Movement Disorders

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Neurology Diagnosis

Two main questions:

- What parts of the nervous system are affected?
- What is the etiology?

Answers based on:

- History
- Clinical examination
- Investigations

Phenomenological Classification of Movement Disorders

- Movement Disorders are classified broadly into two main groups:

  HYPOKINETIC DISORDERS: too little movement

  bradykinesia (slowness of movements)

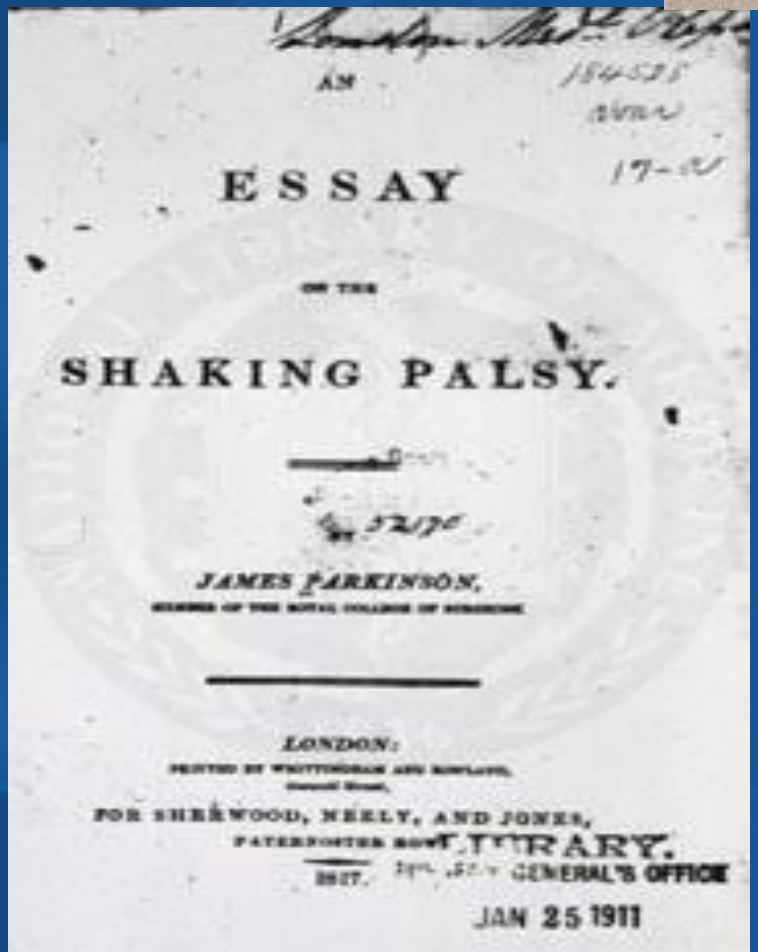
  (Parkinson's Disease and other akinetic rigid syndromes)

  HYPERKINETIC DISORDERS: too much movement

  dyskinesias- (different types of involuntary movements)

Parkinson's Disease

- Published 1817



AN

ESSAY

ON THE

SHAKING PALSY.

JAMES PARKINSON,

LONDON:

FOR SHERWOOD, NEELY, AND JONES,

1817.

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.

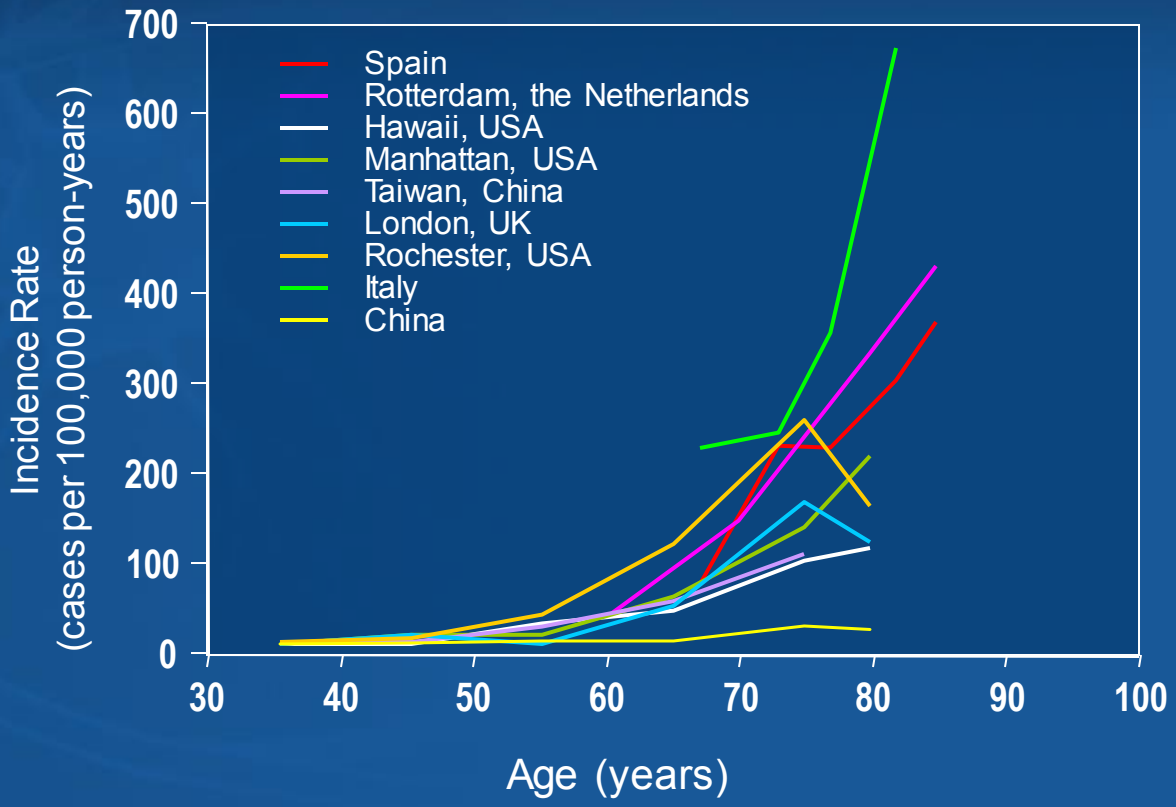
Parkinson's Disease – Definition

- **Parkinson's disease:**
  - A clinical and neuropathological entity characterised by:
    - Bradykinesia
    - Rigidity
    - Tremor
  - Onset usually asymmetric and responsive to dopaminergic treatment
  - No historical or examination clues to indicate secondary parkinsonism (e.g. Wilson's disease, multiple system atrophy)
  - The brunt of the early pathology falls on the dopaminergic nigrostriatal pathway

- **Parkinsonism:**
  - Any bradykinetic-rigid syndrome that is not Parkinson's disease

Epidemiology of Parkinson's Disease – Incidence

- **Idiopathic Parkinson's disease is uncommon before the age of 50**
- **There is a sharp increase in incidence after the age of 60**



Prospective population-based incidence studies of Parkinson's disease

de Lau LM, Breteler MM. *Lancet Neurol* 2006;5:525-35.

Risk Factors for PD

- Increased risk
  - Age
  - Family history
  - Exposure in early life to
    - Well water
    - Pesticides
  - Head injury
- Decreased risk
  - Caffeine
  - Cigarettes

Anatomy of The Basal Ganglia

The Basal Ganglia are “large subcortical nuclei derived from the telencephalon forming connections between the cortex and thalamus providing for the ease and quickness of human movement” .

- Striatum
  - caudate
  - putamen
- Globus Pallidus
  - Externa/Interna
- Substantia Nigra

