# MODULE 6: CEREBELLUM AND BASAL GANGLIA

This module will summarize the important neuroanatomical and key clinical concepts from Chapters 15 and 16 of the textbook for the course. The first part of this module will review the gross anatomy of the cerebellum, viz., the cerebellar lobes, peduncles, and deep nuclei, the microscopic circuitry of the cerebellum, cerebellar output and input pathways, and the vascular supply to the cerebellum.

The second part of this module will summarize the basic anatomy of the basal ganglia, input, output, and intrinsic connections of the basal ganglia, and the four parallel basal ganglia pathways for movement, eye movement, cognition, and emotion.

THE CEREBELLUM

Cerebellar lobes, peduncles, and deep nuclei. The cerebellum is the largest structure in the posterior fossa. It is attached to the dorsal portion of the brainstem (pons and medulla) by three white matter peduncles (feet) and forms the roof of the fourth ventricle. The cerebellum consists of the midline ***vermis***, the ***intermediate part of the cerebellar hemisphere***, and the ***lateral part of the cerebellar hemisphere*** (see figure below).
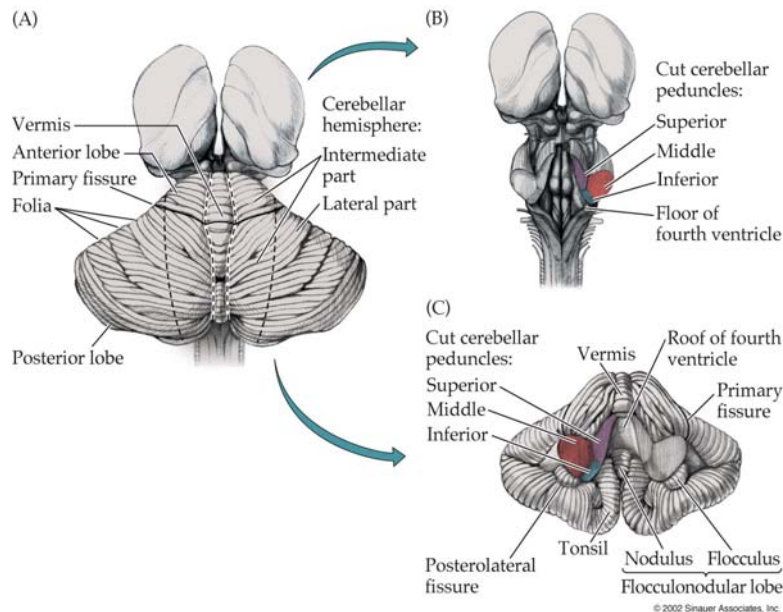
The cerebellum is attached to the brainstem by the ***superior, middle, and inferior cerebellar peduncles***, which contain the input and output fibers of the cerebellum.

All outputs of the cerebellum are carried by the deep cerebellar nuclei and the vestibular nuclei. The cerebellar cortex and deep nuclei can be divided into three functional zones:

A. The **_vermis_** (via **_fastigial nuclei_**) and **_flocculonodular lobes_** (via **_vestibular nuclei_**) are important for control of proximal and trunk muscles and in vestibulo-ocular control, respectively.

B. The **_intermediate part_** of the cerebellar hemisphere (via **_interposed nuclei_**) is involved in control of more distal muscles in the arms and legs.

C. The largest part of the cerebellum is the **_lateral part_** of the cerebellar hemisphere (via **_dentate nuclei_**), which is involved in planning the motor program for the extremities.

These anatomical structures and functions are summarized in the table below (and in your book) along with the motor pathway by which these functions are carried out.

TABLE 15.1 Functional Regions of the Cerebellum		
REGION	**FUNCTIONS**	**MOTOR PATHWAYS INFLUENCED**
Lateral hemispheres	Motor planning for extremities	Lateral corticospinal tract
Intermediate hemispheres	Distal limb coordination	Lateral corticospinal tract, rubrospinal tract
Vermis and flocculonodular lobe	Proximal limb and trunk coordination	Anterior corticospinal tract, reticulospinal tract, vestibulospinal tract, tectospinal tract
	Balance and vestibulo-ocular reflexes	Medial longitudinal fasciculus

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Microscopic circuitry of cerebellum.

