Movement disorders

References:

1. Clinical practice. Diagnosis and initial management of Parkinson's disease. N Engl J Med 2005, 353:1021-1027;

2. Clinical Neurology, fourth edition, P228-252. McGraw-Hill Press;

3. Neurology and Clinical Neuroscience, First edition, P879-982. Mosby Inc.

Movement Disorders

Introduction:

Movement disorders: Impairing the regulation of voluntary motor activity without directly affecting strength, sensation, or cerebellar function.

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Movement Disorders

Introduction:

Extrapyramidal system:

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Movement Disorders

Introduction:

Basal ganglia: No universally accepted anatomic definition. For clinical purposes it may comprise caudate nucleus, putamen, globus pallidus, (subthalamic nucleus, and substantia nigra).

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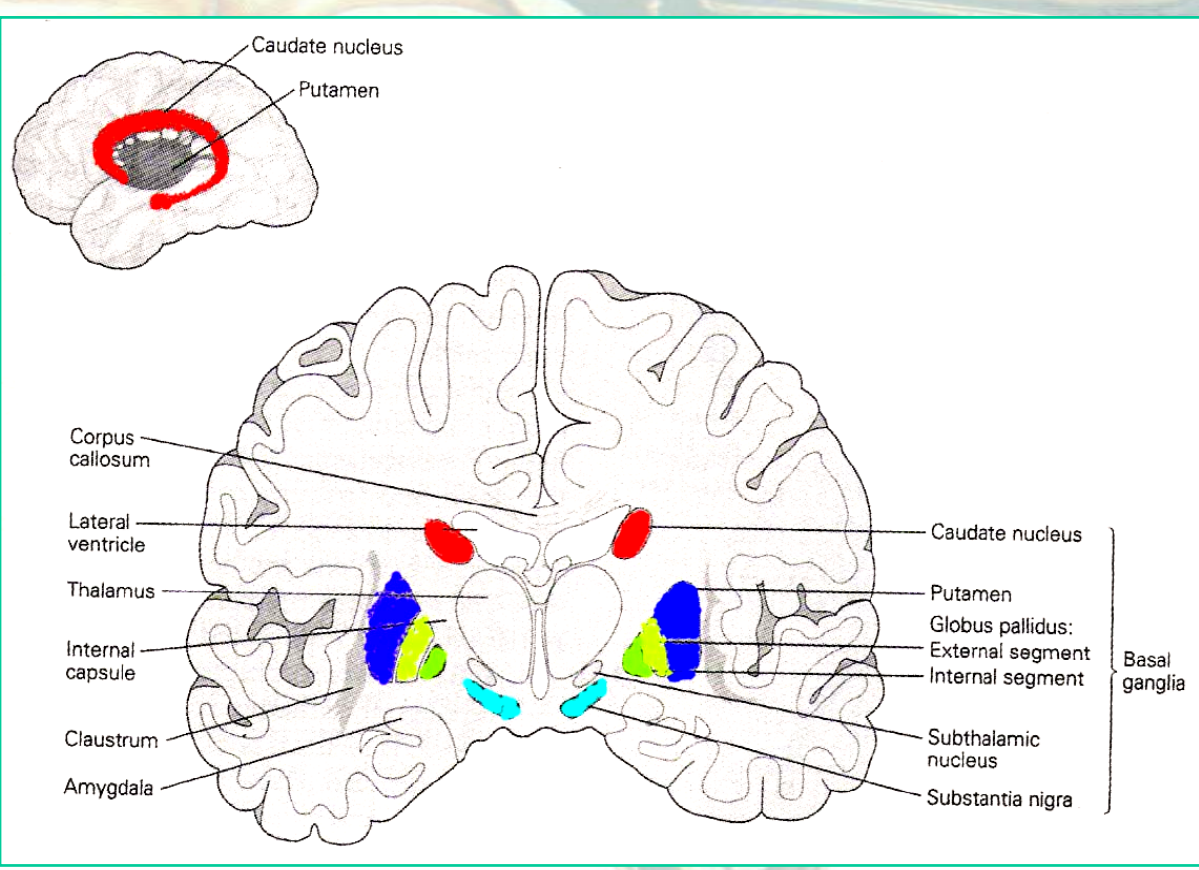
Movement Disorders

Introduction:

Basal ganglia:



Movement Disorders

Introduction:

Corpus striatum:

Neostriatum: Caudate nucleus

Putamen

Paleostriatum: Pallidum

Lentiform nucleus

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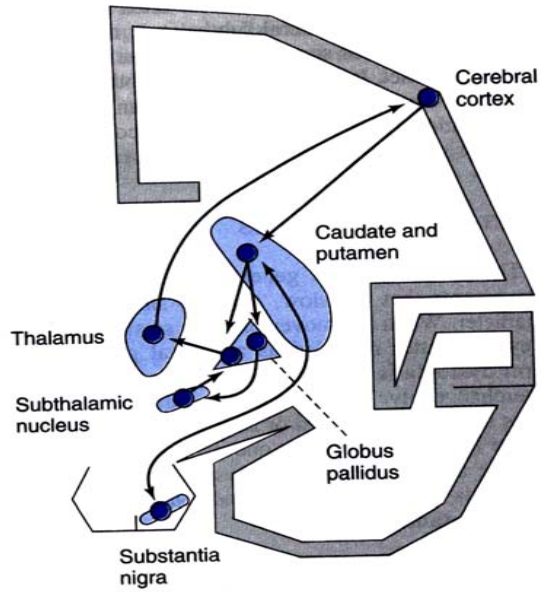
Movement Disorders

Introduction:

Basic neuronal circuitry of the basal ganglia

Basic circuitry of the basal ganglia consists of three interacting neuronal loops:

Corticocortical loop
Nigrostriatal loop
Striatopallidal loop



Movement Disorders

Introduction:

Types of abnormal movements

* Tremor
* Chorea and athetosis
* Hemiballismus
* Tics and habit spasms
* Dystonia
* Myoclonus

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Movement Disorders

* **Tremor:** A steady rhythmic oscillatory movement of the muscles. Tremor may be normal (physiological) or abnormal (pathological)

*Postural tremor

Physiologic tremor

Enhanced physiologic tremor

Familial or idiopathic tremor (essential tremor)

Movement Disorders

* Tremor:

*Intention tremor

Cerebellar disease
Red nuclear tremor
Drug toxicity
Wilson's disease

* Rest tremor

Parkinson's disease
Wilson's disease
Heavy metal poisoning

Movement Disorders

* **Chorea:** Rapid, irregular, jerky movements affacting the face, trunk, and limbs.

Athetosis: Slow, writhing movements which affect all muscle groups.

Choreoathetosis: Two types of movement disorder often occur together.

Movement Disorders

* The disorder arises from diseases of the basal ganglia

Hereditary: Huntington's disease

Static encephalopathy(cerebral palsy):

Sydenham's chorea:

Chorea gravidarum:

Drug toxicity:

Miscellaneous medical disorders:

Cerebrovascular disorders

Structural lesions of the subthalamic nucleus

Movement Disorders

* **Asterixis:** Flapping of hands observed with arms outstretched and hands dorsiflexed. The flap occurs several times a minute.

* **Hemiballismus:** Unilateral violent flinging movements of the proximal limb muscles.
A lesion of contralateral subthalmic nucleus.

Movement Disorders

* **Tics:** Repetitive brief contraction of a muscle or group of muscles.

  Gilles de la Tourette syndrome

* **Habit spasms:** Habitual movements that a person feels the need to make to relieve tension and may be suppressed voluntarily, such as sniffing, blinking.

Movement Disorders

* **Dystonia:** prolonged muscular contraction on attempted voluntary movement, which results in abnormal posturing. Dystonia may be Generalized or Focal.

