PARKINSON DISEASE (PD) and other involuntary movement disorders

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I) Parkinson disease: introduction; etiology and pathogenesis; other akinetic-rigid syndromes; pathology and pathophysiology; epidemiology; clinical manifestations; treatment

II) Drug-induced movement disorders

III) Tremor

IV) Huntington disease and other causes of chorea

V) Ballism

VI) Dystonia

VII) Myoclonus

VIII) Tics

I) Parkinson disease

1. Introduction

Most common neurodegenerative movement disorder and is the most common form of parkinsonism, the clinical syndrome characterised principally by bradykinesia and rigidity

Features of other idiopathic parkinsonian syndromes

(with the exception of vascular parkinsonism where the cause is known) are shown in the table

TABLE 16-1. Parkinsonian Syndromes

Parkinsonian Syndrome	Distinguishing Clinical Features
Progressive supranuclear palsy	Supranuclear ophthalmoplegia, with greatest limitation of downward gaze; axial rigidity; early falls due to rigidity, impaired postural reflexes, neck hyperextension, and inability to look down
Corticobasal ganglionic degeneration	Limb apraxia; cortical sensory impairment; alien-limb phenomenon; asymmetric rigidity; dementia
Diffuse Lewy body disease	Early dementia; prominent visual hallucinations; cognitive fluctuations; extreme sensitivity to extrapyramidal side effects of antidopaminergic neuroleptic drugs
Vascular parkinsonism	"Lower-half" parkinsonism in which rigidity in the legs is greater than in the arms, resulting in slow, shuffling gait
Multiple system atrophy	Early and prominent features of autonomic dysfunction (MSA-A); cerebellar dysfunction (MSA-C); parkinsonism refractory to levodopa (MSA-P); high-pitched, quivering dysarthria

2. Etiology and pathogenesis

Although the ultimate cause of Parkinson's disease is unknown, other, generally rarer, akinetic-rigid syndromes have an identified etiology(next section)

The recognition that MPTP, a synthetic heroin by-product , could produce acute parkinsonism has provided some insight into the etiology of Parkinson's disease itself.

The toxin MPTP crosses the blood-brain barrier and is converted to its active metabolite MPP+ by the enzyme monoamine oxidase type B(MAO-B) in glial cells.

MPP+ , a free radical is concentrated in dopaminergic neurons, entering via the dopamine reuptake mechanism, thereby selectively damaging these cells.

MPP+ is a mitochondrial poison, inhibiting complex I of the respiratory chain, and hence impairing cellular energy production. (figure)

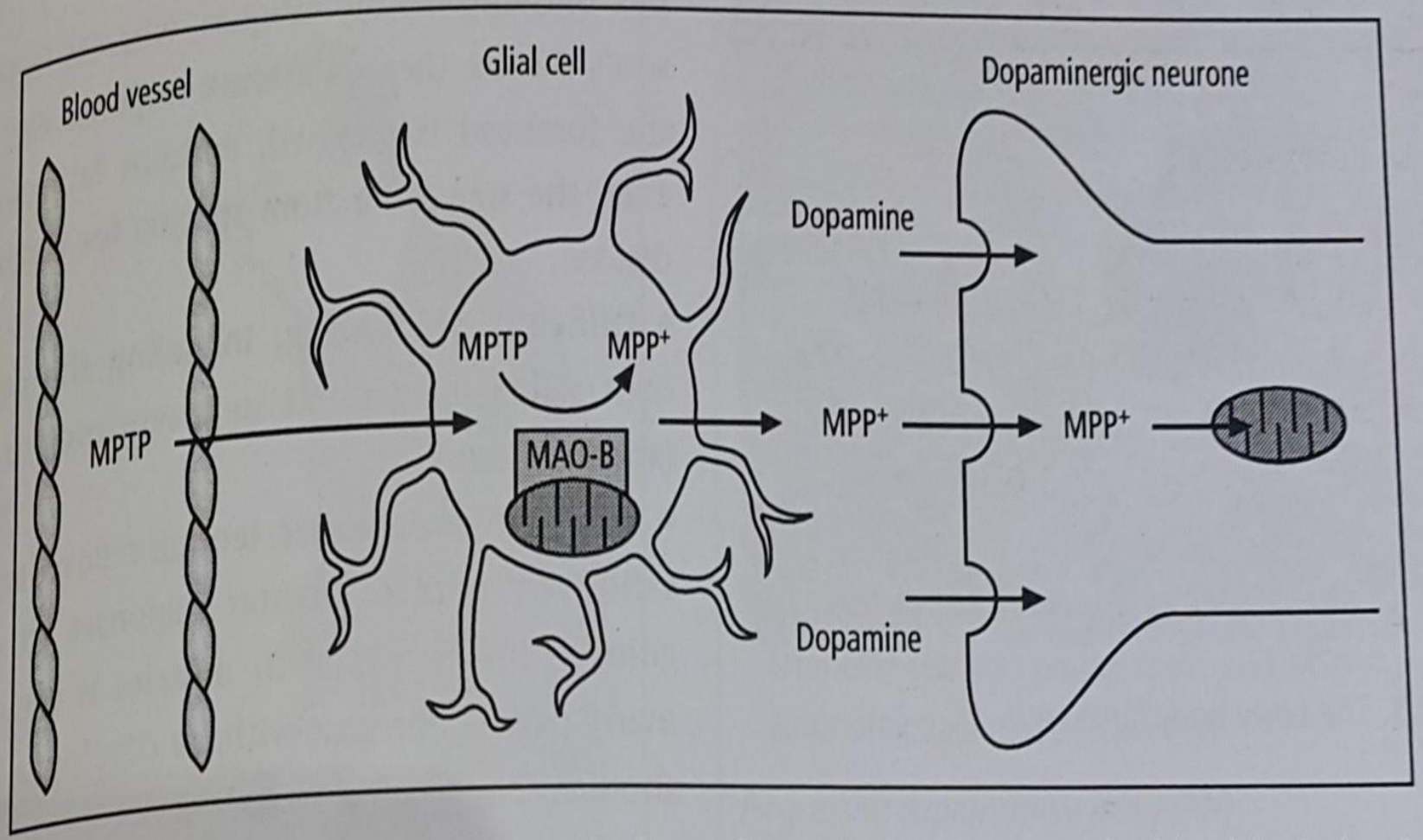


Figure 12.1 MPTP and the aetiology of Parkinson's disease. The toxin MPTP crosses the blood–brain barrier and is converted to its active metabolite MPP+ by the enzyme monoamine oxidase type B (MAO-B) in glial cells. MPP+, a free radical, is concentrated in dopaminergic neurones, entering via the dopamine reuptake mechanism, thereby selectively damaging these cells. MPP+ is a mitochondrial poison, inhibiting Complex I of the respiratory chain, and hence impairing cellular energy production.

The fact that an unusual exogenous toxin may lead to selective CNS damage and Parkinsonism has reinforced the view that idiopathic Parkinson's disease itself may be caused by exposure to a more widely prevalent environmental factor, as yet unidentified, perhaps acting by a similar mechanism to MPTP

Further support for environmental factors includes the following:

- The disease is increasingly common with age (mean age of onset about 60 years)
- Genetic causative factors have been identified but a positive family history is relatively unusual in idiopathic Parkinson's disease

- There is a weak association between Parkinson's disease and various environmental factors, e.g. , exposure to wood pulp and pesticides

3. Other akinetic-rigid syndromes

* Wilson disease:

