



Parkinson's Disease FAQ

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PD 101: Frequently Asked Questions



What is PD?



How did I get it, and can I pass it on?



How can we be sure I have PD?



What are the best medications for PD?



What is the best diet and exercise for PD?



How does it progress, and can I stop its progression?



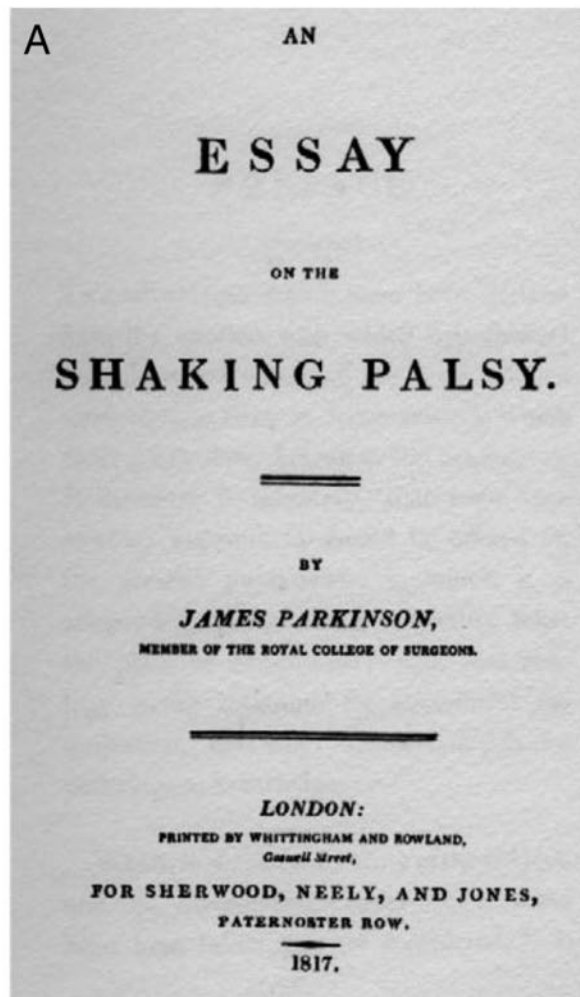
My PD is getting hard to control. Now what?



What is PD?

Sir James Parkinson

An Essay on the Shaking Palsy (1817)



“Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellects being uninjured.”



IN PIAM MEMORIAM
JAMES PARKINSON
OF HOXTON SURGEON AND APOTHECARY

DIPLOMATE OF THE COMPANY OF SURGEONS
MEMBER AND THE FIRST HONORARY MEDALLIST
OF THE ROYAL COLLEGE OF SURGEONS
IN HIS "ESSAY ON THE SHAKING PALSY"

HE FIRST DESCRIBED THE DISEASE
SINCE KNOWN BY HIS NAME

FOUNDER MEMBER OF THE GEOLOGICAL SOCIETY OF LONDON
AND AUTHOR OF "ORGANIC REMAINS OF A FORMER WORLD"
HONORARY MEDALLIST OF THE ROYAL HUMANE SOCIETY

POLITICAL AND SOCIAL REFORMER

BORN AT 1 HOXTON SQUARE 11 APRIL 1755

WHERE HE PRACTISED FOR FORTY YEARS

DIED AT 3 PLEASANT ROW HOXTON

21 DECEMBER 1824

BAPTIZED AND MARRIED IN THIS CHURCH

AND BURIED IN THE CHURCHYARD

A LIFE LONG WORSHIPPER AT THE PARISH CHURCH

ERECTED BY THE NURSING STAFF
OF ST LEONARD'S HOSPITAL



Parkinson's hope

- ▶ “there appears to be sufficient reason for hoping that some remedial process may ere long be discovered, by which, at least, the progress of the disease may be stopped”.

