Introduction to Movement Disorders

Ahmad Elkouzi, MD
Director, Parkinson's Disease Center
Assistant Professor Of Neurology
Neuroscience Institute
Southern Illinois University-SOM

Objectives

- Classify movement disorders
- Recognize main hyperkinetic and hypokinetic movement disorders
- Phenomenology of hyperkinetic and hypokinetic movement disorders
- Know the etiology of some diseases
- Know available options for treatment: medications and interventions

Movement

Too Little (Hypokinetic)

Just Right

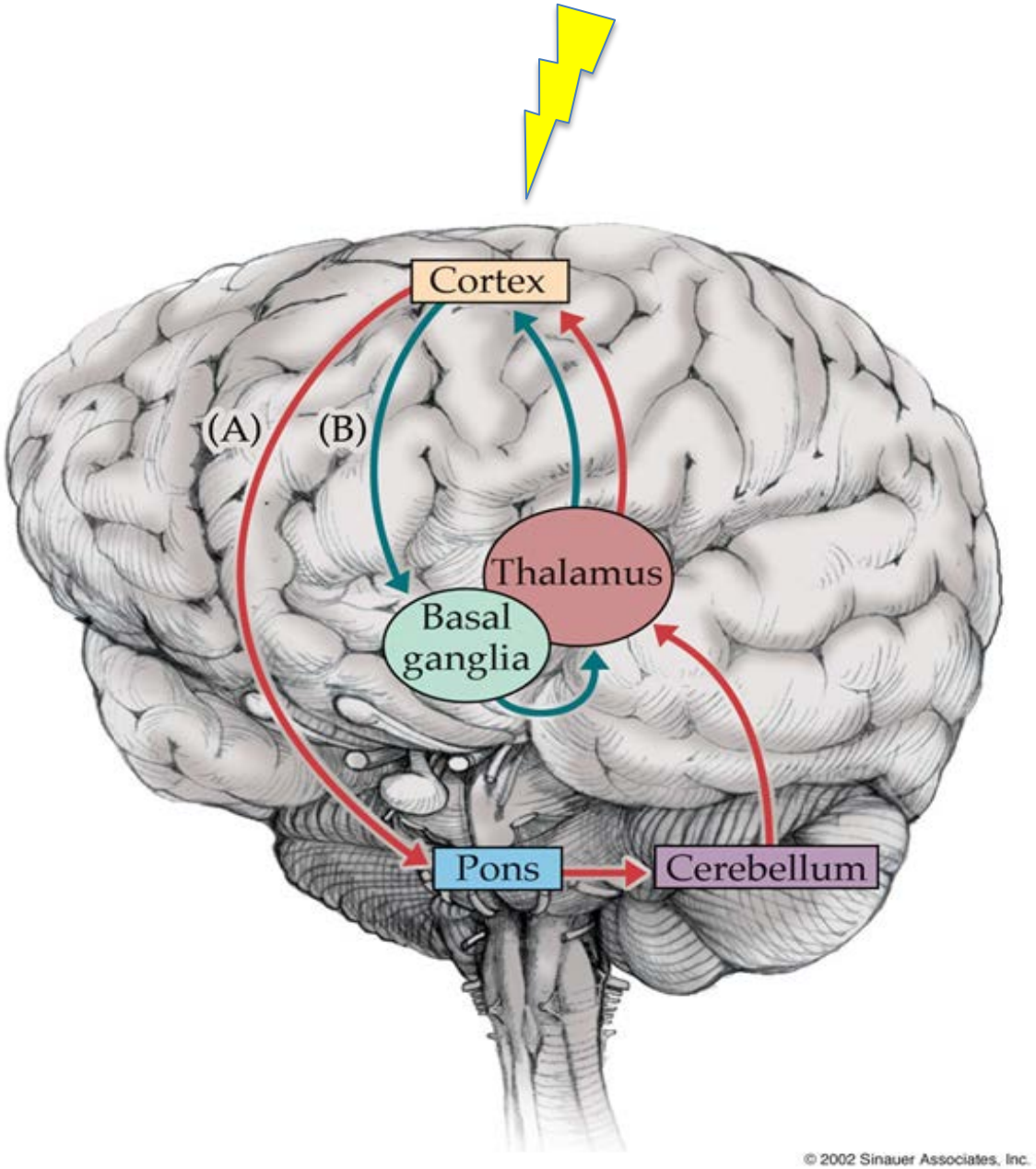
Too Much (Hyperkinetic)

