

The Cerebellum

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An Overall View

THE CEREBELLUM CONSTITUTES ONLY 10% of the total volume of the brain but contains more than one-half of its neurons. The structure comprises a series of highly regular, repeating units, each of which contains the same basic microcircuit. Different regions of the cerebellum receive projections from different parts of the brain and spinal cord and project to different motor systems. Nonetheless, the similarity of the architecture and physiology in all regions of the cerebellum implies that different regions of the cerebellum perform similar computational operations on different inputs.

The symptoms of cerebellar damage in humans and experimental animals give the clear impression that the cerebellum participates in the control of movement. Thus we describe these symptoms because knowledge of them, in addition to being critical for the clinician, constrains conjecture about the exact role of the cerebellum in controlling behavior. The goal of cerebellar research is to understand how the connections and physiology of cerebellar neurons define the function of the cerebellum. Thus a major part of this chapter covers the fundamentals of cerebellar physiology and anatomy.

Finally, there is a relationship between cerebellar operation and more theoretical concepts of “internal models” in motor control (see Chapter 33). A fundamental

precept of modern cerebellar research is that these internal representations of the external world are implemented in the cerebellum. The cerebellum could adjust motor performance by using its learning capabilities to alter the internal models to match any changes in the motor effectors of the external world. Thus at the conclusion of this chapter we discuss cerebellar learning and its possible relationship to internal models.

Cerebellar Diseases Have Distinctive Symptoms and Signs

Disorders of the human cerebellum result in disruptions of normal movement, described originally by Joseph Babinski in 1899 and by Gordon Holmes in the 1920s. These disruptions are in stark contrast to the paralysis caused by damage to the cerebral cortex. We cannot yet link normal cerebellar structure and function to the symptoms of cerebellar damage in humans, but the fact that movements are disrupted rather than abolished and the nature of the disruptions are important clues about cerebellar function.

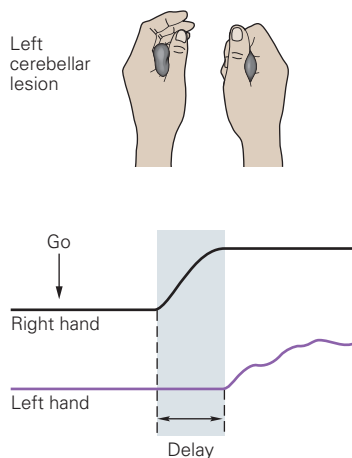
Cerebellar disorders are manifested in four symptoms. The first is *hypotonia*, a diminished resistance to

passive limb displacements. Hypotonia is also thought to be related to so-called “pendular reflexes.” The leg normally comes to rest immediately after a knee jerk produced by a tap on the patellar tendon with a reflex hammer. In patients who have cerebellar disease, however, the leg may oscillate like a pendulum as many as eight times before coming to rest.

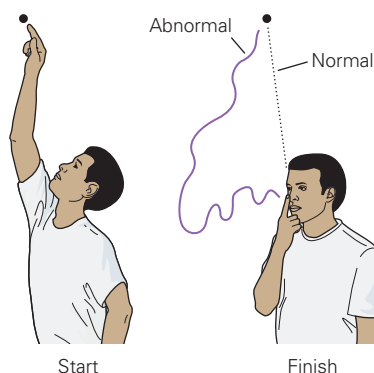
The second symptom is *astasia-abasia*, an inability to stand or walk. Astasia is loss of the ability to maintain a steady limb or body posture across multiple joints. Abasia is loss of the ability to maintain upright stance against gravity. When sitting or standing, many cerebellar patients compensate by spreading their feet, an attempt to stabilize balance by increasing the base of support (see Chapter 41). They move their legs irregularly and often fall.

The third symptom is *ataxia*, the abnormal execution of multi-jointed voluntary movements, characterized by lack of coordination. Patients have problems initiating responses with the affected limb and controlling the size of a movement (*dysmetria*) and the rate and regularity of repeated movements (Figure 42–1). This last deficit, first described by Babinski, is most readily demonstrated when a patient attempts to perform rapid alternating movements, such as alternately touching

A Delayed movement



B Range of movement errors



C Patterned movement errors

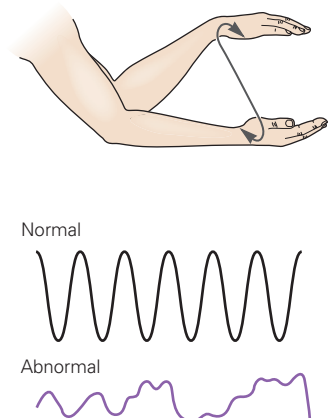


Figure 42–1 Typical defects observed in cerebellar diseases.

A. A lesion in the left cerebellar hemisphere delays the initiation of movement. The patient is told to clench both hands at the same time on a “go” signal. The left hand is clenched later than the right, as is evident in the recordings from a pressure bulb transducer squeezed by the patient.

B. A patient moving his arm from a raised position to touch the tip of his nose exhibits inaccuracy in range and direction

(*dysmetria*) and moves his shoulder and elbow separately (decomposition of movement). Tremor increases as the finger approaches the nose.

C. A subject was asked to alternately pronate and supinate the forearm while flexing and extending at the elbow as rapidly as possible. Position traces of the hand and forearm show the normal pattern of alternating movements and the irregular pattern (*dysidiadochokinesia*) typical of cerebellar disorder.

the back and the palm of one hand with the palm of the other. Patients cannot sustain a regular rhythm or produce an even amount of force, a sign referred to as *dysdiadochokinesia* (Greek, impaired alternating movement). Holmes also noted that patients made errors in the timing of the components of complex multi-joint movements (decomposition of movement) and frequently failed to brace proximal joints against the forces generated by the movement of more distal joints.

The fourth symptom of cerebellar disease is a form of tremor at the end of a movement, when the patient attempts to stop the movement by using antagonist muscles. This *action* (or *intention*) *tremor* is the result of a series of erroneous corrections of the movement. Once a movement is clearly headed in the wrong direction, attempts to make corrections fail repeatedly and the hand oscillates irregularly around the target in a characteristic *terminal tremor*. This behavior clearly suggests that the cerebellum normally is responsible for the properly timed sequence of activation in agonist and antagonist muscles and that loss of proper timing causes movements that, although initiated in the correct direction, cannot be controlled or brought to an accurate endpoint.

One conspicuous feature of cerebellar disorders is a loss of the automatic, unconscious nature of most movements, especially for motor acts made up of multiple sequential movements. One of Holmes's patients, who had a lesion of his right cerebellar hemisphere, reported that "movements of my left arm are done subconsciously, but I have to think out each movement of the right arm. I come to a dead stop in turning and have to think before I start again." Normally movement is controlled seamlessly by cerebellar inputs and outputs; with a malfunctioning cerebellum it seems that the cerebral cortex needs to play a more active role in programming the details of motor actions.

The Cerebellum Has Several Functionally Distinct Regions

The cerebellum occupies most of the posterior cranial fossa. It is composed of an outer mantle of gray matter (the cerebellar cortex), internal white matter, and three pairs of deep nuclei: the fastigial nucleus, the interposed nucleus (itself comprising the emboliform and globose nuclei), and the dentate nucleus (Figure 42-2A).

The cerebellum is connected to the dorsal aspect of the brain stem by three symmetrical pairs of peduncles: the *inferior cerebellar peduncle* (also called the restiform body), the *middle cerebellar peduncle* (or brachium pontis), and the *superior cerebellar peduncle* (or brachium conjunctivum). Most of the output axons of

the cerebellum arise from the deep nuclei and project through the superior cerebellar peduncle. The main exception is a group of Purkinje cells in the flocculonodular lobe that projects to vestibular nuclei in the brain stem.

The surface of the cerebellum is highly convoluted, with many parallel folds called *folia* (Latin, leaves). Two deep transverse fissures divide the cerebellum into three lobes. The primary fissure on the dorsal surface separates the anterior and posterior lobes, which together form the body of the cerebellum (Figure 42-2A). The posterolateral fissure on the ventral surface separates the body of the cerebellum from the smaller flocculonodular lobe (Figure 42-2B). Each lobe extends across the cerebellum from the midline to the most lateral tip.

In the orthogonal, anterior-posterior direction two longitudinal furrows divide three regions: the midline *vermis* (Latin, worm) and the *cerebellar hemispheres*, each of which is split into intermediate and lateral regions (Figure 42-2A).

The cerebellum is also divisible into three areas that have distinctive roles in different kinds of movements: the vestibulocerebellum, spinocerebellum, and cerebrocerebellum (Figure 42-3). The *vestibulocerebellum* consists of the flocculonodular lobe and is the most primitive part of the cerebellum, appearing first in fishes. It receives vestibular and visual inputs, projects to the vestibular nuclei in the brain stem, and participates in balance, other vestibular reflexes, and eye movements.

The *spinocerebellum* comprises the vermis and intermediate parts of the hemispheres and appears later in phylogeny. It is so named because it receives somatosensory and proprioceptive inputs from the spinal cord. The vermis receives visual, auditory, and vestibular input as well as somatic sensory input from the head and proximal parts of the body. It projects by way of the *fastigial nucleus* to cortical and brain stem regions that give rise to the medial descending systems controlling proximal muscles of the body and limbs. The vermis governs posture and locomotion as well as eye movements. The adjacent intermediate parts of the hemispheres also receive somatosensory input from the limbs. Neurons here project to the interposed nucleus, which provides inputs to lateral corticospinal and rubrospinal systems and controls the more distal muscles of the limbs and digits.

