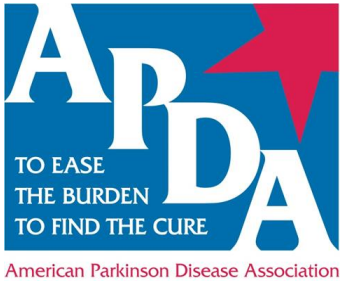
One Size Fits One

PATIENT CENTERED, IMPAIRMENT BASED CARE FOR PERSONS WITH PARKINSON'S DISEASE

ALAPTA ANNUAL CONFERENCE
AUGUST 17, 2019

Welcome!

Parkinson's Care Clinic


ARDA
TO EASE
THE BURDEN
TO FIND THE CURE
American Parkinson Disease Association

Southeast
HEALTH
Neurobalance Program

UAB MEDICINE
Knowledge that will change your world

One Size Fits One

Ellis T., Rochester L. 2018.

The burden of disease…[2-5]

The # of persons with PD worldwide is expected to **DOUBLE by 2030.**

Arthritis

Deconditioning

"On average persons with disabilities report **4-13 secondary conditions**"

The projected total cost to the U.S. alone is expected to be **$52 BILLION ANNUALLY.**

Fatigue

Osteoporosis

Mobility Problems

Muscle/Joint pain

Patient Centered Care

"Care that is respectful and responsive to individual preferences, needs and values, ensuring that the person with Parkinson's Disease (PwP) guides all clinical decision making."

van der Eijk et al. 2011

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Parkinson's disease

Juliana Coleman, MD

Marissa Dean, MD

Jason Crowell, MD

ALAPTA Annual Conference
17 August 2019

Incidence of PD

- Peak age of onset 60 yo
- Lifetime risk 2%
- 1-14/100,000 population per year

Elbaz et al, 2002; Van Den Eeden et al, 2003

Prevalence of PD

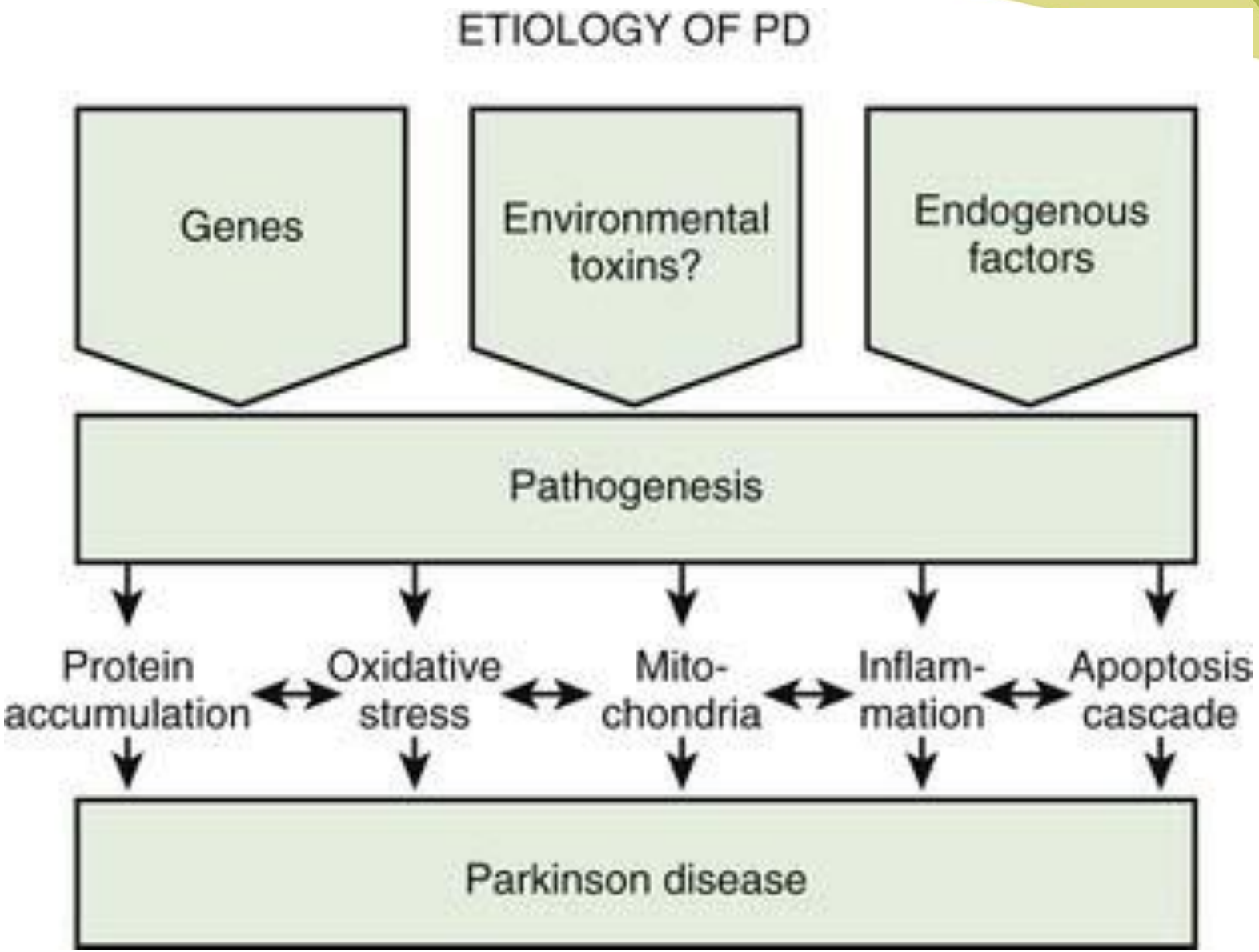
- 1.8% of people over 65 yo
- Risk increases with age
- 2.6% of people 85-89 yo
- More common in males (3:2)

de Rijk et al, 2000; Bowe et al, 2000

Mortality of PD

- Pre-levodopa era: 3x greater risk of death
- Post-levodopa: 1.6x greater risk of death
- Now, patients live >20 years
- Death is usually to an unrelated illness or the effects of decreased mobility, aspiration, or increased falling.

Hoehn and Yahr, 1967; Yahr et al, 1976; Elbaz et al, 2003



Fahn et al, Principles and practice of movement disorders, 2007

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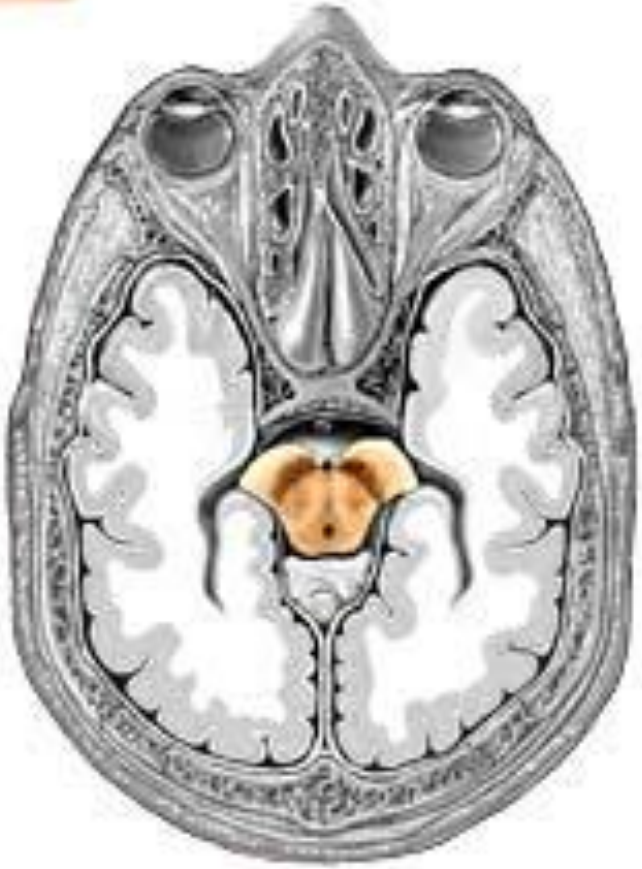
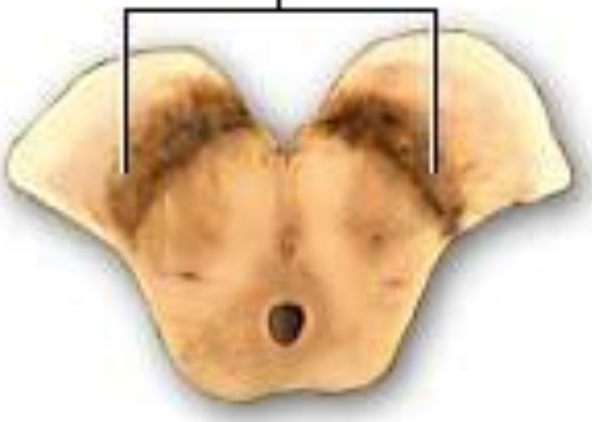
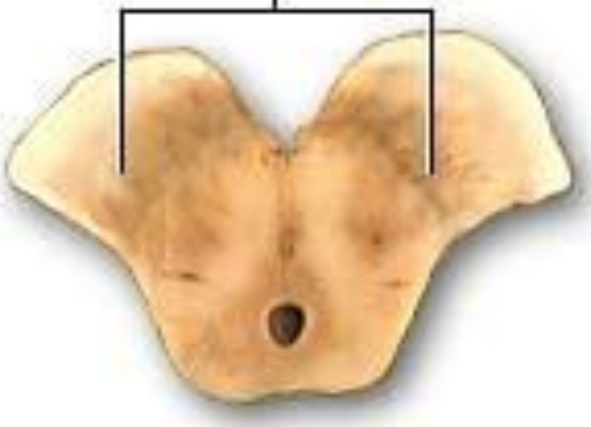
Cut section of the midbrain where a portion of the substantia nigra is visible



Substantia nigra



Diminished substantia nigra as seen in Parkinson's disease



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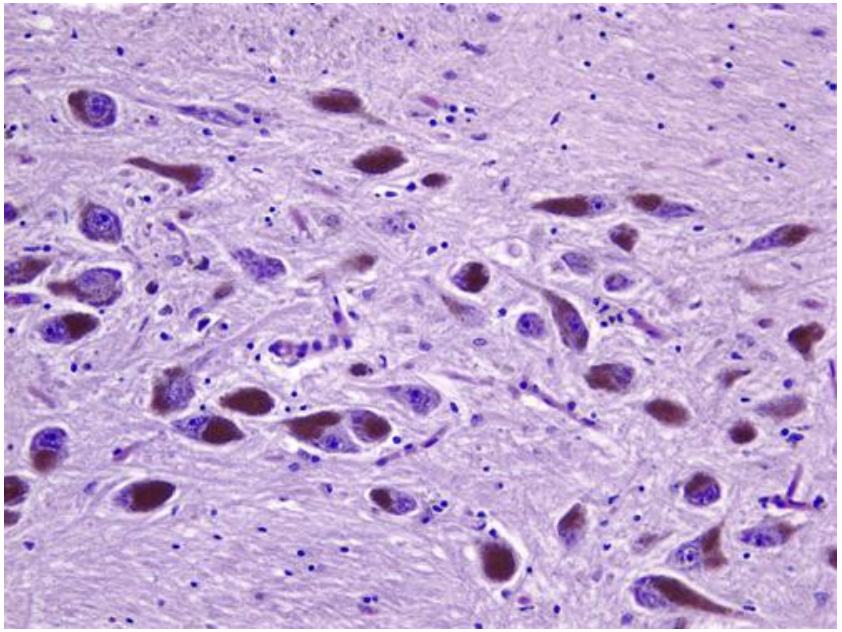
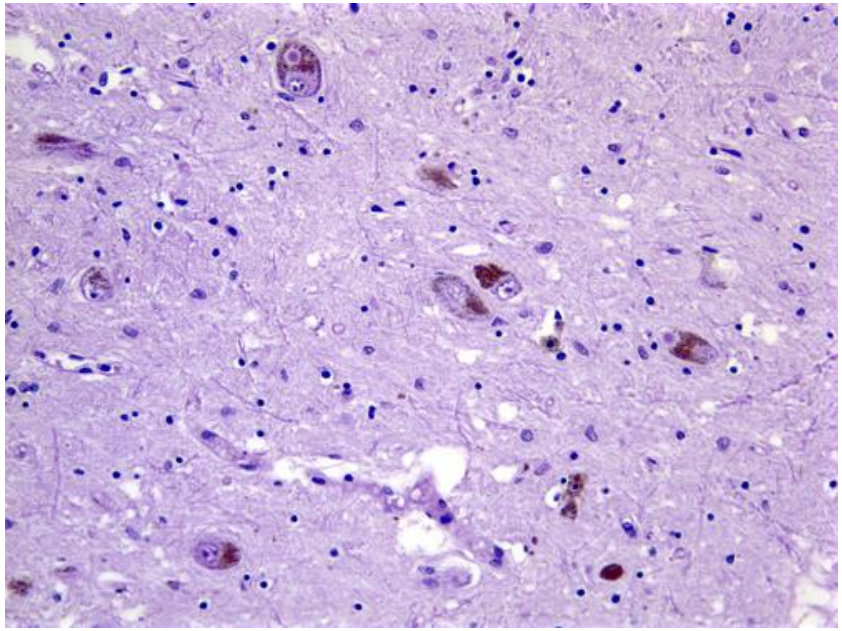
NGHAM

