

DISORDERS OF THE MOTOR SYSTEM

Jeanette J. Norden, Ph.D.

Professor Emerita

Vanderbilt University School of Medicine

THE MOTOR SYSTEM

- To understand disorders of the motor system, we need to review how a *normal **voluntary** and **coordinated** motor movement is made*
- The Motor System is subdivided into 3 “subsystems”
 - **Pyramidal System**
 - **Extrapyramidal System**
 - **Cerebellum**

THE MOTOR SYSTEM

(Voluntary, Coordinated Movement)

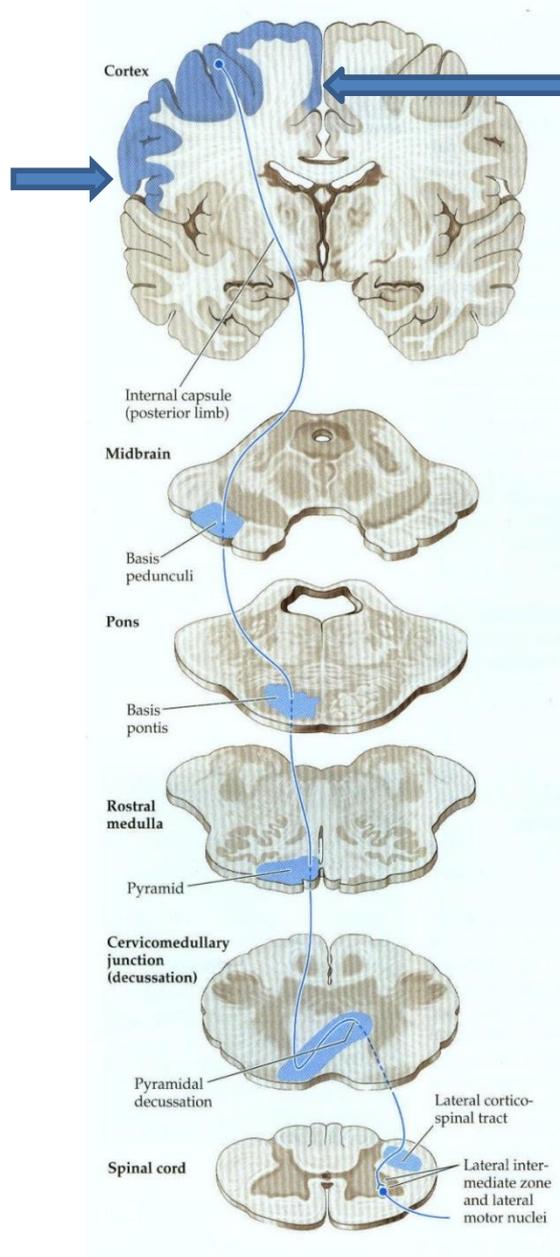
- **PYRAMIDAL SYSTEM (Cortico-Spinal pathways)**
 - **DIRECT Cortico-Spinal pathway: *Involved in the planning and initiation of a voluntary motor movement***
 - **INDIRECT Cortico-Spinal pathway: *Involved in the maintenance of appropriate tone to allow for the movement to be made***
 - ***Only* the Cortico-Spinal pathways (the Pyramidal System) projects to the spinal cord**

Pyramidal System

- Cell bodies of origin of the direct & indirect Cortico-Spinal pathways (together called **Upper Motor Neurons[UMNs]**) are found in **motor cortex or Area 4**, which contains a representation of the contralateral half of the body
- The axons of these neurons travel down through the brain, cross (decussate) in the lowest part of the medulla, and enter the spinal cord
- At appropriate levels, the axons will exit the pathway to synapse onto neurons (called **Lower Motor Neurons [LMNs]**) that will leave the spinal cord to innervate muscle

Direct Corticospinal Tract

The FACE is represented laterally in Motor Cortex



The LEG is represented medially in Motor Cortex

The indirect corticospinal tracts run along with the direct system; together they are called **Upper Motor Neurons**; upper motor neurons synapse onto **Lower Motor Neurons in the spinal cord**; axons of lower motor neurons innervate muscle