The *cerebrocerebellum* comprises the lateral parts of the hemispheres. These areas are phylogenetically most recent and are much larger in humans and apes than in monkeys and cats. Almost all of the inputs to and outputs from this region involve connections with the cerebral cortex. The output is transmitted through the *dentate nucleus*, which projects to motor, premotor, and prefrontal cortices. The lateral hemispheres have

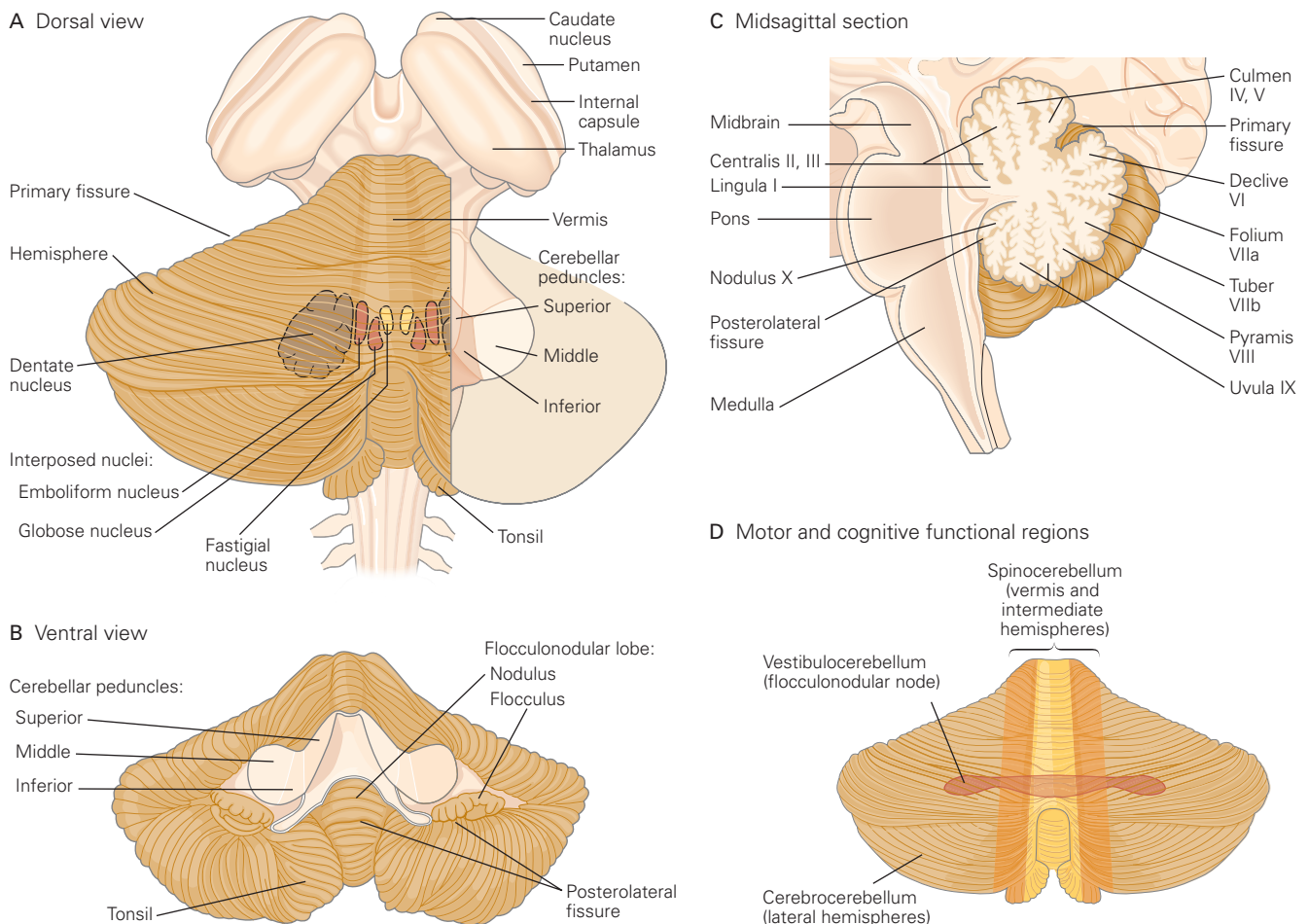


Figure 42-2 Gross features of the cerebellum. (Adapted, with permission, from Nieuwenhuys, Voogd, and van Huijzen 1988.)

A. Part of the right hemisphere has been cut away to reveal the underlying cerebellar peduncles.

B. The cerebellum is shown detached from the brain stem.

C. A midsagittal section through the brain stem and cerebellum shows the branching structure of the cerebellum. The cerebellar lobules are labeled with their Latin names and Larsell Roman numerals. (Reproduced, with permission, from Larsell and Jansen 1972.)

D. Functional regions of the cerebellum. (see also Figure 42-3.)

many functions but seem to participate most extensively in planning and executing movement. They may also have a role in certain cognitive functions unconnected with motor planning, such as working memory. There is now some correlative evidence implicating the cerebellar hemispheres in aspects of schizophrenia (see Chapter 62) and autism (see Chapter 64).

The Cerebellar Microcircuit Has a Distinct and Regular Organization

The cellular organization of the cerebellar microcircuit is striking, and one of the premises of cerebellar

research has been that the details of the microcircuit are an important clue to how the cerebellum works. Four major features of the microcircuit are described in the next four subsections.

Neurons in the Cerebellar Cortex Are Organized into Three Layers

The three layers of the cerebellar cortex possess distinct kinds of neurons and perform different operations (Figure 42-4).

The deepest or *granular layer* is the input layer. It contains a vast number of granule cells, estimated at 100 billion, which appear in histological sections

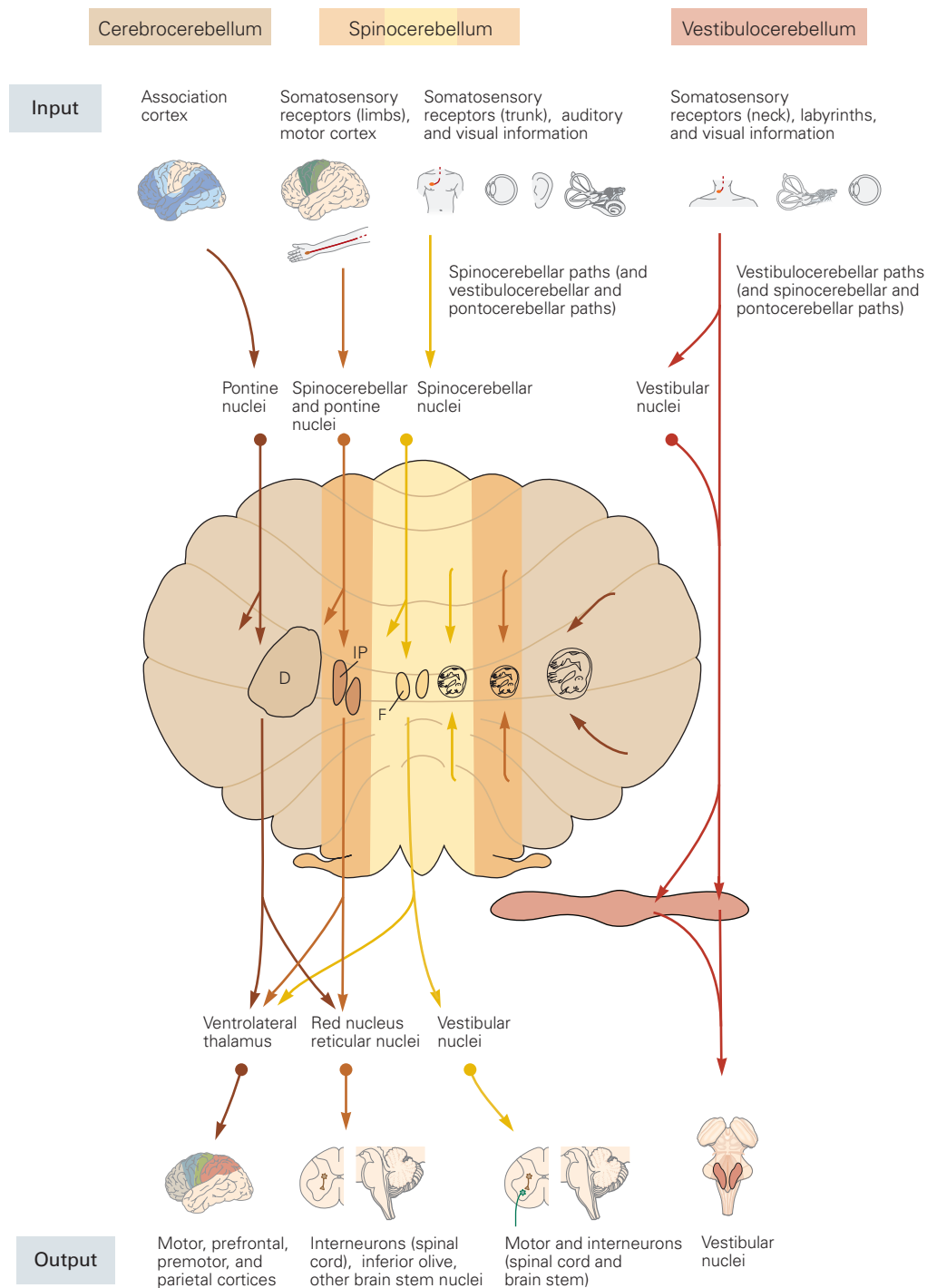


Figure 42–3 The three functional regions of the cerebellum have different inputs and different output targets. In the figure the cerebellum is unfolded, and arrows show the inputs and outputs of the different functional areas. The body maps in

the deep nuclei are based on anatomical tracing and single-cell recordings in nonhuman primates. (D, dentate nucleus; IP, interposed nucleus; F, fastigial nucleus.) (Adapted, with permission, from Thach 1980.)

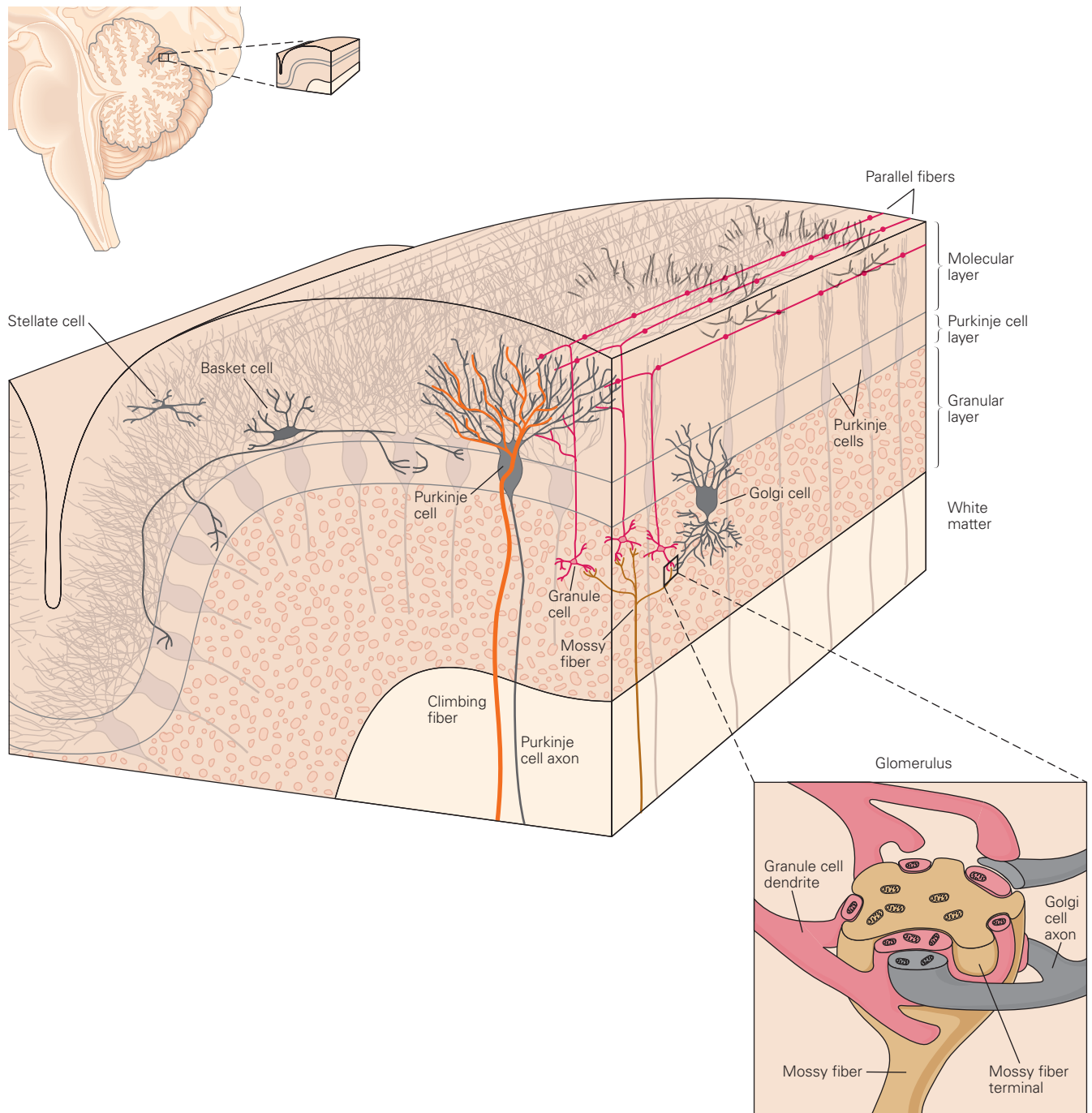


Figure 42–4 The cerebellar cortex contains five types of neurons organized into three layers. A vertical section of a single cerebellar folium illustrates the general organization of the cerebellar cortex. The detail of a cerebellar glomerulus in the granular layer is also shown. A glomerulus is the synaptic

