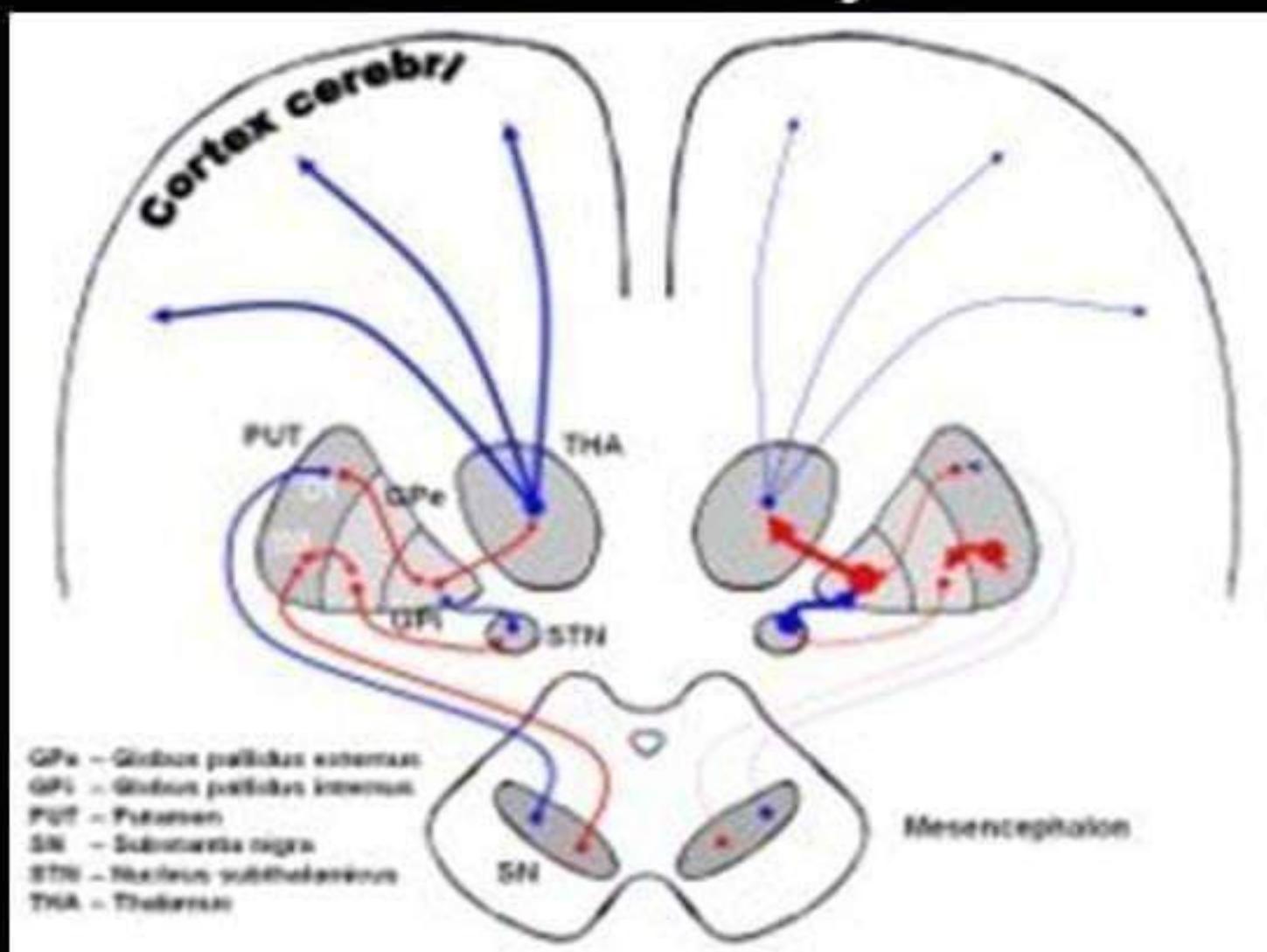


Basal Ganglia

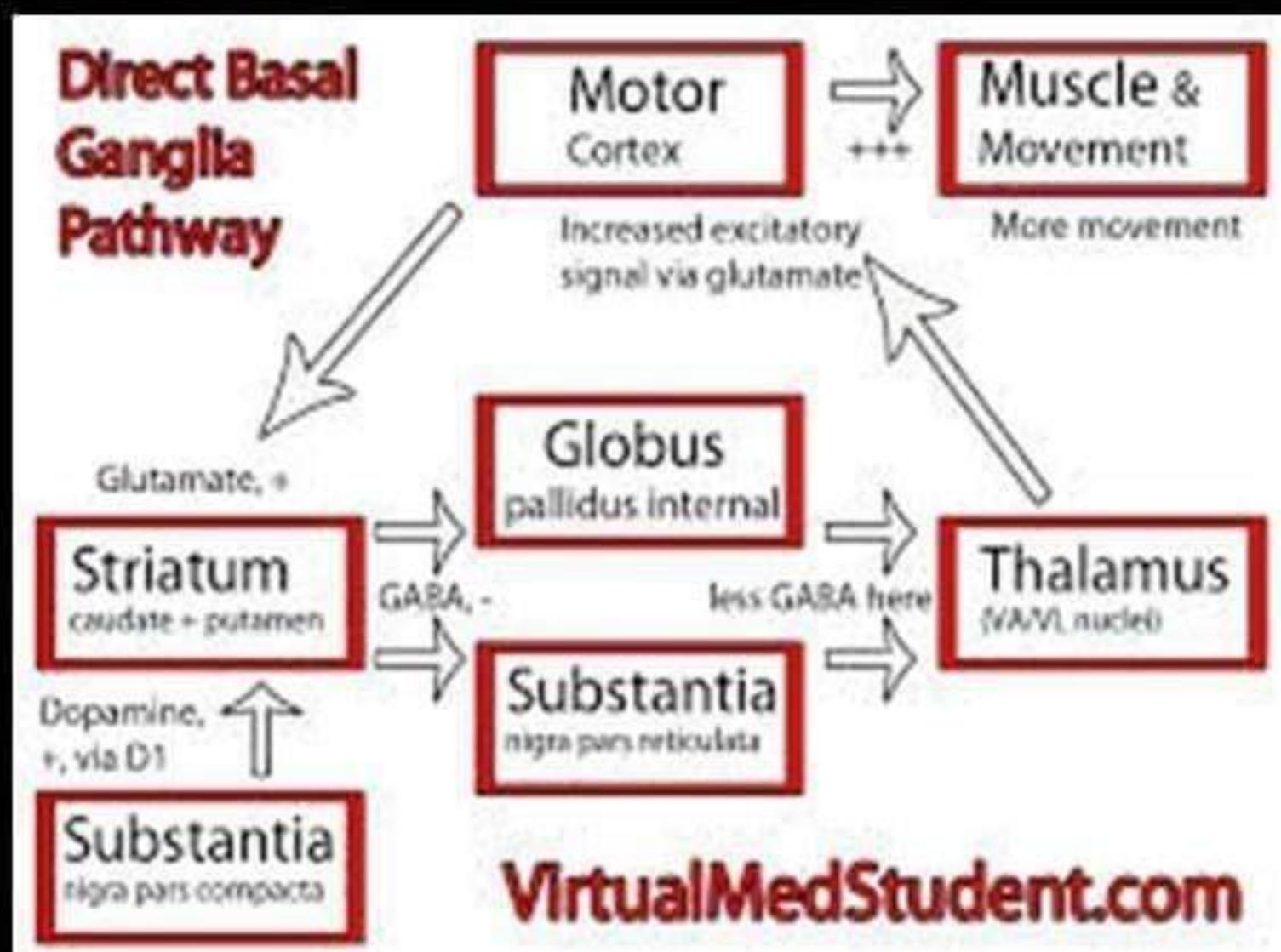
- Direct and Indirect Pathways





Basal Ganglia

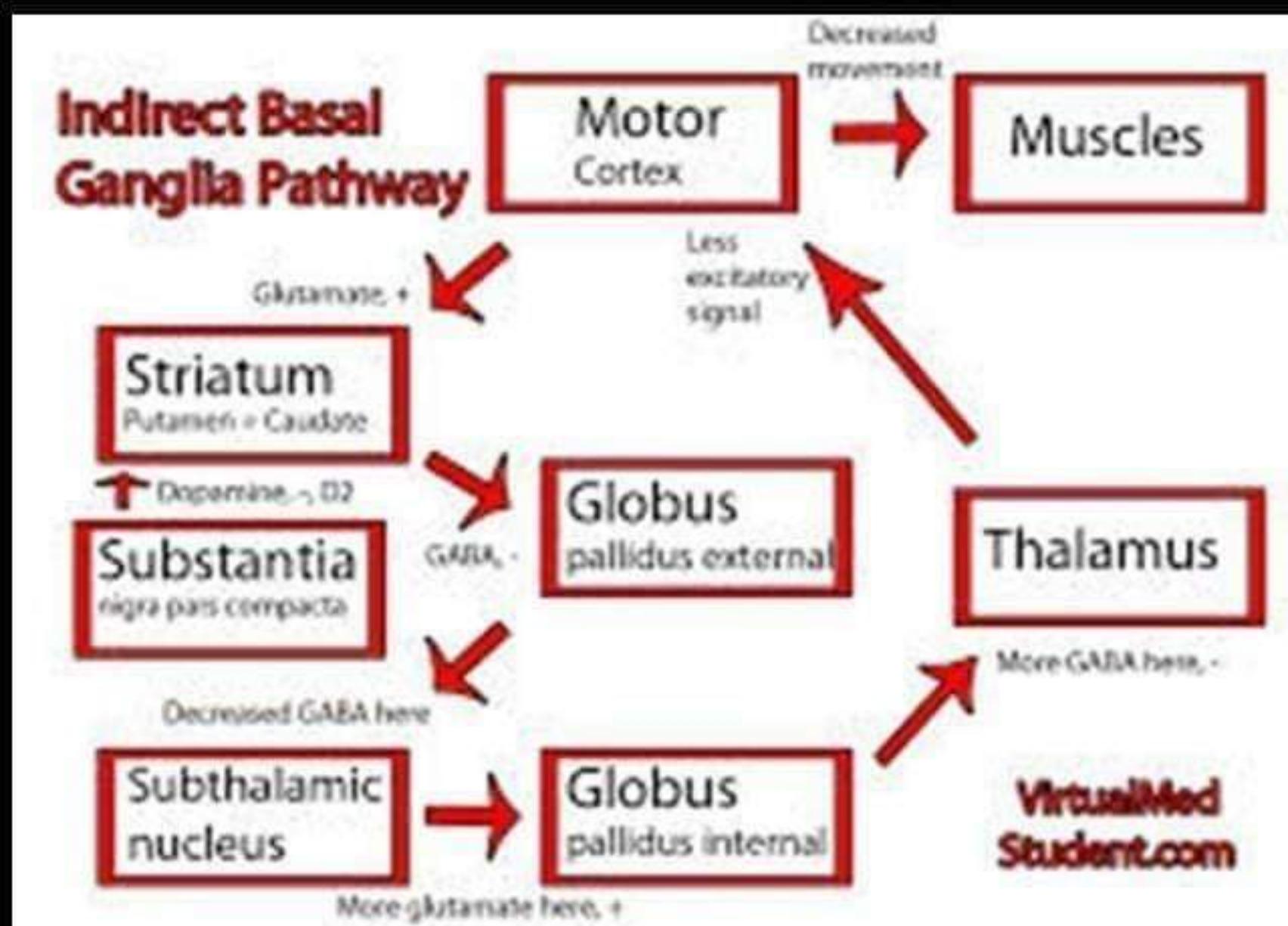
- Direct Pathway





Basal Ganglia

- Indirect Pathway





Epidemiology

Table 1. Epidemiology of Parkinson Disease

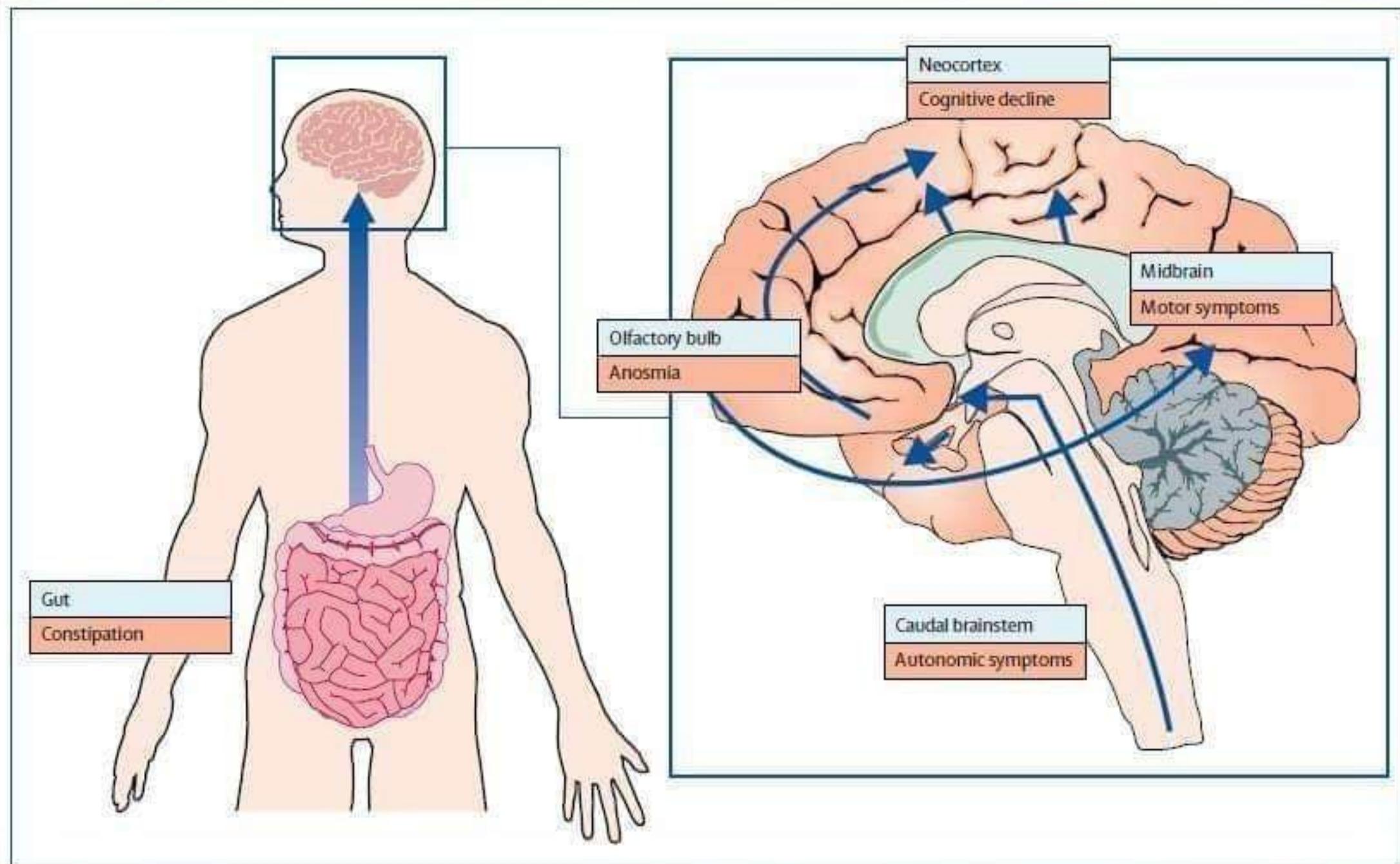
Epidemiological Features	Details
Mean age of onset, y ¹²⁴	65
Men:women ¹²⁵	1.5:1
Incidence, per 1000 person-years ¹²⁵	
Patients aged 55-65 y	0.3
Patients ≥85 y	4.4
Prevalence, % ¹²³	
Total population	0.3
Patients >60 y	1
Idiopathic:hereditary, % ¹²⁶	90:10
Life expectancy ²	Varies with age of onset and occurrence of dementia
Clinical subgroups, % ¹²⁷	
Tremor-dominant	8
Akinetic-rigid	26
Mixed	66
Parkinson disease protective factors ¹²⁸	Cigarette smoking, high coffee consumption
Parkinson disease risk factors ²	Family history of Parkinson disease, pesticide exposure, head injury, constipation ^a

^a Constipation may actually be an early symptom rather than a risk factor.





