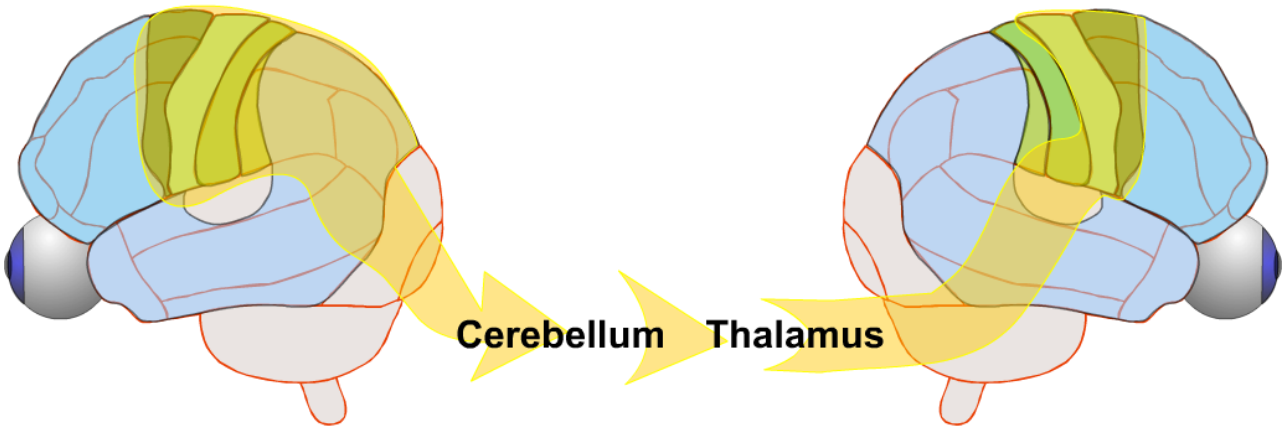
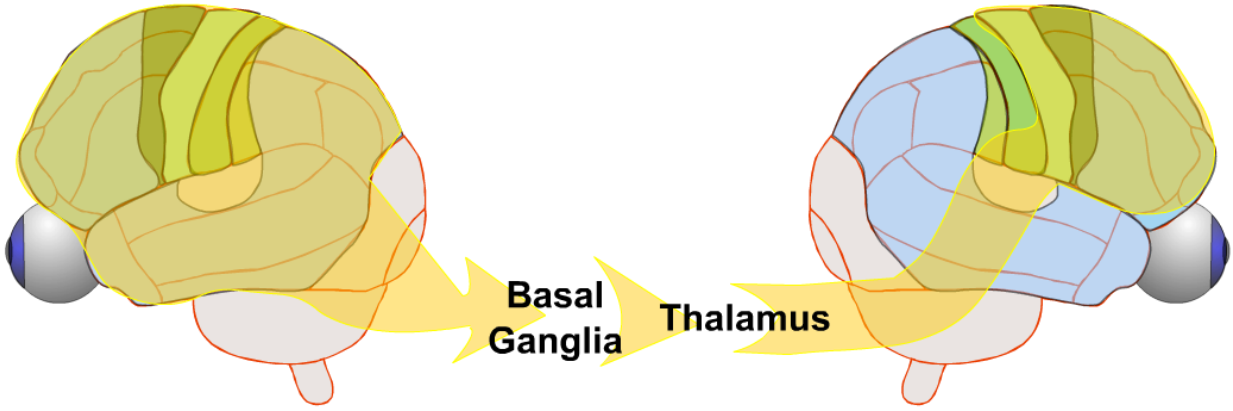
Cerebellum and Basal Ganglia