complex formed by the bulbous axon terminal of a mossy fiber and the dendrites of several Golgi and granule cells. Mitochondria are present in all of the structures in the glomerulus, consistent with their high metabolic activity.

as small, densely packed, darkly stained nuclei. This layer also contains a few larger Golgi interneurons and, in some cerebellar regions, a smattering of other neurons such as cells of Lugaro, unipolar brush cells, and chandelier cells. The mossy fibers, one of the two principal afferent inputs to the cerebellum, terminate in this layer. The bulbous terminals of the mossy fibers excite granule cells and Golgi neurons in synaptic complexes called *cerebellar glomeruli* (Figure 42-4). As we will see later when discussing recurrent circuits in the cerebellum, Golgi cells inhibit granule cells.

The middle, or *Purkinje cell layer*, is the output layer of the cerebellar cortex. This layer consists of a single sheet of Purkinje cell bodies, which are 50 to 80 μm in diameter. The fan-like dendrites of Purkinje cells extend upward into the molecular layer where they receive inputs from the second major type of afferent fiber in the cerebellum, the climbing fibers, as well as from inhibitory and excitatory interneurons. Purkinje cell axons conduct the entire output of the cerebellar cortex, projecting to the deep nuclei in the underlying white matter or to the vestibular nuclei in the brain stem where the GABA (γ -aminobutyric acid) released by their terminals has an inhibitory action.

The outermost, or *molecular layer*, is an important processing layer of the cerebellar cortex. It contains the cell bodies and dendrites of two types of inhibitory interneurons, the stellate and basket cells, as well as the extensive dendrites of Purkinje cells. It also contains the axons of the granule cells, called the *parallel fibers* because they run parallel to the long axis of the folia (see Figure 42-4). The spatially polarized dendrites of Purkinje neurons cover extensive terrain in the anterior-posterior direction, but a very narrow territory in the medial-lateral direction. Because the parallel fibers run in the medial-lateral direction, they are oriented perpendicular to the dendritic trees of the Purkinje cells. Thus each granule cell has the potential to form a few synapses with each of a large number of Purkinje neurons, while making denser connections on a few Purkinje neurons as its axon ascends into the molecular layer.

Two Afferent Fiber Systems Encode Information Differently

The two main types of afferent fibers in the cerebellum, the mossy fibers and climbing fibers, both form excitatory synapses with cerebellar neurons but terminate in different layers of the cerebellar cortex, produce different patterns of firing in the Purkinje neurons, and thus probably mediate different functions.

Mossy fibers originate from cell bodies in the spinal cord and brain stem and carry sensory information from the periphery as well as information from the cerebral cortex. They form excitatory synapses on the dendrites of granule cells in the granular layer (Figure 42-5). Each granule cell receives inputs from just a few mossy fibers, but the architecture of the granule cell axons distributes information widely from each mossy fiber to a large number of Purkinje cells. The mossy fiber input is highly convergent; each Purkinje neuron is contacted by axons from somewhere between 200,000 and 1 million granule cells.

Climbing fibers originate in the inferior olivary nucleus and convey sensory information to the cerebellum from both the periphery and the cerebral cortex. The climbing fiber is so named because each enwraps the cell body and proximal dendrites of a Purkinje neuron like a vine on a tree, making numerous synaptic contacts (Figure 42-5). Each climbing fiber contacts 1 to 10 Purkinje neurons, but each Purkinje neuron receives synaptic input from only a single climbing fiber. The terminals of the climbing fibers are arranged topographically in the cerebellar cortex; the axons from clusters of related olivary neurons terminate in thin parasagittal strips that extend across several folia. In turn, the Purkinje neurons within one strip project to a common group of deep nuclear neurons.

The highly specific connectivity of the climbing fiber system contrasts markedly with the massive convergence and divergence of the mossy and parallel fibers, and suggests that the climbing fiber system is specialized for precise control of the electrical activity of Purkinje cells with related functions.

Mossy and climbing fibers have different effects on the electrical activity of Purkinje cells. Climbing fibers have an unusually powerful influence. Each action potential in a climbing fiber generates a protracted, voltage-gated Ca^{2+} conductance in the soma and dendrites of the postsynaptic Purkinje cell. This results in prolonged depolarization that produces a complex spike: an initial large-amplitude action potential followed by a high-frequency burst of smaller-amplitude action potentials (Figure 42-5). Whether these smaller spikes are transmitted down the Purkinje cell's axon is not clear. In awake animals the climbing fibers spontaneously generate complex spikes at low rates, rarely more than one to three per second. When stimulated they fire single action potentials in temporal relation with specific sensory events.

The climbing-fiber system therefore seems specialized for event detection; the firing rate carries little or no information. Although climbing fibers fire only infrequently, synchronous firing in multiple climbing

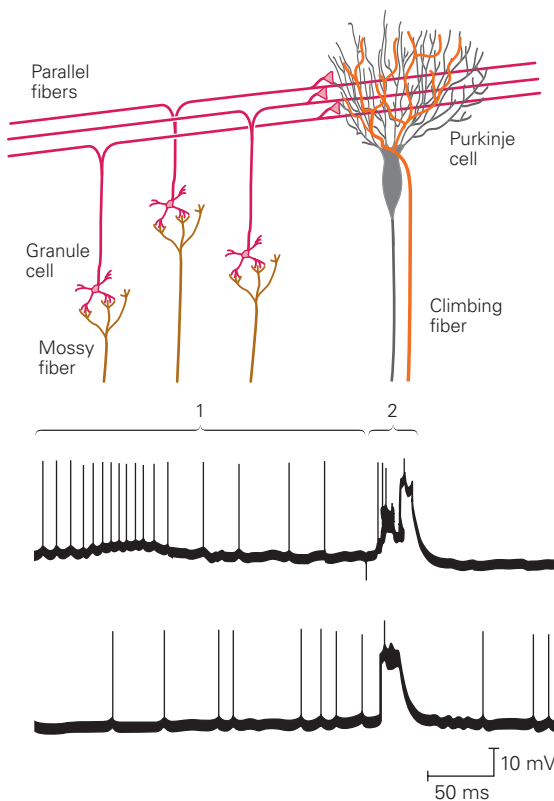


Figure 42-5 Simple and complex spikes recorded intracellularly from a cerebellar Purkinje cell. Simple spikes are produced by mossy fiber input (1), whereas complex spikes are evoked by climbing fiber synapses (2). (Reproduced, with permission, from Martinez, Crill, and Kennedy 1971.)

fibers enables them to signal important events. Synchrony seems to arise partly because neurons in the inferior olivary nucleus often are connected to one another electrotonically.

In contrast, parallel fibers produce only brief, small excitatory potentials in Purkinje neurons. These potentials spread to the initial segment of the axon where they generate simple spikes that propagate down the axon. However, inputs from many parallel fibers are needed to have a substantial effect on the frequency of simple spikes, for each postsynaptic potential is tiny. In awake animals Purkinje neurons emit a steady stream of simple spikes, with spontaneous firing rates as high as 100 per second even when an animal is sitting quietly. Purkinje neurons fire at rates as high as several hundred spikes per second during active eye, arm, and face movements, presumably because of somatosensory, vestibular, and other sensory signals that converge on granule cells through the mossy fibers.

Thus the mossy-fiber system encodes the magnitude and duration of peripheral stimuli or centrally generated behaviors by controlling the firing rate of simple spikes in Purkinje cells.

Parallel Pathways Compare Excitatory and Inhibitory Signals

An important feature of the cerebellar circuit is that excitatory and inhibitory inputs are compared in both the cerebellar cortex and the deep nuclei. In the deep nuclei inhibitory inputs from Purkinje cells converge with excitatory inputs from mossy and climbing fibers (Figure 42-6).

The cerebellum is organized as a series of small, similar modules with close relationships among all the elements of each module. Within a given module a mossy fiber affects target neurons in the deep nuclei

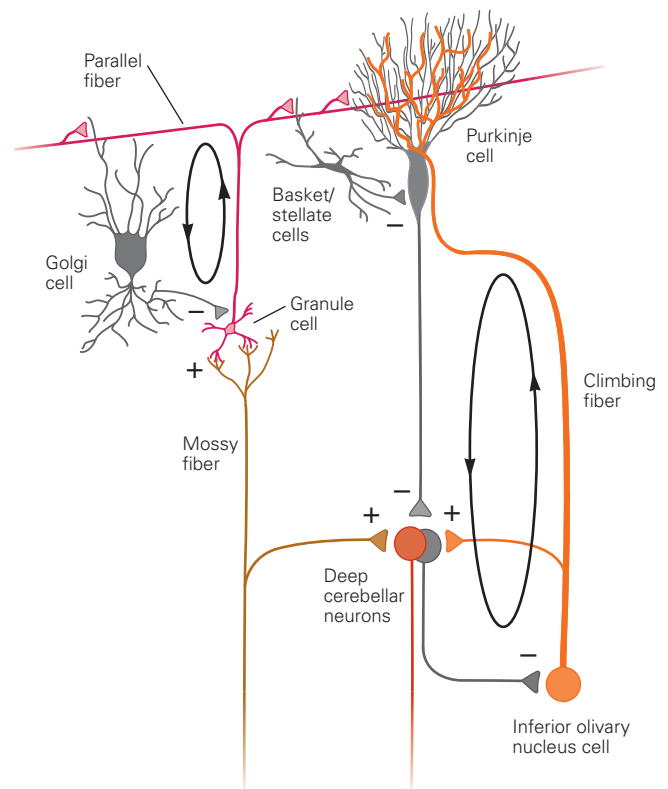


Figure 42-6 Synaptic organization of the cerebellar microcircuit. Excitation and inhibition converge both in the cerebellar cortex and in the deep nuclei. Recurrent loops involve Golgi cells within the cerebellar cortex and the inferior olive outside the cerebellum. (Adapted, with permission, from Raymond, Lisberger, and Mauk 1996.)

in two ways: directly by excitatory synapses and indirectly by pathways through the cortex and the inhibitory Purkinje cells. Thus the inhibitory output of the Purkinje cells modulates or sculpts the excitatory signals transmitted from mossy fibers to the deep nuclei. In almost all parts of the cerebellum the climbing fibers also give off collaterals that excite neurons in the deep nuclei.

