

THE CEREBELLUM

Damage to the cerebellum produces characteristic symptoms primarily with respect to the coordination of voluntary movements. The cerebellum receives information from the skin, joints, muscles, the vestibular apparatus and the eye about positions and ongoing movements. Information is also coming from the cerebral cortex, primarily from cortical areas dealing with planning or initiation of movements. The cerebellum sends information primarily to cell groups that give origin to the central motor pathways, like the motor cortex and the reticular formation of the brain stem.

It is a striking feature of cerebellar organization that the number of afferent fibers leading to the cerebellum is much larger than the number of fibers leading out (in humans about 40:1). This would indicate that considerable integration must take place here.

SUBDIVISIONS, STRUCTURE AND CONNECTIONS

A subdivision of the cerebellum on the basis of functional differences corresponds closely with a subdivision on the basis of differences in where the afferent fibers come from.

The most primitive part occurring first during phylogeny is the flocculonodular lobe or archicerebellum. The rest of the cerebellum is called the corpus cerebelli. This comprises the vermis which forms a narrow zone on both sides of the midline, and the large lateral parts called the cerebellar hemispheres. The medialmost part of the hemispheres, bordering the vermis medially, is called the intermediate zone. The corpus cerebelli is divided by a deep, transversally oriented fissure, the primary fissure into the anterior and posterior lobes. Paleocerebellum: consists of vermis and paravermian zone of the anterior lobe, and the most caudal two lobules of the posterior lobe. The paleocerebellum receives afferent impulses predominantly from the spinocerebellar pathways. The neocerebellum consists of the major part of the posterior lobe and its development is closely related to that of the cerebral cortex. From connective point of view the cerebellum can be divided into vestibulo-; spinal and cerebrocerebellum.

Afferent Connections from the Labyrinth and Vestibular Nuclei

Input from the vestibular nuclei provides the cerebellum with information about the position and movements of the head. Remarkably, some of the fibers in the vestibular nerve bypass the vestibular nuclei: they go to the cerebellum directly. They, too terminate in the vermis and the flocculonodular lobe. Efferents from the flocculonodular lobe end in the vestibular nuclei and can thereby influence the body equilibrium (via the vestibulospinal tract) and eye movements.

Afferent Connections from the Spinal Cord

The dorsal spinocerebellar tract comes from a distinct cell group with fairly large cells at the base of the dorsal horn, forming the column of Clarke. The axons of the cells in the column of Clarke ascend on the same side and enter the cerebellum through the inferior cerebellar peduncle. Primary afferent fibers from muscle spindles and tendon organs end monosynaptically on the neurons of the column of the Clarke. The dorsal spinocerebellar tract conveys information

only from the trunk and the lower extremities and ends in the corresponding parts of the spinocerebellum. The same kind of information from the upper extremities is mediated through the external cuneate nucleus, located laterally in the medulla oblongata.

The ventral spinocerebellar tract originates from cells located mainly laterally in LVII of L4-S3, that is the lamina containing the largest number of interneurons. Most of the axons cross at the segmental level in the cord to the lateral funiculus of the opposite side. However, after having reached the cerebellum through the superior cerebellar peduncle, many of the fibers cross once more. Physiological experiments indicate that they primarily inform about the activity of inhibitory interneurons. Similar information about interneuronal activity in the cervical cord is mediated through the central cervical nucleus and the lateral reticular nucleus in the medulla.

Afferent Connections from the Cerebral Cortex

In humans, by far the largest number of cerebellar afferents arises in the pontine nuclei. The pontocerebellar tract ends primarily in the cerebellar hemispheres. The vast majority of afferents to the pontine nuclei arise in the cerebral cortex (M1, S1, SMA, PM and areas 5, 7 of the parietal cortex). All of these areas are, in various ways, active during or before movements. Presumably, the cerebellum thus receives information about movements that are being planned and about the commands that are sent out from the motor cortex; in response it can modulate the activity of the motor cortex so that the movements are performed smoothly and accurately. The pontine nuclei also receives afferents from the visual cortex, and physiological experiments indicate that these fibers inform primarily about moving objects in the visual field. The pontine nuclei also receive connections from the cingulate gyrus and mammillary bodies. The information from these regions probably contribute to the well known influence of motivation and emotion on movements.

Whereas the lateral parts of the hemispheres are strongly dominated by inputs from the cerebral cortex, and the vermis is dominated by spinal inputs, the intermediate zone receives connections from both the cerebral cortex and the spinal cord. Perhaps the cerebellum compares copies of the motor commands sent from the cerebral cortex with the signals from the periphery providing information about the actual movement that was produced by that command.

