The Cerebellum

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Topics

- What is the cerebellum?
  - What does it do?
  - What are the components of the cerebellum?
  - The functional circuit of the cerebellum.
  - Theories of cerebellar function.
- Parallel Computing

- How do Simple Control Systems work?

- How does the cerebellum work in relation to other parts of the brain?

- What happens when things don’t work?
What Does the Cerebellum do?

- The cerebellum helps to coordinate and optimize motor movement, including timing and precision of movements.
- Damage to particular regions of the cerebellum results in semi-predictable loss of fine motor skills, precision, and timing of movements.
Purkinje cells are GABAergic neurons.

The only output from the cerebellar cortex.

They can be some of the largest cells in the (human) brain.

They are almost always arranged in large, linear arrays.

One Purkinje cell can make over 200,000 synapses.
Mouse Purkinje Cell
Mossy Fibers

- One of two axonal inputs to the cerebellum (This one from the pontine nuclei, spinocerebellar tract, etc.).
- Synapse to granule cells.
Climbing Fibers

- Axonal inputs from the inferior olivary nucleus.

- Synapse with neurons in the deep cerebellar nuclei and with Purkinje cells.

- Excitatory in both cases.

- One climbing fiber may enervate multiple Purkinje cells, but each Purkinje cell will only synapse with one climbing fiber.
Granule Cells

- They are the smallest type of neuron in the human brain.
- They are also the most abundant type of neuron found in the human brain.
- Synapses from mossy fibers. In the granule layer of the cerebellar cortex.
Parallel Fibers

- Axons from granule cells.
- Form T-shaped branches in the molecular layer of the cerebellar cortex.
- Make glutamate synapses with Purkinje cells in the molecular layer of the cerebellar cortex.
Stellate Cells

- Inhibitory interneuron.
- Takes input from the parallel fibers and produces an inhibitory input to the Purkinje cell dendrites.
Basket Cells

- GABAergic interneuron.
- Makes “nests” of synapses with Purkinje cell bodies.
- Modulates the inhibitory action of the Purkinje cells.
Golgi Cells

- Inhibitory Interneuron.
- Receives input from the parallel fibers.
- Provides inhibitory input to the cell bodies of the parallel fibers (granule cells).
- Cell bodies in the granular layer.
- Dendrites in the molecular layer.
Deep Cerebellar Nuclei Cells

- Receives inhibitory stimuli from Purkinje cells and excitatory stimuli from mossy and climbing fiber pathways.
- Nearly all of the output of the cerebellum goes through these cells.
(A) Midline

Primary motor and premotor cortex

VL complex (thalamus)

Cerebellar cortex

Deep cerebellar nuclei dentate/interposed

Superior cerebellar peduncle

Superior colliculus

(B) Primary motor and premotor cortex

Ventral lateral complex (thalamus)

Red nucleus (parvocellular)

Cerebellar cortex

Inferior olive

Deep cerebellar nuclei
Fundamental Unit of the Cerebellum

- Deep cerebellar nuclei (DCN) are stimulated by direct excitatory input from the mossy and climbing fibers.
- The output of the DNC is modulated by the inhibitory Purkinje cells.
- This unit is repeated all throughout the cerebellum.
- The cerebellum houses hundreds of individual “modules,” each containing millions of these units.
- These modules are, for the most part, independent of each other.
Fundamental Unit of the Cerebellum

How it seems to work for motor signals: Purkinje cells and deep cerebellar nucleus (DCN) cells recognize potential errors in motor movements and planning by comparing the concurrent information available to both types of cell. DCN cells then send corrective signals to the upper motor neurons in order to maintain or improve the accuracy of motor actions.

The problem: No one has figured out how exactly this works.
(A) Purkinje cell
At rest

Wrist flexion and extension

(B) Deep nuclear cell
At rest

Wrist flexion and extension
Idea: Signals move slightly slower along certain fibers (such as parallel fibers) than others, which imparts a predictable delay in cerebellar circuits. This delay allows circuits to predict time relationships for motor actions.

Problem: This idea was proposed in 1958, and so far no one has been able to come up with an adequate model of it that matches real-world data.
The Cerebellum as a Sensory Structure

- One possibility is that the cerebellum is responsible for monitoring and adjusting large portions of sensory data upon which the CNS depends. In this way, the cerebellum is not itself responsible for individual behavioral motor actions, but rather it simply influences motor actions so as to maximize the efficiency of other parts of the CNS (I.E., it makes movements that maximize sensory signals).

- Problems: Small number of types of animals studied, small portion of the cerebellum studied.
One possibility is that somewhere in the CNS we store a “map” of the external (space-time) world. In order to coordinate and refine movements, the cerebellum compares the coincidences between goal-directed movement (internal map) and the external world. Thus, the cerebellum acts to transform sensory coordinates into motor coordinates.

