

## **Functional and Morphologic Changes in Anterior Limbic Structures are Observed in Bipolar Disorder**

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Bipolar disorder (BPD) is a psychiatric illness characterized by cycling between episodes of mania, euthymia and depression. Its dynamic and lifelong expression suggests that it is the result of a dysregulation of the neural systems that maintain emotional homeostasis. Recent advances in neuroimaging techniques have implicated components of the anterior limbic system (ALS) in the disease but have done so incompletely. A better understanding of the dysfunctional neural circuits within the ALS could influence the development of more targeted drugs and improve the diagnosis and treatment of BPD.

**Methods:** We obtained structural and functional MRI scans from 32 bipolar and 19 healthy participants while they performed a behavioral task that elicits both emotional and attentional brain activation patterns. Voxel based morphometry (VBM) was used to determine whether differences in gray and white matter density could be used to explain differences in blood flow observed during fMRI. VBM was also used to compare density patterns between patients with more and less severe symptoms.

**Results:** Distinct differences in density were observed in several areas of the anterior limbic system including the posterior cingulate cortex, thalamus and caudate. There were no statistically significant differences in white matter. Both functional and structural abnormalities were observed in the left thalamus. Additionally, patients with more severe symptoms showed a greater reduction in gray matter density in the anterior and posterior cingulate cortex, right caudate and thalamus compared to patients with more mild symptoms.

**Conclusions:** The presence of both structural and functional abnormalities in the left thalamus suggest that its dysfunction may play a more central role in the development of bipolar disorder than was previously considered. More extensive involvement of the cingulate cortex, caudate and thalamus in patients with higher YMRS scores could be explained by a more dynamic model of the brain in BPD. For example, environmental triggers or developmental processes could produce structural changes in the brain that exacerbate the emotional and behavioral deficits observed.