Bradykinetic disorders

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Background information

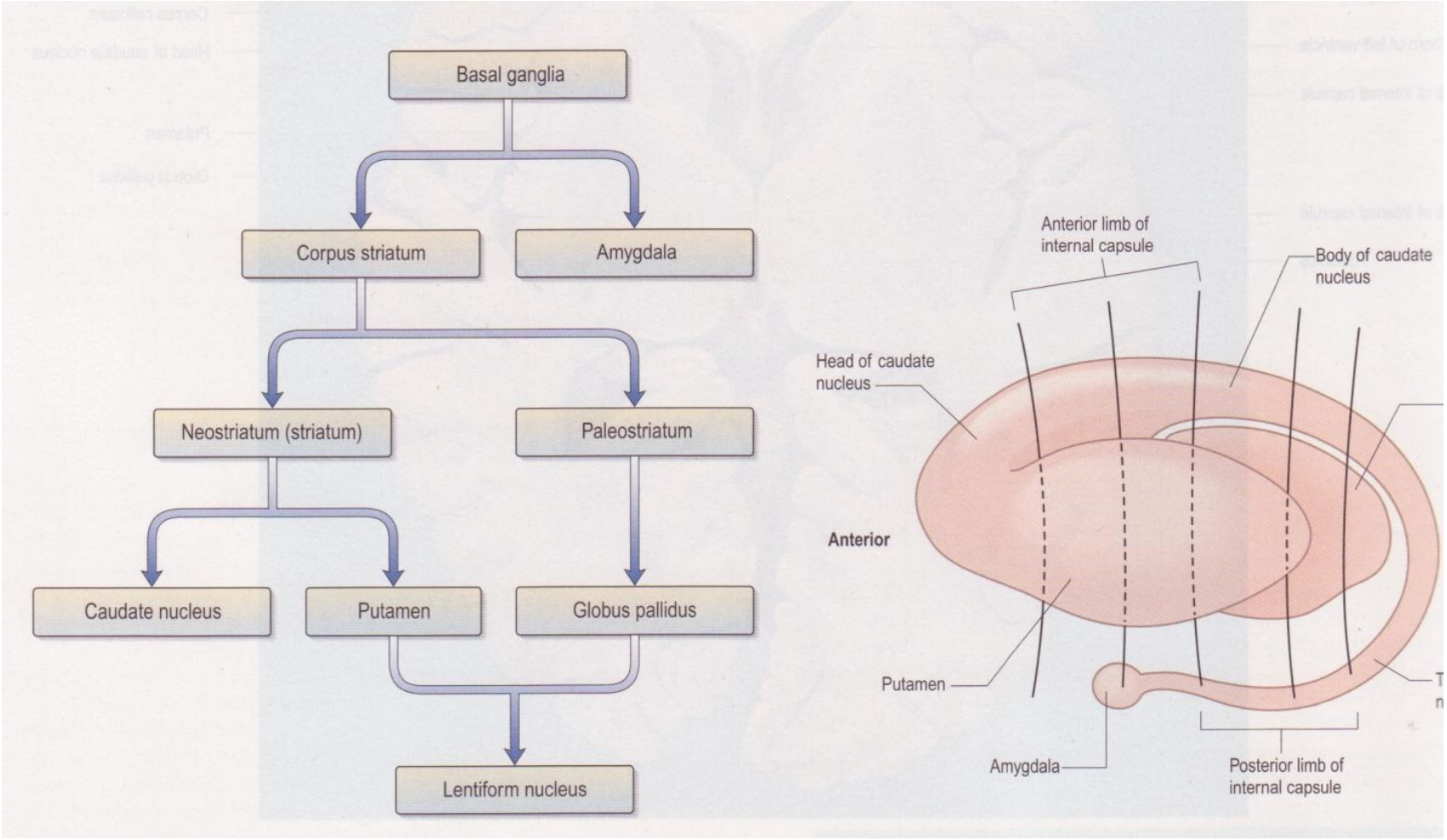
- Movement disorders divided into 2 main groups

- BRADYKINETIC
  - REDUCED
- HYPERKINETIC
  - EXCESSIVE

Bradykinetic

- Slowed ability to start/continue movement
- Impaired ability to adjust the body's position
- Rigidity
- Postural instability
- Loss of automatic associated movements

Anatomy of the Basal Ganglia



Basal Ganglia

BG

↓ (output)