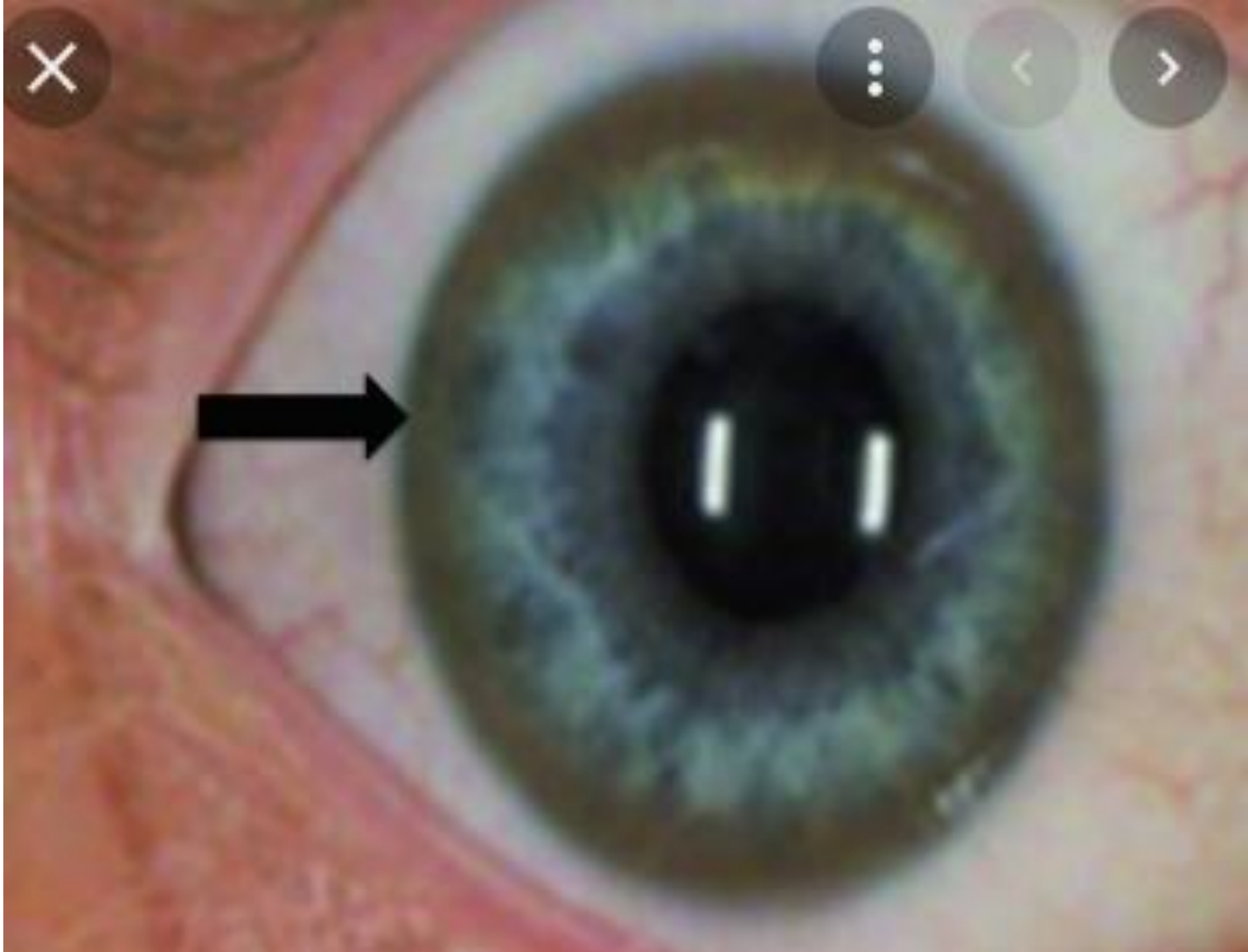
- This is a rare autosomal recessive defect of copper metabolism

- Levels of serum copper and ceruloplasmin, the copper transport protein, are low and copper is deposited in the tissues, particularly the liver and basal ganglia

- The disease may present in childhood with cirrhosis, or in adolescence, where the neurological features dominate

- The neurological features include an akinetic-rigid syndrome, dystonia, cerebellar signs or sometimes neuropsychiatric manifestations, even frank psychosis

- Copper is also deposited in the cornea, as **Kayser-Fleischer rings**, detectable on slit lamp examination



Kayser-Fleischer ring

Classification and external resources

A Kayser-Fleischer ring in a 32-year-old patient who had longstanding speech difficulties and tremor.

- The diagnosis of Wilson's disease, based on serum copper and ceruloplasmin, Kayser-Fleischer rings and, if necessary liver biopsy is important , as the condition is treatable and is fatal without therapeutic intervention

- The mainstay of treatment are the copper-chelating agents trientine and penicillamine, zinc supplementation, and restriction of copper-containing foods such as liver, shellfish, and mushrooms

- Earlier treatment results in better long-term neuropsychiatric and hepatic outcome

- Liver transplantation may be necessary for patients with fulminant symptoms including hepatic failure

* Traumatic: ‘ Punch-drunk syndrome’- chronic head injury in boxers- patients have parkinsonian features often in combination with cerebellar damage and cognitive deficits(dementia pugilistica)

* Inflammatory: Postencephalitic Parkinsonism- following the epidemic of encephalitis lethargica after World War I , patients developed a chronic akinetic-rigid state, with certain characteristic features, particularly oculogyric crises

* Neoplastic: tumours of the basal ganglia presenting with contralateral hemiparkinsonism are extremely rare

* Vascular: Multiple lacunar infarcts may occasionally result in pseudoparkinsonian features, but usually in association with pyramidal and cognitive dysfunction

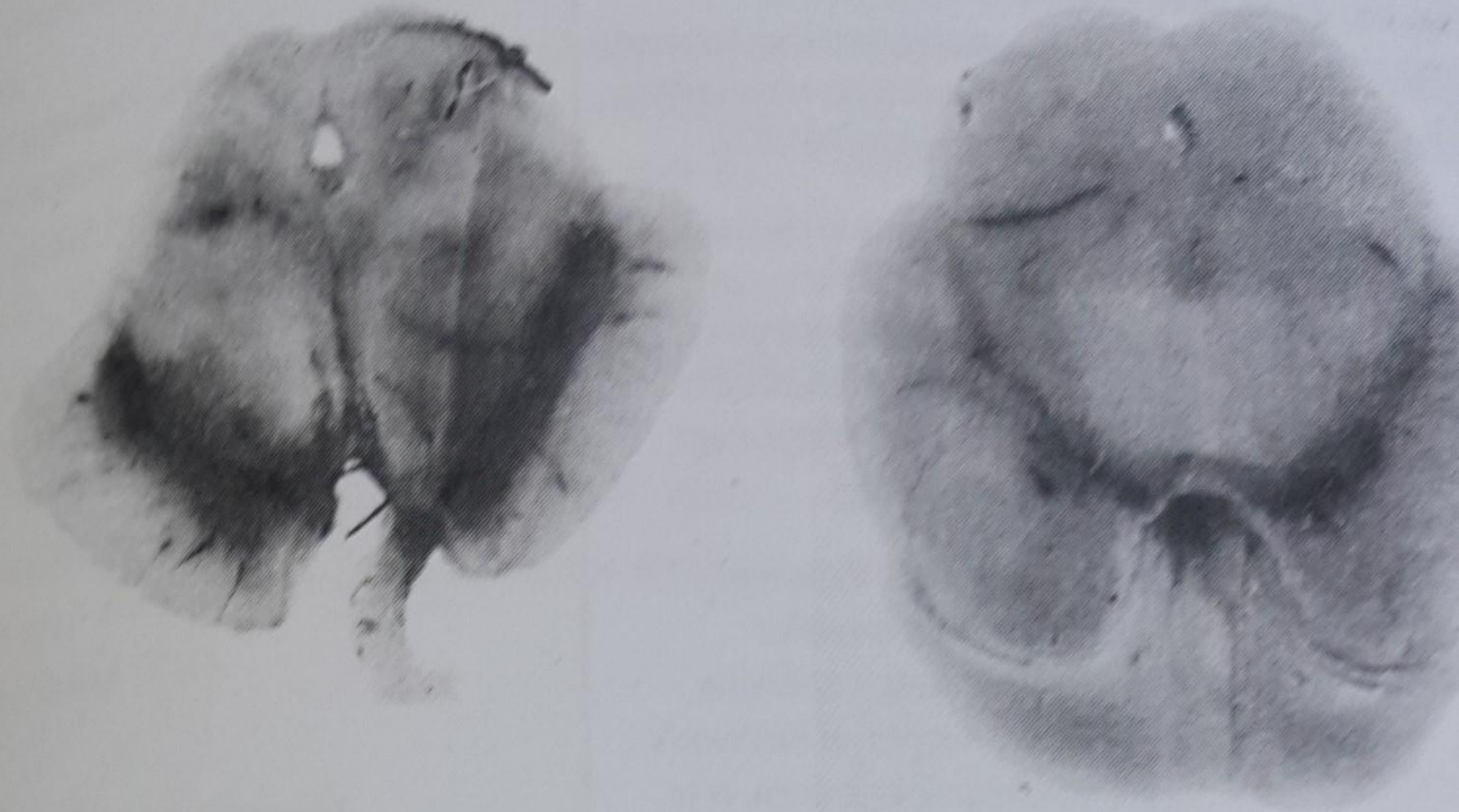
* Drugs: Neuroleptics, antiemetics(metoclopramide) , amiodarone

