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INTERACTION BETWEEN GENETIC RISK FOR ANXIETY DISORDERS AND FUTURE ANXIETY

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The heritability of anxiety disorders range between 30-50%, but efforts to identify specific polymorphisms contributing to this risk have been largely unsuccessful. However, a recent meta-analysis of genomewide association studies identified loci predictive of anxiety disorder (*LOC152225* rs1709393) and anxiety factor scores (*CAMKMT* rs1067327). In addition to replicating these findings in independent samples, it is important to understand what, if any, biological mechanisms implicated in the etiology and pathophysiology of anxiety may mediate these associations. Using data (n = 451) from the ongoing Duke Neurogenetics Study, we examined whether *LOC152225* rs1067327 and *CAMKMT* rs1067327 genotypes were associated with individual differences in threat-related amygdala activity measured using BOLD fMRI. After accounting for gender and ancestrally-informative principal components, we found an additive effect of *CAMKMT* rs1067327 whereby the number of risk alleles was associated with increased threat-related reactivity in the right centromedial amygdala. Further, we found that increased right centromedial amygdala reactivity significantly mediated the association between rs1067327 genotype and future anxiety in the context of recent life stress. These findings provide a putative neural mechanism through which *CAMKMT* rs1067327 genotype conveys anxiety risk.