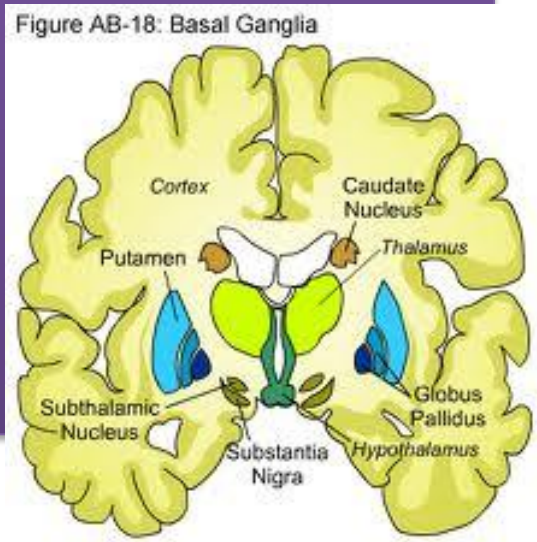
Thalamus

↓

Cerebral Cortex

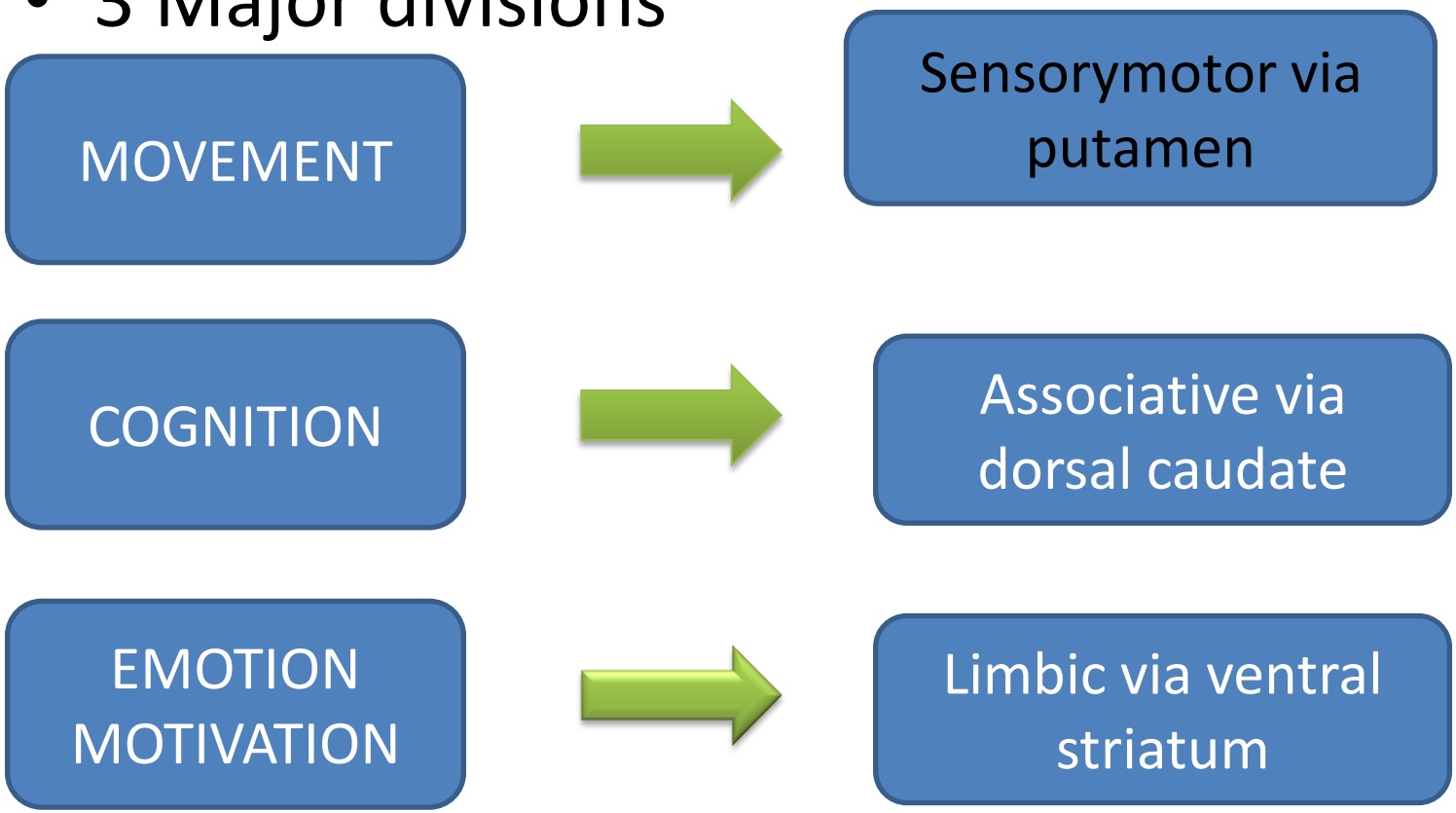
↓

Pyramidal System



Basal Ganglia functions

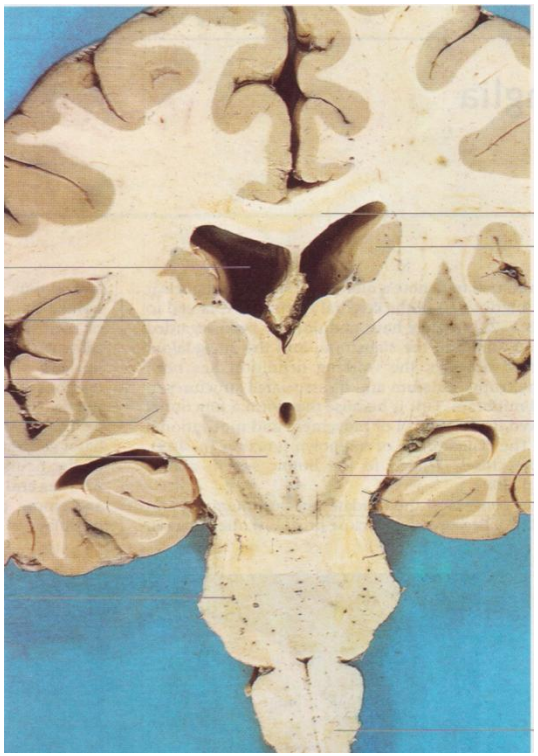
- 3 Major divisions



Basal Ganglia: Functions

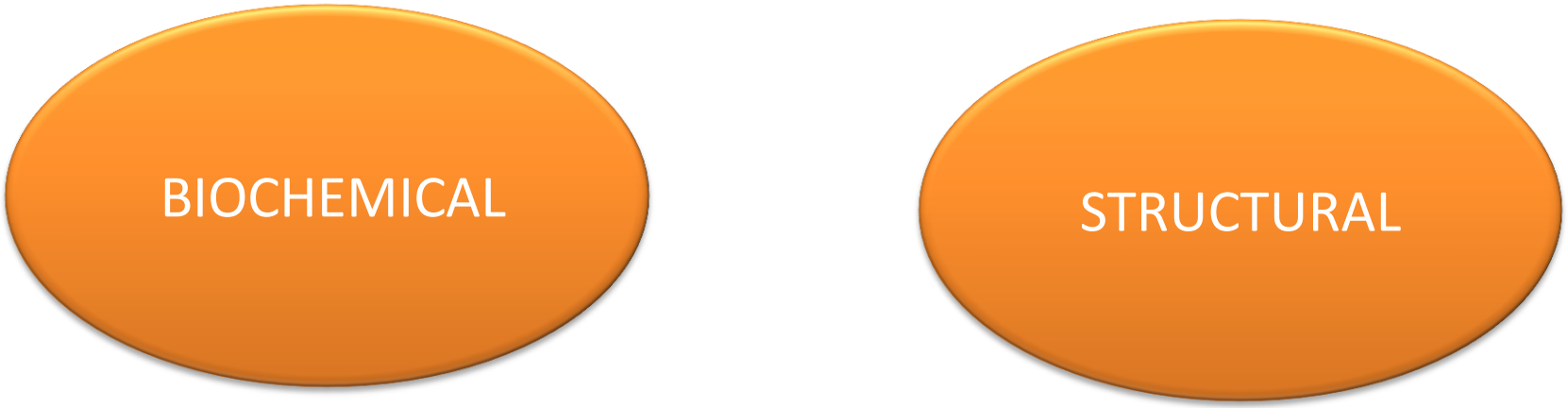
- Movement is modulated by series of excitatory or inhibitory influences

- Lesion will create imbalance of modulation



Basal Ganglia

Disorders



Parkinsonism Classification

1. Primary parkinsonism PD

2. Multisystem degenerations
   - MSA, PSP, CBD

3. Heredodegenerative parkinsonism
   - Wilson's disease, neuroacanthocytosis

4. Secondary/acquired parkinsonism
   - Post-encephalitic, vascular, drugs

AN

ESSAY

ON THE

SHAKING PALSY.

CHAPTER I.

DEFINITION–HISTORY–ILLUSTRATIVE CASES.

SHAKING PALSY. *(Paralysis Agitans.)*

Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from a walking to a running pace: the senses and intellects being uninjured.

Epidemiology of PD

- Prevalence 0.3% of whole population
- 4% of population over 80y
- Mean age of onset 60y
- 5-10% however young onset between 20y and 40y (early < 40y, juvenile < 20y)

