Clinical Case Discussion

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CAMPBELL UNIVERSITY | Jerry M. Wallace School of Osteopathic Medicine

A 70-year-old man presents to the emergency department with syncope.

The patient is a retired police officer who lives with his wife. He describes getting up from a chair after lunch and less than a minute afterward, he lost consciousness and fell. His wife witnessed his fall. He sustained a skin tear on his left forearm but had no head trauma or other injury.

He regained consciousness in less than a minute. He was able recognize his wife and where he was. He had no slurred speech, focal weakness, chest, or abdominal pain. He had no nausea or shortness of breath. He had no tongue bite, or incontinence of bladder or bowel. His wife then called EMS.

His wife indicates that the patient “does not like to see doctors” but he goes to his doctor about twice per year. His wife states the patient has been “slowing down” in recent months and has difficulty with climbing stairs and has become confused while driving.

He denies fever, weakness, fatigue, weight loss or weight gain. ROS is otherwise negative.

PMH:

- HTN
- OA of knees
- BPH

Psurg hx:

- s/p inguinal hernia repair age 40
- s/p appendectomy age 21

Medications:

- Lisinopril 10 mg po daily
- Amlodipine 5 mg po daily
- Tamsulosin 0.4 mg po qhs

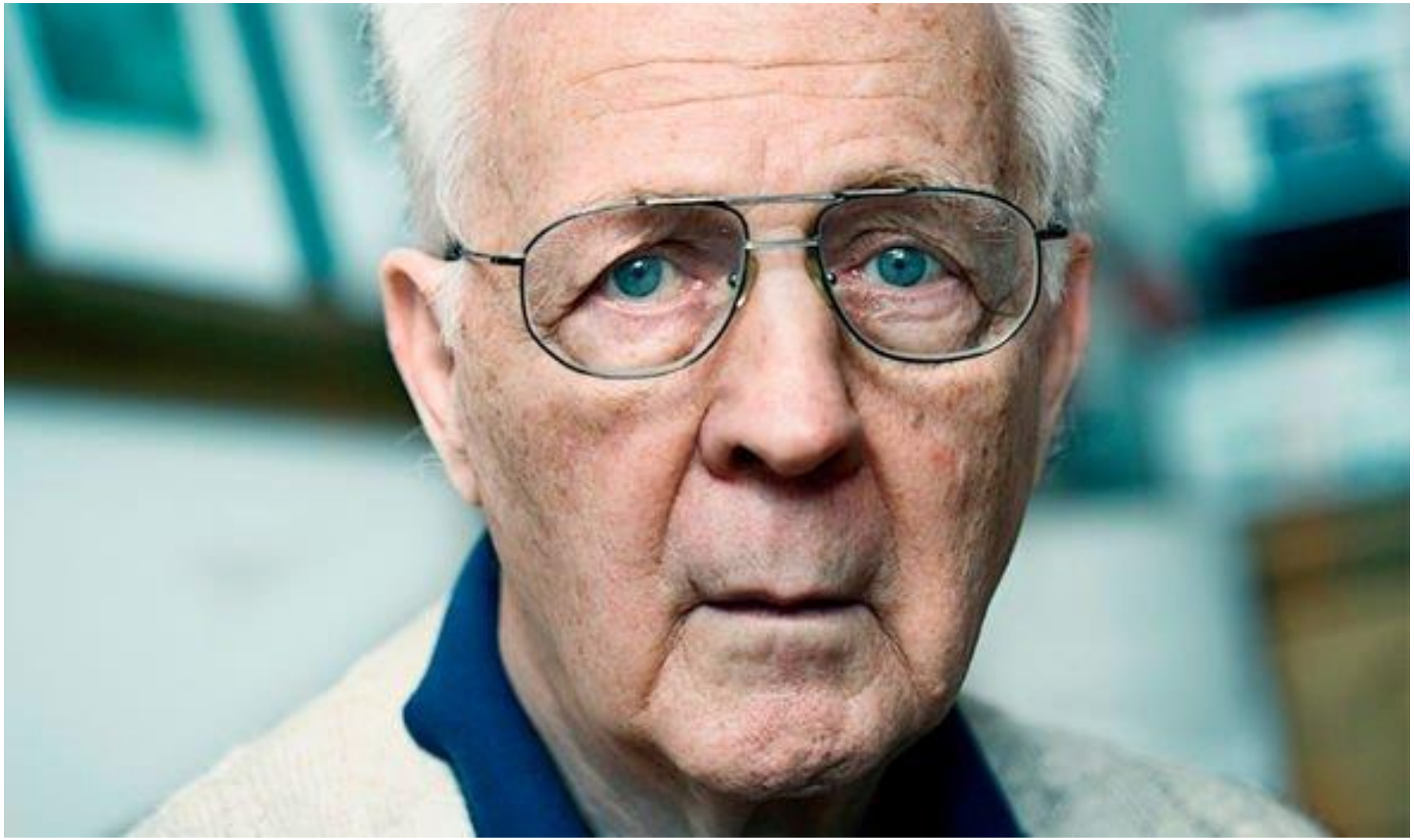
NKDA

Sochx: He is married and lives with his wife. He is a retired police officer. He has never smoked. He drinks alcohol occasionally. There is no history of drug use. He walks for exercise twice per week but has had difficulty completing his walks over the last few months.

Family hx:

- mother d. CVA 87
- father d sepsis 84
- 1 brother age 65, TIA age 62
- 1 sister age 68, HTN

The first step in physical examination, look at your patient.



https://www.express.co.uk/

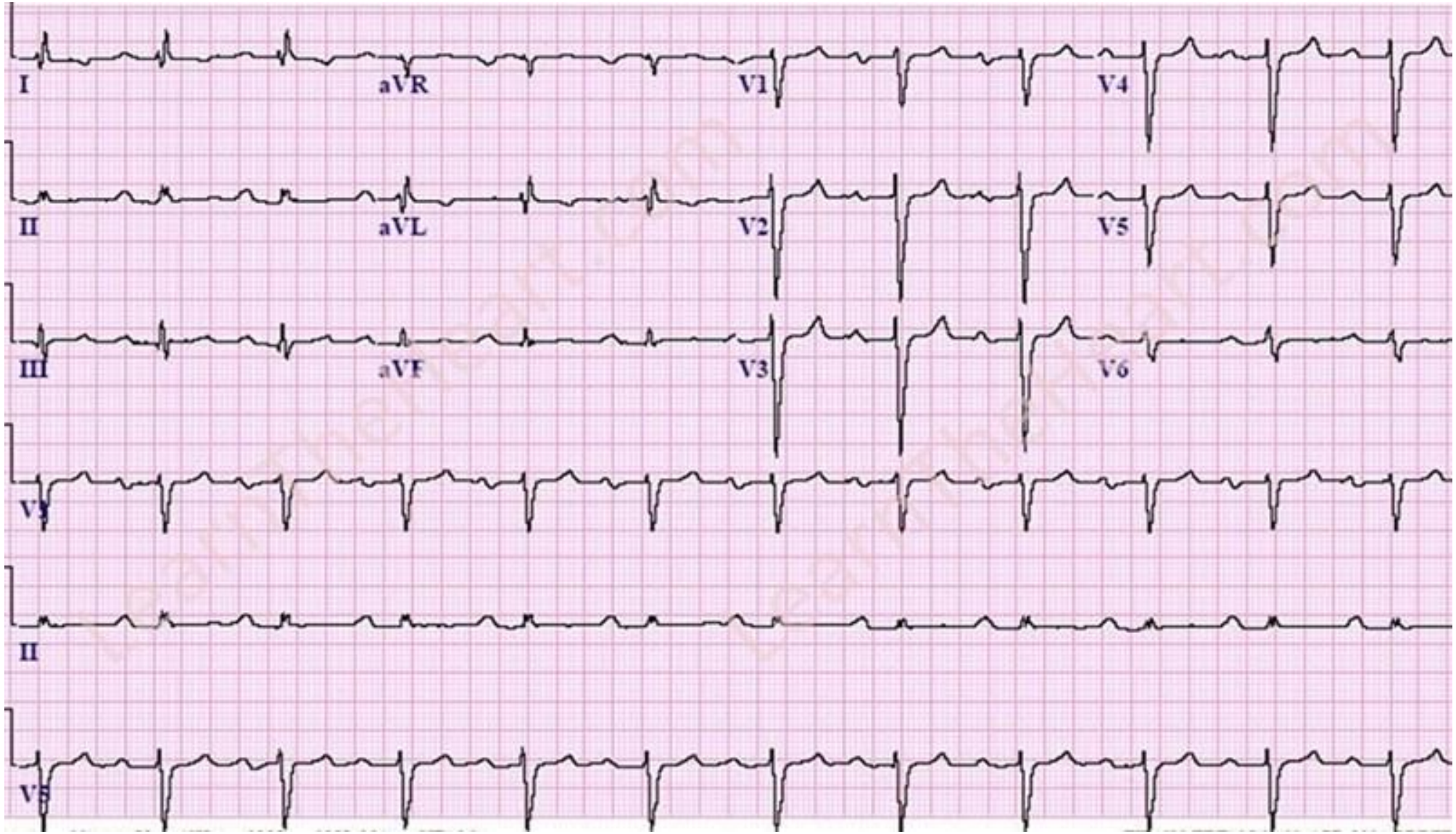
On exam, the patient is an elderly man in no acute distress. He is alert and oriented x 3 and cooperative.
Vitals: bp 105/76 p 72 RR 14 afebrile, O2 sat 94% on RA