From Blumenfeld, 2010

Pyramidal System

- *Damage to the pyramidal system results in paresis [weakness] or paralysis; different “types” of paralysis are associated with UMN and LMN lesions*

Pyramidal System – Clinical Signs/Symptoms

CLINICAL SIGNS ASSOCIATED WITH MOTOR SYSTEM DAMAGE		
UPPER MOTOR NEURON (UMN)		LOWER MOTOR NEURON (LMN)
<p>Affects groups of muscles</p> <p>No atrophy (or only <i>disuse</i> atrophy over time)</p> <p>↑ muscle tone</p> <p>↑ deep tendon reflexes</p> <p>Babinski sign</p>		<p>Can affect single muscles</p> <p>Significant atrophy</p> <p>↓ muscle tone</p> <p>↓ deep tendon reflexes</p> <p>No Babinski sign</p>
<p>SPASTIC PARALYSIS/PARESIS WITH BABINSKI SIGN</p>		<p>FLACCID PARALYSIS/PARESIS</p>

Pyramidal System – Clinical Disorders

- **Polio**; caused by an enteric (gut) virus; example of a **LMN disorder**; illness can range from flu-like symptoms to paralytic polio (flaccid paralysis)
- **Amyotrophic lateral sclerosis** (ALS; also called motor neuron disease or Lou Gehrig's Disease); a neurodegenerative disease that involves **both UMNs and LMNs** (“spastic paralysis in a wasted limb”)
 - **Small % of individuals have a familial form of this disorder (5 - 10%); autosomal dominant in transmission**
 - **Most cases are “sporadic” – without known cause**

THE EXTRAPYRAMIDAL SYSTEM

- *Involved in motor “programs”, habitual behaviors, and in the **modulation of movement***
- *The extrapyramidal system does not project to the spinal cord*
- Exerts influence by modifying the output of the Pyramidal System (modifying firing of Motor Cortex neurons)
- *A lesion involving this system results in either too little (**hypo-kinetic**) movement or too much (**hyper-kinetic**) movement; later in the lecture, we will use Parkinson’s Disease as an example of an extrapyramidal disorder*

