Megan Stevens MD

Parkinson's Disease

Objectives

1. Tremor types
2. Diagnostic process
3. Parkinson's Disease
4. PD treatments
5. What else might it be?

A patient presents in clinic with tremor, worried about Parkinson's Disease...

What is Parkinson's Disease?

James Parkinson 1817

A

AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,

LONDON:

FOR SHERWOOD, NEELY, AND JONES,

1817.

B

FIG. 316.

Paralysis Agitans. *(After St. Leger.)*

Journal of Parkinson's Disease 2 (2012) 181–187
DOI 10.3233/JPD-2012-012108
IOS Press

Fig. 2. James Parkinson's legacy to the field of neurology (A) The frontispiece to his essay on the Shaking Palsy, written in 1
illustration of an individual with Parkinson's disease from William Gower's work *Manual of the Diseases of the Nervous System* written in 1886.

4 cardinal features

Postural instability
Pill rolling rest tremor
Bradykinesia
Rigidity

A

AN

ESSAY

ON THE

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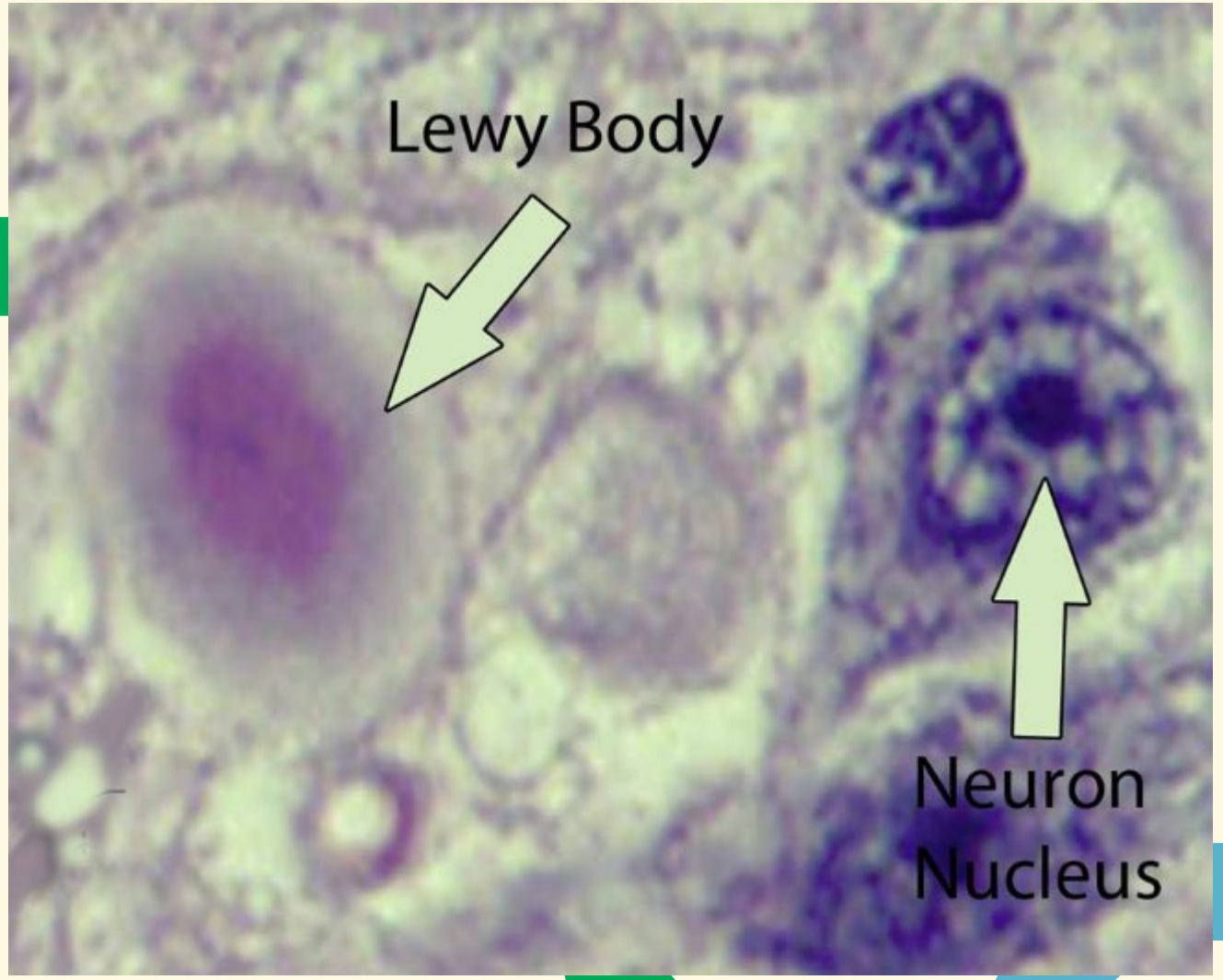
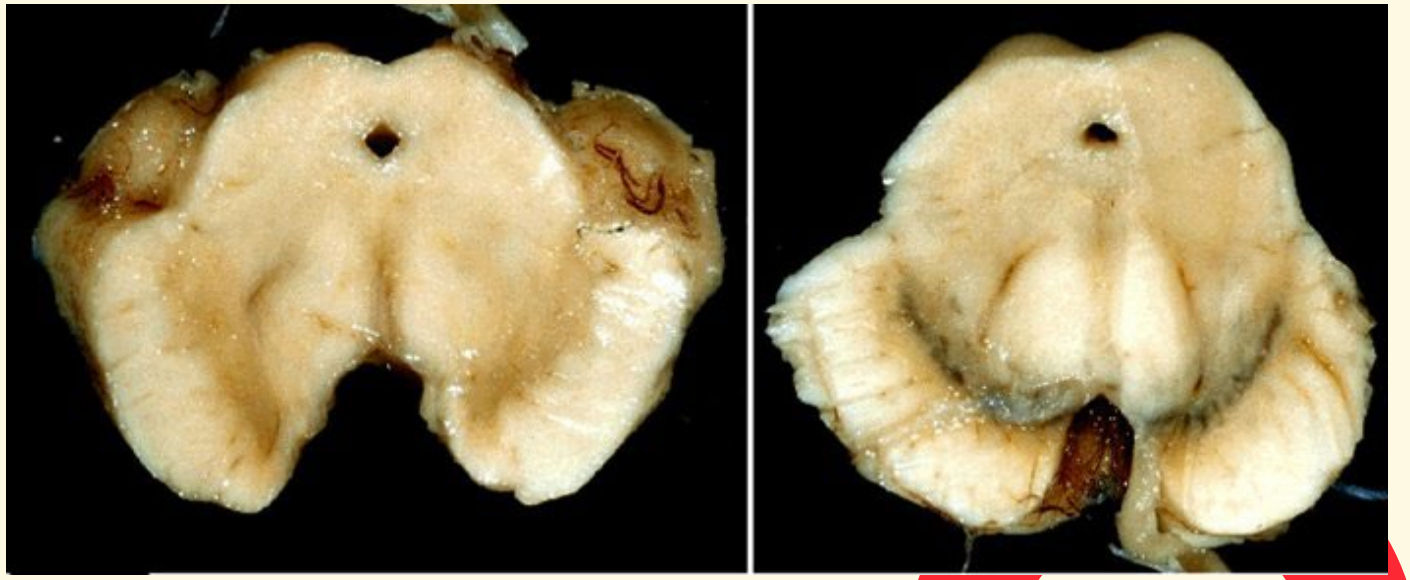