The microscopic circuitry of the cerebellum involves excitatory inputs carried by **_mossy fibers_** and **_climbing fibers_**. These inputs synapse directly or indirectly onto **_Purkinje cells_**, which carry the outputs to the deep cerebellar nuclei and vestibular nuclei. Important local cerebellar neurons include **_granule cells_** and the inhibitory **_Golgi, basket, and stellate cells_**.
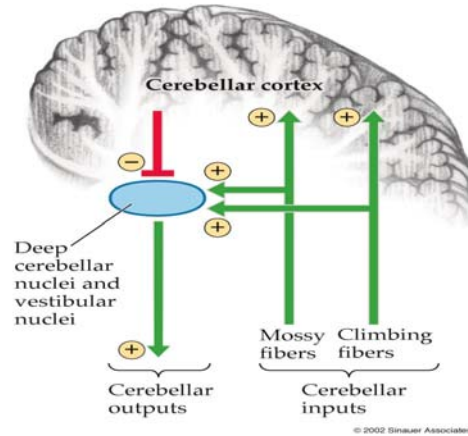
A simple way to remember the excitatory and inhibitory connections of the cerebellar cortex is to recall that all axons projecting ***upward*** are ***excitatory*** (mossy fibers, climbing fibers, granule cell parallel fibers), while all axons projecting ***downward*** are ***inhibitory*** (Purkinje cells, stellate cells, basket cells, Golgi cells). The ***outputs of the deep cerebellar nuclei***, which are not part of the cerebellar cortex, are ***excitatory***.

       Cerebellar input and output pathways. The details of the cerebellar inputs and outputs are complex, and the reader is thus referred to the discussion of these pathways on pages 660-667 in your textbook. The main cerebellar output pathways are summarized in Table 15.2 below.

TABLE 15.2 Main Cerebellar Output Pathways

REGION	DEEP NUCLEI	CEREBELLAR PEDUNCLE	MAIN OUTPUT TARGETS OR EQUIVALENT
Lateral hemispheres	Dentate nucleus	Superior cerebellar peduncle	Ventrolateral nucleus of thalamus (VL), parvocellular red nucleus
Intermediate hemispheres	Interposed nuclei	Superior cerebellar peduncle	VL, magnocellular red nucleus
Vermis	Fastigial nuclei	Uncinate fasciculus[a]	VL, tectum
		Juxtarestiform body[b]	Reticular formation, vestibular nuclei
Inferior vermis and flocculonodular lobe	Vestibular nuclei and fastigial nuclei	Juxtarestiform body[b]	Medial longitudinal fasciculus (eye movement pathways)

[a]The uncinate fasiculus travels with the superior cerebellar peduncle.
[b]The juxtarestiform body travels with the inferior cerebellar peduncle.

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The most clinically important points are that these pathways:
     A. follow a medial to lateral organization
     B. to the lateral motor systems are either ipsilateral or double crossed so that cerebellar lesions cause ipsilateral deficits.

The main cerebellar input pathways are summarized in Table 15.3 below.

TABLE 15.3 Main Cerebellar Input Pathways

INPUT PATHWAY	MAIN ORIGIN(S) OF INPUT	CELLS PROJECTING TO CEREBELLUM	CEREBELLAR PEDUNCLE OR EQUIVALENT
Pontocerebellar fibers	Cortex	Pontine nuclei	Middle cerebellar peduncle
Spinocerebellar pathways			
Dorsal spinocerebellar tract	Leg proprioceptors	Nucleus dorsalis of Clark	Inferior cerebellar peduncle
Cuneocerebellar tract	Arm proprioceptors	External cuneate nucleus	Inferior cerebellar peduncle
Ventral spinocerebellar tract	Leg interneurons	Spinal cord neurons	Superior cerebellar peduncle
Rostral spinocerebellar tract	Arm interneurons	Spinal cord neurons	Superior and inferior cerebellar peduncles
Climbing fibers	Red nucleus, cortex, brainstem, spinal cord	Inferior olivary nucleus	Inferior cerebellar peduncle
Vestibular inputs	Vestibular system	Vestibular ganglia, vestibular nuclei	Juxtarestiform body

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Vascular supply to the cerebellum. Blood supply to the cerebellum is provided by three branches of the vertebral and basilar arteries. They are:

    A. the posterior inferior cerebellar artery (PICA)
    B. the anterior inferior cerebellar artery (AICA)
    C. the superior cerebellar artery (SCA)

The vascular supply to cerebellar is depicted in the figure below on the ventral and dorsal views.