Parkinson Disease

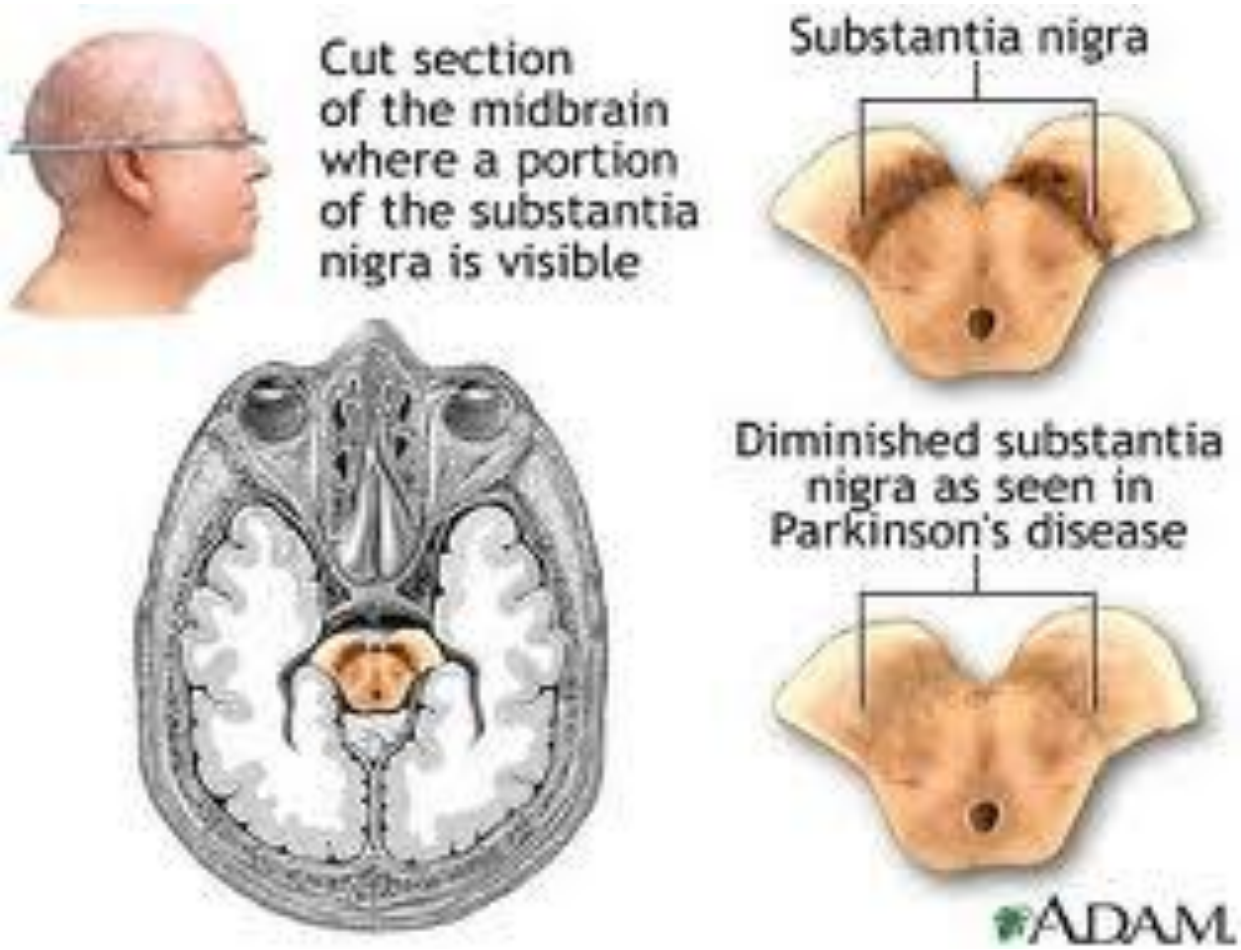
- Neurodegenerative disorder of CNS

Parkinson Disease

- Most sporadic
- Genetic loci PARK1-3 with causative mutations in 6 nuclear genes

  AD or AR disorders
- Genetic factors can contribute to PD susceptibility : PARK10 idiopathic late onset disease