In the cerebellar cortex excitatory and inhibitory inputs converge on Purkinje cells. Parallel fibers directly excite Purkinje neurons but also indirectly inhibit them through disynaptic connections from the stellate, basket, and Golgi interneurons. The short axons of stellate cells contact the nearby dendrites of Purkinje cells, whereas the long axons of basket cells run perpendicular to the parallel fibers and form synapses on the Purkinje cell bodies (Figure 42–4). The stellate cells have an inhibitory regulatory effect on the Purkinje cells that is local in that a stellate cell and the Purkinje cell it contacts are both excited by the same parallel fibers. In contrast, the basket cells create flanks of inhibition of Purkinje cells that are excited by flanking beams of parallel fibers other than the central beam that causes the lateral inhibition.

Recurrent Loops Occur at Several Levels

At the broadest level many parts of the cerebellum form recurrent loops with the cerebral cortex. The cerebral cortex projects to the lateral cerebellum through relays in the pontine nuclei. In turn, the lateral cerebellum projects back to the cerebral cortex through relays in the thalamus. This recurrent circuit is organized as a series of parallel closed loops, such that a given part of the cerebellum connects reciprocally with a given part of the cerebral cortex. Figure 42–7 shows how the cerebellum fits into the greater motor circuits from the cerebral cortex to the spinal cord.

Another recurrent loop involves the cerebellum and the inferior olivary nucleus, the source of all climbing fibers. The deep cerebellar nuclei contain GABAergic inhibitory neurons that project to the inferior olive. If inhibitory inputs from the deep nuclei increase then the firing frequency in inferior olive cells decreases, reducing the amount of excitatory climbing fiber input to cerebellar nuclear and Purkinje cells. This provides each part of the cerebellum a way to regulate its own climbing fiber inputs (see Figure 42–6), another in the many checks and balances built into cerebellar circuitry. Interestingly, the GABAergic fibers from the deep nuclei can regulate the electrotonic coupling between olivary neurons. By selectively disconnecting olivary neurons through inhibition, the nervous system

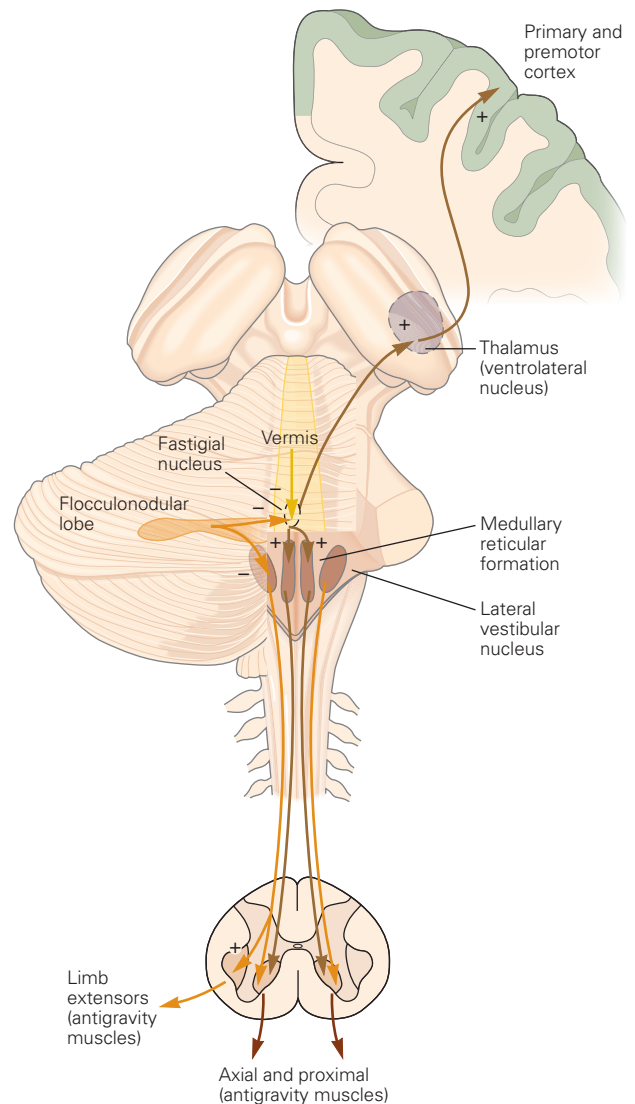


Figure 42–7 The vestibulocerebellum and the vermis control proximal muscles and limb extensors. The vestibulocerebellum (flocculonodular lobe) receives input from the vestibular labyrinth and projects directly to the vestibular nuclei. The vermis receives input from the neck and trunk, the vestibular labyrinth, and retinal and extraocular muscles. Its output is focused on the ventromedial descending systems of the brain stem, mainly the reticulospinal and vestibulospinal tracts and the corticospinal fibers acting on medial motor neurons. The oculomotor connections of the vestibular nuclei have been omitted for clarity.

can activate a specific array of Purkinje neurons synchronously.

The final recurrent loop is contained entirely within the cerebellar cortex and involves Golgi cells. Each Golgi cell receives excitatory inputs from parallel fibers; in turn, its GABAergic terminals provide inhibitory input to the granule cells (Figure 42–6). Golgi cell firing thus suppresses mossy fiber excitation of the granule cells and regulates the firing of the parallel fibers. This loop may shorten the duration of bursts in granule cells. Alternatively, it could limit the magnitude of the excitatory response of granule cells to their mossy fiber inputs. For example, the responses of granule cells could occur only when a certain number of mossy fiber inputs are active, or only when they achieve a threshold frequency of firing. One current idea is that the Golgi cells ensure that only a small number of granule cells are active at any given time, creating a *sparse code* in the input layer of the cerebellar cortex.

The Vestibulocerebellum Regulates Balance and Eye Movements

The vestibulocerebellum, or flocculonodular lobe, receives information from the semicircular canals and the otolith organs, which sense the head's motion and its position relative to gravity (Figure 42–3). Most of this vestibular input arises from the vestibular nuclei in the brain stem. The vestibulocerebellum also receives mossy fiber visual input, both from pretectal nuclei that lie deep in the midbrain beneath the superior colliculus and from the primary and secondary visual cortex through the pontine and pretectal nuclei.

The vestibulocerebellum is unique in that its output bypasses the deep cerebellar nuclei and proceeds directly to the vestibular nuclei in the brain stem. Purkinje cells in the midline parts of the vestibulocerebellum project to the lateral vestibular nucleus to modulate the lateral and medial vestibulospinal tracts, which predominantly control axial muscles and limb extensors to assure balance during stance and gait. Disruption of these projections through lesions or disease impairs equilibrium.

Purkinje neurons in the lateral parts of the vestibulocerebellum project to the medial vestibular nucleus to control eye movements and coordinate movements of the head and eyes (see Chapter 39). Interestingly, this ancient part of the cerebellum has been co-opted in more recent phylogeny by visual guidance of eye movements. In fact, the most striking deficits following lesions of the lateral vestibulocerebellum are in smooth-pursuit eye movement toward the side of the lesion.

A patient with a lesion of the left lateral vestibulocerebellum can smoothly track a target that is moving to the right, but only poorly tracks motion to the left using predominantly saccades (Figure 42–8A).

Patients with lesions of the lateral vestibulocerebellum have normal ocular responses to head turns, but the responses cannot be suppressed by fixation (Figure 42–8B). If, for example, a patient seated in a barber's chair is rotated to the right in the dark, the vestibulo-ocular reflex causes smooth eye rotation to the left and resetting saccades to the right. If the patient is placed in the light and views an object attached to the chair, he or she can use fixation to suppress the smooth eye movements of the reflex. For leftward head rotation, however, the patient cannot do so. These deficits occur commonly if the lateral vestibulocerebellum is compressed by an acoustic neuroma, a benign tumor that grows on the eighth cranial nerve as it courses directly beneath the lateral vestibulocerebellum.

The Spinocerebellum Regulates Body and Limb Movements

The spinocerebellum comprises the vermis and intermediate parts of the cerebellar hemispheres (see Figure 42–2A).

Somatosensory Information Reaches the Spinocerebellum Through Direct and Indirect Mossy Fiber Pathways

The spinocerebellum receives extensive sensory input from the spinal cord, mainly from somatosensory receptors conveying information about touch, pressure, and limb position, through several direct and indirect pathways. This input provides the cerebellum with different reports of the changing state of the organism and its environment and permit comparisons between the two.

Direct pathways originate from interneurons in the spinal gray matter and terminate as mossy fibers in the vermis or spinocerebellum. Indirect pathways from the spinal cord to the cerebellum terminate first on neurons in one of several precerebellar nuclei in the brain stem reticular formation: the lateral reticular nucleus, reticularis tegmenti pontis, and paramedian reticular nucleus.

One fundamental principle of cerebellar operation can be appreciated on the basis of two important pathways from the spinal interneurons. The ventral and dorsal spinocerebellar tracts both transmit signals

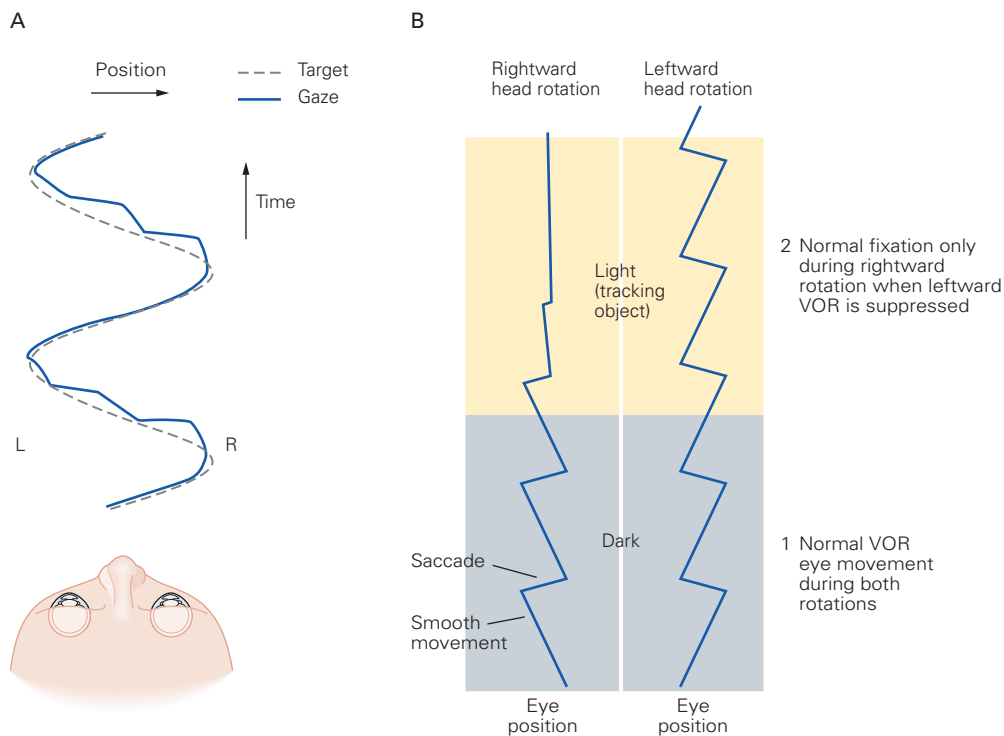


Figure 42-8 Lesions in the vestibulocerebellum have large effects on smooth-pursuit eye movements.