Vascular areas
Key
■ PICA territory
□ AICA territory
■ SCA territory
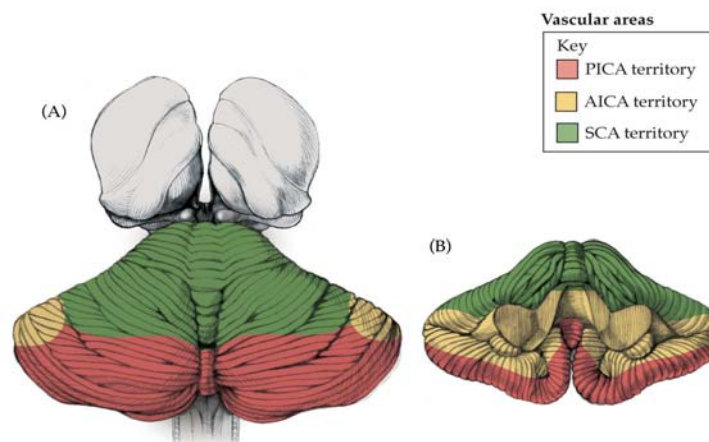
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KEY CLINICAL CONCEPTS – CEREBELLUM

The most common disorder following lesions of the cerebellum is *ataxia*, which is a type of irregular, uncoordinated movement. Because of the anatomical organization of cerebellar pathways, the following principles of localizing cerebellar lesions hold:

A. ***Ataxia is ipsilateral*** to the side of a cerebellar lesion.

B. Midline lesions of the cerebellar ***vermis*** or ***flocculonodular lobes*** cause mainly unsteady gait (***truncal ataxia***) and eye movement abnormalities.

C. Lesions of the ***intermediate*** part of the ***cerebellar hemisphere*** cause mainly ataxia of the ***limbs*** (***appendicular ataxia***). Appendicular ataxia is shown in (B) below.

(A)

(B)
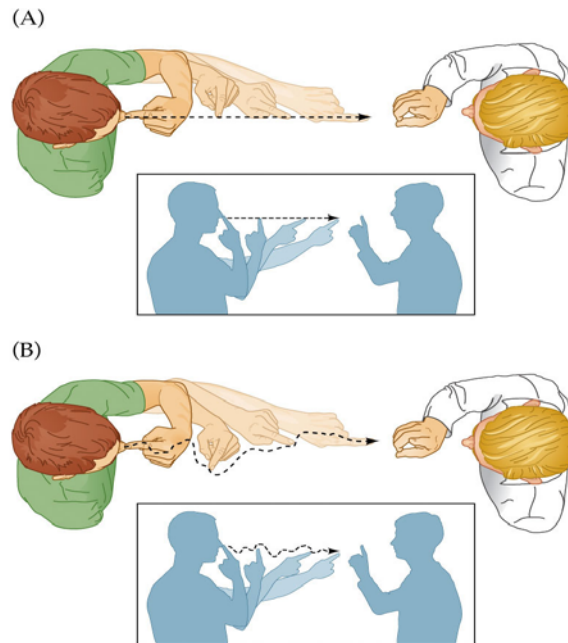
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D. Ataxia is often caused by ***lesions of cerebellar circuitry*** in the brainstem or other locations rather than in the cerebellum itself, which can lead to false localization.

E. Because of the strong reciprocal connection between the cerebellum and the vestibular system, cerebellar lesions are often associated with ***vertigo, nausea, vomiting, and nystagmus***.