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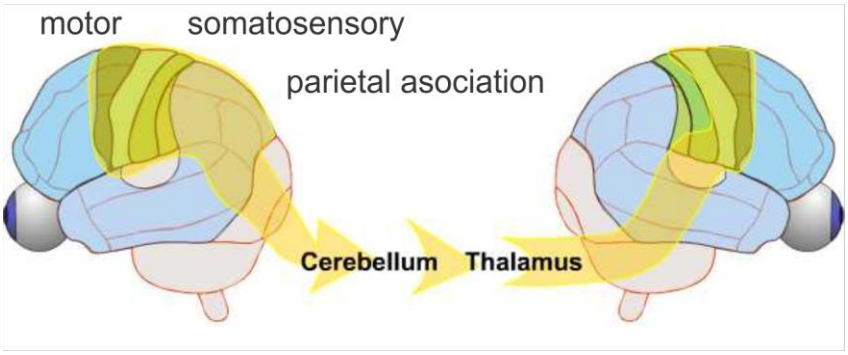
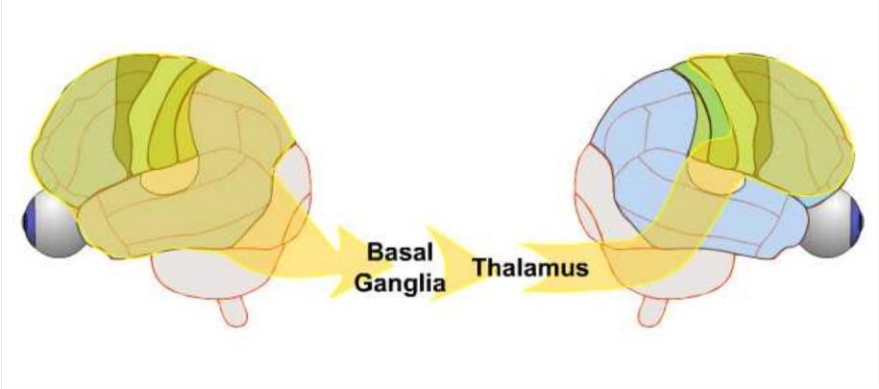
Introduction

The basal ganglia and cerebellum are sub-cortical structures that receive input from wide areas of the cerebral cortex and direct their output, through the thalamus, back to more precisely defined regions.

The cerebellum corrects the errors in each movement command and imparts motor skills. It does so based on input from motor areas, somatosensory areas and parietal association areas, and directs corrections to motor areas. As well, it receives input from and sends corrections to the spinal cord.



The basal ganglia release appropriate movements from the premotor and motor areas. As well, they release appropriate behaviors from the prefrontal association areas. Damage to the basal ganglia is in part responsible for Tourette's syndrome, which results in the release of inappropriate utterances.

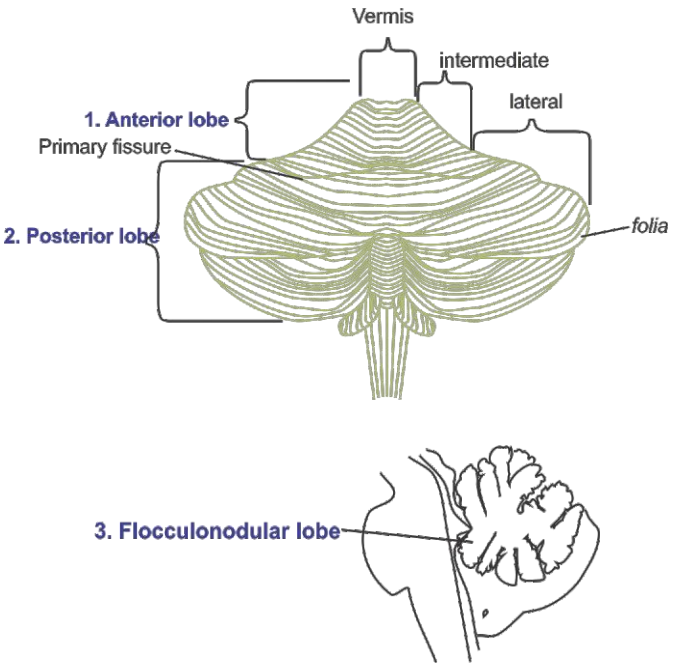


A brief review of cerebellar anatomy

The folia or folds of the cerebellum run horizontally and are more densely spaced than in the cerebral cortex.