Parkinson Disease



Parkinson Disease

Misfolding of alpha synuclein

↓

Lewy Body formation

↓

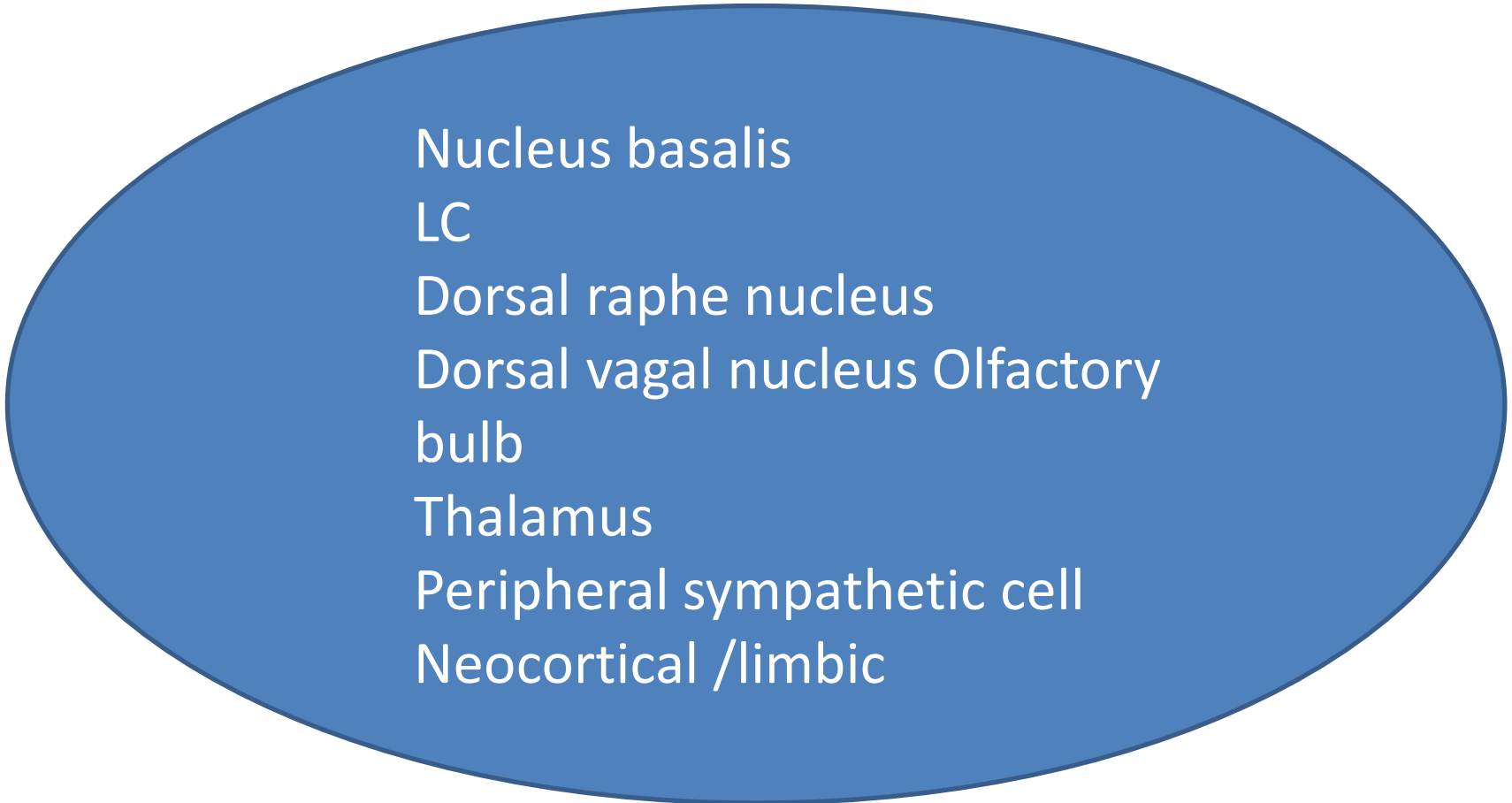
Cellular oxidative stress

↓

Energy depletion

Parkinson Disease

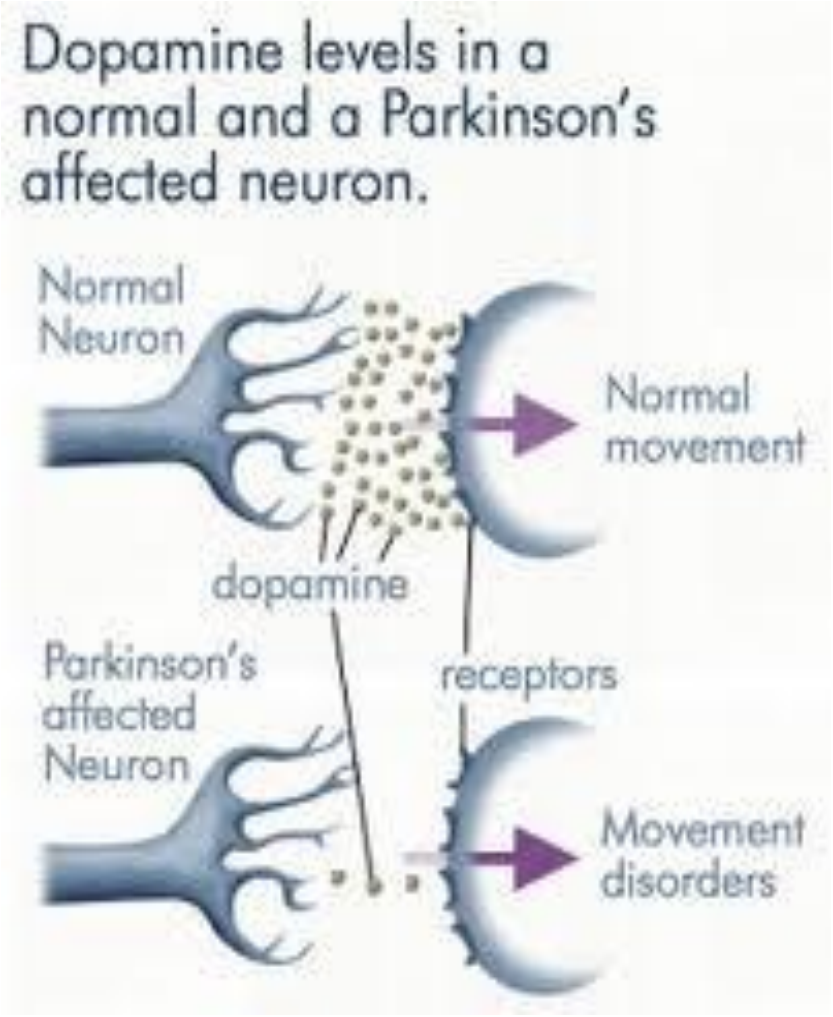
- Also involved
- ? Earlier affected



Parkinson Disease

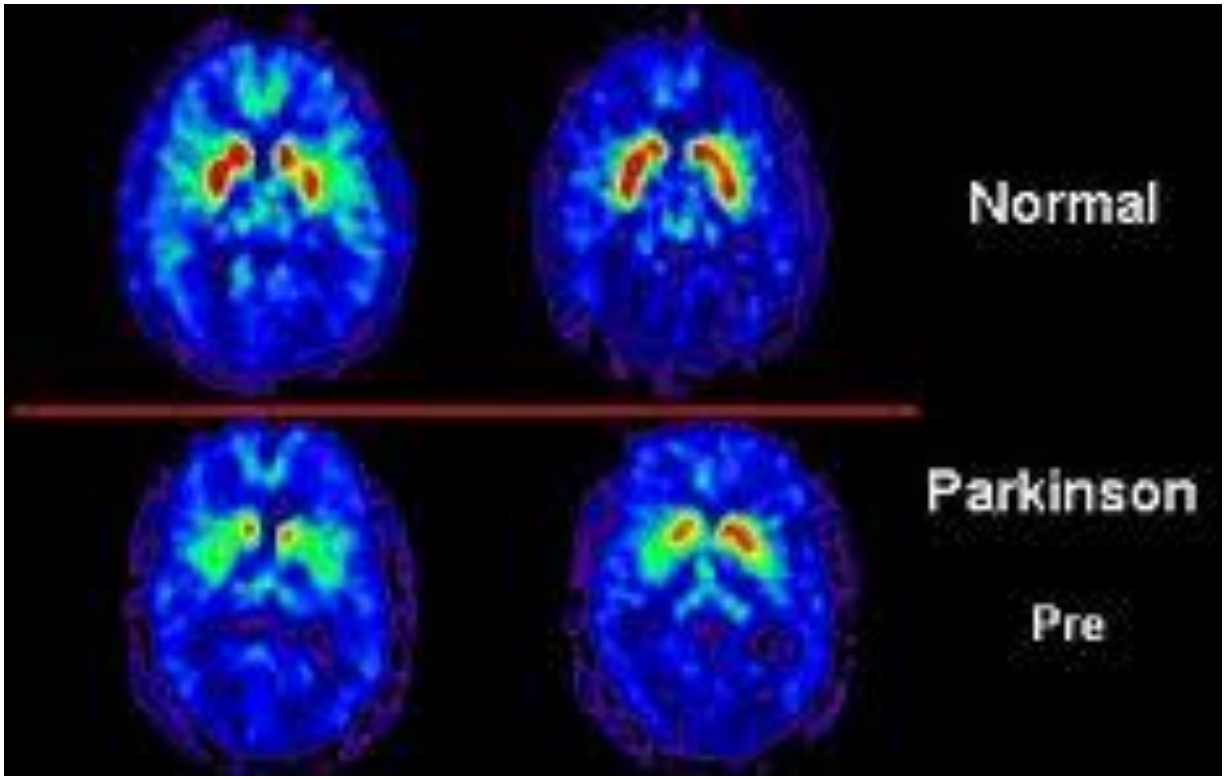
- Reduced SN dopaminergic facilitation of the direct pathway

- Inhibition of indirect pathway



Parkinson Disease

- Increased firing and inhibition of the thalamocortical pathways



Motor Symptoms of PD

- Tremor
- Rigidity
- Bradykinesia
- Postural instability
- Forward-flexed posture
- Decreased arm swing
- Mask face
- Small handwriting

Neuropsychiatric features

Cognitive disturbances

- Planning/abstract
- Attention, slowed speed
- Recalling learned information
- Dementia (6 fold increased)

Mood/behaviour problems

- Depression
- Apathy
- Anxiety
- Impulse control

Psychotic symptoms

Other Clinical Features

Sleep
- Fragmentation
- REM disorder
- Daytime

Autonomic
- Hypotension
- Bladder/Constipation
- Sexual

Sensory
- Pain/Paresthesiae
- Numbness
- RLS

Fatigue

Perception
- Smell

Ophthalmologic
- Decreased blink
- Decreased pursuit
- Up gaze

Diagnosis

- Medical history and examination
- Reduction of motor impairment in response to administration of levodopa strong sign pointing to PD
- May be difficult early
- Lewy bodies on autopsy

PD Society Brain Bank criteria

- Bradykinesia plus either

  Rigidity, resting tremor or postural instability

- Other possible causes need to be ruled out (strokes, head injuries, encephalitis, outonomic symptoms, cerebellar signs, drugs)

PD Society Brain Bank criteria

- Supportive prospective criteria:
- 3 or more with criteria 1: Definite PD:
  - Unilateral onset
  - Resting tremor
  - Progression
  - Asymmetry of motor symptoms
  - Response to levodopa at least 5y
  - Clinical course at least 10y
  - Dyskinesias induced by levodopa