The Inferior Olive

The inferior olive receive information from the spinal cord, cerebral cortex, pretectal nuclei, superior colliculus, red nucleus and project to the cerebellum. The projections from the pretectal nuclei and superior colliculus contributes to control of eye movements and terminate primarily in the flocculonodular lobe.

Structure of the Cerebellar Cortex

The cerebellar cortex has the same structure all over the cerebellum and the structural arrangement of the neural elements is strictly geometric. (see Fig.).

Mossy and Climbing Fibers

The numerous afferent fibers to the cerebellar cortex fall in two categories, which differ in how the fibers end in the cerebellar cortex. The climbing fibers all come from the inferior olive, whereas afferents from nearly all other nuclei end as mossy fibers. The mossy fibers

conducts signals relatively rapidly and end in the granular layer, establishing synapses with the granular cell dendrites. One mossy fiber branches extensively and contacts a large number of granule cells, each of which in turn contacts many Purkinje cells. Thus each mossy fiber influences many Purkinje cells, but the excitatory effect on each is weak, so that many mossy fibers must be active together to provide sufficient excitation (via the parallel fibers) to fire a Purkinje cell. A typical feature of the mossy fibers is that they transmit action potentials with a high frequency and produce Purkinje cell firing with a frequency of 50-100/sec (simple spike).

The climbing fibers end very differently from the mossy fibers: they end with numerous synapses on the dendritic shaft of Purkinje cells. Each Purkinje cell receive branches from only one climbing fiber. Because each climbing fiber forms so many synapses with a Purkinje cell, the total excitatory action is strong. Even a single action potential in a climbing fiber elicits a burst of action potentials in the Purkinje cells it contacts (complex spike).

The mossy fibers are presumably well suited for providing precisely graded information about: movements (the muscles involved, and the direction, speed and force of movements), localization and characteristics of skin stimuli, details concerning motor commands issued from the cerebral cortex. The climbing fibers show an all-or-none action rather than a graded one, corresponding to the theory that the climbing fibers inform about errors in the execution of a movement (giving an error signal when the movement does not correspond to what was intended).

Efferent Connections of the Cerebellum: The Cerebellar Nuclei

The 3 main subdivisions of the cerebellum act largely on the parts of the nervous system from which they receive afferent inputs. In general, the Purkinje cells end in the cerebellar nuclei closest to them. The corticonuclear connections are precisely organized with topographic pattern. Particularly marked is the longitudinal organization, with the vermis sending fibers to the fastigial nucleus, the intermediate zone to the interposed nuclei, and the hemispheres to the dentate nucleus. The neurons of these nuclei then forward the information to the various targets of the cerebellum.

Sagittal Zones and Somatotopic Organization

The cerebellar cortex and the cerebellar nuclei consist of numerous compartments that appear to be able to function independently of each other. (Sagittal macro and microzones). Another aspect of cerebellar localization is that cortical cell groups representing different body parts are spatially segregated -somatotopic organization- fractured somatotopy.

The complex pattern of mossy and climbing fiber inputs to the cerebellar cortex indicates that the cerebellum is divided into numerous smaller functional units. Each unit has the same kind of neuronal machinery to treat the incoming information, whereas they differ in the nature of information they receive and the part of the brain to which they send their "answers".

CEREBELLAR FUNCTIONS

The Vestibulocerebellum Controls Balance and Eye Movements

The dominant afferent inputs to the vestibulocerebellum come from the semicircular canals (which signal changes in head position) and the otolith organs (which signal the orientation of the head with respect to gravity). Secondary afferents arise from the vestibular nuclei. The Purkinje axons from the vestibulocerebellum end primarily in parts of the vestibular nuclei that send ascending connections to the external ocular muscles through the medial longitudinal fasciculus, and to a lesser extent, in parts of these nuclei sending fibers to the spinal cord. The vestibulocerebellum can thus contribute to the control of eye movements and the control of the axial muscles that are used to maintain balance.

The Spinocerebellum Adjusts Ongoing Movements

The principal input to the spinocerebellum is somatosensory information from the spinal cord through the spinocerebellar tracts. The spinocerebellum also receives information from auditory, visual and vestibular systems. These afferent projections are somatotopically organized. The body is mapped in two different areas of the spinocerebellar cortex, one in the anterior lobe and two in the posterior lobe. More refined studies have showed that mossy fiber input from circumscribed peripheral sites diverges to influence several discrete patches of granule cells, each of which excites a small array of Purkinje cells (fractured somatotopy). The spinocerebellum also receives topographically organized projections from the primary motor and somatic sensory cortex.