http://www.nytimes.com/health/guides/disease/parkinsons-disease/print.html

Substantia nigra pars compacta

Collection of pigmented neurons located within the midbrain (upper part of brainstem).



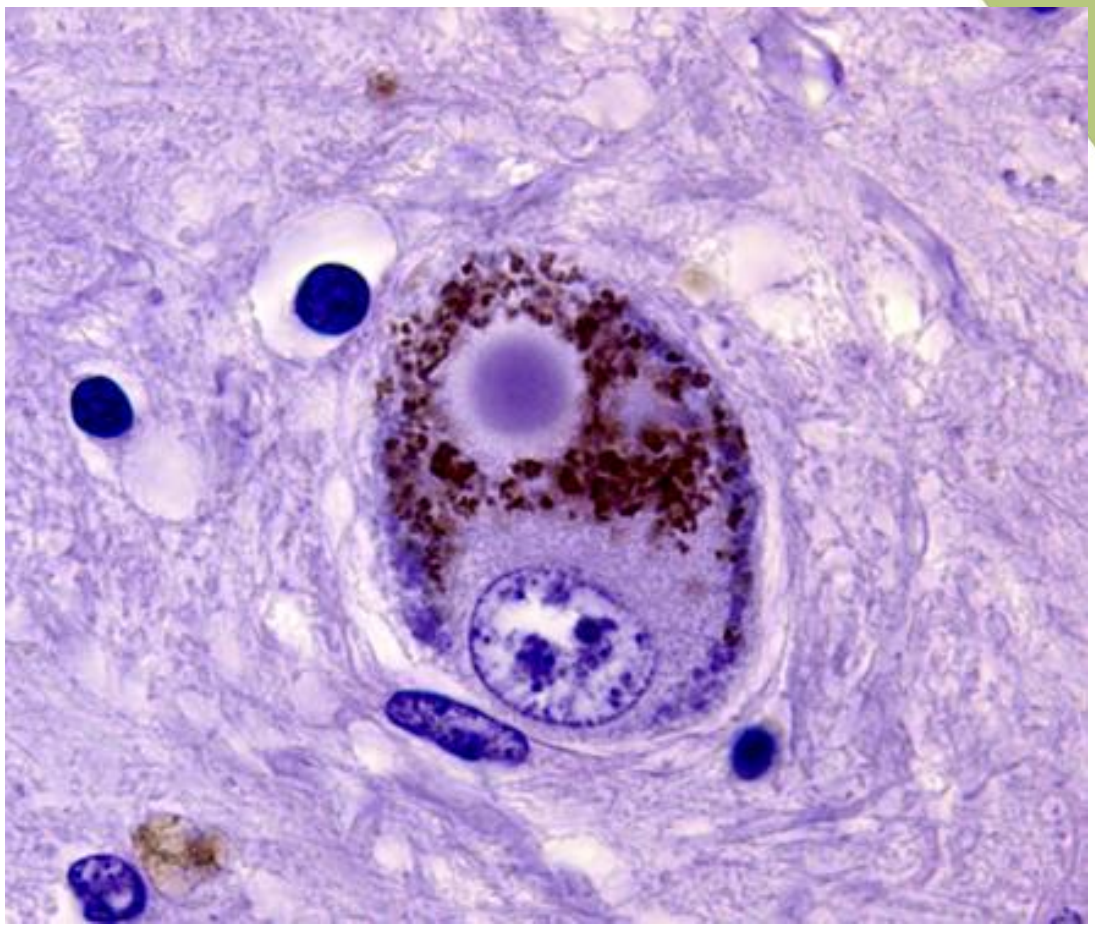


Normal (left) and PD (right). There is loss of these neurons in PD.

http://neuropathology-web.org/chapter9/chapter9dPD.html

Pathology of PD

- 1912, 1914 – Lewy discovered cytoplasmic inclusions (Lewy bodies)
- Almost all patients with PD have Lewy bodies in SN and locus ceruleus.
- Lewy bodies are made up of the protein alpha-synuclein.

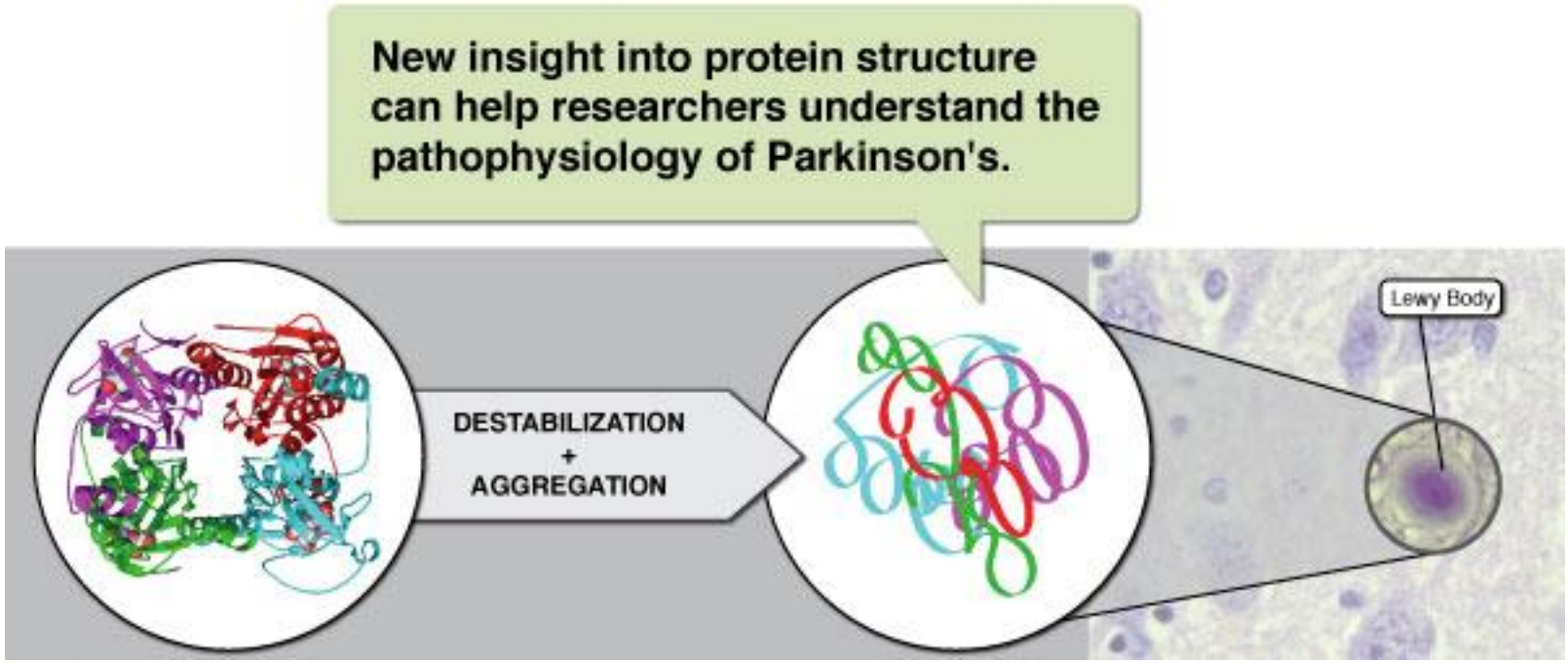


Lewy et al, 1912; Lewy et al, 1914

http://neuropathology-web.org/chapter9/chapter9dPD.html

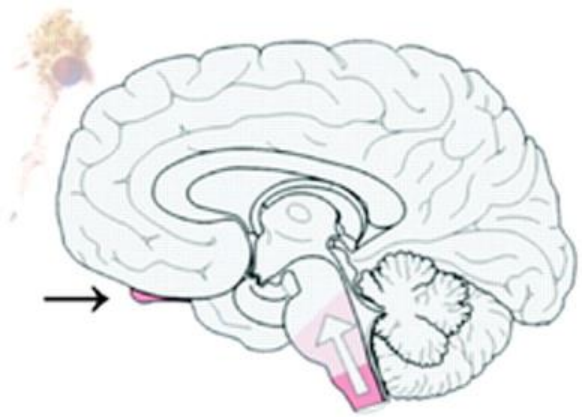
Alpha synuclein

- Soluble protein in cytoplasm.
- Lewy bodies consist of abnormally folded alpha-synuclein.



http://www.labpinions.com/files/science-news/images/Andrew%20Hau/parkinsons-2_0.jpg?1319652492

Braak staging of PD



Braak Parkinson's disease stages 1 & 2
PRECLINICAL

Braak Parkinson's disease stages 3 & 4
CLINICAL PARKINSON'S DISEASE

Braak Parkinson's disease stages 5 & 6
COGNITIVE IMPAIRMENT

Stage 1	**Anterior olfactory nucleus, lower brainstem**
Stage 2	Raphe and locus coeruleus
Stage 3	**Substantia nigra**
Stage 4	Mesocortex and thalamus
Stage 5	**Neocortex association areas, prefrontal cortex**
Stage 6	Entire neocortex (mild in primary motor and sensory areas

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Is the Braak hypothesis valid?

