**The University of Connecticut Schools of Medicine and Dental Medicine**
**Systems Neuroscience,**
**Meds 371**
**MOTOR CONTROL - CEREBELLUM**

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Reading: Purves 2004, Neuroscience, Chapter 18
Kandel et al 2000, Principles of Neuroscience, Chapter 42

GOALS

The cerebellum is a motor control structure responsible for coordination of multijoint movements. It influences the activity of alpha and gamma motor neurons indirectly by communication with the descending motor pathways. The cerebellum helps to maintain equilibrium and coordinate somatic muscle actions for both voluntary and involuntary movements. The cerebellum makes a special contribution to the synergy (synchronization) of muscle action, creating smooth movements from a series of individual muscle contractions. Loss of the cerebellum produces ataxia and uncoordinated movements.

## GROSS ANATOMY OF THE CEREBELLUM

- *Cerebellar cortex* contains 3 lobes: Anterior lobe, posterior lobe, and flocculonodular lobes. These lobes are also divided into medial-to-lateral functional divisions.
- *Deep cerebellar nuclei are the medial (fastigial nucleus in human); interposed, (globosus and emboliformis); and lateral (dentate nucleus in human).*
- *The vestibular nuclei should be treated as a part of the cerebellar complex. They act as outputs for cerebellar cortex as well as inputs.*
- *Cerebellar peduncles carry fibers to and from the cerebellum: Inferior (Restiform body); Middle (Brachium pontis); and Superior (Brachium conjunctivum).*

**SYNOPSIS OF THE BASIC CIRCUIT OF THE CEREBELLUM** (Fig. 1)

**Inputs** to the cerebellum come from brainstem nuclei and terminate in cerebellar cortex and deep nuclei. **Cerebellar cortex** projects to the deep nuclei and **inhibits** the action of the **deep nuclei**.

**Outputs of the cerebellum come from the deep nuclei.** Deep nuclei project to the targets of the cerebellum, that is the corticospinal tract, rubrospinal tract, reticulospinal tracts, and vestibulospinal tracts.

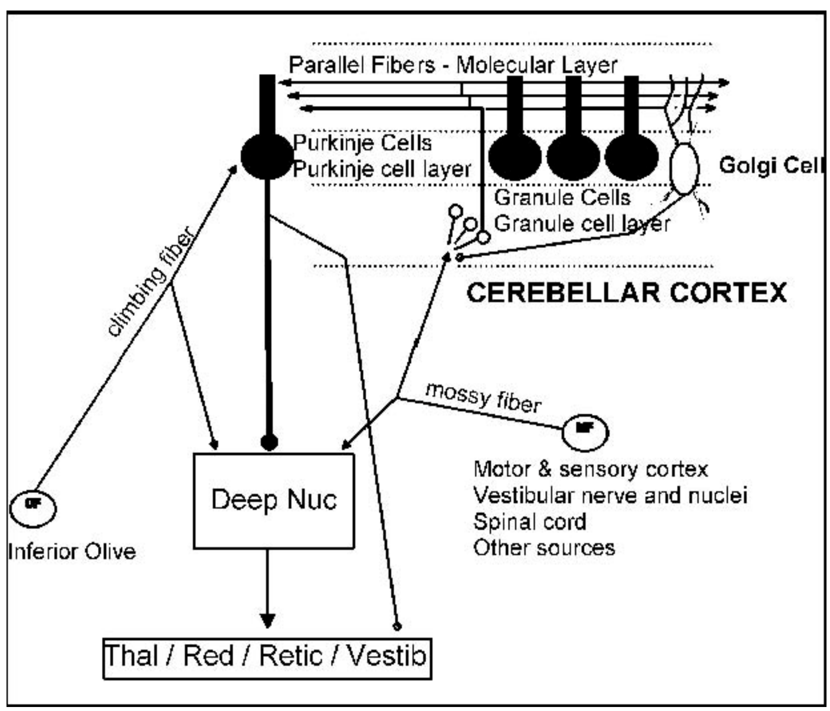


Figure 1

## CELLULAR AND FUNCTIONAL ORGANIZATION OF THE CEREBELLAR CORTEX

**Layers of Cerebellar Cortex**

Cerebellar cortex is composed of three layers.