* Toxins: MPTP, manganese, chronic carbon monoxide poisoning

4. Pathology and pathophysiology

The precise source of PD is not known, but the essential motor manifestations of the disease are due to degeneration of dopaminergic neurons in the substantia nigra pars compacta (figure)

The key histopathologic finding of PD is the Lewy body, which is an alpha-synuclein containing eosinophilic cytoplasmic inclusion that accumulates in neurons in the brainstem,cerebral cortex, and sympathetic autonomic ganglia



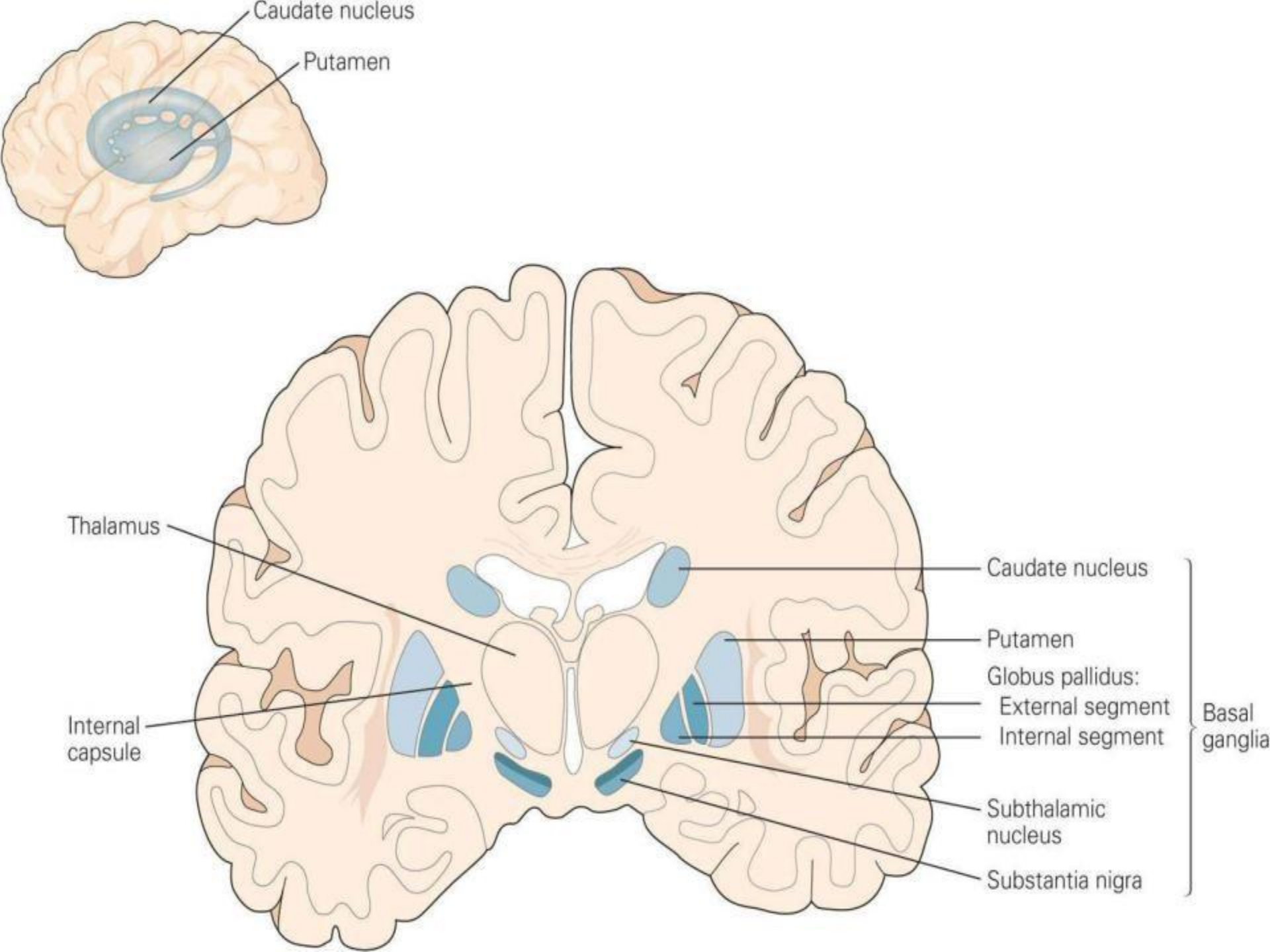
(a)

Figure 12.2 Loss of pigment in the substantia nigra. (a) Normal; (b) Parkinson's disease.

Figure 12.3 The Lewy body (arrowed).

The dopaminergic neurons primarily affected in Parkinson's disease are those projecting from the substantia nigra of the midbrain to the striatum of the basal ganglia(caudate nucleus and putamen)

Macroscopically, atrophy of the substantia nigra in advanced Parkinson's disease is recognizable by loss of the characteristic melanin pigmentation of this region


Caudate nucleus
Putamen
Thalamus
Internal capsule
Caudate nucleus
Putamen
Globus pallidus:
External segment
Internal segment
Subthalamic nucleus
Substantia nigra
Basal ganglia

Microscopically, severe neuronal loss is demonstrable in the substantia nigra, remaining neurons often containing a distinctive intracellular inclusion, the **Lewy body**

Symptoms of Parkinson's disease appear when about 60-80% of nigrostriate dopaminergic neurons have been lost

Pathophysiologically, damage to dopaminergic pathways leads to an imbalance in the extrapyramidal system in favour of cholinergic and other neurotransmitter mechanisms

*Normal dopaminergic pathways are balanced by those utilizing other neurotransmitters, predominantly acetylcholine (ACH)

* Dopaminergic deficiency or cholinergic excess, resulting in an akinetic-rigid syndrome, e.g., idiopathic Parkinson's disease or drug-induced Parkinsonism

(Phenothiazines, Haloperidol and related drugs are neuroleptics and are dopamine antagonists)

* Dopaminergic excess or cholinergic deficiency result in excessive involuntary movements- dyskinesia, e.g., due to overtreatment of Parkinson's disease with dopaminergic drugs, or to degenerative disease of non-dopaminergic pathways , as in Huntington's disease

(which leads to atrophy of both caudate nuclei)

(a)

Normal-dopaminergic pathways balanced by those utilizing other neurotransmitters, predominantly acetylcholine (ACh).

(b)

Dopaminergic deficiency or cholinergic excess, resulting in an akinetic–rigid syndrome, e.g. idiopathic Parkinson's disease or drug-induced Parkinsonism (NB phenothiazines and related drugs are dopamine antagonists).

(c)

Dopaminergic excess or cholinergic deficiency, resulting in excessive involuntary movements – dyskinesia, e.g. due to overtreatment of Parkinson's disease with dopaminergic drugs, or to degenerative disease of non-dopaminergic pathways, as in Huntington's disease.

5. Epidemiology

PD is most common in middle-aged and older patients, affecting approximately 1% of people over 60 years

It is typically a sporadic disorder, but hereditary forms of PD due to mutations in genes such as PRKN, PINK1, LRRK2, and GBA may affect younger patients