Lewy body
- intraneuronal
- cytoplasmic
- alpha synuclein fibril
(Fredrick Lewy 1912)

Substantia nigra

In 1919 Konstantin Tretiakoff shows loss of substantia nigra (AKA dopaminergic neurons) in PD patients



Levodopa shown to improve PD symptoms in published study in 1968

Cotzias GC (March 1968). "L-Dopa for Parkinsonism". The New England Journal of Medicine. ***278*** *(11): 630.*

Back to our patient, we need to evaluate the tremor

TREMOR

Involuntary
Oscillatory
Rhythmic

Most common movement disorder seen by PCP

Tremor types

TREMOR

Rest - no voluntary contraction
Action - voluntary contraction
- Postural - against gravity
- Isometric - against rigid stationary
- Kinetic - with movement
  - Intention - targeted movement
  - Task specific - self explanatory

Tremor descriptors

Parkinson disease

- Asymmetric
- Rest
- High amplitude
- Slow frequency 3-5HZ/4-6Hz
- resolves with muscle activation

Physiologic tremor

- Symmetric
- Invariable
- Low amplitude
- High frequency 8-12 Hz
- Increased by caffeine and stress

Essential tremor

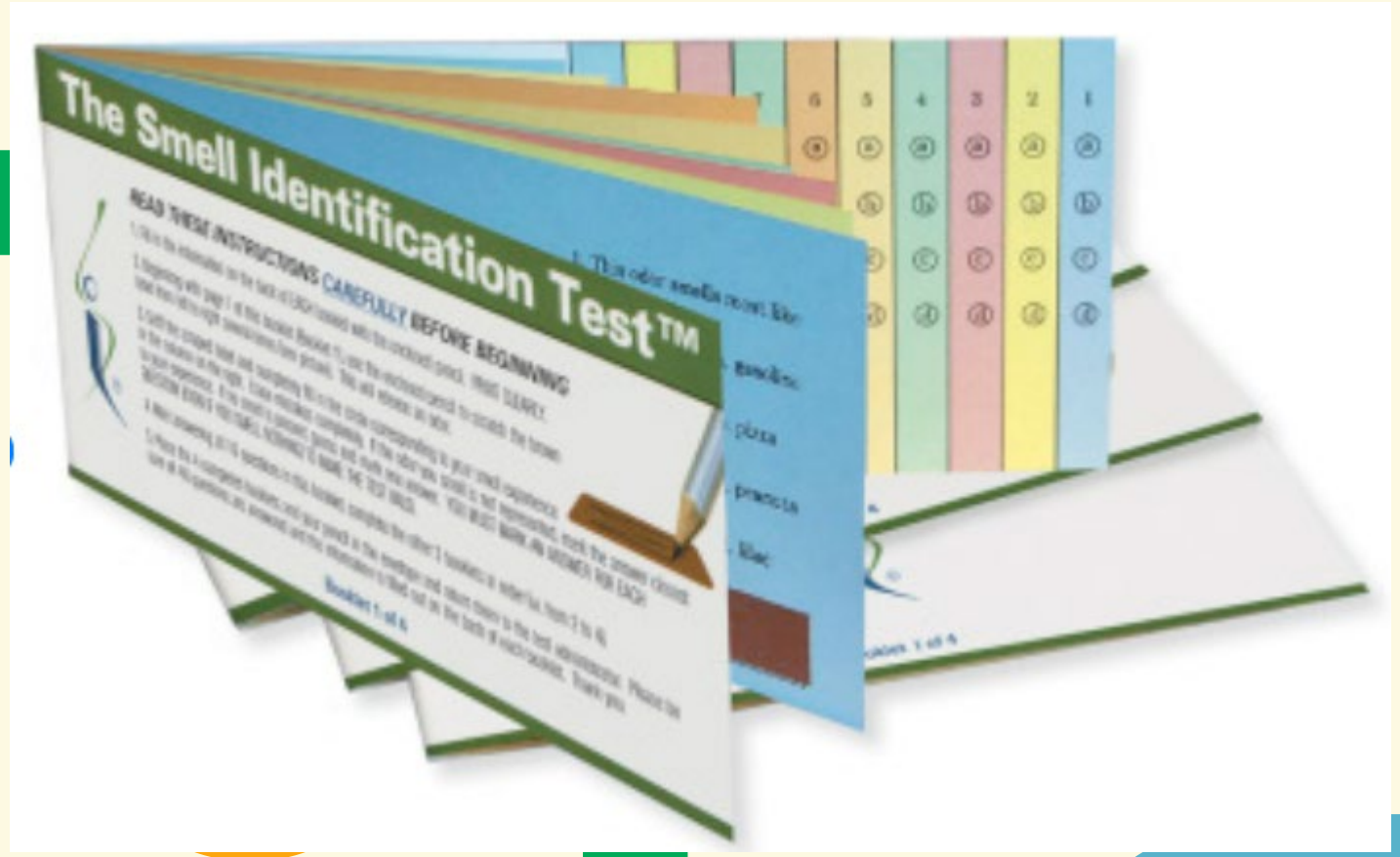
- Symmetric
- Kinetic
- Mid amplitude
- Mid frequency 5-8 Hz
- Alcohol dampens it

Diagnostic process: beyond the tremor

HPI

Onset	**Slowly progressive**
Better/worse	**Better with activation**
Family hx	**Not usually**
Anosmia?	**Yes*** **
Gait change?	**Shuffling/stooped**
micrographia	**yes**
sleep issues	**yes**