A. Sinusoidal target motion is tracked with smooth-pursuit eye movements as the target moves from left (L) to right (R). With a lesion of the left vestibulocerebellum, smooth pursuit is punctuated by saccades when the target moves from right to left.

B. In the same patient responses to vestibular stimulation are normal, whereas object fixation is disrupted during leftward rotation. Each trace shows the eye movements evoked by head rotation while the patient fixates on a target that moves

along with him, first in the dark and then in the light. (1) In the dark the eyes show a normal vestibulo-ocular reflex (VOR) during rotation in both directions: The eyes move smoothly in the direction opposite to the head's rotation, then reset with saccades in the direction of head rotation. (2) In the light the eye position during rightward head rotation is normal: Fixation on the target is excellent and the vestibulo-ocular reflex is suppressed. During leftward head rotation, however, the subject is unable to fixate on the object and the vestibulo-ocular reflex cannot be suppressed.

from the spinal cord directly to the cerebellar cortex but convey two different kinds of information.

The *dorsal spinocerebellar tract* conveys somatosensory information from muscle and joint receptors, providing the cerebellum with sensory feedback about the consequences of the movement. This information flows whether the limbs are moved passively or voluntarily.

In contrast, the *ventral spinocerebellar tract* is active only during active movements. Its cells of origin receive the same inputs as spinal motor neurons and interneurons, and it transmits an efference copy or corollary discharge of spinal motor neuron activity that informs the cerebellum about the movement commands assembled at the spinal cord. The cerebellum is thought to compare this information on planned movement with the actual movement reported by the dorsal spinocerebellar tract

in order to determine whether the motor command must be modified to achieve the desired movement. The dorsal and ventral spinocerebellar tracts provide inputs from the hind limbs, whereas the cuneocerebellar and rostral spinocerebellar tracts provide similar inputs from more rostral body parts.

The idea that the cerebellum compares the actual and expected sensory consequences of movements is supported by studies of a number of movement systems. As a decerebrated cat walks on a treadmill, for example, the firing rate of neurons in the dorsal and ventral spinocerebellar tracts is rhythmically modulated in phase with the step cycle. However, when the dorsal roots are cut, preventing spinal neurons from receiving peripheral inputs that modulate with the step cycle, neurons of the dorsal spinocerebellar tract

fall silent, whereas the firing of neurons of the ventral spinocerebellar tract continues to be modulated.

Recordings from the vestibulocerebellum of monkeys show that Purkinje neurons compare vestibular sensory inputs related to head velocity with corollary inputs related to eye velocity. The simple-spike output from these Purkinje neurons is modulated only when the eye movements are different from those expected from the vestibulo-ocular reflex. The cerebellum participates in the control of smooth eye movement only when the brain stem reflex pathways alone cannot produce the desired motor outputs.

The Spinocerebellum Modulates the Descending Motor Systems

Purkinje neurons in the spinocerebellum project somatotopically to different deep nuclei that control various components of the descending motor pathways. Neurons in the vermis of both the anterior and posterior lobes send axons to the fastigial nucleus. The fastigial nucleus projects bilaterally to the brain stem reticular formation and lateral vestibular nuclei, which in turn project directly to the spinal cord (Figure 42-7).

The spinocerebellum therefore provides important inputs to the brain stem components of the medial descending systems. Its outputs are important for movements of the neck, trunk, and proximal parts of the arm, rather than the wrist and digits, for balance and postural control during voluntary motor tasks. Because these brain stem systems also receive large inputs from descending pathways and from sensory inputs, we think that the cerebellum modulates and initiates, rather than controls, the descending commands to the spinal cord.

Purkinje neurons in the intermediate part of the cerebellar hemispheres project to the interposed nucleus. Some axons of the interposed nucleus exit through the superior cerebellar peduncle and cross to the contralateral side of the brain to terminate in the magnocellular portion of the red nucleus. Axons from the red nucleus cross the midline again and descend to the spinal cord (Figure 42-9). Other axons from the interposed nucleus continue rostrally and terminate in the ventrolateral nucleus of the thalamus. Neurons in the ventrolateral nucleus project to the limb control areas of the primary motor cortex.

By acting on the neurons that give rise to the rubrospinal and corticospinal systems, the intermediate cerebellum focuses its action on limb and axial musculature. Because cerebellar outputs cross the midline twice before reaching the spinal cord, cerebellar lesions disrupt ipsilateral limb movements.

The Vermis Controls Saccadic and Smooth-Pursuit Eye Movements

The vermis is involved in the control of saccades and smooth-pursuit eye movements through Purkinje cells in lobules V, VI, and VII (Figure 42-2C). The cells discharge prior to and during such movements, and lesions of these areas cause deficits in the accuracy of both kinds of movements.

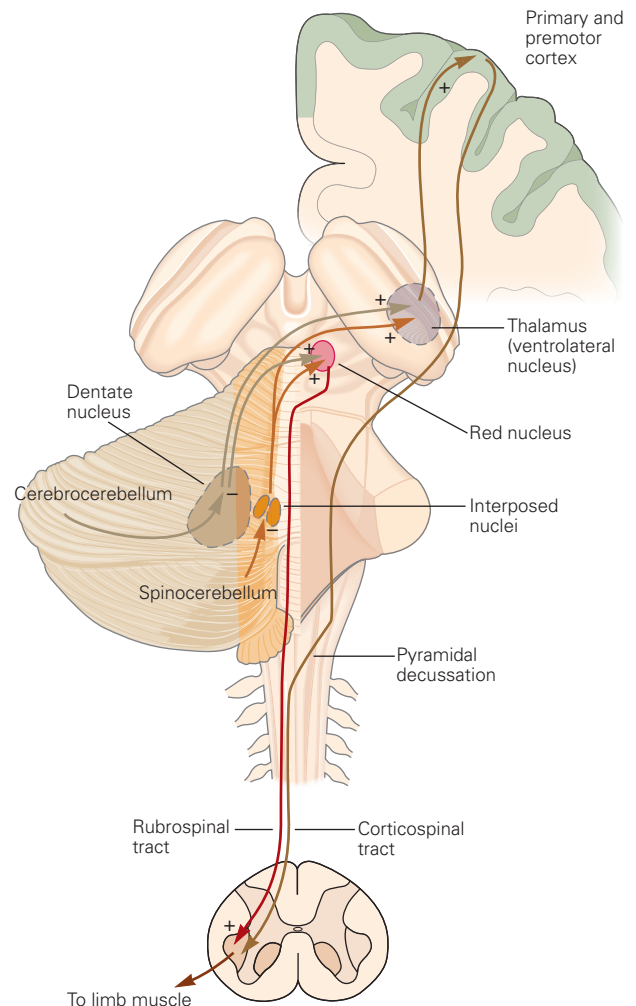


Figure 42-9 Neurons in the intermediate and lateral parts of the cerebellar hemispheres control limb and axial muscles. The intermediate part of each hemisphere (spinocerebellum) receives sensory information from the limbs and controls the dorsolateral descending systems (rubrospinal and corticospinal tracts) acting on the ipsilateral limbs. The lateral area of each hemisphere (cerebocerebellum) receives cortical input via the pontine nuclei and influences the motor and premotor cortices via the ventrolateral nucleus of the thalamus.

The vermis may be the only area of the cerebellum responsible for saccades, but it seems to share responsibility for smooth pursuit with the lateral part of the flocculonodular lobe. The outputs from neurons of the vermis concerned with saccades are transmitted through a very small region of the caudal fastigial nucleus to the saccade generator in the reticular formation. The exact neural pathways for guidance of pursuit by the vermis are not known, but they involve more synaptic relays than the outputs from the lateral part of the flocculonodular lobe, which reach extraocular motor neurons through two intervening synapses. One idea currently being explored is that the vermis also plays a role in motor learning that corrects errors in saccades and smooth-pursuit movements.

Spinocerebellar Regulation of Movement Follows Three Organizational Principles

In addition to confirming that cerebellar lesions in animals have the same effects as in humans, animal studies have provided an initial understanding of what the cerebellum does in healthy people and why lesions of the cerebellum have the effects they do.

Many experiments using monkeys have recorded the action potentials of single neurons in the interposed and dentate nuclei and the intermediate and lateral cerebellar cortex during arm movements. Other experiments have used cooling probes or substances that temporarily inactivate neurons to compare specific aspects of motor behavior in an active and inactive cerebellum. From these experiments we can draw three basic conclusions regarding the function of the spinocerebellum.

First, both Purkinje neurons and deep cerebellar nucleus neurons discharge vigorously in relation to voluntary movements. Cerebellar output is related to the direction and speed of movement. The deep nuclei are somatotopically organized into maps of different limbs and joints, as in the motor cortex. Moreover, the interval between the onset of modulation of the firing of cerebellar neurons and movement is remarkably similar to that for neurons in the motor cortex. This result emphasizes the cerebellum's participation in recurrent circuits that operate synchronously with the cerebral cortex.

Second, the cerebellum provides feed-forward control of muscle contractions to regulate the timing of movements. Rather than awaiting sensory feedback, cerebellar output anticipates the muscular contractions that will be needed to bring a movement smoothly, accurately, and quickly to its desired endpoint. Failure of these mechanisms causes the intention tremor of cerebellar disorders.

Normally a rapid single-joint movement is initiated by the contraction of an agonist muscle and terminated

by an appropriately timed contraction of the antagonist. The contraction of the antagonist starts early in the movement, well before there has been time for sensory feedback to reach the brain, and therefore must be programmed as part of the movement. When the dentate and interposed nuclei are experimentally inactivated, however, contraction of the antagonist muscle is delayed until the limb has overshoot its target. The programmed contraction seen in normal movements is replaced by a feedback correction driven by sensory input. This correction is itself dysmetric and results in another error, necessitating a new adjustment (Figure 42–10).