  Pars compacta/reticulata
- Subthalamic Nucleus

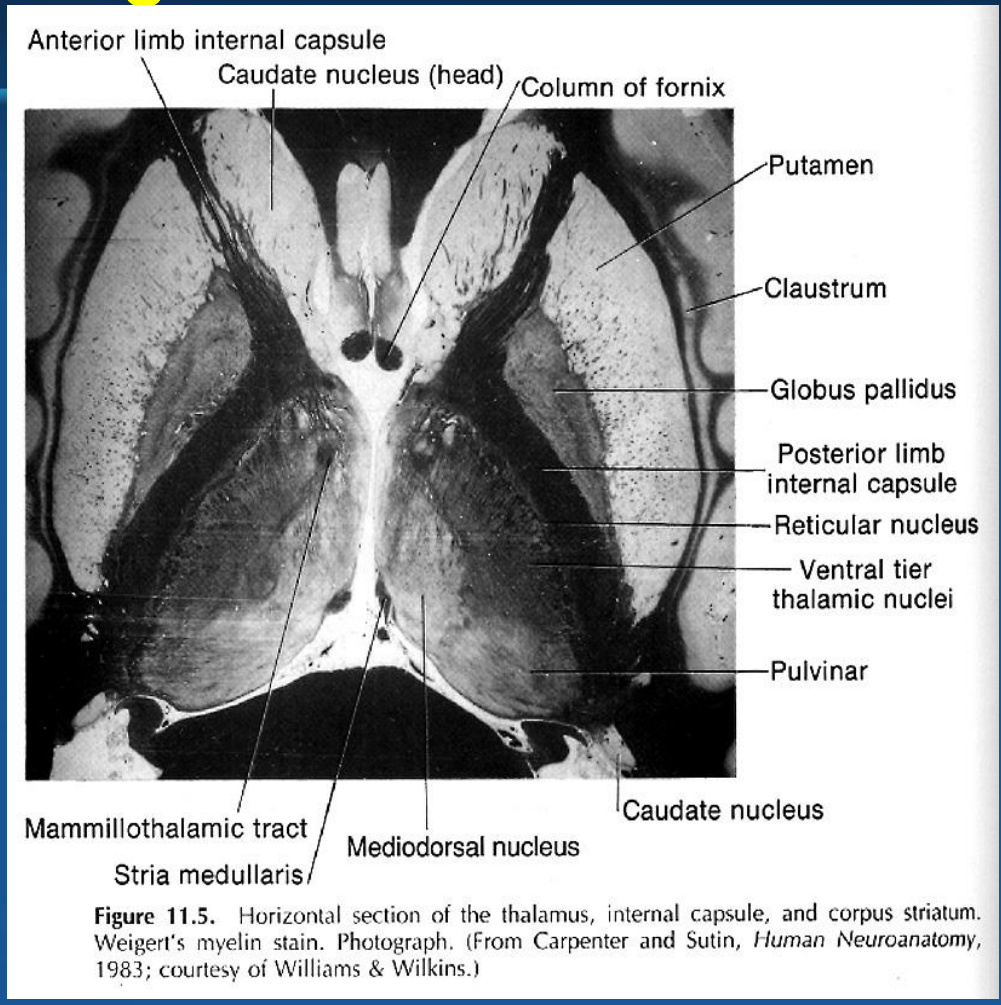
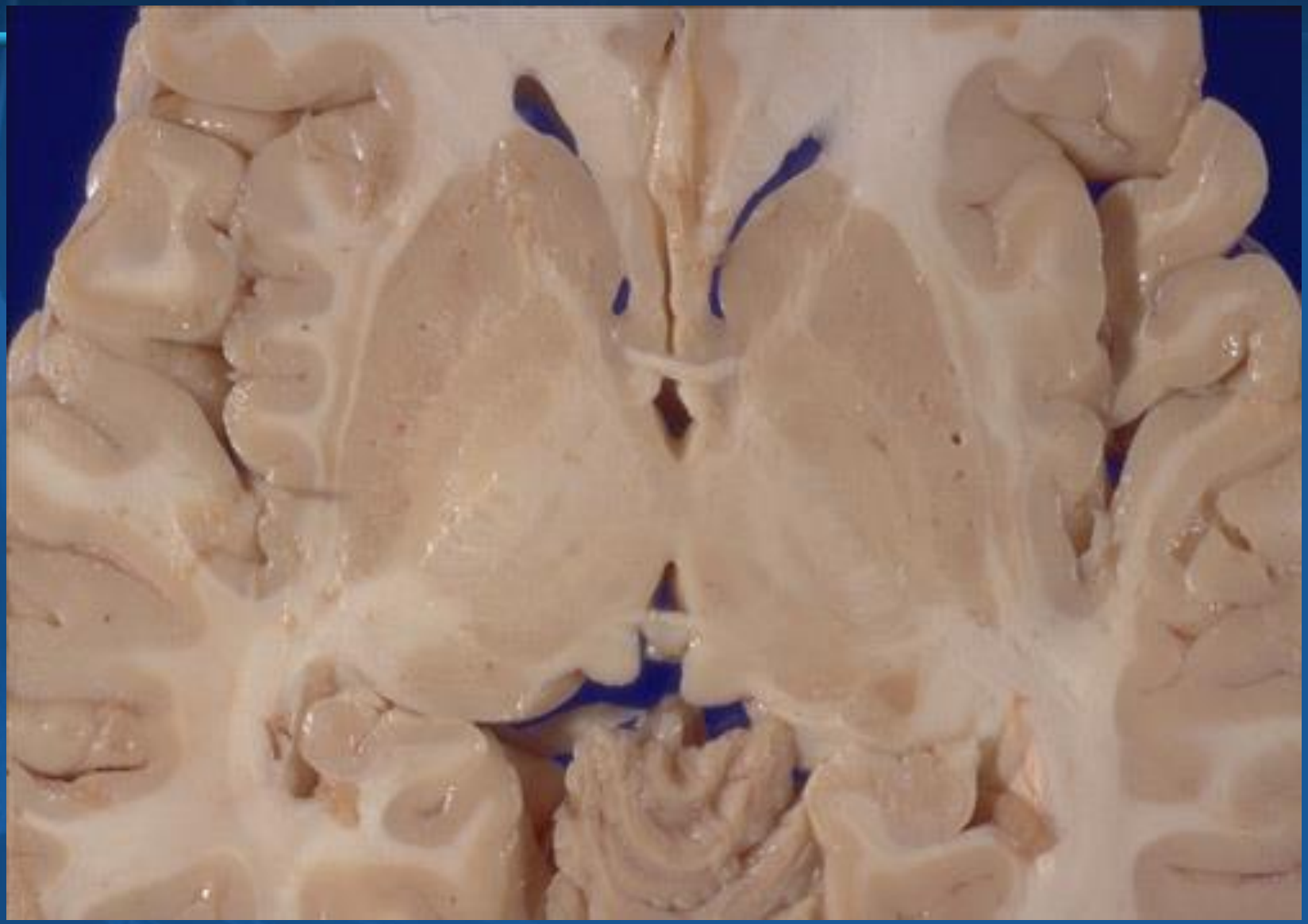
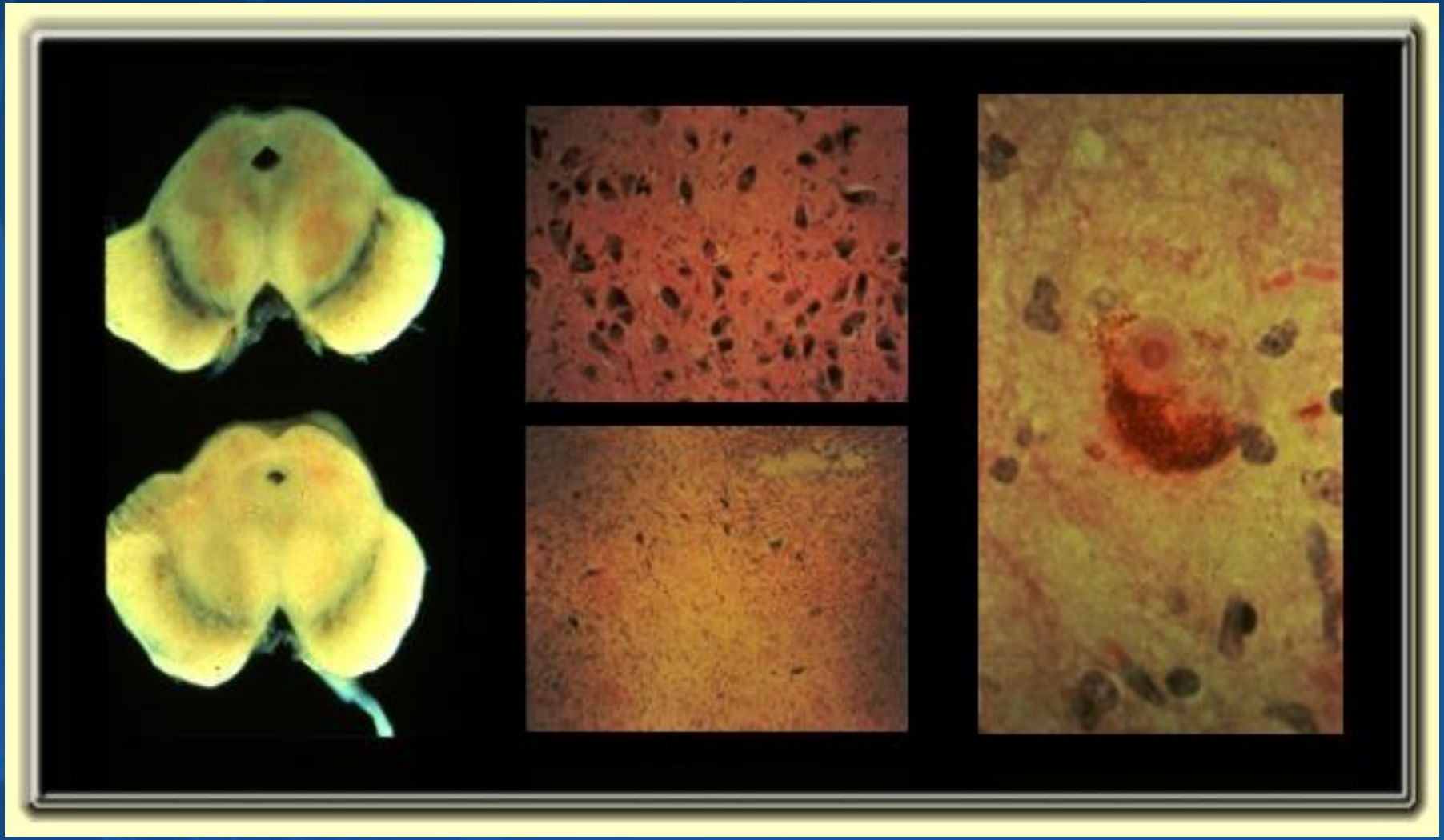


Figure 11.5. Horizontal section of the thalamus, internal capsule, and corpus striatum. Weigert's myelin stain. Photograph. (From Carpenter and Sutin, *Human Neuroanatomy*, 1983; courtesy of Williams & Wilkins.)

Cross section of the Brain at the level of the BG



Pathology of Parkinson's Disease



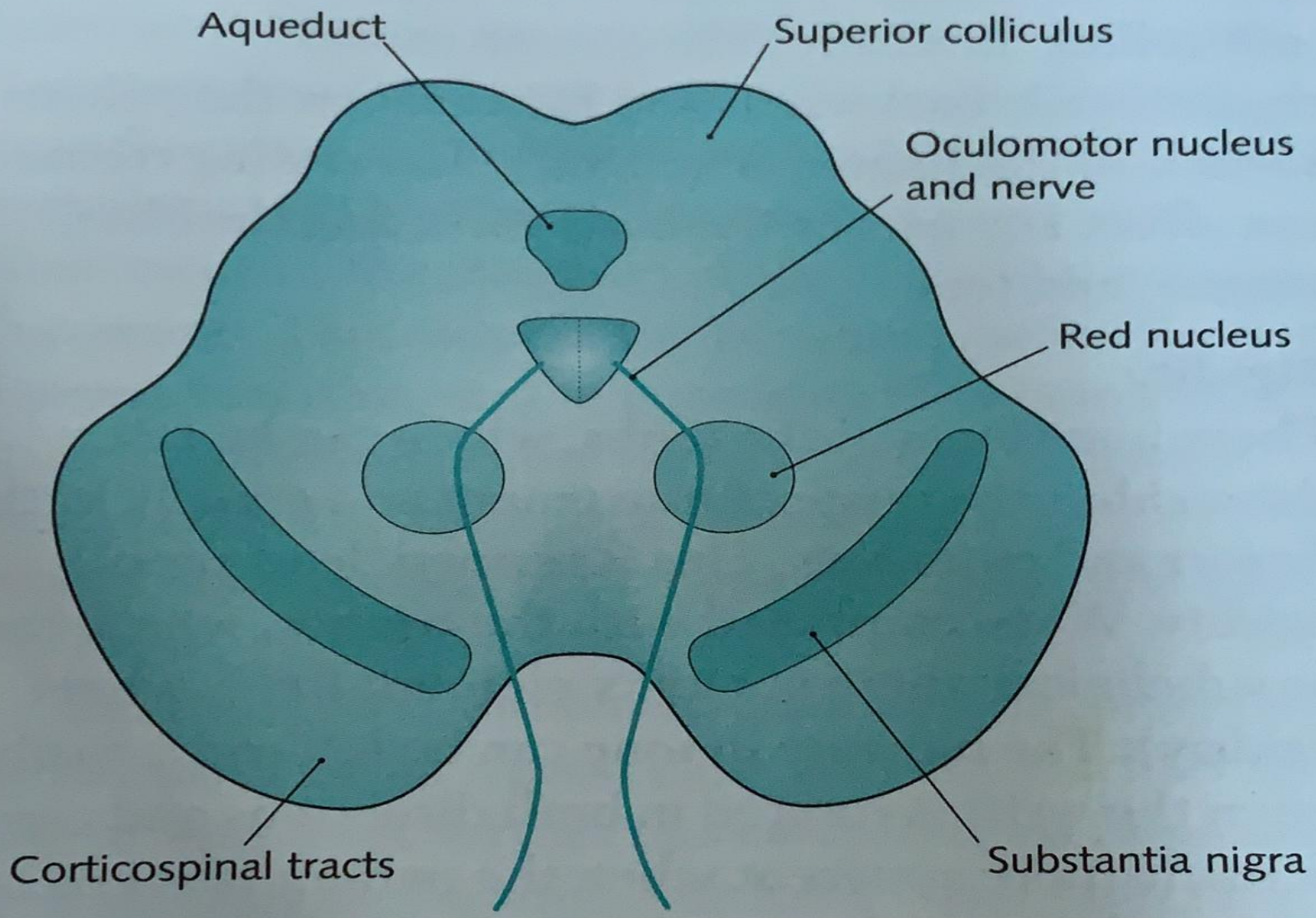
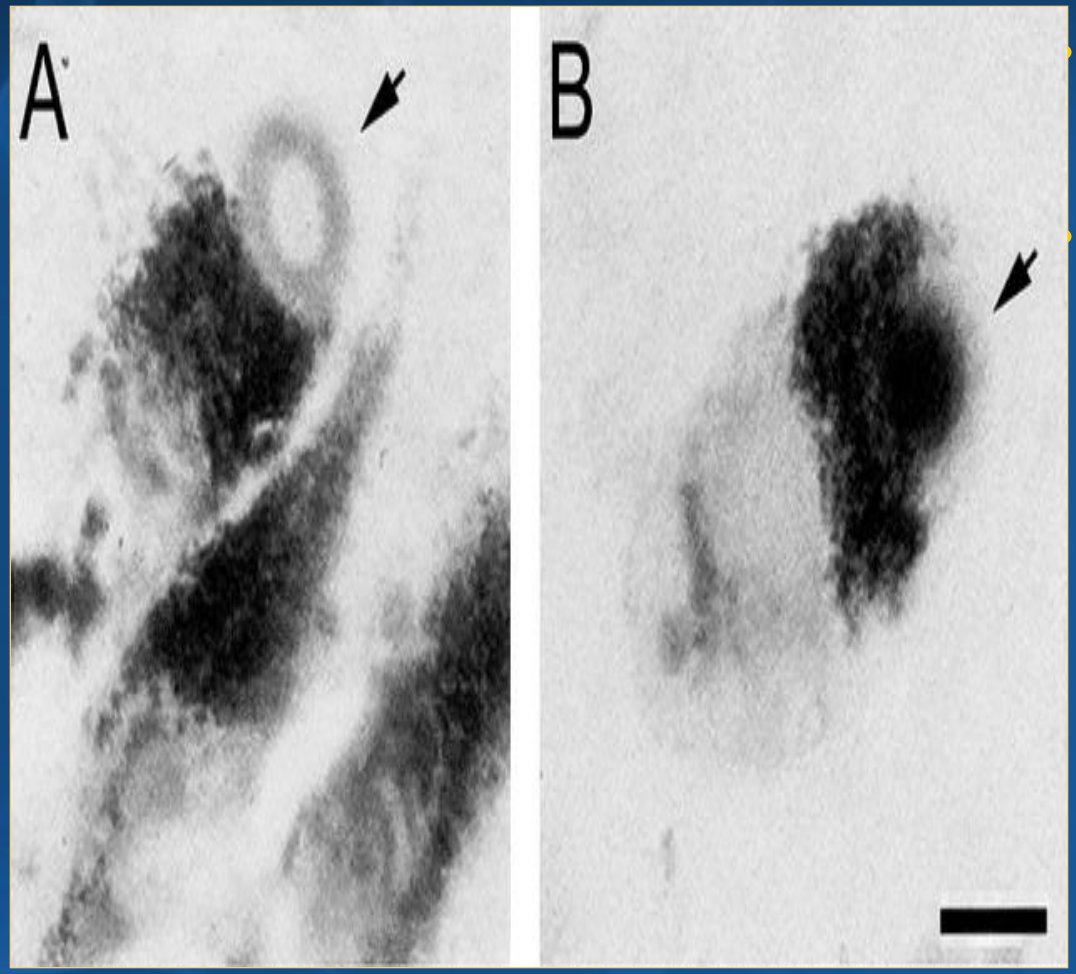


