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PSYCHIATRY, NEUROLOGY, AND THE ROLE OF THE CEREBELLUM

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In this series, Drs. Sanders and Gillig explain how aspects of the neurological examination can aid in differential diagnosis of some common (and some uncommon) disorders seen in psychiatric practice.

ABSTRACT

The cerebellum has long been considered quite separate from the neocortex, and accordingly the understanding of its role has been limited. Recent work has revealed that the cerebellum interacts regularly with the forebrain and it is involved in mood and cognition. In this article, the authors discuss an extensive system of neural circuits connecting the prefrontal, temporal, posterior parietal, and limbic cortices with the cerebellum. Language functions of the cerebellum are described, as well as cerebellar syndromes affecting cognition. The roles of the cerebellum in pain perception, attention deficit disorder, autism, dementia, and schizophrenia are discussed. Practical observations and tests to assess cerebellar function in the psychiatrist's office are described.

INTRODUCTION

Although the cerebellum has an important role in gait and motor function,[1] the importance of the cerebellum to psychiatric disorders has recently been the subject of focus and debate.[2–4] The cerebellum

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has been implicated in perception[5,6] and cognition,[7–9] sometimes referred to as "cerebellar neurocognition."[10]

The cerebellum projects to the prefrontal cortex through dentatothalamic pathways, and the prefrontal cortex sends information back to the cerebellum via the pontine nuclei.[6] In a study of patients with primary cerebellar lesions,[10] cognitive modulation within the cerebellum to the right cerebellar hemisphere for logical reasoning and language and to the left cerebellum for attention and visuospatial skills was found. Single photon emission tomography (SPECT) has supported a "disconnection" in cerebellar-cerebral pathways for many patients who also showed "frontal-like" behavior or affective instability. Baillieux et al[6] argue that the cerebellum plays a role in executive functioning, memory, learning, attention, visuo-spatial regulation, language, and behavioral-affective modulation.

CEREBELLAR-COGNITIVE AFFECTIVE SYNDROME

In 1998, a seven-year study of 20 patients with cerebellar lesions was published by Schmahmann and Sherman.[11] On the basis of this work, it was proposed that there existed a "cerebellar-cognitive affective" syndrome (CCAS), consisting of a) executive dysfunction (e.g. disturbances in planning, set-shifting, abstract reasoning, and working memory and visual-spatial organization and memory; 2) mild language symptoms including agrammatisms and anomia; and 3) behavioral-affective disturbances, consisting of a blunting of affect or disinhibited and inappropriate behavior.

An extensive system of neural circuits connecting the prefrontal, temporal, posterior parietal, and limbic cortices with the cerebellum has been proposed to account for these findings (i.e., motor deficits result from lesions that interrupt cerebellar communication with motor systems; cognitive deficits result from lesions that interrupt cerebellar communication with cerebral association cortex; and psychiatric disorders result from midline vermis lesions that interrupt cerebellar communication with the neocortex and the limbic system).[12]

DEVELOPMENTAL COORDINATION DISORDER

Developmental coordination disorder is a neurodevelopmental syndrome affecting motor, cognitive, and affective functions in five percent of school-age children.[13,14] The symptoms are similar to CCAS (above), and cerebellar involvement of the vermis has been demonstrated. In children with developmental coordination disorder, cerebellar disorder has also been proposed to reflect a disruption of the cerebello-cerebral network involved in the execution of planned actions, visuo-spatial cognition, and affective regulation.[9] Children with this disorder have more abnormal performance on "traditional" (motor) cerebellar neurological tests as well.[15]

POSTERIOR FOSSA SYNDROME

The posterior fossa syndrome (PFS) is most commonly found in children or adolescents with a posterior fossa lesion (e.g., tumor or stroke). These children have transient mutism and behavioral changes. The cause of this syndrome is unclear. At one time it was thought that the muteness was due to damage to the dentate nucleus, which is normally connected via the thalamus to the supplementary motor area.[15] However, a more recent hypothesis for PFS is cerebello-cerebral "diaschisis" (disconnectivity), due to "crossed signals" between the cerebellum and frontal cortex.[16] About 8 to 12 percent of children develop PFS after otherwise successful posterior fossa surgery.

