

A Neuroanatomical Investigation of Generalized Anxiety Disorder

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Generalized anxiety disorder (GAD) affects millions of people in the United States and is characterized by chronic and exaggerated worry. In GAD, aberrant functional activity and connectivity observed for regions of the ventral prefrontal cortex (PFC) and the amygdala has implicated these regions as primary components in regulating the emotional response to threat. The present study was undertaken to investigate whether structural differences in these areas are part of the neurobiological profile of GAD. Structural MRI and DTI were used to compare 49 GAD patients to 39 healthy controls. The patients exhibited volume reductions in the lateral orbitofrontal cortex. Both volumetric MRI and DTI measures indicated reduced structural integrity of the uncinate fasciculus, a major white matter tract connecting the ventral PFC and amygdala. Of the 49 GAD patients, reductions in OFC volume and uncinate fasciculus structural integrity were also observed for the 21 GAD patients with no current comorbid disorders, but not for the 28 GAD patients with at least one comorbid disorder. Correlations with symptom measures indicated unique associations with anxiety (HAM-A) and depression (HAM-D) for the lateral OFC volume and uncinate fasciculus fractional anisotropy (FA). In addition, I examined a common BDNF polymorphism (Val66Met) that has been implicated in prior work on anxiety, depression, and fear conditioning. This genotype did not significantly influence the above areas of interest in this sample, although the study was underpowered for genetic analyses. My findings highlight the importance of the ventral PFC and uncinate fasciculus connectivity in the psychopathology of GAD and warrants further investigation into the functional significance of the OFC in relation to generalized anxiety disorder.