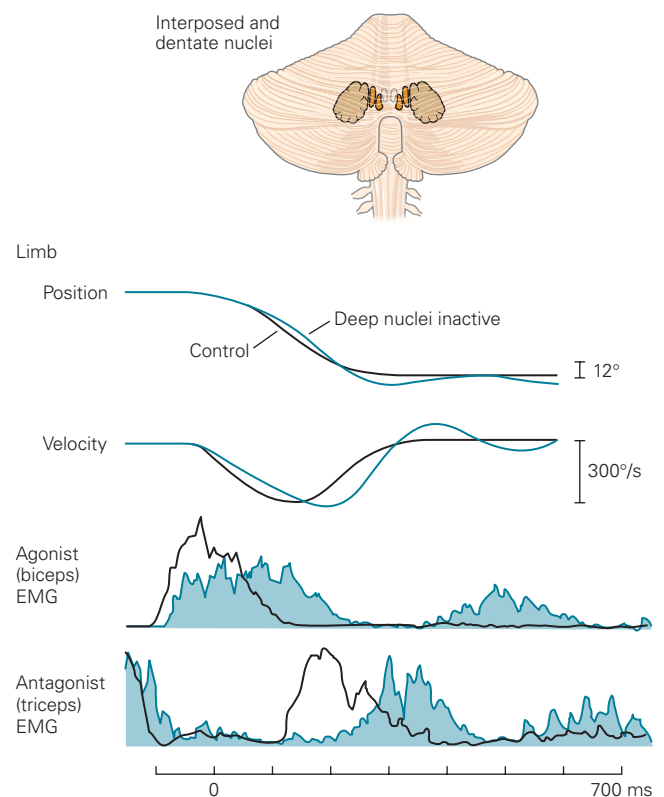


Figure 42–10 The interposed and dentate nuclei are involved in the precise timing of agonist and antagonist activation during rapid movements. The records show arm position and velocity and electromyographic responses of the biceps and triceps muscles of a trained monkey during a rapid movement. When the deep nuclei are inactivated by cooling, activation of the agonist (biceps) becomes slower and more prolonged. Activation of the antagonist (triceps), which is needed to stop the movement at the correct location, is likewise delayed and protracted so that the initial movement overshoots its appropriate extent. Delays in successive phases of the movement produce oscillations similar to the terminal tremor seen in patients with cerebellar damage.

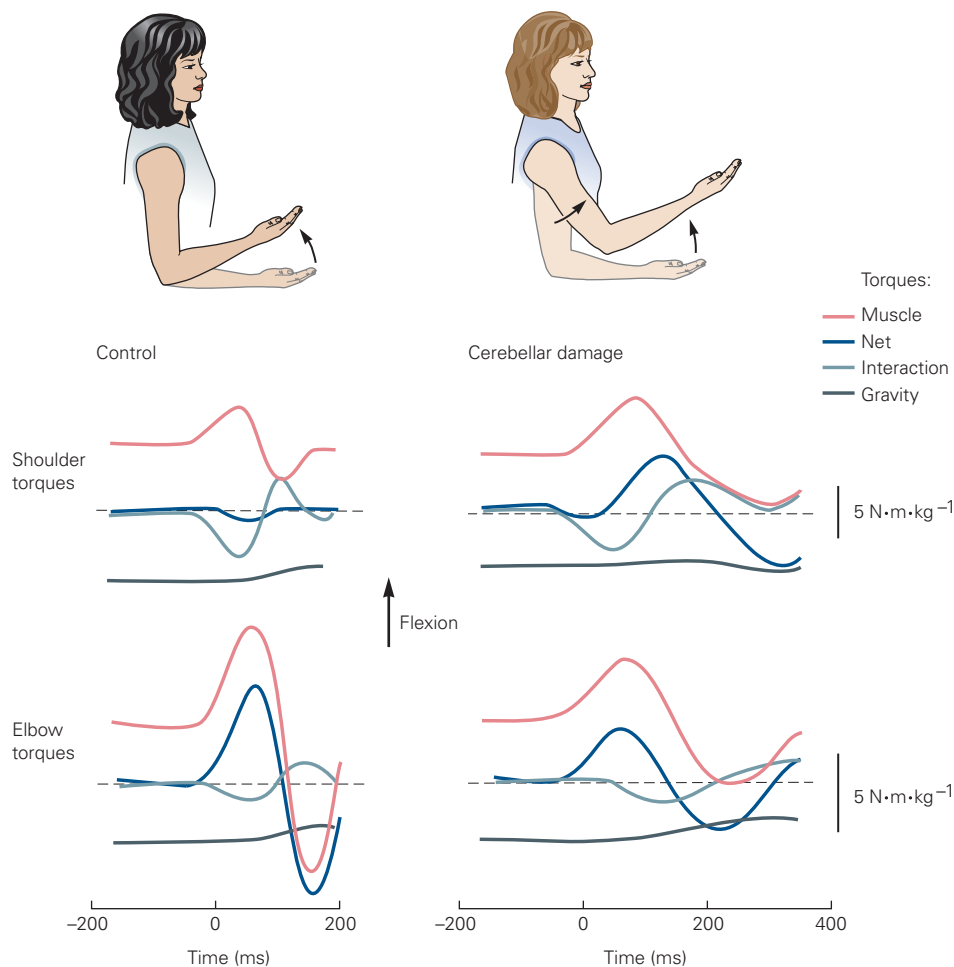


Figure 42–11 Failure of compensation for interaction torques can account for cerebellar ataxia. Subjects flex their elbows while keeping their shoulder stable. In both the control subject and the cerebellar patient the net elbow torque is large because the elbow is moved. In the control subject there is relatively little net shoulder torque because the interaction

torques are automatically cancelled by muscle torques. In the cerebellar patient this compensation fails; the muscle torques are present but are inappropriate to cancel the interaction torques. As a result, the patient cannot flex her elbow without causing a large perturbation of her shoulder position. (Adapted, with permission, from Bastian, Zackowski, and Thach 2000.)

Third, the cerebellum has internal models of the limbs that automatically take account of limb structure. (See Chapter 33 for a discussion of internal models.) An accurate dynamic model of the arm, for example, can convert a desired final endpoint into a sequence of properly timed and scaled commands for muscular contraction. At the same time, an accurate kinematic model of the relationship between joint angles and finger position can specify the joint angles that are needed to achieve an endpoint. Recordings of the output of the cerebellum have provided evidence compatible with the idea that the cerebellum contains kinematic and dynamic models of both arm and eye movements.

Studies of the movements of patients with cerebellar disorders suggest that the interaction torques of a multi-segment limb are represented by an internal model in the cerebellum. Because of the structure of the arm and the momentum it develops when moving, movement of the forearm alone causes forces that move the upper arm. If a subject wants to flex or extend the elbow without simultaneously moving the shoulder, then muscles acting at the shoulder must contract to prevent its movement. These stabilizing contractions of the shoulder joint occur almost perfectly in control subjects but not in patients with cerebellar damage (Figure 42–11). Patients with cerebellar ataxia are unable to compensate for interaction torques.

They experience difficulty controlling the inertial interactions among multiple segments of a limb accounts and greater inaccuracy of multi-joint versus single-joint movements.

In conclusion, the cerebellum uses internal models to anticipate the forces that result from the mechanical properties of a moving limb and may use its learning capabilities to customize internal models to anticipate those forces accurately.

Recent research suggests that excessive variability of Purkinje-cell output can lead to ataxia, suggesting that the regularity of cerebellar activity must be closely regulated to achieve normal movement. In animal models cerebellar symptoms result when deletion of certain ion channels causes the firing of Purkinje cells to become excessively variable even though the mean firing rate is entirely normal when averaged across many repetitions of a movement.

Are the Parallel Fibers a Mechanism for Motor Coordination?

A conspicuous feature of cerebellar structure is the medial-lateral parallel fiber “beam.” Parallel fibers extend up to 6 mm through the molecular layer and excite the dendrites of Purkinje, basket, stellate, and Golgi cells along their course (see Figure 42–4). Basket and stellate axons create inhibitory flanks along the sides of the parallel fiber beam.

One current idea is that the great extent of the parallel fibers allows them to tie together the activity of different cerebellar compartments. Purkinje cells project topographically onto the deep cerebellar nuclei, each of which contains a complete map of body parts and muscles. In each map the representation of the tail is located anteriorly and that of the head posteriorly, with the limbs medially and the trunk laterally. The long trajectory of the parallel fibers could link different body parts in a medial-lateral dimension in different combinations.

In rats trained to reach to a target, for example, Purkinje cells along the medial-lateral parallel fiber beam fire simple spikes simultaneously and in precise synchrony with the movement. Pairs of Purkinje cells that are not situated along the same excitatory beam show no such synchrony. The synchrony may link muscles for multi-muscle movements and synchronize their contractions.

Finally, sagittal splitting of the posterior vermis in children, an operation performed to remove tumors in the fourth ventricle, creates surprisingly little functional deficit. The children can walk and climb

stairs without assistance or obvious abnormality, and they can hop on one leg repeatedly almost as well as healthy children. Nevertheless, a striking deficit occurs when they attempt heel-to-toe tandem gait. Without support they fall after three steps. The discrepancy between the large deficit in tandem gait and the normal one-legged hopping is striking because both require the integration of vestibular, somesthetic, and visual sensation. These observations imply that the severed parallel fibers crossing in the vermis are essential to coordination of the projections to the bilateral fastigial nuclei.

The Cerebrocerebellum Is Involved in Planning Movement

The Cerebrocerebellum Is Part of a High-Level Internal Feedback Circuit That Plans Movement and Regulates Cortical Motor Programs

Clinical observations by neurologists and neurosurgeons initially suggested that, like the rest of the cerebellum, the lateral hemispheres (the cerebrocerebellum) are primarily concerned with motor function. However, recent clinical and experimental studies indicate that the lateral hemispheres in humans also have perceptual and cognitive functions. Indeed, the lateral hemispheres are much larger in humans than in monkeys, just as in humans the frontal regions of the cerebral cortex are greatly expanded.

In contrast to other regions of the cerebellum, which receive sensory information more directly from the spinal cord, the lateral hemispheres receive input exclusively from the cerebral cortex. This cortical input is transmitted through the pontine nuclei and through the middle cerebellar peduncle to the contralateral dentate nucleus and lateral hemisphere (see Figure 42–3).

Purkinje neurons in the lateral hemisphere project to the dentate nucleus. Most dentate axons exit the cerebellum through the superior cerebellar peduncle and terminate in two main sites. One terminus is an area of the contralateral ventrolateral thalamus that also receives input from the interposed nucleus. These thalamic cells project to premotor and primary motor cortex (see Figure 42–9).

The second principal terminus of dentate neurons is the contralateral red nucleus, specifically a portion of the parvocellular area of the nucleus distinct from that which receives input from the interposed nucleus. These neurons project to the inferior olivary nucleus,

which in turn projects back to the contralateral cerebellum as climbing fibers, thus forming a recurrent loop (see Figure 42–6). Neurons in the parvocellular portion of the red nucleus, in addition to receiving input from the dentate nucleus, also receive input from the lateral premotor areas. On the basis of brain imaging, the intriguing suggestion has been made that this loop involving the premotor cortex, lateral cerebellum, and rubrocerebellar tract participates in the mental rehearsal of movements and perhaps in motor learning (see Chapter 33).