- Some non-motor features of PD appear before motor signs, as predicted by Braak.
  - Constipation is commonly seen, up to 20 years prior to motor symptoms.
  - Olfactory dysfunction
- Validation with human autopsy study
  - PD staging held true in majority of patients (67%-86%) with incidental LBs, PSP with LBs, LBD without AD pathology and LBD with AD pathology.
  - PD staging only seen in 6% of AD patients

Savica et al, 2009; Ross et al, 2008; Dickson et al, 2010

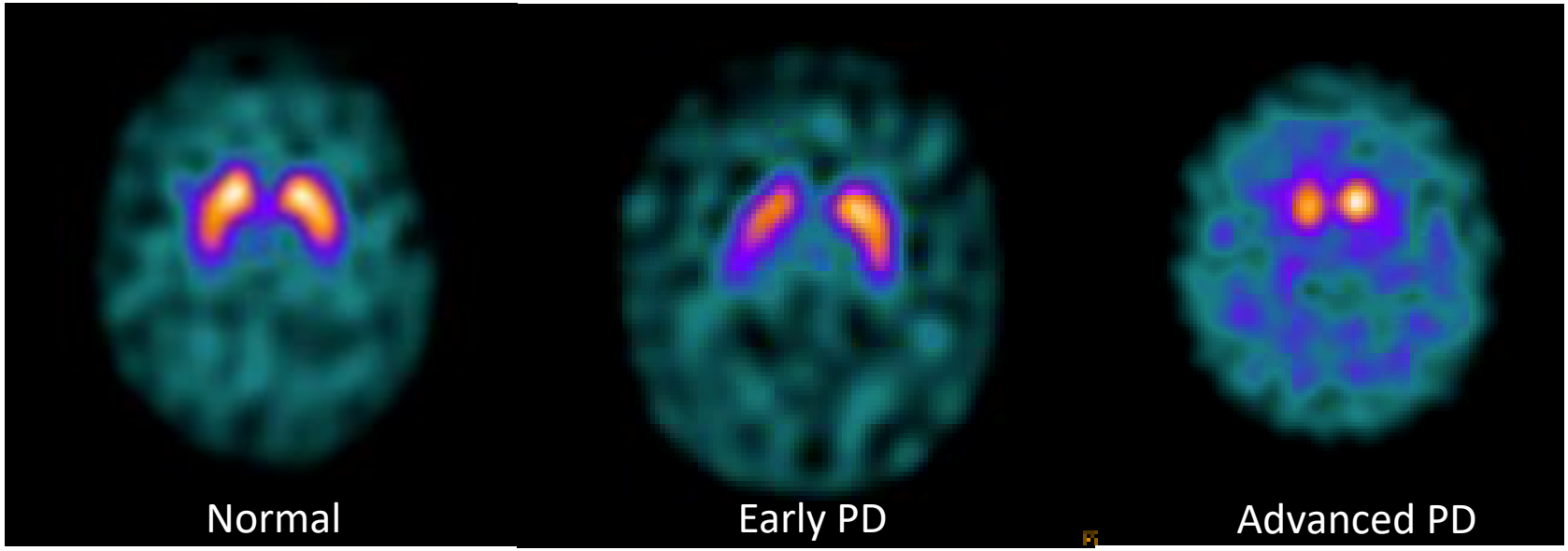
Is the Braak hypothesis valid?

1. Some patients have LB and decreased SNc neurons without LB in lower brainstem.
2. Dementia with lewy bodies often doesn't have brainstem Lewy neurites.
   1. DLB patients excluded in Braak's studies
3. Many elderly patients have Braak pathology (even stage 6) and die without having clinical PD.
4. No correlation between Braak stages and clinical severity of PD.
5. Lewy bodies not always seen in LRRK2 mutations.

Parkkinen et al, 2005; Parkkinen et al 2008; R.E. Burke et al, 2008; Haugarvoll and Wszolek, 2006

Substantia Nigra Imaging

- SNc neurons project to the neostriatum (caudate + putamen).
- In PD, loss of SNc neurons projecting to posterior putamen occurs first.
- Can be seen with FDOPA PET or DAT SPECT scans.
  - Note: abnormal DaT scan can be seen in any parkinsonian syndrome; not just PD.



Pathology and motor symptoms in PD

- Clinical motor features seen after 80% of striatal dopamine content (60% of nigral dopaminergic neurons) are lost.
- How do clinical findings correlate with neuron and dopamine loss in SN?
- SN is involved in the motor circuit, and decreased influence of these neurons within the circuit is thought to contribute to the motor manifestations seen in PD.

Bernheimer et al, 1973

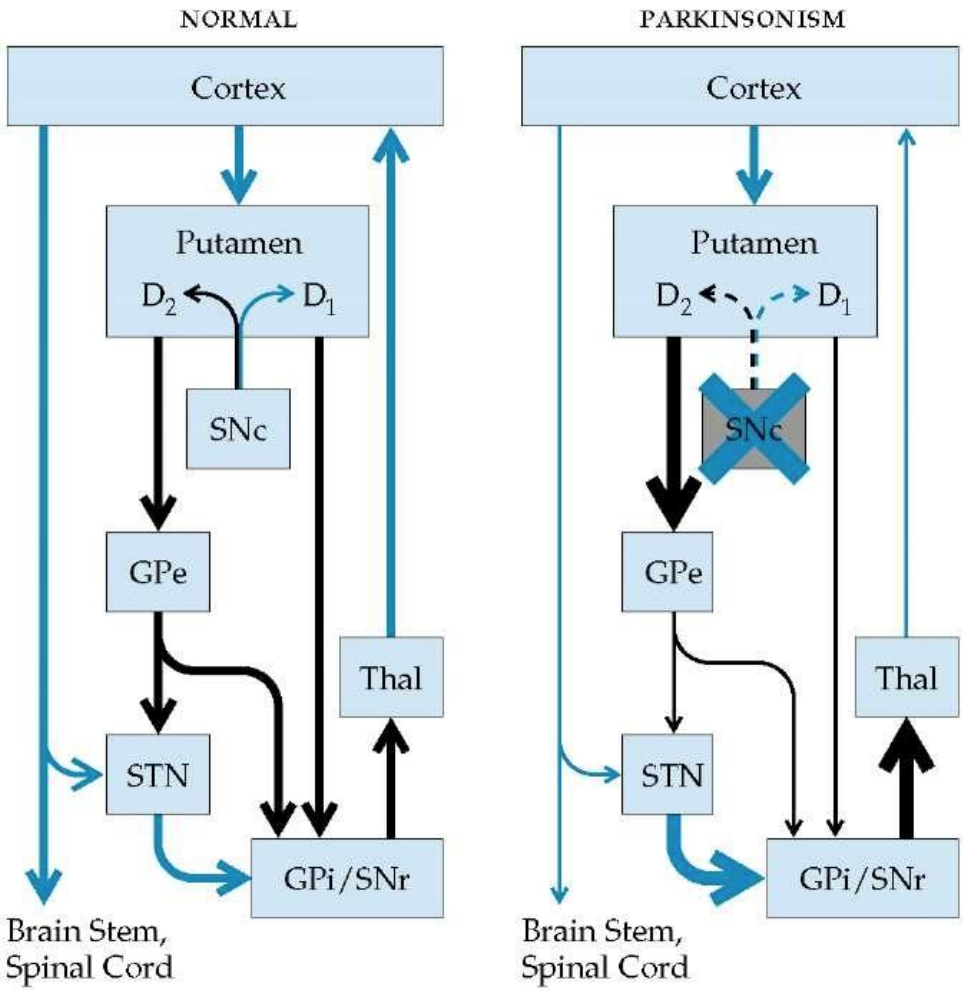
Motor Circuit

Normal:

- Direct pathway: Putamen->GPi/SNr->Thal->Cortex
- Indirect pathway: Putamen->GPe->STN->GPi/SNr->Thal->Cortex

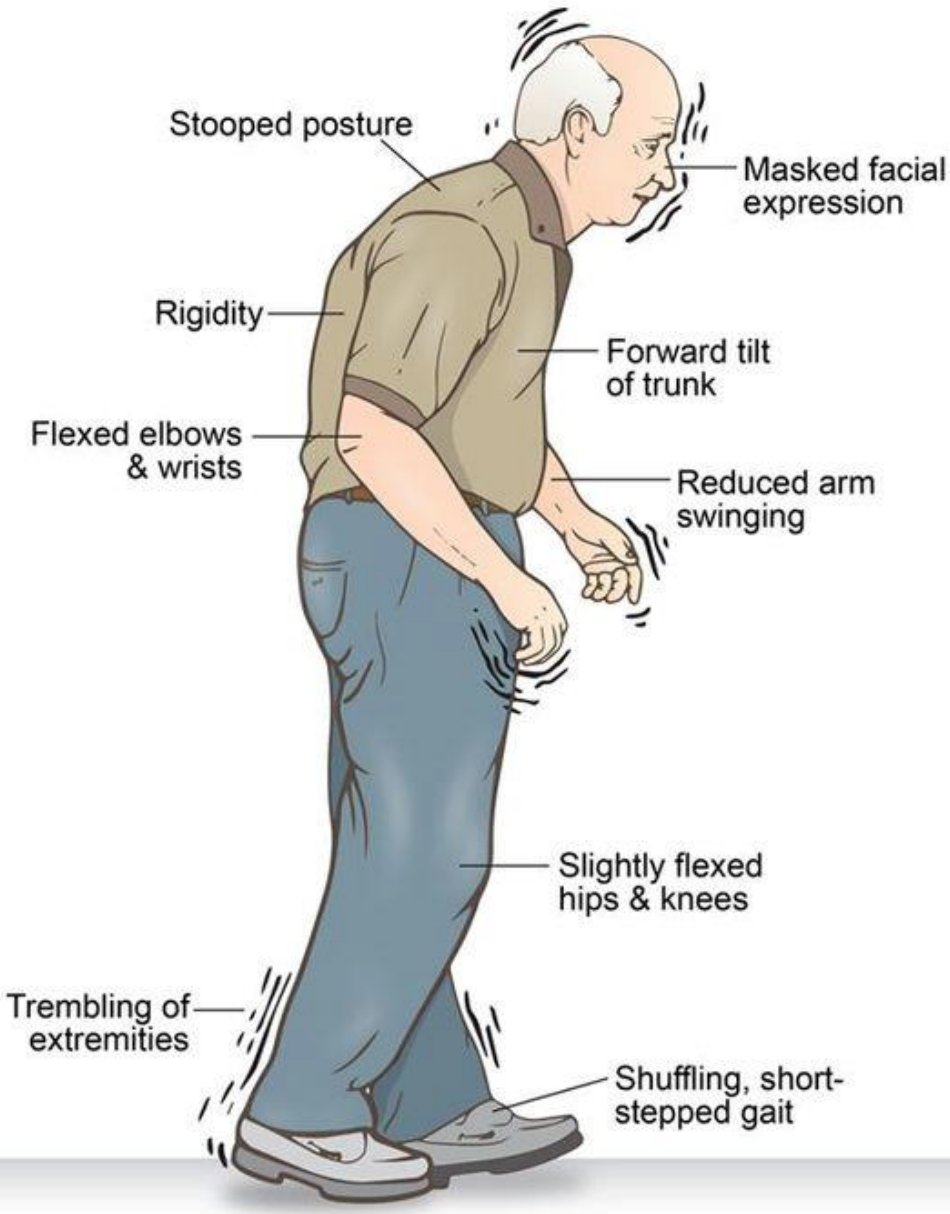
PD:

- Ultimate decreased output from thalamus to cortex



http://what-when-how.com/acp-medicine/parkinson-disease-and-other-movement-disorders-part-1/

Typical appearance of Parkinson's disease



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Making the Diagnosis

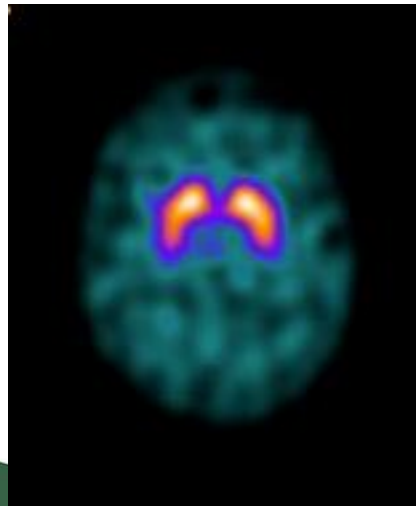
- MDS Clinical Diagnostic Criteria (10/2015)
  - Bradykinesia
  - Tremor and/or rigidity