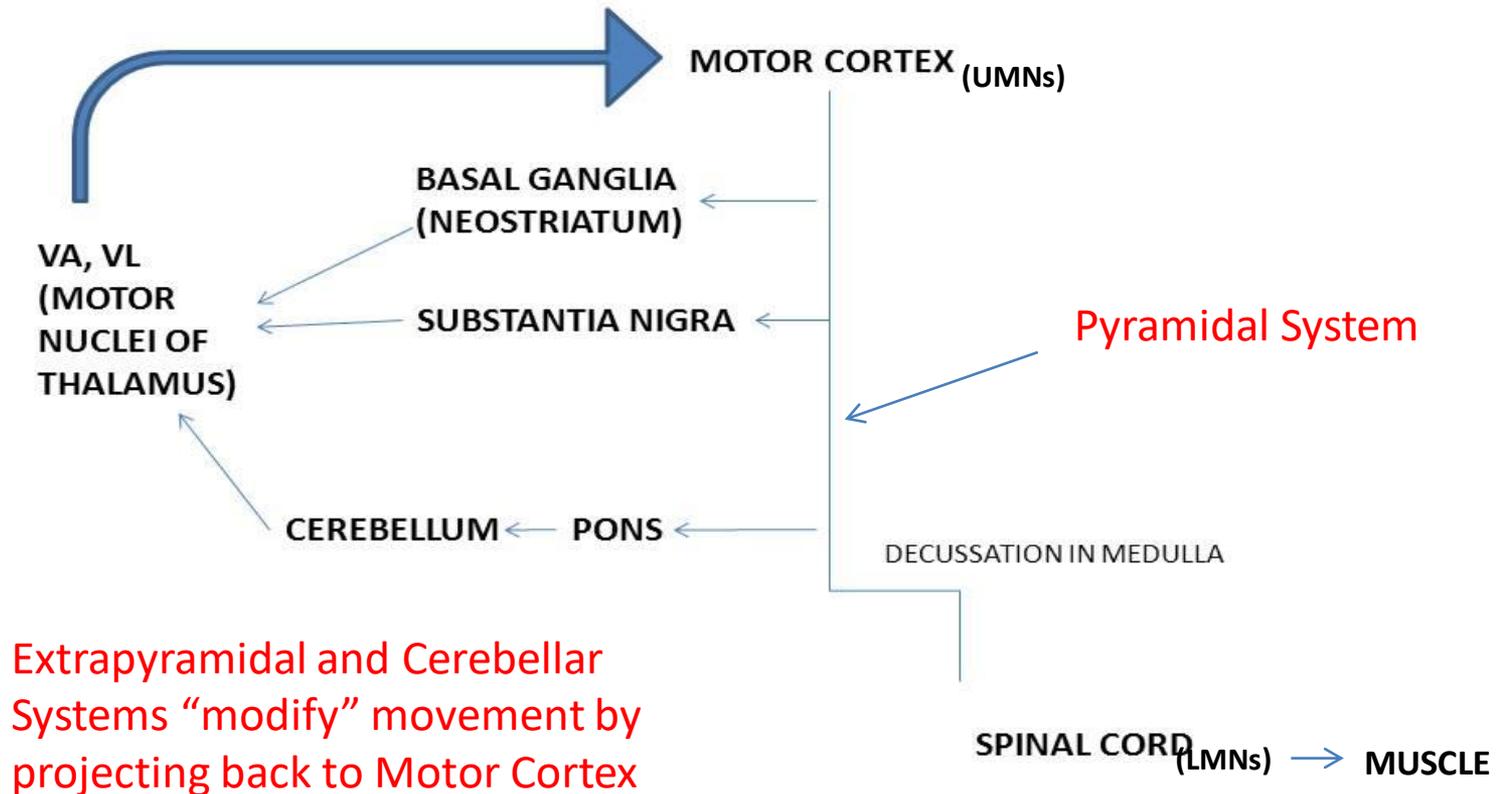
CEREBELLUM

- Involved in equilibrium, posture, muscle tone (old functions); *the proper timing and coordination of learned, skilled motor movement; the correction of movement errors during on-going movement*
- **The cerebellum does not project to the spinal cord**
- Exerts influence by modifying the output of the Pyramidal system
- *A lesion of the cerebellum results (primarily) in ataxia (incoordination)*

Extrapyramidal and Cerebellar Systems – Summary

- ***Neither the extrapyramidal system nor the cerebellum project to the spinal cord***
- ***Both systems exert their influence on motor behavior by modifying the output of Motor Cortex (direct & indirect cortico-spinal pathways of the pyramidal system) which does project to the spinal cord***