  Generalized dystonia:

  & dystonia musculorum deformans:

  & Drugs:

  & Symptomatic dystonia: Wilson's disease:

  & Paroxysmal dystonia:

  Focal dystonia:

  & Cervical dystonia(spasmodic torticollis')

  & Blepharospasm:

  & Oromandibular dystonia:

  & writer's cramp:

Movement Disorders

* **Myoclonus:** Shock-like asymmetrical muscular contractions that occur irregularly.
  Generalized or Focal

Physiologic myoclonus: Nocturnal, Hiccup

Essential myoclonus:

Epileptic myoclonus:

Symptomatic myoclonus:

Movement Disorders

Clinical Evaluation of Patients

* **Hstory:** Age at onset
  Mode of onset
  Progressive mode
  Medical history:
    drug and family history
    general medical history
* **Examination**
* **Investigative studies:**

Parkinson's Disease

Parkinson's disease:

A degenerative disease with initial clinical features that are predominantly the result of loss of dopaminergic neurons in the substantia nigra pars compacta of the midbrain.

Parkinson's Disease

Historical Review:

James Parkinson: The Shaking Palsy published in 1817. Origins in the medulla?

Lewy bodies described in 1912, a hallmark.

Trétiakoff: Cell degeneration in the substantia nigra.

Ehinger and Hornykiewicz: Dopamine deficiency in 1960.

Parkinson's Disease

Epidemiology:

A prevalence of 1-2‰.

Under 45 years :1.3 per 100,000.

75-85 years: 1192.9 per 100,000.

Increasingly common with advancing age, 1% of the population over age of 65 years

Occurs in all ethnic groups

Parkinson's Disease

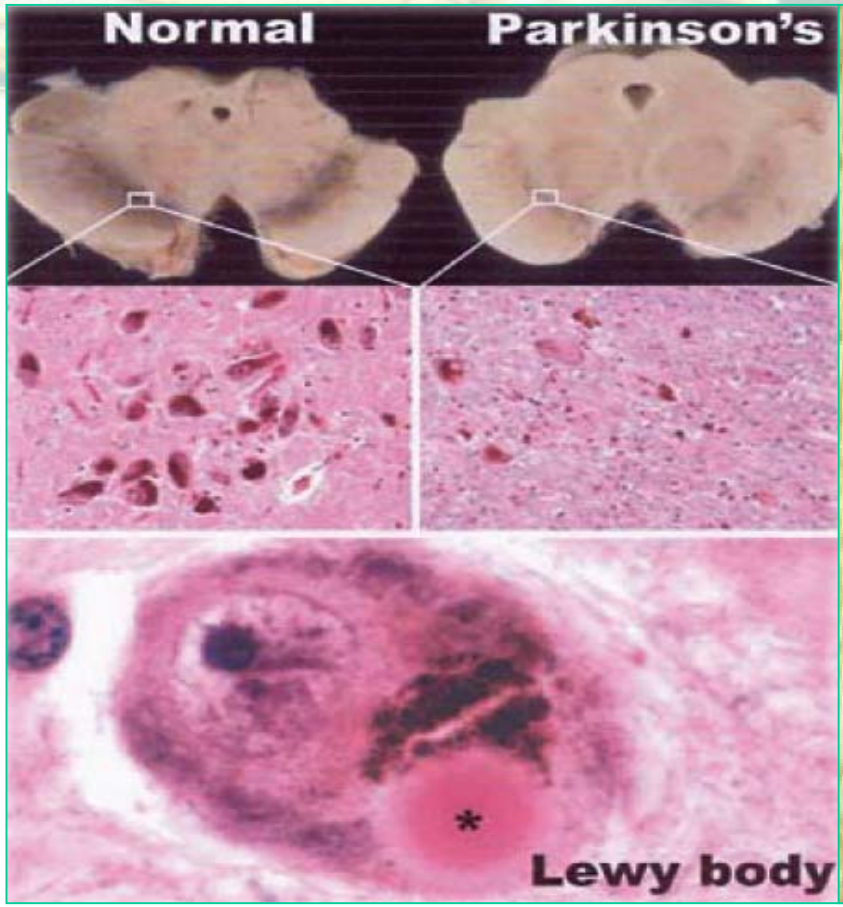
Pathology:

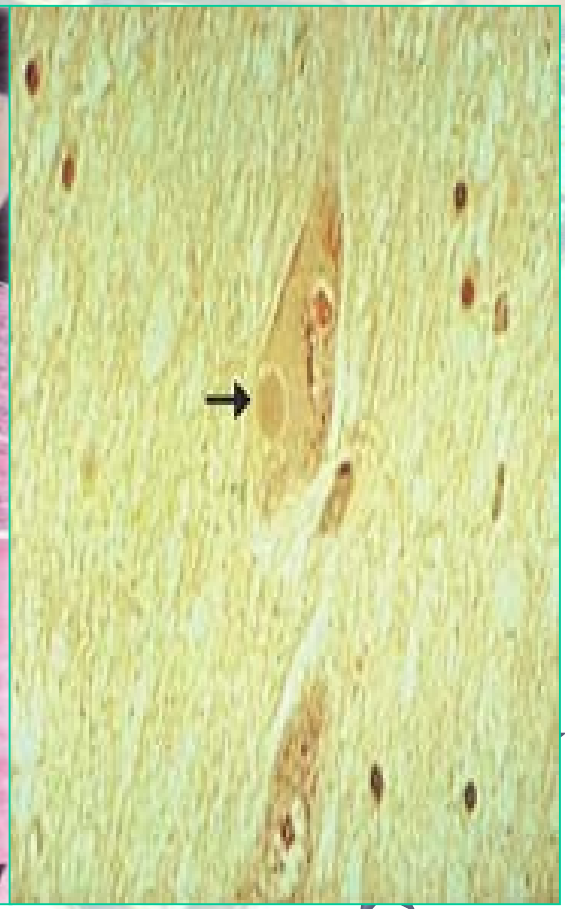
The most constant finding is the loss of pigmented cells in the substantia nigra and other pigmented nuclei in both idiopathic and symptomatic Parkinsonism.

Lewy bodies have attracted considerable attention over the years.

Parkinson's Disease

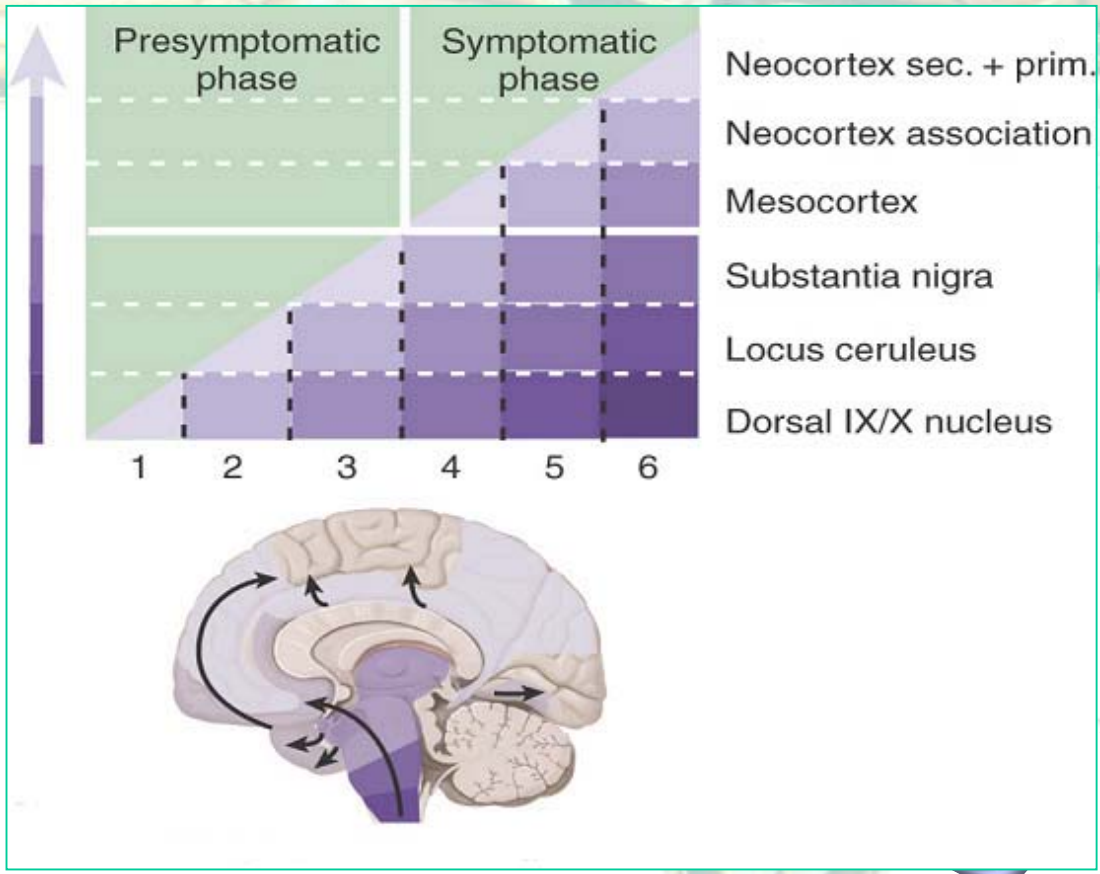
Pathology:





Parkinson's Disease

Pathology: Braak staging of PD



Parkinson's Disease

Etiology:

Idiopathic(Parkinson's disease):

Environmental factors+genetic basis?