Fig. 18.1 Cross-section of the midbrain.

Parkinson's Disease Pathology
Lewy bodies



- Neuronal loss and gliosis in the substantia nigra and other brain regions.
- Lewy bodies, 5-25 μm eosinophilic intracytoplasmic inclusions with a dense core and more transparent halo, and Lewy neurites are typically present. Lewy bodies stain for both α-synuclein and ubiquitin

α-synuclein

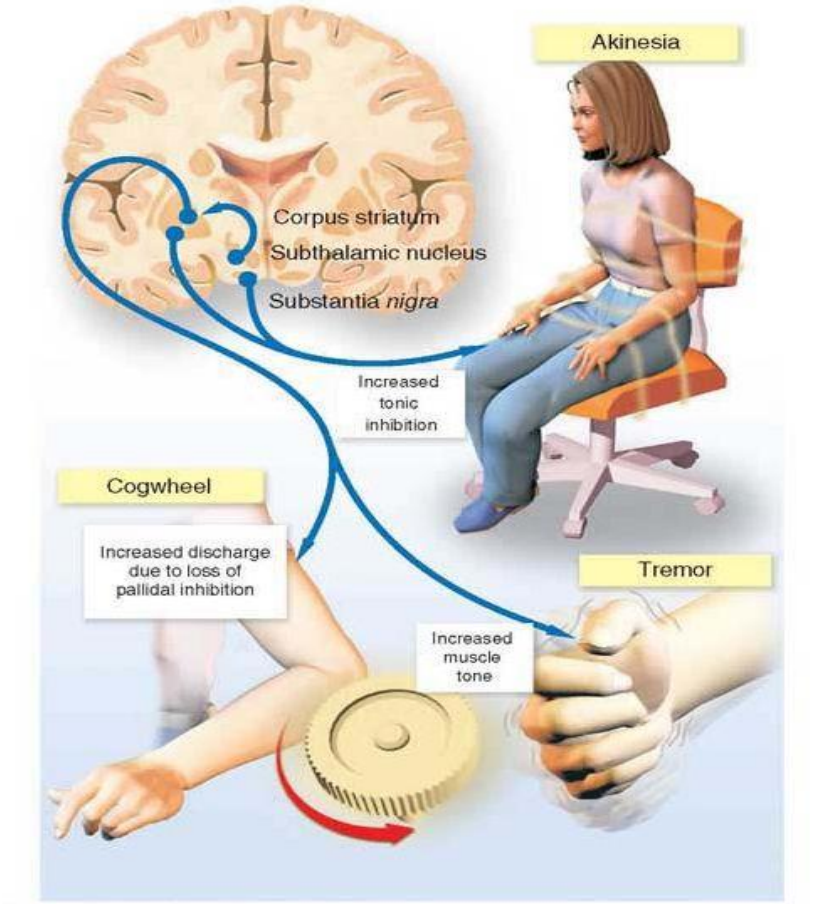
Ubiquitin

Main Biochemical Abnormality

- Marked striatal Dopamine (DA) depletion
- <50% DA loss is asymptomatic
- ~70% DA loss for symptom manifestations
- At death, DA loss > 90%
- Severity of DA loss best correlates with bradykinesia in PD

Diagnosis / differential diagnosis

Cardinal features of Parkinsonism



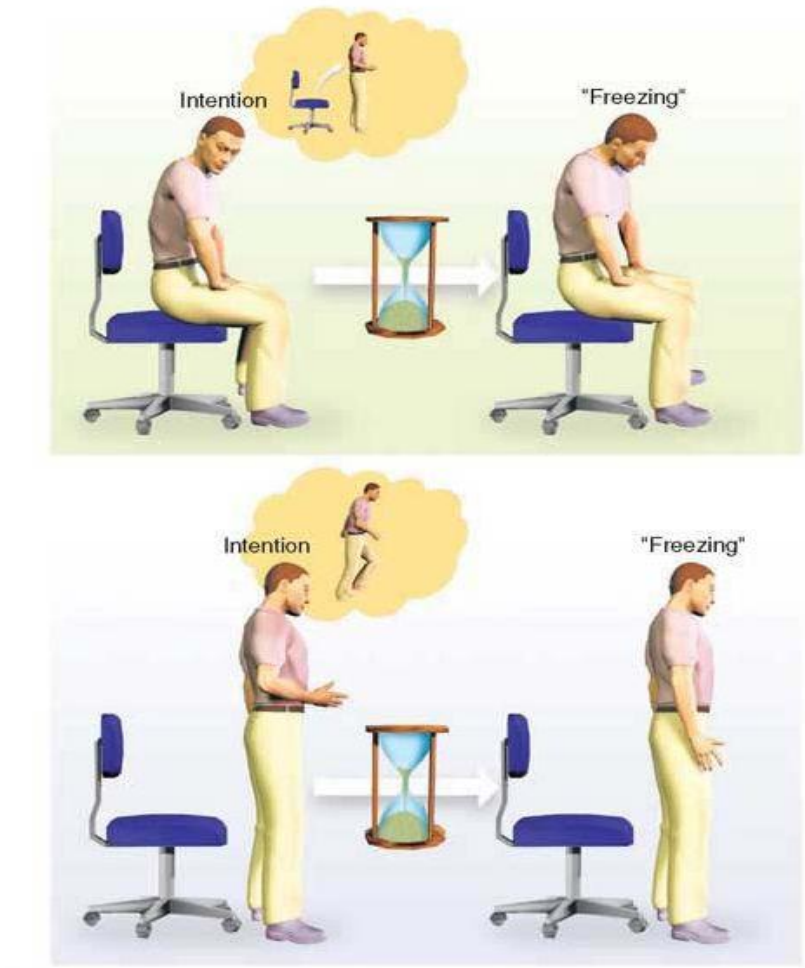
Need 2/3 of:

- Tremor
  - Rest (4-6 Hz)
  - Postural
- Bradykinesia
- Rigidity

-/+ Postural reflex impairment

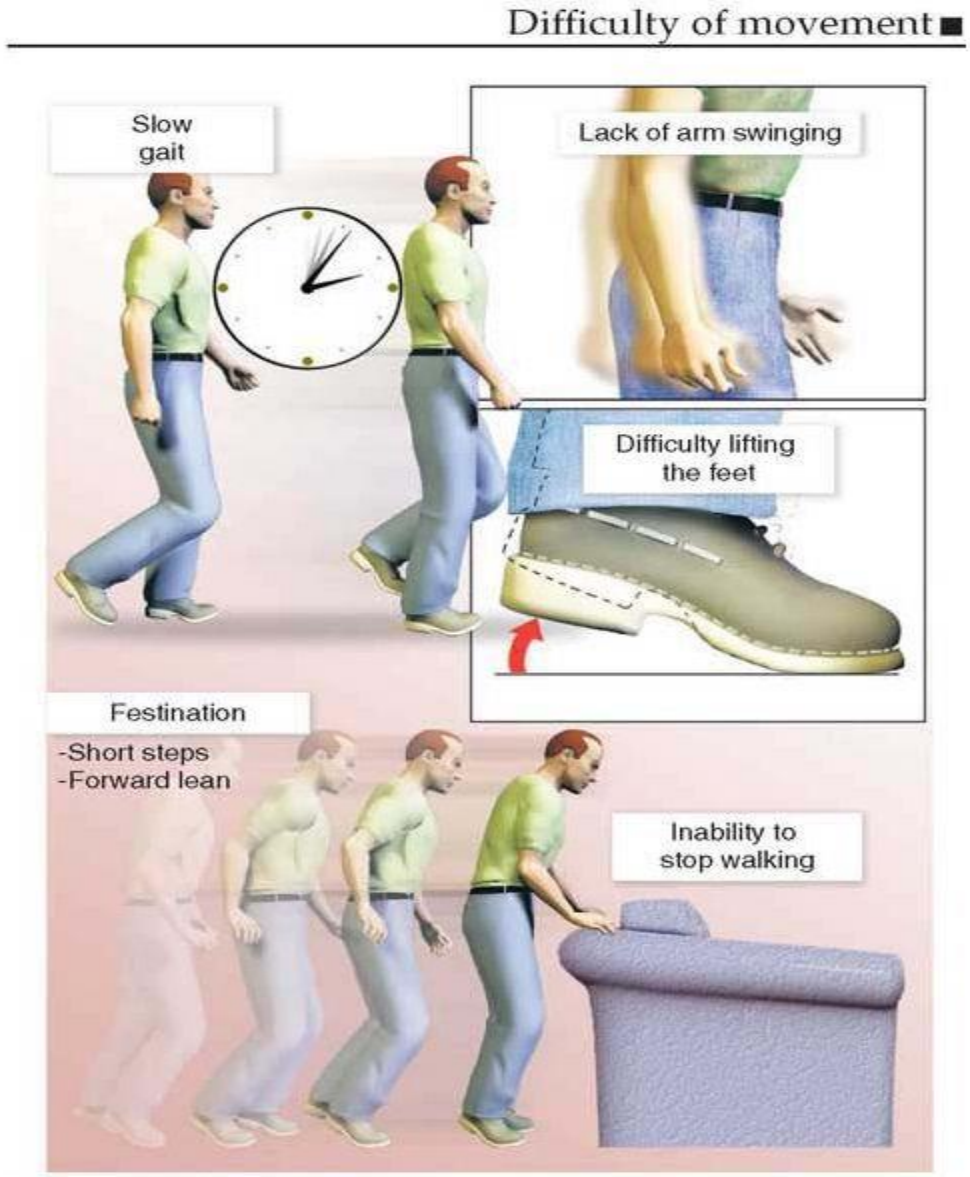
- Tremor
- Rigidity
- Akinesia
- Postural Instability