 Cerebellar infarcts are more common in the PICA and SCA territories than in the AICA territory. Patients with cerebellar infarcts typically present with vertigo, nausea and vomiting, horizontal nystagmus, limb ataxia, unsteady gait, and headache, which can be occipital, frontal, or in the upper cervical region.
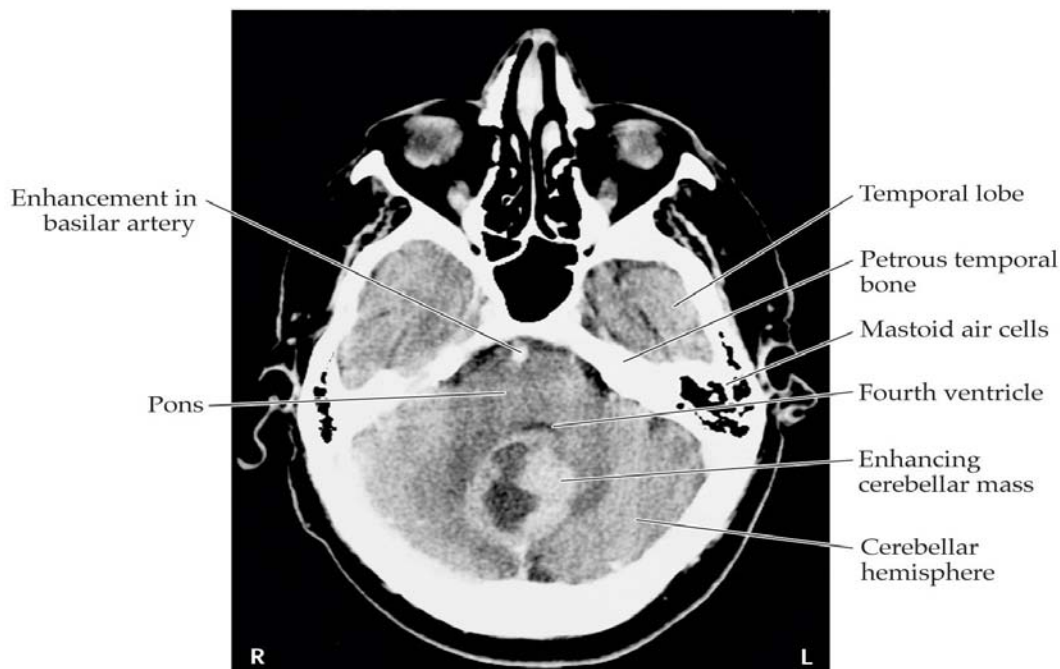
 Cerebellar hemorrhage like spontaneous hemorrhage in other brain regions can occur in the setting of chronic hypertension, arteriovenous malformation, hemorrhagic conversion of an ischemic infarct, metastases, or other causes. Patients usually present with headache, nausea, vomiting, ataxia, and nystagmus.

CLINICAL CASE - CEREBLLUM

Background. A 76 year-old man with a history of cigarette smoking developed progressive **_difficulty walking_** over the course of 1 month. He noticed that when he stood up he felt "whoozy" and described his gait as feeling like he was drunk, saying, "my legs go one way, and I go the other." Family reported he often lost his balance, with **_staggering and unsteadiness_**. He also had frequent mild **_headaches_** that occurred at any time of day or night and seemed to be getting worse.

Examination. Neurological and physical exams were unremarkable except for a **_wide-based, unsteady gait, tending to fall to the left, especially during tandem walking_**. Of note, there was no ataxia on finger-to-nose or heel-to-shin testing, and rapid alternating movements were normal. There was no history of alcohol intake.

Case formulation. The patient had truncal ataxia with NO appendicular ataxia. The symptom suggests the cause may be due to a lesion of the **_cerebellar vermis_**. Other possibilities for this gait disorder include hydrocephalus or a lesion of the frontal lobes. Given the history of cigarette smoking and gradual onset of symptoms, metastatic lung cancer to the vermis should be considered. Axial (transverse, horizontal) head CT scan with intravenous contrast was obtained and is shown below.

Enhancement in basilar artery

Pons

Temporal lobe

Petrous temporal bone

Mastoid air cells

Fourth ventricle

Enhancing cerebellar mass

Cerebellar hemisphere

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Head CT (above) shows an enhancing, cystic lesion visible in the midline cerebellar vermis which turned out to be a lung carcinoma metastasis.

BASAL GANGLIA

The basal ganglia participate in complex networks that influence the descending motor systems. Like the cerebellum, the basal ganglia do not themselves project directly to the spinal cord or periphery, but synapse on other nuclei that do. Patients with basal ganglia lesions can have either hyperkinetic or hypokinetic movement disorders.

Hyperkinetic movement disorders are exemplified by ***Huntington's disease*** in which uncontrolled involuntary movements produce a random pattern of jerks and twists. ***Hypokinetic movement disorders*** are typified by ***Parkinson's disease***, which is characterized by rigidity, slowness, and marked difficulty initiating movements.