Postuma et al., Mov Disord, 2015

Absolute exclusion criteria

- Absence of response to high dose levodopa, despite moderate disease
- Normal DaT scan
- Dopamine blockers (antipsychotics, antiemetics)
- FTD or primary progressive aphasia
- LE parkinsonism for >3 years
- Cerebellar features
- Downward gaze palsy
- Cortical sensory loss or ideomotor apraxia

Postuma et al., Mov Disord, 2015



Supportive criteria

- Need at least 2 for clinically established PD:

  1. Clear and dramatic benefit from levodopa therapy
  2. Levodopa-induced dyskinesias
  3. Resting tremor of limb
  4. Olfactory loss

Postuma et al., Mov Disord, 2015

Red flags

- Wheelchair after 5 years of motor symptom onset
- Recurrent falls (>1/yr) in 3 years
- No progression of symptoms in 5 years
- Bilateral, symmetric parkinsonism
- Absence of non-motor features in 5 years
- Severe dysarthria/dysphonia in 5 years
- Severe dysphagia in 5 years

Postuma et al., Mov Disord, 2015

Red flags

- Inspiratory respiratory dysfunction
- Severe autonomic failure in 5 years
- Contractures in 10 years (anterocollis, hands, feet)
- Unexplained pyramidal tract signs

Motor findings in PD - Bradykinesia

- Bradykinesia: Slowness of movements
  - Decreased amplitude and speed
  - Examine rapid alternating movements
  - Slowness in shrugging/relaxing shoulder or raising arm
  - Micrographia

Espay et al., 2009

Bradykinesia and Gait

- Slow, short-stride, shuffling gait
- Reduced heel strike
- Reduced arm swing when walking
  - decreased automatic/spontaneous movement

Other manifestations of Bradykinesia

- Drooling (failure to swallow saliva)
- Aprosody (loss of inflection during speech)
- Hypophonia (soft speech)
- Hypomimia (loss of facial expression)
- Decreased eye blinking
- Loss of spontaneous movements (such as gesturing)
- Bradyphrenia (slowness of thought)

Bagheri et al., 2009; Lal and Hotaling, 2006; Teulings et al., 2002

Motor findings in PD - Tremor

- Tremor
  - Resting hand tremor (‘pill-rolling’ tremor) is classic
    - Pronation/supination or MCP flexion/extension
  - May also have postural tremor, but will typically be delayed and has same frequency of rest tremor (re-emergent tremor)
  - Frequency 4 to 6 Hz
  - Tremor of chin, lips, jaw also commonly seen
  - Leg tremor
  - Head tremor is infrequent

Jankovic et al., 1999b

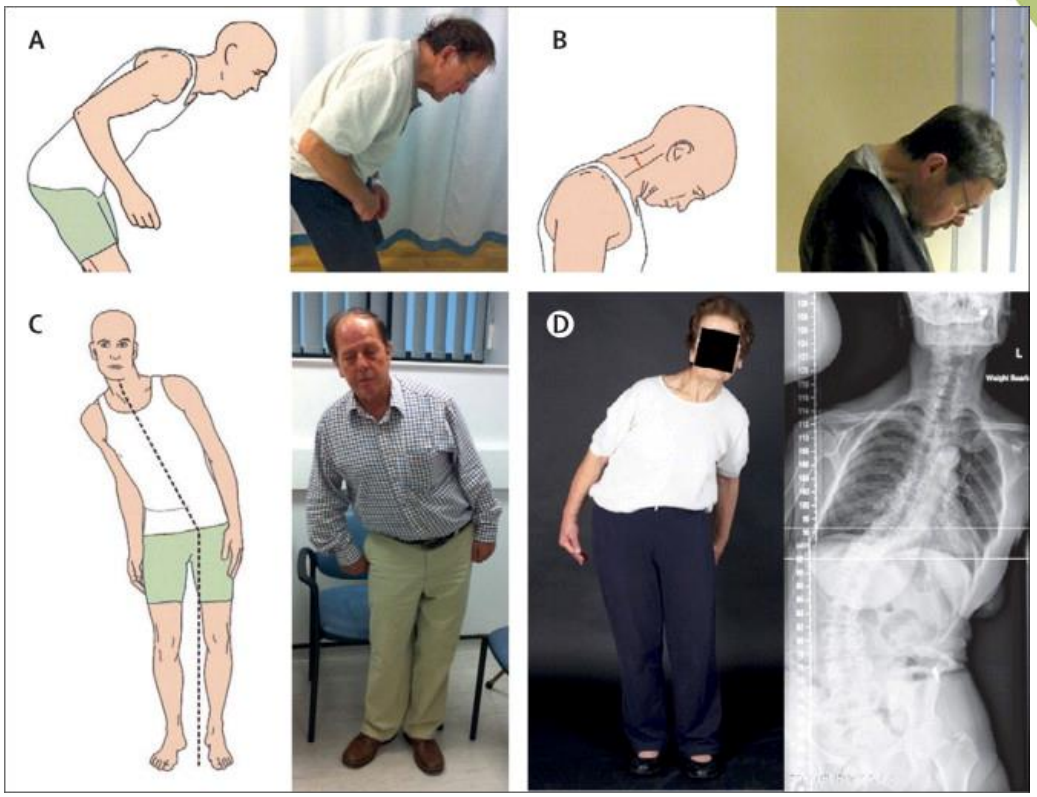
Motor findings in PD - Rigidity

- Rigidity: increased resistance of a joint against passive range of motion
  - No change with velocity
  - Cogwheeling vs lead-pipe
  - Froment's maneuver: increased resistance with voluntary movement of contralateral limb
  - Painful shoulder is common initial symptom
    - Misdiagnosed as arthritis, bursitis, rotator cuff injury

Broussolle et al., 2007; Riley et al., 1989; Stamey et al., 2008

Other manifestations of Rigidity

- Flexed neck and trunk posturing – occurs later in disease
  - Truncal flexion of thoracolumbar spine (camptocormia) worsens during walking and resolves in supine position
  - 'Dropped head'
  - Pisa syndrome (tilting of the trunk and scoliosis)



Doherty et al., The Lancet Neurology, 2011

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Motor findings in PD – Postural reflexes

- Loss of postural reflexes – occurs later in disease
  - Worsens when performing complex motor (carrying groceries while walking up steps) and cognitive tasks
  - Contributes to falls
  - Retropulsion testing (pull test)

Motor findings in PD - Festination

- Festination of gait
  - Loss of postural reflexes + stooped posture
  - Patient walks faster and faster, trying to catch up with center of gravity

Motor findings in PD – Freezing of gait

- Freezing: halting of a motor action
  - Feet can become 'glued to the ground'
- Common Triggers
  - Starting
    - Short, sticking, shuffling steps when initiating walking
  - Turning, Crowded or Cluttered space
  - Doorways
  - Moving in short period of time (crossing street)
  - Destination-freezing and Dual Tasking
- Anxiety and Rushing worsens FOG

Cues/tricks to overcome Freezing

- Visual cues
  - Lasers
  - Strips of tape
- Changing the task
  - Weight shifting
  - Take a step backward
  - March in place
- Tapping the doorway
- Reward mechanisms (chocolate)
- Auditory Cues
  - Rhythms
  - Music
  - Beats

Be Creative!

Other types of Freezing

- Palilalia or freezing of speech
  - Usually, patient will repeat first syllable of the word
- Apraxia of eyelid opening (levator inhibition)
- Freezing of limbs

Progression in PD

- Without treatment:
  - In 5-10 years, severely disabling
  - Death mainly from medical complications

Hoehn & Yahr Stages

Stage 1
Motor symptoms on one side; minimal functional impairment

Stage 2
Symptoms become bilateral

Stage 3
Mild to moderate symptoms with mild loss of balance; functions independently

Stage 4
More severe symptoms with significant loss of balance; requires substantial assistance

Stage 5
Severe symptoms; restricted to bed or wheelchair

Hoehn & Yahr, Neurology. 1967;17:427-442.

Rate of progression

- Different rate for each PD patient
- Rate of progression within same patient is steady
- Tremor-dominant form progresses slower