Bradykinesia

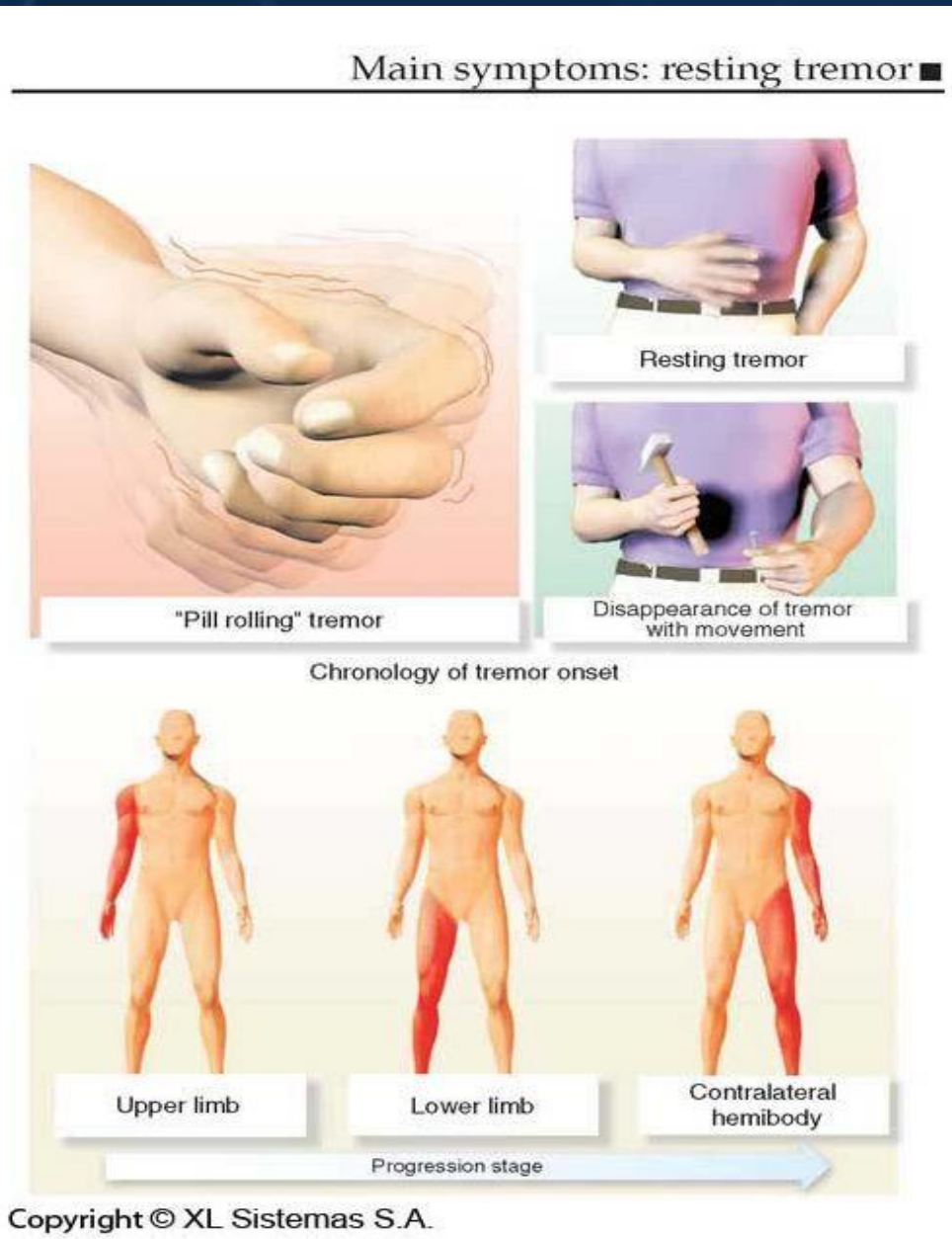


Bradykinesia includes such motor phenomena as delayed initiation, slow performance, low amplitude and intermittent arrests of voluntary movement.

Bradykinesia



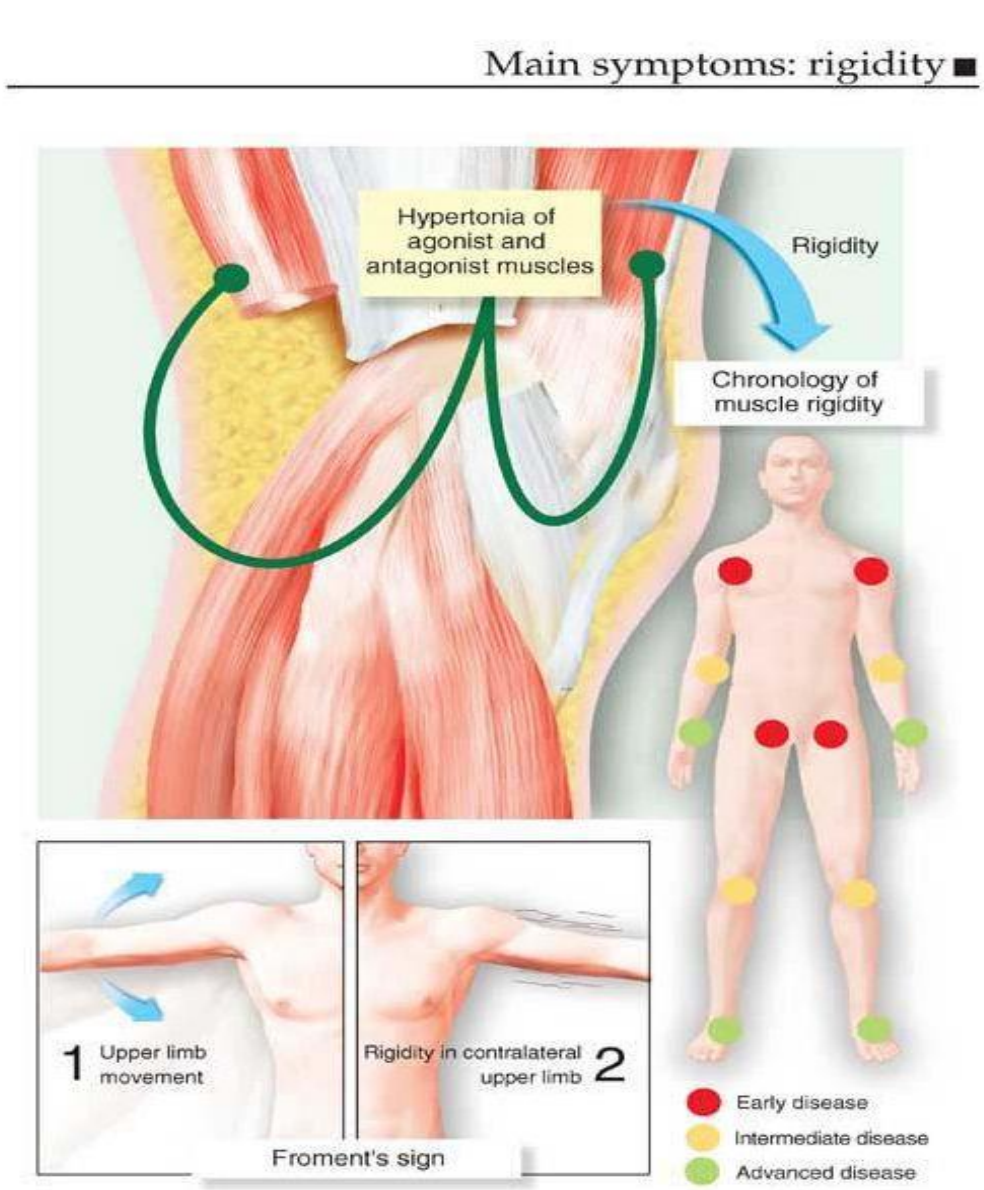
Tremor



The tremor of parkinsonism is seen at rest- frequency is typically 4-6 Hz.

Postural tremor is commonly seen, but is much less specific for the syndrome.