From top to bottom: The cerebellum is divided into three lobes: the anterior, posterior, and flocculonodular lobes.

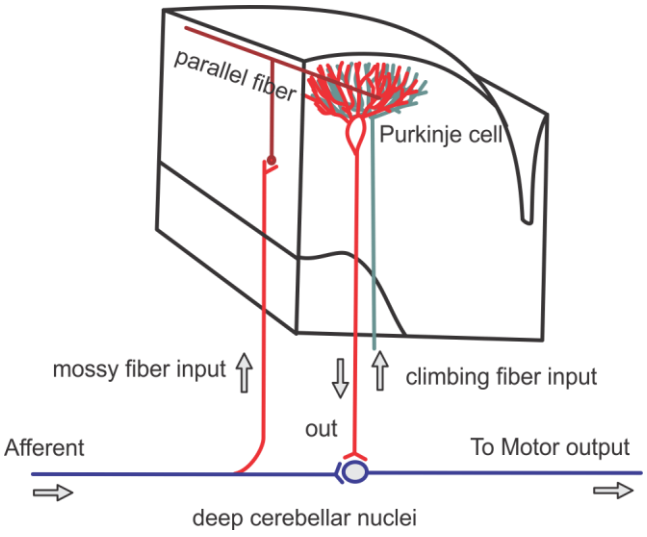
From midline out: It is divided into the vermis, intermediate, and lateral parts.



Basic Circuit

The basic circuit is the same in all parts of the cerebellum. It has three parts:

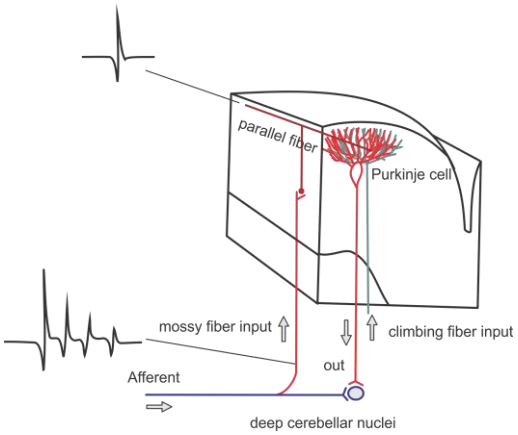
1. Direct path: sensory afferent input projects directly to motor systems via the deep nuclei.
2. Indirect side loop: through parallel fibers to Purkinje cells and back out to the deep cerebellar nuclei. This circuit is used to correct the direct reflex responses.
3. Climbing fiber input: to Purkinje cells. This is the error detection input. This circuit directs the learning to minimize the error.



Parallel and climbing fiber input has a very different effect on Purkinje cells.

i) Many parallel fibers (~200,000) make contact with a single Purkinje cell. Each synapse generates a weak input and many inputs are required to generate a single action potential.

ii) Only one climbing fiber contacts each Purkinje cell but through many synapses. The climbing fiber envelopes the Purkinje cell like a vine on the branches of a tree. Each single input generates a series of spikes. This strong input allows the climbing fiber to be an effective teacher and modify the appropriate parallel fibers' connections.



iii) The only output from the cerebellum is the Purkinje cell. All Purkinje cells inhibit (via Gaba) the deep nuclei.