LANGUAGE

There are linguistic deficits associated with disease or damage to the cerebellum.[17] The right cerebellum normally helps to modulate nonmotor language processes and cognitive function to parts of the brain to which it is reciprocally connected, i.e., the cerebellum modulates (rather than generates) language and cognition, and acts as an interface between cognition and execution.[18] The linguistic impairments that occur with cerebellar lesions are, therefore, different from those produced by cortical lesions. Cerebellar lesions cause a form of "linguistic incoordination" or crudity.[19] A patient might have difficulty generating words grammatically. When asked to generate verbs in response to nouns, the patient might produce some associations that are incorrect responses. For example, instead of saying "lay" or "throw" in response to "brick," the patient might say "red."[20–22]

AGING

Cerebellar volume declines with normal aging.[23] Cerebellar signs become more prominent in healthy older persons.[24] The cerebellum has a role in cognitive associative learning[25] and working memory.[26] In a study of 228 older adults,[27] gray matter volume in the cerebellum predicted general cognitive ability in healthy older persons, with a stronger relationship in men.

ATTENTION DEFICIT HYPERACTIVITY DISORDER

Neurologic "soft signs" including "cerebellar" motor signs have been described in patients with attention deficit hyperactivity disorder (ADHD).[28] Persons with ADHD generally have decreased volume in the posterior inferior cerebellar vermis, and the degree of volume loss has been correlated with parent- and clinician-rated severity measures of ADHD. In sibling comparisons, right cerebellar volume is reduced in the affected sibling but not in the unaffected siblings. There have been recent findings of a genetic association between ADHD and single-nucleotide polymorphisms (SNPs) located in genes that are expressed in the cerebellum.[29–31]

AUTISM SPECTRUM DISORDERS

Autism is associated with repetitive and stereotypic movement, impaired communication, and profound difficulties with social reciprocity.[32] Patients (adults and children) with autism have been found to have a reduction of Purkinje cell density in the cerebellar cortex.[33] Patients with autism also have cytoplasmic inclusions in their Purkinje cells, a reduction in the number of cells, and ectopic grey matter in the deep cerebellar nuclei, as well as an intense neuroinflammatory process extending to the cerebellar white matter.[34]

In Aspergers syndrome, there is a possible abnormality in the development of the cerebello-frontal networks, implying a defect in brain activation during cognitive and motor tasks. White matter defects have been found in specific cerebellar neural pathways with localized abnormalities in the main cerebellar outflow pathway that could prevent the cerebral cortex from receiving cerebellar feedback inputs necessary for successful adaptive social behavior.[33, 34]

Children with autistic spectrum disorder have histopathological abnormalities in the superior peduncles of the cerebellum (increased mean diffusivity, indicating altered microstructural integrity of this output pathway, using diffusion tensor imaging technologies). Children with autistic spectrum disorder also have alterations in the organization of the afferent [inflow] fibers of the middle and inferior cerebellar peduncles, which ultimately connect to the frontal lobe). The fibers are organized differently, but it is not known whether this is a primary or secondary effect of changes in cortical or subcortical structures.[34,35] In general, coordination problems are a common finding in autism spectrum disorders, and frank ataxia is a major feature of Rett syndrome.[36]

PAIN

The cerebellum responds to noxious stimuli, as demonstrated by fMRI studies of pain, which show activation in the cerebellum[5] during both acute and chronic pain.[37,38] Pain has been described as "a multidimensional experience that encompasses sensory discriminative, affective motivational, and cognitive evaluative components."[39] Within the cerebellum, primary afferents conduct noxious input, and the cerebellum modulates noxious input processing and then projects this modulated input to the cortex. The cerebellum responds differentially to innocuous versus noxious stimuli,[40,41] processing the input in different areas of the cerebellum.

