

HOSPITAL PHYSICIAN®

NEUROLOGY BOARD REVIEW MANUAL

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The *Hospital Physician Neurology Board Review Manual* is a peer-reviewed study guide for residents and practicing physicians preparing for board examinations in neurology. Each manual reviews a topic essential to the current practice of neurology.

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Mood Disorders: Neurobiology, Evaluation, and Treatment

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Mood Disorders: Neurobiology, Evaluation, and Treatment

William R. Marchand, MD

INTRODUCTION

Two categories of mood disorders are currently recognized in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR)—unipolar (depressive) spectrum disorders and bipolar spectrum disorders.¹ Despite the high prevalence of depression and the significant burden of suffering caused by unipolar and bipolar syndromes, the neurobiology of mood disorders remains incompletely understood. However, the recent development of functional neuroimaging methods has allowed the characterization of neurobiologic correlates of mood disorders and has contributed to evolving theories of causation. In particular, findings from functional neuroimaging studies—combined with evidence from postmortem lesion, molecular biology, and genetic studies—increasingly implicate neural circuits that regulate emotional behavior in the pathophysiology of mood disorders.

Neural networks allow the functional integration of multiple brain regions to facilitate neural processing. There is considerable evidence that some networks function abnormally in mood disorders. This may occur as a result of underlying molecular pathology. In some cases, however, neural network dysfunction associated with mood disorders also might represent the brain's response or adaptation to illness or be the result of changes related to illness progression. Nonetheless, functional abnormalities of neural networks may be the final common pathway of symptom development and eventually may provide clinically useful biomarkers of illness.

This manual provides an overview of our current understanding of the neurobiology of mood disorders, with a particular focus on abnormalities of neural circuitry associated with these conditions. The aim of this manual is to provide a basic understanding of the current state of knowledge about the etiology of these conditions as well as review the fundamentals of evaluation and treatment.

NEURAL CIRCUITS INVOLVED IN REGULATING EMOTION

In 1937, James Papez, a neuroanatomist at Cornell University, described a neural circuit for regulation of emotion in what had previously been labeled the *limbic lobe* by the French neuroanatomist, Paul Broca. Over time, the concept of an emotional control circuit has been revised, and this circuit is generally referred to as the limbic system (**Figure 1**). Our current understanding is that limbic functions are best described by 2 neural networks that are critical for human affect generation and modulation—the ventral and the dorsal emotional control networks.²

VENTRAL AND DORSAL NETWORKS

The ventral network, which includes the ventral prefrontal cortex, amygdala, insula, ventral striatum, thalamus, orbitofrontal cortex, ventral anterior cingulate cortex, and brainstem nuclei, is involved with the perception of emotional stimuli, the generation of affect, and the production of an autonomic response.² These functions occur primarily by way of the amygdala, which receives sensory inputs from multiple areas. External sensory inputs provide information about the environment and include olfactory input from the olfactory bulb, visual information from the inferior temporal cortex, and auditory information from the thalamus. Internal information about the current state of bodily functions comes from the hypothalamus. The outflow of information from the amygdala provides control over the body's response to the environment. For example, in response to potentially dangerous situations, amygdala output results in sympathetic nervous system activation (fight or flight response) by way of the hypothalamus. Also, output to the reticular pontine nuclei leads to the startle response, and output to the central gray nucleus leads to the freezing behavior seen in fear states. Connections from the amygdala to the hypothalamus result in adrenocorticotropin release and the “stress hormone