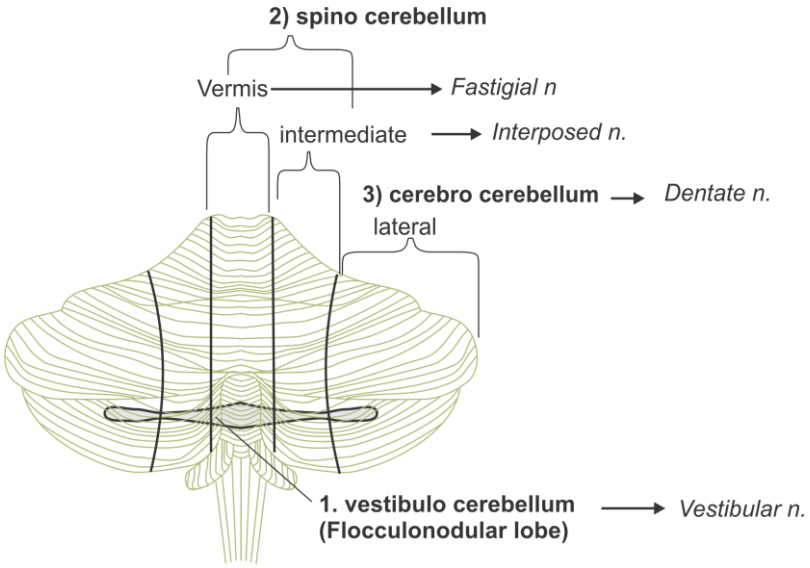
The three functional divisions of the cerebellum

The three subdivisions each send their output to different deep cerebellar nuclei

1) Purkinje cells from the vestibulo cerebellum (the oldest part of the cerebellum) synapse on vestibular nuclei.

2) The spino cerebellum is composed of the vermis and the intermediate cerebellum. Purkinje cells, from the vermis, synapse on the fastigial nuclei. Those from the intermediate cerebellum, synapse on the interpositus nuclei.

3) The cerebro cerebellum, the newest part, projects to the motor and premotor cortex via the dentate nuclei.



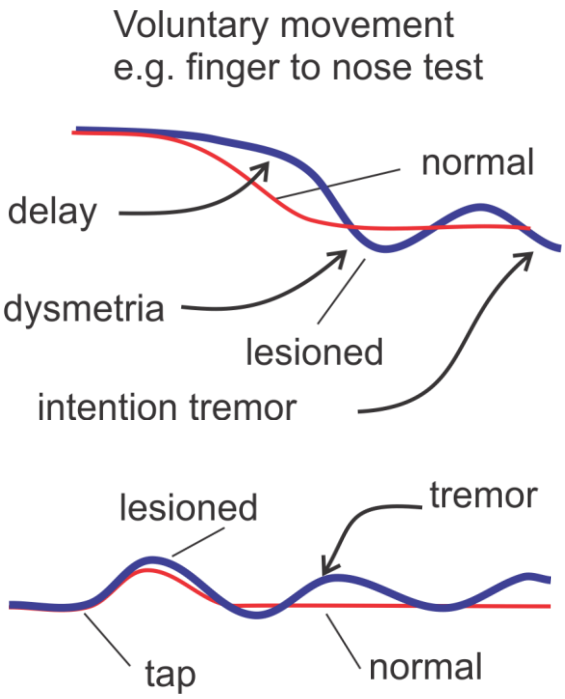
The main function of each sub-division

1) Vestibulo cerebellum **input:** vestibular organs. **output:** to legs, trunk, and eye muscles. **function:** tunes balance (stance & gait) & VOR.	*Disorders patients exhibit:* Ataxic gait and wide based stance (looks drunk) due to poor sense of balance. Imbalance becomes worse when eyes are closed. (Romberg sign). Nystagmus even when stationary.
2) Spino cerebellum **input:** directly from the spinal cord. (somatosensory & muscle afferents), visual and auditory systems. **output:** to spinal cord. **function:** tunes and adjusts ongoing movements and muscle tone (e.g. during walking).	Ataxic gait due to poor control of leg muscles. Falls when walking heel-to-toe ("drunk driver test"). Hypotonia.
3) Cerebro cerebellum **input:** from cerebral cortex (a copy of the motor command, sent down the spinal cord) **output:** to motor and premotor cerebral cortex **function:** add skill to movements.	Ataxia during skilled movement initiation: delay in initiation, dysmetric (inaccurate) movements, tremor. Fails the finger to nose test.