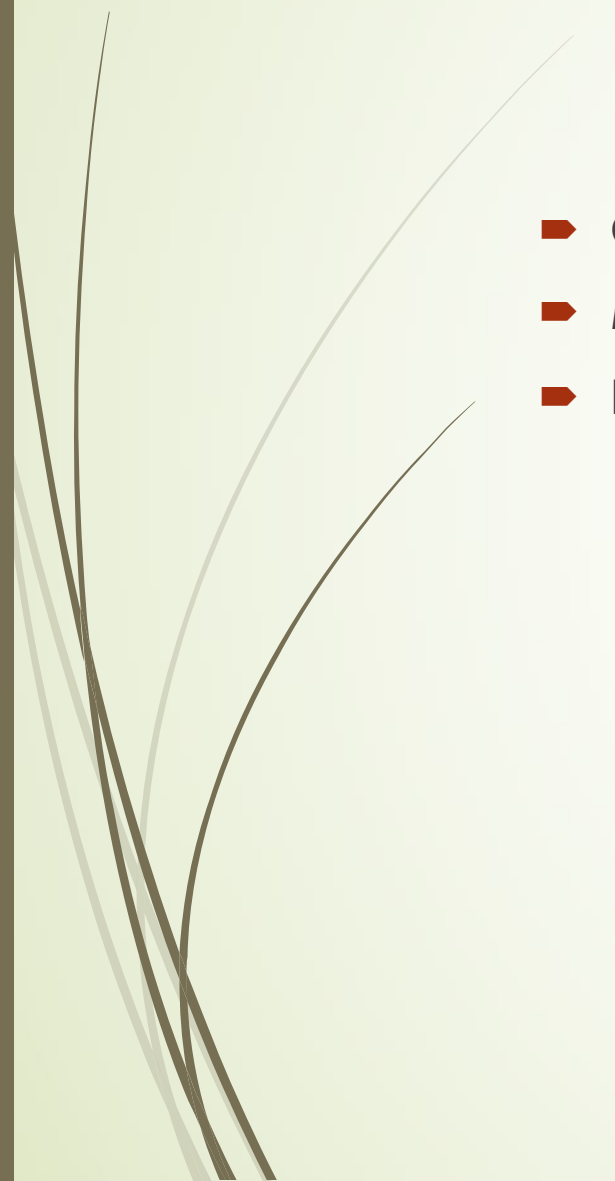
Parkinson's Disease

A tale of
imbalances





Three Imbalances of PD

- Chemical Imbalance
 - Molecular Imbalance
 - Electrical Imbalance
- 



Chemical Imbalance in PD

Lack of dopamine

Excess acetyl choline

Arvid Carlsson and Dopamine

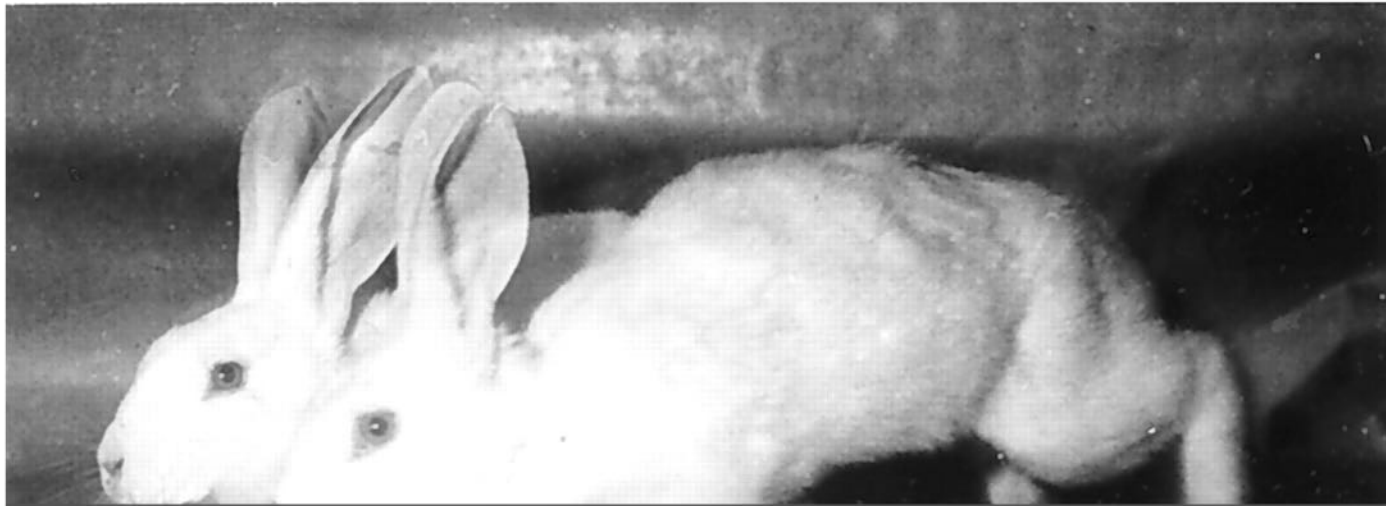
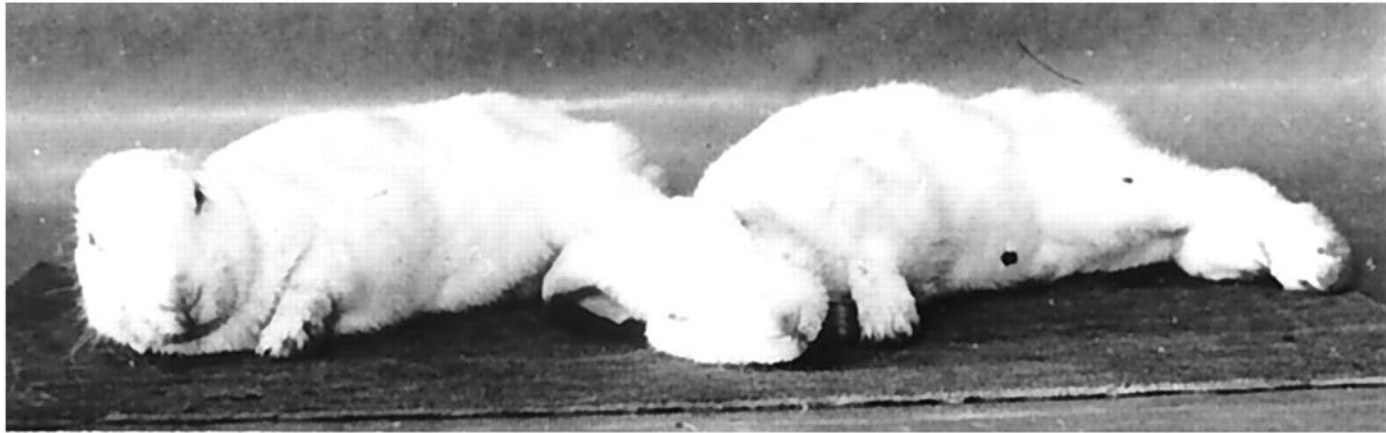
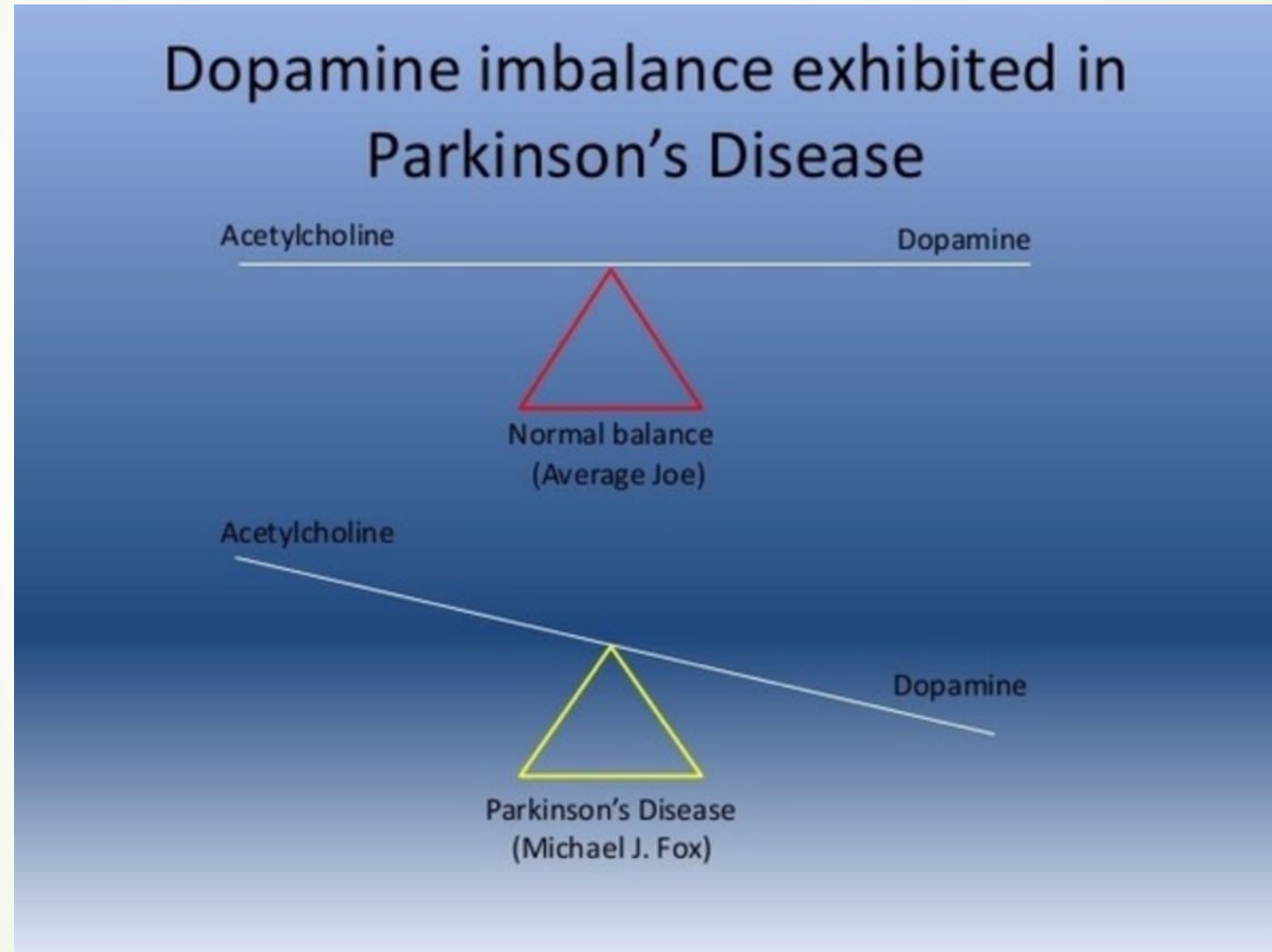


Figure 2

Reversal of reserpine's effects by DOPA. (**Top**) Rabbits treated with reserpine (5 mg/kg intravenously). (**Bottom**) The same rabbits 15 min after D-L-DOPA (200 mg/kg intravenously). [From (41)]