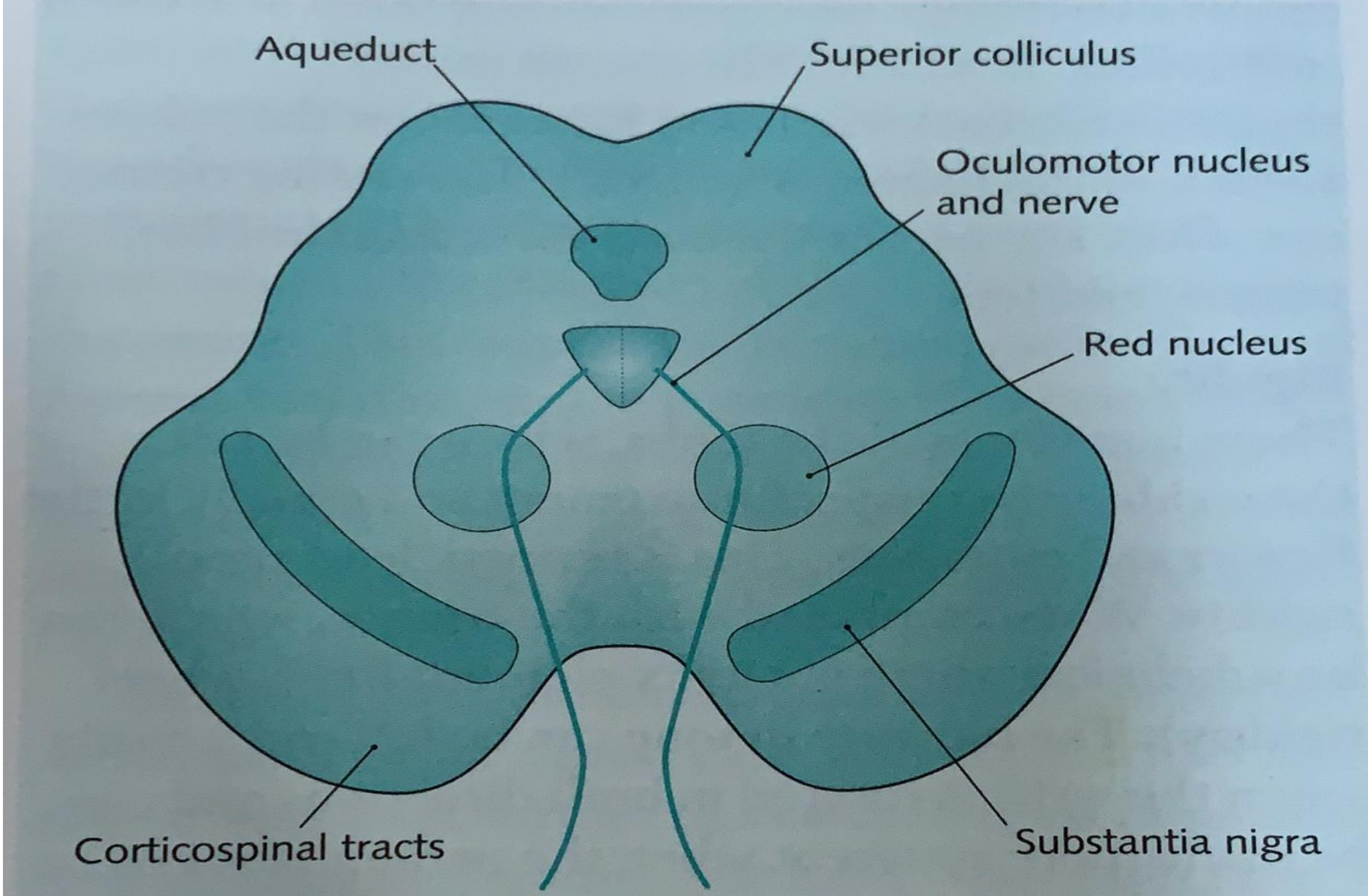


Fig. 18.1 Cross-section of the midbrain.

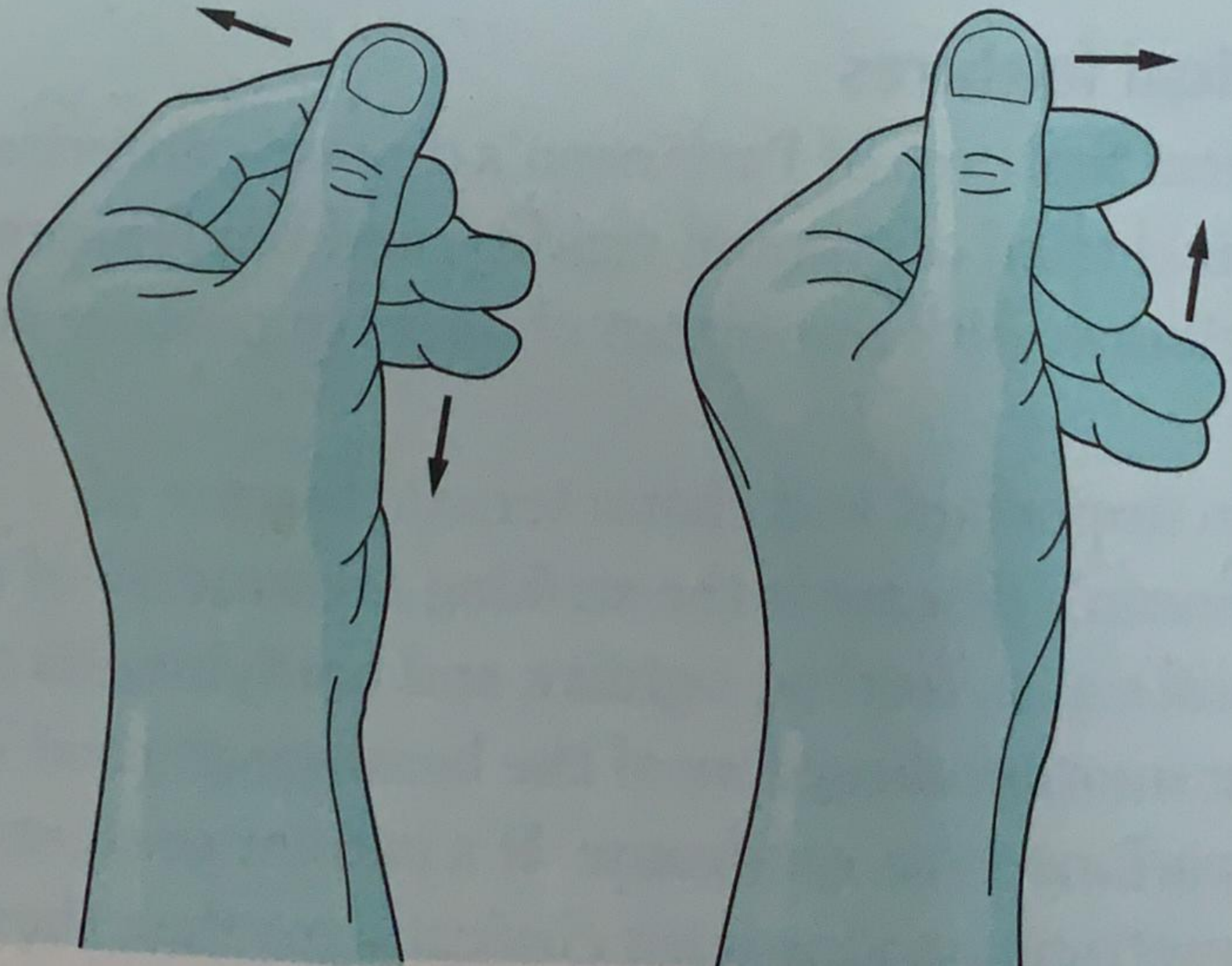
6. Clinical manifestations

The 4 cardinal motor manifestations of PD are tremor, rigidity, bradykinesia, and postural instability

Approximately 80 % of patients with PD have a resting tremor, which is characteristically asymmetric, involves the hands, recurs about 4 times per second

(4 Hz), and is worse with distraction

A" pill-rolling" tremor involving the thumb and forefinger is classic(figure)