Basal ganglia anatomy. The basal ganglia are a collection of gray matter nuclei located deep within the white matter of the cerebral hemispheres. The main components of the basal ganglia are the ***caudate nucleus, putamen, globus pallidus, subthalamic nucleus, and substantia nigra*** (see figure below).
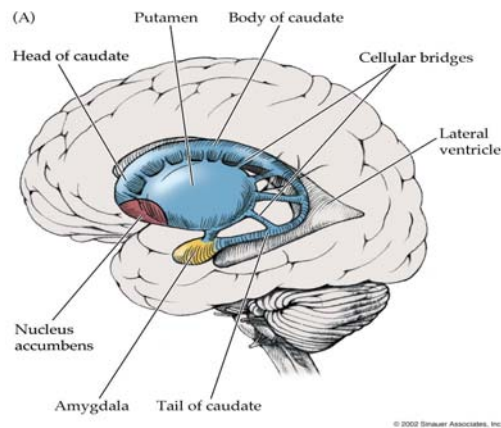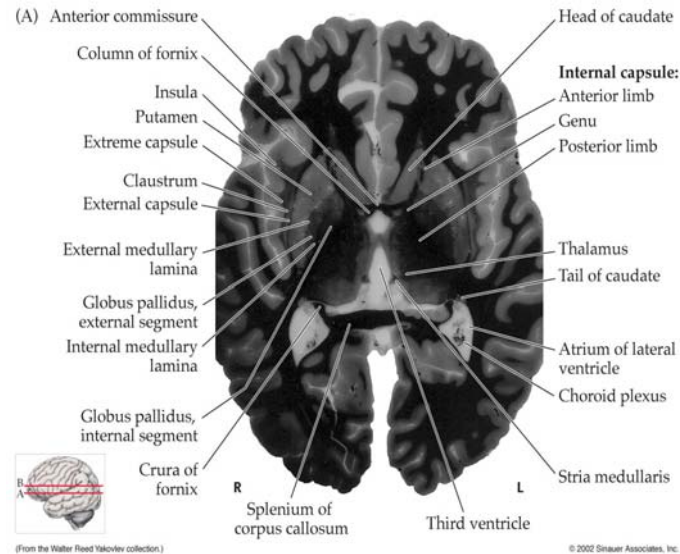

The striatum includes the caudate nucleus and the putamen, while the lentiform nucleus includes the putamen and globus pallidus (see Table 16.1 below).

TABLE 16.1   Basal Ganglia[a]

Striatum	Caudate	
	Putamen	Lenticular nucleus
	Globus pallidus	
	Subthalamic nucleus	
	Substantia nigra	

[a]The nucleus accumbens and ventral pallidum can also be considered part of the basal ganglia.

The relationships among the basal gangliar structures are best appreciated through examination of horizontal or coronal brain sections (see a horizontal section below).

(A) Anterior commissure
Column of fornix
Insula
Putamen
Extreme capsule
Claustrum
External capsule
External medullary lamina
Globus pallidus, external segment
Internal medullary lamina
Globus pallidus, internal segment
Crura of fornix
Splenium of corpus callosum

Head of caudate
Internal capsule:
Anterior limb
Genu
Posterior limb
Thalamus
Tail of caudate
Atrium of lateral ventricle
Choroid plexus
Stria medullaris
Third ventricle

R   L

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Note in the brain section above, the internal capsule forms a sideways V-shaped demarcation with the thalamus and caudate nucleus lying medial to the internal capsule and the lentiform nucleus lying lateral.

Input, output, and intrinsic connections of the basal ganglia.

All inputs, including inputs from motor and premotor **cortex**, other cortical regions, dopaminergic inputs from the **substantia nigra** (pars compacta part), and inputs from the **thalamic** intralaminar nuclei enter the basal ganglia circuitry **via the striatum**.

All outputs, including those to the thalamic ventral anterior **(VA)** and ventral lateral **(VL)** nuclei, other thalamic nuclei, brainstem **reticular formation**, and **tectum** leave **via the internal segment of the globus pallidus** and the **substantia nigra pars reticulata**.