Dopamine/acetylcholine imbalance





Molecular Imbalance in PD

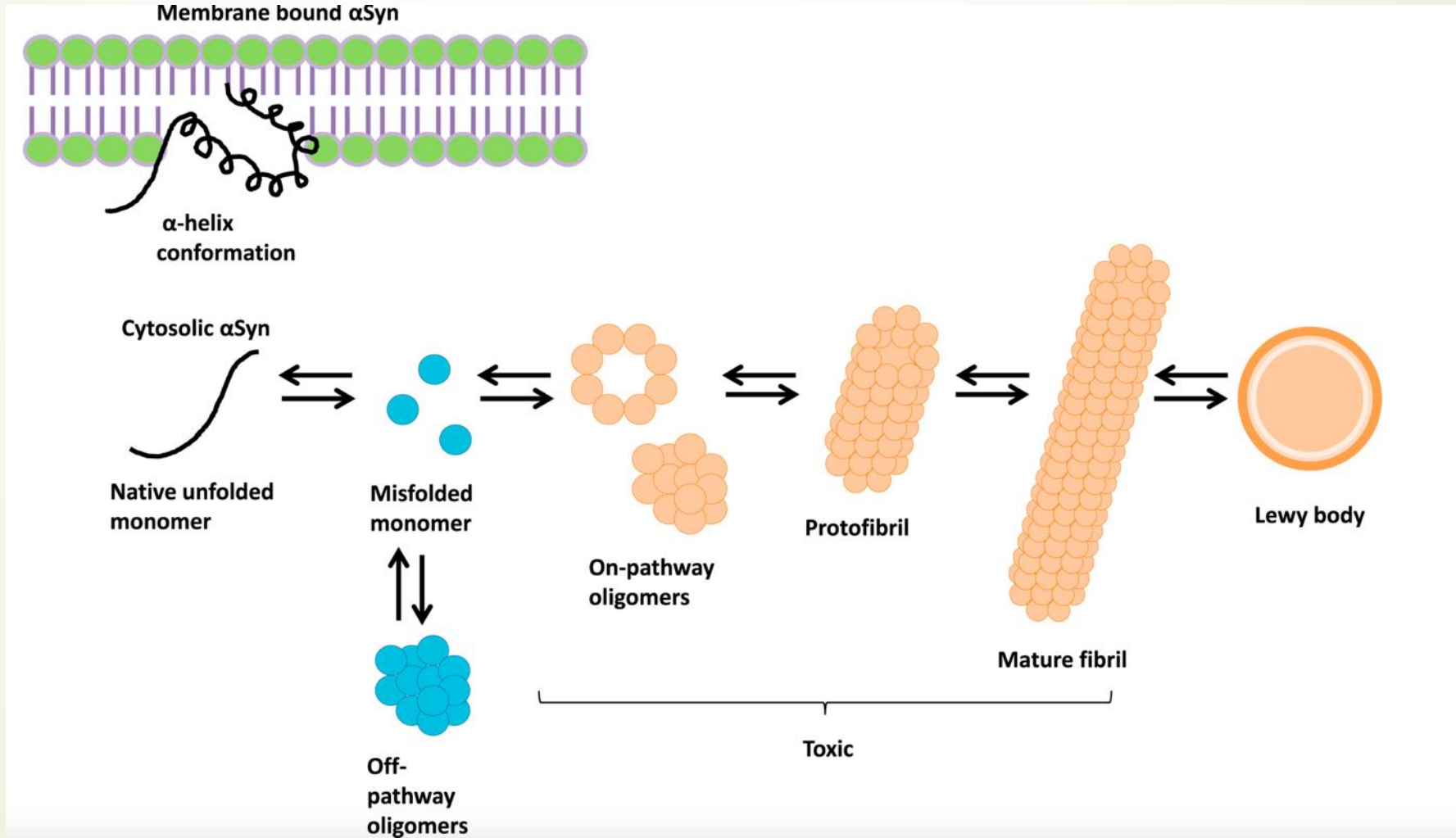
Excess alpha-synuclein production

Decreased alpha-synuclein clearance

Lewy Body in a PD Brain



Alpha-synuclein and the Lewy Body



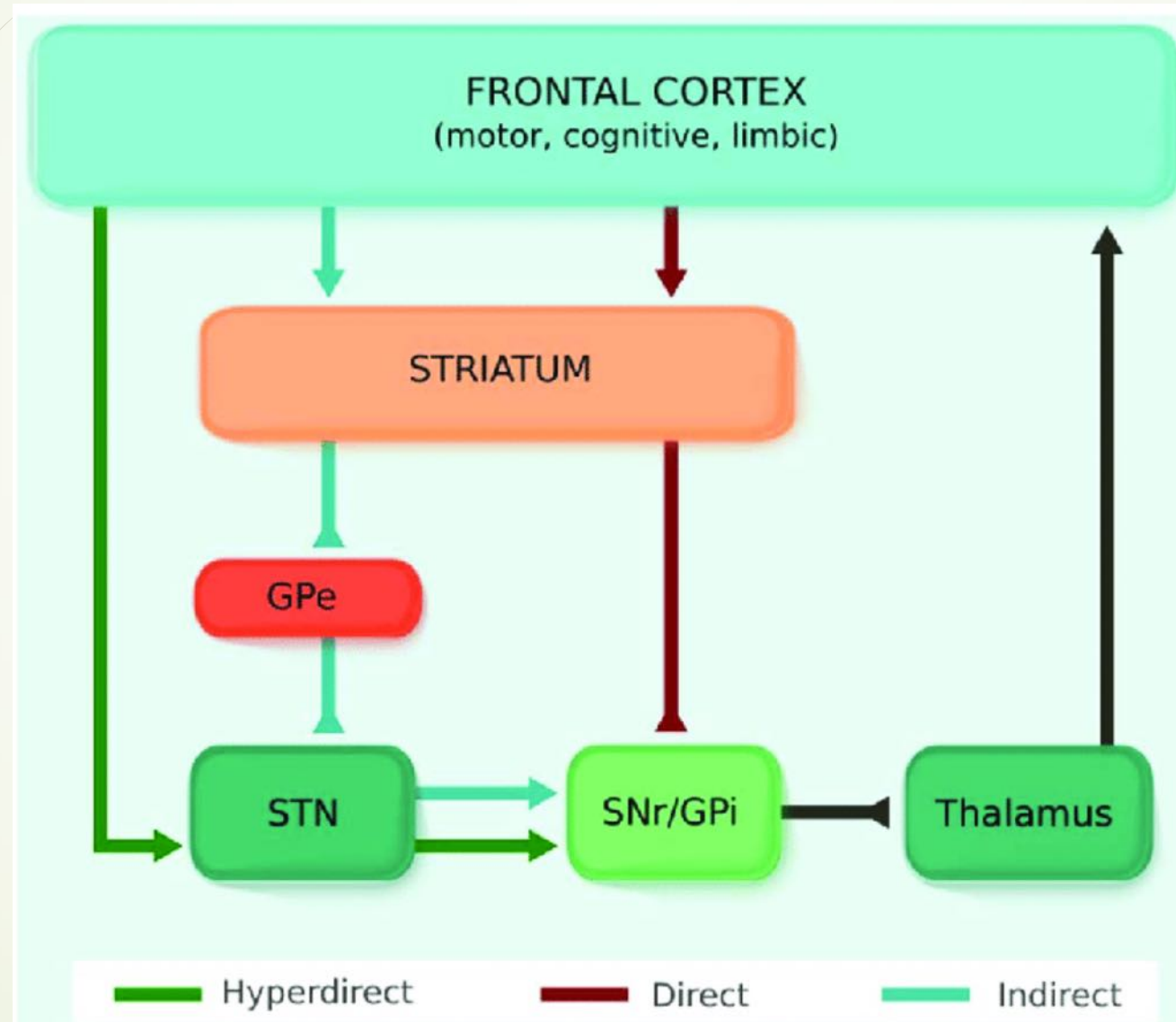


Electrical Imbalance in PD

Excess indirect pathway electrical activity

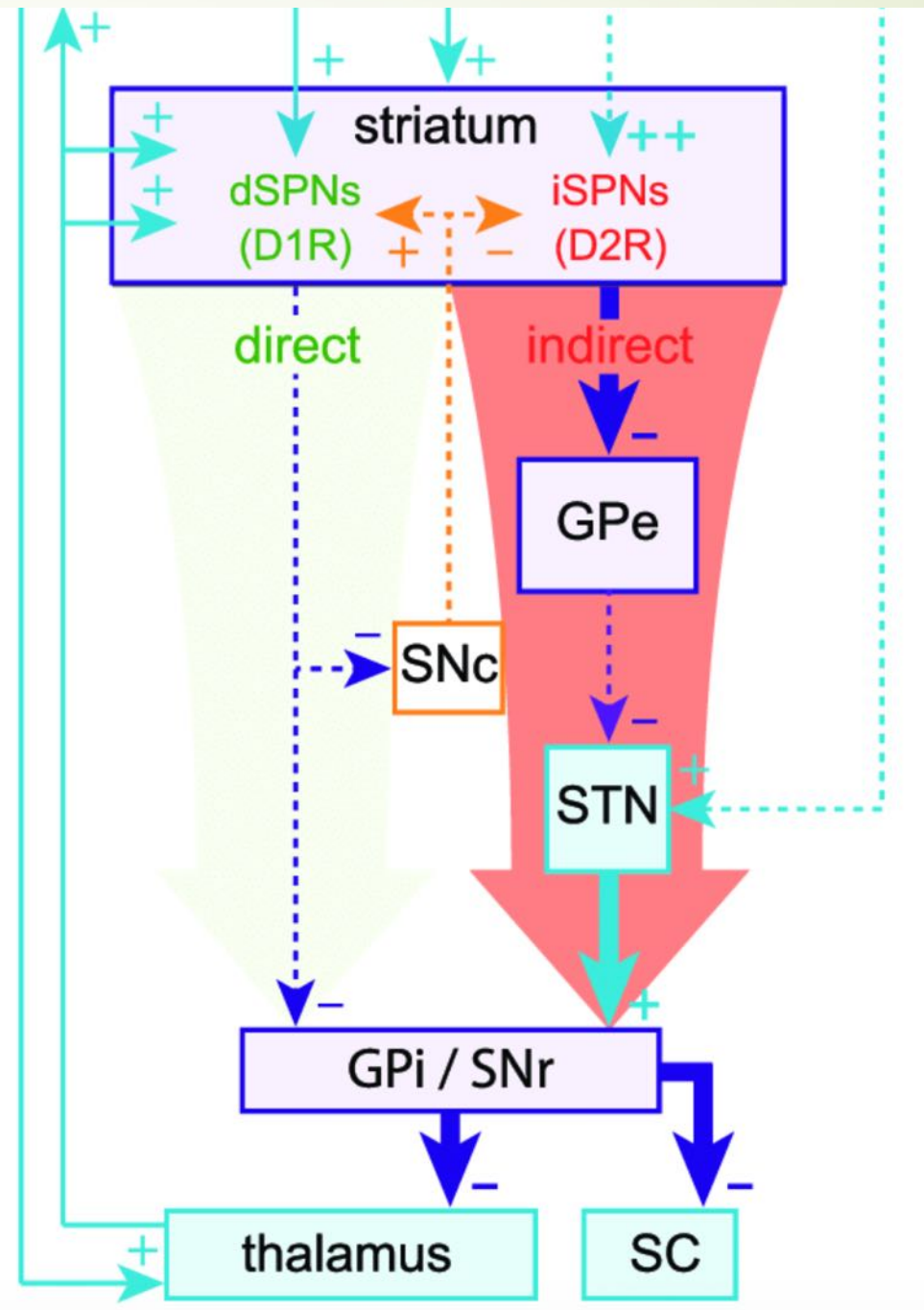
Decreased direct pathway electrical activity