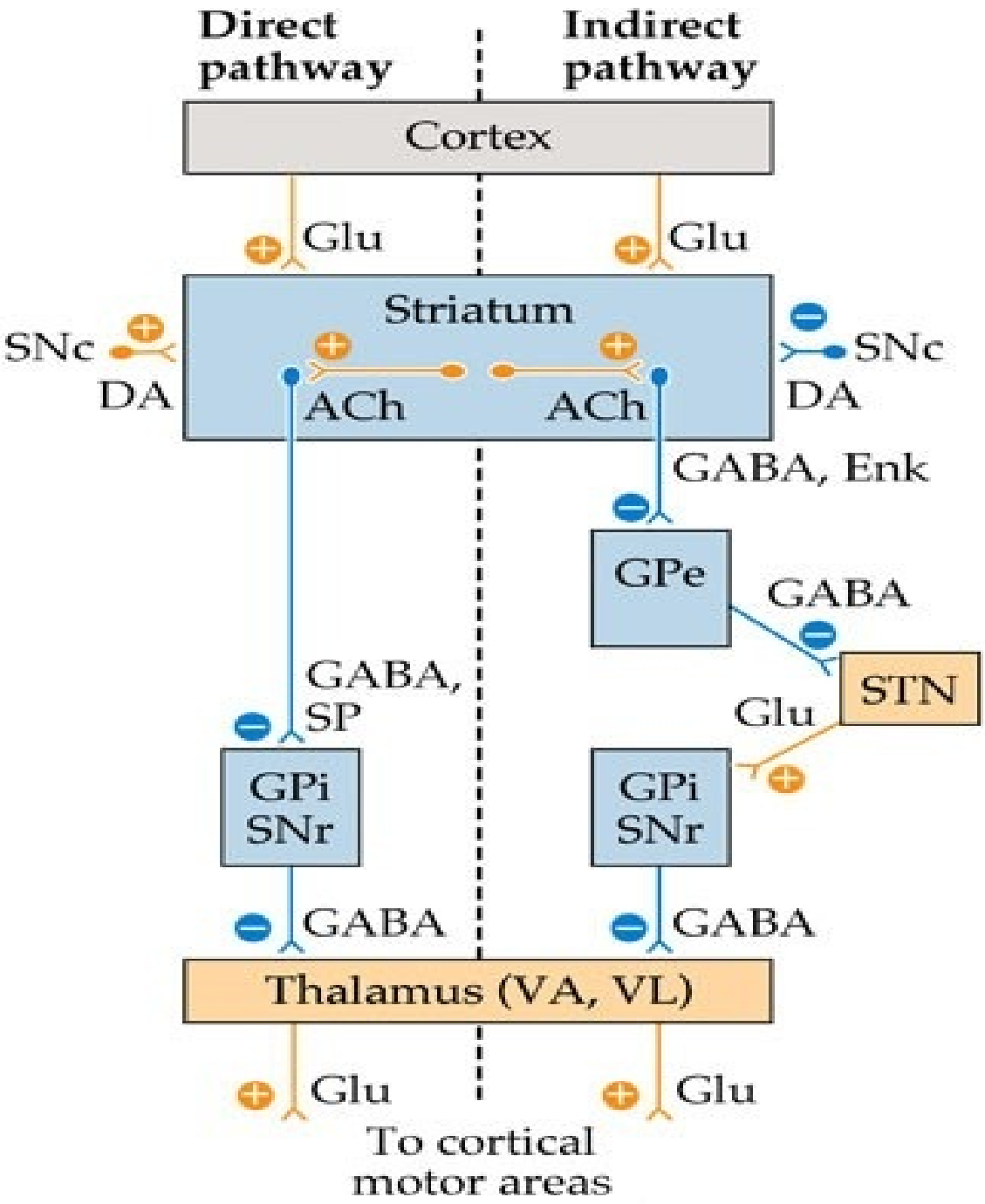
Courtesy of : C spears, MD

Classification

- Hypokinetic movement disorders:
  - Parkinson's disease
  - Atypical parkinsonism (PSP, MSA, LBD, CBD, etc..)

- Hyperkinetic movement disorders:
  - Tremors
  - Dystonia
  - Myoclonus
  - Chorea
  - Tics
  - Hemifacial spasm
  - Tardive dyskinesia
  - RLS

