

Psychiatric and Cognitive Complications of Diseases Affecting the Cerebellum

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Psychiatric disorders frequently complicate degenerative brain diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease, and strokes. Common psychiatric manifestations of these diseases include depression, anxiety, explosive temper outbursts, irritability, and apathy. It is now clear that these psychiatric conditions are not psychological reactions to the experience of having a devastating neurological disease. Instead, psychiatric disorders, like problems with walking, balance, coordination, and cognition (thinking and memory), are a direct consequence of the neurological diseases, and stem from damage to regions of the brain that control mood, thought, and emotion. Most importantly, many of these psychiatric disorders can be successfully treated.

In two centuries of study of the cerebellum and cerebellar diseases, attention has almost exclusively focused on the role of the cerebellum in regulating movement and coordination. However, the frequency of psychiatric complications in other neurodegenerative diseases led us to suspect that psychiatric disorders may also commonly complicate cerebellar degenerative diseases, such as the spinocerebellar ataxias. Our suspicions were fueled by case reports of psychiatric symptoms in patients with various cerebellar diseases. For instance, 20 individuals reported by Schmahmann and Sherman, most with cerebellar strokes, all had some combination of cognitive and emotional changes following cerebellar damage. In addition, neuroanatomical studies have conclusively demonstrated that the cerebellum is connected to other brain regions known to regulate thought, emotion, and behavior, including the frontal cortex (located behind the forehead and responsible for so-called executive functions like planning and judgment), the limbic

system (several linked brain regions that together regulate emotion), and the hypothalamus (a small region near the bottom of the brain that regulates many drives and appetites). Also, studies of healthy individuals using sophisticated techniques for measuring brain activation have shown that the cerebellum participates in the processing of language, time, spatial orientation, decision making, and emotion.

The goal of our research was to answer, at least preliminarily, a series of questions about the psychiatric and cognitive aspects of diseases causing cerebellar degeneration: Do individuals with cerebellar degeneration have more cognitive and psychiatric difficulties than a comparable population of healthy individuals? What types of cognitive deficits and psychiatric disorders are most common in individuals with cerebellar degeneration? How does this compare with another degenerative movement disorder, Huntington's disease (HD), in which degeneration occurs in a different brain region (the basal ganglia)? Can psychiatric and cognitive complication be detected during standard clinical evaluations of individuals with cerebellar degeneration? Can we combine the answers to these questions to provide useful guidelines for the treatment of psychiatric and cognitive complications of cerebellar degeneration?

To address these questions, we compared three groups of individuals. The first consisted of 31 volunteers with neurodegenerative diseases affecting the cerebellum. Most of these individuals had either hereditary or nonhereditary forms of spinocerebellar ataxia, with an average of 12 years between the onset of disease and participation in our study. The second group consisted of 21 individuals with HD, with disease onset also occurring an average of 12 years before participation in ►►

our study. The third group consisted of 29 neurologically healthy volunteers. Almost all members of this group were the spouses of individuals with cerebellar degeneration or HD group. One reason we chose spouses to serve as a comparison group is that they are exposed to the psychological stress of living with a chronic illness without having the illness themselves. The average age, education, and pre-illness cognitive abilities of the three groups were nearly identical. All participants in the study received a detailed psychiatric examination by an experienced neuropsychiatrist (Dr. Leroi, who specializes in psychiatric problems in individuals with neurological disorders). We also obtained information from a person who knew the study participant well, and from medical records. Study participants were also given a variety of tests of thinking, learning, and memory.

The most important finding of our study was that *80% of individuals with cerebellar degeneration had a clinically significant psychiatric disorder that arose during the course of their neurological illness*, double the rate of the neurologically healthy individuals and about the same rate that we found in individuals with HD. The most common psychiatric diagnosis in the cerebellar group was mood disorder. Over 65% of the individuals with cerebellar degeneration developed a mood disorder at some time after the onset of their neurological illness, usually a form of depression.