Electrical Pathways in PD



Imbalance in PD

Overactive indirect pathway suppresses movement and causes muscle rigidity





How did I get PD and
can I pass it on?



PD and gene-environment interaction

Some PD Genes

- SNCA (alpha synuclein)
- Parkin
- LRRK2
- GBA

Environment

- Pesticides
- Well water
- Welding??
- Mining??



Can I pass it on?

- Approximately 10% of PD has a definite inheritance pattern
- Autosomal dominant (50% probability)
 - SNCA
 - LRRK2
- Autosomal Recessive (25% probability)
 - Parkin
 - PINK-1
- Outside of research setting gene testing is not recommended



How can we be sure I
have PD?



Patient comments on diagnosis

- ▶ “All the doctor did was have me make some movements with my hands and legs and watch me walk and then he told me I had Parkinson’s disease! How is that possible?”
 - ▶ “I don’t believe my diagnosis. Aren’t there a bunch of other diseases it could be?”
 - ▶ “How can they know for sure? I want a test to prove whether I do or do not have Parkinson’s disease!”
-
- ▶ SOURCE: APDA Website



UK Brain Bank Criteria



- Bradykinesia
- At least one of the following
 - Muscular rigidity
 - Rest tremor
 - Postural instability
- Exclude atypical or secondary causes of parkinsonism
- Supportive criteria
 - Unilateral/asymmetric
 - Rest tremor
 - Excellent response to levodopa
 - Levodopa responsive for 5+ yrs
 - Clinical course of 10+ yrs

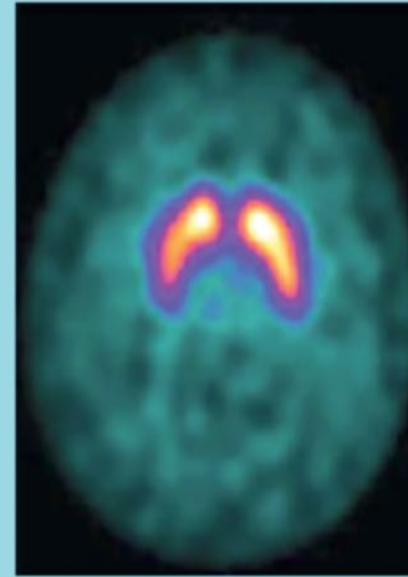
DATSCAN IMAGING

DaTscan imaging tags the dopamine transporter molecule in the brain and provides a rough estimate of the dopamine level in the brain

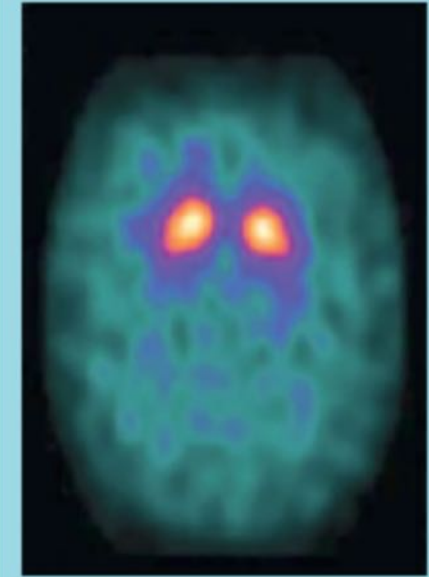
It is not a quantitative measure

It has a false positive and false negative error rate

It is not required to make a diagnosis and is not sufficient to make a diagnosis



Axial dopaminergic SPECT of a normal brain¹⁴



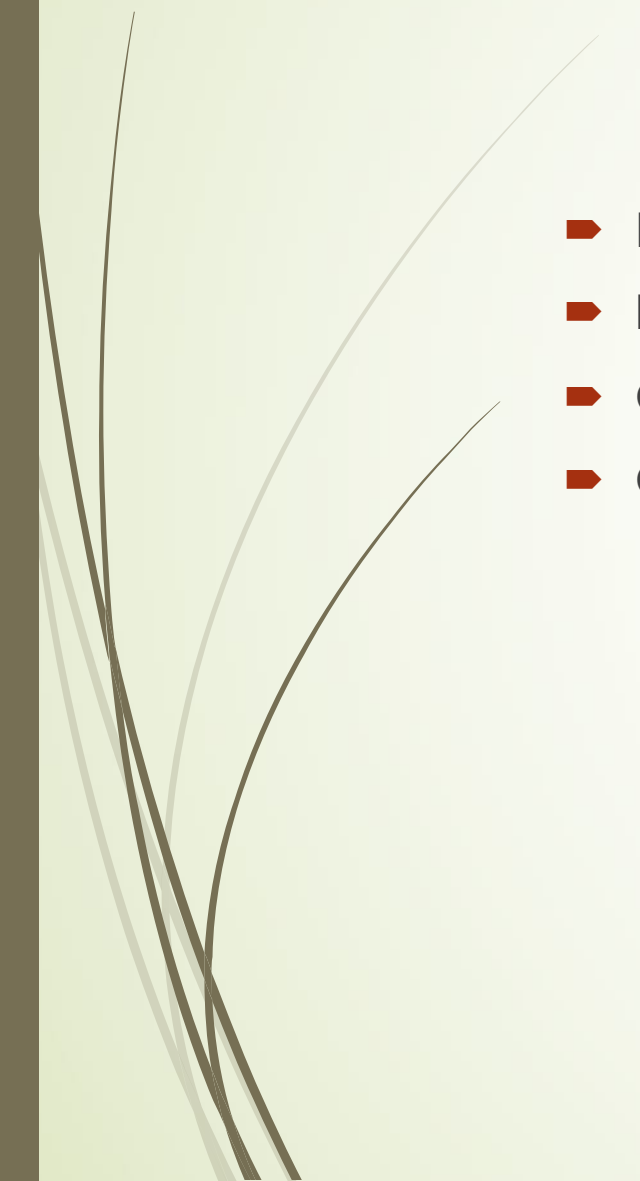
Axial dopaminergic SPECT of a brain demonstrating changes associated with Parkinson's disease (reduced uptake in the putamen)¹⁴



What are the best
medications for PD?

