Mechanisms of Ataxia

Ataxia is derived from the Greek word for “disorderly.” Originally a general term that was applied to a number of different medical disorders of heartbeat, gait, and movement, “ataxia” is now used more specifically to mean the incoordination of movement following damage of the sensory or cerebellar system. The purpose of this update is to review the causes and possible mechanisms of ataxia. A better understanding of the possible mechanisms of ataxia could lead to improved treatment strategies for this challenging group of patients.

Neural Structures Associated With Ataxia
Ataxia can result from damage to several different motor or sensory regions of the central nervous system, as well as from peripheral nerve pathology. One of the most common causes of ataxia is damage to the cerebellum, often caused by stroke, disease, or tumor. Cerebellar damage generally results in ataxia of voluntary limb movement or gait, and also can result in high-amplitude tremor that accompanies movement. If there is damage to only one cerebellar hemisphere, the resultant symptoms will manifest on the side of the body ipsilateral to the lesion.

Theoretically, damage to any of the pathways that provide cerebellar input or output also can result in ataxia of voluntary limb movement or gait. These structures include dorsal and ventral spinocerebellar pathways, pontine nuclei (disruption of the corticopontocerebellar pathway), and any of the three cerebellar peduncles (through which run all of the cerebellar input and output fibers). Demyelinating diseases such as multiple sclerosis can cause profound ataxia via the loss of myelin in the cerebellum or any of its pathways. Discrete damage to structures that receive cerebellar input, such as the thalamus, also can result in varying degrees of ataxia and tremor.


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Ataxia may also occur following disruption of proprioceptive input from the periphery. Thus, “sensory ataxia” can result from damage to the afferent portions of peripheral nerves (eg, large-fiber neuropathies), the dorsal nerve roots entering the spinal cord (eg, tabes dorsalis), the dorsal column of the spinal cord, the medial lemnisci of the brain stem, the sensory-receiving regions of the thalamus, and sometimes the parietal cortex. Damage to any of these structures can cause ataxia of voluntary limb movement or gait, depending on lesion location and size.

**Distinctions Between Cerebellar and Sensory Ataxia**

Ataxia due to cerebellar damage can be distinguished from that due to sensory loss by observing movements performed with and without vision. Individuals with sensory ataxia show a marked worsening of symptoms when their eyes are closed. Individuals with cerebellar ataxia show only a minimal worsening of symptoms when their eyes are closed, although cerebellar and sensory ataxia may both cause increased reliance on visual feedback during movement.

**Potential Mechanisms of Ataxia: Interaction Torques and Multijoint Movements**

The mechanism that underlies ataxia is not yet understood. Many studies addressing this issue have tested the voluntary limb movements of subjects with either cerebellar damage or peripheral neuropathy. Often, the studies of individuals with cerebellar lesions have used paradigms that test movement at one joint in a highly instrumented manner. These studies of single-joint movements have uncovered some abnormal findings that appear to be related to classic components of ataxia. However, these studies often go on to generalize that control over one particular parameter is a specific and fundamental function of the cerebellum.

Several researchers have found that patients with cerebellar pathology exhibit hypermetria (ie, overshoot their target) when they are asked to make rapid, single-joint step tracking movement to a target. Commonly, the abnormal findings that occur with this task are (1) agonist muscle activity is reduced in magnitude and prolonged in time (resulting in similar deficits of acceleration) and (2) antagonist muscle activity is delayed (resulting in delayed deceleration). These researchers concluded that the fundamental role of the cerebellum is to modify agonist muscle activity or control the timing of onset of antagonist muscle activity. However, in a study in which patients with cerebellar pathology were asked to make rapid reversals in a movement (testing for dysdiadochokinesia), the primary finding was that the patients had an inability to cease activity of an antagonist muscle so that the agonist muscle could begin the second phase of the movement. In this study, the cerebellum was hypothesized to play a role in the cessation of antagonist activity. A more recent study examined the ability of patients with cerebellar pathology to adjust for added inertia at the hand during a single-joint wrist movement. With the addition of an inertial mass, the patients exhibited increasing hypermetria because they were unable to adjust the magnitude of the antagonist muscle activity to decelerate and stop the movement appropriately. Thus, the results of this study support the hypothesis

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that the cerebellum functions to modify the magnitude of antagonist muscle activity.

Overall, the studies of patients with cerebellar dysfunction making single-joint movements have provided evidence for variables that the cerebellum may control, such as timing or amplitude scaling in the agonists, the antagonists, or both muscle groups. When considering findings from these studies, however, it appears that the controlled variable changes depending on the constraints of the task. Thus, it becomes clear that the mechanism to explain all of these deficits is more complicated than, for instance, just agonist magnitude scaling or any other single proposed explanation. Instead, what appears to be critical is the relationship between activities of multiple muscles relative to the load (inertia) that has to be moved. Another interesting observation regarding this work is that no mechanism proposed in these studies of single-joint movements has ever been found to explain the profound deficits observed in more natural multijoint movements. Furthermore, other researchers have compared the effects of cerebellar lesions on both single-joint and multijoint movements and have found relatively mild or even no deficits in single-joint movements compared with profound deficits in multijoint movements.