The **intrinsic connections** of the basal ganglia may be divided into a **direct pathway** from the striatum to the output nuclei, and an **indirect pathway** that reaches the output nuclei via a detour through the subthalamic nuclei (see figures below for details of these connections).
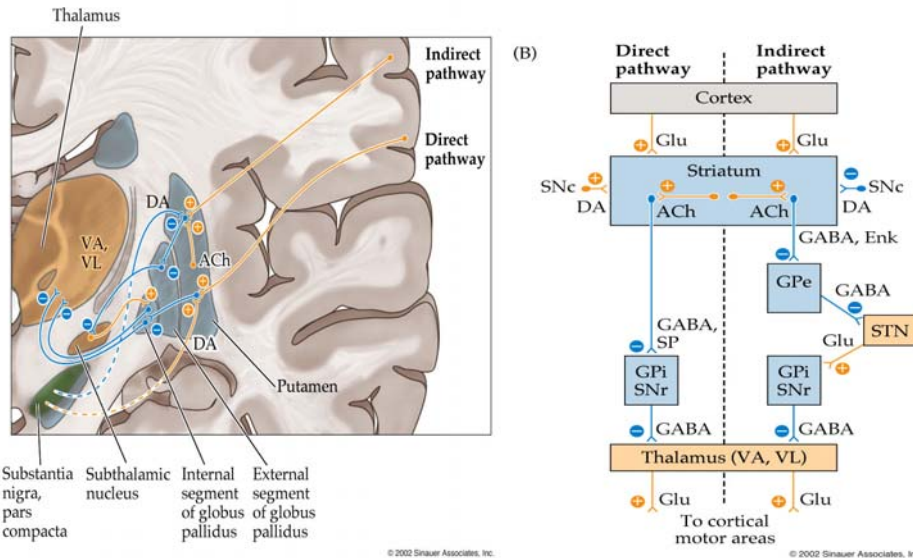
Figure above is Figure 16.7 (A) and (B) taken from page 700 of your textbook. Note on (A) the striatum is represented by the putamen only, although the caudate has the same connections as well. In (B) above, GPi = globus pallidus interna, GPe = globus pallidus externa, SNc = substantia nigra, pars compacta, STN = substantia nigra, VL = ventral lateral nucleus, VA = ventral anterior n.

      Parallel basal ganglia pathways for movement, eye movement, cognition, and emotion. Four parallel channels of information processing have been described.

      The best known is the motor channel (described in the section above). In the ***motor channel***, cortical inputs travel mainly to putamen, and outputs arise from the internal segment of the globus pallidus and substantia nigra pars compacta to reach the VA and VL nuclei of the thalamus. From the thalamus, the motor channel continues to the supplemental motor area (SMA), premotor cortex, and primary cortex.

      A separate ***oculomotor channel*** subserves regulation of eye movements. Input for this pathway is predominantly from the body of the caudate, and output is to the frontal eye fields and supplemental eye fields of the frontal lobes. The ***prefrontal channel*** is probably important for cognitive functions involving the frontal lobes. Input is from the caudate (primarily the head), and output reaches the prefrontal cortex.

      Finally, the ***limbic channel*** is an important pathway through the basal ganglia that is involved in limbic regulation of emotions and motivational drives. Inputs arise from ***limbic cortex***, hippocampus, and amygdala, and project to ***nucleus accumbens*** and other regions of the ventral striatum. Outputs arise from ***ventral pallidum*** to reach the ***dorsomedial*** nucleus and ***ventral anterior*** nuclei of ***thalamus***. Projections from these thalamic nuclei reach the limbic cortex of the anterior cingulated gyrus and medial orbital frontal gyri. The limbic channel is likely to play a central role in many neurobehavioral and psychiatric disorders.

KEY CLINICAL CONCEPTS – BASAL GANGLIA

An understanding of the neurotransmitters and intrinsic basal ganglia connections provides a framework for understanding the hyperkinetic and hypokinetic movement disorders. In ***hyperkinetic movement disorders***, such as Huntington's disease, the ***inhibitory output*** from the basal ganglia ***to*** the ***thalamus*** (and thus to cortex) is ***decreased***, leading to a relative ***disinhibition*** of the descending ***motor*** systems. The most common examples include lesions of the ***subthalmic nucleus*** (STN), such as stroke, causing ***hemiballismus*** (wild flinging movements of extremities contralateral to STN lesion), and loss of inhibitory GABAergic neurons from the striatal neurons of the indirect pathway in early ***Huntington's disease***.

In ***hypokinetic movement disorders***, the inhibitory output from the basal ganglia to thalamus is increased, resulting in a relative paucity of movements. Examples include degeneration of dopaminergic neurons in substantia nigra pars compacta that project to the striatum in ***Parkinson's disease***.

Movement disorders. The slow, clumsy, stiff movements and hyperreflexia resulting from corticospinal, upper motor neuron lesions is called ***spasticity***. Irregular, uncoordinated movements caused by lesions of the cerebellar circuitry are called ***ataxia***. Abnormal movements caused by basal ganglia dysfunction is often called ***dyskinesia***, meaning simply "abnormal movement." Basal ganglia dysfunction causing dyskinesia is often referred to as an ***extrapyramidal*** motor disorder because the extrapyramidal system was once mistakenly thought to be an independent pathway, running parallel to the pyramidal (corticospinal) tracts, traveling from the striatum to spinal cord.

