

Functional MRI investigation of ADHD Comorbidity in Adolescent Bipolar Patients

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Background: Bipolar disorder is a common, life-long illness that typically begins in adolescence or early adulthood. Several studies suggest that more than half of bipolar adolescents may also be diagnosed with attention deficit hyperactivity disorder (ADHD). Because of the high rate of co-occurrence of these disorders there has been a perceived confusion in differentiating their clinical presentations. Adolescents with bipolar disorder are often initially misdiagnosed and treated with medications for ADHD that may exacerbate their symptoms. Furthermore, the widely varying estimates of comorbidity have led to suggestions that the apparent co-occurrence of these disorders may be related to diagnostic ambiguity rather than a clear clinical distinction. This question is complicated by the very limited data available on the neurobiology of adolescent bipolar disorder or ADHD.

Impulsivity and inattention are two cardinal features associated with bipolar disorder as well as ADHD. Neuronal control of mood appears to involve brain regions that also regulate attention. Indeed, some investigators have suggested that in the presence of a mood disorder, attention disturbances may represent a marker of dysfunction in brain regions that modulate mood. We have previously observed significantly decreased neuronal activation in adolescent bipolar patients performing an attention task, centered in the medial temporal cortex, anterior cingulate, anterior insula, and striatum, suggesting that bipolar adolescents have dysfunction in brain regions involved in regulation of both mood and attention. The population we previously studied combined bipolar adolescents with and without comorbid ADHD. Comparing regional brain activation in adolescent bipolar patients without comorbid ADHD with activation in bipolar adolescents with ADHD, during performance of an attention task may help to clarify the differential neurobiology of these disorders and lead to a greater understanding of the relationship between bipolar disorder and ADHD. In addition, comparing these patient groups may help to identify neurobiological markers that differentiate bipolar patients with comorbid ADHD, thereby facilitating earlier recognition and more specifically targeted treatment. In this study we utilized functional magnetic resonance imaging (fMRI) to compare neuronal activation in bipolar patients adolescents with and without comorbid ADHD during performance of a simple attention task.

Methods: Twelve bipolar adolescents with a comorbid diagnosis of ADHD, and fifteen bipolar adolescents without any comorbid psychiatric condition participated in fMRI scans during which they were asked to participate in a very simple attention task (single digit CPT-IP, during which subjects were asked to press a button when the same digit appeared twice in a row). All patients were manic at the time of the scan, and no patients were yet receiving medication. A voxel-by-voxel regression analysis, controlling for task performance, was performed between groups.

Results: Bipolar adolescents with ADHD demonstrated decreased activation in the dorsolateral prefrontal cortex and anterior cingulate (blue in Figure 1) and increased activation in the parietal cortex (yellow in Figure 1) compared with bipolar adolescents without ADHD. Task performance did not significantly differ between groups.

Discussion: These findings suggest that bipolar adolescents with ADHD have greater functional deficits in frontal brain regions associated with attention, and may be using secondary attention regions, such as those found in the parietal cortex, to compensate for frontal neuropathology. These findings have significant clinical implications in suggesting that bipolar adolescents with ADHD constitute a distinct subgroup that may require uniquely tailored clinical interventions to achieve clinical stability.

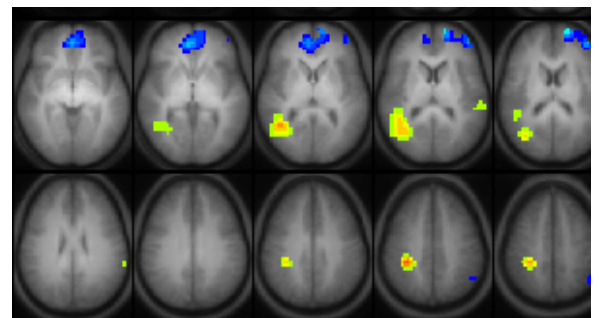


Figure 1.