Lesions of the cerebro cerebellum result in ataxia

Ataxia consists of:

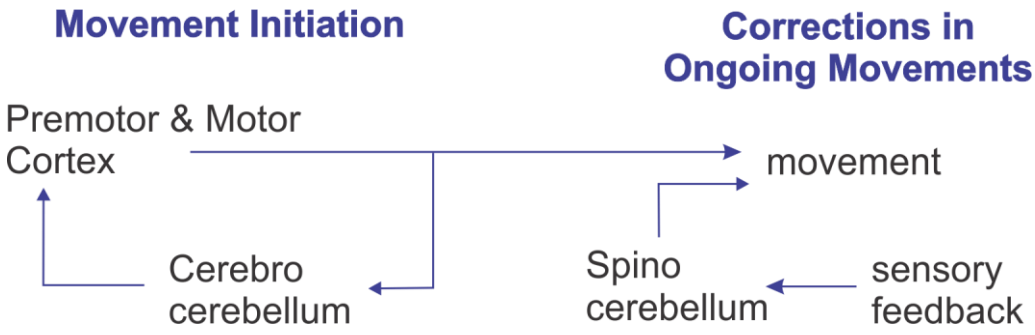
1) delayed initiation of movement. Also slower initiation of movement because agonist muscle activity is less phasic.
2) dysmetria: movement overshoots (or undershoots) target.
3) intention tremor: occurs after a movement to a target location or when perturbed from holding a particular position.



Tremor is not present at rest i.e. when not attempting movement or when not attempting to hold a limb in a particular position.

Tremor is produced by a series of over-responses of the long loop reflex through the motor cortex.

Overall Function: Motor Set- adjusts reflexes so that they are appropriate to the task. Example: Lift a box. Your initial lift is adjusted to the expected weight of the box by the cerebro cerebellum. The skill required to complete the lift is added by the spino cerebellum.



The cerebellar role in motor learning

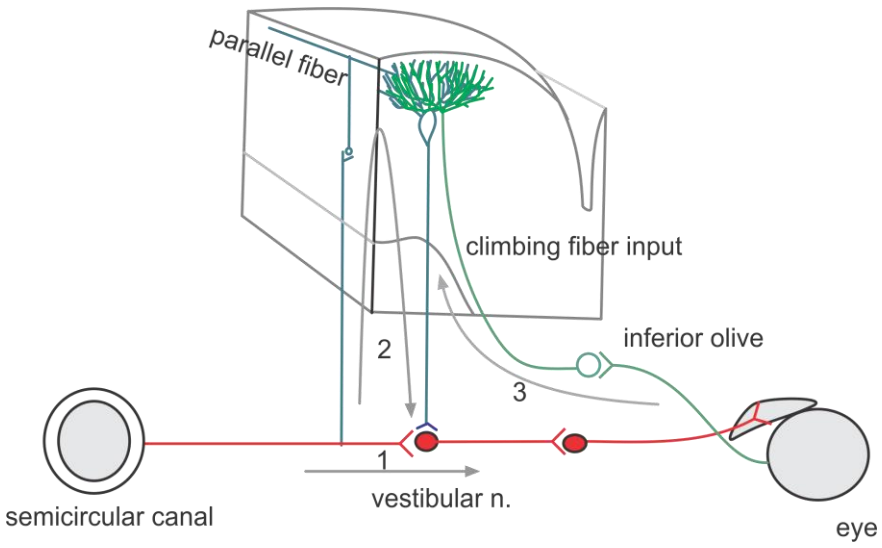
Example 1: Adjustment of the VOR

When the head turns, the vestibulo ocular reflex rotates the eye by an equal amount in the opposite direction and thus keeps the image still on the retina.