The dorsal and ventral spinocerebellar tracts are the direct pathways from the trunk and legs and the cuneo- and rostral spinocerebellar tracts are the direct pathways from the arms and neck. Signals in the dorsal spinocerebellar tract faithfully reflect sensory events in the periphery and provide the cerebellum with information about evolving movements. The ventral spinocerebellar neurons are principally driven by central commands that regulate the locomotor cycle. This internal feedback allows the cerebellum to monitor the operation of spinal circuits.

The fastigial nucleus receiving Purkinje axons from the vermis sends its efferents to both the vestibular nuclei and the reticular formation. Thus, motoneurons can be influenced via the vestibulospinal and reticulospinal tracts. The fastigial nuclei also have crossed ascending projections that reach the ventrolateral nucleus of the thalamus. From here the information is relayed to the primary motor cortex. Through both its ascending and descending projections, the medial region of the cerebellum controls mainly the cortical and brainstem components of the medial descending systems. This region of the cerebellum regulates axial and proximal musculature.

The efferents from the intermediate zone reach the interposed nucleus which modulate cortical commands for movement through their connections to the brainstem and cortical components of the lateral descending systems: the rubrospinal and corticospinal tracts. The interposed nuclei project to the contralateral magnocellular portion of the red nucleus in the brain stem via the superior cerebellar peduncle. Many of these fibers continue rostrally to the ventral lateral nucleus of the thalamus, where they end on neurons projecting to the limb areas of motor cortex. By acting on the cells of origin of the rubrospinal and corticospinal systems, the intermediate zone and the interposed nucleus focus their action on distal limb muscles.

Because both the ascending fibers from the cerebellum to the motor cortex and the descending fibers from the cerebral cortex to the spinal cord are crossed, the deficits produced by the lesions of the intermediate zone affects limbs on the same side of the lesion.

The spinocerebellum controls the execution of movement and regulates muscle tone. It carries out these functions by regulating the peripheral muscular apparatus to compensate for small variations in loads encountered during movement and to smooth out small oscillations.

This control is thought to be dependent both on information that the spinocerebellum receives from cortical motor areas about the intended motor command and on feedback from the spinal cord and periphery, which provides details about the evolving movement. These inputs allow the spinocerebellum to correct for deviations from the intended movement.

The Cerebrocerebellum Coordinates the Planning of Limb Movements

The cerebrocerebellum receives most of its input from sensory and motor cortices and from premotor and posterior parietal cortices. These regions do not project directly to the cerebellum but rather to the pontine nuclei, which then distribute cortical information to the contralateral cerebellar hemisphere through the brachium pontis. The lateral zone of the cerebellar cortex projects to the dentate nucleus, which sends fibers through the superior cerebellar peduncle to the ventral lateral nucleus of the thalamus. These nuclei also receive fibers from the basal ganglia, but they end in different parts than the cerebellar fibers, which implies that the basal ganglia and the cerebellum also influences different part of the cortex. Impulses from the cerebellar hemispheres pass primarily to M1, SMA, whereas the basal ganglia via the thalamus act mainly on the PM and prefrontal cortex. The dentate nucleus also projects to the parvocellular component of the red nucleus. This portion of the red nucleus does not contribute to the rubrospinal tract but is part of a complex feedback circuit that sends information back to the cerebellum, primarily through the ipsilateral olivary nucleus.

The lateral parts of the cerebellar hemispheres are largely devoted to achieving precision in the control of rapid limb movements and in tasks requiring fine dexterity. Lesions on either side of the dentate nuclei or the overlying cortex produce four kinds of disturbances: 1) delays in initiating and terminating movement, 2) terminal (intention) tremor at the end of the movement, 3) disorders in the temporal coordination of movements involving multiple joints 4) disorders in the spatial coordination of hand and finger muscles. The cerebrocerebellum contributes to the preparation of movement while the spinocerebellum is more concerned with movement execution and feedback adjustments. The role played by the cerebrocerebellum in programming movement is particularly critical for multijoint movements and in those requiring fractionated movements.

According to current view the basal ganglia and lateral cerebellum process information originating in the sensory association cortex. This processing is critical for planning movement and preparing the motor system to act. Eventually, the processed information forms the commands for movement issued by the lateral cerebellum and the basal ganglia to the premotor and motor cortical areas. These motor areas execute movement and inform the spinocerebellum of the ongoing commands. In turn, the spinocerebellum then corrects for errors that have occurred or compensates for impending errors in the commands for movement.

CEREBELLAR DYSFUNCTIONS

Isolated damage to the flocculonodular lobe in animals produces disturbances of the equilibrium. Similar symptoms occur in humans with tumor of the nodulus. Eye movements may also be disturbed in patients with cerebellar lesions. This manifests itself as spontaneous nystagmus.