1. Molecular layer
2. Purkinje cell layer
3. Granule cell layer

**The Purkinje Cell is the main projection neuron of the cerebellar cortex.** Purkinje cells project to the deep cerebellar nuclei where they makes GABAergic inhibitory synapses.

**Inputs to the Purkinje cell:**

**Climbing fibers** come from cell bodies in the **inferior olive** (Fig. 1). These make excitatory, glutamatergic synapses on Purkinje cells and basket cells. A single climbing fiber synapses many times on the same Purkinje cell. Stimulation of climbing fibers produces a powerful excitation of the Purkinje cells, the complex spike, which results in a burst of multiple action potentials.

**Synopsis of Olivo-Cerebellar, climbing fiber Pathway**

1. Origin – Inferior olive
2. Course –inferior cerebellar peduncle (Restiform body)
3. Laterality – Crossed Topographical Organization - Yes
4. Destination – Cerebellar cortex and deep nuclei.

**Mossy fiber--parallel fibers input to Purkinje cell** (Fig. 1). All other inputs to the cerebellar cortex come from mossy fibers. Stimulation of mossy fibers activates the granule cells whose axons make the parallel fibers of the cerebellar cortex and synapse on the Purkinje cells. Many Purkinje cells along a single folia are linked together by excitation from the same group of parallel fibers (the axons of the granule cells). This large number of Purkinje cells, yoked together, will represent adjacent muscles and adjacent joints in the somatotopic representation of the body. The linkage of the parallel fiber provides coordination that can influence the actions at multiple adjacent joints and body parts. Stimulation of mossy fibers also activates the deep cerebellar nuclei.

**Synopsis of mossy fiber pathways**

1. Origin – All other cerebellar inputs including spinal cord, reticular formation, pontine nucleus.
2. Course – all cerebellar peduncles
3. Laterality – Mixed
4. Topographical Organization - Yes
5. Destination – mossy fibers terminate on granule cells of the cerebellar cortex and in the deep nuclei. Axons of granule cells (parallel fibers) then synapse on Purkinje cells.

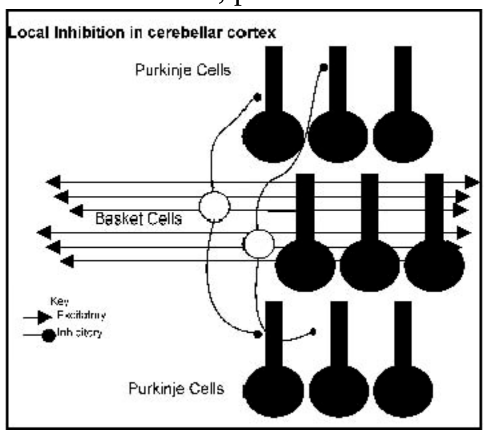

Figure 2

**Intrinsic cells**

Four cell types have their axons restricted to the cerebellar cortex and are responsible for much of the local processing in the cerebellar cortex. The granule cell is the smallest and most numerous neuron type in the cerebellar cortex (Fig. 2). Axons from granule cells are the parallel fibers in the molecular layer that synapse on the Purkinje, Golgi, Basket, and Stellate neurons. The Golgi cell (Fig. 1) is a larger inhibitory intrinsic cell in cerebellar cortex with dendrites in both the granule cell layer and in the molecular layer. It makes feed-back inhibitory projections (GABA) to granule cells. The Basket and Stellate cells (Fig. 2) are in the molecular layer. They provide feed-forward GABAergic inhibition of the Purkinje cell.

**PREVIOUSLY LEARNED AND NEWLY LEARNED COORDINATED MOVEMENTS IN THE CEREBELLUM**

Cerebellum influences **multi-joint** movements the most. It is needed to link together different muscle groups, smooth out, and coordinate their contractions. The action of the cerebellar cortex on the deep nucleus is to modulate/modify the firing rate of the deep nucleus.