Differential diagnosis

- Postural, action and intention tremors
- Alzheimer's disease
- Multiple cerebral infarction
- Drug-induced
- Parkinson plus syndromes

Imaging

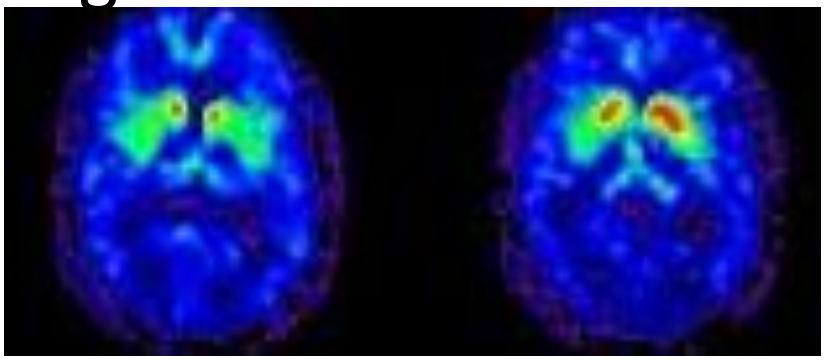
CT and MRI imaging of patients with pure PD usually appear normal

used to rule out secondary causes of parkinsonism, incl. BG tumours, vascular pathology and hydrocephalus

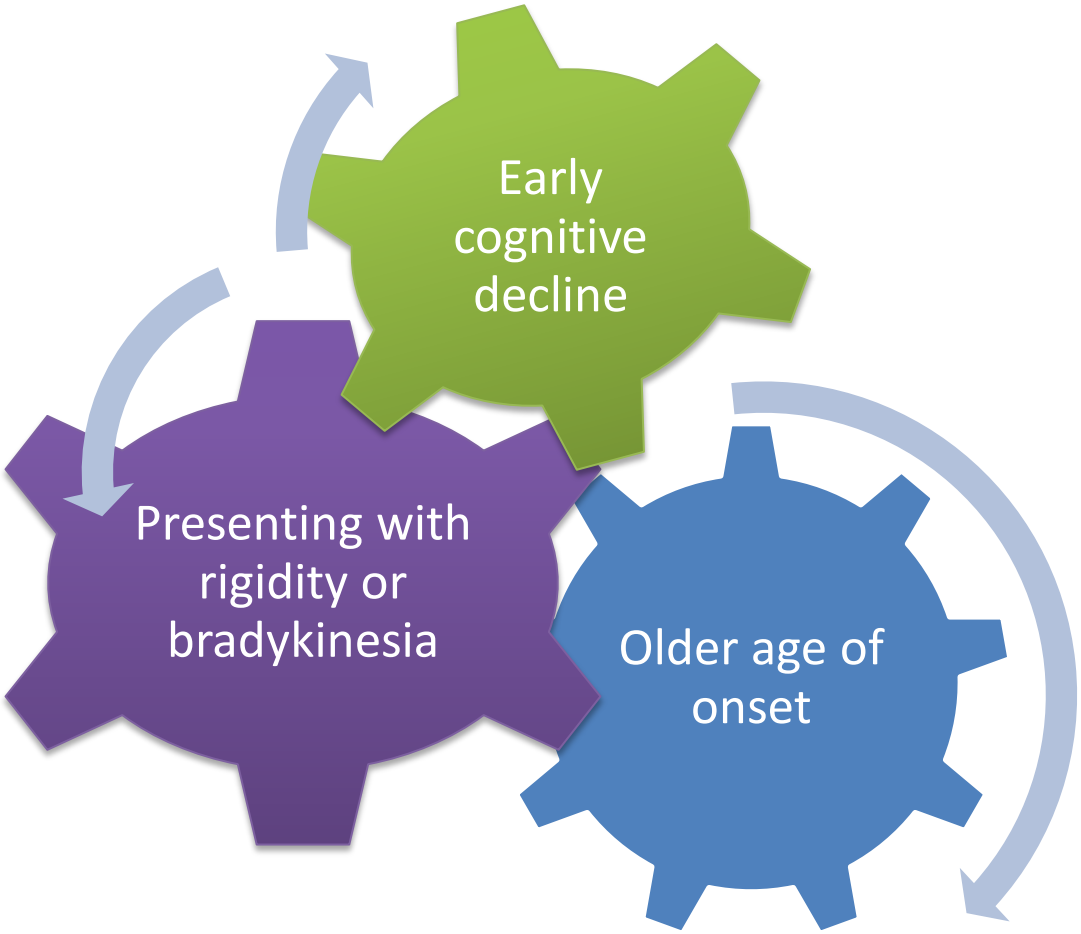
Imaging

PET and SPECT radiotracers can measure Dopaminergic function

A pattern of reduced Dopaminergic activity in the BG can aid in the diagnosis of the disease