Here it is important to point out that a "clinical" depression (sometimes referred to as "major depression") is different than the sadness or blues that are a part of everyday emotional life. While low mood is usually a part of clinical depression, some or all of a long list of other symptoms are also present and may be even more prominent than low mood: **loss of interest in usual activities, excessive anxiety or agitation, irritability or apathy, change in sleep patterns, changes in appetite or sex drive, pessimism, poor concentration or slowed thinking, agitated or slowed movements, low energy, and thoughts about death or suicide.** Episodes of depression typically last weeks to months, but may be longer or shorter. This type of depression

is caused by abnormalities in brain function, and is not a psychological reaction to adverse events in a person's life. It is useful to think about clinical depression as an emotion that takes on a life of its own, no longer closely tied to life events.

25% of the individuals with cerebellar degeneration developed personality changes, compared to 50% of individuals with HD and none of the neurologically healthy individuals. In a clinical context, "personality change" means a marked change from the previous personality of an individual that is sufficient to cause problems at work, at home, or in relationships with others. New and problematic personality characteristics in individuals with cerebellar degeneration and HD included mood instability (rapid and volatile mood changes), disinhibition, apathy, suspiciousness, and silly child-like behavior. It was not unusual for several of these changes to occur in the same individual.

In our evaluation of cognitive function, we found that 10% of individuals with cerebellar degeneration were sufficiently impaired to meet standard criteria for dementia (with dementia defined as impairment in multiple aspects of cognition sufficiently severe to interfere with usual life activities). An additional 10% had less severe cognitive impairment. None of the neurologically healthy individuals had cognitive impairment, while cognitive impairment was apparent in 70% of individuals with HD. On more sophisticated testing, it was again apparent that cognitive impairment was less severe in individuals with cerebellar degeneration than with HD. Executive function, rather than memory, verbal skills, or spatial orientation, was the most prominent type of cognitive difficulty experienced by individuals with cerebellar degeneration.

To confirm the results of this study, we also examined the neurological records of 133 individuals with cerebellar degeneration referred to our clinic for genetic testing. The referring neurologists detected psychiatric difficulties in 40% of these patients, and cognitive impairment in 30%. The rates were lower

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in those individuals with only cerebellar degeneration, and higher in those in whom other brain regions were also affected. Since diagnoses were made by clinical neurologists during routine evaluations, it is not surprising that the rate of psychiatric and cognitive disorders were different than in our primary study. Nonetheless, the conclusions of this secondary study are consistent with our primary study: psychiatric disorders and cognitive impairment are common in patients with diseases that cause cerebellar degeneration, these problems are of sufficient severity to attract attention on routine clinical examinations, and that these problems are more likely to occur when neurodegeneration involves regions of the brain in addition to the cerebellum.

Given that psychiatric disorders and cognitive impairment are relatively frequent complications to degenerative diseases of the cerebellum, what can be done? The ultimate answer, of course, is to prevent or cure the degeneration itself. There is much room for optimism on this front, but effective treatments have proven elusive. In the meantime, as we have learned in the treatment of HD and other neurodegenerative disorders, it is possible to substantially improve the quality of life of individuals with neurodegenerative diseases and their families by treatment of cognitive and especially psychiatric disorders.

All treatment efforts must *start with education*. It is essential that individuals with diseases affecting the cerebellum and their family members know that psychiatric and cognitive problems may arise during the course of their illness. Just like troubles with balance or coordination, psychiatric and cognitive problems are a part of the disease, and are not the fault of the affected individual, family members, or health care providers. The presence of these complications does not imply moral failure or a deliberate effort on the part of the patient to undermine efforts to help them. All parties involved should remain optimistic that environmental and pharma-

cological interventions may remove at least some of the burden imposed by these conditions.

The recognition of depression is essential, since, among all the common complications of cerebellar disease, it may be the most treatable. The approach to treatment is multi-pronged, and includes antidepressants, support, and environmental changes. There is no data in cerebellar disease indicating which of the many currently available antidepressants is most effective, and hence the choice of an antidepressant is based on experience with treatment of depression in other neurodegenerative disorders. A reasonable first choice is one of the serotonin specific reuptake inhibitors (SSRIs), of which Prozac (fluoxetine) is the most famous example. It is prudent to start with a relatively low dose and advance the dose relatively slowly, since individuals with neurodegenerative disorders are more prone than other people to become confused if drug doses are too high or are advanced too fast. Antidepressants can be advanced to a standard therapeutic dose if necessary and if side effects are tolerable. After 1-2 months of no response to one antidepressant at a typical dose it is reasonable to switch to another agent. Patients, family members, and doctors should remember that side effects often emerge prior to beneficial effects, and often spontaneously resolve. Physicians and other medical providers can be very helpful in providing support and guidance during the initiation of treatment with antidepressant medicine, reminding patients and family that treatment takes time and carefully assessing side effects. Helpful environmental interventions often involve establishing a "structure" for the patient, including setting regular hours for sleep, eating, exercising, and getting out of the home. Meanwhile, the patient can be freed from burdensome responsibilities, which then can be gradually reinstated as the patient improves. As always, treatment must be individualized.