HEENT:	PERRL; EOMI; Conjunctivae without injection oropharynx: moist mucous membranes; dentition fair
Neck:	Full ROM; supple; no adenopathy; no thyromegaly; trachea midline
Car:	r/r/r without r/m/g
Lungs:	CTA
Abd:	non-distended, soft, nontender, no organomegaly
Extr:	no edema; dp pulses 1+ B/L
Skin:	There is a 2 cm skin tear on the L forearm which is now bandaged

Now what???

wbc	14.8
hgb	13.1
hct	39.3
platelets	320,000

Na	134
K	3.8
CL	110
CO2	16
BUN	12
Cr	1.2
Glc	90



FIRST-DEGREE AV BLOCK

Helio.com

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Orthostatic bp and HR readings . . .

Lying:	bp 105/70	p 80
Sitting:	bp 90/50	p 90
Standing:	bp 70/40	p 100

Very orthostatic.

He is slowly hydrated overnight with normal saline at 100 ml/hr.

His lisinopril, amlodipine and tamsulosin are stopped.

The following morning, he feels a little better.
Repeat vital signs:

Lying	bp 100/70	p 80
Sitting	bp 95/65	p 90
Standing	bp 80/40	p 95

Not as orthostatic but still symptomatic with lightheadedness.

Fall in a 70-year-old man with orthostatic hypotension: differential diagnosis

V	Vascular	Cardiac arrhythmia
I	Infectious	
N	Neoplastic	
D	Drugs	Anti-HTN meds, alpha-1 blocker
I	Iatrogenic, Inflammatory	
C	Collagen Vascular	
A	Allergic, autoimmune	
T	Trauma	
E	Endocrine	Hypothyroidism, adrenal insufficiency

TSH 4.8 (normal)

Cosyntropin stimulation test:

Normal 8am ACTH Range: 10 to 60 pg/ml

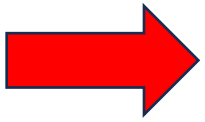
Normal 8 am Cortisol Range: 5 to 25 mcg/dl

8am
ACTH
Cortisol

ACTH 10 pg/ml

Cortisol 5 mcg/dl

Administer
Cosyntropin
(ACTH) 250
mcg IV x 1



8:30 am
Cortisol

Cortisol 18 mcg/dl

9:00 am
Cortisol

Cortisol 27 mcg/dl

Cortisol > 20 = NORMAL ADRENAL FUNCTION

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What are we missing?

A neurologic exam!

CNs: II, III: vision: visual fields are 20/30 in each eye with corrective lenses

III, IV, VI: PERRL; EOMI

V: facial sensation intact

VII: face symmetric, “mask” facies

VIII: hearing adequate

IX, X: elevates soft palate symmetrically; gag intact

XI: shoulder shrug 5/5, symmetric

XII: tongue midline

Sensation: light touch, vibratory sense intact throughout

Cerebellar: finger to nose testing normal

Reflexes: 1+ throughout, toes downgoing B/L

Gait: narrow-based

Motor:

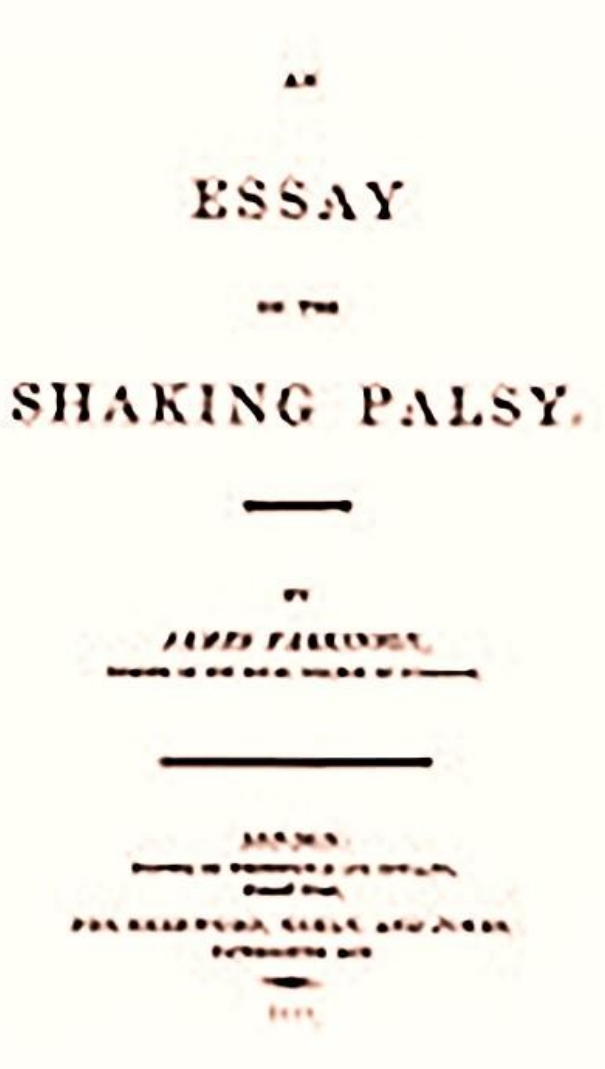
Bulk: normal in all four extremities

Tone: mildly increased rigidity in all four extremities

Strength: 5/5 wrist ext, forearm flex, forearm ext, hip flex, leg ext, leg flex, first toe dorsiflexion

Parkinson's Disease

Dr. James Parkinson, an English surgeon and apothecary described the disease in his essay, the “Shaking Palsy” in 1817.



ESSAY

ON THE

SHAKING PALSY.

Jankovic J, UpToDate 2023

The same condition, “kampavata” (shaking with lack of muscular movement”) was described in the ancient Indian medical system, the Ayurveda, over 4500 years ago!

Very Well Health.com

In ancient times, the *Mucuna puriens* plant was used to treat this condition. This plant was later found to contain levodopa

Jankovic J, UpToDate 2023

Parkinson's Disease (PD) Epidemiology

- As of 2016, 6.1 million patients with PD worldwide
- Incidence begins to increase in fifth decade
- But, 25% of PD patients are diagnosed before age 65
- Male to female ratio: 1.4:1
- Having a first-degree relative with PD increases the risk of PD by two to three times

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Environmental Exposures Associated with PD

- Pesticides
- Air pollution
- High dairy product consumption
- Urban or industrial areas with copper, manganese or lead
- Organic solvents

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Environmental Exposures Associated with PD

- Rural areas
- Farming/agriculture work
- Well water
- High dietary intake of iron, especially with manganese
- Reduced vitamin-D from sunlight and dietary intake