Berg et al., 2015; Iannilli et al., 2017; Slabik and Garaschuk, 2023


The Smell Identification Test™
READ THESE INSTRUCTIONS CAREFULLY BEFORE BEGINNING


A
Sniffin' Sticks

Medication list review

Antipsychotics 1st
Haloperidol
Droperidol
Fluphenazine
Pimozide
Perphenazine

Antipsychotics 2nd
Risperidone
Olanzapine
Aripiprazole
Lurasidone
Clozapine
Ziprasidone
Quetiapine

Other
Tetrabenazine
Reserpine
Prochlorperazine
Metaclopramide
Valproic acid

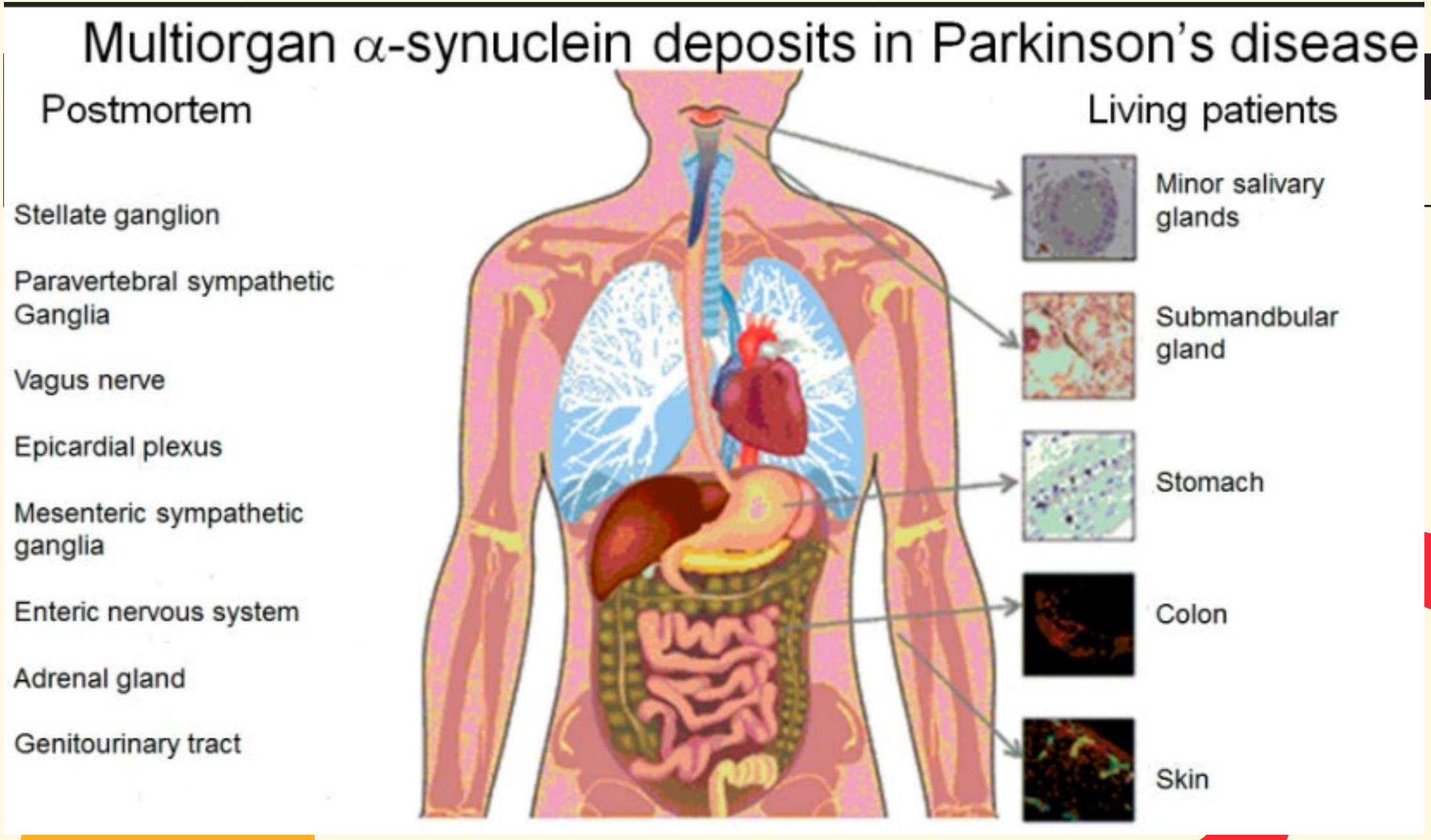
6-12 month wash out

Review of systems

Depression
Anxiety
Constipation
Change in memory
Weight loss
Anemia
Soft voice
Illegible handwriting
RLS
drooling
Seborrheic dermatitis
Acting out dreams
Insomnia
Daytime sleepiness
Fatigue
Loss of smell
Shoulder pain
DM2, HTN, cancer
Urinary problems

Santiago JA et.al. Biological and Clinical Implications of Comorbidities in Parkinson's Disease Front Aging Neurosci. 2017; 9: 394

Multiorgan α-synuclein deposits in Parkinson's disease



Surguchov A. Parkinson's Disease: Assay of Phosphorylated α-Synuclein in Skin Biopsy for Early Diagnosis and Association with Melanoma. *Brain Sciences*. 2016; 6(2):17. https://doi.org/10.3390/brainsci6020017