Lesions of the Cerebrocerebellum Disrupt Motor Planning and Prolong Reaction Time

In the first half of the 20th century, neurologists identified two characteristic motor disturbances in patients with localized damage in the cerebrocerebellum: variable delays in initiating movements and irregularities in the timing of movement components. The same defects are seen in primates with lesions of the dentate nucleus.

Clinical observations suggest that the cerebrocerebellum has a role in the planning and programming of hand movements, and recordings of the activity of neurons in the dentate nucleus in primates support this idea. Some neurons in the dentate nucleus fire some 100 ms before a movement begins and even before the discharge of neurons in either the primary motor cortex or interposed nuclei, which are more directly concerned with the execution of movement. The onset of firing in the primary motor cortex, and thus the onset of movement, can be delayed experimentally by inactivating the dentate nucleus (Figure 42–10). Nevertheless, movement is simply delayed, not prevented, demonstrating that the dentate nucleus is not absolutely necessary for the initiation of movement.

The Cerebrocerebellum May Have Cognitive Functions Unconnected with Motor Control

When patients with cerebellar lesions attempt to make regular tapping movements with their hands or fingers, the rhythm is irregular, and the motions are variable in duration and force. Based on a theoretical model of how tapping movements are generated, Richard Ivry and Steven Keele inferred that medial cerebellar lesions interfere only with accurate execution of the response, whereas lateral cerebellar lesions interfere with the timing of serial events. This timing defect was not limited to motor events. It also affected the patient's ability to judge elapsed time in purely mental or

cognitive tasks, as in the ability to distinguish whether one tone was longer or shorter than another or whether the speed of one moving object was greater or less than that of another.

This demonstration that the cerebellum is responsible for a cognitive computation independent of motor execution prompted other researchers to investigate purely cognitive functions of the cerebellum. For example, Steve Petersen, Julie Fiez, and Marcus Raichle used positron emission tomography to image the brain activity of people during silent reading, reading aloud, and speech. As expected, areas of the cerebellum involved in the control of mouth movements were more active when subjects read aloud than when they read silently.

In a task with greater cognitive load subjects were asked to name a verb associated with a noun; a subject might respond with “bark” if he or she saw the word “dog.” Compared with simply reading aloud, the word-association task produced a pronounced increase in activity within the right lateral cerebellum. In agreement with this study, a patient with damage in the right cerebellum could not learn a word-association task.

Functional magnetic resonance imaging provides evidence that the lateral cerebellum has a role in other cognitive activities. For example, solving a pegboard puzzle involves greater activity in the dentate nucleus and lateral cerebellum than does the simple motor task of moving the pegs on the board. Interestingly, the active area of the dentate nucleus is the area that receives input from the part of the cerebral cortex (area 46) involved in working memory. The dentate nucleus appears to be particularly important in processing sensory information for tasks that require complex spatial and temporal judgments, which are essential for complex motor actions and sequences of movements.

The Cerebellum Participates in Motor Learning

Climbing-Fiber Activity Produces Long-Lasting Effects on the Synaptic Efficacy of Parallel Fibers

On the basis of mathematical modeling of cerebellar function and the striking features of the cerebellar microcircuit described earlier in the chapter, David Marr and James Albus independently suggested in the early 1970s that the cerebellum might be involved in learning motor skills. Along with Masao Ito, they proposed that the climbing-fiber input to Purkinje neurons modifies the response of the neurons to mossy-fiber inputs and does so for a prolonged period of time.

Subsequent experimental evidence has supported the theory. Despite the low frequency of their discharge, climbing fibers modulate the input of parallel fibers to Purkinje cells. In particular, climbing fibers can selectively induce *long-term depression* in the synapses between Purkinje neurons and parallel fibers that are activated concurrently with the climbing fibers. Long-term depression has been analyzed in slices and cultures of cerebellum, where it is possible

to record the postsynaptic potentials of Purkinje cells following stimulation of climbing fibers and parallel fibers. Many studies have found that concurrent stimulation of climbing fibers and parallel fibers depresses the Purkinje cell responses to subsequent stimulation of the same parallel fibers but not to stimulation of parallel fibers that had not been stimulated earlier along with climbing fibers (Figure 42–12A). The resulting depression can last for minutes to hours.

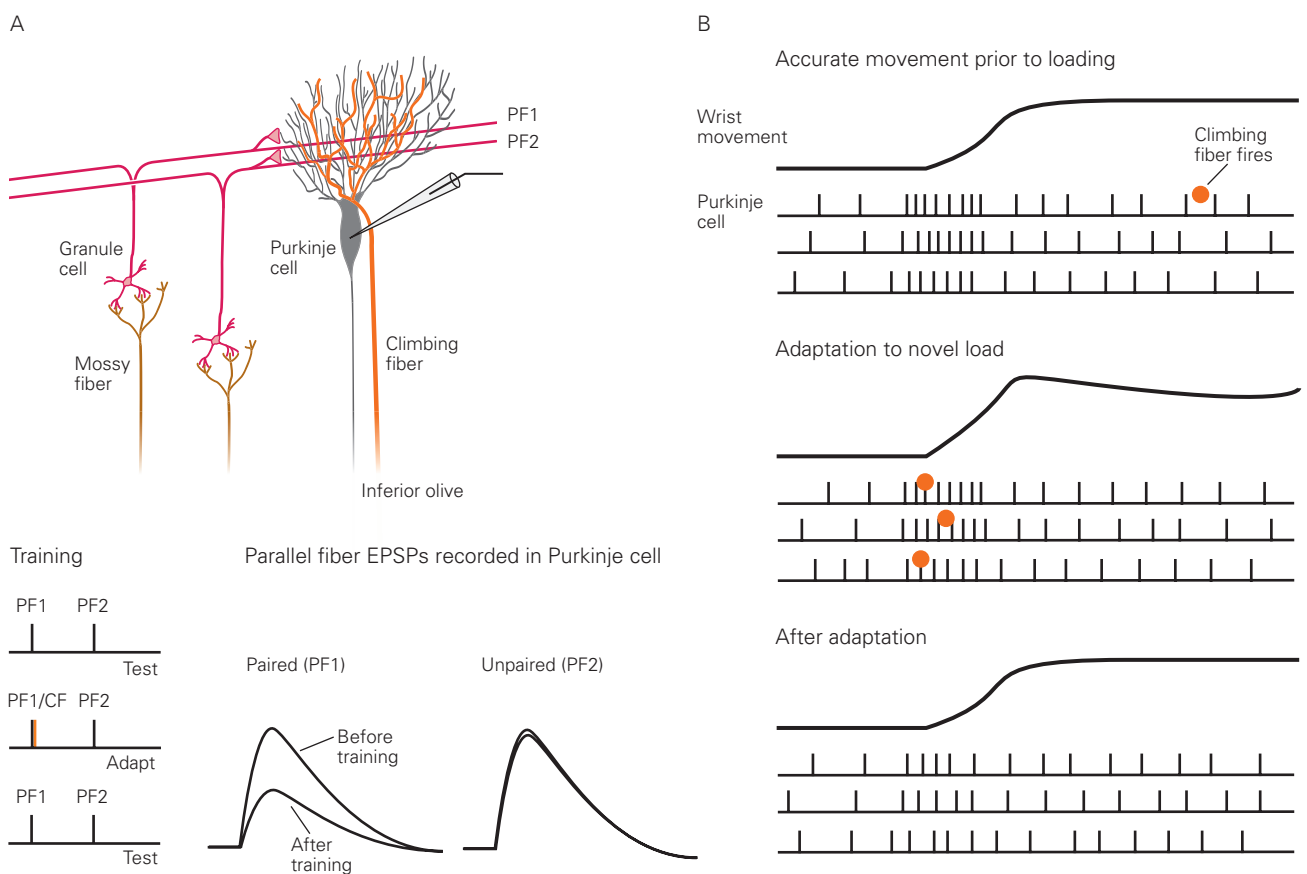


Figure 42–12 Long-term depression of the synaptic input from parallel fibers to Purkinje cells is one plausible mechanism for cerebellar learning.

A. Two different groups of parallel fibers and the presynaptic climbing fibers are electrically stimulated in vitro. Repeated stimulation of one set of parallel fibers (PF1) at the same time as the climbing fibers produces a long-term reduction in the responses of those parallel fibers to later stimulation. The responses of a second set of parallel fibers (PF2) are not depressed because they are not stimulated simultaneously with the presynaptic climbing fibers. (CF, climbing fiber; EPSP, excitatory postsynaptic potential.) (Adapted, with permission, from Ito et al. 1982.)

B. Top: An accurate wrist movement by a monkey is accompanied by a burst of simple spikes in a Purkinje cell, followed later by discharge of a single climbing fiber in one trial. **Middle:** When the monkey must make the same movement against a novel resistance (adaptation), climbing-fiber activity occurs during movement in every trial and the movement itself overshoots the target. **Bottom:** After adaptation the frequency of simple spikes during movement is quite attenuated, and the climbing fiber is not active during movement or later. This is the sequence of events expected if long-term depression in the cerebellar cortex plays a role in learning. Climbing fiber activity is usually low (1/s) but increases during adaptation to a novel load. (Adapted, with permission, from Gilbert and Thach 1977.)

What functional effects might this long-term depression have? According to the theories of Marr and Albus, altering the strength of certain synapses between parallel fibers and Purkinje cells shapes or corrects eye and limb movements. During an inaccurate movement the climbing fibers respond to specific movement errors and depress the synaptic strength of parallel fibers involved with those errors, namely those that had been activated with the climbing fiber (Figure 42–12B). With successive movements the parallel fiber inputs conveying the flawed central command are increasingly suppressed, a more appropriate pattern of simple-spike activity emerges, and eventually the climbing-fiber error signal disappears.

Learning Occurs at Multiple Sites in the Cerebellar Microcircuit

Initial studies of cerebellar learning focused on the vestibulo-ocular reflex, a coordinated response that keeps the eyes fixed on a target when the head is rotated (see Chapter 40). Motion of the head in one direction is sensed by the vestibular labyrinth, which initiates eye movements in the opposite direction to maintain the image in the same position on the retina.

When humans and experimental animals wear glasses that change the size of a visual scene, the vestibulo-ocular reflex initially fails to keep images stable on the retina because the amplitude of the reflex is inappropriate to the new conditions. After the glasses have been worn continuously for several days, however, the size of the reflex becomes progressively reduced (for miniaturizing glasses) or increased (for magnifying glasses). Adaptation of the vestibulo-ocular reflex can be blocked in experimental animals by lesions of the lateral part of the vestibulocerebellum, indicating that the cerebellum also has an important role in this form of learning, as discussed below.