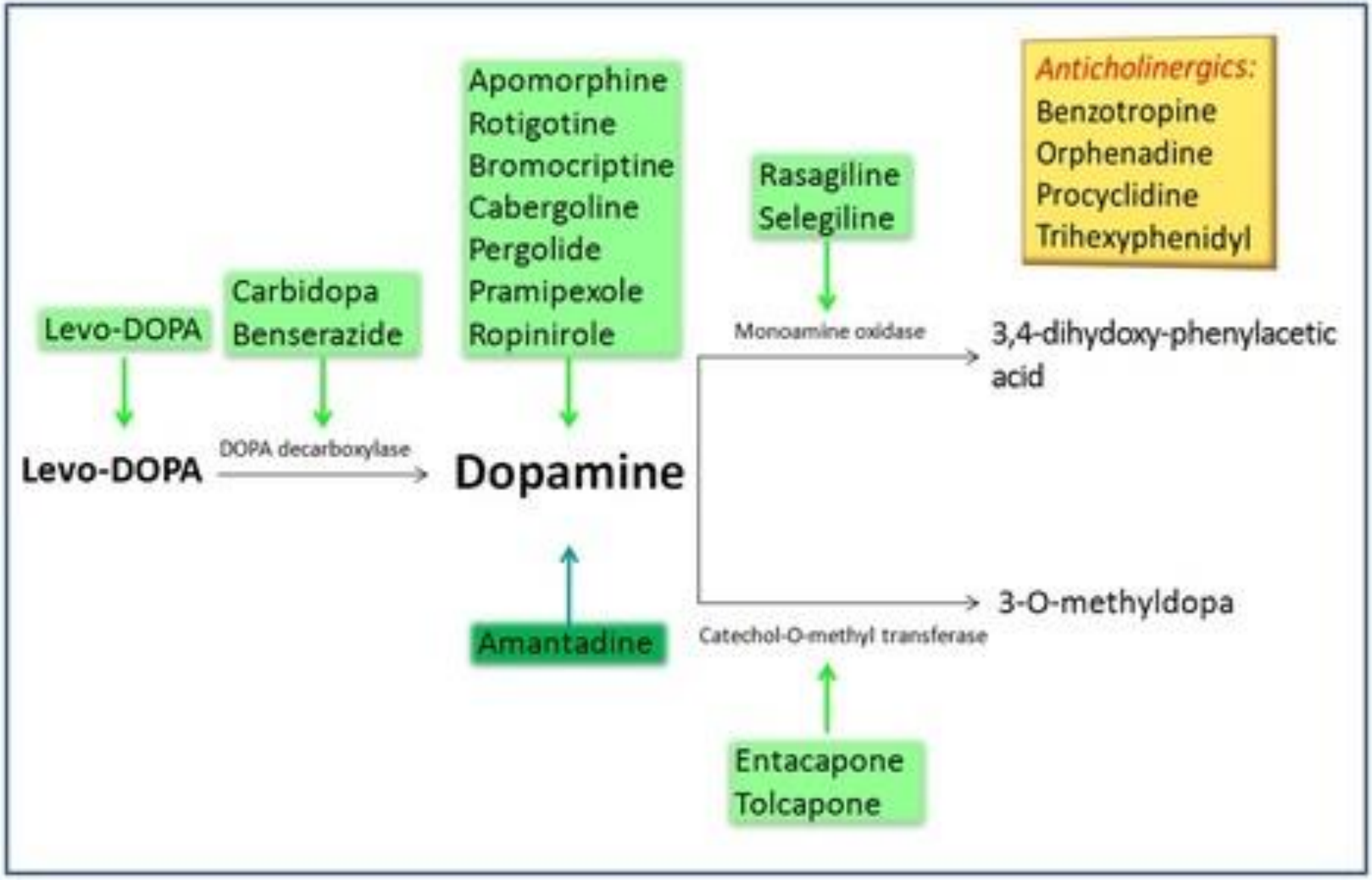
Post et al., 2007

Other influences of progression

- Stress
  - Emotional and medical
- Illness
- Therapy

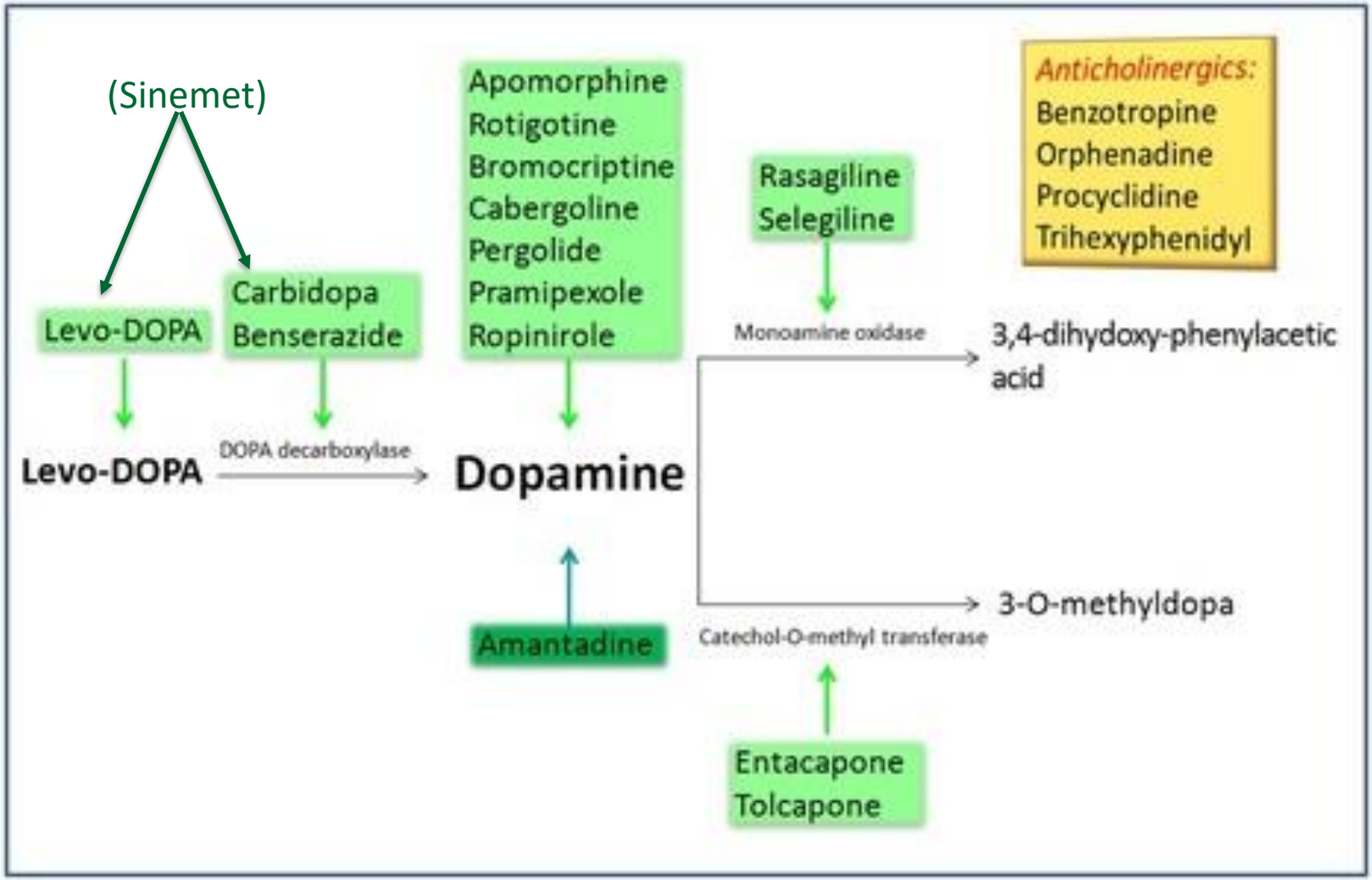
Tanner and Goldman, 1996; Onofrj and Thomas, 2005.

Medications Used in Parkinson disease



https://you.38degrees.org.uk/petitions/free-medication-for-people-with-parkinson-s

Medications Used in Parkinson disease

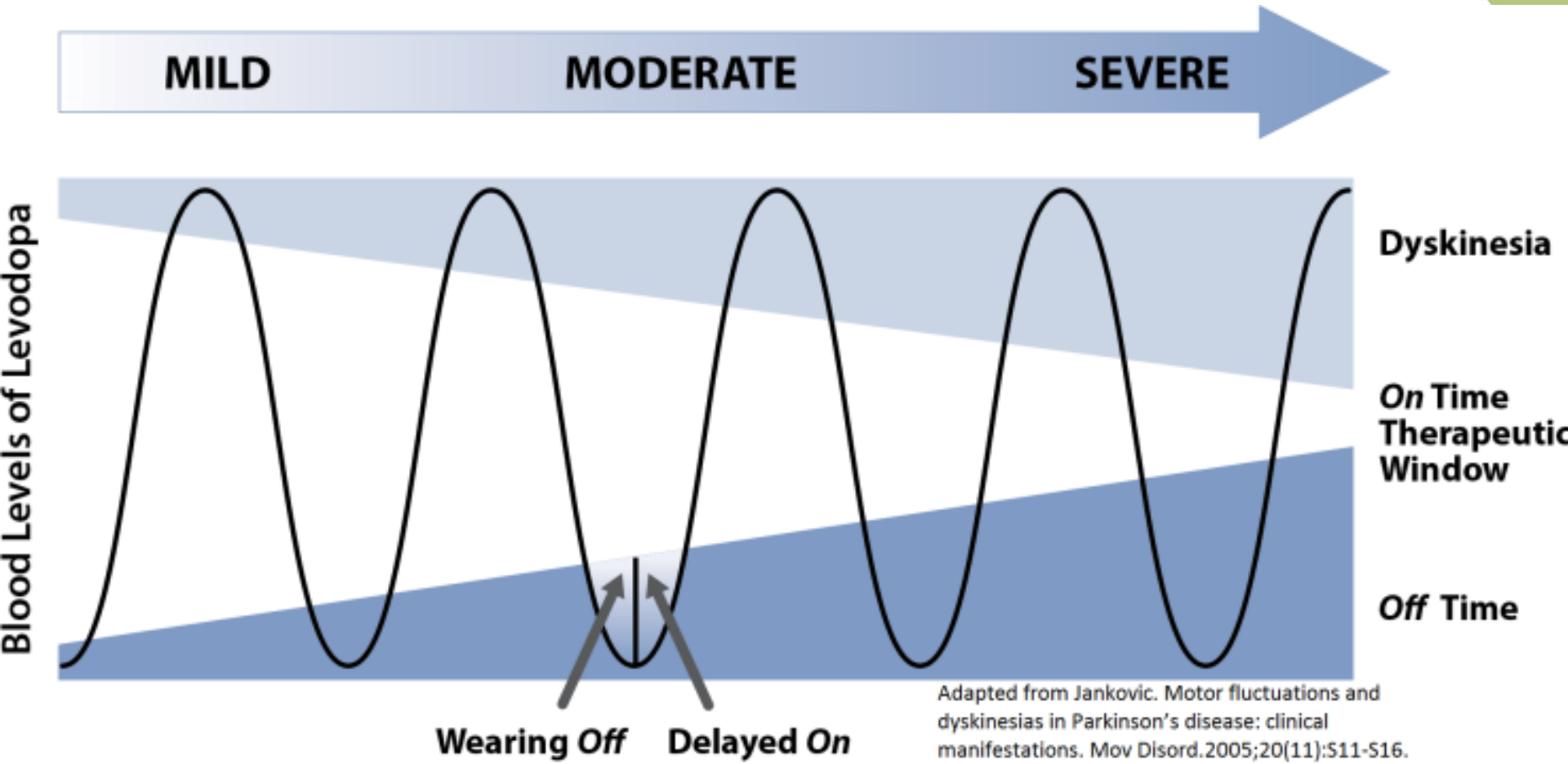


https://you.38degrees.org.uk/petitions/free-medication-for-people-with-parkinson-s

Sinemet (carbidopa/levodopa)

- Precursor to dopamine and converted to dopamine in vivo
- Bioavailability is best with:
  - Ratio is usually 25mg/100mg
  - Immediate release is most predictable

Motor Fluctuations

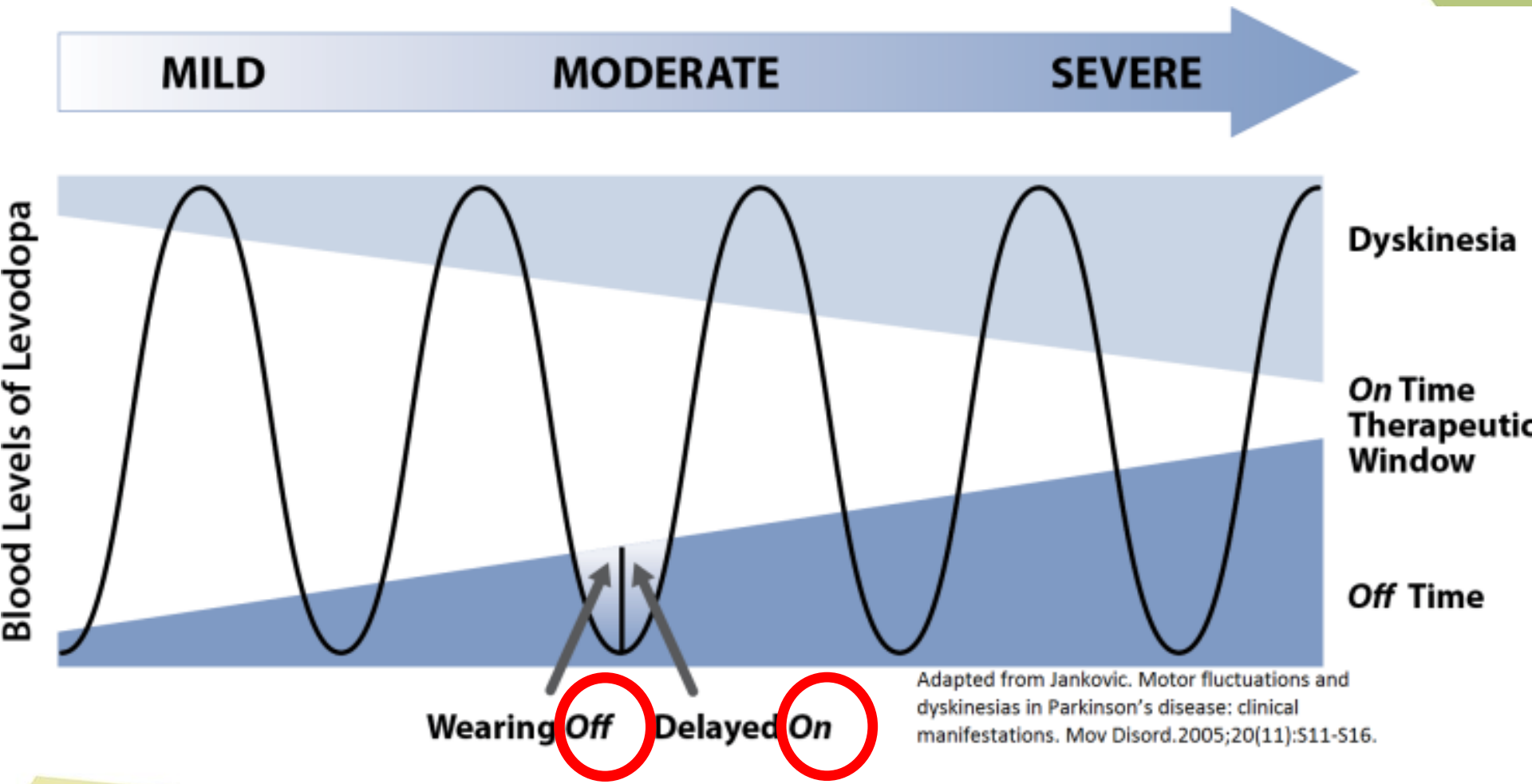


Adapted from Jankovic. Motor fluctuations and dyskinesias in Parkinson's disease: clinical manifestations. Mov Disord.2005;20(11):S11-S16.

