The Cerebellum

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The word "cerebellum" is derived from a Latin word meaning "little brain". Given the scope of its function and the number of neurons that comprise the cerebellum, "little brain" is an apt description. The vast number of neurons in the cerebellum belies its modest size. While it occupies some ten percent of total brain volume, half of the brain's neurons are cerebellar neurons. It is difficult to succinctly describe the cerebellum's functions. However, for the purposes of the present review, it will suffice to say that the cerebellum plays a significant role in motor control, integrating sensory input and motor commands in order to finely adjust and balance the relationship between these two streams of information. The lecture that pertains to this material was both concise and expressive. Consequently, the present document does not serve to briefly summarize that material, but rather, offers supplementary information to broaden the reader's understanding of the cerebellum and to pique curiosity.

Anatomy. Two fissures in the cerebellum divide it into three lobes. The cerebellum is a layered structure with an outer layer of grey matter and an inner layer of white matter, resembling the gross organization of the cerebrum. The spatial organization of cells in the cerebellum is quite regular, resembling a repeating pattern. The cerebellar cortex (the outer layer) contains many small granule cells. These cells contribute greatly to the cerebellum's high number of neurons. Granule cells receive input from the pons, whose axons (called "Mossy fibres" in this case) simultaneously project to the deep cerebellar nuclei (these will be described later). The cerebellar cortex also contains large Purkinje cells, which receive input from granule cells (via parallel fibres) and send inhibitory projections to nuclei below the cortex. The Purkinje cells play a critical role in exerting control over motor commands. The large number of parallel fibre inputs (numbering around 200,000 per cell) to the Purkinje cells testifies to the enormous computational burden shouldered by these cells. Note that the Purkinje cells also receive input from inferior olive neurons via the climbing fibres.

The aforementioned nuclei (collections of cell bodies) lie below the cerebral cortex. These include the fastigial nuclei, interpositus nuclei, dentate nuclei and vestibular nuclei. The output of these nuclei is directed to muscles, such as limb muscles and eye muscles. The deep nuclei are the final stop in the path motor commands take through the cerebellum.

Cerebellar anatomy suggests that this structure has a rather heavy computational responsibility. The number of axons projecting to the cerebellum is 40 times greater than the number of axons that project from the cerebellum.

Movement. As indicated above, the cerebellum is a key contributor in motor control and so it is valuable to learn something about movement in general. Movements generated by the nervous system are of three types: reflexive, rhythmic and voluntary. Voluntary movements will be the focus of this section. All voluntary movements are initiated in order to reach a goal. Take for example a reach-and-grasp movement. The goal is to contract the muscles of the arm in such a way as to produce a desired movement trajectory, bringing the hand in contact with a target object.

Voluntary movements are subject to the laws of physics, of course. Their successful execution also depends on the nervous system's ability to compensate for events that would serve to perturb movement. Simple thought experiments illustrate this general principle. To perform an accurate reaching movement, the nervous system must appreciate the dynamics of the arm. It's an odd, multi-segment thing that behaves in strange ways when

forces (like muscle contractions) are applied to its joints. The nervous system must appreciate these dynamics and compensate for them. In the course of generating a reaching movement, the arm may collide with an obstacle. The nervous system must be able to deal with this physical event and the consequences it has on movement.

The nervous system uses two different control strategies to compensate for the various physical events that affect movement. These are feedback control and feed-forward control. These will be considered in the following sections.

Feedback control. The nervous system continually monitors sensory input. During a reaching movement, for example, the nervous system is provided with a steady flow of information from muscle spindle afferents, as well as information from joint receptors and cutaneous mechanoreceptors. Vision also provides information about the movement.

Voluntary movements are generated in order to reach a goal (for example, bringing the hand to a target object). The goal is associated with a particular pattern of sensory input. In the case of the reach-and-grasp movement considered above, a successful reach is marked by spindle input that signals specific muscle lengths, by cutaneous input that signals contact between the hand and the target object, by visual input that signals the position of the hand in the target location and so on. Generally speaking, the nervous system needs to compare the desired output (that is, the sensory information pertaining to the desired state, like reaching the target object) with the actual output. Returning once again to the above example, in the course of a reaching movement mistakes may be made. Alternatively, the movement may be impeded by an obstacle of some sort. These physical events create a discrepancy between what the nervous system wants and what is actually happening. In feedback control, the nervous system compares desired output with actual output and implements changes in order to reduce the difference between desired output and actual output. Feedback control is adjustment based on error.

Patients who are devoid of spindle afferents and cutaneous afferents are faced with the challenge of moving with virtually no feedback control, aside from that afforded by vision. These patients cannot maintain their hands in one position. They cannot maintain a stable grasp, either. Force and position begin to drift, as they cannot detect fatigue of their muscle fibres.

Feed-forward control. In addition to using sensory input to correct errors, the nervous system can use sensory input to *anticipate* errors. Feed-forward control refers to adjustments of motor commands that are meant to compensate for predicted physical events and the consequences they have on movement. In the example of the reaching movement, visual input can signal the presence of an obstacle before the hand reaches it, or before the movement is executed at all. This information can be used by the nervous system to generate a feed-forward motor command that takes the obstacle into account. Feed-forward control is proactive; feedback control is reactive.