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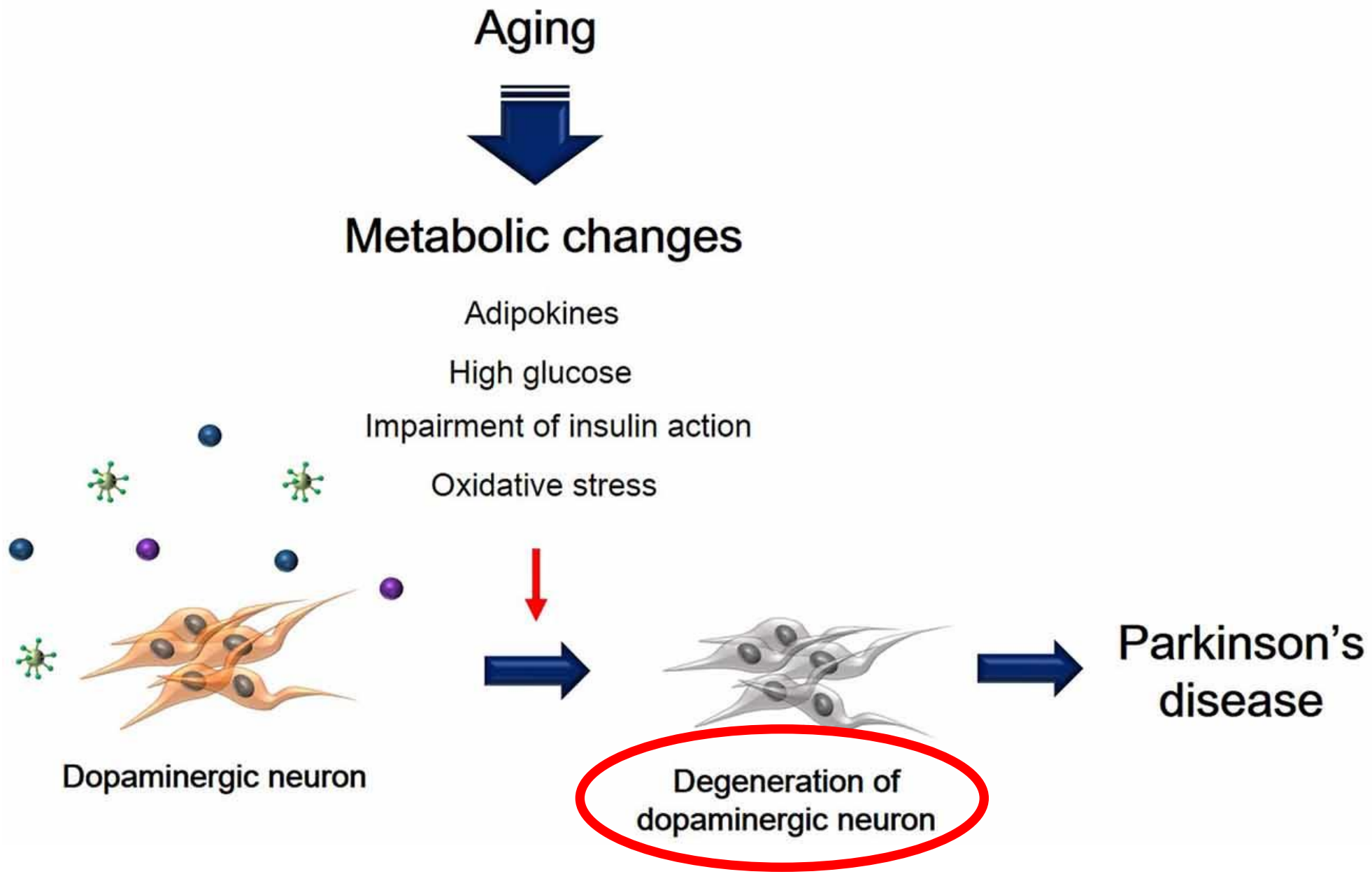
Pathophysiology of Parkinson's Disease



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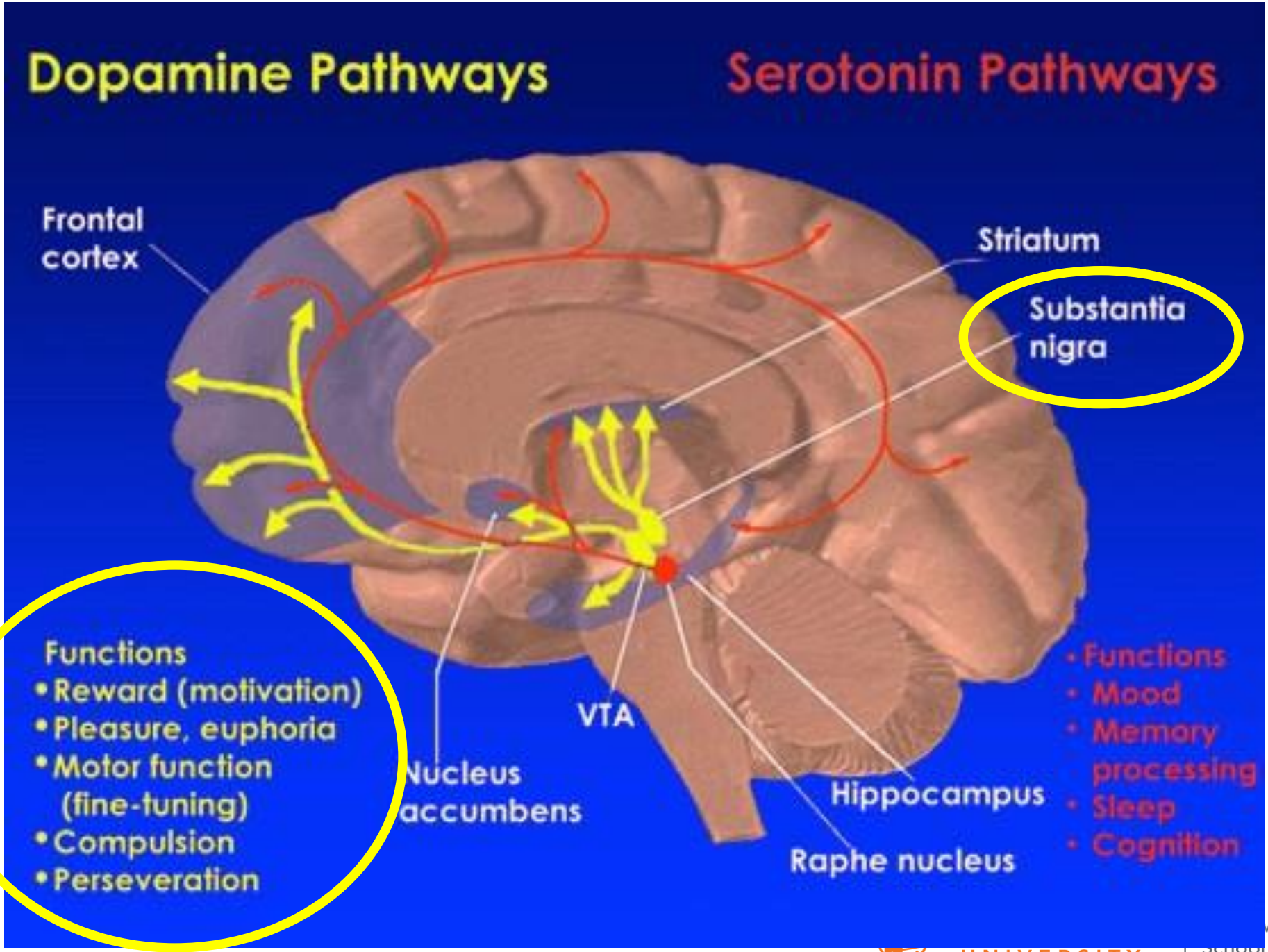
Dopamine Pathways
Serotonin Pathways
Frontal cortex
Striatum
Substantia nigra
Functions
• Reward (motivation)
• Pleasure, euphoria
• Motor function (fine-tuning)
• Compulsion
• Perseveration
VTA
Nucleus accumbens
Hippocampus
Raphe nucleus
• Functions
• Mood
• Memory processing
• Sleep
• Cognition