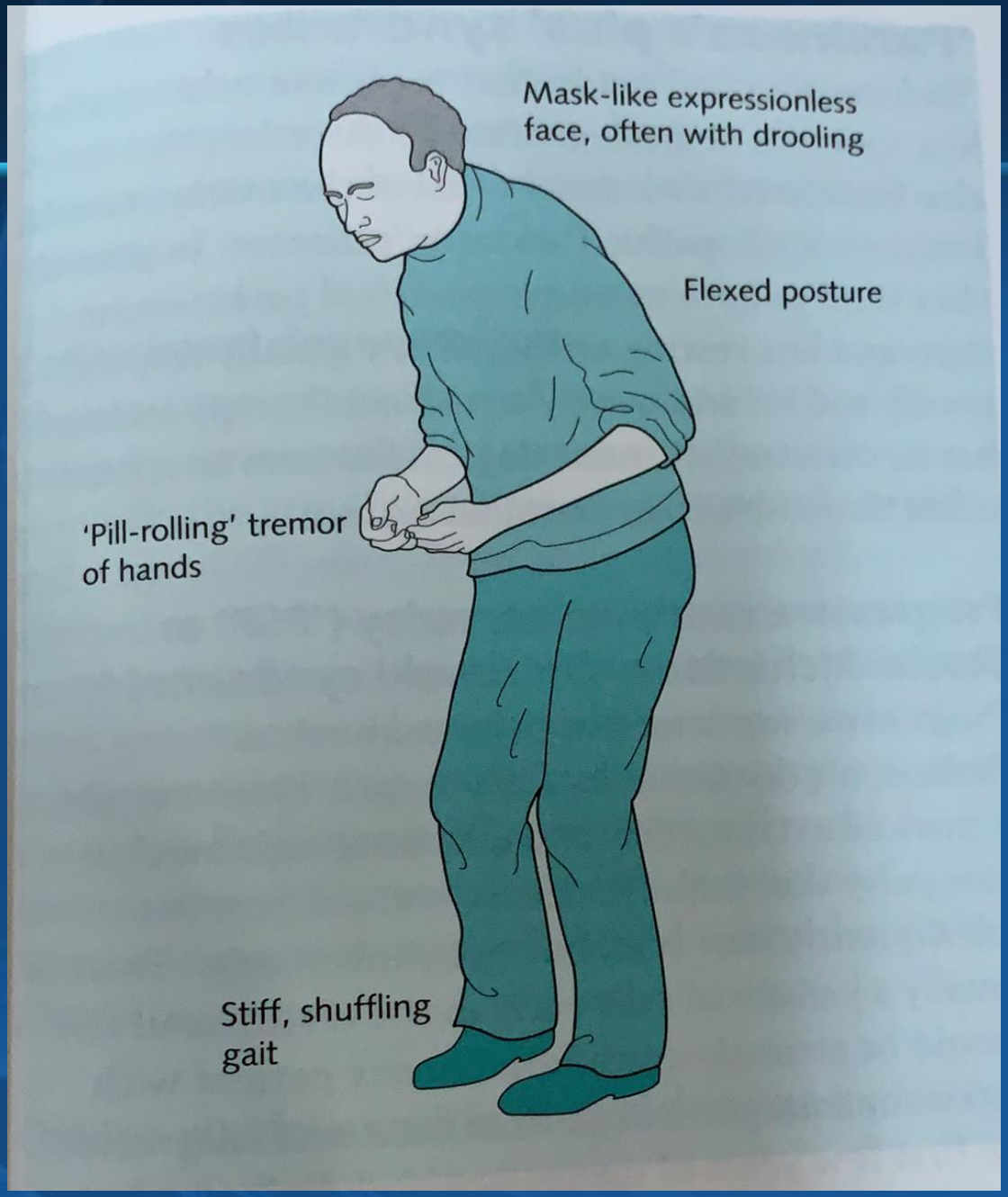
Rigidity

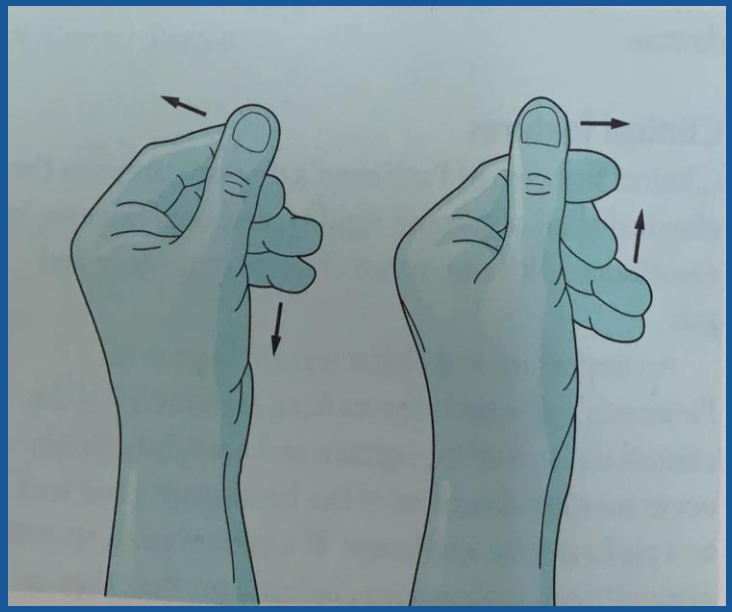


Rigidity describes increased resistance to passive range of motion in the neck or limbs. Rigidity is present in both flexor and extensor muscles, where it is relatively symmetric.

Rigidity, unlike spasticity, is not velocity dependent.

Differences between spasticity and rigidity	
Spasticity	**Rigidity**
Lesion in upper motor neuron	Lesion in basal ganglia and connections
Increased tone more marked in flexors in arms and extensors in legs	Increased tone equal in flexors and extensors
Increased tone most apparent early during movement ('clasp-knife effect')	Increased tone apparent throughout range of movement (Lead pipe rigidity)
Reflexes brisk with extensor plantars	Normal reflexes with flexor plantars


Mask-like expressionless face, often with drooling
Flexed posture
'Pill-rolling' tremor of hands
Stiff, shuffling gait



Classification of Parkinsonism

- Primary (Degenerative)
- Secondary

Degenerative Parkinsonism

- Parkinson's disease
  - Sporadic
  - Hereditary forms
- Multiple system atrophy
- Dementia with Lewy bodies.
- Progressive supranuclear palsy (PSP)
- Corticobasal degeneration

Degenerative Parkinsonism 2

- Huntington's disease
  - Juvenile presentation (Westphal variant)
  - Later in disease course.
- **Wilson disease**
- Acquired hepatolenticular degeneration
- Parkinsonism Dementia Complex of Guam
- PKAN (Hallervorden-Spatz disease)
- Basal Ganglia calcification : Fahr’s Disease.
- Chorea-acanthocytosis

Secondary Parkinsonism

- Post-encephalitic
- Post-traumatic
- Vascular/SDH
- Metabolic: Wilson's disease, Hypo/hyper-parathyroidism
- Hydrocephalus and Space-occupying lesion
- Toxic
  - Manganese
  - MPTP
  - Carbon monoxide
  - Cyanide
- Drug-induced
  - DA-receptor blockers
    - Antipsychotics
    - Anti-emetics
    - Ca-channel blockers
  - Anticonvulsants
    - Phenytoin
    - Valproic acid
  - Antiarrhythmics
    - Amiodarone
  - Others
    - Lithium

Young Onset Parkinsonism

- IPD (Sporadic)
- Familial PD.
- Wilson's Disease.
- Huntington's Disease.
- Dopa-Responsive Dystonia.
- Hallervorden-Spatz Disease.
- Neuroacanthocytosis.
- Neuroferrtinopathy.

What is this sign/disease

Kayser-Fleischer Rings of Wilson Disease

Hereditary Parkinsonism

		locus	protein
PARK1	AD	4q21-23	α-synuclein
PARK2	AR	6q25.2-27	Parkin
PARK3	AD	2p13	?
PARK4	AD	4p15	?
PARK5	AD	4p14	UCH-L1
PARK6	AR	1p35-36	PINK1
PARK7	AR	1p36	DJ-1
PARK8	AD	12q12	LRRK2/dardarin
PARK9	AR	1p36	?
PARK10	AD	1p32	?
PARK11	AD	2q36-37	?

Classification of Parkinsonian Syndromes in a Community

- Idiopathic PD ~ 85% of all PS cases
- Drug-induced parkinsonism (DIP) 7% - 9%
- MSA ~ 2.5%
- PSP and CBD ~ 1.5%
- Vascular parkinsonism ~ 3%
- PS due to MPTP, CO, Mn, recurrent head trauma is extremely rare
- No definite new cases of encephalitic lethargica since l960s

Causes of Acute Parkinsonism

- Structural-Stroke, Subdural hematoma, Hydrocephalus
- Drug induced- Neuroleptics, Antiepileptics, Antidepressants, Chemotherapeutic agents, Amiodarone
- Toxic-MPTP,Carbon monoxide,Carbon disulfide, Manganese, Cyanide, Methanol
- Infectious-Viral encephalitis, HIV,Whipple disease, Postinfectious
- Metabolic-Central pontine myelinolysis
- Wilson disease, Rapid-onset dystonia-parkinsonism
- Psychiatric – Catatonia, Psychogenic

Diagnosis of Parkinson's Disease

UK Parkinson's Disease Society

Brain Bank Criteria

Step 1

1. Bradykinesia AND
2. At least one of the following:
   - Muscular rigidity
   - 4-6 Hz rest tremor
   - Postural instability
     - -- Not visual
     - – Not vestibular
     - – Not cerebellar
     - – Not sensory

Diagnosis of Parkinson's Disease

Step 2: Exclusion Criteria

- Repeated Strokes with stepwise progression of Parkinsonian features
- Repeated head injury
- Hx of definite encephalitis
- Oculogyric crises
- Neuroleptic treatment at onset of symptoms
- More than one affected relative
- Sustained remission
- Unilateral > 3years

……. Contd.

Diagnosis of Parkinson's Disease

Step 2: Exclusion Criteria

- Supranuclear gaze palsy
- Cerebellar signs
- Early severe autonomic involvement
- Early severe dementia, apraxia
- Babinski's sign
- Tumor or Communicating Hydrocephalus on CT
- No response to large doses of levodopa

Diagnosis of Parkinson's Disease

Step 3: Supportive Criteria

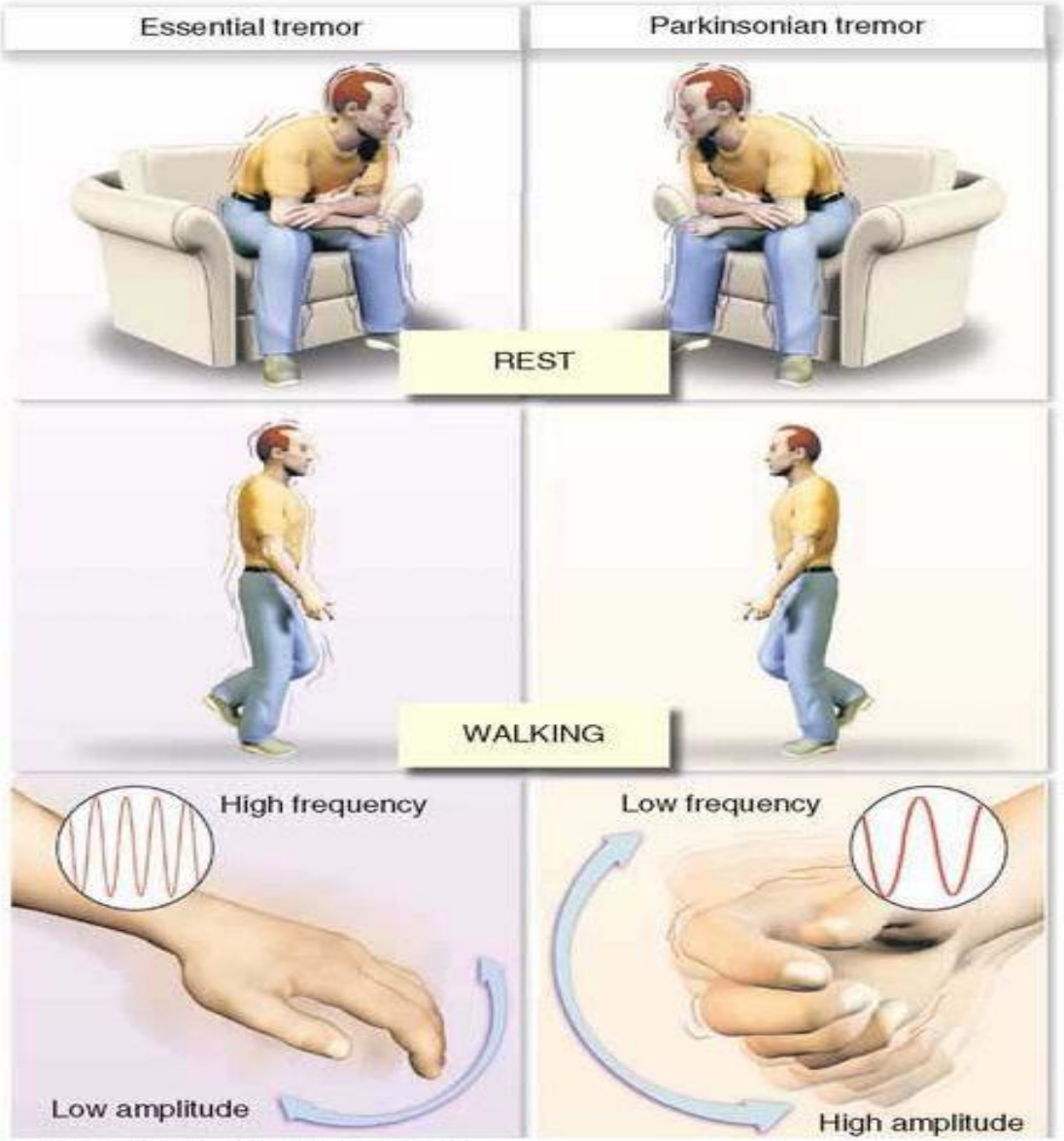
- Unilateral onset
- Rest tremor present
- Progressive disorder
- Persistent asymmetry affecting side of onset most
- Excellent response (70–100%) to levodopa
- Severe levodopa induced chorea
- Levodopa response for five years or more
- Clinical course of 10 years or more