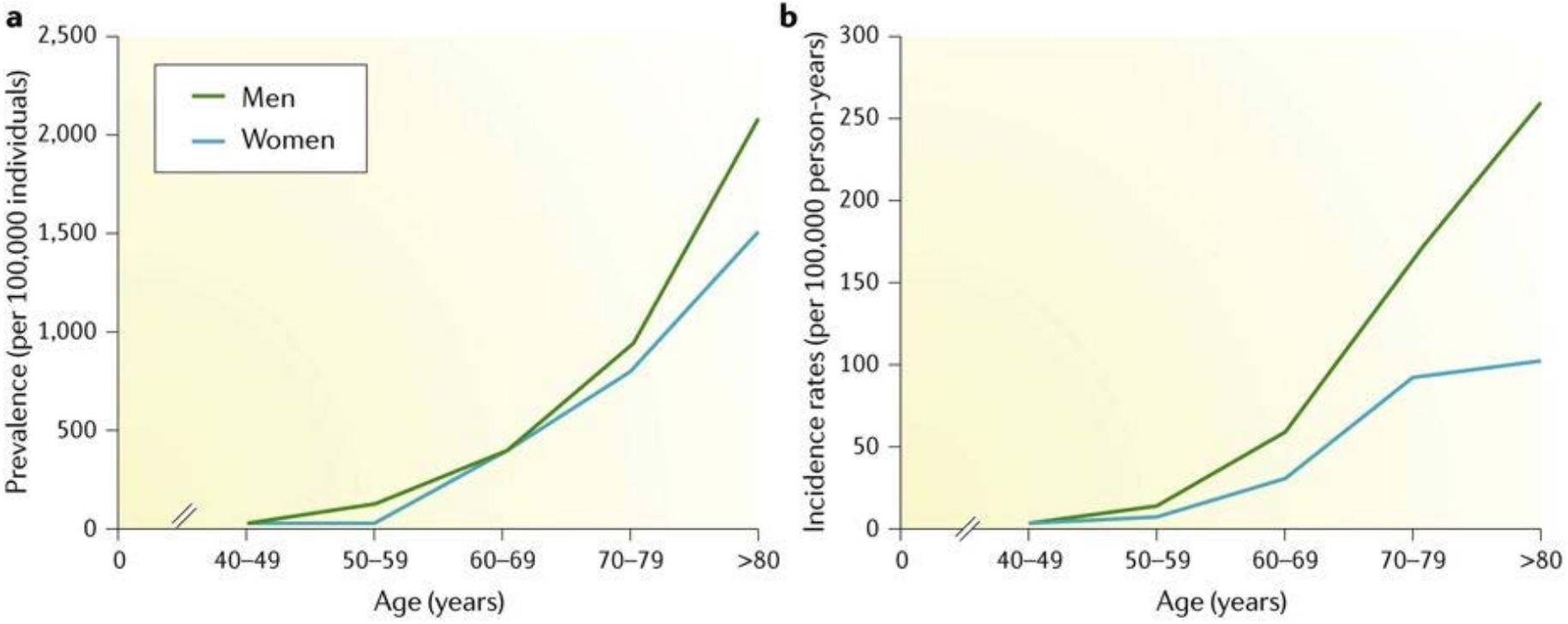



Direct pathway
Indirect pathway
Cortex
Glu
Glu
Striatum
SNc
DA
ACh
ACh
SNc
DA
GABA, Enk
GPe
GABA
STN
Glu
GABA, SP
GPi SNr
GPi SNr
GABA
GABA
Thalamus (VA, VL)
Glu
Glu
To cortical motor areas

Parkinson’s disease

Epidemiology

- Worldwide incidence estimates of Parkinson disease range from 5 to >35 new cases per 100,000 individuals yearly
- Parkinson disease is rare before 50 years of age, but the incidence increases 5–10-fold from the sixth to the ninth decade of life.
- The global prevalence, conservatively estimated at 0.3% overall, likewise increases sharply with age to >3% in those >80 years of age
- Mortality is not increased in the first decade after disease onset, but increases thereafter, eventually doubling compared with the general population.
- The number of people with Parkinson disease is expected to double between 2005 and 2030
- Parkinson disease is twice as common in men than in women in most populations, although in a few populations, including one study from Japan, no difference or even a female excess was observed.
- A protective effect of female sex hormones, a sex-associated genetic mechanism or sex-specific differences in exposure to environmental risk factors might explain this male preponderance, although disparities in health care could also contribute.