Key Points: Parkinsonism

Clinical features	• Tremor at rest • Bradykinesia • Rigidity • Gait/balance impairment • Mask facies • Micrographia • Orthostatic hypotension

Now what???

Symptomatic treatment of orthostatic hypotension

Stop antihypertensive medication

Look for and treat anemia

Trial of oral midodrine

Midodrine

Pharmacologic feature	
Class	Alpha-1 agonist
Initial dose	2.5 mg po tid
Maximal dose	10 mg po tid
Time of onset	1 hour
Half-life	3 to 4 hours
Side Effects	**Supine hypertension.** **May reach 200 mm Hg in 7% of patients** **Titrate slowly and use minimum effective dose to relieve hypotension with standing**
Cost	2.5-mg tab: $1.50; 5-mg tab: $3.00; 10-mg tab:

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Our patient is started on midodrine 2.5 mg po tid

He continues to work with physical therapy for gait training.
On the following day, his repeat orthostatic are as follows:

Lying	bp 130/85	p 70
Sitting	bp 120/70	p 80
Standing	bp 100/68	p 82

He is still mildly lightheaded when he stands and starts to walk.

You increase the midodrine to 5 mg po tid

On the following day, his repeat orthostatic are as follows:

Lying	bp 150/90	p 72
Sitting	bp 130/80	p 80
Standing	bp 110/78	p 86

His lightheadedness on standing has resolved.

Diagnostic Criteria for Parkinson's Disease

- Bradykinesia:
  - Slowness of movement PLUS
  - Decrement in amplitude/speed OR progressive hesitations/halts as movements continue

PLUS

- Rigidity: velocity-independent resistance ("lead pipe") to passive movement of large joints while patient is relaxed

PLUS

- Resting tremor: observed in a fully resting limb. Tremor is suppressed by movement

- There are other supportive criteria and "red flags" excluding Parkinson's disease for which expert consultation is recommended.