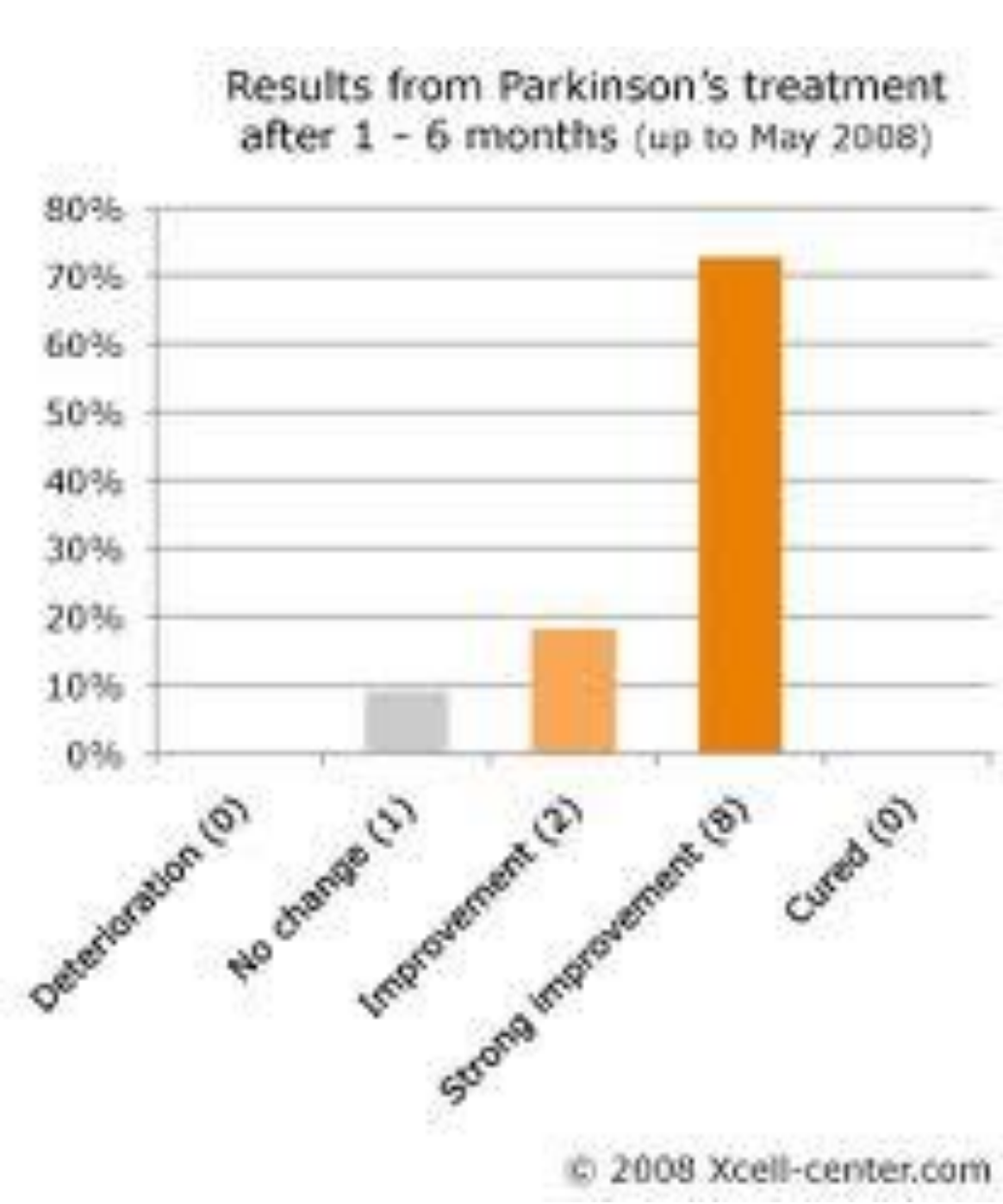
Predict rapid progression



Treatment

At present there is no cure for PD

- Medication, surgery and multidisciplinary management can provide relief from the symptoms


Results from Parkinson's treatment
after 1 - 6 months (up to May 2008)
80%
70%
60%
50%
40%
30%
20%
10%
0%
Deterioration (0)
No change (1)
Improvement (2)
Strong improvement (8)
Cured (0)
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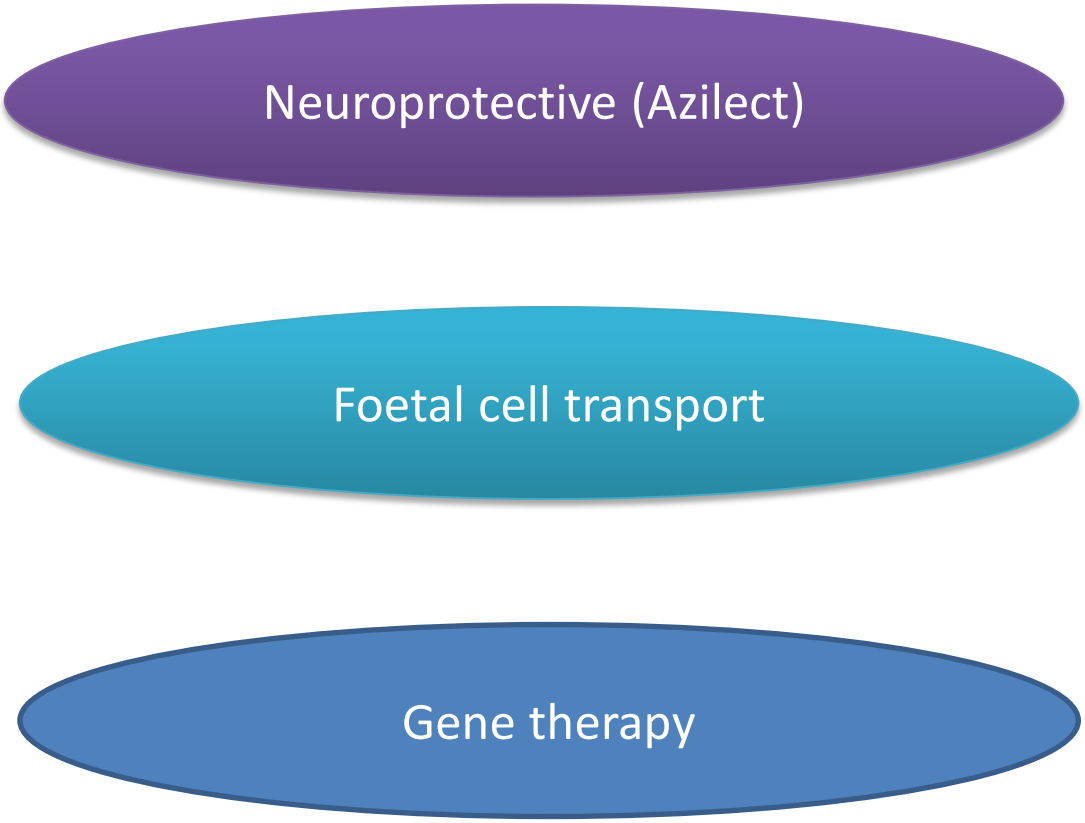
Treatment of PD

Increase levels of dopamine in the brain in attempt to slow down disease progression

Lifestyle modification control motor symptoms in the early stages

Surgical treatment (DBS)

Novel Approaches in PD



Treatment

- Treatment differ for every person
- Treatment changes as disease progresses
- Goal

To provide control of signs and symptoms for as long as possible while minimizing adverse effects

Treatment

Studies demonstrates that disease can deteriorate quickly if treatment is not instituted at/shortly after diagnosis

Early onset disease

MOA-B

Levodopa

Dopamine Agonist

Anti-cholinergic

Amantidine

Advanced disease

Levodopa small dosages more frequently

COMT-inhibitors

Carbidopa-levodopa

Greatest effect

Fewer adverse effect in short term

Long-term side effects

↓

Motor fluctuations

Dyskinesias

Dopamine Agonist

- Symptom relief at lower risk of developing motor complications

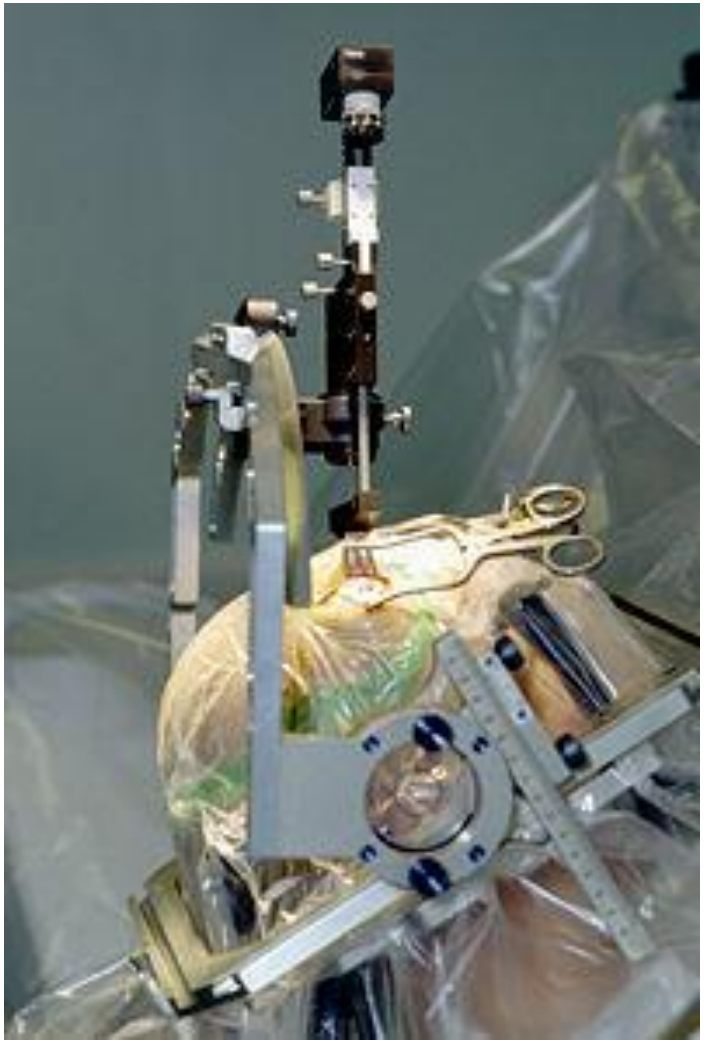
Problems

Orthostatic hypotension, sleepiness, hallucinations, edema, pleural effusion, retroperitoneal fibrosis, pathological gambling/ sexual behavior, restrictive valvular disease