During a **normal movement** that is already learned (Fig. 3):

1. Purkinje cell activity is driven by mossy fiber/parallel fiber inputs. Simple spikes.
2. Many Purkinje cells are activated together because of the parallel fibers that link different parts of the cerebellar cortex.
3. Purkinje cell activity inhibits the deep nuclei. GABA synapses.
4. Deep nuclei are always firing. They receive excitatory inputs from all mossy fiber and climbing fiber inputs.
5. When Purkinje cells fire, the firing rate of the deep nucleus cell DECREASES. Conversely, if Purkinje cells DO NOT fire, the firing rate of the deep nucleus cell INCREASES.

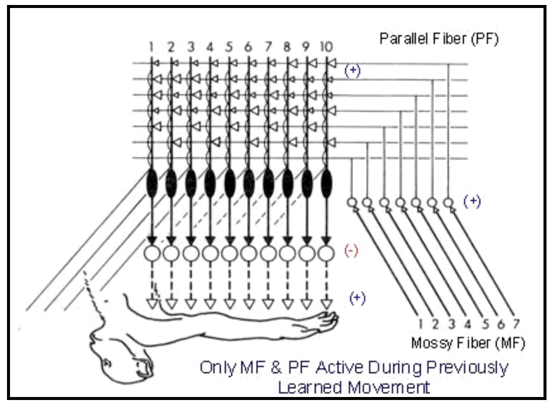

Figure 3

During a **new movement** or when a existing motor program needs to be adjusted (Fig. 4):
(example: more strength is needed because there is greater resistance than expected.)

1. Both CF and MF/PF Systems are Active  Climbing fibers are activated. Complex spikes. Mossy fiber/parallel fiber inputs must be activated AT THE SAME TIME as the climbing fibers.
2. Learning occurs because synapses are modified. **Long Term Depression** (LTD).
3. During LTD, the strength of the synapse is decreased.
4. The Purkinje cell fires less after LTD.
5. Because the Purkinje cell fires less after LTD, it inhibits the deep cerebellar nuclei less.
6. Because the deep cerebellar nucleus is inhibited less, its firing rate increases. The makes the excitation from the cerebellum on the CNS target greater.

## THE THREE FUNCTIONAL DIVISIONS OF CEREBELLUM

Functional subdivisions are ***defined by the afferent connections*** to the cerebellum.

1. Vestibulocerebellum: Flocculonodular lobe. Defined by inputs from vestibular ganglia and nuclei.
2. Spinocerebellum: Anterior lobe and medial part of posterior lobe called the vermis and paravermal cortex. Inputs from spinal cord.
3. Cerebrocerebellum: Lateral part of posterior lobe. Inputs from the cerebral cortex via the pons.

## VESTIBULOCEREBELLUM

***The flocculonodular syndrome*** represents a lesion of the ***vestibular cerebellum.*** The lesion is in the flocculonodular lobe or uvula. Thus the inputs to superior, medial, and inferior vestibular nuclei are lost. The patient has difficulty maintaining equilibrium and normal posture. The cerebellum influences the vestibular system and the ***vestibulospinal tracts*** with direct inputs to the vestibular nuclei. These systems help the body and eyes adjust to changes in balance, posture, and acceleration, especially through the axial muscles. Outputs of the cerebellum to the vestibular nuclei are unusual in that there are two antagonistic outputs, an excitatory one from the deep cerebellar (fastigial) nucleus, and an inhibitory one (GABA) from Purkinje cells. Some regard the vestibular nuclei as deep cerebellar nuclei because the receive this direct Purkinje cell input.