Feed-forward control relies on more than just sensory input. Experience is also used to guide feed-forward motor commands, as experience allows the organism to anticipate mechanical perturbations. The nervous system is capable of storing the nature and location of obstacles in memory. It also relies on its movement experience to anticipate the physical consequences of different types of movements. Unlike the flailing arms of neonates, the arm movements of healthy adult humans fully compensate for the dynamics of the limb.

Feed-forward control is particularly important during the execution of fast movements or during movements that are affected by fast perturbations, the speed of which defy effective feedback control. Feed-forward control is also required during the execution of skilled,

precisely timed, coordinated movements. Proficiency in a motor skill is made possible through anticipation of the mechanical events associated with movement. Seasoned baseball pitchers can throw a ball accurately at high speed and compensate for subtle changes in posture, ball mass and so on. Novice throwers have difficulty anticipating every perturbation and rely more heavily on feedback control.

A number of observations of human movement suggest that many movements are fully planned in advance of their execution. This suggests the presence of feed-forward control. For example, reaching movements executed to targets over different distances, presented randomly from trial to trial, are identical in terms of their acceleration and velocity profiles. These kinematic features of movement are simply scaled up or down, proportional to the distance of the target. If it was the case that these different movements were not planned in advance of their execution, their velocity and acceleration profiles would not have single peaks. Instead, they would have multiple peaks as a consequence of pure feedback control making adjustments throughout the course of movement.

A broad view of cerebellar function. The effects of cerebellar lesions hint at the cerebellum's role in motor control. Lesions result in cerebellar ataxia. Ataxic patients have difficulty executing coordinated, accurate movements. It appears that the temporal and spatial aspects of their motor control are impaired. Balance and muscle tone are negatively affected in ataxic patients. They also have difficulty learning motor skills and performing a number of cognitive tasks. Ataxic patients, however, are not deficient in terms of the strength of muscle contraction they can produce. Also, their sensory thresholds remain unchanged.

The cerebellum is deeply concerned with integrating information about movement goals, movement commands and sensory feedback. The disproportionately high ratio of input axons to output axons testifies to the cerebellum's role as an information processor. The output of the cerebellum projects mainly to premotor and motor areas in the cerebral cortex and brainstem, so its intimate link to motor control cannot be denied. Finally, the cerebellum contains many modifiable synapses, which are crucial for learning. Below is a brief consideration of fibres in the cerebellar cortex.

Simple and complex spikes. Climbing fibres originate in the inferior olivary nucleus. They convey sensory input and signals from the cerebral cortex. Climbing fibres exert powerful excitatory effects on Purkinje cells, creating a big, complex spike (as opposed to the little, simple spikes generated by parallel fibres). Frequency of simple spikes encodes magnitude and duration of stimuli or centrally generated signals. Complex spikes are relatively infrequent and so they are ill suited for conveying information regarding the magnitude of stimuli. Rather, they appear to signal the timing of events. Different phases of natural behaviour are correlated with simultaneous discharge of particular groups of Purkinje cells. Cells in the inferior olivary nucleus can fire at the same time. Accordingly, synchronous signals in climbing fibres can cause simultaneous complex spikes in groups of Purkinje cells.

The activity of climbing fibres leads to significant long-term depression of parallel fibres that are firing concurrently. This may play a role in the learning of motor skills.

The cerebellum is divided into distinct regions, each of which receives different input. The input to these regions and the output from these regions reveals something about their contribution to motor control.

The vestibulocerebellum. Information from the semicircular canals and otolith organs is

delivered to the vestibulocerebellum. The vestibular nuclei give rise to Mossy fibres that terminate in the vestibulocerebellum. Purkinje neurons in this region of the cerebellum exert their effects on axial and limb muscles through the lateral and medial vestibulospinal tracts. These Purkinje cells also influence neck and eye muscles via the medial longitudinal fasciculus. Lesions to the vestibulocerebellum or its projections impair one's ability to use vestibular information to control eye movements during head rotation, or limb/body movements during standing and walking. Patients who have sustained lesions of this nature can move their limbs accurately while lying down or while the head and body are fixed, however.

The spinocerebellum. The ventral and dorsal spinocerebellar tracts are projections to the spinocerebellum from the ventral and dorsal spinal interneurons. The spinocerebellum is thus provided with sensory information arising from leg proprioceptors and with descending motor commands. Before reaching the cerebellum, this information is relayed to precerebellar nuclei in the brainstem reticular formation. In this manner, the cerebellum is provided with several versions of the current state of the organism and its environment. The cerebellum is thus in a ready position to compare these different signals, in addition to monitoring outgoing motor commands.

The spinocerebellum contains the fastigial nuclei. These send projections to the reticular formation and lateral vestibular nuclei, which in turn project to the spinal cord. The fastigial nuclei also send projections to the thalamus, which sends axons to the primary motor cortex (in particular, to representations of proximal muscles. The spinocerebellum influences control of neck, face, mouth and proximal limb muscles. Its role in gait and balance is clear.