Conditions Mimicking Parkinsonism

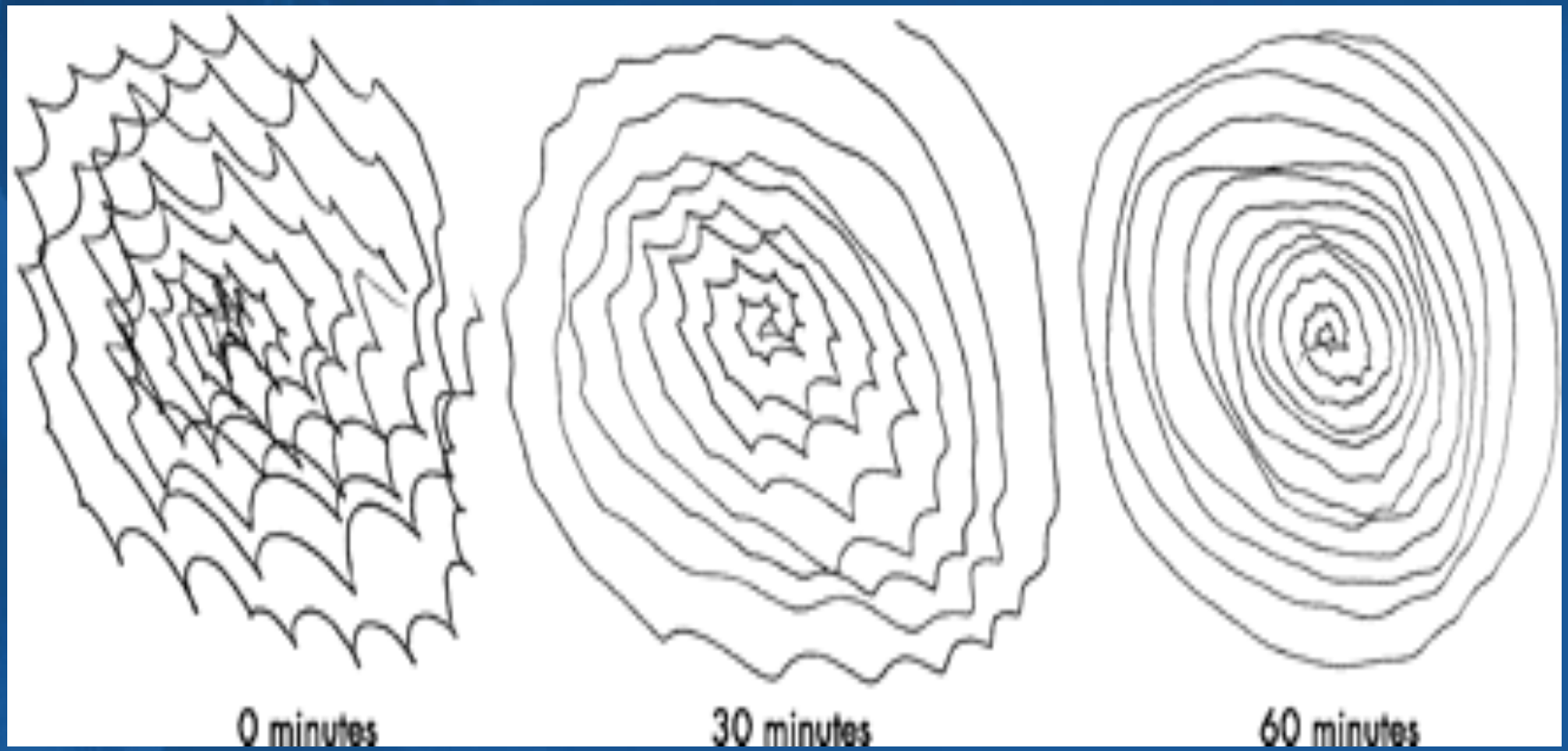
- Essential Tremor.
- Normal pressure Hydrocephalus.
- Cerebrovascular Disease.
- Elderly patients with slowness and tremor.

Other types of tremor: differential diagnosis ■

from Parkinson's disease



Response of Essential Tremor to Alcohol



Essential Tremor

- Essential tremor is an action tremor characterised by rhythmic shaking of the arms in almost every case; it may also involve tremor of the head, tongue, lower limbs, voice and face.
- Essential tremor is commonly autosomal dominant, so a family history is important.
- Enhanced physiological tremor is commonly misdiagnosed as essential tremor.
- First-line agents for the treatment of essential tremor include propranolol and primidone. DBS (Vim nucleus of thalamus) for severe cases

Differential diagnosis of essential tremor

- Enhanced physiological tremor
- Parkinson's disease
- Cerebellar tremor
- Dystonia
- Psychogenic tremor
- Orthostatic tremor
- Wilson's disease—younger than 40 years
- Task specific tremor
- Holmes's (rubral) tremor

Non-Motor Symptoms of Parkinson's Disease

Neuropsychiatric symptoms

Depression, apathy, anxiety
Anhedonia
Attention deficit
Hallucinations, illusions, delusions
Dementia
Obsessional behaviour (can be drug-induced) and repetitive behaviour
Confusion
Delirium (could be drug-induced)
Panic attacks

Sleep disorders

Restless legs and periodic limb movements
Rapid eye movement (REM) sleep behaviour disorder and REM loss of atonia
Non-REM sleep-related movement disorders
Excessive daytime somnolence
Vivid dreaming
Insomnia
Sleep-disordered breathing

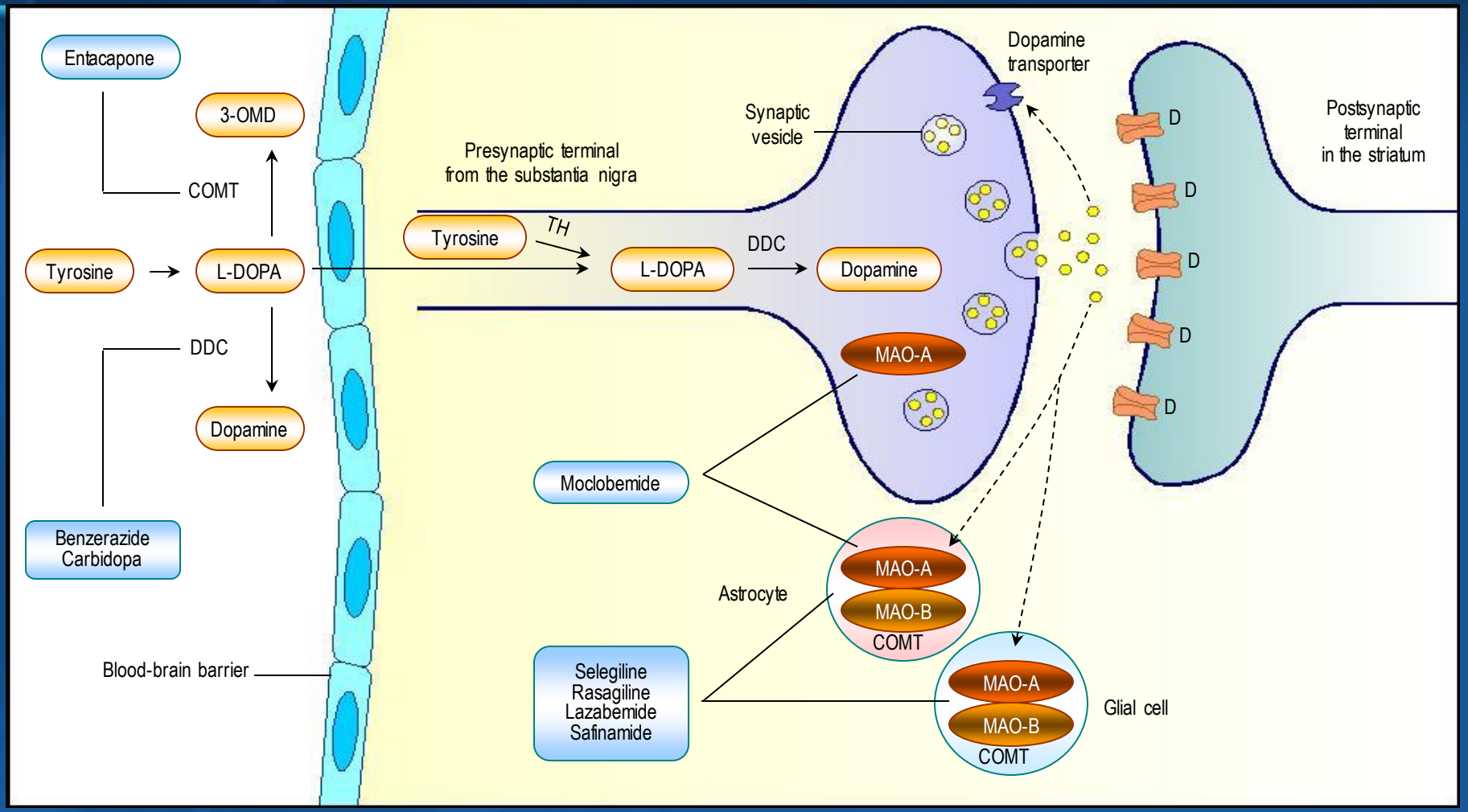
Autonomic symptoms

Bladder disturbances
- Urgency
- Nocturia
- Frequency

Sweating
Orthostatic hypotension
Falls related to orthostatic hypotension
Coat-hanger pain
Sexual dysfunction
Hypersexuality (likely to be drug-induced)
Erectile impotence
Dry eyes

Drug Therapy in PD

The Basis for Symptomatic Drug Therapy of Motor Symptoms in Parkinson's Disease



Abbreviations: DDC, dopa decarboxylase; TH, tyrosine hydroxylase; L-DOPA, levodopa; MAO-A, monoamine oxidase A; MAO-B, monoamine oxidase B; COMT, catechol-O-methyltransferase; D, dopamine receptors; 3-OMD, 3-O-methyldopa

Drug Therapy – Symptomatic Treatment of Motor Symptoms-Dopaminergic agents

- Levodopa
  - Levodopa + carbidopa
  - Levodopa + benserazide
  - COMT inhibitors (entacapone, tolcapone)
- Selective MAO-B inhibitors
  - Selegiline
  - Rasagiline
  - Safinamide
- Dopamine agonists
  - Non-ergot
    - Pramipexole
    - Ropinirole
    - Rotigotine
    - Piribedil
  - Ergot
    - Bromocriptine
    - Pergolide
    - Cabergoline
    - Dihydroergocryptine
    - Lisuride