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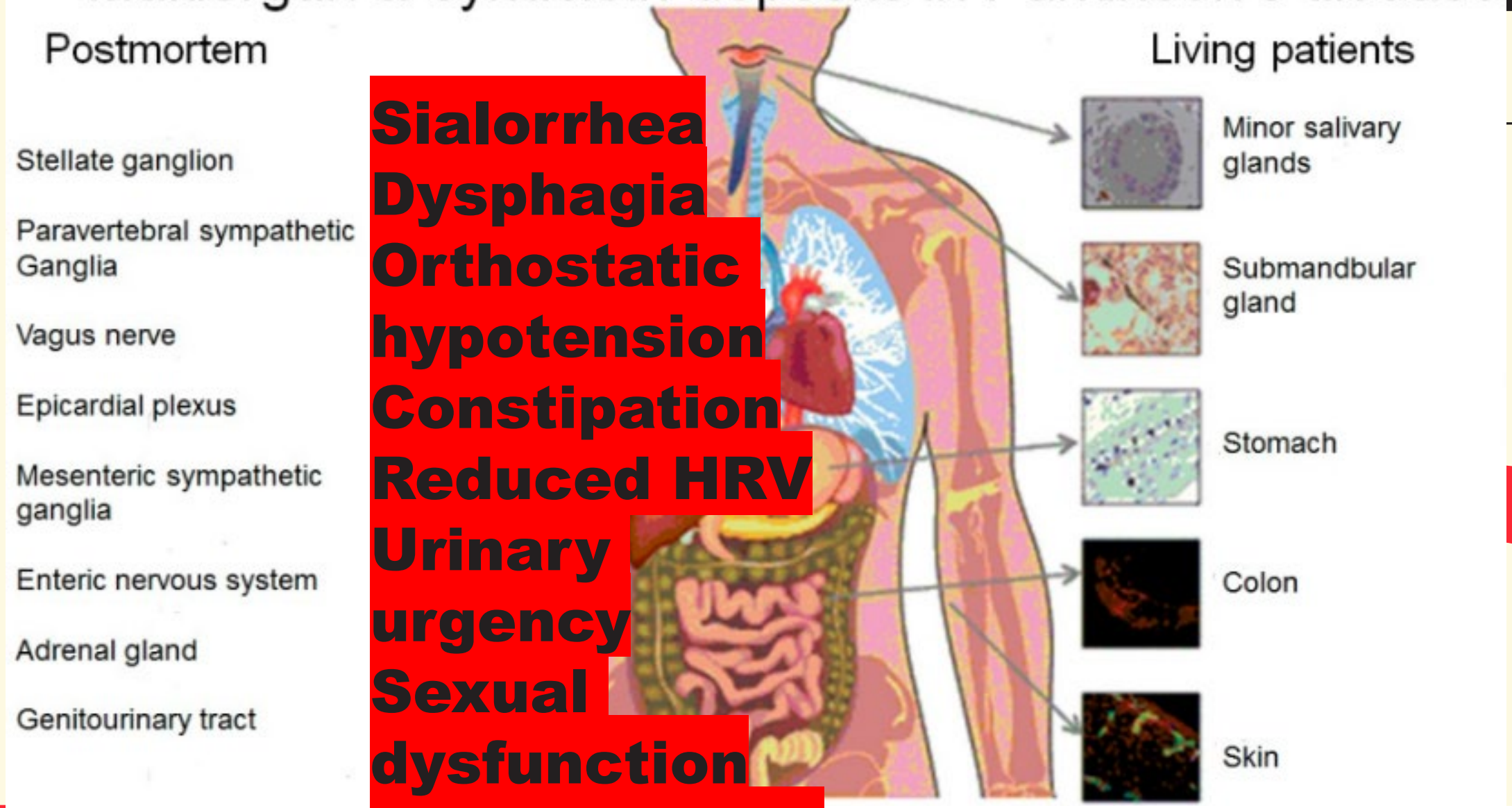
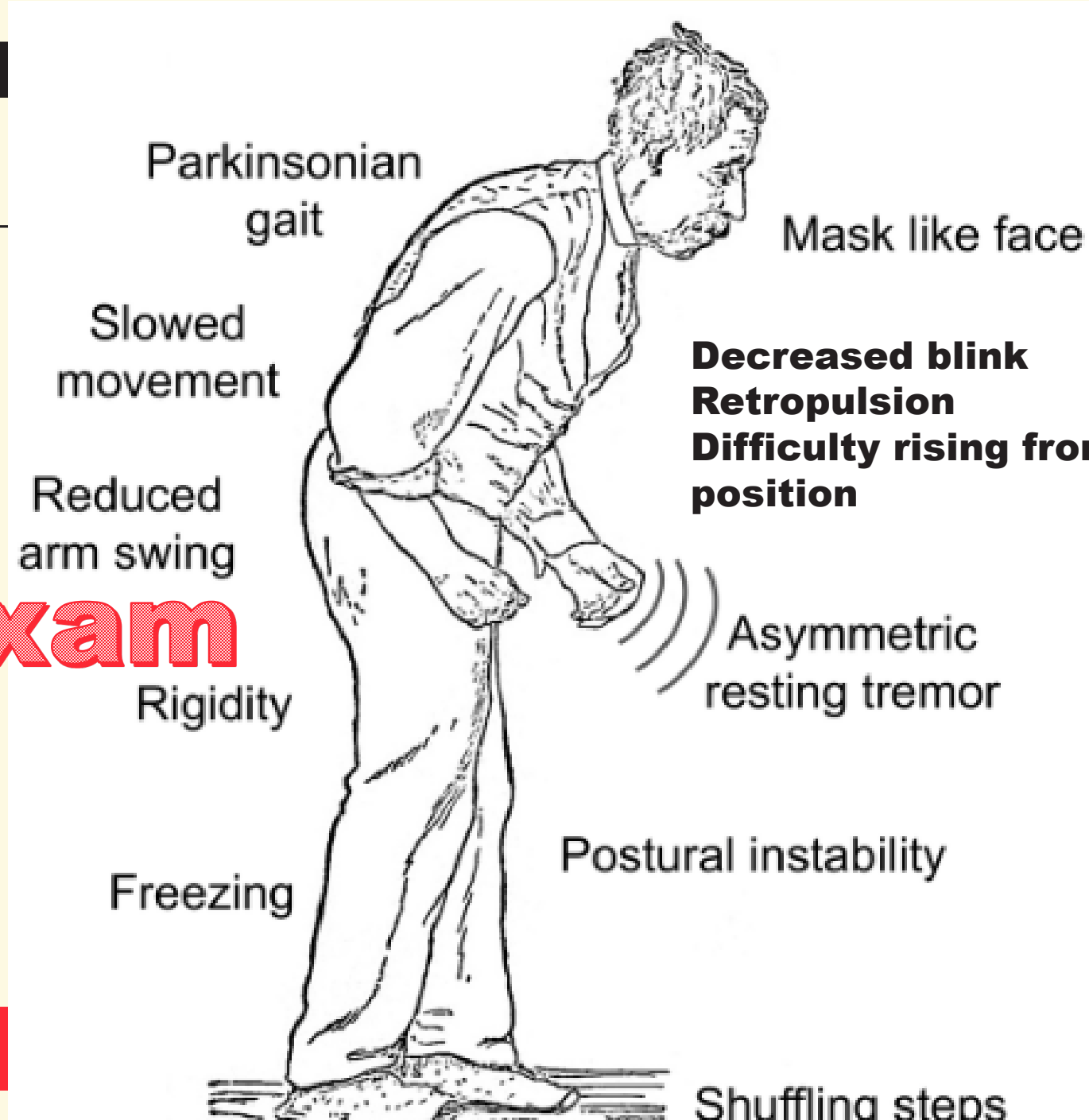