This is achieved by:

1) a direct pathway from the canals that contract the appropriate eye muscles, and

2) an indirect pathway through parallel fibers and Purkinje cells which provides ongoing corrections



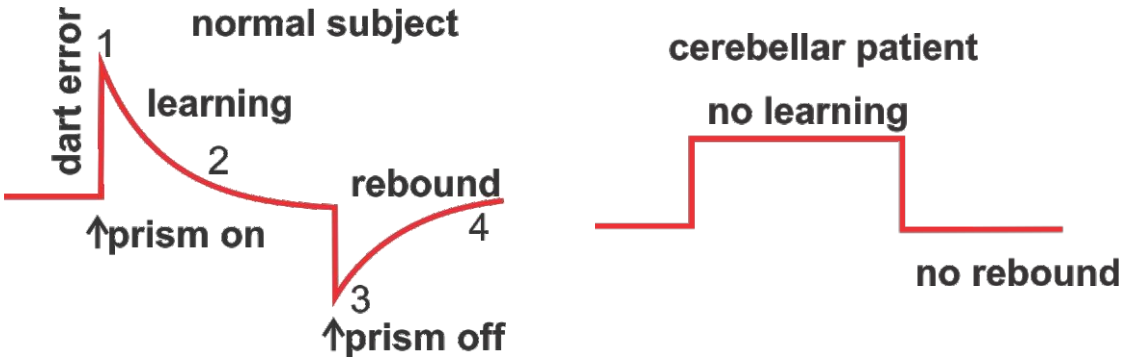
3) When VOR is not working properly (i.e. the eye is not rotating enough) a slip of the image is sensed by the eye and sent to the cerebellum via the inferior olive climbing fiber input.

Climbing fibers input semi-permanently alter the synapses of concurrently activated parallel fibers. When the VOR is restored to normal (i.e. no slip of the image on retina) climbing fiber activity stops. Thus climbing fibers instruct the action of parallel fibers (motor learning or adaptation).

Example 2: Prisms in front of your eyes alter where things appear to be

1) When you throw a series of darts with prisms, the dart board appears displaced to one side and you miss.
2) Gradually your cerebellum helps you correct for this.
3) When you take the prisms off, you again miss the dartboard but in the opposite direction.
4) Your cerebellum again corrects this.
Without the cerebellum, the error persists and there is no rebound when the prisms are removed.

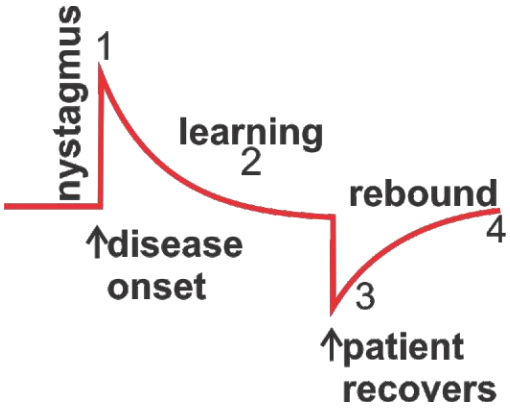
Glasses have similar effect to prisms. The VOR is recalibrated whenever new lenses are prescribed.



Example 3: Changes in the VOR when the canal properties are affected

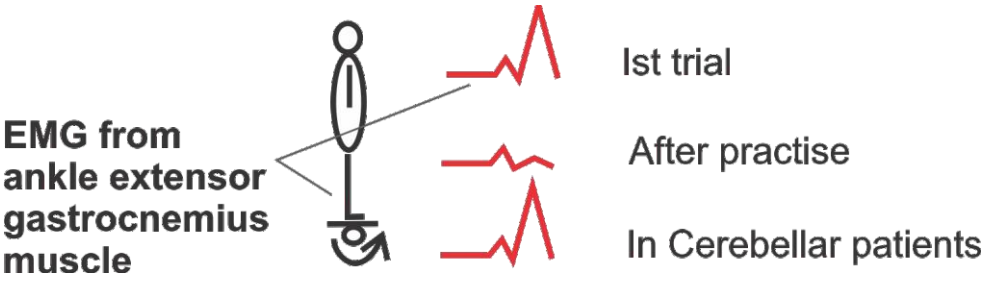
In Meniere's disease, the vestibular afferents are affected but often only temporally.