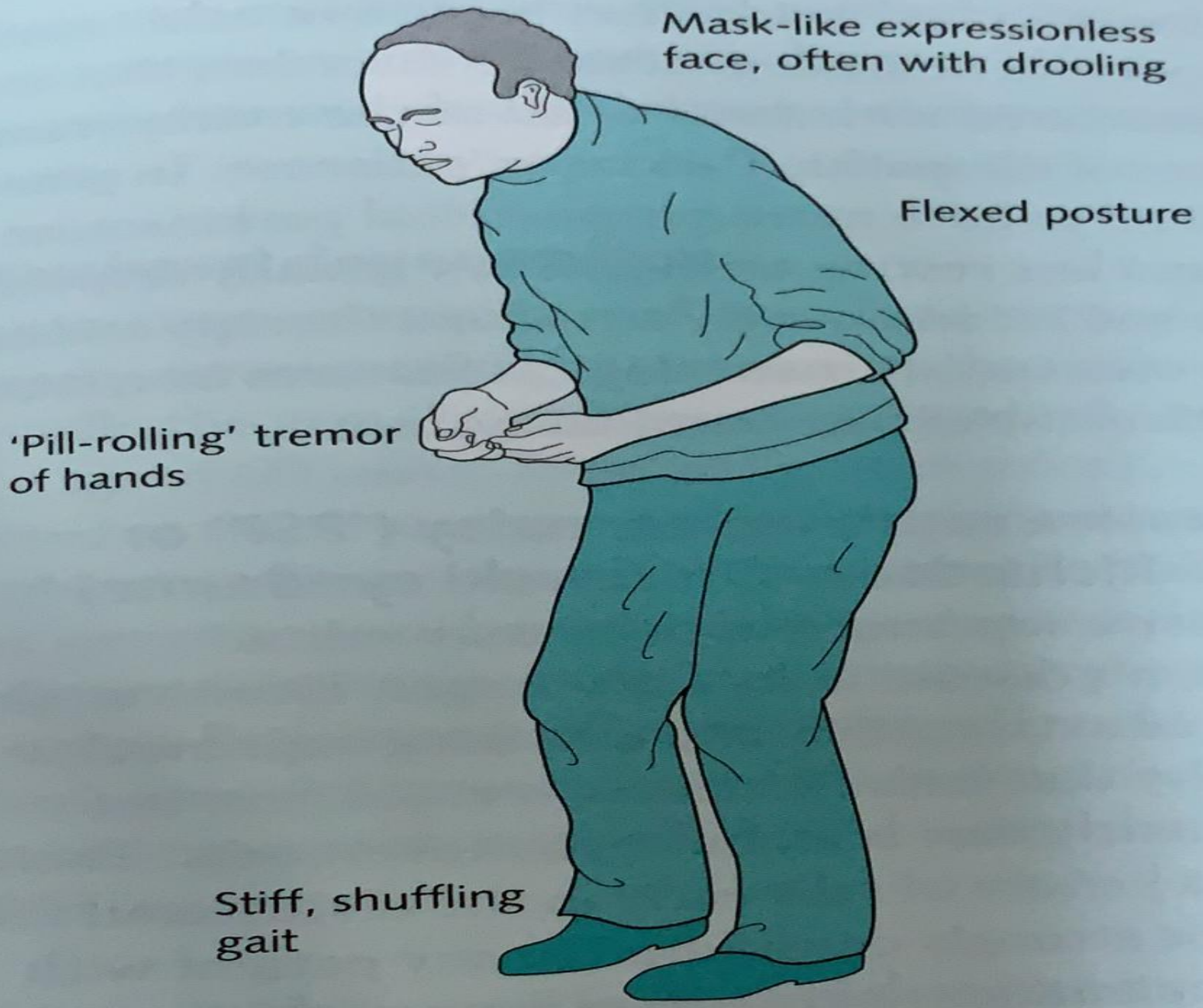
Bradykinesia or slowness of movement is often the most disabling feature of PD and involves both axial and appendicular muscles.

Speech and swallowing difficulties in PD are manifestations of bradykinesia

Rigidity is an increase in muscle tone, which is equal in both flexion and extension of a body part, different than spasticity(table)

In patients with PD , rigidity tends to be greater in the limbs than in the trunk(figure)

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

Postural instability is the final cardinal motor manifestation of PD: patients with advanced PD have difficulty with postural control and tend to fall backward when pulled from behind

PD also has important " nonmotor" features.

Rapid eye movement (REM) sleep behaviour disorder is characterised by violent enacting of dreams.The patient's bed partner will describe them as fighting, kicking, or running while asleep.

This phenomenon is due to the failure to induce muscle atonia in REM sleep and often predates overt PD by many years

Other non-motor symptoms include:

- Depression : is common and may arise independently of the degree of motor dysfunction

- Hallucinations: Vivid, formed visual hallucinations may occur, particularly at night, and need not necessarily indicate cognitive impairment or psychosis

- Psychosis: Worsening hallucinations and delusions may escalate to full-blown psychosis, particularly in patients who also have cognitive impairment

- Dementia: Cognitive impairment is a common accompaniment of advanced Parkinson's disease

- Sleep disorder: Insomnia is common in Parkinson's disease and may relate to immobility, mood disturbance, hallucinations and various sleep-related behavioural and movement disorders

- Autonomic symptoms:

The skin may have a greasy seborrheic texture

Constipation is common, as are bladder disturbance and erectile dysfunction

Other autonomic features, e.g., postural hypotension, are relatively milder than in multiple system atrophy

- Anosmia: it is a feature of Parkinson's disease which may antedate the onset of motor symptoms by many years

7. Treatment

The most effective medical treatment of PD is replacement of deficient endogenous dopamine with levodopa.(Indeed , if this does not help, one should consider the possibility of other illnesses other than idiopathic PD)

Levodopa is combined with carbidopa, an inhibitor of peripheral dopa decarboxylase, which allows the levodopa to cross the blood-brain barrier and reach its target, while reducing peripheral dopaminergic side effects including nausea, vomiting and postural hypotension

Initially levodopa is quite effective for most patients with PD, but over time it loses its effectiveness , and disabling dyskinesias develop

The long-term treatment of PD is complicated (table)

The monoamine oxidase B inhibitors rasagiline and selegiline may provide slight benefit to patients with PD and are often used in the early stages of the disease as monotherapy or as a supplement to levodopa

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.

The dopamine agonists pramipexole and ropinirole are also options for the treatment of mild or early PD

These medications may improve symptoms and reduce levodopa requirement, thereby minimizing the long-term probability of dopamine-related dyskinesias

Rotigotine is a dopamine agonist available in patch form and is designed to prevent excessive fluctuation in drug levels

Other medications are used for specific applications in PD :

*Anticholinergics including benztropine and trihexyphenidyl are used to treat tremor but generally have little effect on other PD symptoms

*Amantadine is helpful in the management of

dyskinesias and dystonia associated with PD

*The catechol-O-methyl transferase inhibitor entacapone inhibits levodopa metabolism, thereby extending the duration of levodopa action in patients who experience “ wearing off”.

Drug treatments are summarized in the table

TABLE 16-3. Pharmacologic Treatment of Parkinson Disease

Drug	Mechanism of Action	Dosing	Side Effects
Levodopa/carbidopa	Dopamine precursor/ dopa decarboxylase inhibitor	Start with a half of a 25/100 tablet bid; increase dose as needed; typically dosed 3–5 times a day	Anorexia, nausea, psychosis, hallucinations, orthostatic hypotension, dyskinesia
Trihexyphenidyl	Anticholinergic	Start with 1 mg bid–tid; increase to 4 mg tid as needed	Dry mouth, constipation, urinary retention, confusion, hallucinations, narrow-angle glaucoma
Benztropine	Anticholinergic	Start with 0.5–1 mg at bedtime; increase to 2 mg qid as needed	As above
Amantadine	NMDA antagonist	100 mg bid	Hallucinations, leg edema, *livedo reticularis*
Pramipexole	Dopamine agonist	Start with 0.125 mg tid; titrate gradually to 1.5 mg tid as needed	Lightheadedness, sleep attacks, pathologic gambling, and other impulse control disorders
Ropinirole	Dopamine agonist	Start with 0. 25 mg tid; titrate gradually to 1 mg tid as needed	As above
Rotigotine patch	Dopamine agonist	2 mg qd; titrate to 6 mg qd	As above, patch site reactions
Entacapone	COMT inhibitor	200 mg with each L-dopa dose	Nausea, diaphoresis, lightheadedness
Rasagiline	MAO-B inhibitor	1 mg qd	Dizziness, flulike syndrome
Selegiline	MAO-B inhibitor	5 mg bid	Confusion, orthostatic hypotension, nausea

COMT, catechol *O*-methyl transferase; MAO-B, monoamine oxidase B; NMDA, *N*-methyl d-aspartate.