Braak Hypothesis





1. Tremor



Cogwheeling Rigidity



Bradykinesia



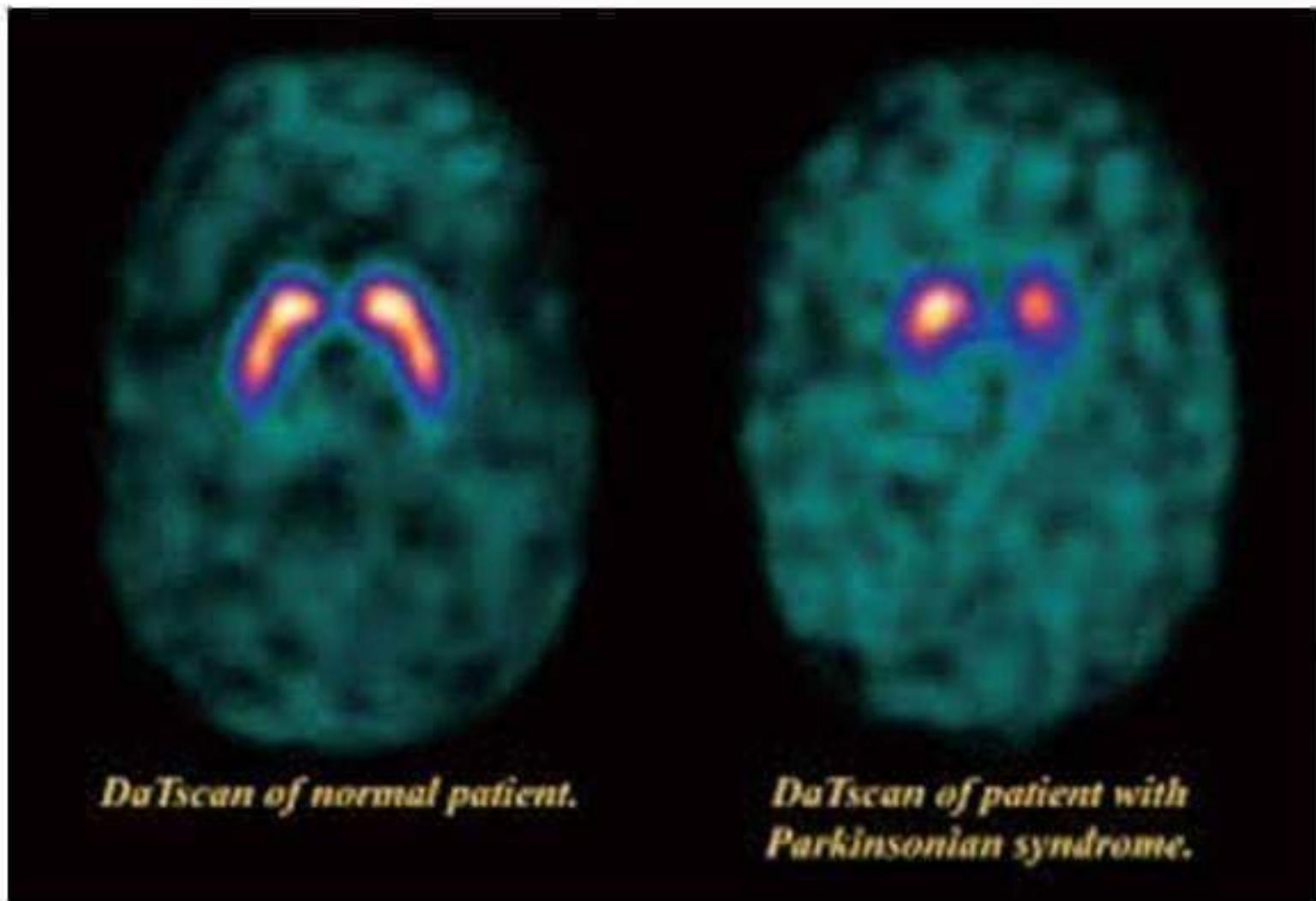
Abnormal Gait



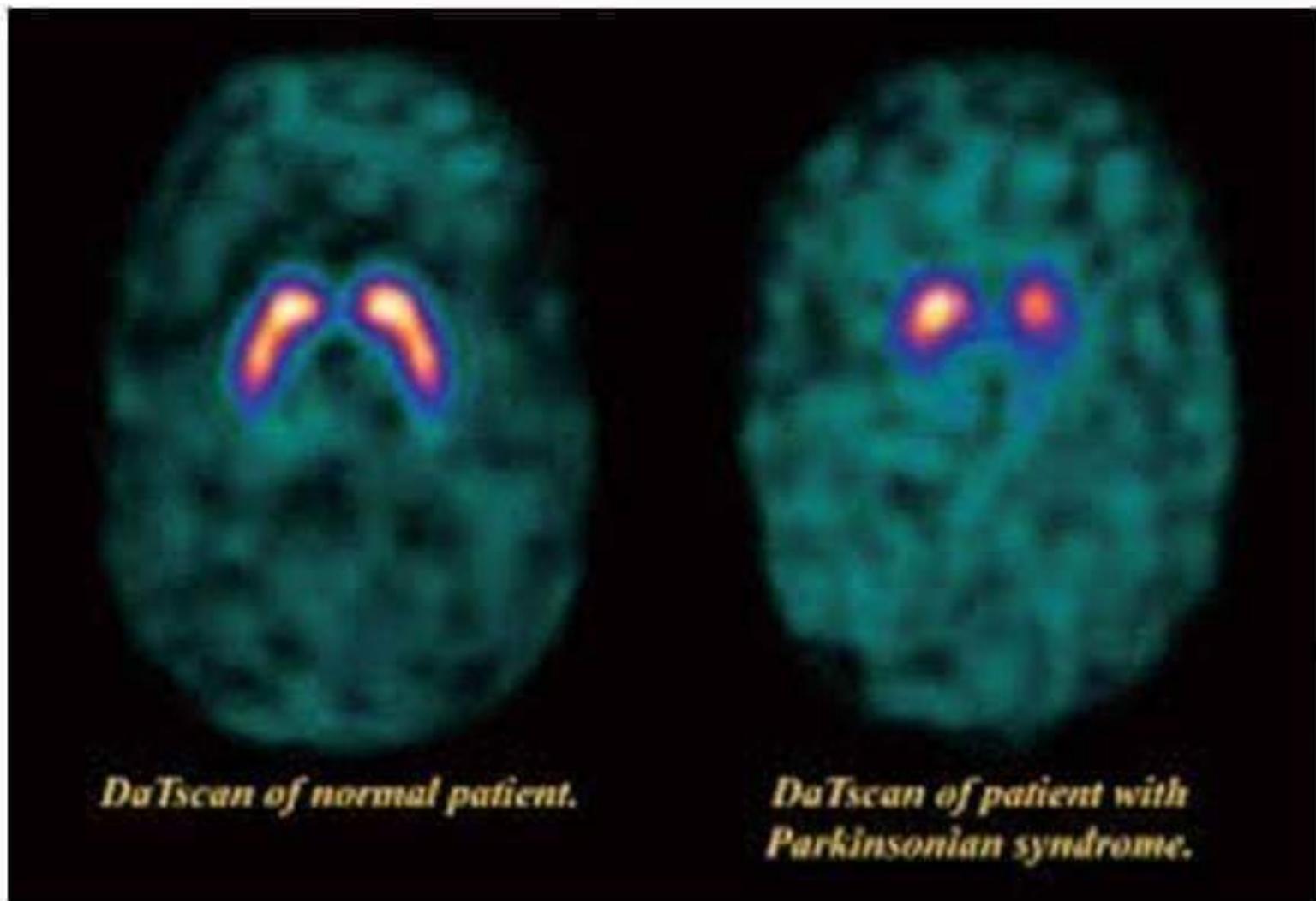
Postural Instability



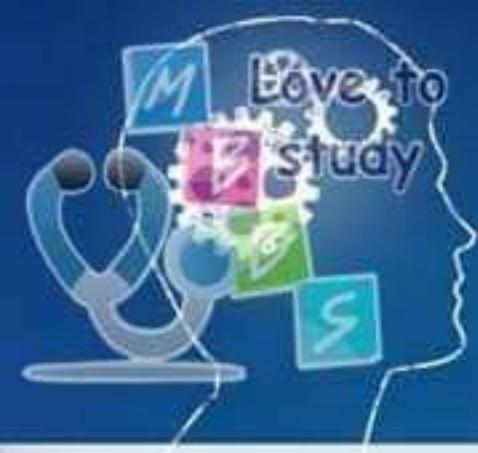
Glabellar Reflex



DAT Scan



DAT Scan



All that shakes is not PD

Table 2 Features differentiating Parkinson's disease from essential tremor

Feature	Parkinson's disease	Essential tremor
Age at onset (y)	55–75	10–80
Family history	+/-	++
Tremor frequency (Hz)	4–6	5–10
Tremor characteristics	Supination-pronation	Flexion-extension
Influencing factors		
Rest	Increases	Decreases
Action	Decreases	Increases
Mental concentration	Decreases	Increases
Writing	Decreases (micrographia)	Increases (tremulous)
Walking	Increases	Decreases
Alcohol	—	Decreases
Postural tremor	Re-emergent	Without latency
Kinetic tremor	+/-	Yes
Limb tremor	Asymmetric	Symmetric
Distribution other than limbs	Face, jaw, lips, chin	Head, voice
Neuroimaging—dopaminergic system	Marked dopaminergic deficit	Mild dopaminergic deficit
Mid-brain sonography	Marked hyper-echogenicity	Mild hyper-echogenicity
Neuropathology	Nigrostriatal degeneration, Lewy bodies	Mild cerebellar degeneration, Lewy bodies in the substantia nigra, brainstem and cerebellum some cases
Treatment	Anticholinergics, amantadine, dopaminergic drugs, deep brain stimulation	Alcohol, beta-blockers, primidone, topiramate, gabapentin, botulinum toxin, deep brain stimulation

PD vs Essential Tremor



All that shakes is not PD

Parkinson Plus Syndromes

- Multiple system atrophy
- Progressive supranuclear palsy
- Parkinsonism-dementia-amyotrophic lateral sclerosis complex
- Corticobasal ganglionic degeneration
- Diffuse Lewy body disease



Carbidopa/Levodopa

- Sinemet
- Sinemet CR
- Apokyn
- Parcopa
- Rytary
- Stalevo





Dopamine Agonists

- Mirapex (Pramipexole)
- Mirapex ER
- Requip (Ropinirole)
- Requip XL
- Neupro (Rotigotine)





MAO-B & COMT Inhibitors

- Azilect (Rasagiline)
- Zelapar (Selegiline)
- Comtan (Entacapone)