Damage to the anterior lobe in experimental animals produces primarily a change of the muscle tone. In decerebrate animals, the decerebrate rigidity increases (loss of inhibitory input to the vestibulo and reticulospinal neurons). In humans, more marked is the unsteadiness of

walking (gait ataxia) in patients with damage mainly affecting the anterior lobe vermis and intermediate zone.

The Neocerebellar Syndrome

Lesions involving large part of the cerebellum, including the neocerebellum results incoordination of the voluntary movements. The following symptoms are characteristic:

- 1) ataxia: involves the limbs, particularly the distal extremities, and is associated with deviations of the gait and stance toward the lesion.
- 2) dysmetria: the inability to gauge distance correctly, resulting in premature arrest of movement or overshooting
- 3) asynergia loss of coordination in the innervation of muscle groups needed for the performance of precise movements. Individual muscle groups function independently and are incapable of complex orchestrated movement patterns (decomposition of movements).
- 4) dysdiadochokinesia: rapid alternating movements of agonist/antagonist muscles cannot be performed. Alternating movements, such as rapid pronation and supination of the hands, are slow, hesitating, and arrhythmic.
- 5) intention tremor: an action tremor that is evident when an object is pointed at. It becomes more severe as the finger or toe approaches the object. This tremor is usually associated with damage to the dentate nucleus or superior cerebellar peduncle.
- 6) rebound phenomenon: caused by an inability to adjust promptly to changes in muscle tension. For example, a patient's arm pressed against the hand of the examiner cannot immediately relax when the examiner withdraws his hand but follows the hand with an uncontrolled hitting motion.
- 7) scanning speech: asynergia of the muscles of speech results in slow, hesitant, and poorly articulated speech with inappropriate emphasis on individual syllables that cause some words to be uttered explosively.

RECENT THEORIES INTERPRETING CEREBELLARR FUNCTIONS

One hypothesis is that the cerebellum has a special role in timing movements. While cortical areas primarily select the effectors needed to perform a task, the cerebellum provides the precise timing needed for activating these effectors.

The timing hypothesis can account for the cerebellar symptom of hypermetria. Rapid movements require both agonist and antagonist activity. One argument for the biphasic pattern is that it enables a person to move at fast speeds that are not reliant on sensory feedback. An initial agonist burst propels the effector rapidly in the correct direction with little opposing resistance. Then the antagonist brakes the movement. This requires that the timing of the agonist and antagonist must be precise. In this view, the cerebellum's contribution to rapid movements establishes a temporal pattern across the muscles. The cerebellum can predict when the

antagonist should be activated to terminate movement at the right location. If the cerebellum is lesioned, the agonist burst is sufficient to initiate the movement, but the animal cannot anticipate when the brake is needed. Other signals, such as feedback from the moving limb, may now be required to trigger the antagonist. Given delays in neural transmission, it is likely that the antagonist will be delayed and the animal will overshoot the target.

The timing hypothesis offers a novel slant on the role of the cerebellum in motor learning. Cerebellar lesions are most disruptive to highly practiced movements, which present the greatest need for precise timing. This point is highlighted in an experiment involving a simple model of motor learning, eye blink conditioning. When a puff of air is directed at the eye, a reflexive blink is produced, a response designed to minimize potential eye damage. If a neutral stimulus such as tone is presented in advance of the air puff on a consistent basis, the animal comes to blink in response to the tone. The acquired response is highly adaptive: by blinking to the tone, the animal's eye closes before the air puff. This conditioned response is timed to reach amplitude at the onset of the air puff. Lesions of the deep cerebellar nuclei abolish the learned response. The fact that the animal continues to blink reflexively in response to the air puff indicates that the lesion has produced a learning deficit and not a motor problem. The anticipatory, learned responses are still present following lesions of the cerebellar cortex, however, they are timed inappropriately, and, thus no longer adaptive.

The cerebellum has purely cognitive functions

Functional magnetic resonance imaging data have provided evidence that the cerebellum has purely cognitive functions independent of motor control. For example, Peter Strick and co-workers showed that 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 area activated in the dentate nucleus corresponds to the area receiving input from the part of the cortex (Brodmann area 46) involved in working memory. Another example in which cognitive activity could be isolated from sensory stimulation of movement is shown in Gao et al., experiments (Fig.). Activity in the dentate nucleus increased dramatically when subjects were required to evaluate sensory information consciously. Thus the dentate nucleus appears to be particularly important in acquiring and processing sensory information for tasks requiring complex spatial and temporal judgements, which are essential for programming complex motor actions and sequence of movements.