Chou K, UpToDate 2023

Differential diagnosis of Parkinson's Disease

Differential Diagnosis of Parkinson's Disease

Disorder	**Core Clinical Features**	**Features Distinguishing it from Parkinson's Disease**
Essential tremor	Bilateral action tremor in upper extremities	• Tremor not present at rest unless severe • No involvement of face or legs • Family history • Relieved with alcohol

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Differential Diagnosis of Parkinson's Disease

Disorder	**Core Clinical Features**	**Features Distinguishing it from Parkinson's Disease**
Dementia with Lewy Bodies	• Dementia • Visual hallucinations • Fluctuating cognition • Parkinsonism	Dementia begins before or at the same time as motor symptoms

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Differential Diagnosis of Parkinson's Disease

Disorder	Core Clinical Features	Features Distinguishing it from Parkinson's Disease
Multisystem atrophy	• Parkinsonism and/or cerebellar dysfunction • Autonomic failure • Pyramidal signs (Babinski signs)	• Poor response to levodopa • Symmetric motor symptoms • Early falls • Relatively preserved cognitive function • Nocturnal stridor

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Differential Diagnosis of Parkinson's Disease

Disorder	Core Clinical Features	Features Distinguishing it from Parkinson's Disease
Progressive supranuclear palsy	• Gait disturbance with falls • Ophthalmoparesis • Parkinsonism	• Poor response to levodopa • Early falls • No tremor • Pseudobulbar affect

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Differential Diagnosis of Parkinson's Disease

Disorder	Core Clinical Features	Features Distinguishing it from Parkinson's Disease
Corticobasal degeneration	• Asymmetric movement disorder • Orobuccal or limb apraxia • Cortical sensory deficits • Alien limb phenomenon • Cognitive dysfunction	• Poor response to levodopa • Aphasia • Apraxia • Cortical sensory loss

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Differential Diagnosis of Parkinson's Disease

Disorder	Core Clinical Features	Features Distinguishing it from Parkinson's Disease
Huntington's Disease	• Chorea • Psychiatric illness • Dementia • Parkinsonism with older age of onset	• Abnormal eye movements • Motor impersistence • Family history (autosomal dominant)

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Differential Diagnosis of Parkinson's Disease

Disorder	Core Clinical Features	Features Distinguishing it from Parkinson's Disease
Frontotemporal dementia with parkinsonism	• Frontotemporal dementia • Parkinsonism	• Family history (autosomal dominant) • Earlier age of onset • Early memory impairment

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Differential Diagnosis of Parkinson's Disease

Disorder	Core Clinical Features	Features Distinguishing it from Parkinson's Disease

Spinocerebellar ataxia	• Progressive cerebellar syndrome
	• Symptoms are variable:
	  • Oculomotor
	  • Retinal
	  • Pyramidal
	  • Extrapyramidal
	  • Sensory
	  • Cognitive
		• Younger age of onset
		• Family history (autosomal dominant)

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Secondary Parkinsonism

- Medication-induced
  - Antipsychotics
  - Metoclopromide
- Vascular
- Toxic, for example:
  - Carbon monoxide
  - Organic solvents
- Metabolic, for example:
  - Hypoparathyroidism
  - Chronic liver failure
  - End-stage kidney disease