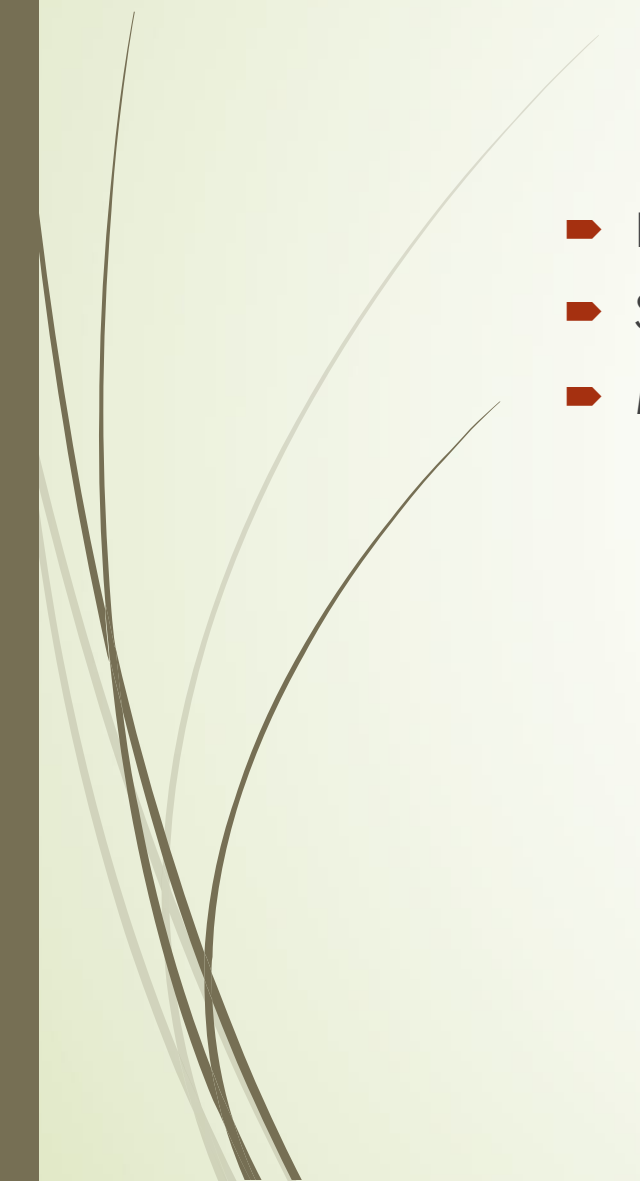


Levodopa is still the gold standard

- Levodopa (L-DOPA) is a precursor to dopamine
 - In the brain it is enzymatically converted to dopamine
 - Combined with carbidopa to prevent breakdown outside the brain
 - Combination carbidopa/levodopa is called Sinemet
- 



Levodopa

- Half-life of levodopa is approximately one hour
 - Short half-life leads to pulsatile stimulation
 - Motor fluctuations and/or dyskinesia typically occur around 5-year mark
- 



MEDICATIONS FOR PD

Levodopa Variants

- ▀ Sinemet
- ▀ Sinemet CR
- ▀ Stalevo
- ▀ Parcopa
- ▀ Inbrija inhaler

Adjunct Medications

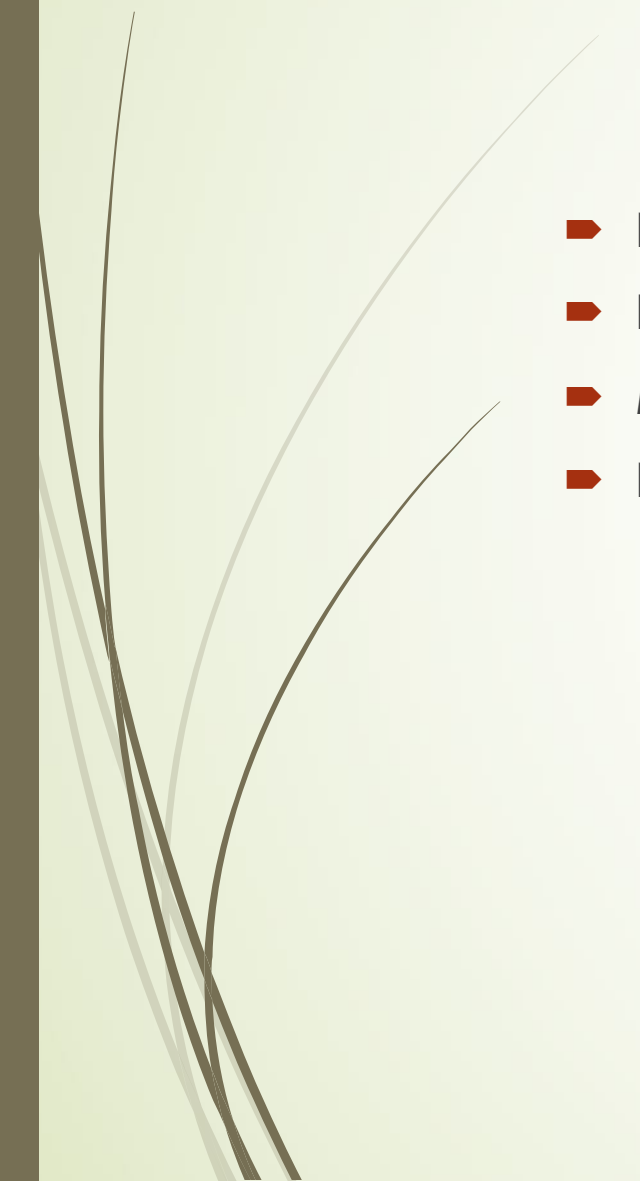
- ▀ Dopamine Agonists
 - ▀ Mirapex, Requip
 - ▀ Neupro patch
 - ▀ Apokyn injections
- ▀ MAO-Inhibitors
 - ▀ Selegiline, Azilect
 - ▀ Xadago
- ▀ Anticholinergics
 - ▀ Artane, Cogentin
 - ▀ Amantadine



What is the best diet
and exercise?



DIET AND PD

- No need for gluten free diet unless there is also celiac disease
 - Keto diets may be too restrictive for someone with PD
 - Mediterranean and MIND diets are sustainable and helpful
 - No need to avoid protein but some patients may need to time meds
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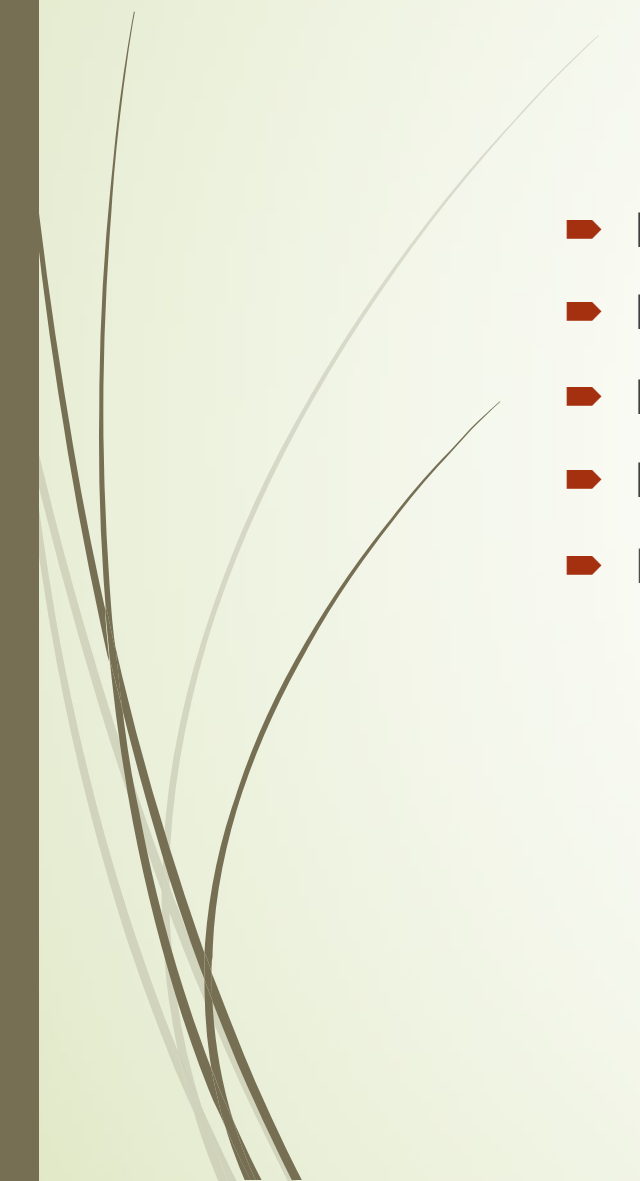
MIND DIET