MAO-B inhibitors

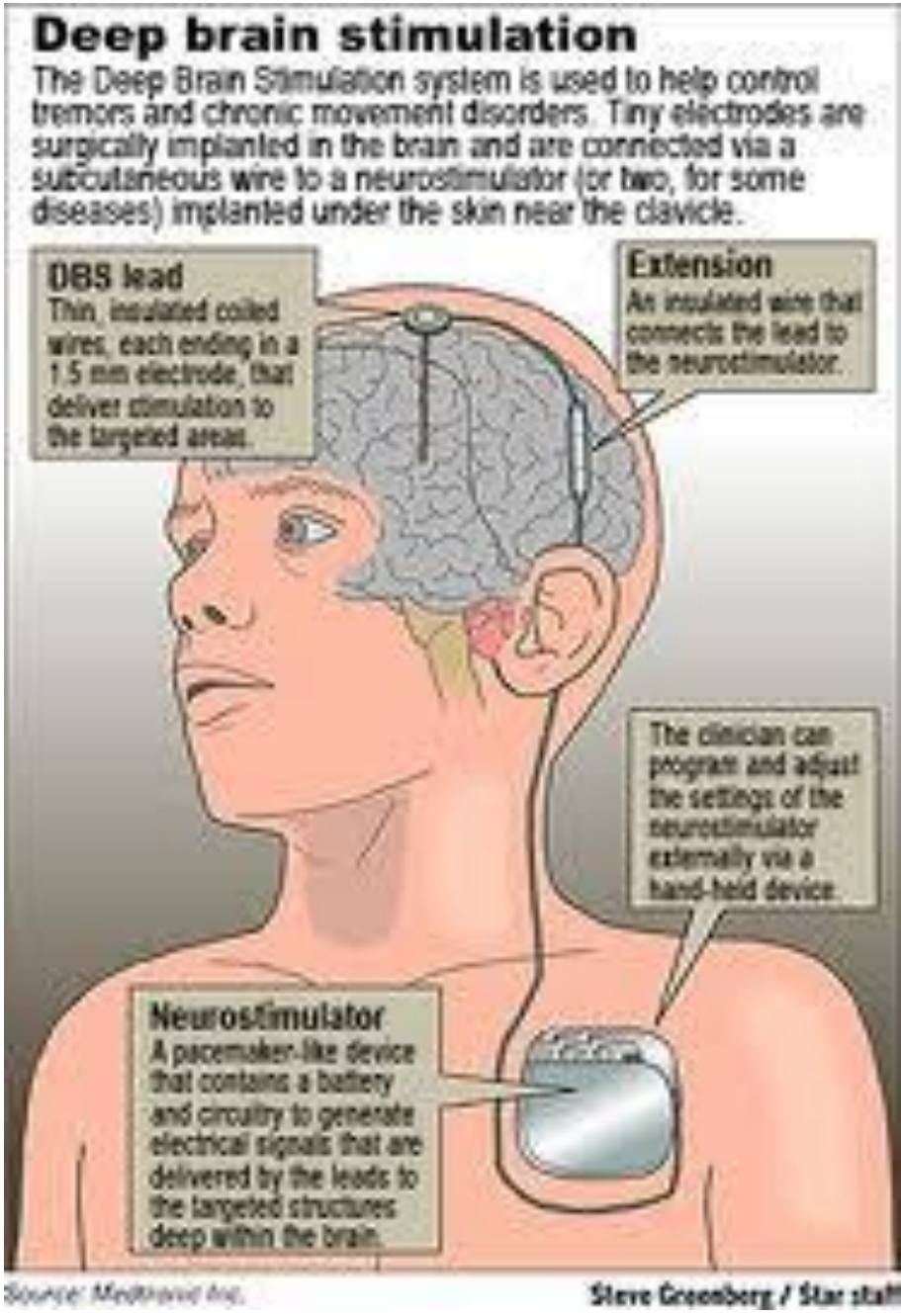
Azilect

Deep Brain Stimulation



Deep Brain Stimulation

- Implanted into affected area, with a wire under the skin to battery-operated pulse generator implanted near the collarbone
- Programmed to send continuous electrical pulses to the brain


Deep brain stimulation
The Deep Brain Stimulation system is used to help control tremors and chronic movement disorders. Tiny electrodes are surgically implanted in the brain and are connected via a subcutaneous wire to a neurostimulator (or two, for some diseases) implanted under the skin near the clavicle.
DBS lead
Thin, insulated coiled wires, each ending in a 1.5 mm electrode, that deliver stimulation to the targeted areas.
Extension
An insulated wire that connects the lead to the neurostimulator.
The clinician can program and adjust the settings of the neurostimulator externally via a hand-held device.
Neurostimulator
A pacemaker-like device that contains a battery and circuitry to generate electrical signals that are delivered by the leads to the targeted structures deep within the brain.
Source: Medtronic Inc.
Steve Greenberg / Star staff

Dementia with Lewy Bodies

Prominent disruption of attention and visual spatial abilities
Visual hallucinations
Parkinsonism Depression

Multisystem Atrophy

Include disorders with various combinations of pyramidal, extrapyramidal, cerebellar, autonomic features

Corticobasal Degeneration

Akinetic rigidity
Apraxia
Alien limb
Cortical sensory loss
Dystonia and tremor
Aphasia
Myoclonus

Huntington's Disease

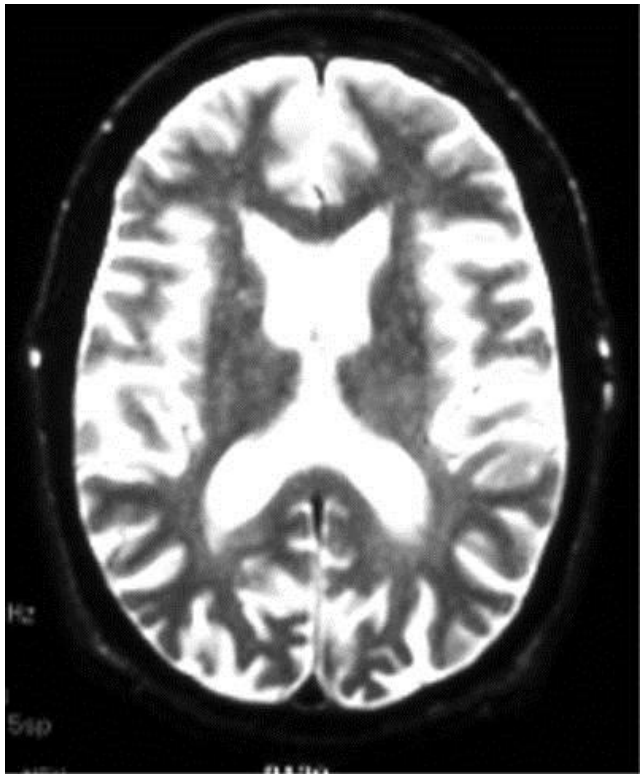
- 1/10 000
- Equal sex bias
- AD
- CAG trinucleo-
- tide repeat disorder⇉ worsened disease, earlier onset