The common abnormal movements are ranked below in the table by movement speed from slowest to fastest:

TABLE 16.3 Ranking of Common Movement Disorders by Movement Speed

Bradykinesia, hypokinesia	SLOW
Rigidity	
Dystonia	
Athetosis	
Chorea	
Ballismus	
Tics	
Myoclonus	FAST
Tremor	Slow or fast depending on type

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These common abnormal movement disorders are described below:

Bradykinesia = means "slowed movements"

Hypokinesia = means "decreased amount of movements"

Akinesia = means "absence of movement"

Rigidity = is increased resistance to passive movement of a limb

Dystonia = is an abnormal, often distorted position of the limbs, trunk, or face that is sustained.

Athetosis = is characterized by twisting movements of the limbs, face and trunk that sometimes merge with faster choreic movements.

Chorea = literally means "dance"; characterized by nearly continuous involuntary movements that have a jerky or constant varying quality.

Ballismus = movements of the proximal limb muscles with a large-amplitude rotatory or "flinging" quality.

Tics = a sudden brief action preceded by an urge to perform it and followed by a sense of relief.

Myoclonus = considered the faster of all movement disorders; a sudden rapid muscular jerk that can be focal, unilateral or bilateral.

**_Tremor_** = rhythmic or semirhythmic oscillating movements.

CLINICAL CASE – BASAL GANGLIA

Background. This patient is a 53 year-old right-handed man who was referred to the neurologist for progressive bradykinesia, tremor, rigidity, and unsteady gait. The patient was well until 10 years ago when he noticed some slowness and difficulty using his right arm. This gradually progressed, and 2 years later he developed occasional shaking of the right arm and leg. He was diagnosed with Parkinson's disease at that time and started on Simemet (levodopa plus carbidopa) which provided significant benefit at first. Later the tremor spread to involve his whole body, and he became progressively slower and stiffer, complaining that he often had difficulty initiating movements.

Neurological examination. Motor exam revealed **_4 Hertz tremor_** of the head and all extremities, worse on the right side and **_worse at rest_**, **_cogwheel rigidity_**, especially of the right arm, and finger tapping and rapid alternating movements slowed bilaterally.

There was no pronator drift, and power (strength) was 5/5 (normal) throughout. Mental status exam was normal except for ***micrographia***. Cranial nerve exam was normal except for ***masklike*** decreased ***facial expression*** and slightly hypophonic voice. Reflexes were normal except for failure to extinguish glabellar tap (positive Myerson's sign). He was unable to rise from a chair without assistance. ***Gait*** was ***slow and stiff***, with ***stooped posture***, short steps, and decreased arm swing. Sensory exam was normal.

    Case formulation. The patient had all the typical core features of idiopathic Parkinson's disease including bradykinesia, cogwheel rigidity, resting tremor, stooped gait with short steps, decreased arm swing, significant benefit from levodopa, and gradual progression over a period of years. Parkinson's disease is caused by loss of dopaminergic neurons in the substantia nigra pars compacta (depigmentation of the substantia nigra is shown in Figure 16.10 [A] taken from the textbook on page 713. [B] shows a Lewy body in SNpc).
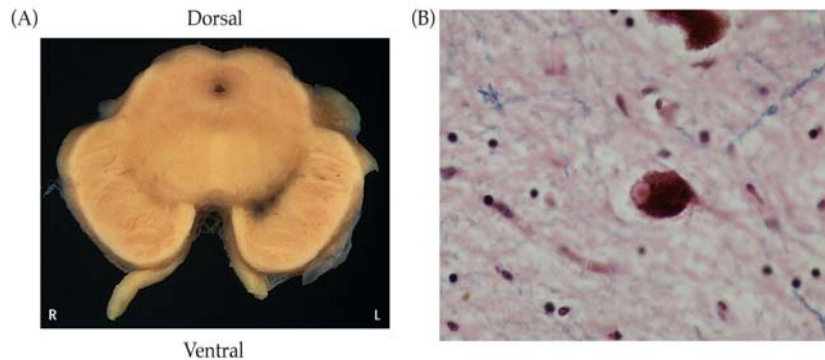
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