Non-dopaminergic agents

- Anticholinergic agents:
  - Trihexyphenidyl
  - Benztropine
- NMDA antagonists
  - Amantadine

Main Mechanisms of Action of Therapeutic Interventions in Parkinson's Disease

	Action			
Drugs	**Promote dopamine synthesis**	**Activate specific receptors**	**Prolong dopamine availability**	**Prolong levodopa bioavailability**
Dopaminergic	Levodopa	DAs	MAO-B inhibitors	COMT inhibitors
Antiglutamatergic	Amantadine*			
Anticholinergic†		Trihexyphenidyl Benztropine		
Surgery	**Lesion** Thalamotomy Pallidotomy Subthalamic nucleotomy	**DBS** Thalamus Pallidum Subthalamic nucleus	**Transplantation‡** Foetal mesencephalic cells	
Rehabilitation procedures	Physical therapy Occupational therapy Speech therapy			

Levodopa in the Management of Parkinson's Disease

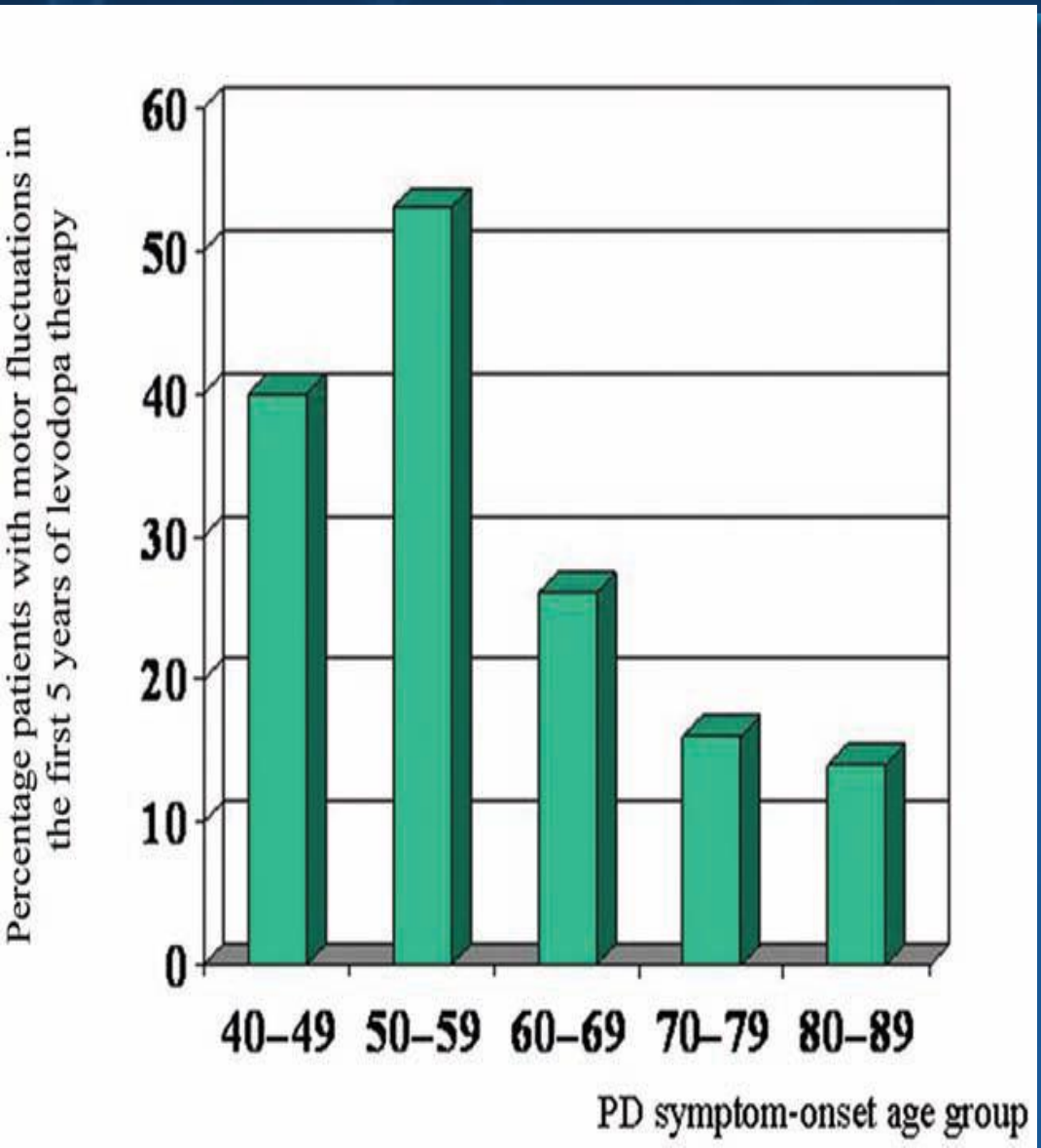
- First of the dopaminergic drugs
  - Used since late 1960s
- Highly effective drug
  - Relatively rapid relief of bradykinesia, rigidity and associated pain
  - Reduces tremor in many patients

Levodopa improves quality of life and life expectancy in patients with PD

Levodopa in the Management of Parkinson's Disease

- Must be metabolised to dopamine to be effective
- Addition of dopa decarboxylase inhibitors (DDIs) (benserazide, carbidopa) is required to limit additional peripheral side effects
- Absorption delayed or diminished by large neutral amino acids or agents that slow transit time, antacids and anticholinergics
- Short half-life causes pulsatile stimulation of dopamine receptors

Levodopa induces motor complications



- Up to 80% of PD patients suffer from motor fluctuations and dyskinesias after approximately 5 to 10 years of treatment with levodopa
- 50 to 75% of patients develop motor fluctuations 3 to 6 years after initiating therapy
- 70% of young-onset PD patients develop motor complications after 3 years

Dopamine Agonists in the Treatment of Parkinson's Disease

- First-line therapy in early PD in younger patients
  - Rare motor complications
    - Delay the use of levodopa and related motor complications
  - Good side-effect tolerance
    - Avoid ergot dopamine agonists: rare but serious fibrotic reactions
- Agonist monotherapy can provide control of motor symptoms for several years in some patients
- Adjunctive treatment in more advanced PD
- Putative neuroprotection with some agents, particularly pramipexole and ropinirole

Clinical Pharmacology of Dopamine Agonists

Drug	Dopamine receptor interaction	Interaction with other receptors		Half-life (h)
		NA	5-HTP	
Non-ergot				
Pramipexole	D2	±	-	10
Ropinirole	D2	-	-	6
Rotigotine	D2 > D1	+	+	5-7 (td)
Apomorphine	D2/D1	-	-	0.5 (sc)
Ergot				
Bromocriptine	D2	+	+	3-6
Pergolide	D2 > D1	+	+	15
Cabergoline	D2	+	+	65

All mentioned D2-family agonists have D_3/D_2 subtype affinity ratio > 1 except for bromocriptine.
Abbreviations: NA, noradrenaline; 5-HT, 5-hydroxytryptophan; td, transdermal; sc, subcutaneous

Definition of motor complications

- **Motor complications**: The dyskinesias and motor fluctuations which occur during the long term management of patients with Parkinson's disease
- **Motor fluctuations**:

  (1) Predictable wearing *OFF*

  (2) unpredictable ON–OFF fluctuations

  (3) sudden OFF periods
- **Dyskinesias**:

  (1) Peak dose dyskinesias

  (2) diphasic dyskinesias

  (3) OFF period dystonia

TABLE 16-2. Therapeutic Strategies in Parkinson Disease

Scenario/Problem	Therapeutic Approach
Initial treatment	Levodopa, dopamine agonist, or MAO inhibitor
Poor or no response to initial treatment	Increase levodopa dose and consider alternative diagnoses
Tremor-predominant disease	Anticholinergic or amantadine
Overnight or early morning bradykinesia	Consider overnight controlled-release preparation of levodopa
Levodopa-induced hallucinations	Discontinue concurrent therapy with anticholinergics, amantadine, selegiline, or dopamine agonists
	Decrease dose of levodopa
	Low-dose atypical antipsychotic (with quetiapine, clozapine, or pimavanserin)
"Wearing off"	More frequent dosing
	Extended release formulation of levodopa
	Add COMT inhibitor
Dyskinesia	Reduce dose of levodopa
	Add or increase dose of dopamine agonist
	Change dopamine agonist
	Add amantadine
	Consider deep brain stimulation

COMT, catechol *O*-methyl transferase; MAO, monoamine oxidase.

Phenomenological Classification of Movement Disorders

- Movement Disorders are classified broadly into two main groups:

  HYPOKINETIC DISORDERS: too little movement

  bradykinesia (slowness of movements)

  (Parkinson's Disease and other akinetic rigid syndromes)

  HYPERKINETIC DISORDERS: too much movement

  dyskinesias- (different types of involuntary movements)

Hyperkinetic Disorders

- Five main types:
  - Tremor
  - Tics
  - Chorea
  - Myoclonus
  - Dystonia

Decide which group does the patient best fit

Tremor

- **Definition**: Rhythmic oscillation of a body part.
- Tremors can be classified as:
  - *Rest*: occurs when affected body part is at rest
  - *Postural*: occurs when arms are outstretched
  - *Kinetic*: occurs during movement of body part.

Tremor

Resting tremor:

- Parkinson's disease and other parkinsonian disorders, dystonic tremor, one component of rubral tremor, severe ET,

Postural:

- Essential tremor, Physiological
- PD, Dystonic tremor etc

Kinetic:

- Cerebellar disorders

Chorea

Definition: Irregular, brief, purposeless movements that flit from one body part to another

Many causes: Acquired and inherited

-Drugs/ Oral contraceptives

- Basal ganglia lesions

- Sydenham's chorea

-Antiphospholipid antibody syndrome

-Huntington's disease/ HD like diseases

-Neuroacanthocytosis

Huntington's Disease

- An AD trinucleotide (CAG) repeat expansion disorder with the cardinal manifestations of chorea, psychiatric disease and cognitive decline.
- Chorea involves limbs ,head and face
- Motor impersistence (of grip, tongue protrusion or gaze fixation) is a classic feature
- Caudate atrophy on MRI

Tics

- Brief, repetitive and stereotyped movements or vocalisations.
- Tics are usually suppressible for a short period of time, but at the expense of mounting inner tension.
- Very common: 3-4% of the population are affected at some time in their lives, almost always starting in childhood.

Motor:	- eye blinking
	- head jerks
	- arm/leg jerks
	-complex sequence
Vocal:	- sniffing
	- grunting
	- snorting

Gilles de la Tourette Syndrome

- Typically, onset of persistent multiple motor and vocal tics, often with associated psychiatric disturbance [Attention deficit hyperactivity syndrome (ADHD); Obsessive compulsive disorder (OCD); copropraxia; coprolalia]

Myoclonus

- **Definition**: Brief shock-like jerks.