THE COMPONENTS OF THE MOTOR SYSTEM WORK TOGETHER TO PRODUCE A MODULATED AND COORDINATED MOVEMENT



CLINICAL CORRELATION: PARKINSON'S DISEASE

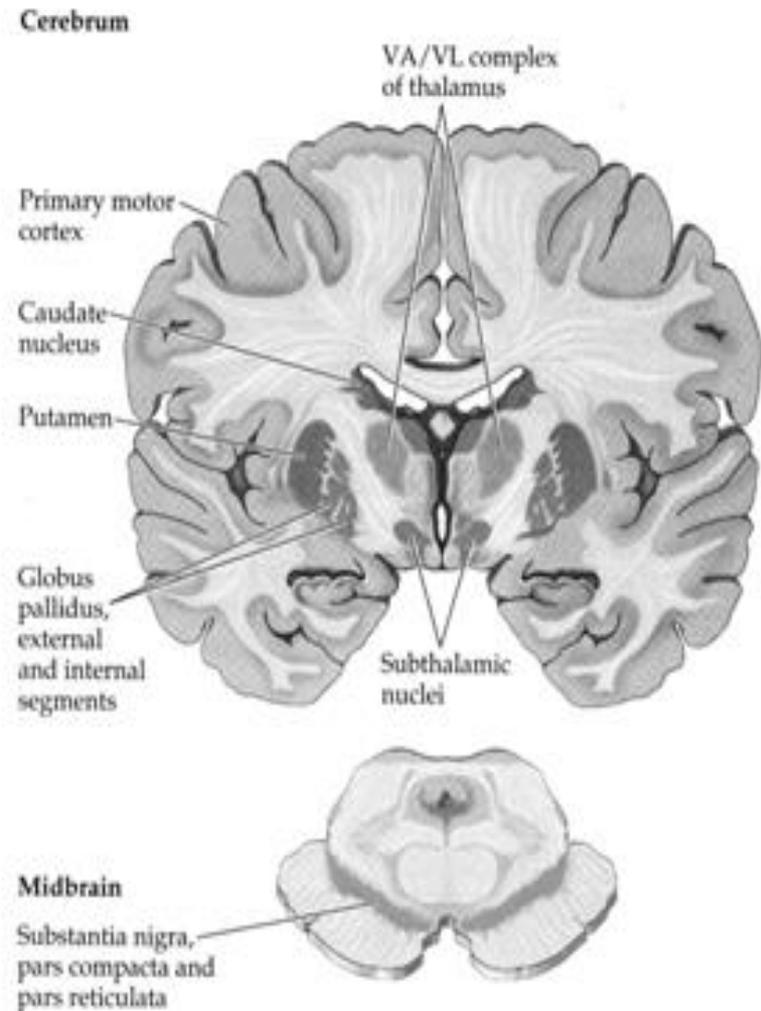
- Parkinson's Disease is an ***extrapyramidal motor system disorder*** in which specific neurons in the extrapyramidal motor system degenerate, resulting in the inability to *modulate* movement appropriately

NUCLEI OF THE EXTRAPYRAMIDAL MOTOR SYSTEM

Nuclei of the Extrapyraxidal Motor System

- Caudate & putamen (neostriatum)
- Globus pallidus
- Subthalamic nucleus
- **Substantia nigra***

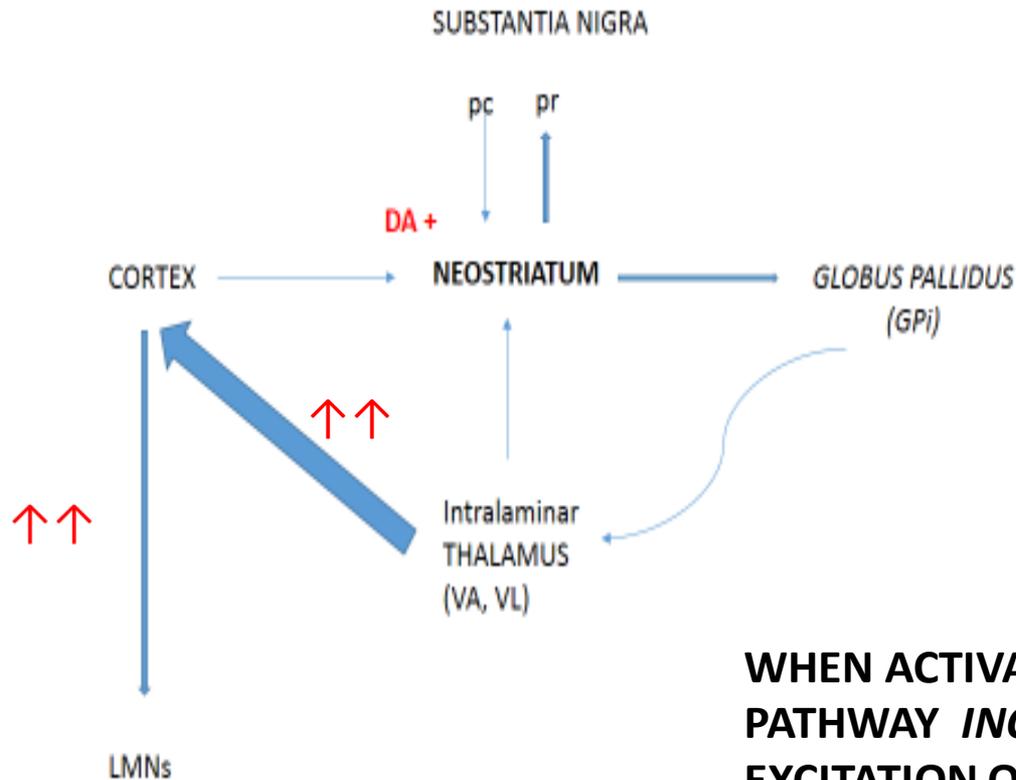
**Signs/symptoms of Parkinson's Disease occur when 80-85% of substantia nigra neurons are lost*