ON and OFF

- ON
  - The medications are working
  - (Possibly with some dyskinesia)
- OFF
  - Patients' medication is not sufficient to control their symptoms
  - Usually, it has been metabolized, and it is time for a new dose!
  - You may hear the words "wearing off" which is when the benefit is waning!

Motor Fluctuations



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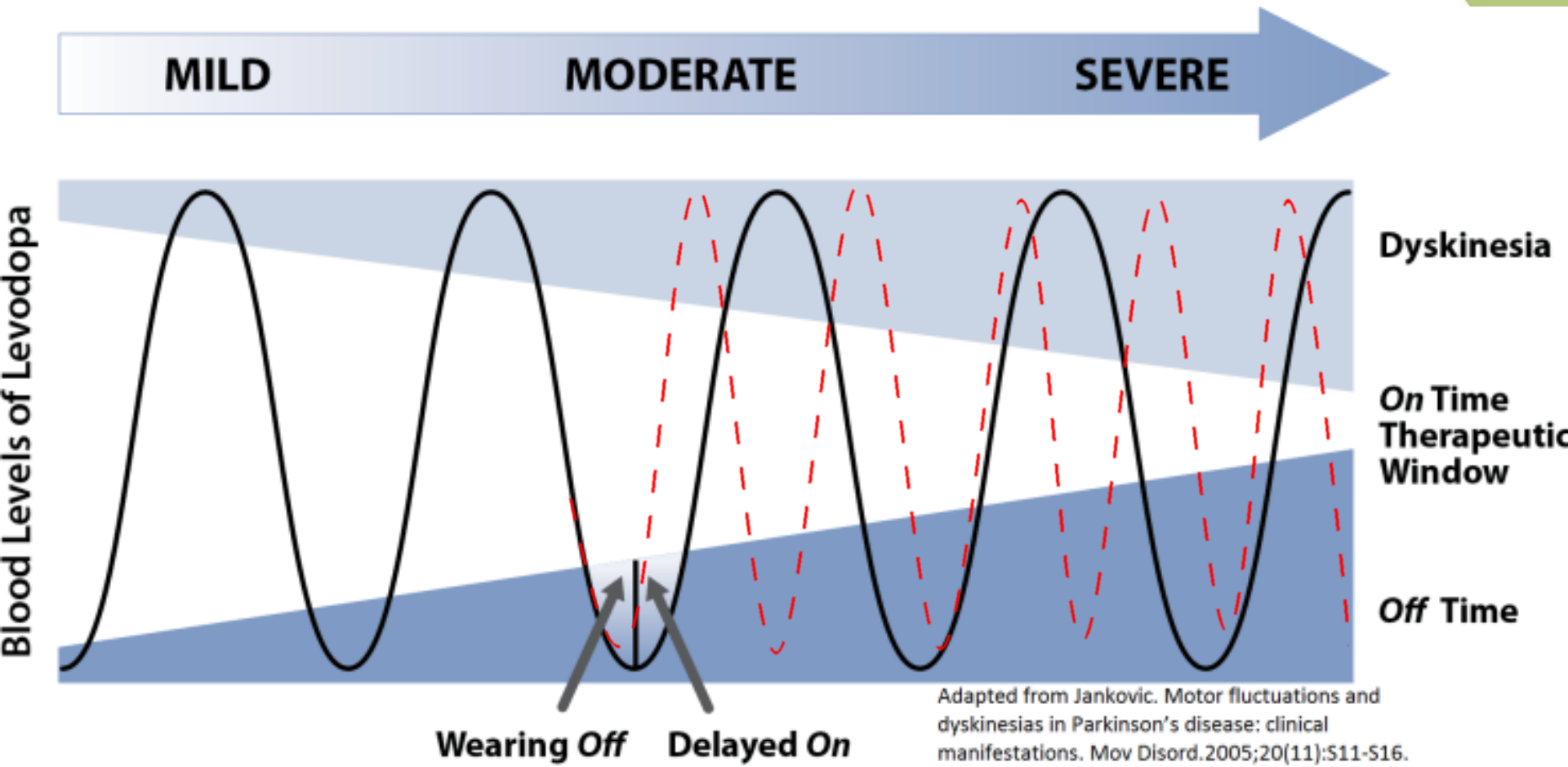
Motor Fluctuations – Increase frequency



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Dyskinesia Video

- A familiar face with dyskinesia
- Multiple patients, start at 2:45 - 3:10

Marconi et al., MD, 1994

Dystonia Video

Why this matters to Physical Therapists:

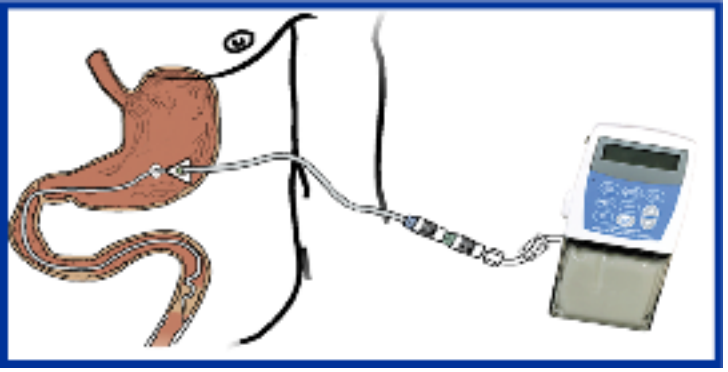
- Why is your patient having fluctuating abilities?
- What can you do about it?
  - Extra dose?
  - Better time of day?

There are other ways to give Levodopa!

- Inhaled Levodopa (Inbrija) - New!
  - Good for sudden OFF's and morning OFF's
  - Begins to work after 10 min

- Duopa Pump
  - 16 hour continuous infusion during the daytime hours
  - The patient can give themselves an additional booster dose prn
  - The pump is secure and should not interfere with therapy generally
  - Cannot do aqua therapy

LeWitt., et al. MD 2016
Fernandez, et al. MD 2015



- FDA approved in 2016
- Used in Europe since 2004

Duopa.com
Parkinson.org

MANY WAYS

Are you wondering about carrying the Duopa pump?

We get it. You're wondering if this medical device will suit you. You want to know how it will fit, look, and feel on your body.

These are all good questions, and the good news is you're not the first to ask. That's why we created 5 carrying options, so you can decide which style works best for you.

Already using Duopa?

While you may be using the carrying bag that came with your pump, take a look at other carrying cases that may suit you.

Refer to the Instructions for Use for the carrying case that you use.