Dopamine Agonists

- Mirapex (Pramipexole)
- Mirapex ER
- Requip (Ropinirole)
- Requip XL
- Neupro (Rotigotine)





Motor Complications

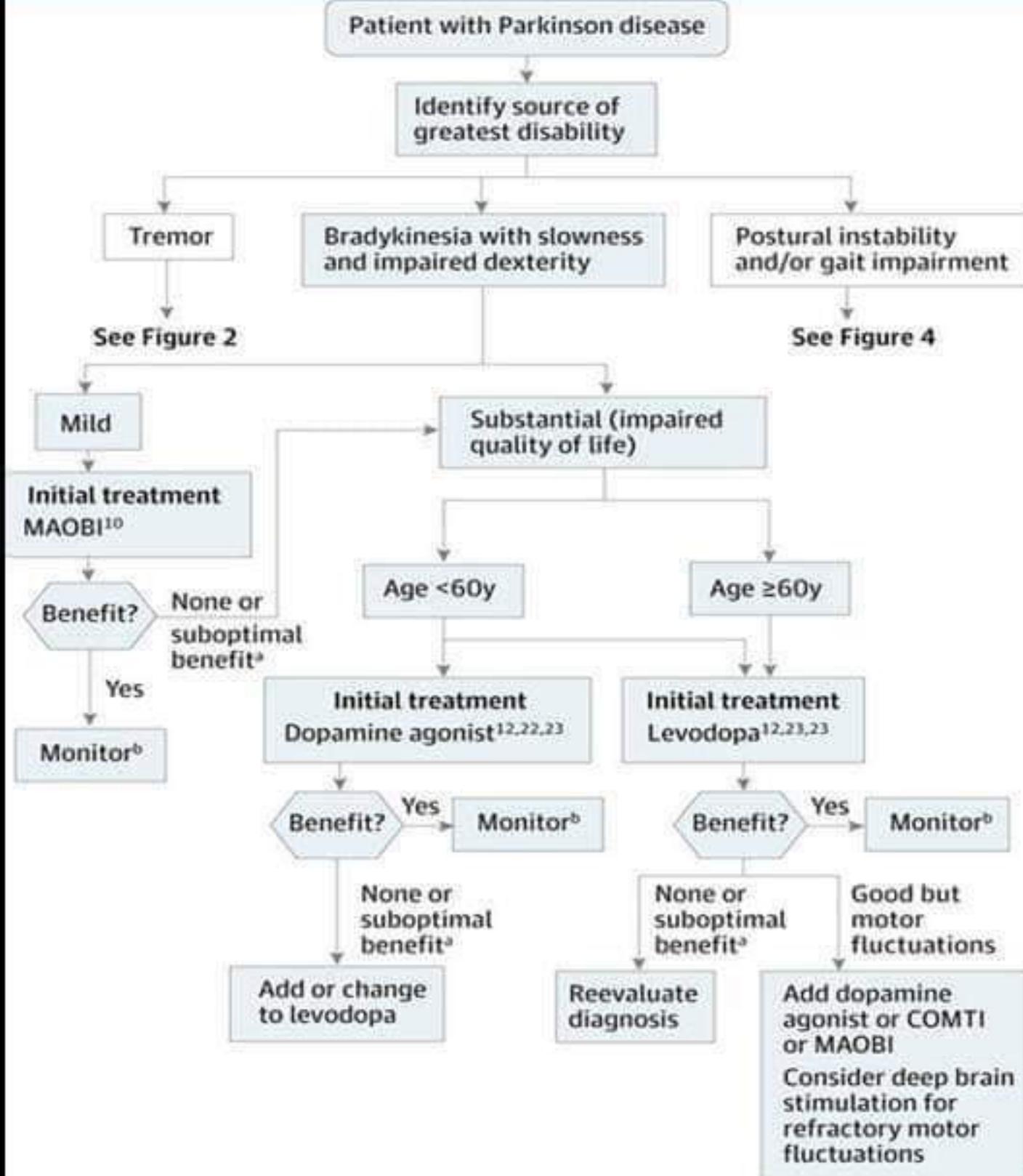
Table 3. Adverse Effects of Dopaminergic Treatment^a

Symptom	Adverse Effect	Time to Onset After Treatment Initiation	Frequency, % ^b
Motor complications	Motor fluctuations	3-5 y	~40 by 4-6 y; ~70 by ≥9-15 y
	Dyskinesia	3-5 y	~35 by 4-6 y; >85 by ≥9-15 y
Impulsive and compulsive behaviors	Impulse control disorders	Any time	~15
	Dopamine dysregulation syndrome	Any time	Up to 4
	Punding	Any time	Up to ~15
Nausea		Immediate	~15
Hallucinations		Generally later in disease course; earlier in older patients	>70 by 20 y