Sialorrhea
Dysphagia
Orthostatic hypotension
Constipation
Reduced HRV
Urinary urgency
Sexual dysfunction
hyperhydrosis

Surguchov A. Parkinson ylated α-Synuclein in Skin Biopsy for Early Diagnosis and Association with Melanoma. *Brain Sciences*. 2016; 6(2):17. https://doi.org/10.3390/brainsci6020017

Physical exam



camptocormia

Shuffling gait

retropulsion

A systematic review American Academy of Neurology (AAN) 2006 :
levodopa or apomorphine challenge tests for DX
could help BUT
30% with negative challenge have it
20-30% with a positive test have alternate Dx

TESTING

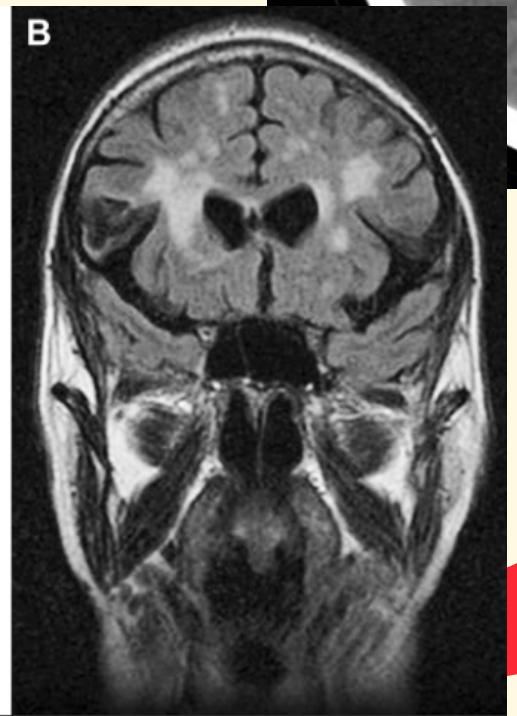
Medication trial of at least 1,000mg levodopa daily for 2 months

Carbidopa/levodopa 25mg/100mg tabs
Work up to 1 tab 3 times a day at 8am noon and 4
Increase to 1.5 tabs 3 x a day the following week
Increase to 2 tabs 3 x a day the following week