FOOD	AMOUNT
Green leafy vegetables	6 or more servings per week
Other vegetables	1 serving per day
Berries	2 servings per week
Nuts	5 or more servings per week
Olive oil	Primary cooking oil
Whole grains	3 servings per day
Fish	1 serving per week
Poultry	2 or more meals per week
Wine	No more than 1 glass per day



EXERCISE AND PD

- Increased blood flow to brain
 - Increased BDNF (nerve growth factor) in the brain
 - Improved balance
 - Improved cognitive function
 - Natural antidepressant
- 



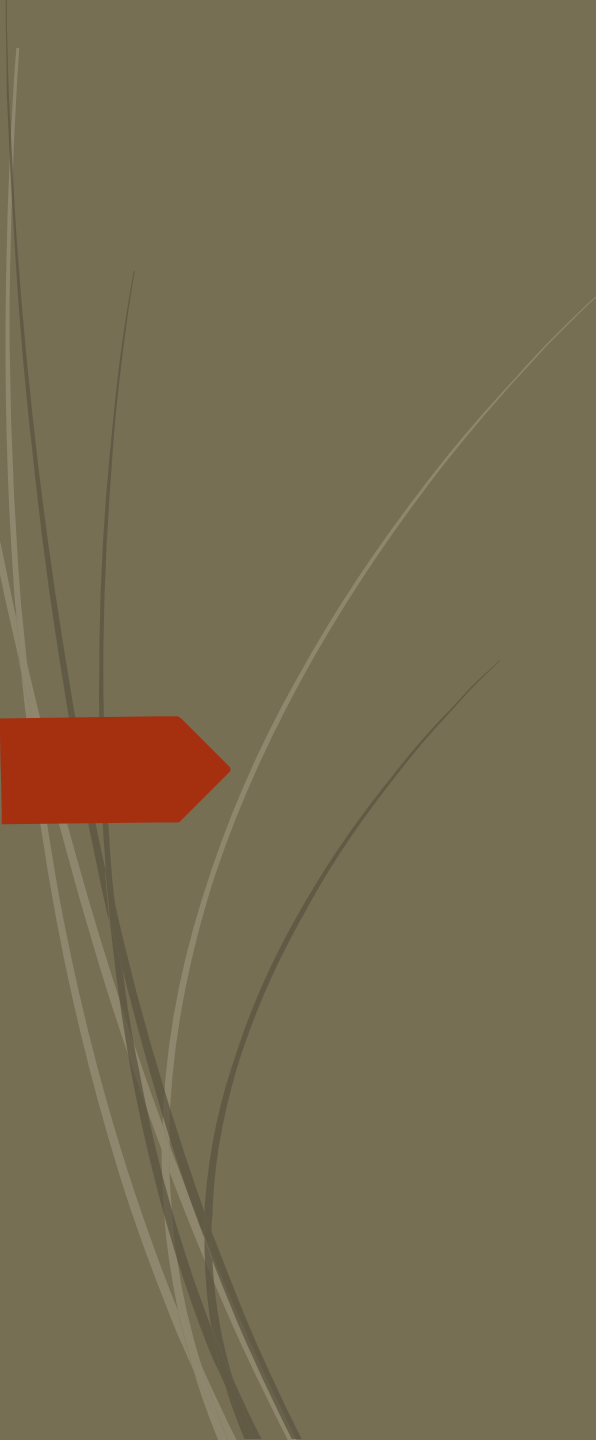
Which Exercise?

- Choose what fits
- Include aerobic activity
- Avoid pain (No pain is a big gain)
- Some options
 - Walk
 - Swim
 - Rock Steady Boxing
 - Water aerobics
 - Tai Chi



The bare minimum

- ➡ For PD's sake keep moving
- 



How does PD progress
and can progression be
stopped?