1) At the onset of this disease, an imbalance in the VOR generates a nystagmus.
2) Over a few days, the nystagmus subsides because the cerebellum rebalances the VOR.
3) When the patient gets well, the nystagmus again reappears because the cerebellum had adjusted the balance.
4) This nystagmus disappears as the cerebellum restores the balance.



Example 4: Learning new postural reflexes

Imagine learning to balance yourself on a platform placed on top of a ball.



Normally when standing on a solid floor, a stretch of the extensor means that you are leaning forward too far and the correct reflex response is to contract the extensor.

When on this platform, this same reflex causes you to fall.

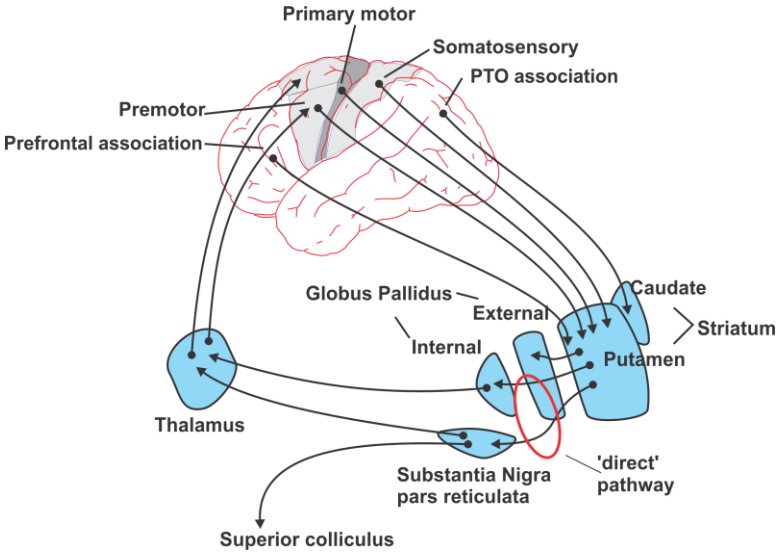
You must learn to relax the extensor when the platform stretches it. Gradually the cerebellum learns to suppress this reflex contraction.

No learning occurs if the cerebellum is damaged.

Summary

- The cerebellum acts like a repair shop.
- It learns to adapt the motor systems to new tasks, i.e. to learn new motor skills.
- Motor disorders produced by lesions outside the cerebellum are quickly masked by this repair shop.
- Cerebellar lesions produce motor disorders because the repair shop is damaged and old disorders are unmasked.
- Deficits persist if they exceed the capacity of the repair shop, e.g. one cannot compensate for a totally paralyzed muscle.

The circuit of the basal ganglia

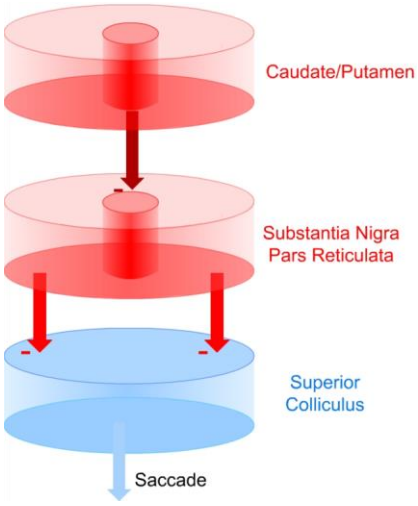


The basal ganglia are part of a loop that begins and ends in the cerebral cortex. The cerebral cortex (motor, somatosensory and association areas) projects to striatum (caudate and putamen) then to globus pallidus and substantia nigra then to thalamus, and finally back to prefrontal association, premotor and motor cortex, the regions involved in selecting movements and behaviours.

The overall function of this loop is to select a particular movement or sequence of movements, or behaviours, while suppressing others, (vs. that of the cerebellum: to add skill to each movement).

For eye movements the substantia nigra tonically suppresses the superior colliculus. This inhibition prevents distracting visual input from triggering unwanted saccadic eye movements. When a saccade is desired, the caudate/putamen inhibits a region of the substantia nigra. This removes the brakes from a region of the superior colliculus, releasing the selected saccade.