Med associated dyskinesia

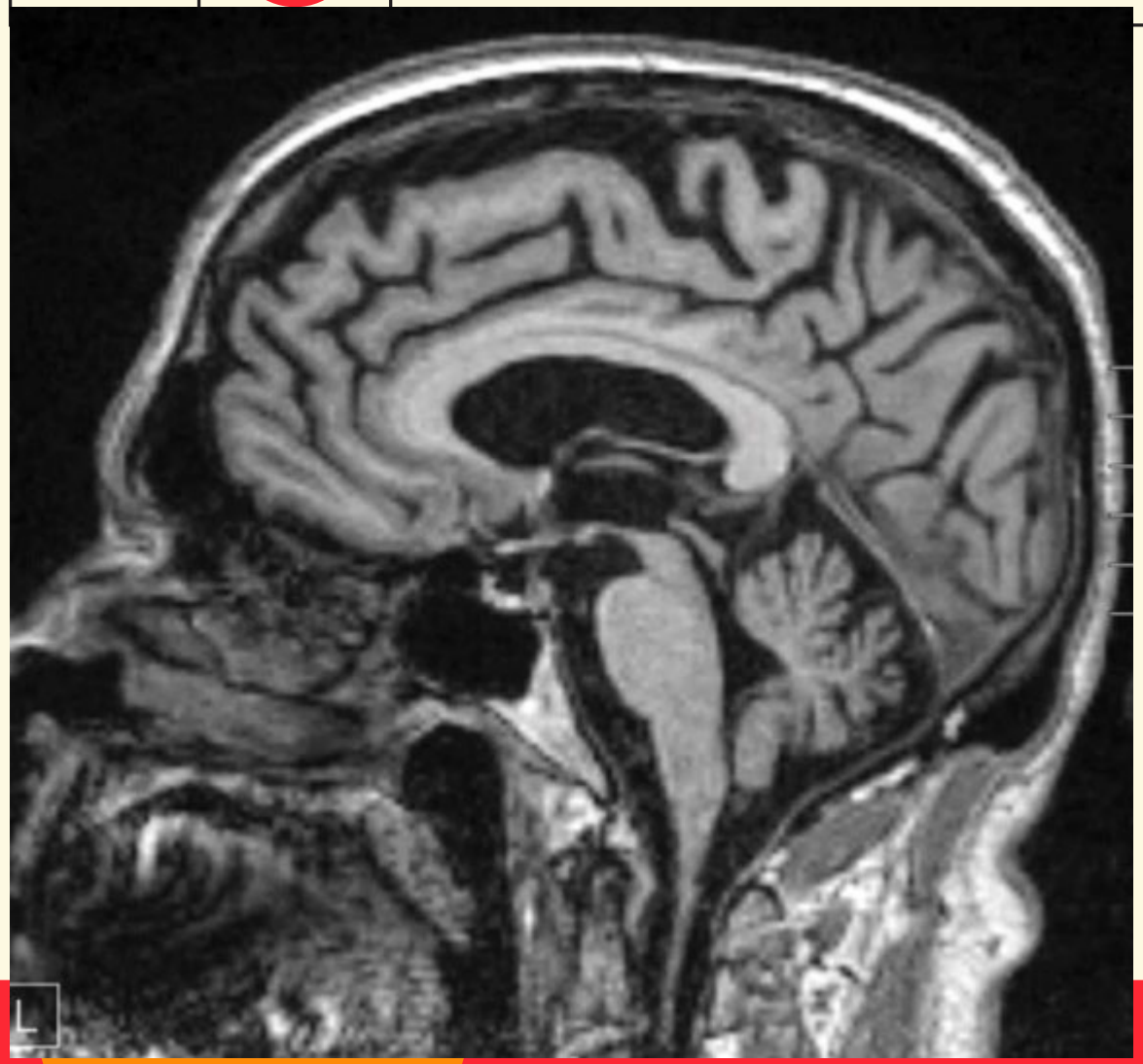
Imaging

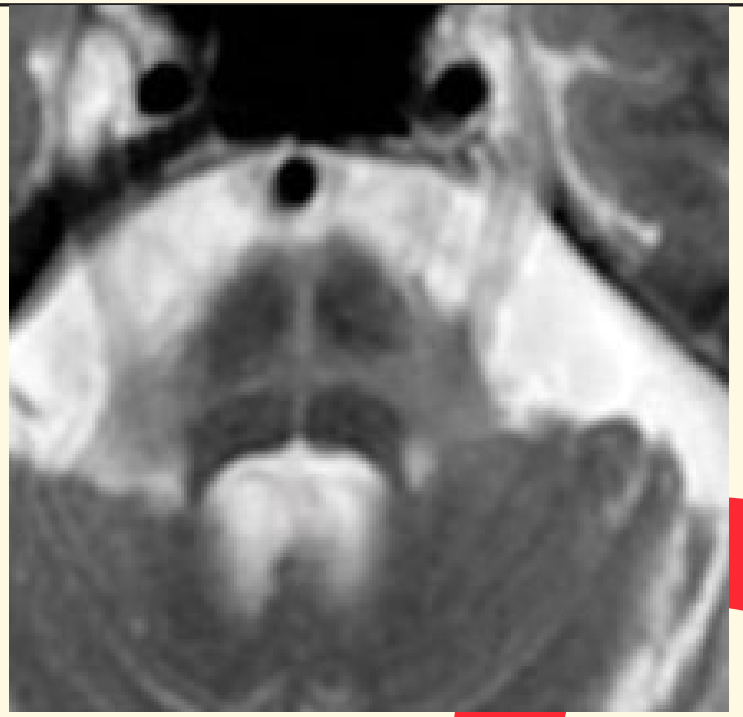
SDH
Hydrocephalus
Stroke
BG calcifications



https://radiopaedia.org/cases

Brain MRI

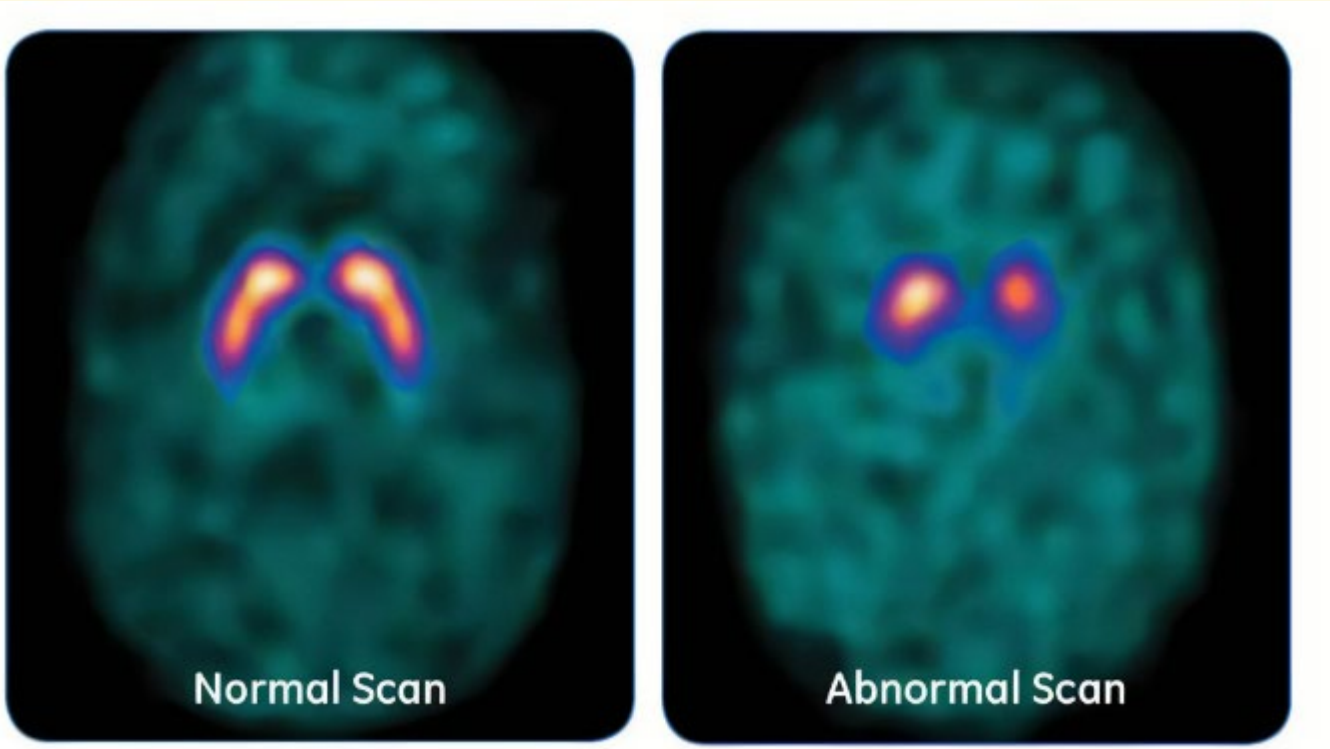




McFarland NR, Hess CW. Recognizing Atypical Parkinsonisms: "Red Flags" and Therapeutic Approaches. Semin Neurol. 2017 Apr;37(2):215-227. doi: 10.1055/s-0037-1602422. Epub 2017 May 16. PMID: 28511262; PMCID: PMC5961706.