Many causes –

-Physiological,

-Fragment of epilepsy

-Metabolic encephalopathies/ Hypoxia

- Progressive myoclonic ataxia/epilepsy

-SSPE/CJD/other encephalitides

Dystonia

- Involuntary muscle spasms leading to abnormal posturing of limbs and writhing movements (athetosis).
- P*rimary dystonia*: without any structural damage often inherited
- *Secondary dystonia*: Due to variety of environmental or heredodegenerative causes with structural damage to the CNS
- *Paroxysmal dystonia*: brief episodes of dystonia/dyskinesia

- Focal
- Segmental
- Generalized

Three features unique to dystonia

- **Task-specificity:** selective activation of involuntary movements by specific tasks (e.g. writing, using a computer mouse, playing a musical instrument).
- **Geste antagoniste:** a sensory trick that improves the dystonic phenotype while it is applied (touching the chin, touching the eyes, holding an object between the teeth).
- **State function:** variation in severity of dystonia with specific actions (walking backwards but not forwards, speaking but not eating).

Treatment of dystonia

- All children with dystonia should receive a trial of levodopa, in order not to miss the diagnosis of dopa-responsive dystonia.
- "ABCs" of dystonia Rx : Artane (trihexiphenidyl), baclofen, clonazepam
- Other useful drugs-diazepam,L-Dopa,Amantadine,AED,DA
- Add one drug at a time, titrate to efficacy or until side effects develop.
- Polypharmacy is the rule rather than the exception.
- Tardive dystonia responds particularly well to tetrabenazine.
- Botox and surgery

Primary dystonia:

Two main phenotypes depending on age of onset

Young onset: (below 28 yrs)
lower limb onset,
spreads,
tends to generalise;
cranial-cervical
less affected/spared
often familial: DYT1 gene +ve

Prevalence: 3/100,000

Adult onset:
affects upper body;
focal or segmental;
cranio-cervical most common
(F>M)
mostly sporadic
Non-DYT-1
Prevalence: 8, 33, 58*, and even 732**/ 100,000

Dopa Responsive dystonia

- An inherited condition characterised by early onset dystonia and parkinsonism.
- Responds very well to small doses of levodopa, and response lasts for life.
- Many people with DRD are misdiagnosed as having other conditions e.g cerebral palsy.
- *Therefore, levodopa should be considered in all patients with dystonia, particularly those with young onset.*

Drug-induced MD

Acute dystonic reactions/oculogyric crisis

- Acute dystonic reactions are best treated with anticholinergic agents and benzodiazepines
- This reaction is short-lived and does not produce long-term consequences

Parkinsonism

- This may occur as the result of long-term use of any neuroleptic agent
- The symptoms are similar to those seen in Parkinson disease, but tremor is less common and patients tend to be less responsive to levodopa

Neuroleptic malignant syndrome

- This occurs when patients are exposed to high doses of dopamine-blocking medications or when levodopa or dopamine agonists are withdrawn rapidly
- The syndrome includes fever, autonomic instability, encephalopathy, and muscular rigidity
- The offending agent must be stopped , but a combination of bromocriptine, dantrolene, and benzodiazepines is usually required to control the muscle rigidity

Drug class	Examples of drugs
Psychiatric	Risperidone, ziprasidone Haloperidol Clozapine, loxapine, quetiapine Chlorpromazine, fluphenazine, thioridazine Thiothixene Olanzapine
Antiemetics	Prochlorperazine, promethazine
Properistaltic	Metoclopramide, domperidone
Antiparkinsonian	Dopamine agonists, Levodopa

Tardive dyskinesia

- This is a disorder that occurs after chronic exposure to dopamine-blocking agents- leading to receptor hypersensitivity ??
- Commonly observed movements include chewing , grimacing, lip smacking, and tongue thrusting
- The trunk is commonly affected
- The limbs may be affected
- Treatment of TD is challenging:

-- The dopamine-depleting agent tetrabenazine may be helpful

Tardive syndromes are movement disorders distinguished by their late emergence in the course of treatment and their potential persistence for months to years, even in the face of stopping or reducing neuroleptic medication.

Symptoms develop in association with using a neuroleptic medication for at least a few months.

Symptoms may develop after a shorter period of medication use in older people.

Acute and Tardive Akathisia

Antiemetics
Droperidol
Metoclopramide
Prochlorperazine
Promethazine
Antiepileptics
Carbamazepine
Psychotropics
Lithium
Haloperidol
Molindone
Phenothiazines (e.g. chlorpromazine, fluphenazine, mesoridazine, perphenazine, thioridazine, trifluoperazine)
Olanzapine (high dose)
Pimozide
Risperidone (high dose)
Thioxanthenes (e.g. thiothexene)

Active and Tardive Stereotypies

Antiemetics
Metoclopramide
Prochlorperazine
Antiepileptics
Phenytoin
Psychotropics
Amoxapine
Haloperidol
Molindone
Phenothiazines
Olanzapine (high dose)
Pimozide
Risperidone (high dose)
Thioxanthenes

Acute and Tardive Dystonia

Antiemetics
Droperidol
Metoclopramide
Prochlorperazine
Promethazine
Psychotropics
Amoxapine
Haloperidol
Molindone
Phenothiazines
Olanzapine (high dose)
Risperidone (high dose)
Thioxanthenes

Parkinsonism

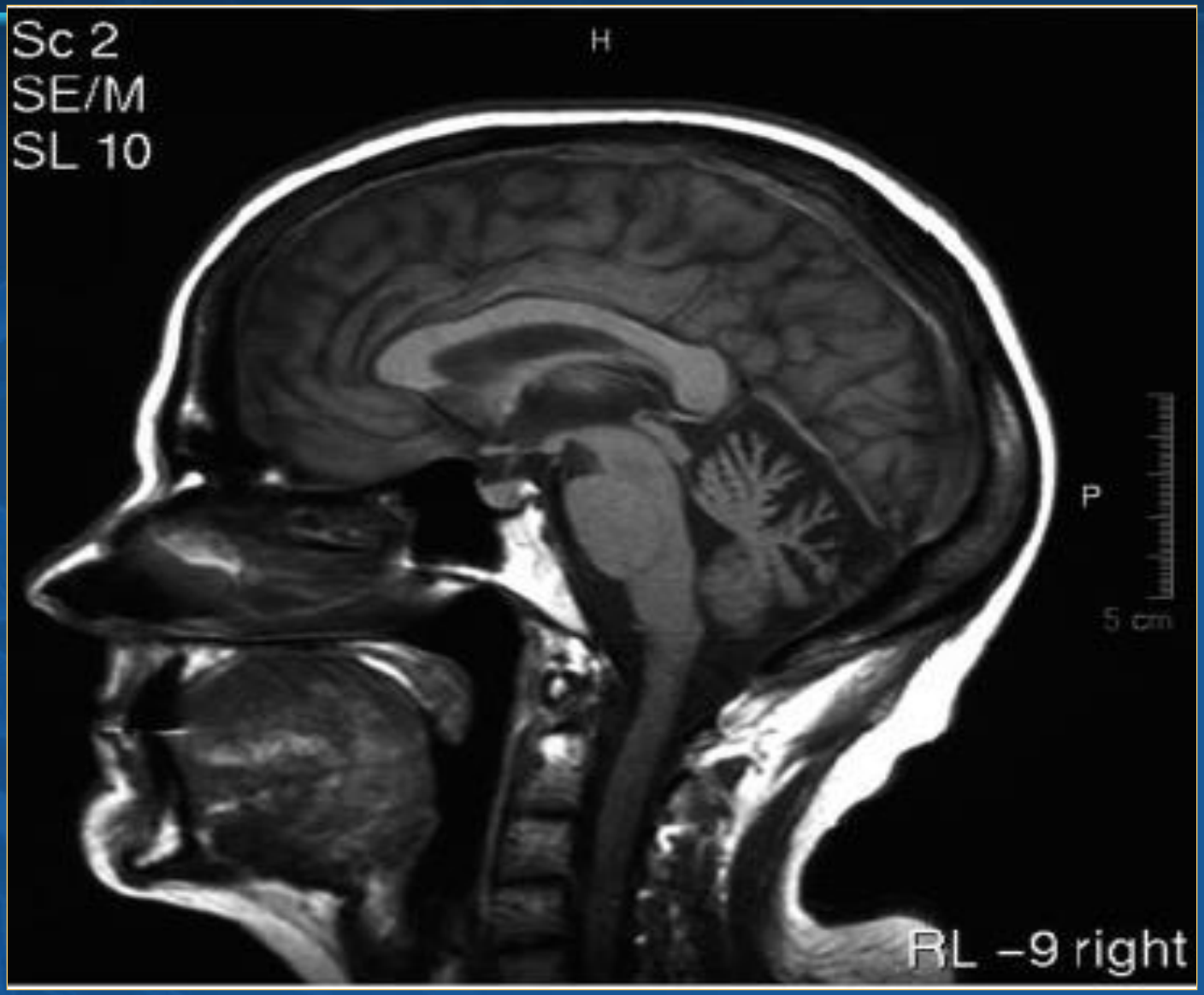
Antiemetics
Droperidol
Metoclopramide
Prochlorperazine
Promethazine
Antiepileptics
Valproate
Cardiovascular Agents
Alpha-methyldopa
Reserpine
Psychotropics
Amoxapine
Haloperidol
Molindone
Phenothiazines
Olanzapine (high dose)
Risperidone (high dose)
Thioxanthenes
Vestibular Sedatives
Cinnarizine
Flunarizine
Miscellaneous
Pimozole

Serotonin Syndrome

- Serotoninergic stimulation (e.g. SSRI + triptan or tramadol)
- Myoclonus, tremor, agitation, sweating, fever

Drug class	Examples of drugs
Selective serotonin reuptake inhibitors (SSRIs) and selective serotonin and norepinephrine reuptake inhibitors (SNRIs)	Sertraline Paroxetine Fluoxetine Citalopram Escitalopram Venlafaxine Desvenlafaxine Duloxetine
Monoamine oxidase inhibitors	Amitriptyline Nortriptyline Clomipramine Imipramine
Other psychiatric	Lithium Trazodone (serotonin modulator) Bupropion (dopamine/norepinephrine reuptake inhibitor)
Antiepileptic	Valproic acid
Antiemetic and properistaltic	Ondansetron Metoclopramide
Antibiotics, antiviral	Linezolid Ritonavir
Analgesics, relaxants	Tramadol Fentanyl Meperidine Cyclobenzaprine
Cough and cold	Dextromethorphan

Ataxias



Definition

- Ataxia (Gk. Taxis = Order; means lack of order)
- Ataxia denotes a syndrome of imbalance and incoordination involving gait, limbs, and speech and usually results from the disorder of the cerebellum or its connections
- It is characterized by dyssynergia, dysmetria, dysdiadochokinesia
- It is a disorder of rate, range, direction and force of movements

Examination

- Neck tilt and titubation
- Nystagmus and other ocular movement abnormalities
- Dysarthria
- Intention tremor
- Hypotonia
- Past pointing
- Rebound phenomenon
- Macrographia
- Stance
- Ataxic Gait
- Pendular knee jerk

Differentiation of sensory and cerebellar ataxia

- Sensory ataxia is due to severe sensory neuropathy, ganglinopathy or lesions of the posterior column of the spinal cord. e.g. Sjogren's syndrome, cisplatin, CCNU, Para-neoplastic disorders, SACD, Tabes dorsalis.

Cerebellar ataxia	Sensory ataxia
Scanning speech	Normal speech
Nystagmus and other ocular signs	Absent
Sensory exam normal, Romberg test negative	Sensory loss, Romberg's test postive
Pendular reflexes	Hypo to aeflexia
Reeling, ataxic gait	Stamping gait

Thank You