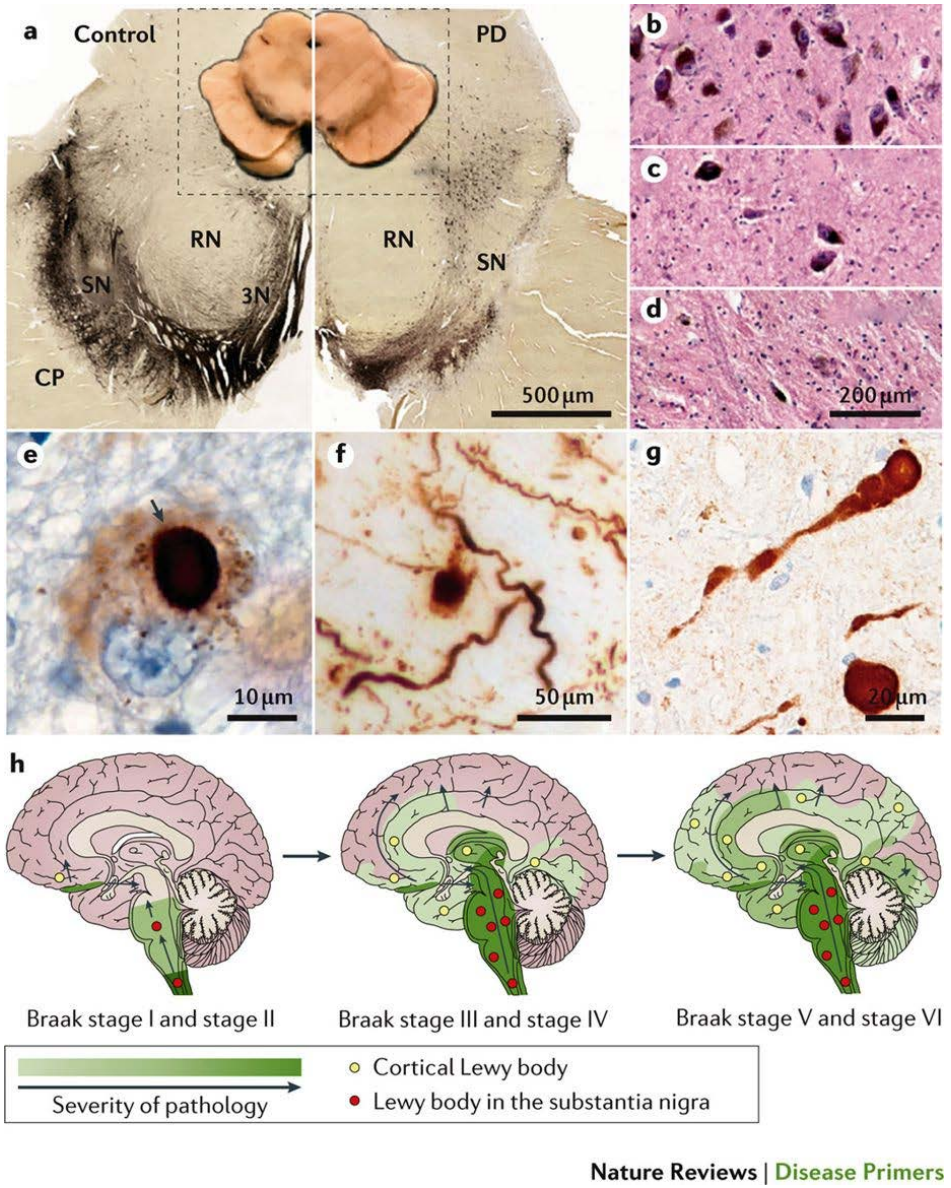
Nature Reviews | Disease Primers

Pathophysiology

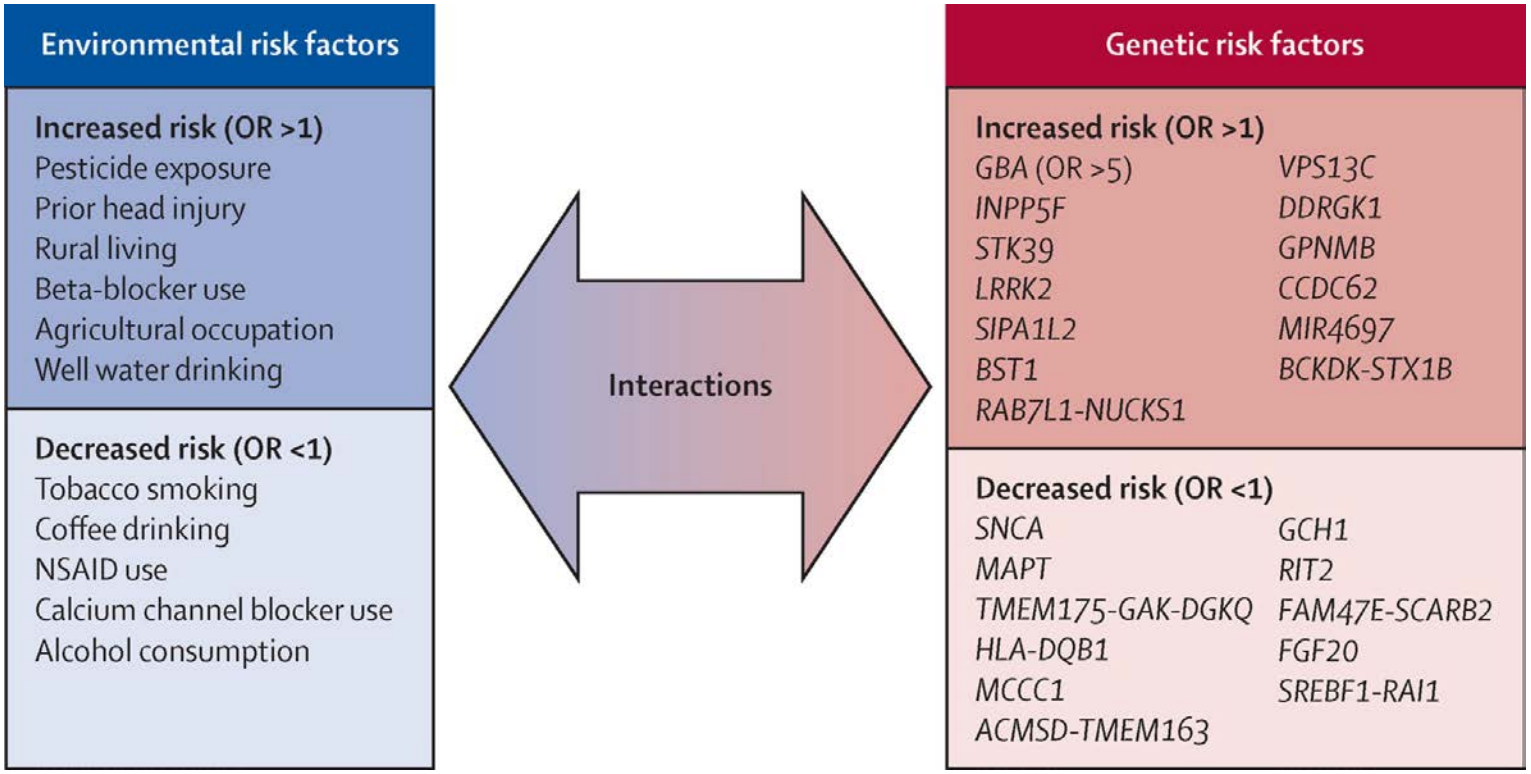
SN

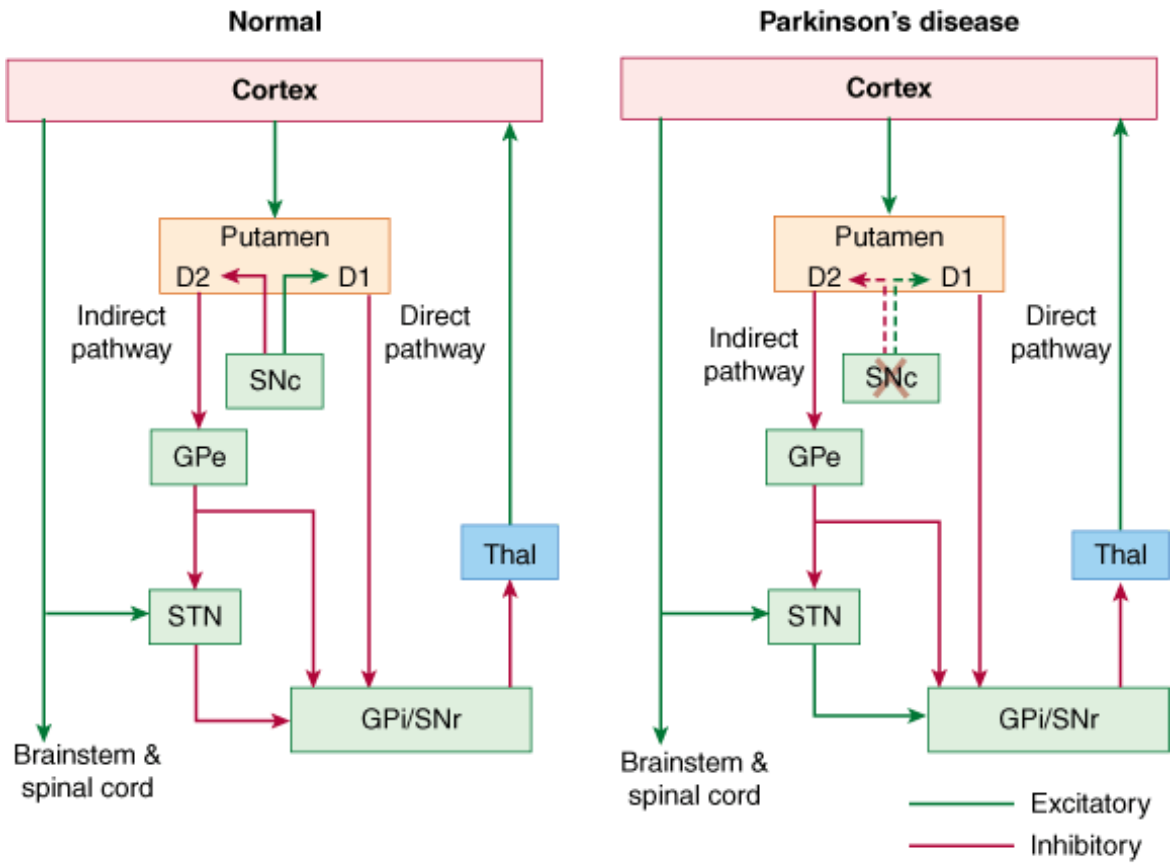
Lewy body

Braak staging



Parkinson's Disease





Source: Watts RL, Standaertt DG, Obeso JA: *Movement Disorders, 3rd Edition*: http://www.accessphysiotherapy.com