TESTING

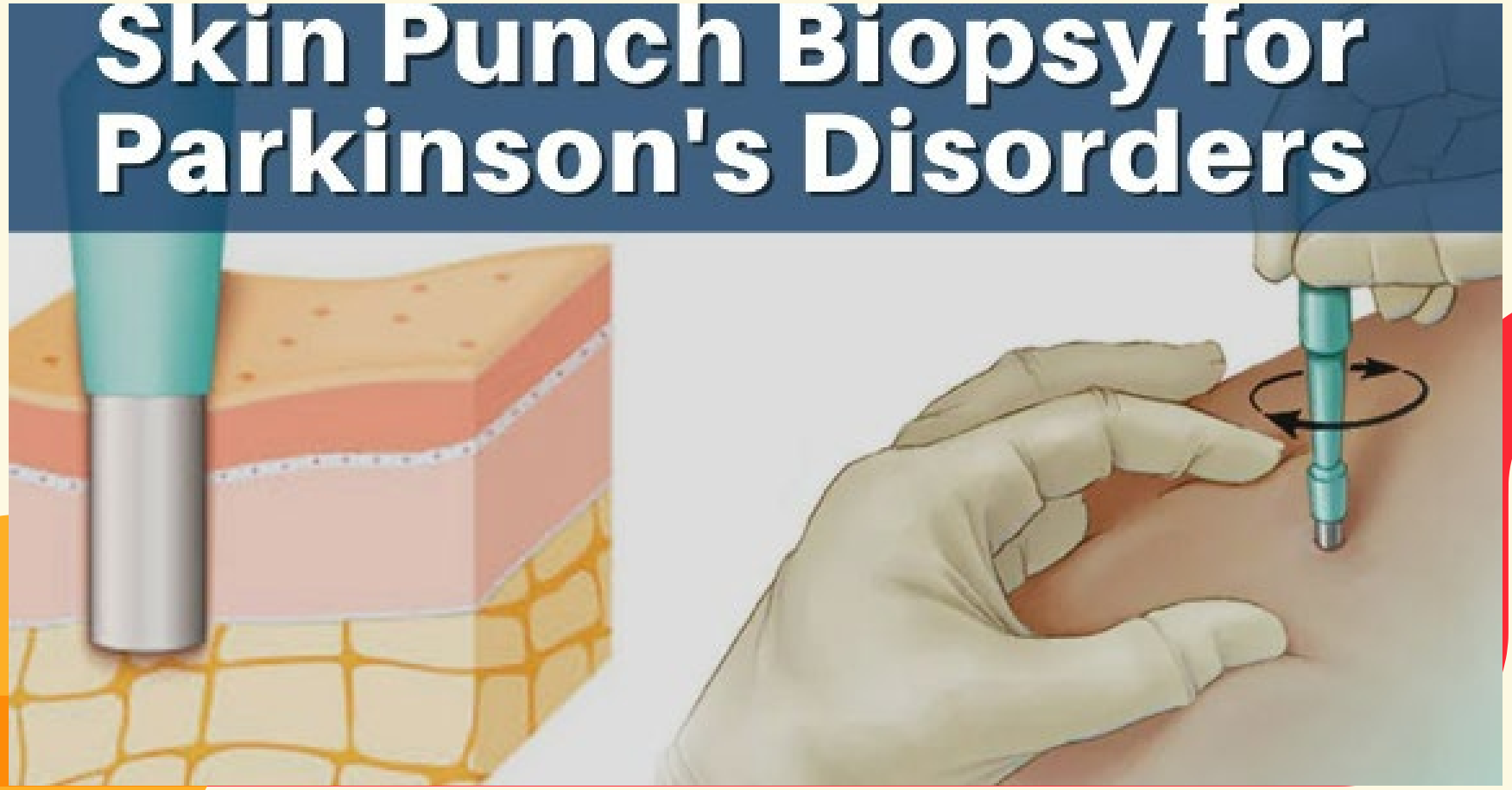
Dat scan can differentiate Parkinson's and Parkinson's plus from controls

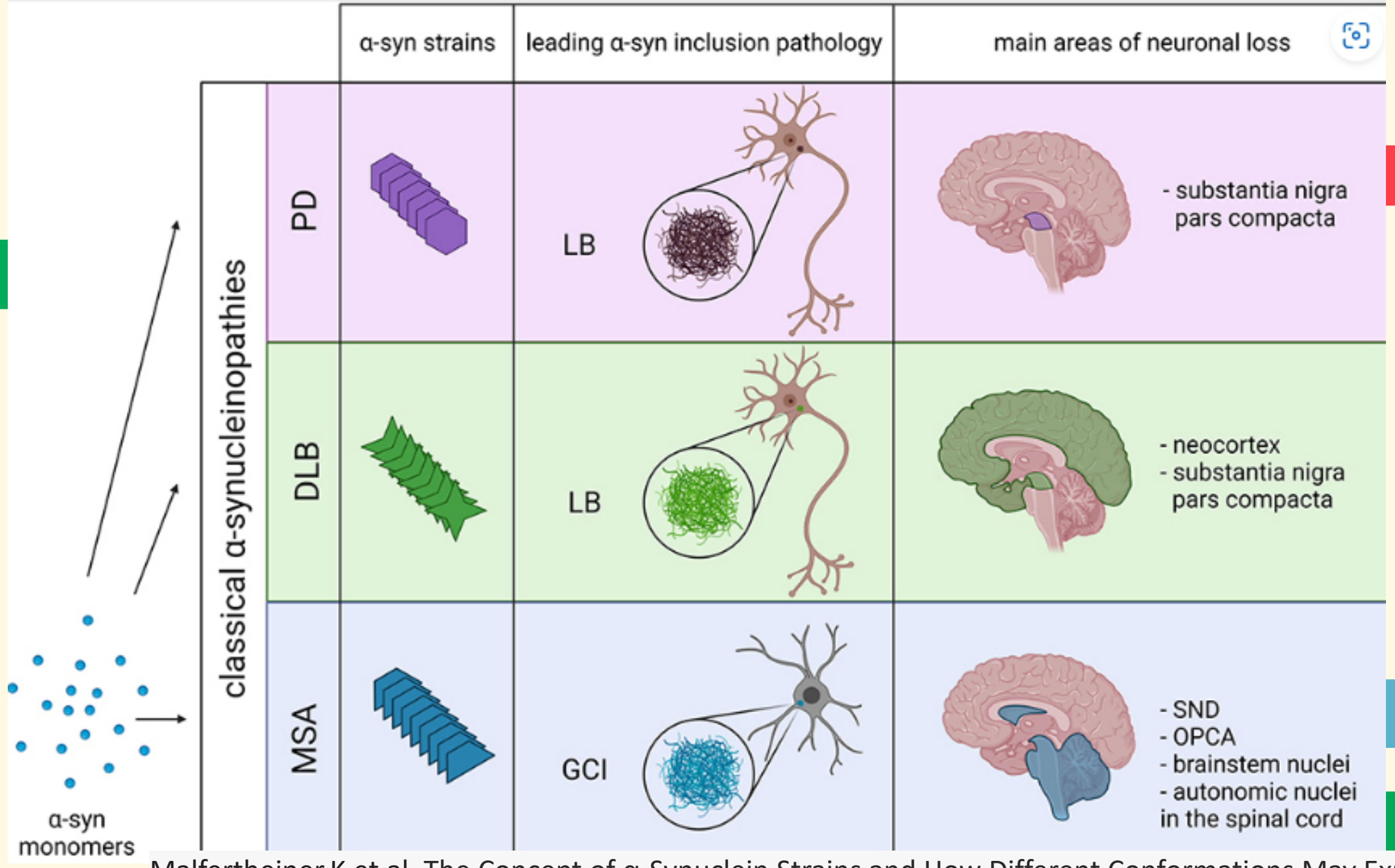


What is a DaTscan and should I get one? | APDA (apdaparkinson.org)