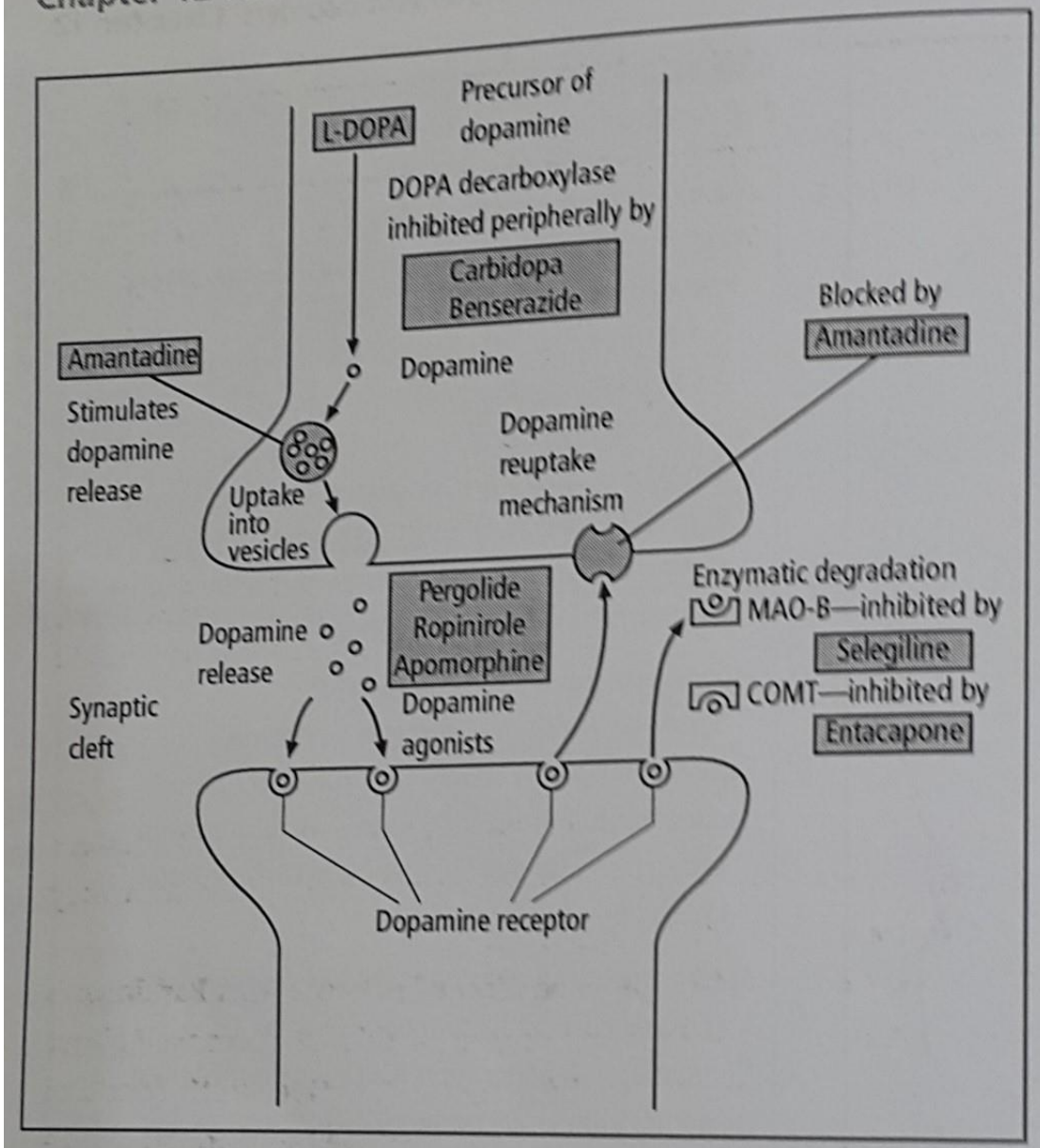


Figure 12.6 Actions of drugs which improve dopaminergic transmission in Parkinson's disease. Amantadine, a weak antiparkinsonian drug, appears to act by several mechanisms. In addition to those illustrated which relate directly to dopaminergic transmission, there are also indirect effects via pathways utilizing other neurotransmitters, e.g. glutamate.

Deep brain stimulation of the subthalamic nucleus (STN) and globus pallidus internus may be helpful in patients with advanced disease

II) Drug-induced movement disorders

Medications which block dopamine receptors including antipsychotic medications (both traditional dopamine blockers and newer, atypical agents) and the promotility agent metoclopramide may produce a variety of movement disorders

A) Acute dystonic reactions

They occur when patients are introduced to dopamine-blocking medications or given high doses of dopamine blockers to which they are not accustomed

Intermittent or sustained contraction in any of the muscles in the face, limbs, or trunk may occur

Forced contraction of the extraocular muscles and tonic deviation of the eyes may occur

Acute dystonic reactions are best treated with anticholinergic agents and benzodiazepines

This reaction is short-lived and does not produce long-term consequences

B) 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

C) 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

D) Tardive dyskinesia (TD)

This is a disorder that occurs after chronic exposure to dopamine-blocking agents

Commonly observed movements include chewing , grimacing, lip smacking, and tongue thrusting

The limbs, trunk, and even diaphragm may be affected

Treatment of TD is challenging:

- Withdrawal of the offending agent often makes the movements worse

- The dopamine-depleting agent tetrabenazine may be helpful

III) Tremor

Tremor is an involuntary oscillatory movement of a body part(arm, leg, head, jaw, lips, palate)

It can be divided into resting (occurring when the body part is at rest), postural (occurring when maintaining a fixed posture) , or action (occurring on movement)

Postural and action tremors usually accompany each other

The term intention tremor is applied when an action tremor worsens as the body part approaches its target

Common types and causes of tremors are:

- Resting tremor: idiopathic Parkinson disease, other parkinsonian syndromes

- Postural/action tremor: essential tremor, physiologic tremor, drugs (e.g., theophylline, beta-agonists), alcohol, orthostatic tremor

- Intention tremor: cerebellum and cerebellar outflow tract dysfunction (e.g. , infarction, multiple sclerosis, tumor, Wilson disease, drugs)

Essential tremor (ET) is the most common tremor and overall, the most common movement disorder

It can begin at any age and tends to get worse over time

Because there is often a family history, the term "familial tremor" is sometimes applied

The tremor is a postural and action tremor, which involves the hands, head, and voice

It often improves with small quantities of alcohol, though this is not recommended as a treatment strategy

The most effective treatment options are propranolol and primidone

Deep brain stimulation of the ventral intermediate nucleus of the thalamus may help patients with disabling ET refractory to medications

IV) Huntington disease and other causes of chorea

Chorea is an irregular ,twisting or jerky movement of a group of muscles

In most cases, chorea flows from one muscle group to an adjacent group in a random-appearing pattern

Chorea is usually accompanied by athetosis, a writhing movement of the limbs

Motor impersistence often occurs with chorea: two examples are the darting tongue and milkmaid grip, which are seen in patients with Huntington disease (HD)

Causes of chorea

* Hereditary: Huntington disease(HD), HD-like syndromes, neuroacanthocytosis, dentatorubral pallidoluysian atrophy, Wilson disease

* Drugs: neuroleptics, antiparkinsonian medications

* Toxins: alcohol, anoxia, carbon monoxide

* Metabolic: hyperthyroidism, nonketotic hyperglycemia, hepatocerebral degeneration

* Pregnancy: chorea gravidarum

* Immunologic: SLE, antiphospholipid syndrome, post-streptococcal (Sydenham chorea)

* Vascular: caudate infarction or hemorrhage

Huntington disease (HD)

*Clinical manifestations

HD, an autosomal dominant neurodegenerative disorder is the most important and serious cause of chorea

HD is characterized by chorea, cognitive impairment, dystonia, and psychiatric illness

Symptoms usually appear between the ages of 35 and 45 years and include the triad of chorea,behavioral changes or personality disorder(frequently obsessive-compulsive disorder) , and dementia

