Duke Neurogenetics Study. Threat-related amygdala reactivity was assayed using an emotional face-matching task while functional magnetic resonance imaging data were acquired. Neuroticism was assessed with self-report. We tested whether 11 genome-wide significant single nucleotide polymorphisms (SNPs) were associated with neuroticism through GWAS. Covariates in analyses included sex and ancestrally-informative principal components.

We found that the risk alleles of three (*TYRP1* rs10809559, *SBF2* rs13923776, *PAFAH1B1* rs12938775) SNPs were associated with elevated amygdala reactivity (all $\beta>0.032$, all $p<0.04$). The *PAFAH1B1* rs12938775 allele associated with neuroticism in the GWAS was also associated with neuroticism in our dataset ($\beta=3.31$, $p<0.016$), however, neither *TYRP1* rs10809559 nor *SBF2* rs13923776 were (both $p>0.68$). We conclude that common genetic risk for neuroticism is associated with elevated threat-related amygdala reactivity. Increased threat-related amygdala response may be a genetically influenced neural mechanism conferring neuroticism and risk for psychopathology.