SCHIZOPHRENIA

Schizophrenia may be associated with a fundamental disturbance in the timing of neural processes.[42–45] At one point, it was proposed that patients with schizophrenia had enhanced cerebellar excitability during conditioning tasks[42,43] and this excitability resulted in motor and cognitive incoordination due to temporal processing errors.[42,44] Recent reviews[46] have not supported a cerebellar contribution to affective symptoms, however, and fMRI studies, in general, have found cerebellar hypoactivation in schizophrenia.[46]

Cerebellar volume alone is not associated with global cognitive functioning in schizophrenia[47] although severity of incoherence of speech and the presence of neologisms has been correlated with reduced activity in the cerebellar vermis.[48,49] Another study found a correlation between cerebellar white matter volume and severity of thought disorder.[50] Patients with cerebellar neurological motor signs have been found to have more severe negative symptoms, poorer premorbid social adjustment, and smaller total cerebellar volume.[51,52]

The presence or absence of cerebellar neurological soft signs can discriminate between patients with schizophrenia versus control groups. The most common abnormalities are found on the Romberg test and tests of tandem gait. Patients with schizophrenia also have problems predicting proprioceptive consequences of self-generated movements[53] and have problems with smooth pursuit eye movements.[54–57] A recent fMRI study investigating effects of a CNS selective cholinesterase inhibitor (rivastigmine) found that improvement of behavioral measurements correlated with increased rCBF in the cerebellum.[58] It is currently being debated whether this result was due to enhanced attention, or rather related to a predominantly sensory role of the cerebellum,[59] with the cerebellum functioning in the role of error detection and timing[60] as an internal timing system,[61] which is damaged in patients with schizophrenia.

CEREBELLAR SIGNS AND SYMPTOMS

Brain disorders that affect the cerebellum are reflected in a) loss of muscle tone (especially with an acute lesion); b) incoordination of volitional movement, with abnormalities in the rate, range, and force of movement, so that there is irregular acceleration and deceleration of the movement resulting in an intention tremor; c) minor muscle weakness, fatigability, and impairment of associated movements; and d) problems maintaining equilibrium.

Balance. Lesions that involve the superior cerebellar peduncle, which ascends to the thalamus, or the dentate nucleus, which indirectly projects to the premotor cortex, cause the most severe and enduring cerebellar symptoms. However, lesions of the cerebellar vermis, which is in the midline, cause more severe disturbances of equilibrium and gait.

Hypotonia. Hypotonia can be tested by tapping the wrists of the outstretched arms. The affected limb will be displaced through a wider range than normal, due to the hypotonic muscles reduced ability to fixate the arms. Pendularity in the knee-jerk reflex due to defective tonic contraction of the quadriceps

and hamstring muscles is also seen in cerebellar disease.

Volitional movement. The patient may overshoot the mark (past-pointing or hypermetria) when reaching for something and then correct the error by a series of secondary movements side-to-side (intention tremor). This is demonstrated in the upper extremities with the finger-to-nose test, and in the lower extremities with heel-to-shin.

Tremor. A head tremor of about 3- to 4-second movements in the anterior-posterior direction (titubation) may accompany a cerebellar midline lesion.

Speech. Cerebellar lesions are associated with several disorders of speech. The patient may speak slowly and with slurring or else have a scanning dysarthria with variable intonation, such that the words are broken up into syllables as if "scanning" a line of poetry for meter. There may be explosive speech where, after an involuntary interruption, a syllable is spoken with less or more force than is natural.

Eye movements. Eye movement may be impaired, with voluntary gaze accomplished by a series of jerky movements (saccadic dysmetria). On attempted fixation, the eyes may overshoot the target and then oscillate through several cycles until fixation is attained, similar to the problems the patient has with volitional movements.

CONCLUSION

The function of the cerebellum is relevant to the psychiatrist because the cerebellum has been implicated in affect and cognition and is damaged in important psychiatric disorders including schizophrenia In this article we reviewed some neural circuits connecting the prefrontal, temporal, posterior parietal, and limbic cortices with the cerebellum. Language functions of the cerebellum were described, as well as other cerebellar syndromes affecting cognition. The roles of the cerebellum in pain perception, ADHD, autism, dementia, and schizophrenia were described. Practical observations and tests to assess cerebellar function in the psychiatrist's office were outlined.

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