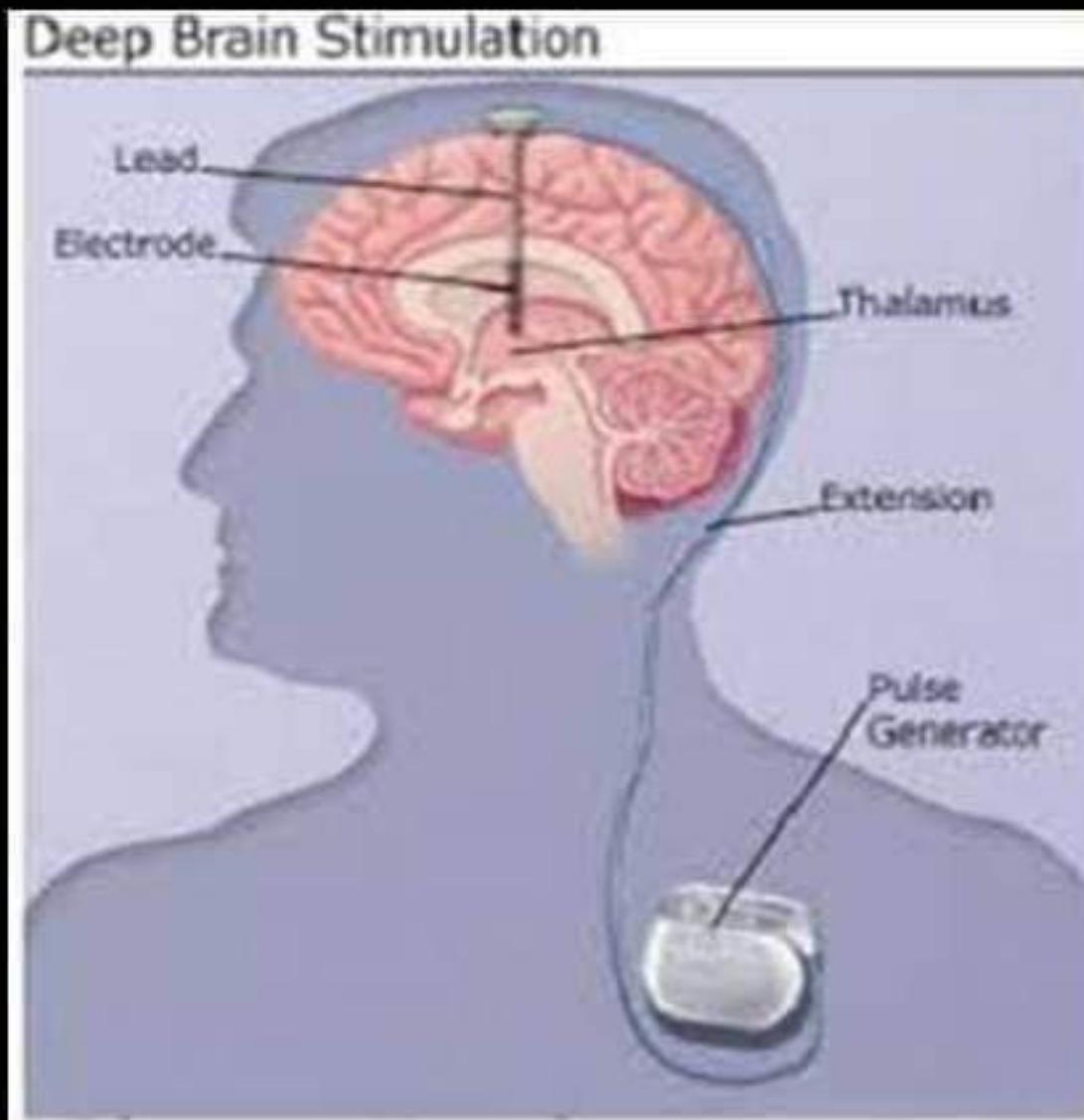


Algorithm



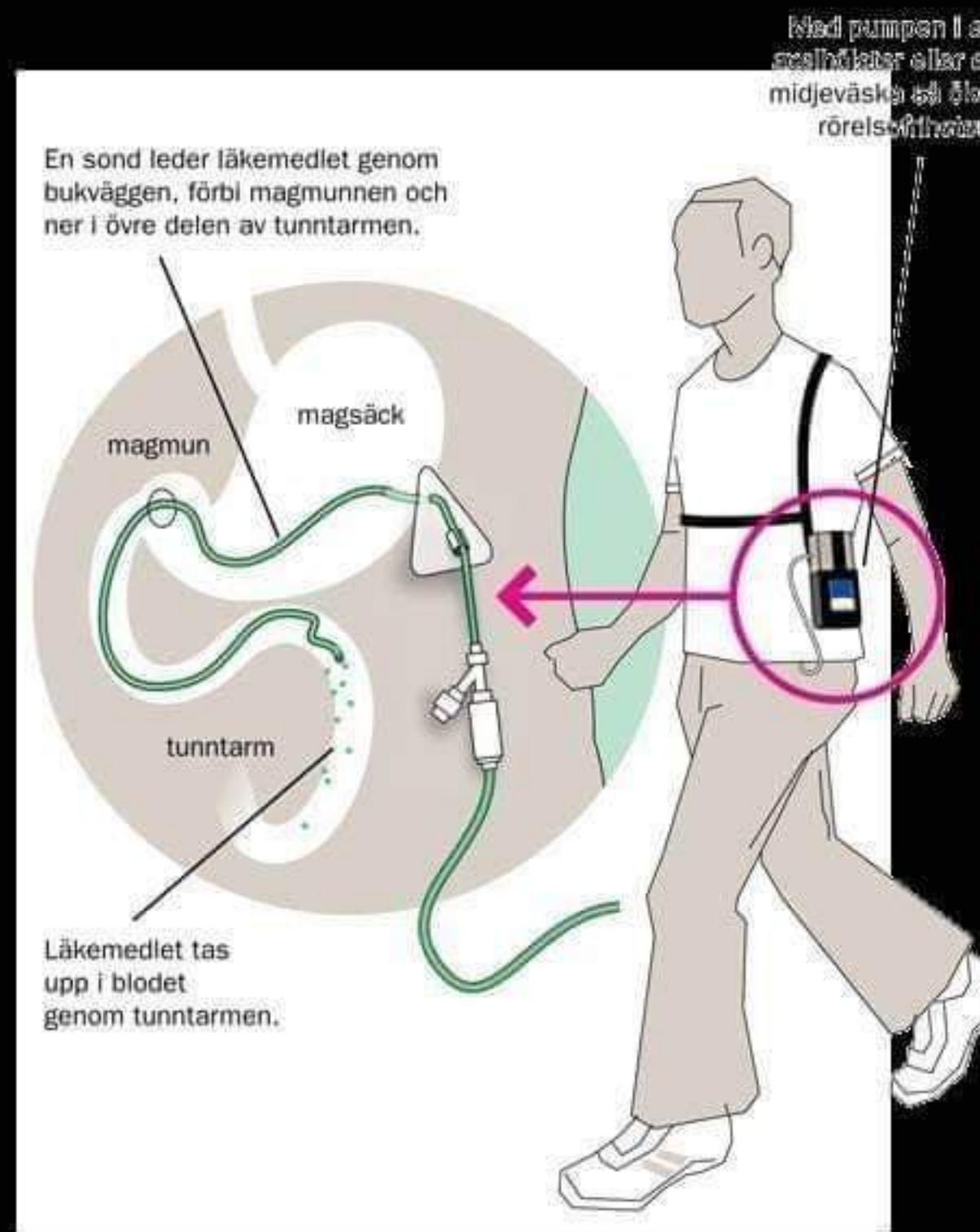


Surgical Intervention





Intestinal Infusion





Treatment of Non-Motor Symptoms

Table 5. Treatment of Nonmotor Symptoms of Parkinson Disease

Nonmotor Symptom	Medication	Dosage	Level of Recommendation*	Adverse Effects
Nausea	Domperidone ^a	10 mg thrice daily; max, 20 mg 4 times daily	U	Cardiac arrhythmia, sudden cardiac death, breast pain, drowsiness, dry mouth, headache, hot flashes, and nausea
RBD	Clonazepam	0.25-2 mg at bedtime	U	Sedation and confusion
	Melatonin	3-15 mg at bedtime	U	Daytime sleepiness, dizziness, and headache
	Citalopram	10-20 mg once daily	U	Akathisia, anorexia, nausea, drowsiness, and sexual dysfunction
Depression	Fluoxetine	10-50 mg once daily	C	Same as citalopram
	Paroxetine	20-40 mg once daily	U	Same as citalopram
	Sertraline	25-200 mg once daily (rarely >100 mg)	U	Same as citalopram
	Venlafaxine extended release	37.5-225 mg once daily	B	Drowsiness, insomnia, sexual dysfunction, and gastrointestinal symptoms
Hallucinations	Nortriptyline	25-150 mg/d single or divided	C	Anticholinergic effects ^a , orthostatic hypotension, ventricular arrhythmias, heart block, drowsiness, sexual dysfunction, and weight gain
	Desipramine	25-150 mg/d single or divided	B	Same as nortriptyline
	Clozapine	6.25-150 mg at bedtime or divided (often effective in very low doses)	B	Agranulocytosis, seizure, myocarditis, cardiomyopathy, and sedation
PD-MCI	Quetiapine	12.5-400 mg at bedtime or divided	C	Extrapyramidal symptoms and sedation
	Rivastigmine ^a	1.5-6 mg twice daily; transdermal patch, 4.5-9.8 mg/24 h	C	Gastrointestinal symptoms, bradycardia, vivid dreams, and exacerbation of rest tremor