TESTING

skin biopsy for alpha synucleinopathies





Malfertheiner,K et.al. The Concept of α-Synuclein Strains and How Different Conformations May Explain Distinct Neurodegenerative Disorders Front. Neurol., 04 October 2021 Sec. Movement DisordersVolume 12 - 2021

TESTING

EVALUATION with MOVEMENT DISORDER SPECIALIST

Dr Ellen Valadez

Parkinson's disease

Movement Disorder Society clinical diagnostic criteria for Parkinson Disease – Executive summary/completion form

The first essential criterion is parkinsonism, which is defined as bradykinesia, in combination with at least one of rest tremor or rigidity. Examination of all cardinal manifestations should be carried out as described in the MDS-Unified Parkinson Disease Rating Scale.[1] Once parkinsonism has been diagnosed:

Diagnosis of clinically established PD requires:

1. Absence of absolute exclusion criteria
2. At least two supportive criteria, and
3. No red flags

Diagnosis of clinically probable PD requires:

1. Absence of absolute exclusion criteria
2. Presence of red flags counterbalanced by supportive criteria
   If one red flag is present, there must also be at least one supportive criterion
   If two red flags, at least two supportive criteria are needed
   No more than two red flags are allowed for this category

MDS critieria

Supportive criteria (check box if criteria met)

☐ 1. Clear and dramatic beneficial response to dopaminergic therapy. During initial treatment, patient returned to normal or near-normal level of function. In the absence of clear documentation of initial response a dramatic response can be classified as:

a. Marked improvement with dose increases or marked worsening with dose decreases. Mild changes do not qualify. Document this either objectively (>30% in UPDRS III with change in treatment), or subjectively (clearly-documented history of marked changes from a reliable patient or caregiver)

b. Unequivocal and marked on/off fluctuations, which must have at some point included predictable end-of-dose wearing off

☐ 2. Presence of levodopa-induced dyskinesia

☐ 3. Rest tremor of a limb, documented on clinical examination (in past, or on current examination)

☐ 4. The presence of either olfactory loss or cardiac sympathetic denervation on MIBG scintigraphy

Absolute exclusion criteria: The presence of any of these features rules out PD:

Let’s break it down

BRADYKINESIA +
resting tremor
OR
BRADYKINESIA +
rigidity

Supportive features

1) Improvement in either rigidity, tremor or bradykinesia on levodopa
2) Levodopa associated dyskinesias
3) Unilateral rest tremor
4) olfactory function loss
5) denervation of cardiac sympathetic function on MIBG scan

And no red flags...

PD treatments

Oral medications

First line: Carbidopa-levodopa
- take with carbs not protein
- watch for nausea, OH

Dopamine agonists, ropinirole , pramipexole
- younger patients at high risk for dyskinesias
- watch for las vegas syndrome/sleepiness

MAO-B selegiline, rasagiline
- once daily, milder benefit

Amantadine useful for prominent tremor, milder benefit

Anticholinergics trihexyphenidyl, benztropine
- milder benefit, cognitive side effects

Other treatments

PT, OT, ST
Big and Loud therapy

Levodopa through J tube

DBS

Keep up nutrition!

Treating more than tremor

Orthostatic hypotension midodrine droxidopa

Dementia donepezil

Depression SSRIs

RBD melatonin and clonazepam

What else might it be?

RED FLAGS

Rapid gait impairment /wheelchair in 1st 5 years (PSP)

No progression in motor symptoms in 1st 5 years

Bulbar dysfunction (PSP)

Severe autonomic features in 1st 5 years (MSA)

Recurrent falls in 1st 3 years(PSP)

RED FLAGS

Inspiratory sighs/stridor (MSA)

anterocollis and /or contractures in feet and hands in 1st 10 years (dystonia, MSA)

No associated sleep issues, autonomic issues, or psychiatric issues in 1st 5 years

pyramidal signs/weakness hyperreflexia

Symmetric involvement

RED FLAGS

Anterocollis present in 42% with MSA 5.8% PD

Doherty KM, Gershanik OS, Bloem BR. Postura.. deformities in Parkinson's disease. *Lancet Neurol* 2011;10:538–549

Exclusionary

cerebellar signs
downward vertical gaze palsy (PSP)
probable FTD or PPA
lower limbs only for 3 years (vascular)
DA depleting med in last year
no response to levodopa
cortical sensory loss or ideomotor apraxia (CBD)
normal DAT scan
alternative dx deemed more likely by expert

PARKINSON PLUS

Parkinson-plus syndromes			
Lewy body dementia (LBD)	Multiple system atrophy (MSA)	Progressive supranuclear palsy (PSP)	Corticobasal ganglionic degeneration (CBD)
Parkinsonism plus **synuclein**	Parkinsonism plus **synuclein**	Parkinsonism plus **tau**	Parkinsonism plus **tau**
• Early dementia • Hallucinations • Neuroleptic sensitivity **Fluctuating cognition**	Early autonomic dysfunction: • Orthostatic hypotension • Erectile dysfunction • Incontinence **Cognition preserved**	• Downgaze impairment **Ophthalmoplegia** • Axial rigidity • Other brainstem symptoms: dysphagia, oral dyskinesia, dysphonia	• Asymmetry • Apraxia **Alien limb** **Cortical sensory loss**

https://youtu.be/ebaVzX-mR24?si=RGyzen4Sx1h8zsL7

Toxic
- MPTP, manganese, carbon monoxide

Metabolic
- Hypoparathyroidism
- Liver failure
- Extrapontine myelinolysis
- ESRD with DM
- DM2

Infectious
- HIV, neurosyphilis, prion disease, PML, toxo

drug induced (DA antagonists)

vascular

structural- cSDH,tumor, head trauma, NPH

genetic- Wilson’s

Summary

If you are looking for more information:

Marino BLB, de Souza LR, Sousa KPA, Ferreira JV, Padilha EC, da Silva CHTP, Taft CA, Hage-Melim LIS. Parkinson's Disease: A Review from Pathophysiology to Treatment. Mini Rev Med Chem. 2020;20(9):754-767. doi: 10.2174/1389557519666191104110908. PMID: 31686637.

Thank you