EXTRAPYRAMIDAL MOTOR SYSTEM

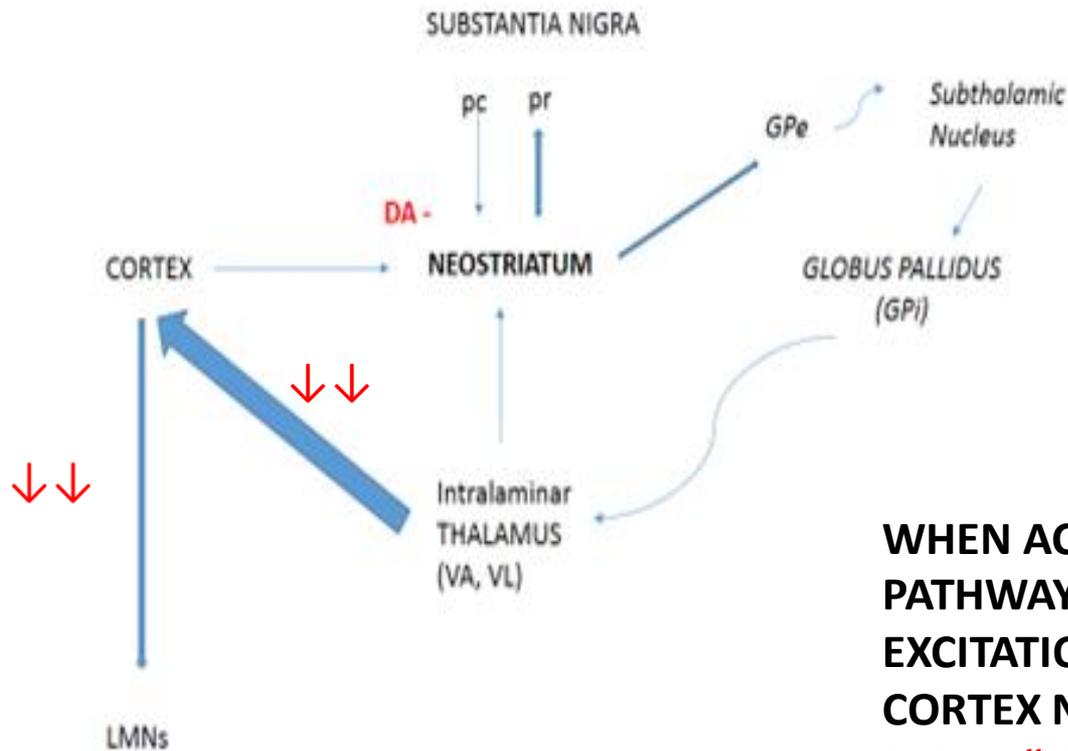
- At rest, neurons in the neostriatum are quiescent (not firing)
- When motor cortex initiates a motor movement, collateral axons of the cortico-spinal pathway *inform* the neostriatum about the intended movement
- This activates two *antagonistic* pathways in the neostriatum
- These two pathways are “modulated” in their activity by the **substantia nigra** via the chemical **DOPAMINE**