Not actual patients

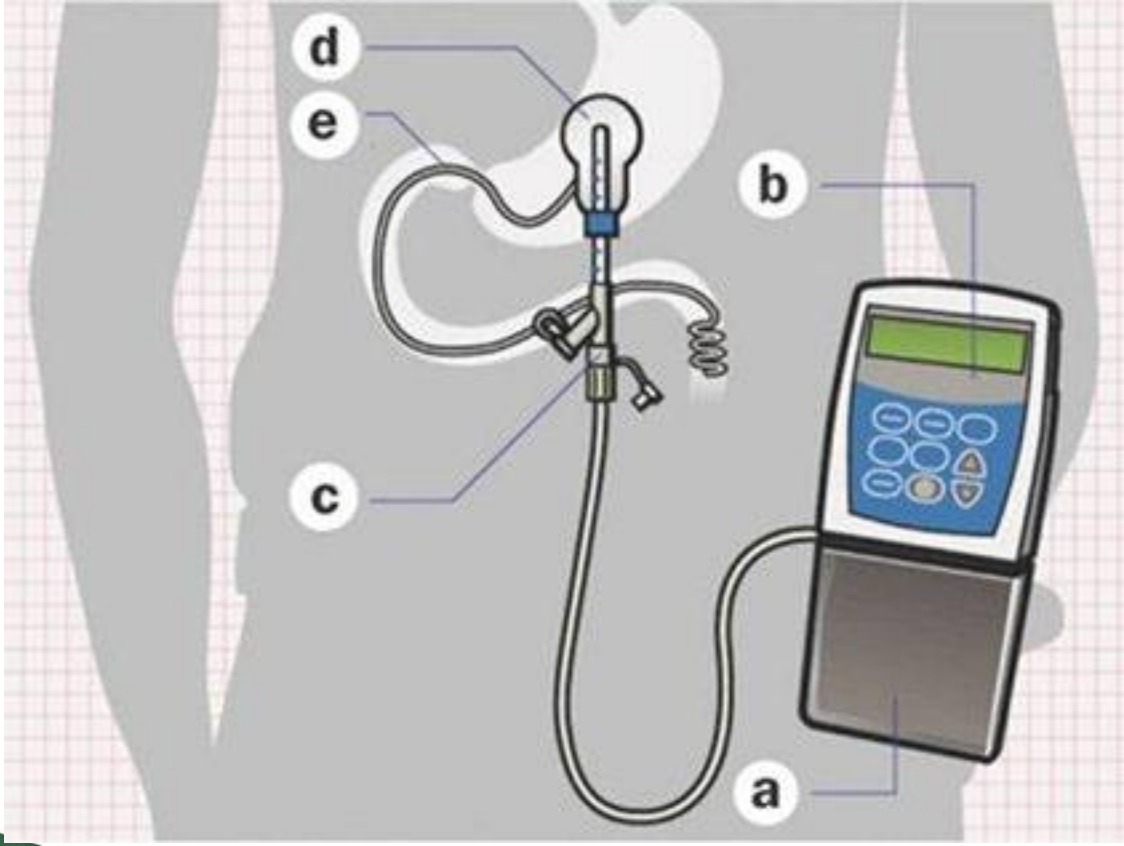
HIP PACK

PAGE 4

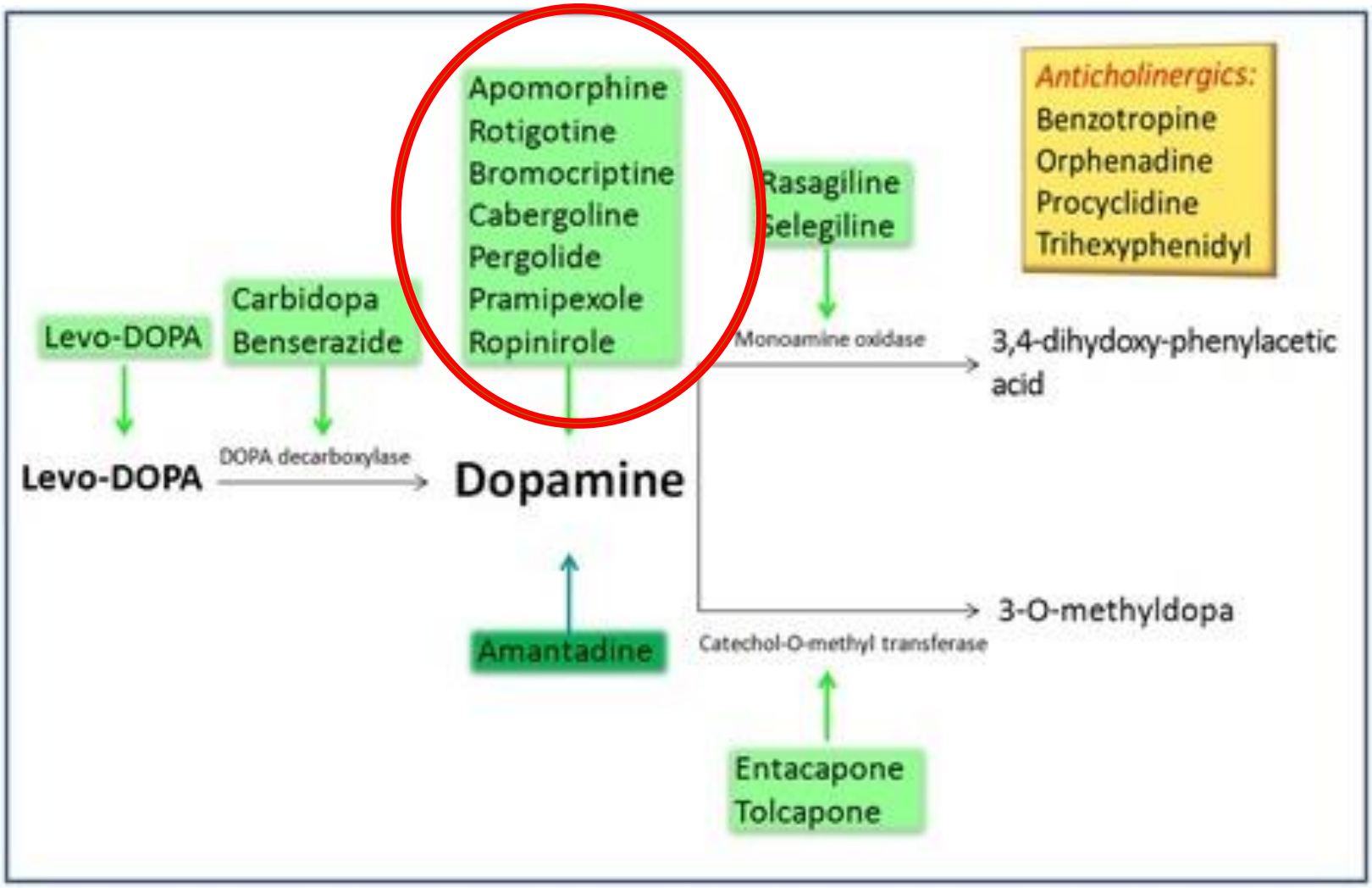
LIGHTWEIGHT VEST

PAGE 6

Please see full Important Safety Information on pages 14-15 and accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/duopa_pi.pdf.



Medications Used in Parkinsons



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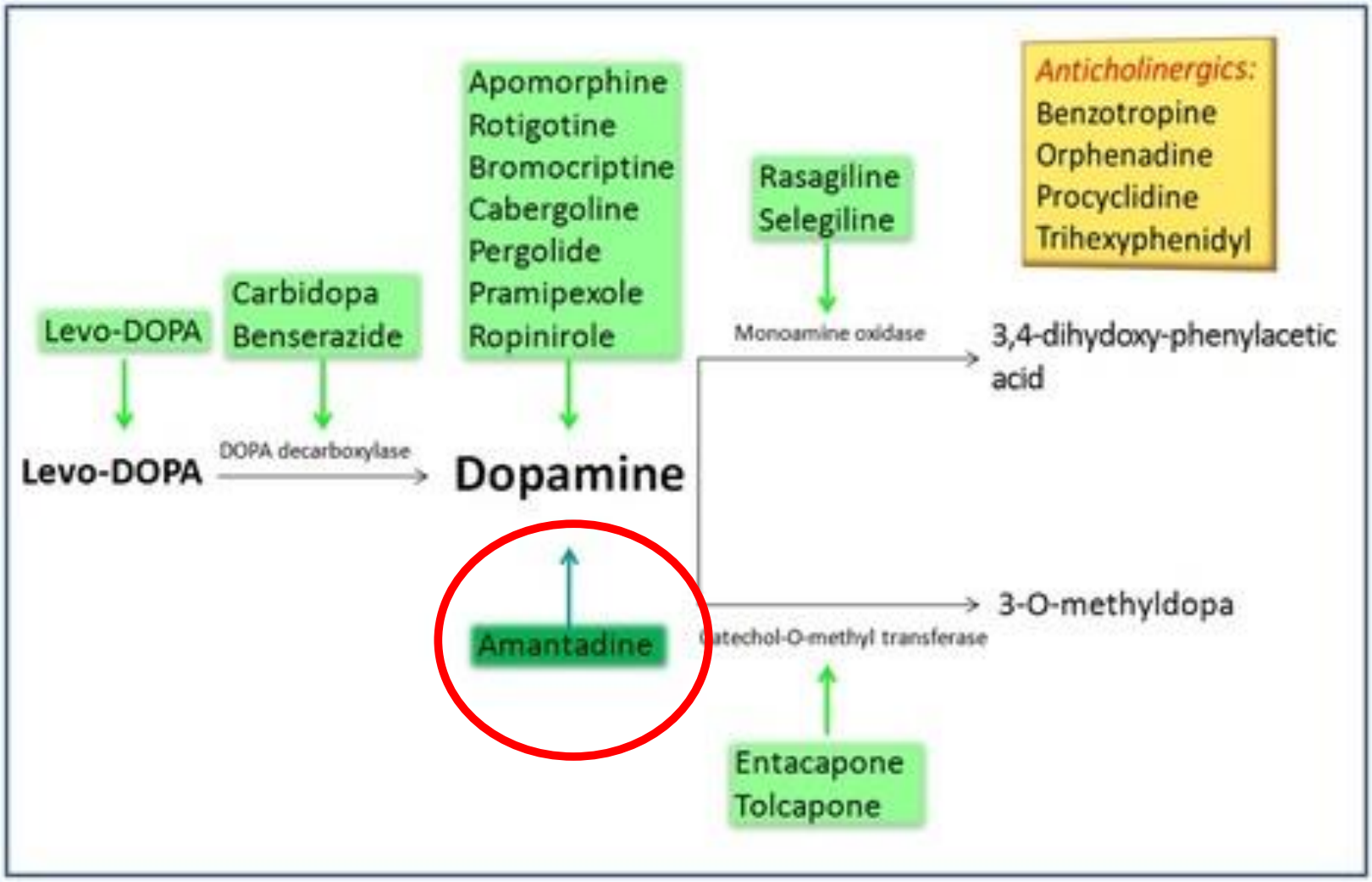
Dopamine Agonists Adverse Effects

- Nausea, orthostatic hypotension, somnolence, sleep attacks, hallucinations, delusions, LE swelling
- Impulse control disorders
  - Gambling
  - Excessive Eating
  - Hypersexual behaviors
  - Hobbying
  - Punding

Medications Used in Parkinson disease

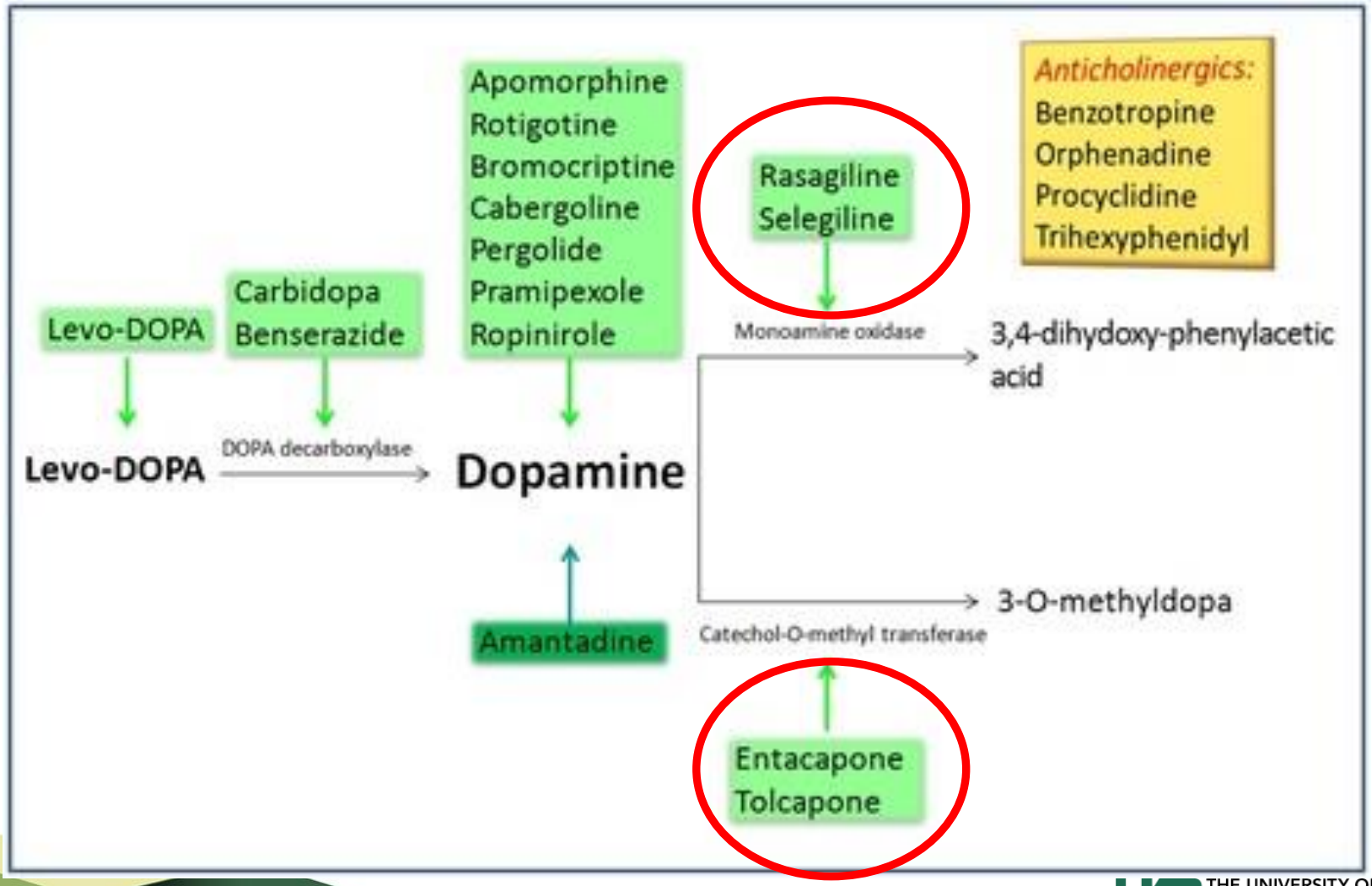


https://you.38degrees.org.uk/petitions/free-medication-for-people-with-parkinson-s

Amantadine

- Hallucinations
- Confusion/worsened memory
- Dry mouth and Dry Eyes
- Insomnia
  - (can also be a benefit and help lessen fatigue/drowsiness)

Medications Used in Parkinson disease



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COMT and MAO inhibitors

- Typically most beneficial as adjuncts
- Entacapone can cause diarrhea
- Rasagiline is $$$

In general, for patients with PD, when…

- Motor fluctuations in patients who are medication responsive
  - Early wearing off
  - Dyskinesias
- Severe tremor, unresponsive to medications
- Intolerable side effects from oral medications

Deep Brain Stimulation (DBS)

1997

Approved by the FDA for essential tremor

- Thalamus

2002

Approved by the FDA for Parkinson's disease and dystonia

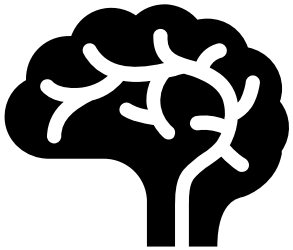
- Subthalamic nucleus
- Globus pallidus interna

Today

Over 150,000 people worldwide have received DBS for essential tremor, Parkinson's disease, dystonia, and obsessive-compulsive disorder.