PDD	Atomoxetine	Target dose, 80 mg once daily	U	Alopecia, dry mouth, sexual dysfunction, gastrointestinal symptoms, dizziness, and increased heart rate and blood pressure
	Rivastigmine	1.5-6 mg twice daily; transdermal patch, 4.5-9.8 mg/24 h	B	Same as rivastigmine
	Donepezil	5-10 mg once daily	B	Same as rivastigmine
	Galantamine	4-12 mg twice daily	U	Same as rivastigmine
Orthostatic Hypotension	Fludrocortisone	0.05-0.1 mg once or twice daily	C	Hypertension, metabolic abnormalities (including hypokalemia), gastrointestinal symptoms, and myopathy
	Domperidone ^a	10 mg thrice daily; max, 20 mg 4 times daily	C	Same as domperidone
	Midodrine	2.5-10 mg thrice daily	U	Hypertension, nausea, weakness, heartburn, headache, scalp tingling, and chills
Dysautonomia	Pyridostigmine	50 mg thrice daily	U	Hypertension, gastrointestinal symptoms, sweating, and increased salivation/bronchial secretions
	Indometacin	50 mg thrice daily	U	Hypertension, edema, metabolic abnormalities, gastrointestinal symptoms, headache, and renal damage
	Yohimbine	2 mg thrice daily	U	Blood pressure changes, sexual dysfunction, hallucinations, seizure, and renal failure
Salivation	Droxidopa	300 mg thrice daily	U	Hypertension, tachycardia, nausea, vomiting, and headache
	Glycopyrrolate	1 mg thrice daily	B	Anticholinergic effects ^a
	Atropine	1-2 drops of 1% concentration up to 4 times daily	U	Same as glycopyrrolate
	Ipratropium bromide	1-2 sprays (23 µg); max, 4 times daily	U	Same as glycopyrrolate
Dysphagia	BTA	Varies by formulation	B	Dysphagia, dry mouth, and injection-associated discomfort
	BTB	Varies by formulation	B	Same as BTA