Familial Parkinsonism: genetic factors

Symptomatic Parkinsonism:

Drugs- or toxin-induced:

Encephalitis Lethargica:

Other neurological diseases: Stroke

Parkinson's Disease

Etiology: Genetic Factors:

	Inheritance	Locus	Onset(y)	LB	Gene
Park1	Autosomal dominant	4q21	40s	+	α-Sunuclein
Park2	Autosomal recessive	6q25	20s	-	Parkin
Park3	Autosomal dominant	2p13	60s	+	?
Park4	Autosomal dominant	4q21	30s	+	α-Sunuclein
Park5	Autosomal dominant	4p15	50s	+	UCH-L1
Park6	Autosomal recessive	1p36	30s	?	Pink-1
Park7	Autosomal recessive	1p36	30s	?	DJ1
Park8	Autosomal dominant	12p	-	±	LRRK2
Park9	Autosomal recessive	1p36	-	?	?
Park10	Autosomal recessive	1p32	-	?	?
Park11	?	2q36-37		?	?

Parkinson's Disease

Etiology:

Genetic Factors:

PSP, CBD: tau H1 haplotype
FTDP-17 complex: tau mutation
X-linked parkinsonism-dystonia(Lubag)
SCA2 in Chinese: ataxin 2
SCA3/MJD: ataxin 3
Fragile X mental retardation: CGG repeat in FMR-1 gene NB premutation

Parkinson's Disease

Etiology:

Genetic Factors: Genetic association?

Wilson's disease

Hallevorden-Spatz syndrome: PANK2

Dopa responsive dystonia:

GTP cyclohydrolase 1

Dystonia-parkinsonism:

Na-K pump mutation

Parkinson's Disease

Etiology:

Genetic Factors:

Genetic association?

Parkinson's Disease

Etiology:

Environmental Factors:

Risk increase of rural residency, in particular young-onset PD

Herbicide and pesticide exposure:

MTPT implication:

Carbon monoxide:

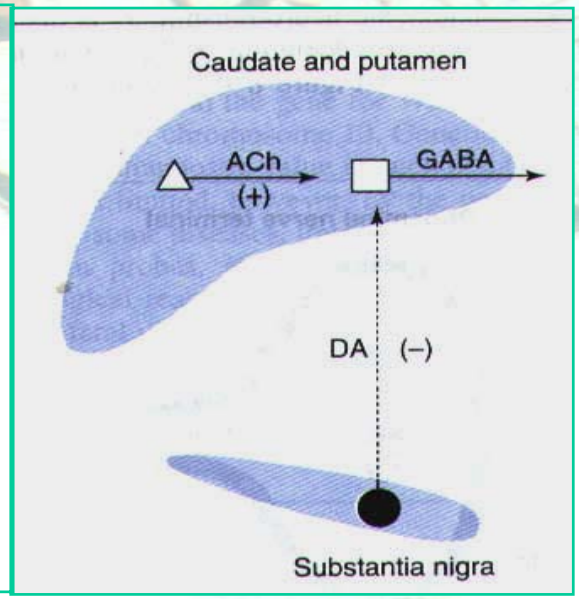
Manganses and other metal ions:

Smoking and coffee:

Parkinson's Disease

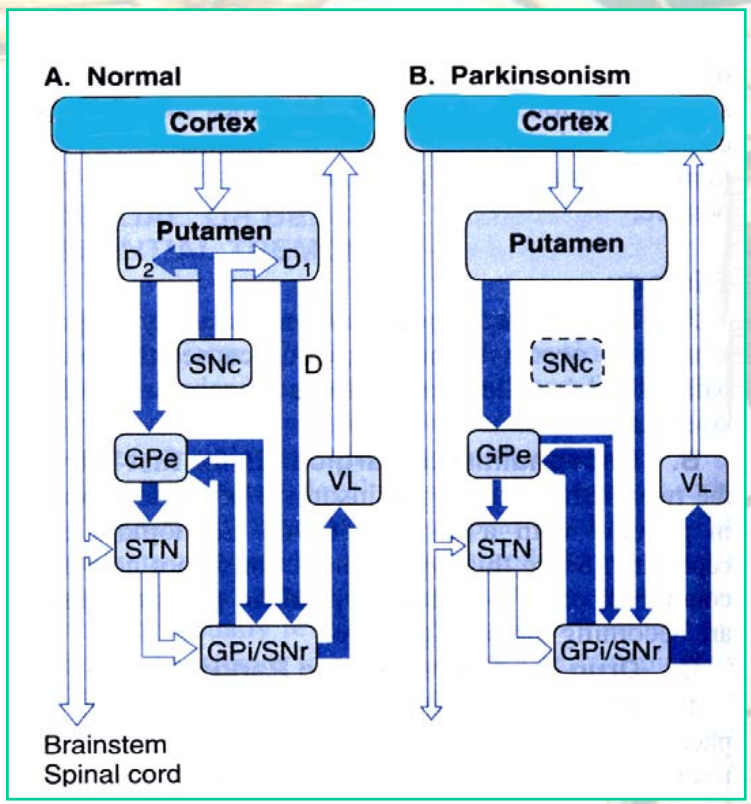
Pathogenesis:

Dopamine depletion due to degeneration of the dopaminergic nigrostriatal system leads to an imbalance of dopamine and acetylcholine.