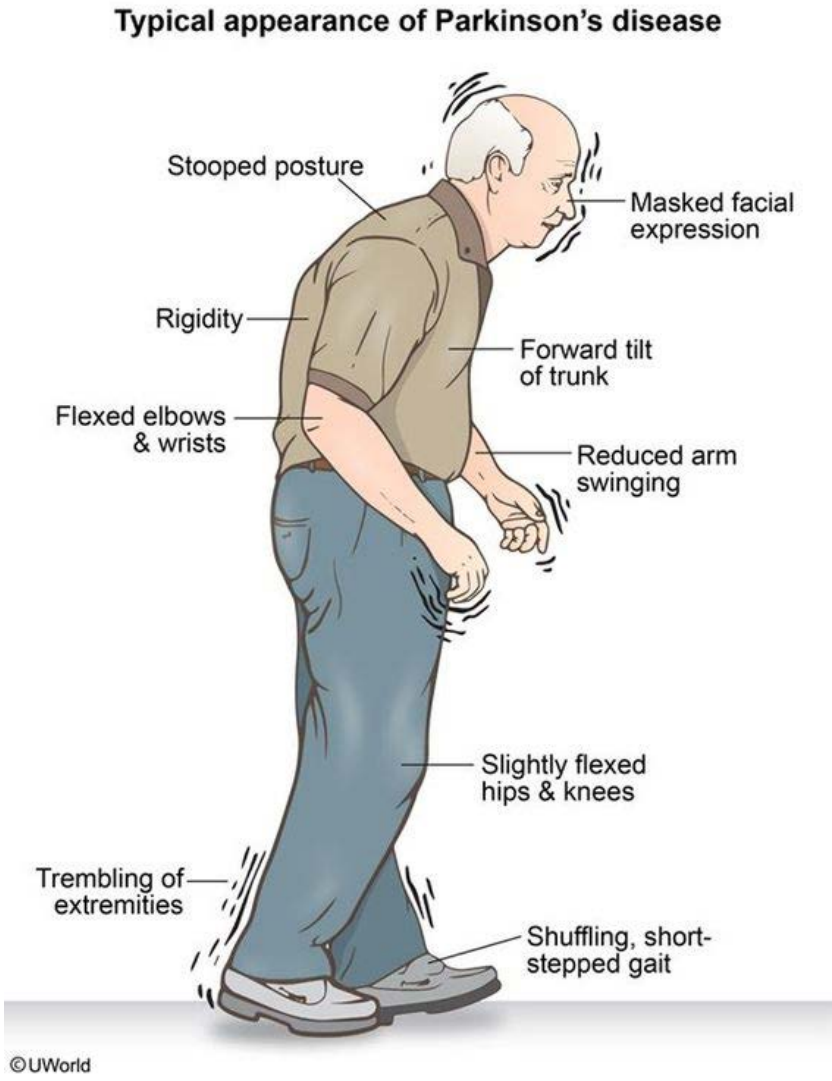
TRAP

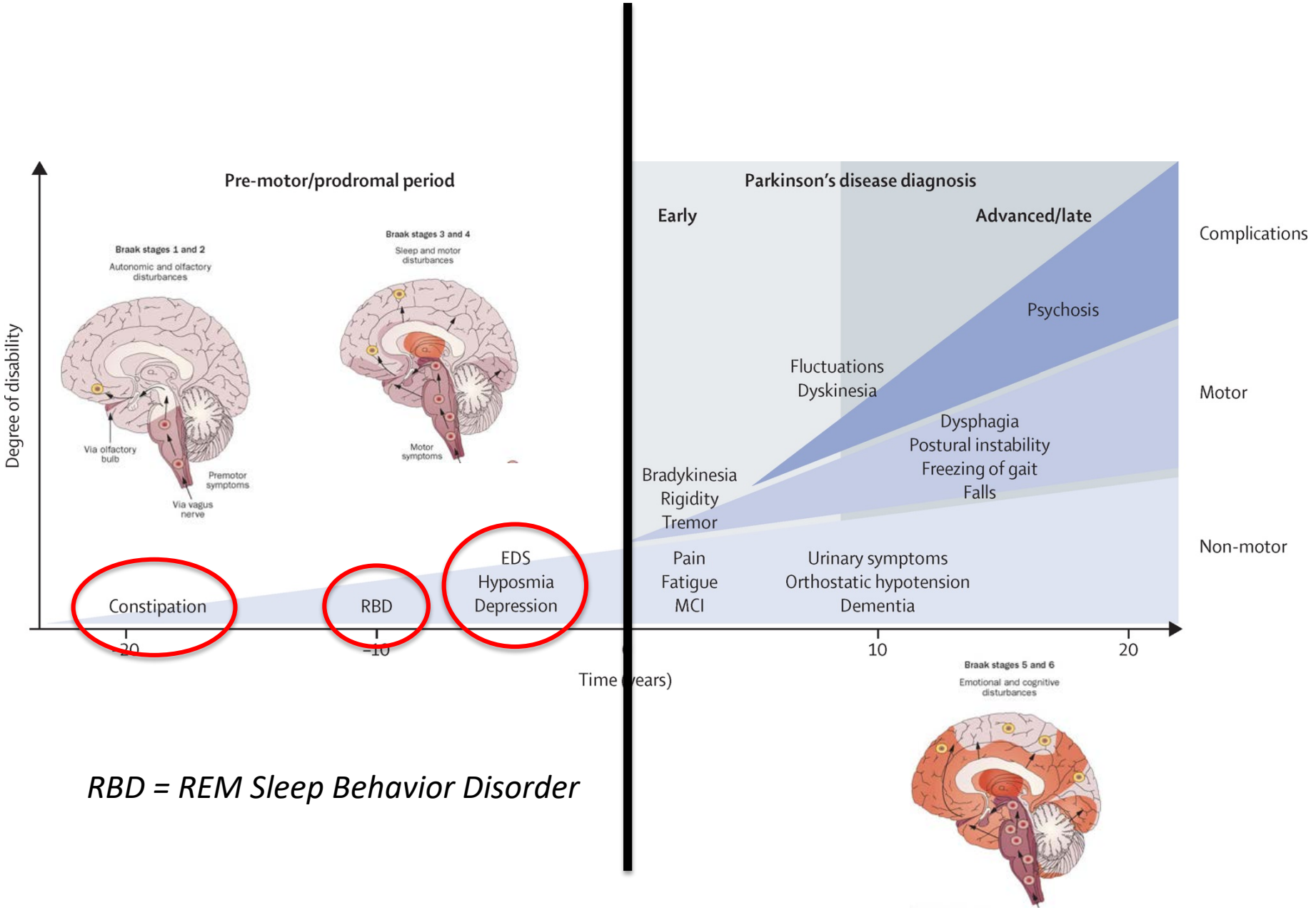
Tremor (4-6 hz resting)