How does DBS work?

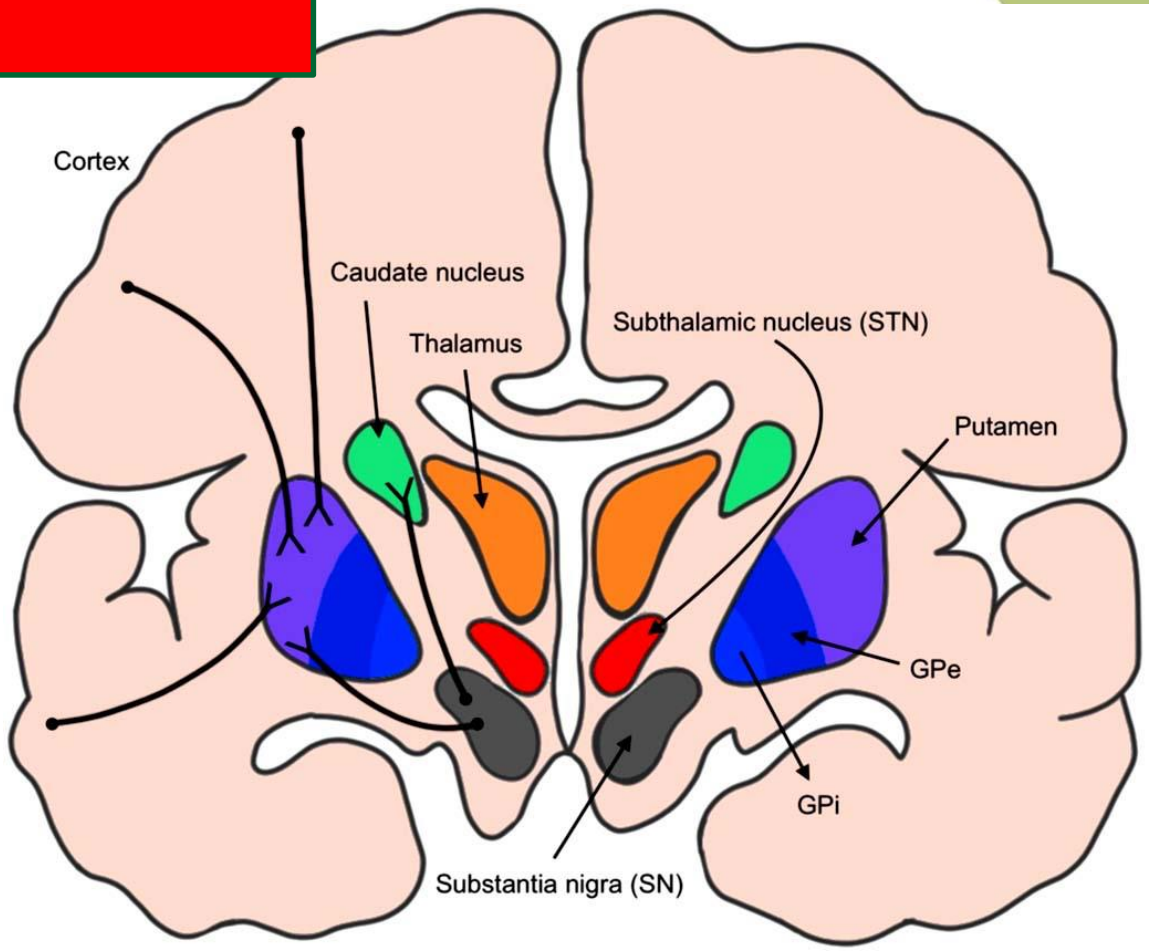
Nobody knows, for sure



Interference with an abnormal signal in the brain

Subthalamic nucleus

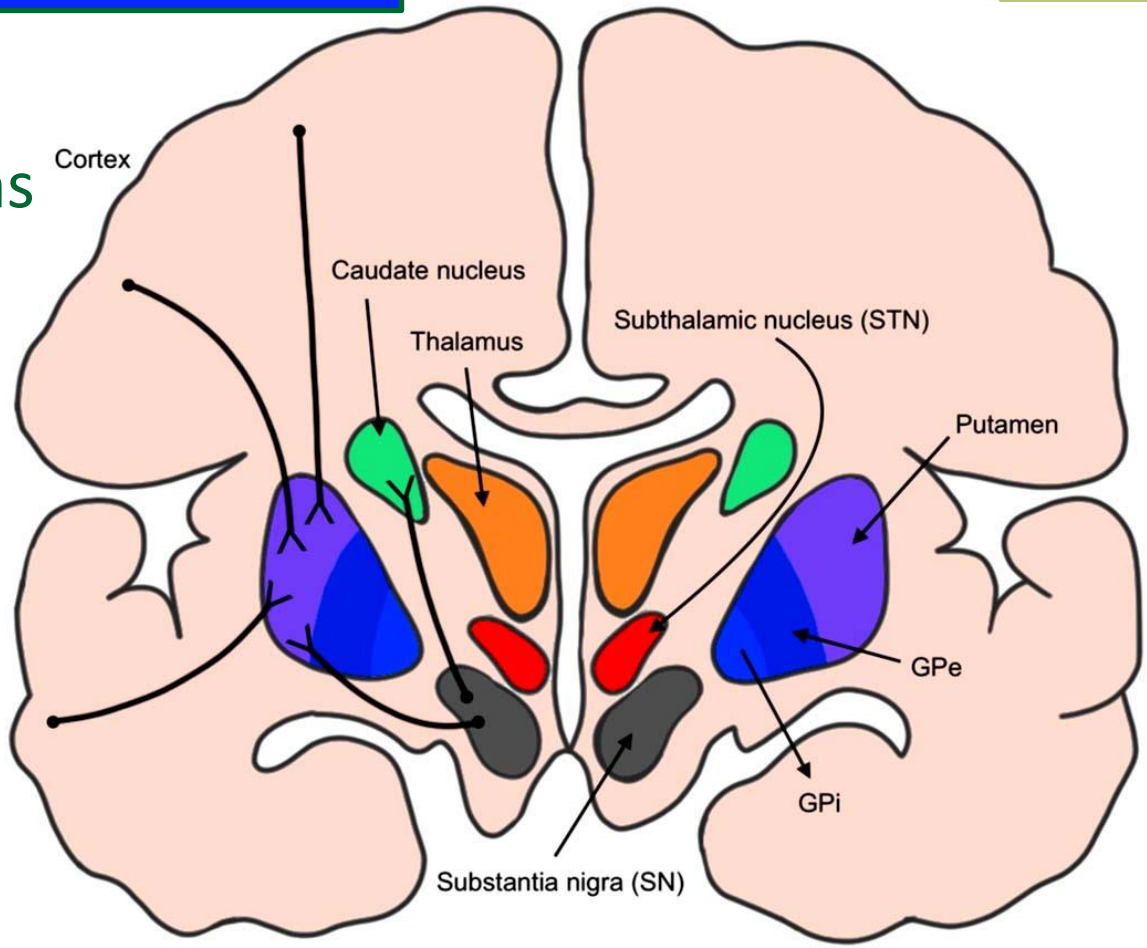
- Tremors
- Slowness
- Stiffness



https://www.bioscience.org/2018/v23/af/4586/figures.htm

Globus pallidus interna

- Classic motor symptoms
- Dystonia
- May block dyskinesias



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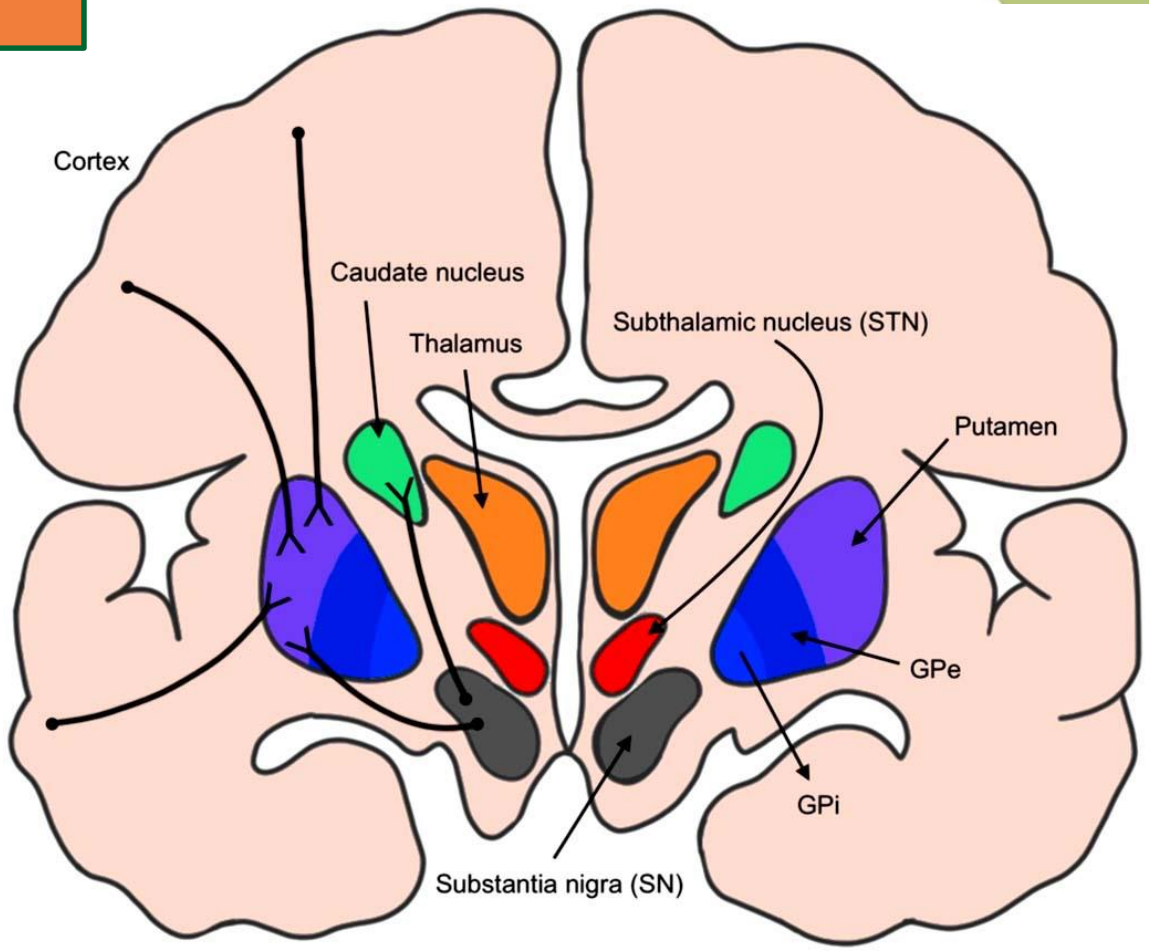
Thalamus-VIM

- Tremor



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How long does DBS work?

It is not a cure; it doesn't prevent progression of disease.

But, after ~20 years of implantation, research shows the device continues to help many symptoms of PD, especially tremor and dyskinesias.

Take Home Points

- Each person is unique
- Gait problems are common in advanced PD and the treatment requires some creativity
- Ask your patients a few basic questions to try to optimize their time at Physical Therapy
- Please feel free to get in touch with us, the medical providers, to discuss possible concerns!
- We love PT's! You guys are the miracle workers!

Questions?