### Input to the vestibulocerebellum: The Vestibulo-Cerebellar Pathway

1 Origin – Vestibular ganglia AND vestibular nuclei; **8th nerve** (Fig. Course – 8th nerve, fastigio-bulbar tract.

2 Laterality – Ipsilateral

3 Topographical Organization - NA

4 Destination – Mossy fiber inputs to flocculonodular lobe of cerebellar cortex and deep nuclei.

### Output from Vestibulo-cerebellum (Fig. 4)

1. Origins -
   a. Fastigial nucleus (makes excitatory synapses)
   b. Purkinje cells of flocculonodular lobe, vermis (makes GABAergic synapses)
2. Course – fastigio-bulbar tract that is medial to the middle and inferior cerebellar peduncles in the deep white matter
3. Laterality – ipsilateral
4. Topographical Organization - Yes
5. Destination – Lateral vestibular nucleus

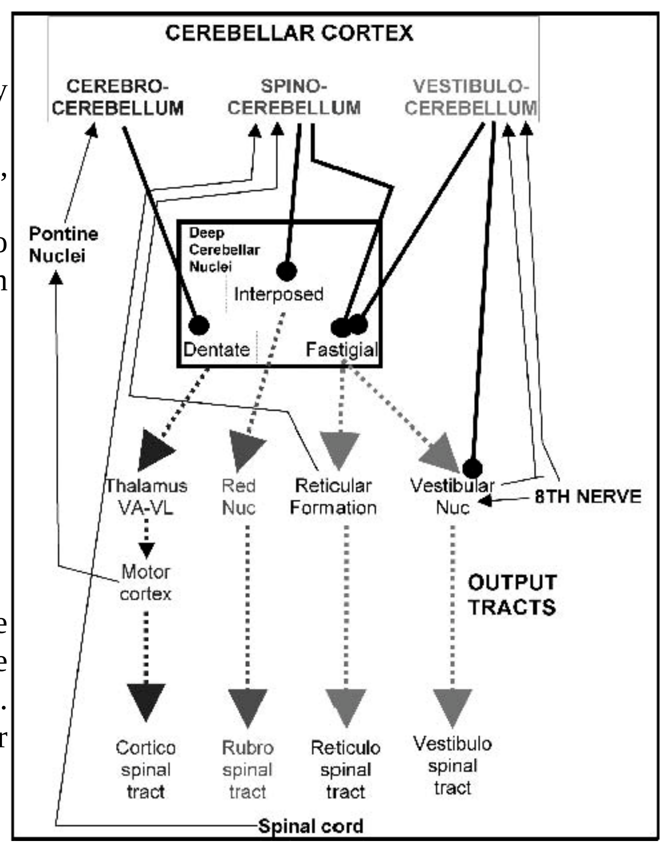

Figure 4

## SPINOCEREBELLUM

-- the vermis, paravermis, and anterior lobe

***The anterior lobe syndrome*** represents the loss of the spinocerebellum. Lesions seen in the anterior lobe (often alcohol related) and vermis of posterior lobe. There is an increase of postural reflexes, extensor rigidity (hypertonia), and locomotion is altered. Symptoms are somatotopically organized. As in the flocculonodular syndrome, there is a loss of direct inhibition of cerebellar Purkinje cells to the lateral vestibular nucleus. Spinal cord inputs and cerebellar outputs to reticular formation and red nuclei are lost and these losses disrupt posture and the coordination of proximal limb muscles.

**Spinal cord inputs define the spinal cerebellum**
Spinocerebellar afferents are the major contributors to a somatotopic organization in the cerebellar cortex. However, the body is represented on the surface of the cerebellar cortex by more than one somatotopic map. Spinal cord inputs provide SENSORY FEEDBACK INFORMATION from the spinal cord during a movement.

*Trigeminal inputs* to cerebellum also carry somatosensory information about the head. They come from the spinal trigeminal nucleus. Somatosensory afferents also come from the reticular formation.
Outputs of the spinocerebellum are either descending or ascending and influence somewhat different functions.