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Secondary Parkinsonism

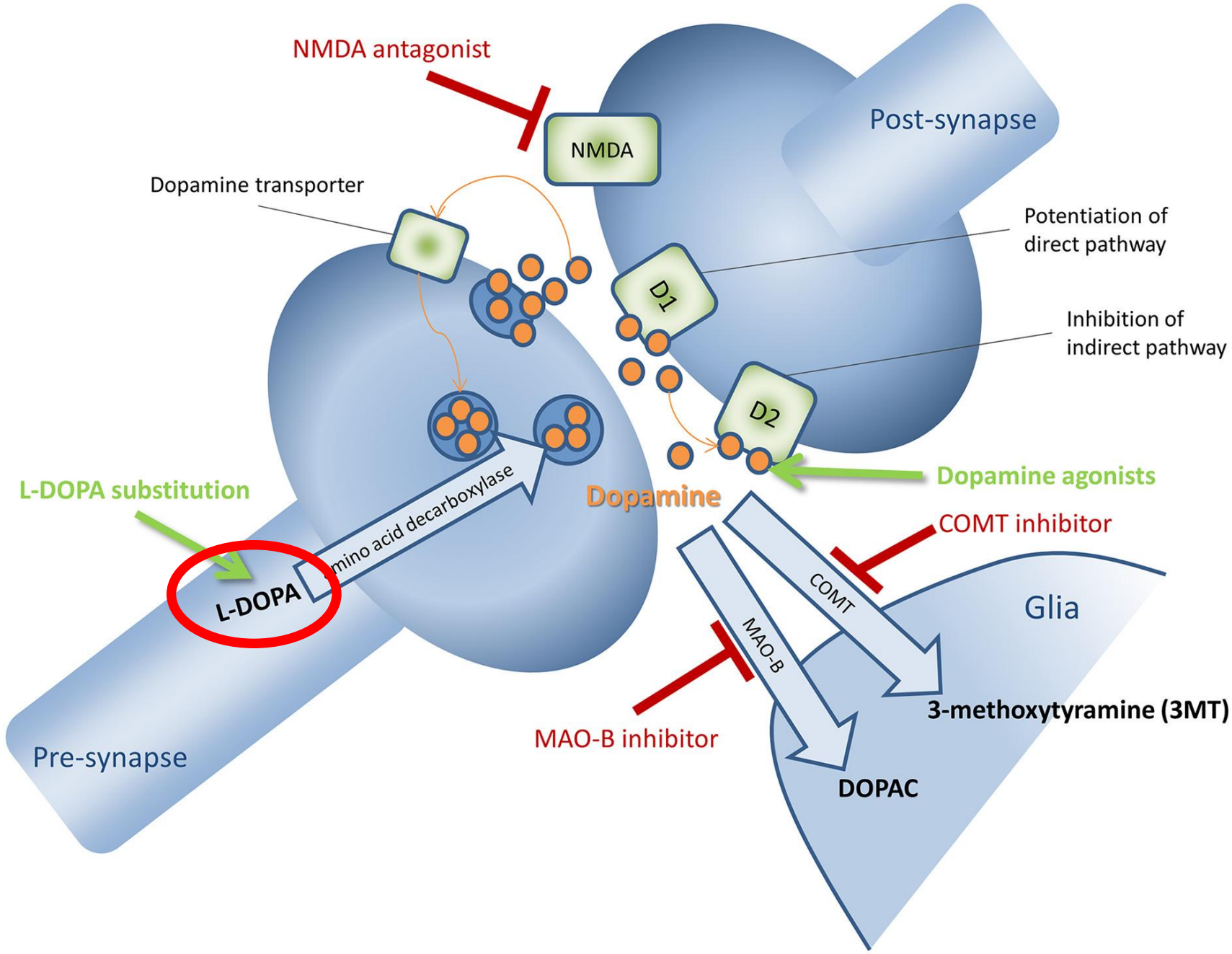
- Structural, for example:
  - Normal pressure hydrocephalus
  - Chronic subdural hematoma
  - Tumor
  - Head trauma
- Infectious, for example:
  - HIV/AIDS
  - Neurosyphilis
  - Prion disease
  - Progressive multifocal leukoencephalopathy (PML)
  - CNS Toxoplasmosis
- Genetic, for example:
  - Wilson's disease

Chou K, UpToDate 2023

You request a neurology consultation and the neurologist confirms the diagnosis of early Parkinson's disease.

The neurologist starts the patient on carbidopa-levodopa immediate release 25 mg/100mg 0.5 tab po tid.

Pharmacologic Therapy to Improve Dopaminergic Neural Pathways in Parkinson's Disease



Wiley Online Library.com

Key Points: Parkinson's Disease

Management	• No medication available to slow the progression
	• Symptomatic treatment
	  • Dopamine precursor: Levodopa
	  • Decarboxylase inhibitor: Carbidopa
	  • Dopamine agonist: pramipexole
	  • Catechol-0-methyltransferase inhibitor: entacapone
	  • Monoamine oxidase type B inhibitor: amantadine
	  • Antipsychotic agent: quetiapine
	  • Norepinephrine precursor: droxidopa

Carbidopa-levodopa (immediate-release)

Pharmacologic feature	
Class	• Dopamine crosses the blood-brain barrier to supplement strial dopamine lacking in Parkinson's disease. • Carbidopa inhibits the breakdown to levodopa via decarboxylation in the peripheral blood
Initial dose	25 mg/100 mg tab: 0.5 tab po tid with meals; must be titrated with expert consultation

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Carbidopa-levodopa (immediate-release)

Pharmacologic feature	
Maximal dose	Levodopa 2,000 mg po daily Carbidopa 200 mg po daily
Time of onset	30 to 60 minutes
Half-life	90 to 120 minutes

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Carbidopa-levodopa (immediate-release)

Pharmacologic feature	
Side Effects	• Nausea • Somnolence • Dizziness • Headache • Confusion • Hallucinations • Delusions • Agitation • Psychosis • Orthostatic hypotension
Cost	$1.61/tablet

Spindler M, UpToDate 2023

Our patient is looking better. His orthostatic vitals remain improved. He continues to work with physical therapy and has a more steady and stable gait.

He continues carbidopa/levodopa 25/100 0.5 tab po tid plus Midodrine 5 mg po tid.

He is discharged to home with his family with outpatient physical therapy and follow up with neurology and his primary care physician.

Questions?

Thank you!