The three may occur together at onset, or one may precede the others by years

* Diagnostic evaluation

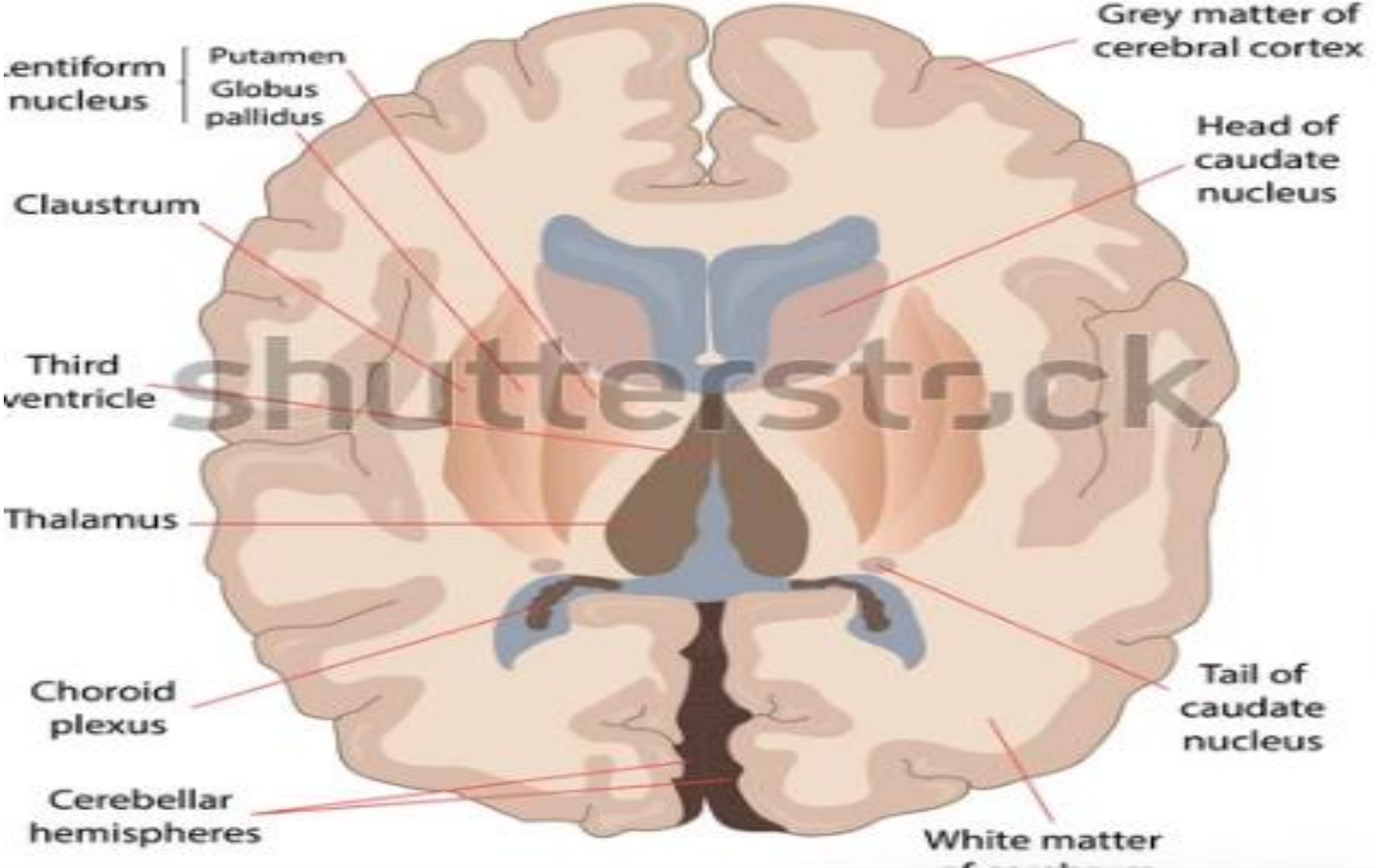
Diagnosis is by personal and family history, clinical signs, imaging, and genetic testing

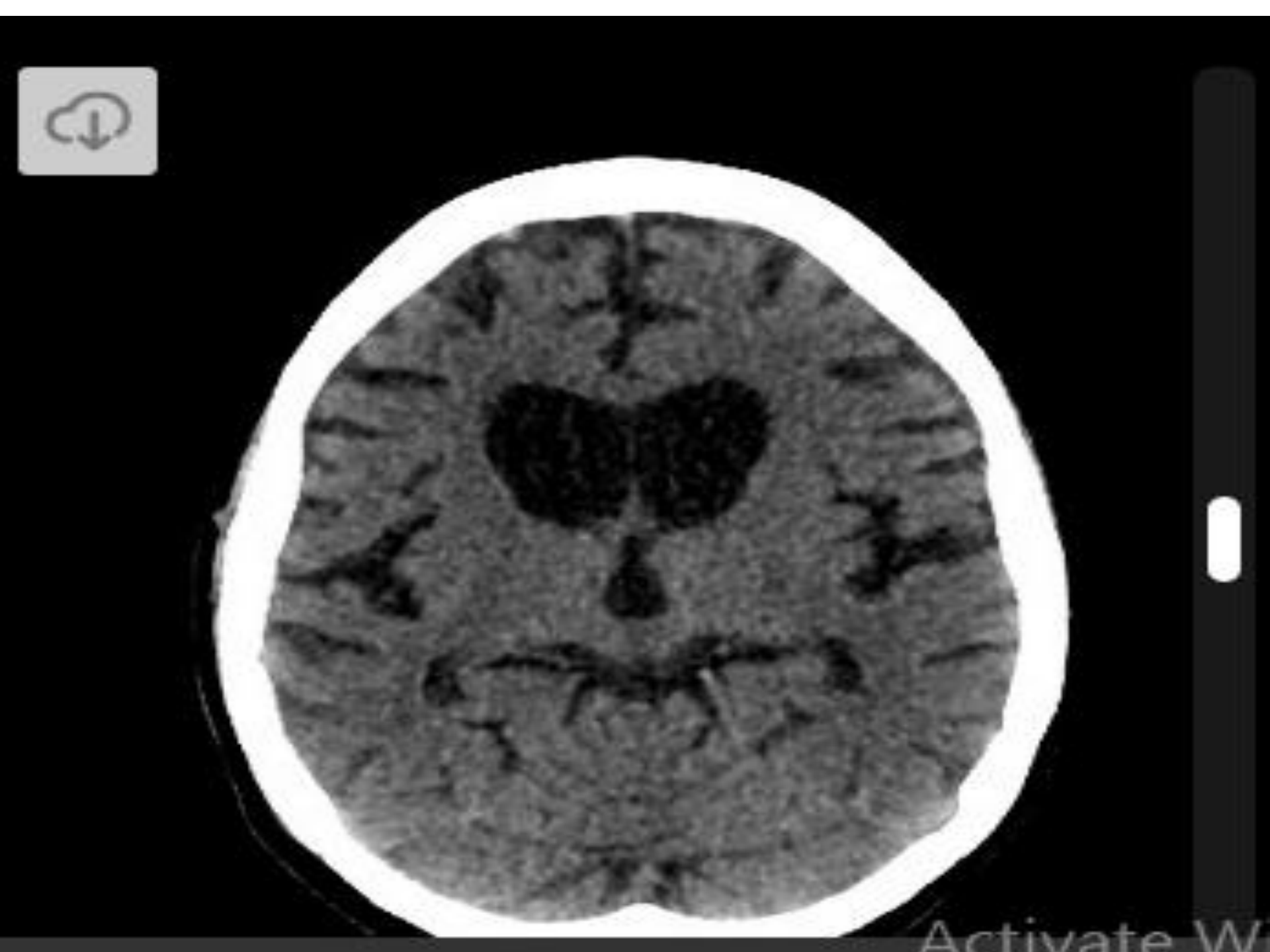
Caudate atrophy , sometimes severe, is the characteristic finding on magnetic resonance imaging (MRI)

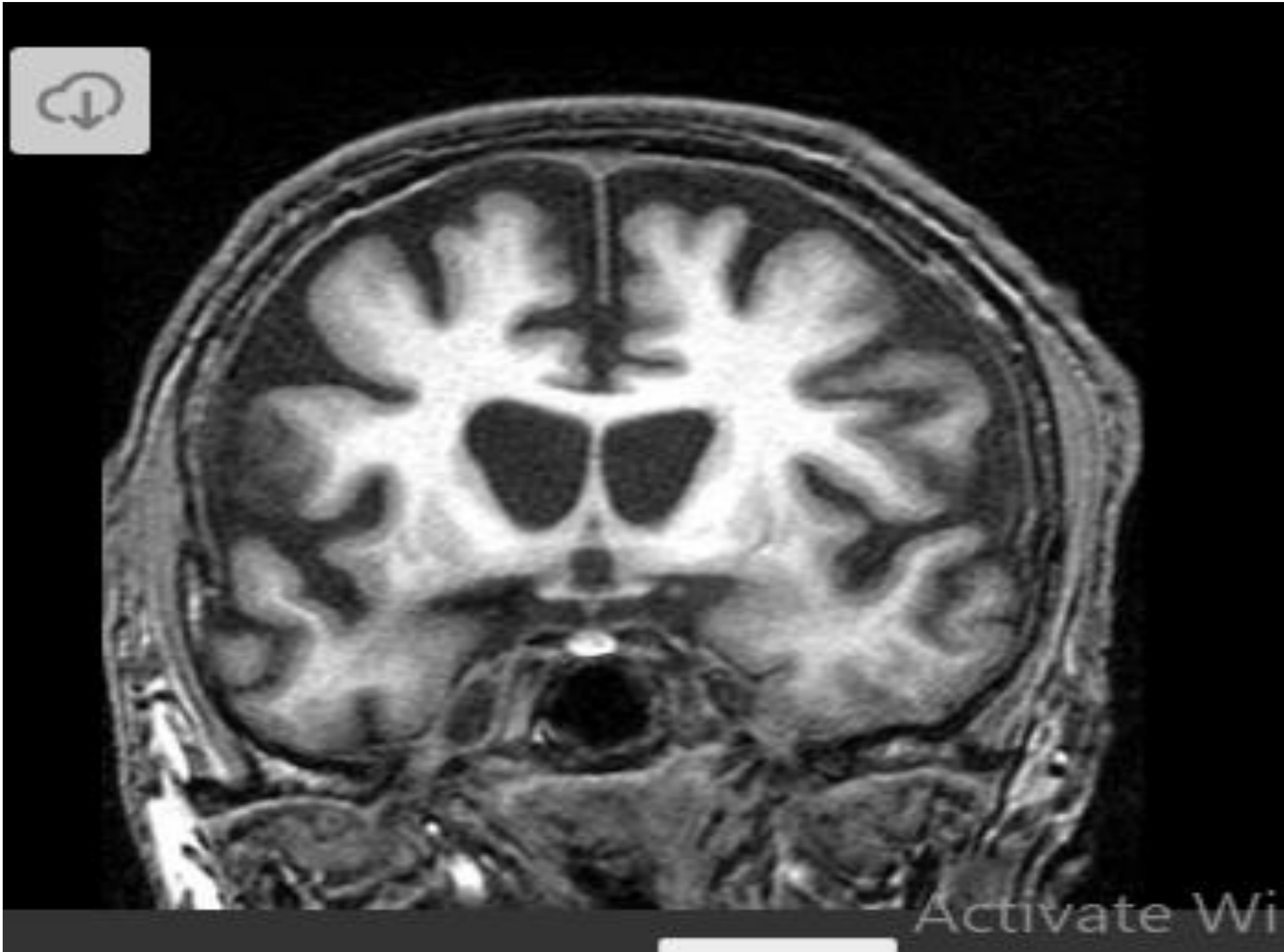
Definitive diagnosis is made by finding an expansion of more than 40 cytosine-adenine-guanine trinucleotide repeats in the HTT gene on chromosome 4