Huntington's Disease

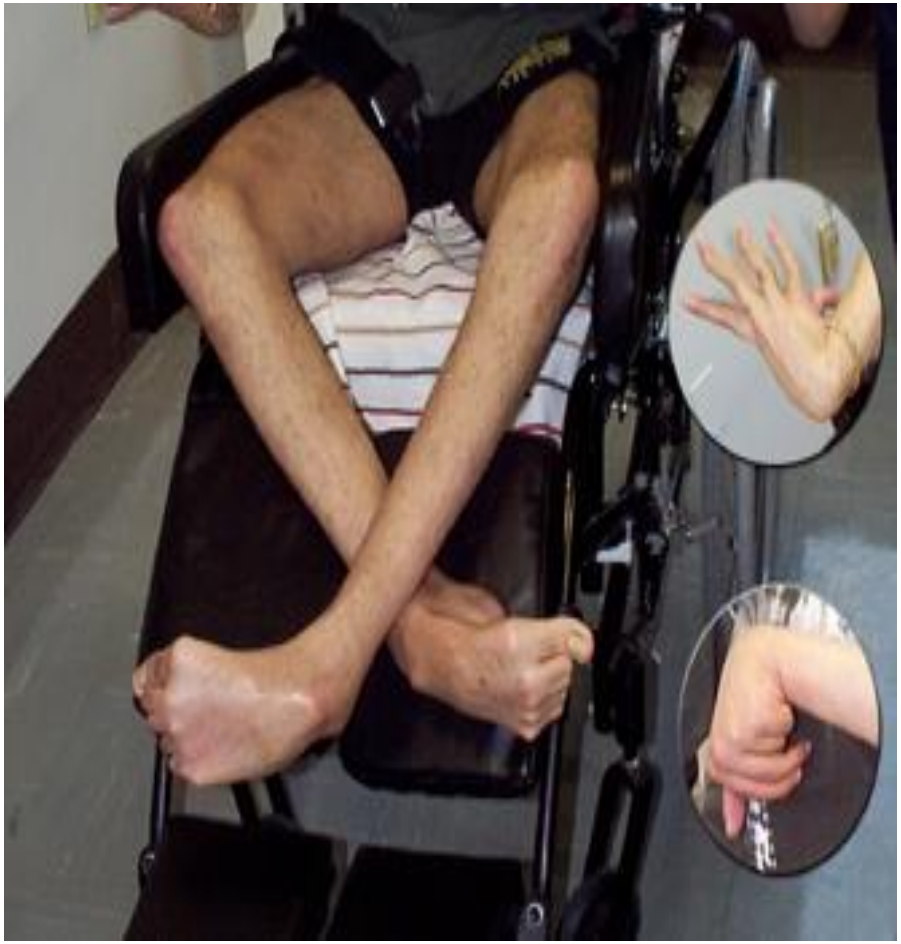
Devastating, progressive movement disorder associated with psychiatric and cognitive decline, leading to a terminal state of dementia and immobility

Huntington's Disease

Fragments of huntingtin protein containing expanded polyglatamine may be neurotoxic

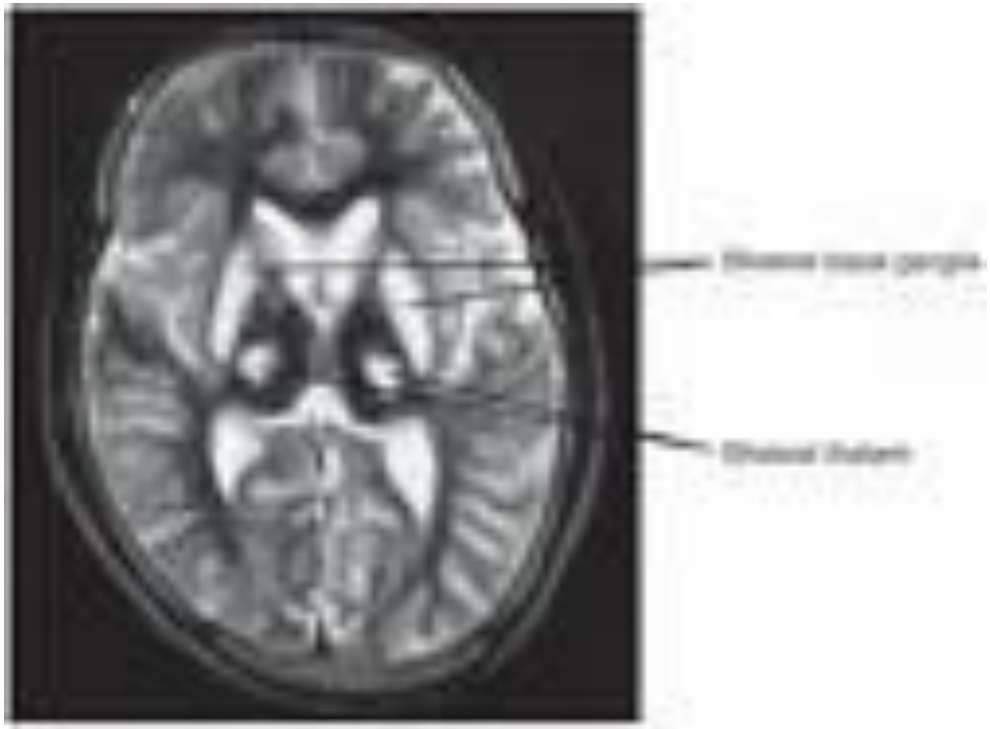


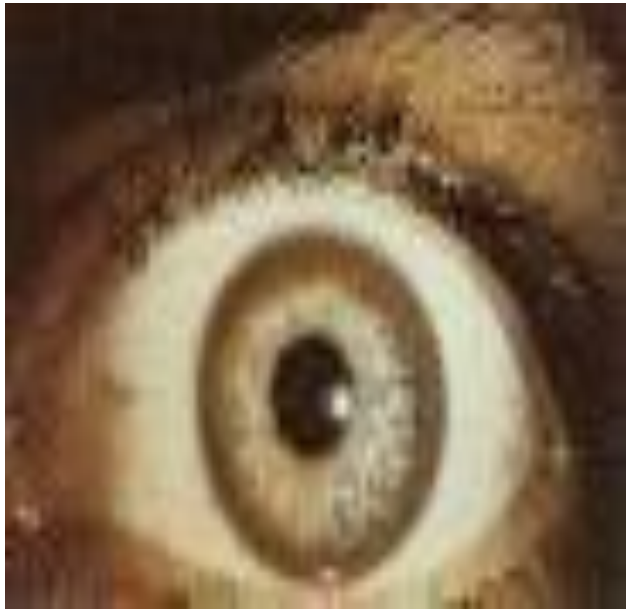
Wilson's Disease



- Hepatolenticular degeneration
- 30/mil
- AR
- Defect of cellular copper export

Wilson's Disease





Wilson's Disease