The spinocerebellum also contains the interposed nuclei. These send projections to the red nucleus, which sends its axons to the spinal cord. The same nuclei also send projections to the thalamic regions that synapse on limb areas of the primary motor cortex. Axial and limb muscles are influenced by this system.

Damage to the interposed nucleus reduces activity in the rubrospinal and corticospinal tracts, leading to reduced muscle tone. Dysmetria in limb movements also results, seemingly due to a loss of timing, direction and extent of movements. Ataxia also results, leaving hand trajectories curved. Patients notice these errors and try to correct, which results in more movement errors. The limb oscillates around the target.

Experiments have revealed that these errors are due to compromised feed-forward control. In healthy monkeys (and humans for that matter), when the limb is being voluntarily held in a given position, a sudden perturbation causing elbow extension is quickly corrected. The perturbation stretches the biceps muscle, leading to a stretch reflex as the muscle contracts. To prevent the hand from overshooting its intended position, the triceps muscle contracts in a timely manner and slows the hand down. The contraction of the triceps is not due to stretch reflex, but rather, is an anticipatory movement. In monkeys with lesions to the interposed and dentate nuclei, anticipatory contractions of the triceps are not observed. Instead, the limb oscillates about the desired position as alternative stretch reflexes shift the hand to either side of the target.

During voluntary movement, antagonist muscles contract in a predictive fashion to accurately reach a movement target. Lesions to the dentate and interposed nuclei delay these muscle contractions. The feed-forward command is replaced by a feedback correction and so the effector misses the target, corrects for this error, misses again, corrects for this new error, and so on. Similarly, human patients with cerebellar lesions cannot compensate for interaction torques that arise in limb joints during reaching movements.

The cerebrocerebellum. Sensory information from the cerebral cortex is sent to the cerebrocerebellum. Purkinje cells in this region send projections to the dentate nuclei. From here, neural signals travel to the ventrolateral thalamus (the interposed nuclei send their projections here as well) and from there to premotor and primary motor areas in the cerebral cortex. These Purkinje cells also send projections to the red nucleus, which connects to the inferior olivary nucleus, which from there sends signals back to the cerebellum. This is a feedback loop.

Lesions to the cerebrocerebellum delay initiation of movement (slow reaction time) and create irregularities in movement timing. Many movements (like a reach-and-grasp) are composed of several component movements, which must be executed more or less at once to create a smooth, successful movement. Lesions of the cerebrocerebellum result in a serial execution of these components. The movement is decomposed, essentially. Patients report having to consider each portion of a movement individually.

These effects suggest that the cerebrocerebellum is involved in movement planning and programming (especially where the hand is involved). The cerebrocerebellum also appears to be involved in purely cognitive tasks (e.g. judging elapsed time, word association, peg board tasks).

Motor learning. The cerebellum plays a key role in learning motor skills. Tasks that entail learning to compensate for aberrations in visual feedback or the presence of perturbing forces rely on an intact cerebellum. Imaging studies have shown pronounced activity in the cerebellum during and following acquisition of novel motor skills.

It is thought that the climbing fibres provide error signals. The climbing fibres depress activity of concurrently active parallel fibres, allowing correct movements (those associated with no error) to emerge. Climbing fibres likely detect differences between expected and actual sensory input.

In the course of motor learning, kinematic features of the movements suggest that the nervous system shifts from a largely feedback control strategy to one that is primarily feed-forward. Take for example the visuomotor rotation task. In this task, participants use their hands to guide the motion of a cursor to targets that appear on a screen. Under normal conditions, participants are able to accurately guide the cursor in straight lines to the targets. With a visuomotor rotation in place, however, participants initially are unable to guide the cursor in a straight line to the target, resulting in curved trajectories. A visuomotor rotation is a perturbation of visual feedback, where the cursor's direction of motion is rotated about the start position. With practice, participants regain the ability to guide the cursor in straight lines directly to the targets, even with a visuomotor rotation in place.

Curved trajectories suggest the presence of feedback control. Participants who are first exposed to a visuomotor rotation cannot proficiently anticipate the effects of the rotation. Their trajectories miss the target and this is followed by a corrective movement to bring the cursor back on target. This is adjustment based on error. With practice, trajectories become straight. Practice grants participants the ability to fully compensate for the visuomotor rotation. The extent of learning can be assessed during trials when the visuomotor rotation is suddenly and unexpectedly removed. The typical result of this is a perturbed movement - an after-effect. The trajectories are curved once again, appearing as mirror images of the curved trajectories that occurred when the visuomotor rotation was first imposed. This kinematic feature reveals that after extensive practice, the hand moves in such a way to precisely counteract the visuomotor rotation in a predictive fashion.

This task bears some resemblance to prism goggle tasks, where participants are instructed to throw balls at targets while wearing goggles that shift the visual world, for example, by 30 degrees to the left. Patients with cerebellar lesions have difficulty learning this motor task, although they can devise strategies for overcoming the altered visual feedback. When the goggles are removed, the patients do not exhibit after-effects.