**INPUT: Spinocerebellar and Cuneocerebellar Tracts** (Fig. 4)
1. Origin –
a. Dorsal Spinocerebellar - Clarke's nucleus of thoracic spinal cord
b. Ventral Spinocerebellar – interneurons in layers V-VII of lumbar cord (L3-L6)
c. Cuneocerebellar - lateral (accessory) cuneate nucleus
d. Trigeminocerebellar - spinal trigeminal nucleus

2. Course – lateral white matter of spinal cord; lateral medulla via inferior cerebellar peduncle (ventral in superior penducle)
3. Laterality – uncrossed
4. Topographical Organization - yes; dorsal and ventral spinocerebellar tract for lower limb; cuneocerebellar for upper limb.
5. Destination – Mossy fiber inputs to vermis and paravermis of cerebellar cortex and deep nuclei.

*Descending projections* influence the RETICULOSPINAL TRACT. This system is important for the maintenance of posture and general muscle tone, especially as it relates to axial, extensor muscles and gamma motor neurons. Important for ongoing execution of movement.

**OUTPUT: Descending Fastigio-Reticular (bulbar) Pathway** (Fig. 4)
1. Origin – Fastigial deep cerebellar nucleus
2. Course – Fastigiobular tract
3. Laterality – Contralateral
4. Topographical Organization - yes
5. Destination – Reticular formation of the pons and medulla, origin of the RETICULOSPINAL tract.

*Ascending projections* from the spinocerebellum control of the proximal limbs via RUBROSPINAL TRACT. Minor projections are also found to the ventrolateral (VL) and ventro-anterior (VA) nuclei of thalamus. Functionally, the output to the red nucleus is important it relates to the cortico-rubrospinal tract.

**OUTPUT: Ascending Interposed-Red Nucleus Pathway** (Fig. 4)
1. Origin – Interposed deep cerebellar nuclei
2. Course – Brachium conjunctivum (superior cerebellar peduncle)
3. Laterality – Contralateral
4. Topographical Organization - yes
5. Destination – Red Nucleus, origin of the RUBROSPINAL TRACT

**CEREBROCEREBELLUM - NEOCORTEX - INPUTS**
***The neocerebellar syndrome*** represents a loss of the cerebrocerebellum. Lesions of cerebellar hemispheres, posterior lobe, and especially the dentate nucleus produce this syndrome. Symptoms are hypotonia, ataxia (awkwardness), tremor (intention), and disruption of skillful volitional movements. There is no somatotopic organization of the symptoms. This type of lesion impairs the cerebellar modulation of motor cortex activity. Lack of excitatory inputs to thalamus (VA-VL) from the dentate nucleus decreases excitability of alpha/gamma systems controlled by corticospinal pathway.

**Pontine inputs to the cerebellum define the cerebrocerebellum.** They provide MOTOR AND SENSORY information since the afferents to the pontine nuclei are primarily from the neocortex. Projections from motor and premotor cortex send an EFFERENT COPY of the motor program. Information goes to cerebellum from motor cortex before, during, and after a movement. Projections from parietal, temporal, and occipital lobes provide SENSORY INFORMATION to the cerebellum.

**INPUT: Ponto-Cerebellar Pathway** (Fig. 4)
1. Origin – the pontine nuclei.
2. Course – middle cerebellar peduncle (brachium pontis)
3. Laterality – Contralateral
4. Topographical Organization - Yes
5. Destination – Terminate in lateral lobe of cerebellar cortex as mossy fibers and deep nuclei.

**Outputs of cerebrocerebellum** influence the action of the motor cortex. The dentate nucleus projects to the frontal lobes, including motor cortex, via a synapse in the thalamus (VA,VL). For voluntary movement, the cerebrocerebellum will influence the CORTICOSPINAL TRACT that emerges from the motor cortex of the precentral gyrus. Functionally, this output of the cerebellum is directly concerned with the initiation, planning, and timing of voluntary movement. It is involved in the comparison of sensory activity with the intended motor program.

**OUTPUT: Dentato-Thalamic Pathway** (Fig. 4)
1. Origin – Dentate deep cerebellar nucleus.
2. Course – superior cerebellar peduncle (brachium conjunctivum)
3. Laterality – Contralateral
4. Topographical Organization - Yes
5. Destination – VA, VL nuclei of dorsal thalamus, diencephalon.