Classical conditioning of the eye-blink response also depends on an intact cerebellum. In this form of associative learning a neutral stimulus such as a tone is played while a puff of air is directed at the cornea, causing the eye to blink just before the end of the tone. If this paradigm is repeated many times, the brain learns the tone's predictive power and the tone alone is sufficient to cause a blink. Michael Mauk and his colleagues have shown that the brain also can learn about the timing of the stimulus so that the eye blink occurs at the right time. It is even possible to learn to blink at different times in response to tones of different frequencies.

The cerebellum is also involved in learning limb movements that depend on eye-hand coordination.

Adaptation of such movements can be demonstrated by having people wear prisms that deflect the light path sideways. When a person plays darts while wearing prisms that displace the entire visual field to the right, the initial dart throw lands to the left side of the target by an amount proportional to the strength of the prism. The subject gradually adapts to the distortion through practice, so that the darts land on target within 10 to 30 throws (Figure 42–13). When the prisms are removed, the adaptation persists, and the darts hit the right side of the target by roughly the same distance as the initial prism-induced error. Patients with a damaged cerebellar cortex or inferior olive are severely impaired or unable to adapt at all in this task.

Extensive analysis of the cerebellum during adaptation of the vestibulo-ocular reflex, classical conditioning of the eye-blink response, and voluntary arm movements has led to a coherent theory about the cerebellum's role in motor learning. Learning occurs not only in the cerebellar cortex, as postulated by Marr, Albus, and Ito, but also in the deep cerebellar nuclei (Figure 42–14). Available evidence is compatible with the long-standing suggestion that inputs from climbing fibers provide instructive signals that lead to changes in synaptic strength within the cerebellar cortex.

The original hypothesis of learning in the cerebellum focused on long-term depression of the synapses from parallel fibers to Purkinje cells, one of a group of possible sites where climbing fibers cause plasticity. But there are additional sites of synaptic and cellular plasticity throughout the microcircuit, notably in the deep cerebellar nuclei. Learning seems to be implemented through complementary synaptic changes in the cerebellar cortex and deep nuclei. The cerebellum appears to be the learning machine envisioned by the earliest investigators, but its learning capabilities may be even greater and more widely localized than imagined.

As outlined in Chapter 33 and earlier in this chapter, many operations performed by the motor system may be based on internal models. If the brain has accurate internal models of the dynamics and kinematics of the arm, for example, then it can compute signals that generate accurate movements. Synaptic plasticity could be the mechanism that creates and maintains accurate internal models. One important function of learning in the cerebellum may be to provide continuous tuning of internal models in the cerebellum. By using sensory feedback to adjust synaptic and cellular function, cerebellar internal models can be tuned to create commands for movements that are rapid, accurate, and smooth.

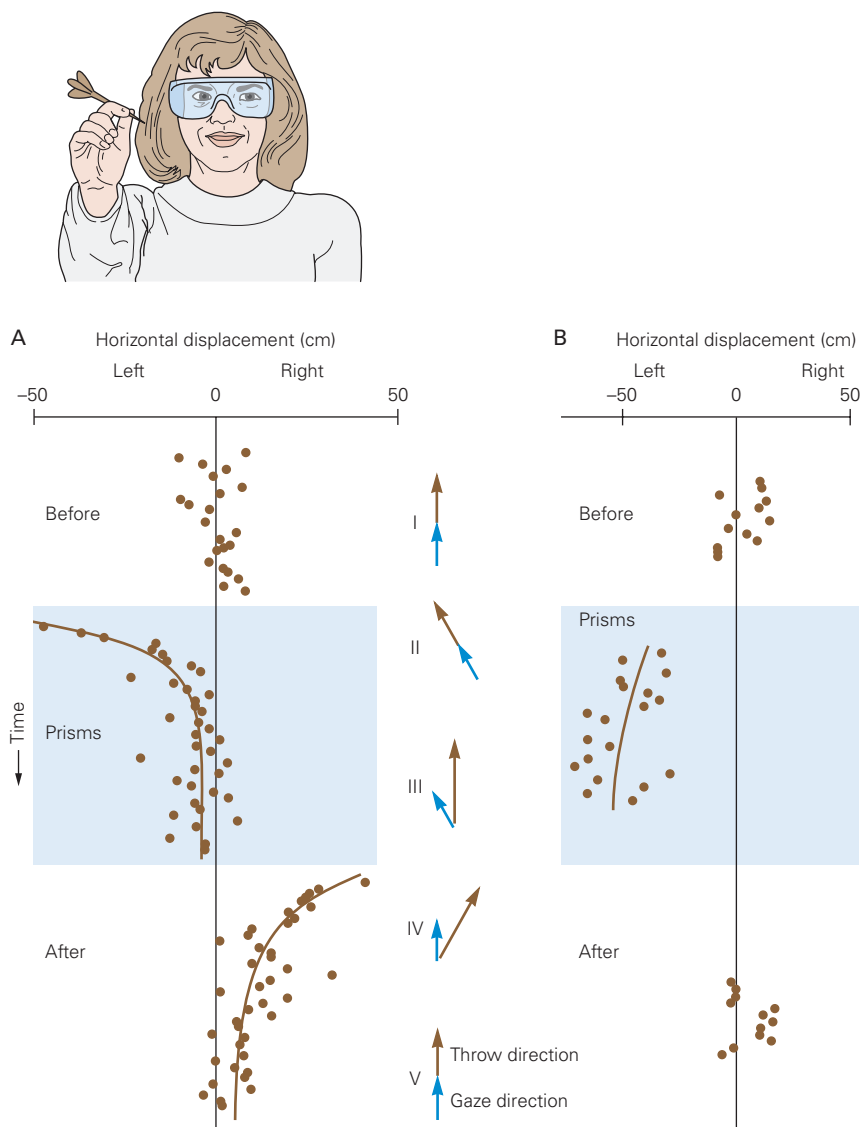


Figure 42-13 Adjustment of eye-hand coordination to a change in optical conditions. The subject wears prisms that bend the optic path to her right. She must look to her left along the bent light path to see the target directly ahead. (Adapted, with permission, from Martin et al. 1996a, 1996b.)

A. Without prisms the subject throws with good accuracy. The first hit after the prisms have been put in place is displaced left of center because the hand throws where the eyes are directed. Thereafter hits trend rightward toward the target, away from where the eyes are looking. After removal of the prisms the subject fixes her gaze in the center of the target; the first throw hits to the right of center, away from where the eyes are directed. Thereafter hits trend toward the target. Data during and after prism use have been fit with exponential curves. Gaze and throw directions are indicated by the **blue** and **brown** arrows, respectively, on the right. The inferred gaze direction assumes that the subject is fixating the target.

Before donning the prisms the subject looks at and throws toward the target (I). Just after donning prisms, when her gaze is directed along the bent light path away from the target, she throws in the direction of gaze, away from the target (II). After adapting to the prisms she directs her gaze along the bent light path away from the target but directs her throw toward the target (III). Immediately after removing the prisms she directs her gaze toward the target; her adapted throw is to the right of the direction of gaze and to the right of the target (IV). After recovery from adaptation she again looks at and throws toward the target (V).

B. Adaptation fails in a patient with unilateral infarctions in the territory of the posterior inferior cerebellar artery that involve the inferior cerebellar peduncle and inferior lateral posterior cerebellar cortex.

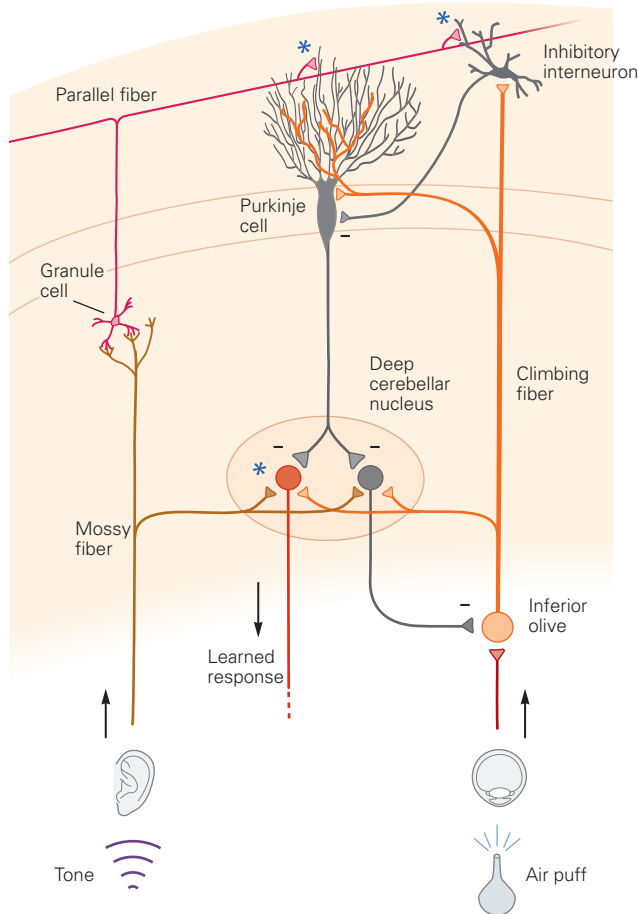


Figure 42–14 Learning can occur in the cerebellar microcircuit both in the cerebellar cortex and in the deep cerebellar nuclei. The diagram is based on classical conditioning of the eyelid response (combining a tone and air puff), but describes equally well adaptation of the vestibulo-ocular reflex when head turns are associated with image motion on the retina (see Chapter 40). Sites of learning are denoted by asterisks. (Adapted, with permission, from Carey and Lisberger 2002.)

An Overall View

Whereas lesions of other motor processing centers result in paralysis of voluntary movements, lesions of the cerebellum result in large errors in movements. How do these errors occur?

The organization of the inputs and outputs of the cerebellum indicates that the cerebellum compares internal feedback signals that report the intended movement with external feedback signals that report the actual motion. On a very short time scale during the execution of the movement, the cerebellum is able to generate corrective signals that help to make

movements accurate. These corrective signals are feed-forward or anticipatory actions that operate on the descending motor systems of the brain stem and cerebral cortex. When these mechanisms fail because of lesions of the cerebellum, movement develops characteristic oscillations and tremors.

The corrective control of movement by the cerebellum is complemented by important cerebellar contributions to motor learning. Although some aspects of a movement can be adjusted “on-the-fly” during the movement, much about the movement must be well planned in advance, and planning necessarily incorporates adjustments of motor programs based on learning. The cerebellum may have a role in motor learning through the ability of the climbing fibers to depress activity in the parallel fibers. Because of their low firing frequencies, climbing fibers have only a modest capacity for transmitting moment-to-moment changes in sensory information. Instead, they may be involved in detecting error in a movement and changing the program for the next movement.

Finally, the cerebellum seems to have a role in some purely mental operations. In many respects these operations appear to be similar to the cerebellum’s motor functions. For example, the different regions of the lateral hemisphere appear to be particularly important for forms of both motor and cognitive learning that depend on repeated practice.

Stephen G. Lisberger
W. Thomas Thach

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