Basal Ganglia

Horizontal Sections through Cerebrum



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* Pathology

Pathologic examination shows severe destruction of the caudate and putamen (striatal and nigral GABA-ergic neurons) and loss of neurons in the cerebral cortex (layer 3)

The molecular mechanisms of HD are unclear but involve accumulation of abnormal intracellular proteins which triggers cell death

* Treatment

Pharmacologic management of dementia and chorea often involves dopaminergic antagonists, including neuroleptic drugs, but it is far from adequate

Neuroleptics can ameliorate the chorea, but the other neuropsychiatric symptoms ultimately prove disabling

Unfortunately, HD is a progressive and ultimately fatal disorder; death occurs 10 to 20 years after onset

Suicide is not rare in at-risk and early-onset HD patients

Genetic counseling is crucial

V) Ballism

Ballism is a brief flinging movement of a limb, most often unilateral (hemiballismus)

The classic lesion responsible for hemiballismus is an ischemic stroke in the contralateral subthalamic nucleus, though lesions in other components of the basal ganglia may be causative

In many cases, ballism resolves on its own, but dopamine-blocking agents may be helpful if this spontaneous improvement does not occur

VI) Dystonia

Dystonia is a sustained contraction of agonist and antagonist muscles producing twisting movements or abnormal postures

Dystonia may be focal (affecting one body part), segmental (affecting one region), or generalized (affecting multiple body parts)

The abnormal movements are worsened by movement and relieved by sensory tricks such as touching or stroking the affected body part

Focal dystonia is more common in adults, and various body parts have characteristic dystonias

Torticollis is excessive contraction of the neck muscles resulting in a fixed head position; it is often quite painful

Blepharospasm involves sustained contraction of the orbicularis oculi and forced closure of the eyelids

Spasmodic dysphonia involves the laryngeal muscles and may result in choppy or strangled speech (adductor spasmodic dysphonia) or a breathy voice quality (abductor spasmodic dysphonia)

Writer's cramp is a focal dystonia of the hand and arm muscles that prevents a patient from using a writing implement properly

In general, botulinum toxin injections are the best treatment option for focal dystonias

Generalized dystonias are more common in children than in adults

The most common of these is **DYT-TOR1A dystonia**, an autosomal dominant disorder caused by a mutation in the gene that encodes the protein torsin A

DYT-TOR1A dystonia starts in childhood or adolescence and often begins in the foot and leg muscles

Treatment options include anticholinergic agents such as trihexyphenidyl, or baclofen, benzodiazepines and deep brain stimulation of the globus pallidus interna

The **dopa-responsive dystonias** are an important group of childhood-onset dystonias and are caused most often by a mutation in the *gene* encoding the enzyme GTP cyclohydrase 1

Parkinsonism may accompany the dystonia

As the name suggests, this group of conditions is responsive to dopamine

For this reason, a trial of levodopa is warranted in all children who develop dystonia

Dystonias may also occur as a manifestation of other central nervous system disorders including Wilson disease, Parkinson disease, Huntington disease, anoxic brain injury, stroke, multiple sclerosis, and medication-induced movement disorders

VII) Myoclonus

Myoclonus is a sudden jerking movement of a muscle that is sufficient to move a joint

Asterixis is a negative form of myoclonus in which a patient is suddenly, but briefly , unable to hold the arms and hands up against gravity, resulting in an erratic and repetitive downward jerking movement

Both are signs of central nervous system dysfunction

The etiologic categories of myoclonus are physiologic, essential, epileptic, and symptomatic:

* Physiologic: hypnic jerks (sleep starts), anxiety and exercise induced

* Essential

* Epileptic: primary generalized epilepsies (e.g., juvenile myoclonic epilepsy), myoclonic epilepsies

(often associated with progressive encephalopathy e.g., Lafora body disease, Unverricht-Lundborg disease, sialidosis)

* Symptomatic: metabolic encephalopathy (uremia, liver failure, hypercapnia), Wilson disease, Creutzfeldt-Jakob disease and other advanced dementias, hypoxic

(post-anoxic brain injury or Lance-Adams syndrome)

Physiologic myoclonus includes common movements such as jerks that occur just at sleep onset(" sleep starts" or " hypnic jerks") and hiccups

Essential myoclonus occurs in isolation without other neurologic symptoms or signs. It may occur in familial and sporadic forms and may be responsive to small quantities of alcohol

Epileptic myoclonus occurs as a manifestation of juvenile myoclonic epilepsy and other " benign" epilepsy syndromes, and with some of the more malignant progressive myoclonic epilepsies

Symptomatic myoclonus accompanies a wide variety of metabolic disturbances and neurodegenerative diseases

Clonazepam and valproate are often effective in controlling myoclonus, but an underlying source should be identified and treated if possible

VIII) Tics

Tics are abnormal , brief muscle contractions that may involve the face, extremities, or speech

They tend to vary in intensity and are irregular in frequency , sometimes occurring in runs of multiple tics and often suppressible for short periods of time

Patients with tics describe an internal sensation of an urge to move or perform the tic, with a sense of relief after the tic has occurred

Stress tends to exacerbate tics

Tics can be divided into motor and vocal tics

These, in turn can be divided into simple and complex tics

Simple motor tics involve eye blinks, facial grimaces, and shoulder shrugs

Complex motor tics include spitting and finger cracking

Examples of simple vocal tics include grunting, throat clearing, and coughing

Complex vocal tics are more extensive vocal utterances of several words blurted out, including foul language

(coprolalia)

Tics are most often idiopathic, but head trauma, encephalitis, and cerebrovascular disease may produce tics

Gilles de la Tourette syndrome is a pediatric-onset disorder in which patients develop motor and vocal tics

It has a presumed genetic origin, but a single responsible gene mutation has not been identified

Boys tend to be affected more often than girls

Multiple motor and vocal tics are present; they may change over time and even go into periods of *remission*

There is a tendency for tics to improve in adulthood

Obsessive-compulsive disorder, attention- deficit hyperactivity disorder , and depression often accompany Tourette syndrome

Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) are a combination of tics, obsessive-compulsive disorder, and anxiety following group A beta-hemolytic streptococcal infection

The etiology of PANDAS is controversial , but presumably the streptococcal infection triggers an autoimmune reaction against the basal ganglia

The symptoms are temporary and respond to treatment with antibiotics and immunomodulatory therapy

Tic treatment options include dopamine antagonists

(haloperidol, risperidone, and pimozide are used most commonly), guanfacine, clonazepam, and clonidine

In many cases, tics improve during youth and disappear by the teenage years or early adulthood