Bipolar Disorder and Advances in Neuroimaging: A Progressive Match

By Stephen M. Strakowski, MD

Despite being a common and significant illness, the neurophysiologic basis of bipolar disorder was relatively little studied until the advent of advanced neuroimaging techniques, primarily magnetic resonance imaging technologies, allowed in vivo and noninvasive examination of the human brain. Consequently, neuroimaging studies of bipolar disorder proliferated in the past decade.

In this issue of CNS Spectrums, experts from Harvard University in Boston, McLean Hospital in Belmont, Massachusetts, and the University of Cincinnati College of Medicine in Ohio, describe recent progress and the direction of future research in the neuroimaging study of bipolar disorder.

Perry F. Renshaw, MD, PhD, and colleagues review reports of structural (morphometric) imaging techniques applied to the study of the neuroanatomy of bipolar disorder. The authors note that morphometric studies suggest abnormalities within fronto-limbic-striatal-pallidal-thalamic circuits that modulate human emotional and cognitive behavior. Moreover, they note that several new imaging techniques permit more sophisticated measurements of brain structures than classic volumetric measurements. These techniques include voxel-based morphometry, shape analysis, cortical surface mapping, and diffusion tensor imaging. These instruments will refine the current neuroanatomic models of bipolar disorder and guide future studies of brain function and dysfunction.

Extending morphometric findings, Deborah A. Yurgelun-Todd, PhD, and Amy J. Ross, PhD, review recent functional magnetic resonance imaging findings that inform models of the functional neuroanatomy of bipolar disorder. As they note, functional magnetic resonance imaging permits examination of brain activation in response to specific cognitive tasks that allows researchers to “shape” brain response to better understand both brain function and dysfunction. The authors observe that contemporary studies provide some support for the “ventral-dorsal hypothesis,” which suggests that mood episodes are associated with hypoactivity of the dorsal prefrontal cortex and hyperactivity of ventral prefrontal, coupled with reduction of inhibitory input from subcortical (eg, striatal) regions and dysfunctional modulation of these networks by the extended amygdala. They note a number of limitations to current studies that require ongoing investigation to address.

Melissa P. DelBello, MD, and colleagues then contrast findings between adults and children with bipolar disorder. Although some of the neuroimaging and magnetic resonance spectroscopy findings observed in adults with bipolar disorder have also been observed in affected children and adolescents, this is not always true. These differences suggest that normal neurodevelopmental processes occurring in childhood and adolescence interact with neural events leading to bipolar disorder, potentially affecting age at onset, clinical treatment response, and, of course, results in neuroimaging studies. Understanding these interacting processes may clarify what must occur in the brain in order to precipitate the first affective episode in a vulnerable individual.

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Finally, Caleb M. Adler, MD, and colleagues integrate recent neuroimaging studies in order to develop a specific functional neuroanatomic model of bipolar disorder. They propose that bipolar disorder arises from functional, structural, and neurochemical abnormalities within discrete prefrontal-striatal-thalamic-amygdala networks (ie, the anterior limbic network) that modulate human emotional and cognitive behavior. Specifically, they suggest that symptoms of bipolar disorder do not simply arise from discrete localized brain lesions, but rather are emergent properties of dysfunction of these brain networks. Their discussion provides a model for future testing of this suggestion.

The discussions in this issue highlight the improvements made in our conceptualization of the brain basis of bipolar disorder. Recent studies have advanced models of bipolar neuropsychophysiology from historical oversimplified and nonspecific “right hemisphere dysfunction” hypotheses to more focused models proposing specific biochemical abnormalities within specific prefrontal-striatal-thalamic networks that modulate mood and behavior. These models are imminently testable and provide a framework to continue to refine and advance our understanding of the neural basis of bipolar disorder. Ultimately, this will only improve our ability to develop targeted effective treatments in order to improve the lives of people affected by this common psychiatric condition.

REFERENCES