The basal ganglia play a similar role in movement generation. The basal ganglia normally exert a constant inhibitory influence on thalamic regions that excite the premotor and motor cortex, preventing them from becoming active at inappropriate times. To initiate a movement, the basal ganglia remove the brakes from a region of the thalamus releasing selected movements and behaviours from the cortex. Dopamine facilitates this release of inhibition.

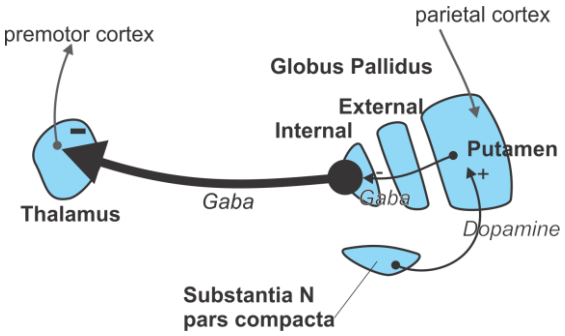


A fine balance must be maintained between suppression of all movements and the release of inappropriate movements. The correct balance is maintained by **the substantia nigra pars compacta**. It provides a excitatory (D1 dopamine) input to the putamen.

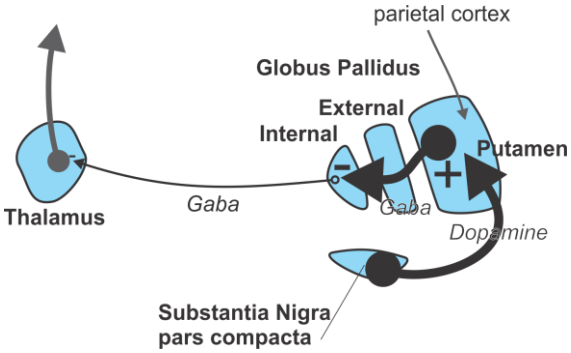
Parkinson's patients

These patients have difficulty initiating movement because of degeneration of the dopaminergic projection from substantia nigra pars compacta.

Under-activity in direct pathway produces too much inhibition of thalamus and prevents the initiation of movements.



Parkinson's patients are treated with L- Dopa. With too much L-Dopa, excess activity occurs in the direct path which results in too little inhibition of thalamus and the generation of spontaneous movements (chorea) as in Huntington's disease.



Summary of motor deficits in cerebellar diseases and of the basal ganglia (Parkinson's)

Cerebellar disease	**Parkinson's disease**
1) Ataxia: Can initiate movements but they are not accurate a) slow to start b) dysmetria- errors in size and speed c) decomposition - joints do not act together	*1) Akinesia:* resistance when initiating voluntary movements. Need an external sensory trigger to initiate movement; e.g. use a visual trigger to initiate walking because cannot initiate movement from internal working memory (in frontal lobe) Bradykinesia: slow movements
2) Intention tremor: when trying to reach target no tremor at rest sway while standing	*2) Tremor at rest:* often less during a movement (starts in hands -"pill rolling")
3) Hypotonia	*3) Rigidity* (co-contraction of agonist and antagonist muscles)
4) Symptoms may improve with time	*4) Symptoms* usually get worse

Practice problems

1. In the cerebellar repair shop of the VOR (vestibular ocular reflex)

a) the VOR is modulated by excitatory input from Purkinje cells.
b) the mossy fiber input signals retinal slip.
c) the climbing fiber input from the inferior olive produces complex spikes in Purkinje cells.
d) the mossy fiber activity stops when normal VOR function is restored.
e) the adaptation occurs in the lateral cerebro cerebellum.

2. The motor deficits in cerebellar diseases include

a) rigidity.
b) dysmetric movements.
c) a tremor which is most prominent when at rest.
d) symptoms which usually get worse.
e) the need of external sensory trigger to initiate movements.

Answers

1. c)
2. b)

See also: http://www.tutis.ca/NeuroMD/L6CerBG/CerBGProb.swf