THE “GO” PATHWAY OF THE EXTRAPYRAMIDAL MOTOR SYSTEM



WHEN ACTIVATED, THIS PATHWAY *INCREASES* EXCITATION OF MOTOR CORTEX NEURONS - **THUS, IT IS A “GO” PATHWAY**

THE “NO-GO” PATHWAY OF THE EXTRAPYRAMIDAL MOTOR SYSTEM



WHEN ACTIVATED, THIS PATHWAY *DECREASES* EXCITATION OF MOTOR CORTEX NEURONS - **THUS, IT IS A “NO-GO” PATHWAY**

CLINICAL SYNDROMES OF THE EXTRAPYRAMIDAL MOTOR SYSTEM

- **DIVIDED INTO**

- ***HYPO-KINETIC (too little movement) DISORDERS:***
Parkinson's disease/Parkinsonism

- ***HYPER-KINETIC (too much movement) DISORDERS:***
Huntington's chorea, ballismus, and dystonia

- ***Parkinson's Disease is a progressive and irreversible hypo-kinetic disorder in which there is too little "go", and too much "no-go"***

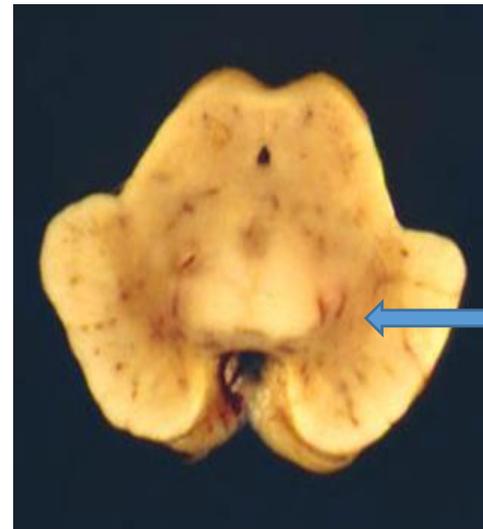
PARKINSON'S DISEASE, Cont.

- **LOSS OF SUBSTANTIA NIGRA NEURONS CAN BE SEEN ON GROSS EXAMINATION; these are the neurons that utilize **dopamine** to modulate activity of extrapyramidal motor system nuclei**