Unlike depression, the goal for management of personality change or impaired cognition is not elimination of the condition, but ►►

rather adaptation to it. Medicines, typically antipsychotics drugs (such as haloperidol, resperidone, or olanzapine) or mood stabilizers (such as valproate or gabapentin) may prove useful in minimizing moodiness or irritability. Apathy may improve with stimulants (such as amphetamines) or other agents affect the chemistry of the dopamine system (such as amantadine). There is no evidence that pharmacologic treatment improves the cognitive impairment of cerebellar degeneration, though the issue has never been systematically examined.

Establishing routines that emphasize the strengths of the affected individual often prove very helpful in managing personality change and cognitive impairment. For instance, a set schedule of regular daily activities, minimizing change from day-to-day, is often helpful for patients who react with anger, suspicion, or confusion to change. New routines with increased stimulation may be of some value in overcoming apathy. Learning the proper response to irritability (ignoring it, switching to another topic of conversation, or distraction by introduction of a different activity) may help prevent escalation of temper into verbal or physical violence. Patients may partially compensate for mild cognitive impairment by keeping lists and allowing themselves more time for tasks. The stress on patients and families of more severe cognitive impairment or personality change may be decreased by removing the responsibility of the patient for performing tasks which are beyond their capacity (maintaining finances, supervising small children, driving, employment), while maintaining the patient's responsibility for tasks within their capacity. Such interventions require considerable delicacy.

Developing, implementing, revising, and maintaining treatment for cognitive and psychiatric complications of cerebellar disease requires an accurate assessment of the patient's strengths and weaknesses, individualization of treatment, and flexibility to change the plan as needed. Neurologists and primary care physicians with expertise in depression and personality change may assume overall

management of the treatment. In more complicated cases, or with neurologists or primary care physicians who are less comfortable with these issues, consultation with a psychiatrist with experience in the complications of neurodegenerative diseases may be necessary. Neuropsychological testing can provide precise information on cognitive strengths and weakness, and occupational therapists can assess an individual's capacity to perform both routine and more complicated tasks of daily living. Involvement of the family is essential in every step of the process of diagnosis and treatment.

To summarize, diseases that result in cerebellar degeneration are commonly complicated by cognitive impairment and psychiatric disorders, especially depression. These complications are probably more frequent and more severe when other brain regions in addition to the cerebellum are also involved. Based on our current knowledge of neurodegenerative diseases affecting other brain regions, both pharmacologic and non-pharmacologic interventions may prove helpful to patients with cerebellar degeneration and their families. Successful treatment is dependent on thorough evaluation and careful individualization to the strengths, weakness, and environment of each affected person.

Those with interest are referred to the three publications that describe in detail the studies summarized here:

Leroi I, O'Hearn E, Marsh L, Lyketsos CG, Rosenblatt A, Ross CA, Brandt J, Margolis RL. Psychopathology in degenerative cerebellar diseases: A comparison to Huntington's disease and normal controls, *American Journal of Psychiatry*, 159 (2002):1306-1314.

Brandt J, Blau C, Leroi I, O'Hearn E, Rosenblatt A, Margolis RL. Cognitive impairments in cerebellar degeneration: a comparison with Huntington's disease. *Journal of Neuropsychiatry and Clinical Neurosciences*, in press.

Liszewski CM, O'Hearn E, Leroi I, Ross CA, Margolis RL. Cognitive impairment and psychiatric symptoms are common in cerebellar degenerative disease, *Journal of Neuropsychiatry and Clinical Neurosciences*, in press. ❖