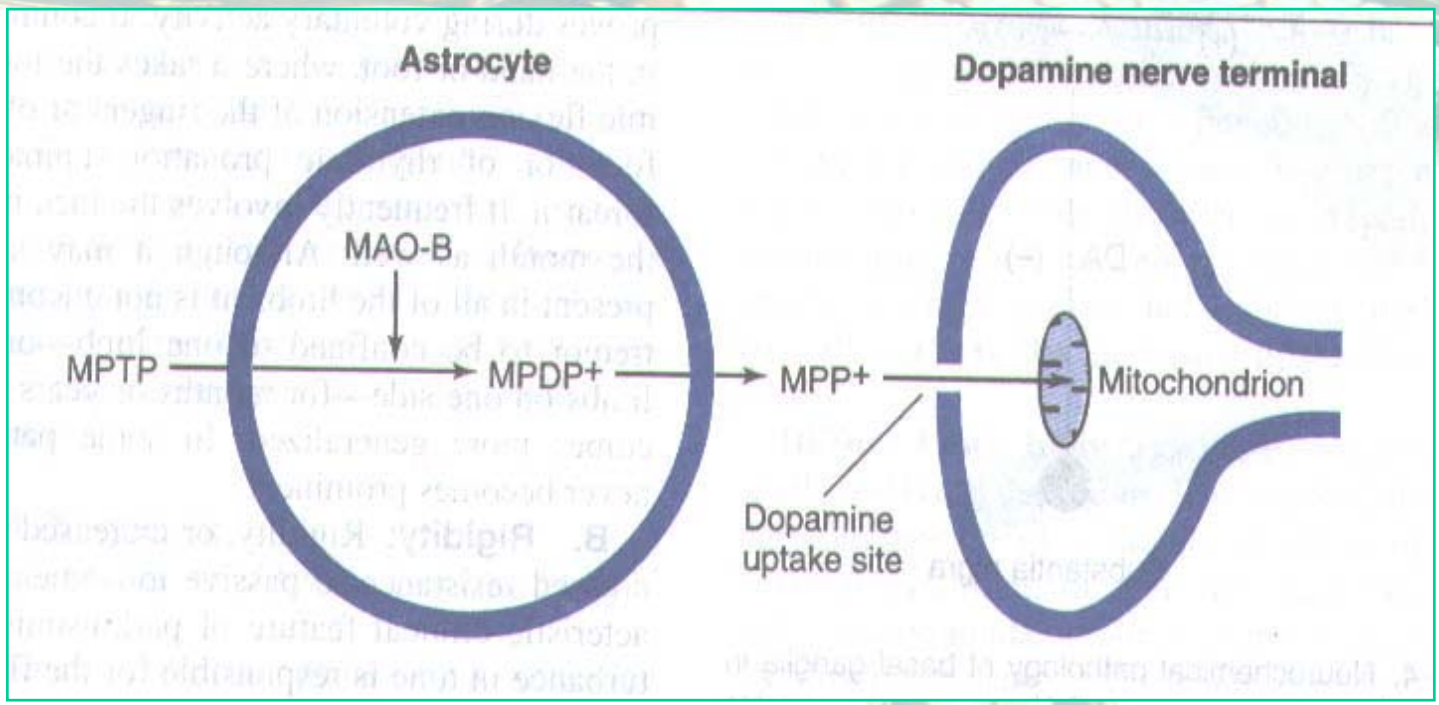
Parkinson's Disease

Pathogenesis:



Parkinson's Disease

Pathogenesis



Parkinson's Disease

Pathogenesis:

Cu/Iron-associated pathogenesis:

Oxidative stress:

Mitochondrial dysfuction:

Parkinson's Disease

Clinical Findings:

Presyptomatic phase:

Olfactory dysfunction

Rapid eye movement behavior disorder

Constipation

Parkinson's Disease

Clinical Findings:

Motor symptoms:

* Tremor
* Rigidity:
* Hypokinesia:
* Abnormal gait and posture:

Parkinson's Disease

Clinical Findings:

Nonmotor symptoms:

* Cognitive decline and Dementia:
* Other clinical feature:
  Seborrhea of skin, drool and sweating, blepharoclonus, constipation

Parkinson's Disease

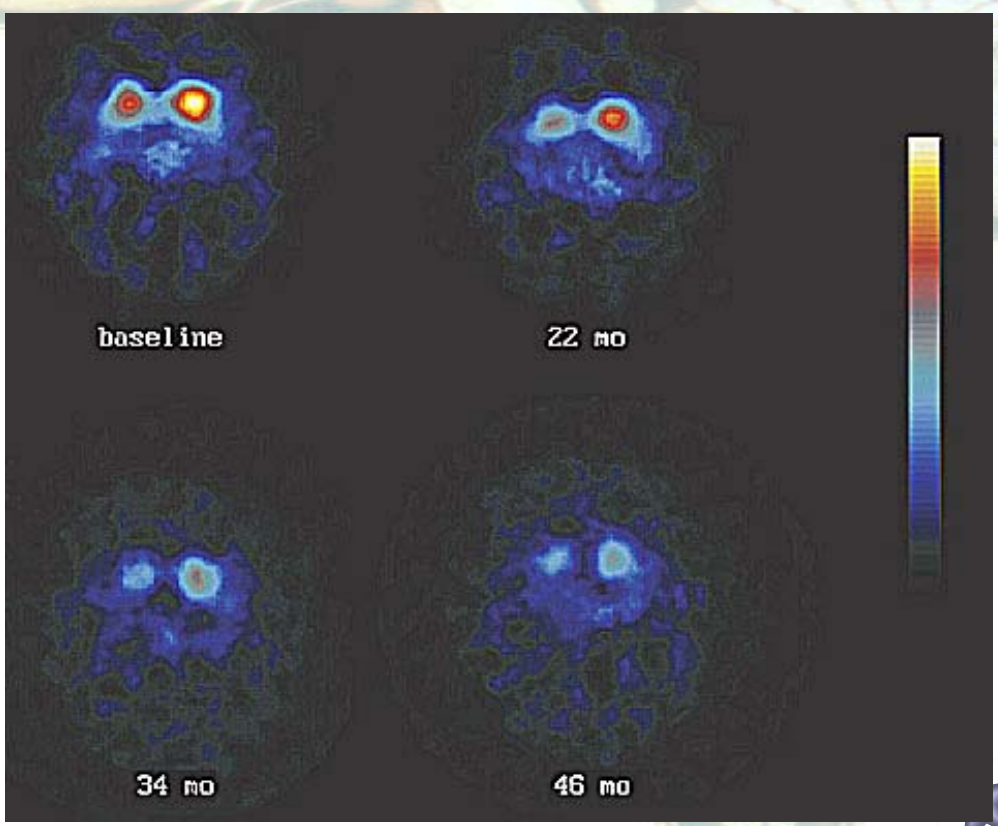
Clinical Findings:

Symptoms less responsive to dopaminergic therapy

Motor	Postural instability, gait disorders, speech problems
Mental changes	Depression, anxiety & apathy, dementia
Autonomic NS dysfunction	Orthostatic hypotension, constipation, sexual dysfunction, urinary problems, Sweating
Sensory phenomenon	Pain, dysesthesias
Sleep disturbances	Sleep fragmentation, sleep apnea, REM behavioral disorder

Parkinson's Disease

Clinical Findings: Investigate studies:



Parkinson's Disease

Clinical Findings: Investigate studies:

UPDRS:

Hoehn & Hayr staging:

Parkinson's Disease

Diagnosis:

Any combination of

tremor,

rigidity,

bradykinesia,

progressive postural instability

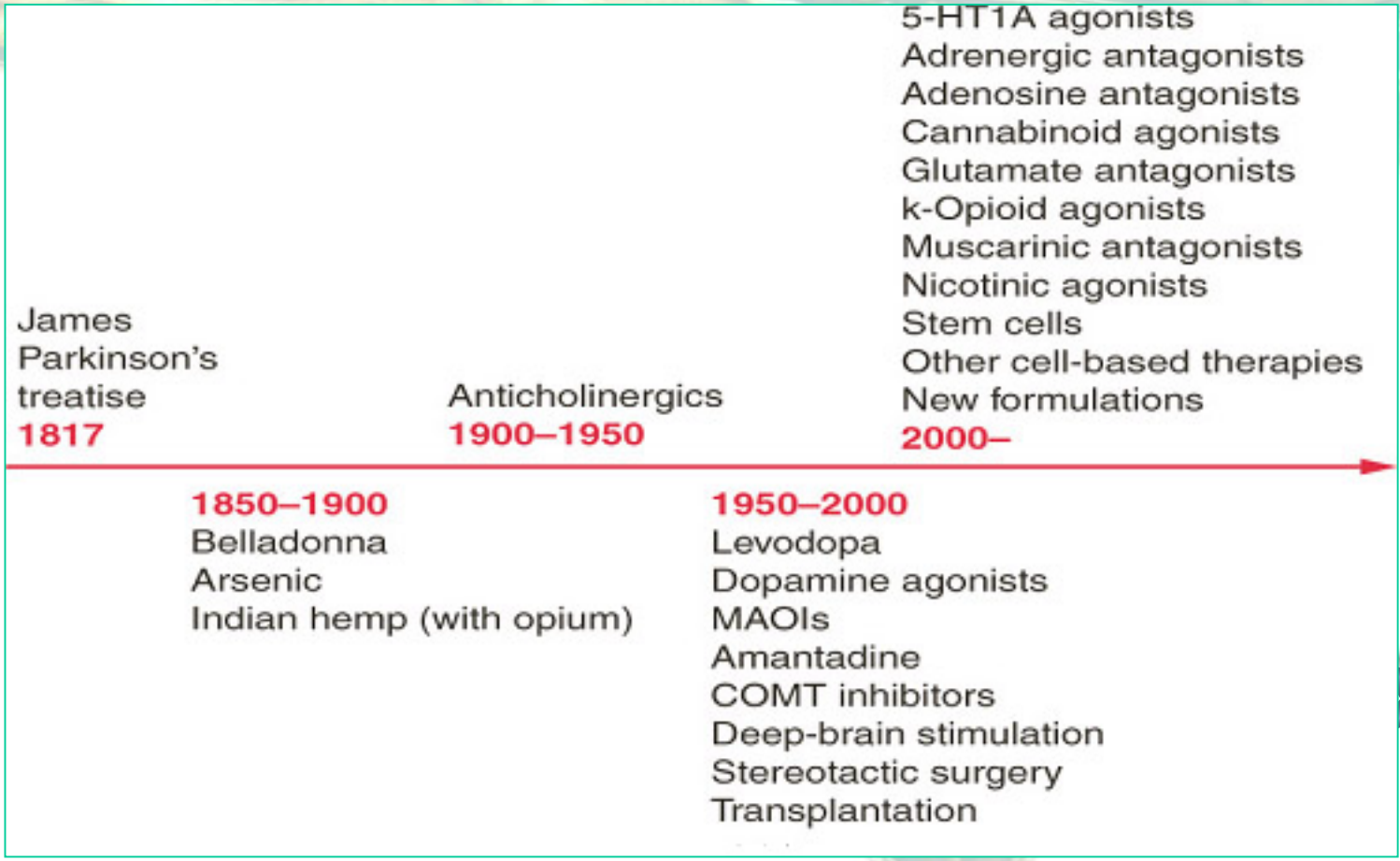
Parkinson's Disease

Differentiation:

* Parkinson's disease and syndromes:
* Parkinson plus and Multiple system atrophy : Striatonigral degeneration
  progressive supranuclear palsy
* Senile tremor:
* Familial or idiopathic tremor:
* Alcoholism:
* Thyrotoxicosis and Hepatic cirrhosis :
* Other :

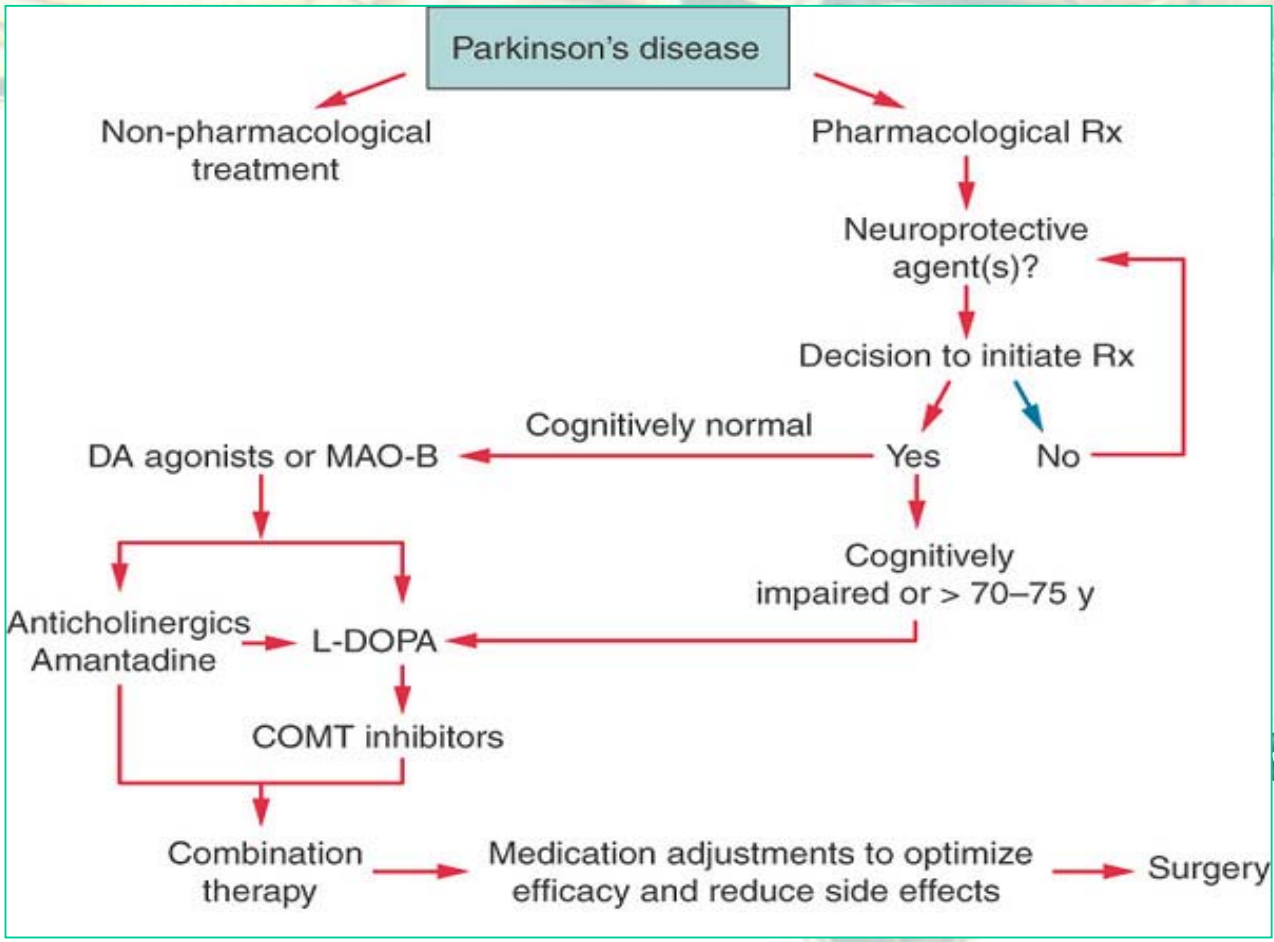
Parkinson's Disease

Treatment:



Parkinson's Disease

Treatment:



Parkinson's Disease

Treatment:

* Amantadine:

An antiviral agent. To act by releasing dopamine from striatal neurons, blocking re-intake of the dopamine, and anticholinergic property?

To patients with mild symptoms, it improves all of the clinical features of parkinsonism.

Parkinson's Disease

Treatment:

* Anticholinergic drugs:

More helpful in alleviating tremor and rigidity than bradykinesia.

Treatment is started with a small dose.

Parkinson's Disease

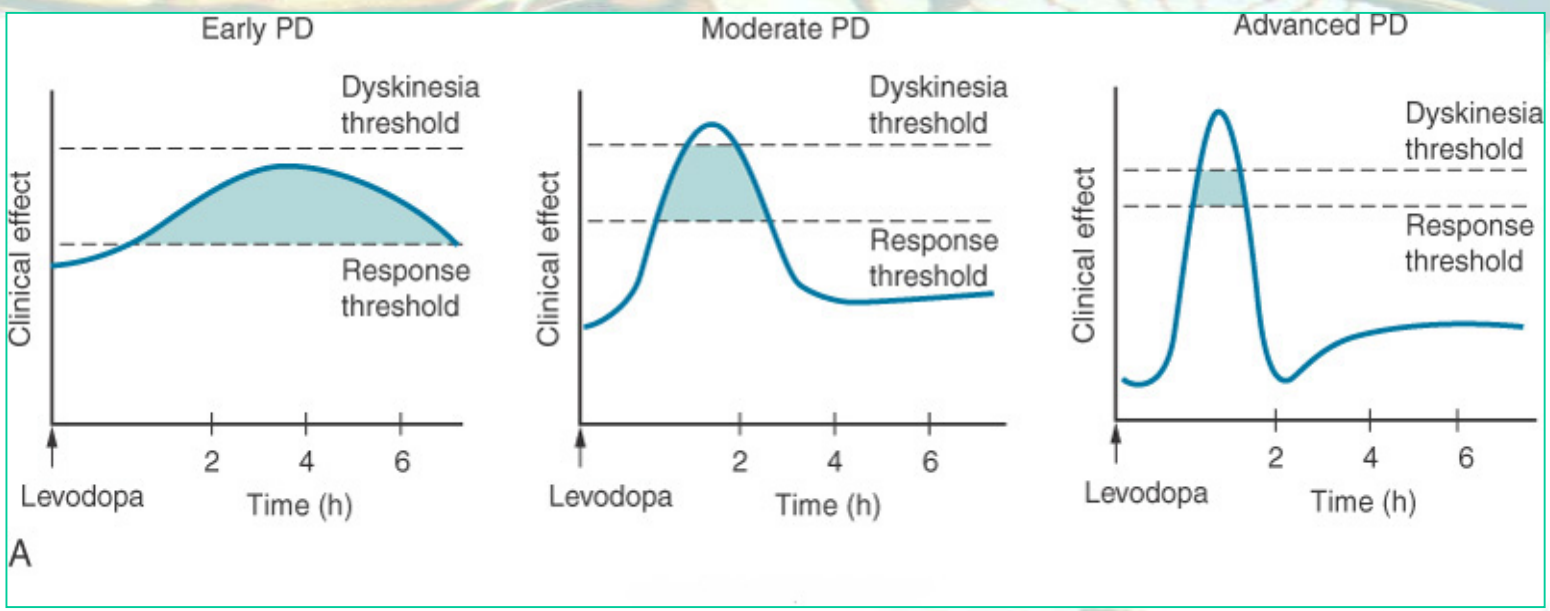
Treatment:

* Levodopa:

Converted in the body to dopamine, it improves all of the major features of Parkinson's disease, but does not stop progression of the disorder.

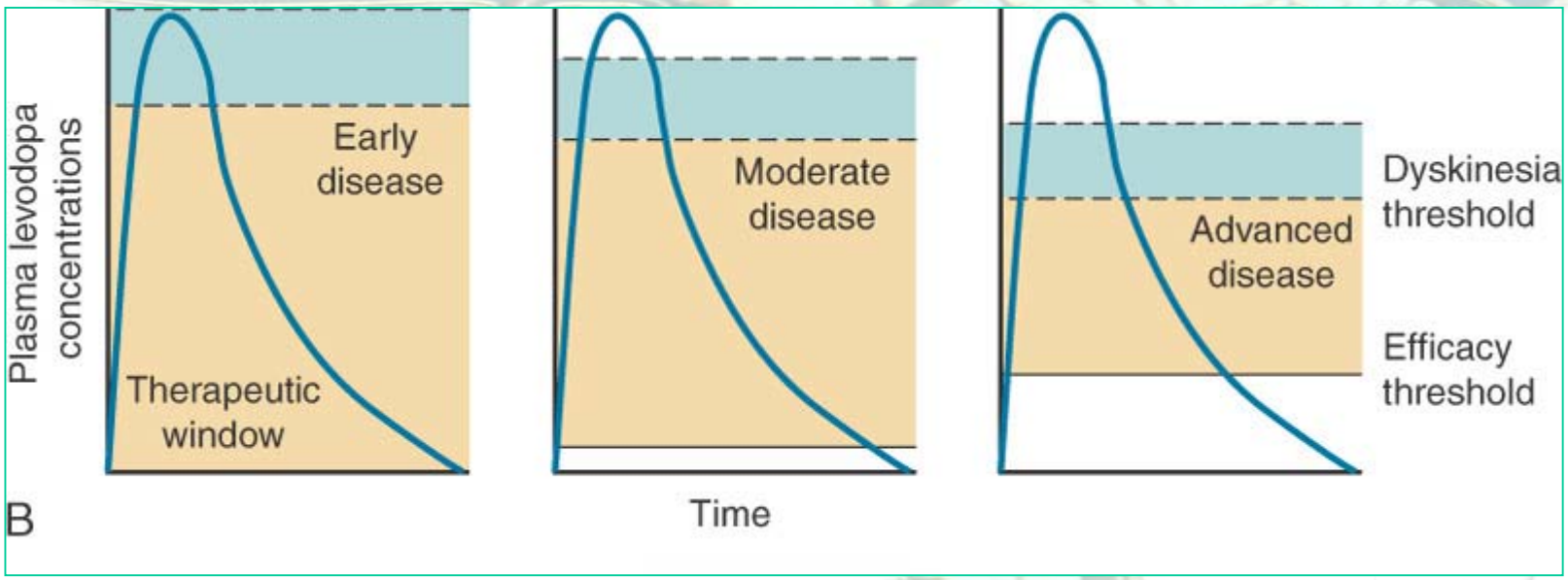
Parkinson's Disease

Treatment: Levodopa:



Parkinson's Disease

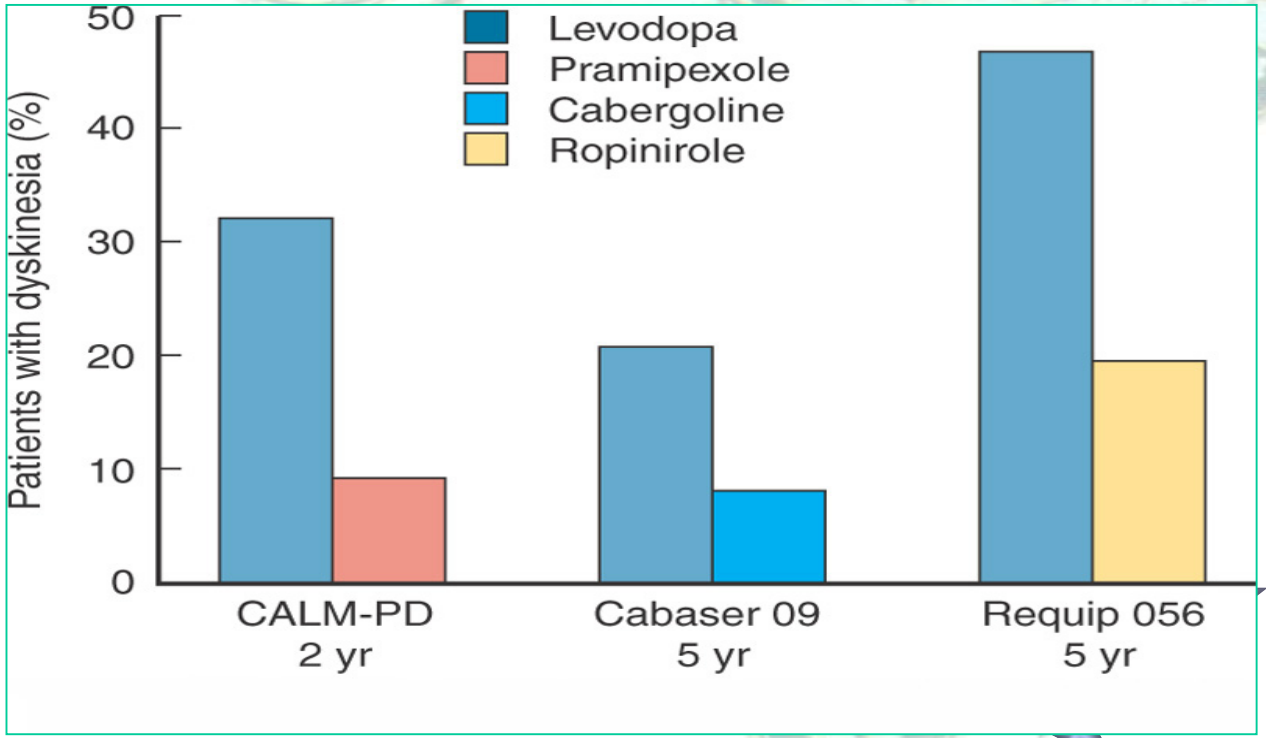
Treatment: Levodopa:



Parkinson's Disease

Treatment:

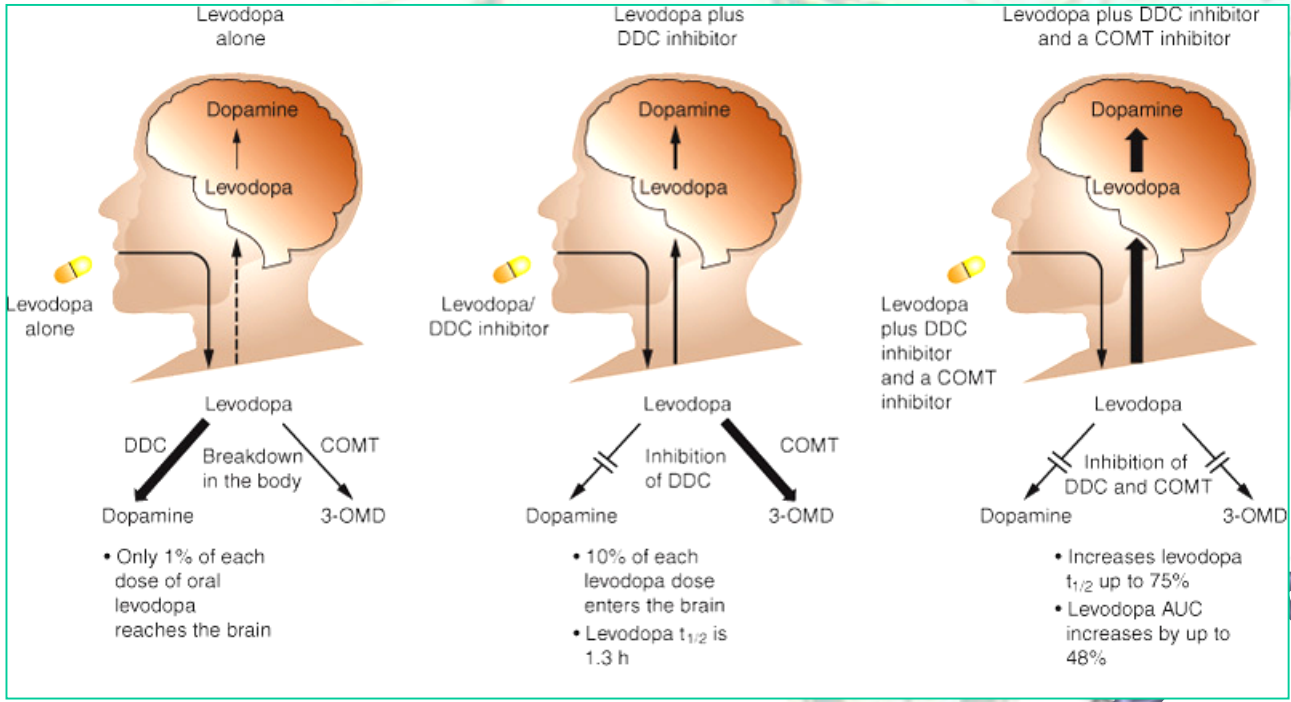
Dopamine agonists:



Parkinson's Disease

Treatment:

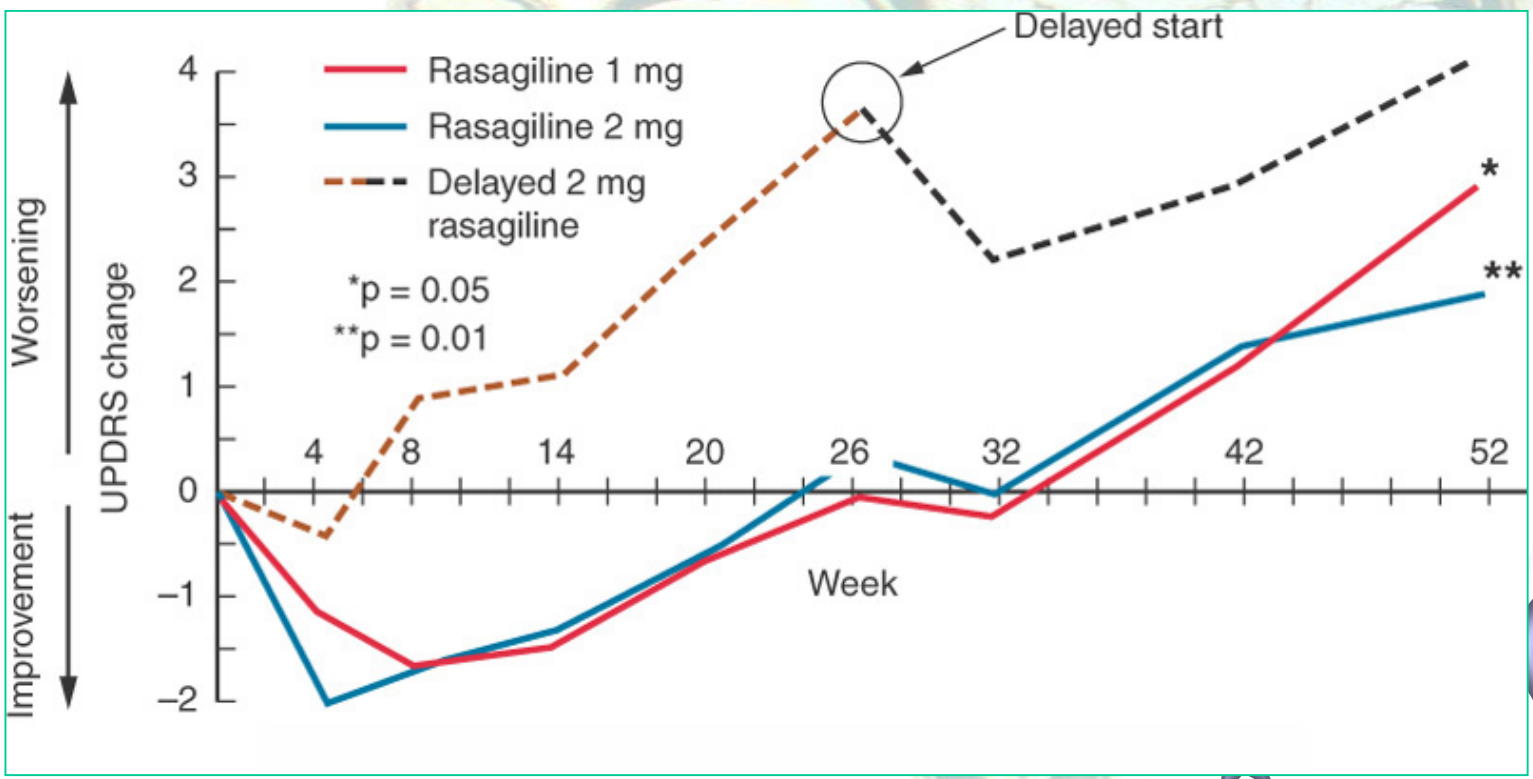
Catechol-O-methyltransferase inhibitors



Parkinson's Disease

Treatment:

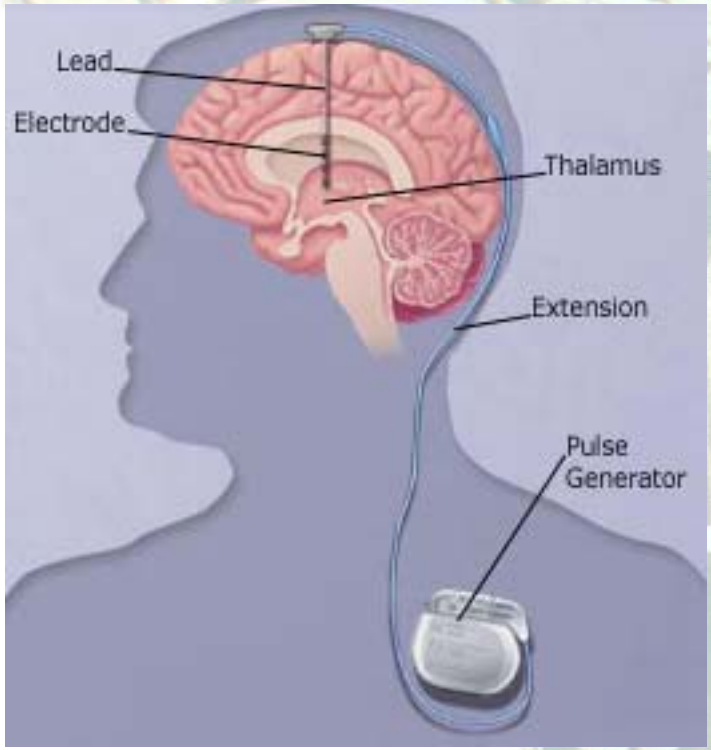
Monoamine oxidase-B inhibitors



Parkinson's Disease

Treatment:

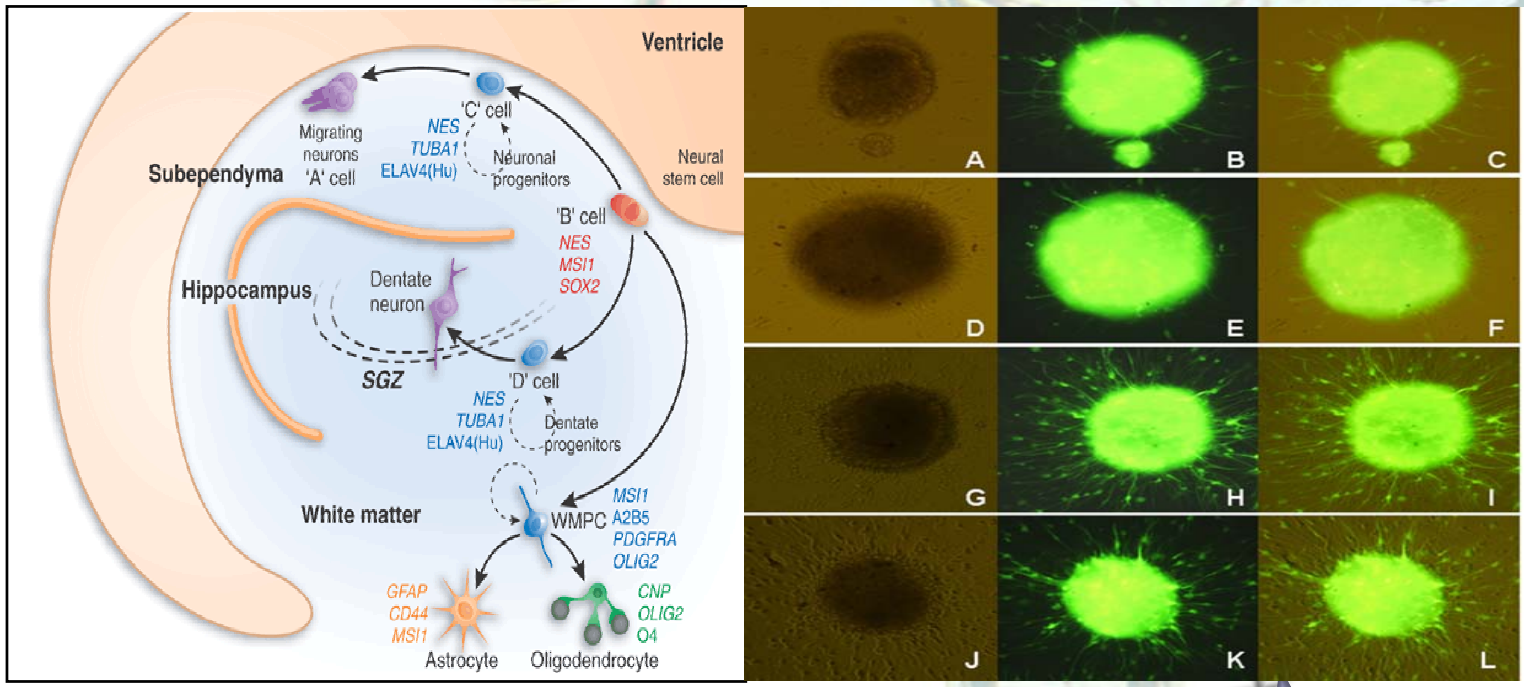
Surgery and Deep brain stimulation:



Parkinson's Disease

Treatment:

Stem cell therapy:



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Parkinson's Disease

Treatment:

Neural protection:

- Dopamine agonists
- MAO-B inhibitors
- Coenzyme Q_{10}

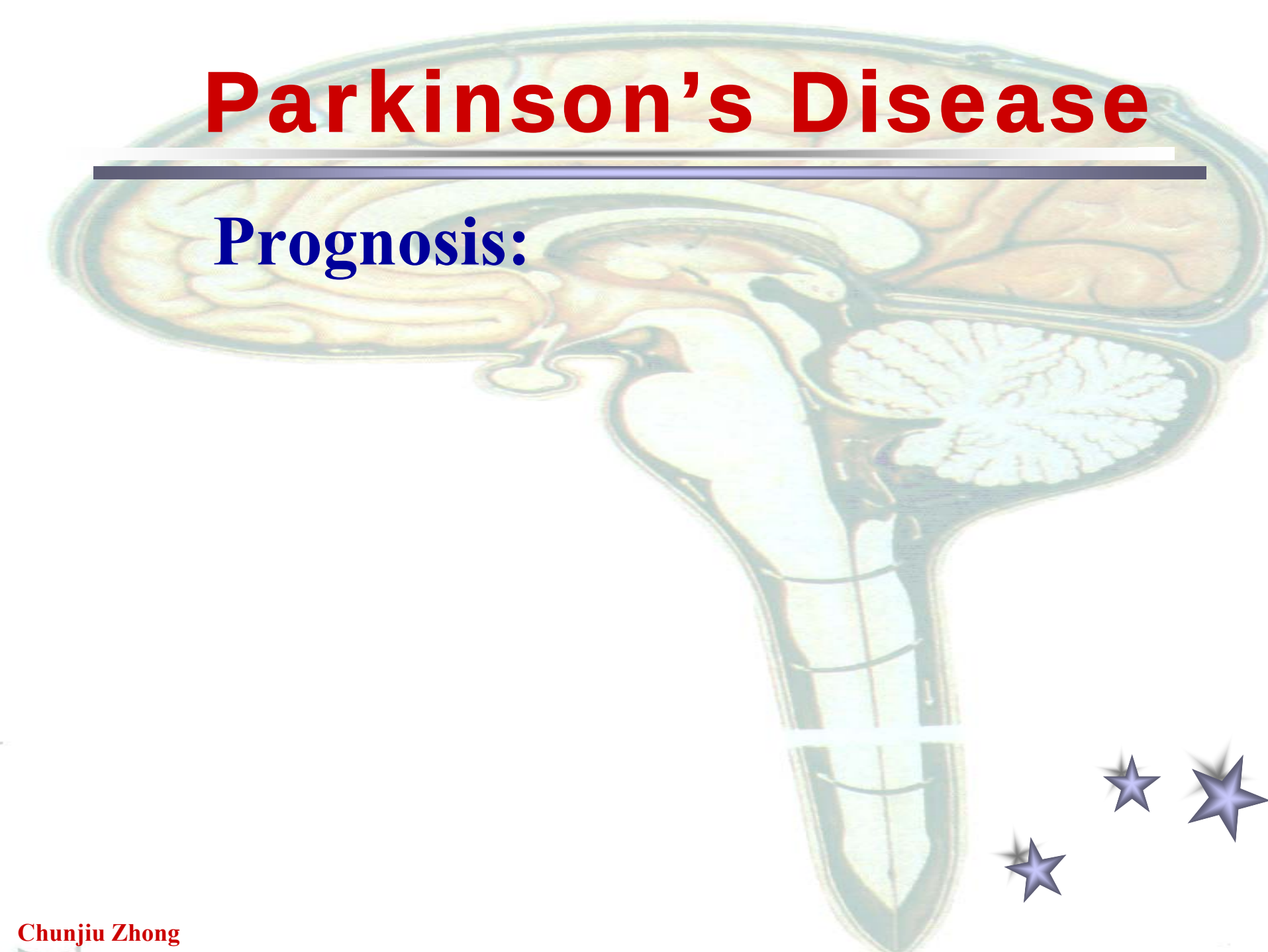
Parkinson's Disease

Treatment:

Physical therapy
and aids for daily living:

Parkinson's Disease

Prognosis:



Wilson's Disease

Etiology and Pathogenesis:

Clinical Features:

Treatment:

Prognosis:

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