This is a more complete model, but we still lack the computational power to confirm it.
It’s been known for some time that the cerebellum plays an important part in motor learning (e.g., playing an instrument, chopping an onion, etc.). The general idea is that climbing fibers convey special signals which represent errors to parallel fiber-Purkinje cell synapses; these signals induce long-term depression of the synapses. In this way, individual cerebellar circuits can be modified over time.
Partial sectioning of lateral rectus tendon

With patch

Position
Target

Eye  Time →

-3°

Position

Time →

With patch

Position

Time →

With patch

Position

Time →

25°
In lampreys and hagfish, the cerebellum is barely distinguishable from the brainstem.
In most other fish, it is a quite a bit larger.
In mormyrids, the cerebellum is actually larger than the rest of the brain. Most of it is dominated by the valvula, which receives input from the electric organ.
Amphibians have considerably smaller cerebellums than most fish.

This probably has to do with the combination of slow movement and the reduction of dimensions for motor coordination in comparison to fish.
Evolution and Comparative Function of the Cerebellum

- Reptiles have larger cerebellums in relation to amphibians.
- This probably relates to a more active lifestyle and more complex motor actions.
Birds have a larger cerebellum than reptiles. We can see more folding and differentiation (more similar to a human cerebellum).

This probably has to do with increased activity, dimensionality of flight, and intelligence.
Evolution and Comparative Function of the Cerebellum

- In general: The cerebellum’s size relates to the activity level and complexity of an animal.

- Brains are expensive to maintain, so if you don’t need it, then it will go away (e.g., amphibians).

- Some animals have larger than expected cerebellums due to the specialized nature of how they use them (e.g., mormyrid fish).
Parallel Computing

- The traditional method of solving a computational problem is to use serial processing:

![Diagram showing serial processing](image-url)
Serial processing is generally efficient for doing linear calculations, but becomes inefficient (or inapplicable) for non-linear problems (such as coordinating multiple tasks).
One solution is to break the problem down into separate discrete sections and assign a separate processor to each section.
Parallel Computing

- The cerebellum is set up well to solve parallel processing problems because of its structure: Multiple “modules,” relatively isolated from each other, containing discrete processing units.
Generally speaking, most problems can be broken into separate steps, each of which may be more efficiently dealt with using serial or parallel processing methods. The cerebellum may be the part of the brain that is utilized for the parallel sections of computational problems, while other brain areas handle the serial computations.
The cerebellum is, then, just one piece in a larger computational scheme.
Control Systems

- The most basic control system consists of an instructor (P) a controller (CT) and a controlled object (CO). Feedback can be integrated into the system with a sensory system (SS).
In this model, error signals can be extrapolated by comparing the outputs of the CO (a) with the output of the cerebellum (b).
Putting it together

In this model, the instructor sends a signal to the cerebellum and the controller. The cerebellum computes the “ideal” space-time trajectory of movement, while the CO begins making the movement. If there is a discrepancy between the output of the CO and the signal from the instructor, then corrections can be made.
Damage to the flocculonodular lobe tends to result in problems with balance and equilibrium. A simple test for this type of damage: Walk in a straight line.
Damage to the cerebrocerebellum tends to result in problems with voluntary and planned movements. Simple test: Reach out and touch a small point/area.

- **Dysarthria**: Problems with speech articulation.
- **Dysmetria**: Problems judging distance.
- **Dysdiadochokinesia**: Problems performing rapid, alternating movements.
- **Tremors**
Pathology of the Cerebellum

Damage to the peduncles tends to result in a wide range of problems, generally involving sensory input. The most common are vision and hearing problems (vertigo, deafness), loss of temperature and pain response, facial palsy.

- Nystagmus: Eye-drift.
- Diplopia: Abnormal alignment of the eyes.
- Dysphagia: Difficulty swallowing.
- Horner's syndrome: One side of face: eye/vision problems (drooping eyelids etc.), lack of sweating on that side of the face.
Causes of Damage to the Cerebellum

- Physical trauma.
- Tumors.
- Hypertension (can lead to cerebellar hemorrhage).
- Several (rare) chronic degenerative conditions.
- Prion diseases (see textbook).
- Most common cause:
Alcohol

- Most common symptoms:
  - Wernicke’s encephalopathy.
  - Oculomotor dysfunction.
  - Gait ataxia.

- Often associated with vitamin B1 deficiency.

- Over time, regular consumption of alcohol (even moderate amounts) can lead to a decrease in the number of cerebellar Purkinje cells. It’s unclear as of yet what the direct implications of this are.
Alcohol Pathways

- Increases Golgi cell excitability, enhancing GABAergic pathways between Golgi cells and granule cells. The spontaneous firing rate of Golgi cells is increased.

- Longer term influence: alcohol changes the climbing fiber-Purkinje cell synapses. Changes metabotropic NMDA activity at synapse. Result: LTD is inhibited.

- Same story at the parallel fiber-Purkinje cell synapses.
Applications: Brain Surgery

- Violinist Undergoes Brain Surgery.