From a mechanical perspective, the task of controlling each of the multiple degrees of freedom associated with a multijoint movement is not equivalent to that of controlling each of the elemental single-joint movements separately. If several elemental single-joint commands were executed simultaneously, a normal multijoint movement would not be generated; instead, a very disorganized movement would arise. Movement of one segment that is linked to another segment passively causes intersegmental "interaction torques" (including Coriolis, centripetal, and inertial torques) to occur at the involved joints. For example, during a reach involving multiple joints, elbow movement will cause an interaction torque to occur at the shoulder, and shoulder movement will cause an interaction torque to occur at the elbow. These torques are velocity and acceleration dependent and will increase in magnitude as movements are made more rapidly. In the course of a reach involving multiple joints, individuals without neurological problems must exploit interaction torques when the torques assist with the intended movement and must counter the torques when they oppose the intended movement. Thus, the muscles acting at a joint normally produce the correct amount of torque to combine with any interaction torques generated by movement of linked joints.

Recent evidence supports the idea that persons without neurological problems predictively adjust for intersegmental interaction torques occurring during a given movement. Aoki found that anticipatory electromyographic activity occurring in muscles crossing the elbow joint was specific to counter interaction torques caused by wrist flexion and extension. This anticipatory response in the elbow muscles was independent of the wrist muscles used, but was instead related to the mechanical effects of the wrist movement at the elbow joint. Other studies of anticipatory postural adjustments to rapid arm displacements during standing provide further evidence that the nervous system predictively anticipates and counters the mechanical effects of moving limb segments.

Recent studies of individuals with peripheral sensory neuropathies and cerebellar ataxia provide compelling evidence that ataxia may result from an inability to exploit or counter intersegmental interaction torques. Sainburg et al. studied subjects with large-fiber sensory neuropathies, causing complete loss of proprioception in their arms, as they made planar multijoint arm movements. Subjects were asked to trace lines oriented in different directions by moving "out" along the line and then reversing and moving back "in" along the line. When the subjects were not allowed to view their arm, they made characteristic errors at the "reversal" phases, which were greatest in the directions where the interaction torque acting at the elbow was large. These errors were also in the direction that would be predicted by the interaction torque. The conclusions from this study were that interaction torques are normally accounted for in a predictive manner and that proprioceptive information about the limb is required for this mechanism in the absence of vision.

Bastian et al. showed that subjects with cerebellar damage compensate abnormally for interaction torques generated during a multijoint reaching movement. In this study, control subjects and subjects with cerebellar disorders made vertical-plane reaching movements after receiving instructions for slower and for faster movements. The faster movements increased the magnitude of the interaction torques and the need to compensate for them. When subjects with cerebellar disorders moved faster, they were unable to fully adjust for interaction torques. Often, the torque produced by their muscles did not counter the interaction torque and allowed the interaction torque to excessively affect the movement. This inability to adjust for interaction torques resulted in an abnormal (ataxic) pattern of reaching, with the elbow and shoulder joints moving at inappropriate rates relative to one another and the fingertip overshooting the target (hypermetria). When subjects with cerebellar disorders were asked to move slowly and accurately, they tended to "decompose" the reach into a series of shoulder movements and then elbow movements and undershoot the target slightly (hypometria). Decomposition was hypothesized to represent a compensatory strategy.
that would reduce the interaction torques occurring at
the moving joint, although interaction torques would
still occur at the stationary joint. Under this hypothesis,
co-contraction of the muscles about the stationary joint
to "stiffen" it would be the optimal simplification stra-
tegy, thus reducing the need to dynamically account for
interaction torques. In sum, this study of cerebellar
ataxia indicates that the interaction torques during
faster movements are not appropriately countered or
exploited and that decomposition of movement sacri-
fices coordination to produce better accuracy.

A final piece of evidence supports the idea that the
cerebellum is involved in predictively adjusting for the
mechanical effects of moving segments. This evidence
comes from studies of anticipatory postural reactions.
Normally, when the arm is moved rapidly during stand-
ing, preparatory and concurrent muscle activity occurs
in the trunk and legs to counter inertial effects of the
moving limb.18-20 Subjects with cerebellar damage have
also been studied performing rapid arm raises in a
standing position and were found to produce abnor-
manally timed sequences of preparatory and concurrent
postural muscle activity relative to the arm raise.23 Sub-
jects with cerebellar disease generated leg and trunk
muscle activity that occurred too early to be effective in
countering the inertial effects of the arm movement.
Because the postural adjustment was not appropriately
coordinated with the arm movement, postural stability
was diminished in the subjects with cerebellar damage.

Summary
Ataxia, or incoordination of movement, is a disorder
that can be caused by damage to several different
nervous system structures. Common causes of ataxia
include damage of the cerebellum and damage of sen-
sory structures. Sensory ataxia is distinguishable from
cerebellar ataxia, because the sensory ataxia causes
symptoms to worsen when movements are made with
the eyes closed. The basic mechanism underlying ataxia
is not yet understood, although studies indicate that ataxia
may be due in part to an inability to coordinate the
relative activity of multiple muscles and adjust move-
ments at a given joint for the effects of other moving
joints (interaction torques). Based on these findings, it
could be reasoned that treatments focusing on strategies
to reduce the complexity of a movement by minimizing
the number of moving joints or by stabilizing against the
inertial effects of limb movement will improve func-
tion.7,12-14,21-28 Further testing of treatments for ataxia,
however, is needed. Ataxia may be best treated by teaching
people to avoid rapid multijoint movements and instead
make slower movements limited to single joints.

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