PD Progression over 40 years

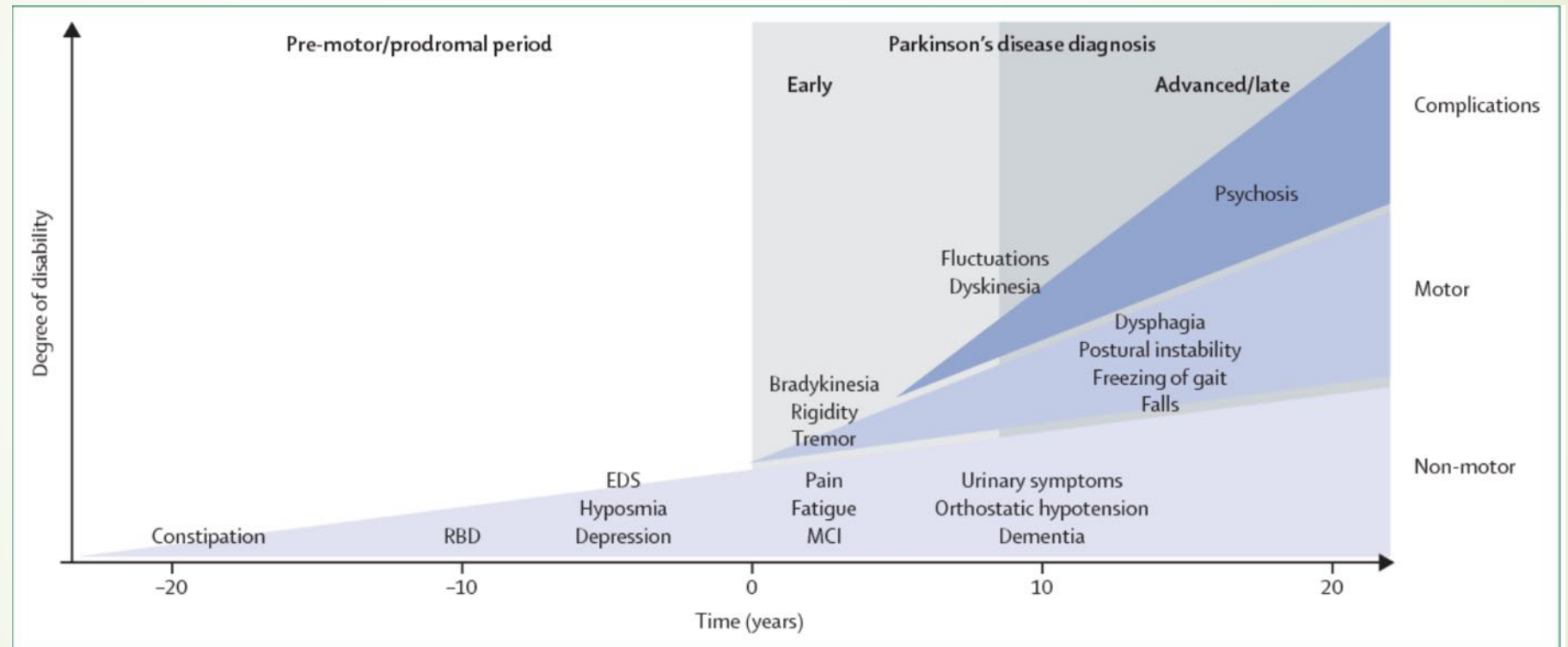


Figure 1: Clinical symptoms and time course of Parkinson's disease progression

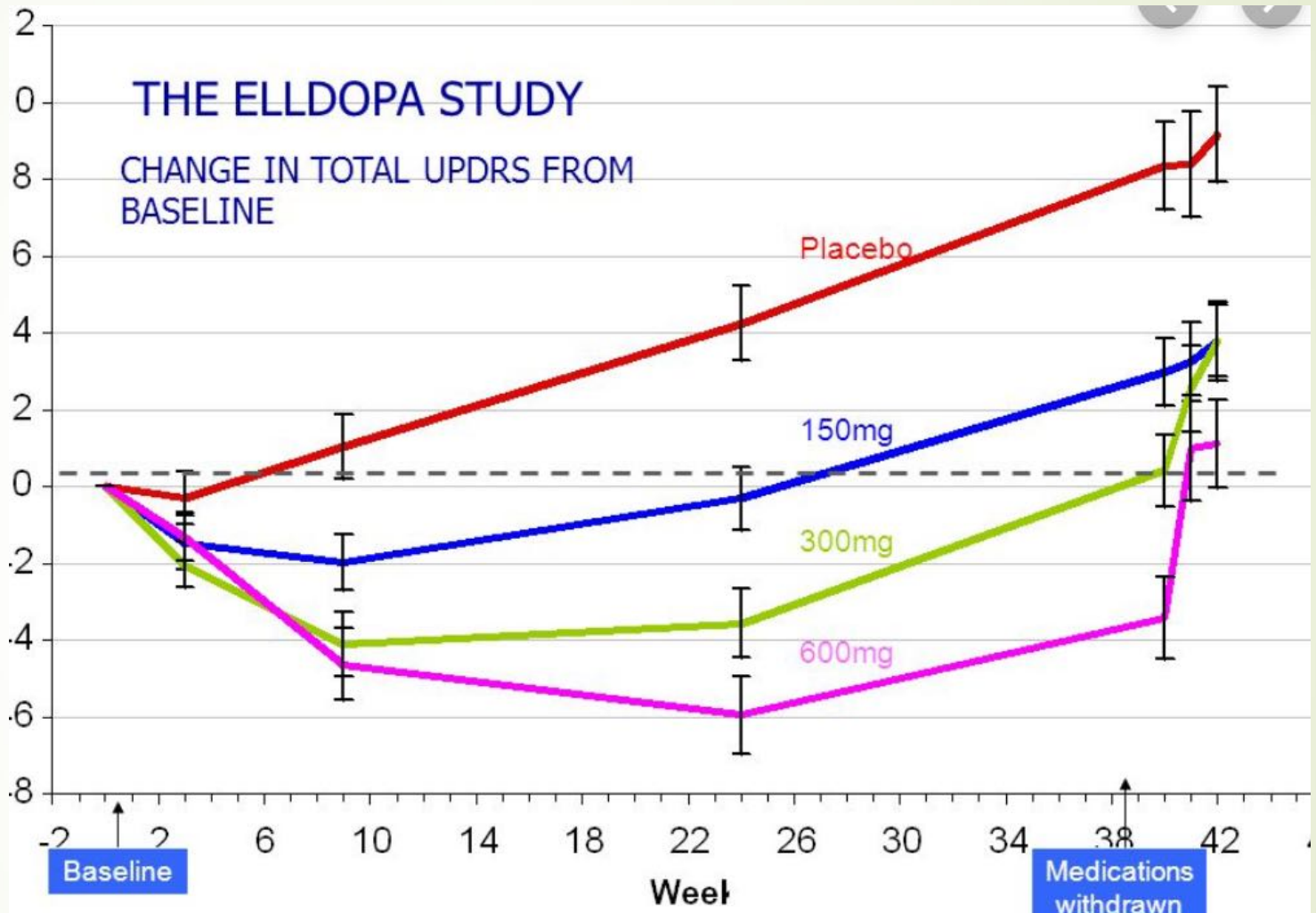


Neuroprotective medications??

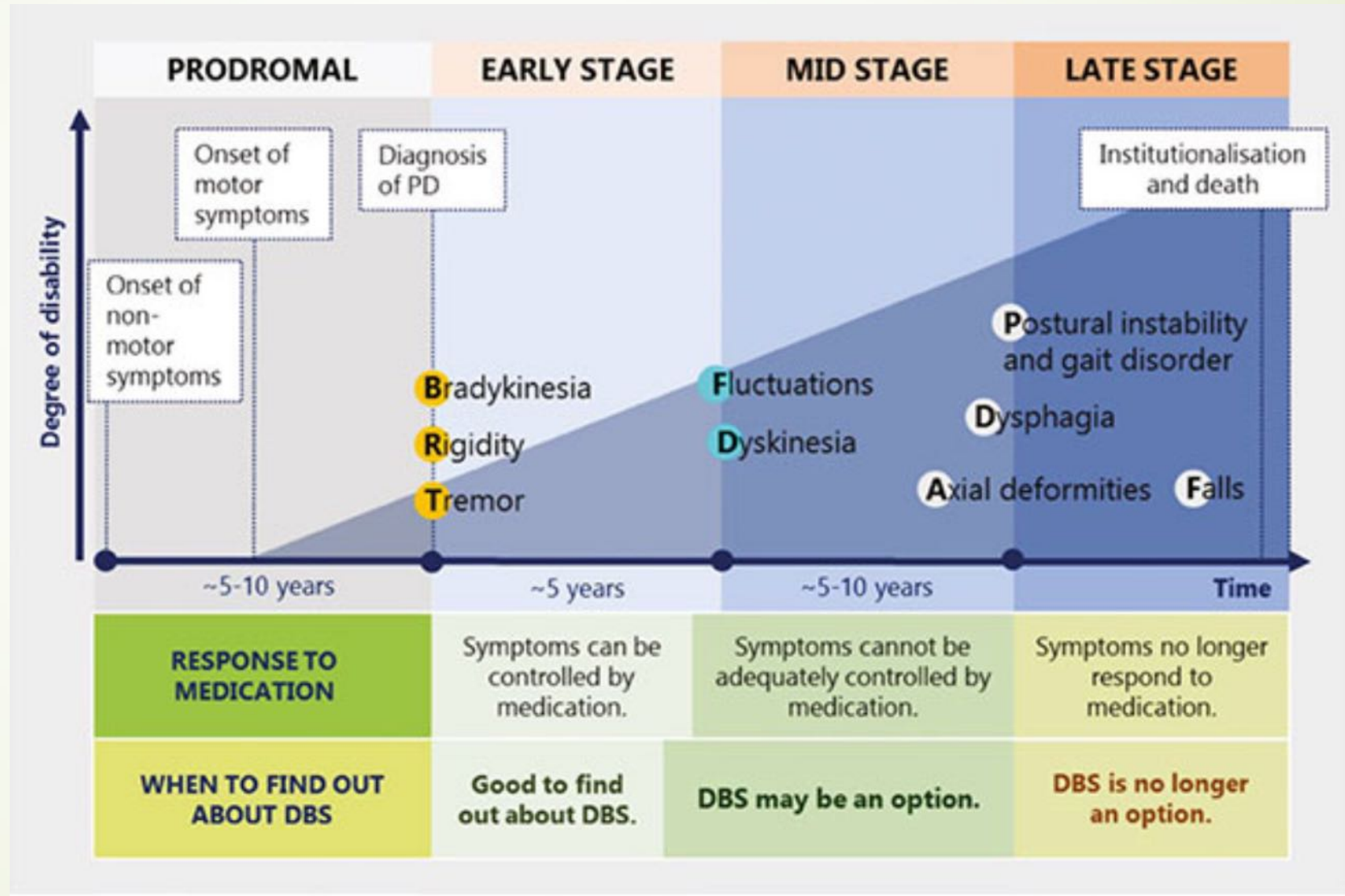
STUDY	DRUG	RESULT
DATATOP	Selegiline	Selegiline not neuroprotective but reduced symptoms and delayed levodopa for 6 months
ADAGIO	Rasagaline	Met 5 out of 6 endpoints but not deemed neuroprotective by FDA
PRECEPT	Coenzyme Q10	No significant difference from placebo

ELLDOPA STUDY (Fahn et al.)

