

The Role of the Cerebellum in Neurobiology of Psychiatric Disorders



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KEYWORDS

• Cerebellum • Mood disorders • Schizophrenia • Attention deficit • Autism

KEY POINTS

- The cerebellum, not only literally but also functionally, can be expounded as the *diminutive of cerebrum*.
- The cerebellum primarily, by itself, does not generate any motor, emotive, or cognitive outputs; but it plays a modulatory, rather than generative, role in nearly all human cerebrum functions.
- Just like an *equalizer* device in sound recording, the cerebellum, by its close interconnections with supratentorial structures, serves as a device to adjust our cerebrum tones and maintain the balance in our performance in all domains.

INTRODUCTION

For a long time, the cerebellum was only known for its role in movement coordination. Although the emotional and behavioral disturbances were described in patients with cerebellar diseases as early as 1831, until recently, the role of cerebellum in nonmotor aspects of the brain function was largely ignored.¹ In fact, the discovery of the involvement of cerebellum in emotion processing goes back to the eighteenth century, when Gall, the Swiss founder of phrenology, mentioned the cerebellum as the primary anatomic locus of love.²

After a long period of latency, by the mid twentieth century, Snider and colleagues hypothesized the role of the cerebellum on the *non-motor centers of cerebrum*.³ Later in 1970, it was shown that chronic stimulation of cerebellum not only improves seizure control but also improves emotional symptoms, such as aggression, anxiety, and depression, in the affected patients. In 1998, Schmahmann and Sherman⁴ discussed the possibility of a cerebellar contribution to emotions and behaviors, publishing the

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first systematized work on the subject. They studied 20 patients with cerebellar lesions and described their psychiatric symptoms. The newly delineated clinical entity was called cerebellar cognitive affective syndrome (CCAS). Schmahmann is now a research pioneer in this field; he categorized the affective part of the CCAS into 5 axes: attentional control, emotional control, autism spectrum disorders, psychosis spectrum disorders, and social skills set.⁵

This article aims to review the current evidences supporting the role of cerebellum in the pathophysiology of psychiatric disorders, including studies using volumetric and/or functional imaging techniques, genetic and molecular studies, and clinical reports. The implication of these findings, their potential use, and future directions are also discussed.

CEREBELLUM AND EMOTIONAL CONTROL

Bipolar Mood Disorder and Major Depressive Disorder

Mood disorders are among the most frequent psychiatric illnesses. The lifetime prevalence of major depressive disorder is about 12%, and approximately 2.5% of the population has bipolar mood disorder. Mood disorders are characterized by pervasive dysregulation of mood that is accompanied by cognitive, biorhythmic, and psychomotor activity disturbances.^{6,7} Unfortunately, our knowledge about the cause and pathophysiological basis of bipolar disorder is very limited. The neural system involved in mood regulation is very complex, and extensive interconnecting neural networks are involved.

Current theories in the pathophysiology of mood disorders mainly focus on 3 cortical-striatal-limbic circuits:

1. Orbital frontal circuit
2. Ventromedial emotion circuit
3. Dorsal cognitive circuit

The last circuit includes dorsolateral and dorsomedial frontal cortices. There are several neuroanatomical, electrophysiological, functional neuroimaging, and clinical evidences that indicate the role of the cerebellum in emotion regulation and affective disorders.

Limbic system including the Papez circuit is the neural substrate for emotional experience and expression. The cerebellum influences various substructures in the Papez circuit. Specifically, cerebellum nuclei and vermis are closely interconnected with midbrain substructures.^{8,9} The fastigial nucleus has projections to the ventral tegmental area. Cerebellum is not only directly interconnected to the septum, hippocampus, amygdala, and hypothalamus but is also indirectly connected to the nucleus accumbens, the mesolimbic center for reward. The cingulate cortex, which plays a crucial role in motivation and drives, is also interconnected with the cerebellum. Electrophysiological studies corroborate these interconnections.¹⁰ As mentioned before, those brainstem areas are concerned with motivation, emotions, and drives. Even neocortical areas implicated in higher-order emotional processing, including prefrontal cortex, posterior parietal lobe, superior temporal lobe, and parahippocampus, are closely connected to the cerebellum.⁸ Considering these closed cerebrocerebellar circuits, cerebellar vermis is appropriately named “limbic cerebellum”¹⁰ and “emotional pacemaker.”¹¹

Cerebellar volume

There are many volumetric studies on people who suffer affective disorders. Reduced cerebellar volume has been reported in several studies and case reports in both bipolar mood disorder and unipolar depression. The probable mediating factors include

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