Pigmented neurons in the Substantia Nigra



NORMAL

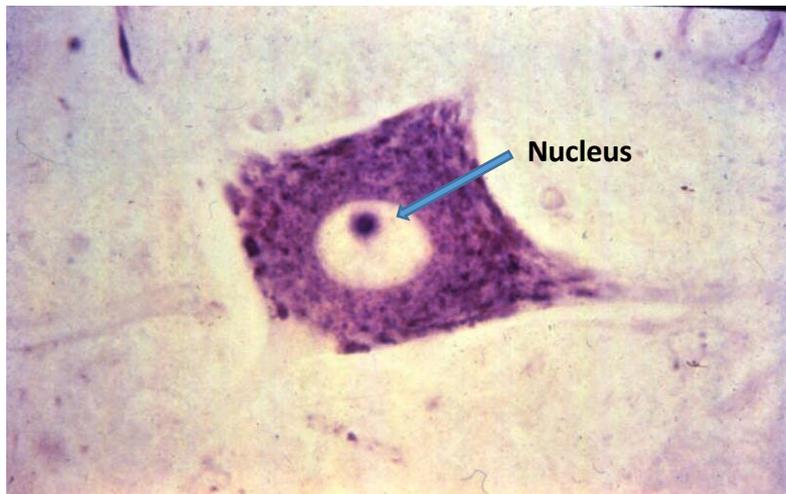


Loss of neurons in the Substantia Nigra

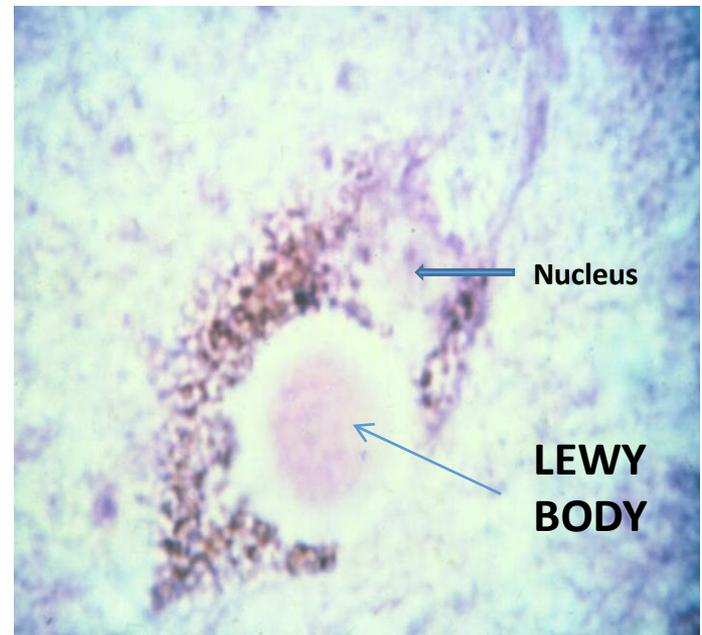
**PARKINSON'S
DISEASE**

PATHOLOGY OF PARKINSON'S DISEASE

- CHARACTERIZED BY PRESENCE OF ABNORMAL INCLUSION BODIES, CALLED “LEWY BODIES” (INTRACELLULAR AGGREGATES OF **SYNUCLEIN**); THESE INCLUSIONS MAY KILL THE NEURON



Normal Neuron



ETIOLOGIES

PARKINSON'S DISEASE (Primary Parkinson's) - loss of ~85% of substantia nigra neurons (and thus loss of dopamine)

- **IDIOPATHIC** – sporadic; cause unknown; **risk ↑↑ with age**
- **GENETIC** – small fraction of cases (~5-10%) familial – autosomal dominant inheritance; number of “pre-disposing” genes have been identified as well

PARKINSONISM (also called Secondary Parkinson's)

- **ENCEPHALITIC INFLAMMATION**
- **STROKE**
- **CO POISONING**
- **TOXIC** (herbicides, pesticides, drugs [both recreational and prescription])

CLINICAL SIGNS/SYMPTOMS

- **AKINESIA or HYPOKINESIA** (loss of normal movement; failure to move body normally)
- **BRADYKINESIA** (slowness of movement; difficulty beginning or ending movement)
- **DYSKINESIA** (abnormal movement – “resting” tremor)
- **ALTERNATIONS IN MUSCLE TONE** (muscles are firm and tense)
- **IMPAIRED POSTURAL REFLEXES**
- **OTHER (MICROGRAPHIA, SOFT VOICE, IMPAIRED SWALLOWING, PROFOUND PHYSICAL AND EMOTIONAL FATIGUE, DEPRESSION)**
- ~25% of patients will develop **DEMENTIA** (progressive mental decline)

TREATMENTS

- **Pharmacological:** to restore dopamine
 - Sinemet (to replace dopamine); patients may develop L-dopa induced abnormal movements (dyskinesias)
- **Surgical:**
 - Transplantation of nervous system neurons that utilize dopamine or closely related neurotransmitters
 - Ablation (lesioning of particular nuclei in the extrapyramidal system to effectively increase “go” and decrease “no-go”)
 - **Deep brain stimulation (DBS):** a reversible interruption of normal transmission in specific nuclei to decrease activity in the “no-go” system
- **Exercise, Physical Therapy**

TAKE-HOME MESSAGES

- *If you or your loved ones experience progressive*

- **Loss of smell**
- **Decreased movement**
- **Tremor**
- **Softness of voice**

Notify your Primary Care Physician

- ***While we do not have a cure, in most patients symptoms can be managed; in addition, physical therapy programs can help individuals maintain independence for as long as possible and help with “activities of daily living [ADLs]” and “mobility”***