- All levodopa doses were superior to placebo
- Higher dose provided more symptomatic benefit
- However dosing at 600 mg led to higher incidence of dyskinesia



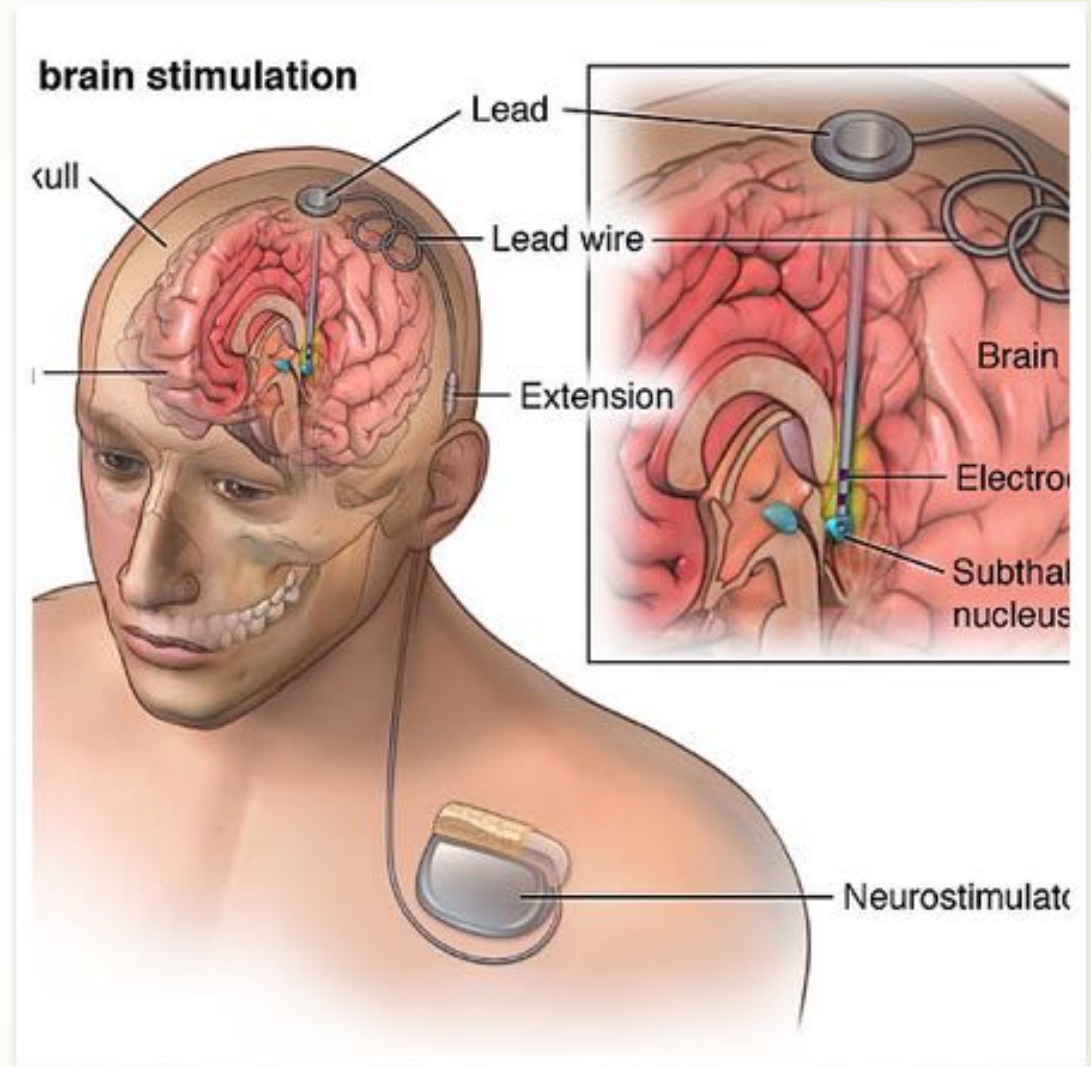
PD Progression



Deep brain stimulation


A pacemaker for the brain

- Electrode is inserted into centers deep within the brain
- Electrode is connected with a wire to a pacemaker that is under the skin below the collar bone
- DBS helps reduce tremor and other symptoms from Parkinson's disease






When to consider DBS?

- ▶ Tremor that is not controlled by medications
 - ▶ On-Off fluctuations become severe and unpredictable
 - ▶ Troublesome dyskinesias
 - ▶ Any patient with inadequate quality of life with medications
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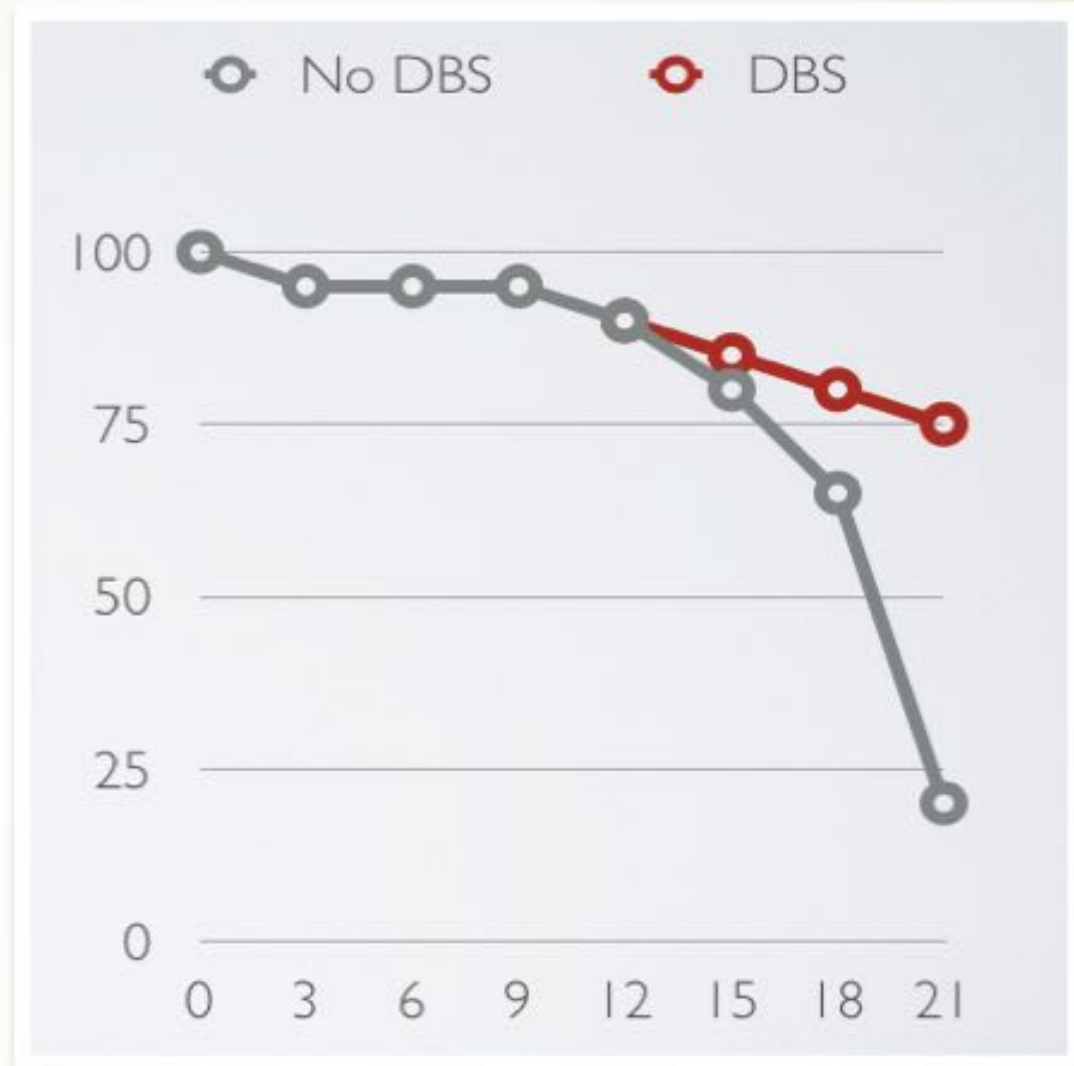


WHAT TO EXPECT FROM DBS

- Tremor is the symptoms that improves the most
 - Severity and duration of the off state is reduced
 - Dyskinesias are improved
 - NO improvement in cognition
 - NOT a cure or replacement for PD medications
- 

DBS and disease progression

- PD has a honeymoon phase followed by a phase of unpredictable medication response followed by more rapid decline
- DBS helps delay the rapid decline





Risks of DBS

- 2% risk of brain hemorrhage with severe stroke like symptoms
- 3-5% infection
- Temporary numbness, double vision etc. can be adjusted by DBS programming
- Very rare: lead breakage or migration
- Poor placement of DBS electrode




MRI-FUS versus DBS

	MRI-FUS	DBS
EXPERIENCE	2 years 200 cases with tremor	20 years Over 100,000 PD and ET
TARGETING	MRI only	MRI plus brain mapping
REVERSIBLE?	No	Yes: DBS turned off
HARDWARE	No	Yes



Contraindications to FUS

- Pacemaker or unstable heart condition
 - Abnormal bleeding or blood thinners
 - History of stroke or brain tumor
 - Skull density ration of 0.45 or less of CT head
- 



Take Home Messages

- Stay informed through PD foundations
- See a movement disorders neurologist
- Take a holistic approach: meds, diet, exercise, lifestyle
- Consider surgical options

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