Rigidity (cogwheeling & lead pipe)

Akinesia / Bradykinesia

Postural Instability





RBD = REM Sleep Behavior Disorder

Parkinson's Disease

- Diagnostic criteria

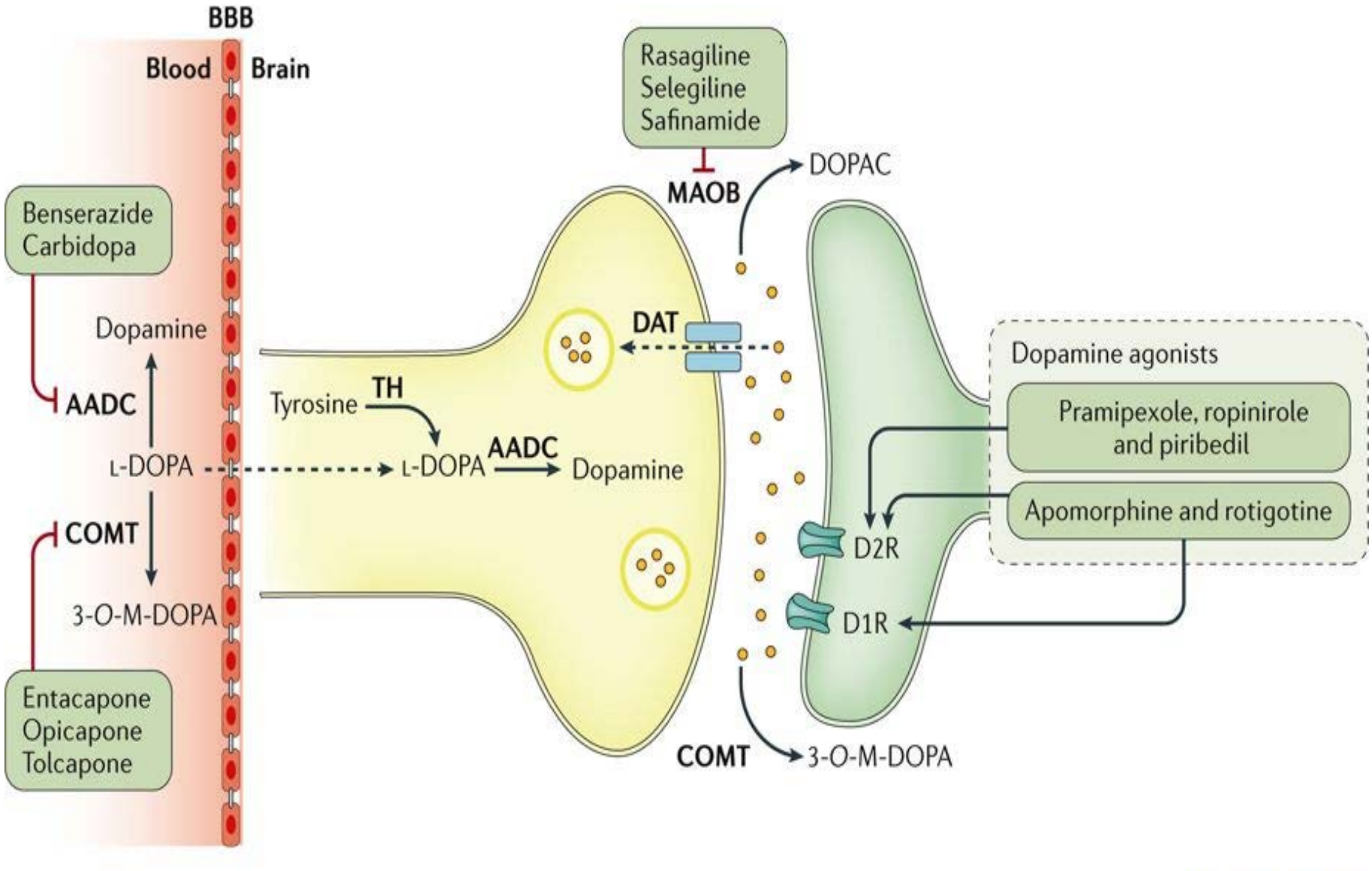
Bradykinesia

Plus ≥ 1 of the following

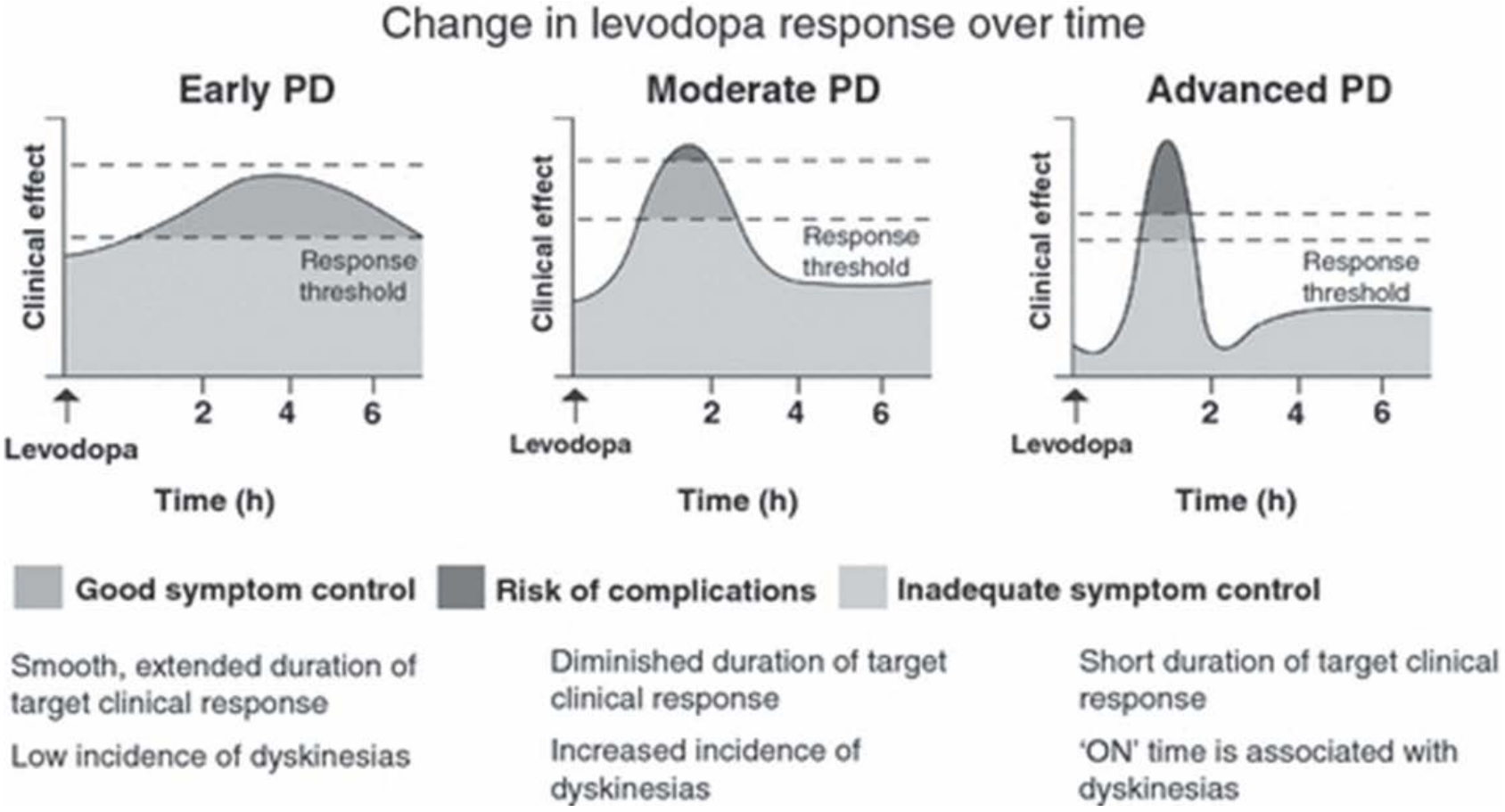
Resting tremor (4-6hz)

Rigidity

Postural instability



Nature Reviews | Disease Primers


Change in levodopa response over time
Early PD
Moderate PD
Advanced PD
Clinical effect
Response threshold
Levodopa
2
4
6
Time (h)
Good symptom control
Risk of complications
Inadequate symptom control
Smooth, extended duration of target clinical response
Low incidence of dyskinesias
Diminished duration of target clinical response
Increased incidence of dyskinesias
Short duration of target clinical response
'ON' time is associated with dyskinesias

Duopa

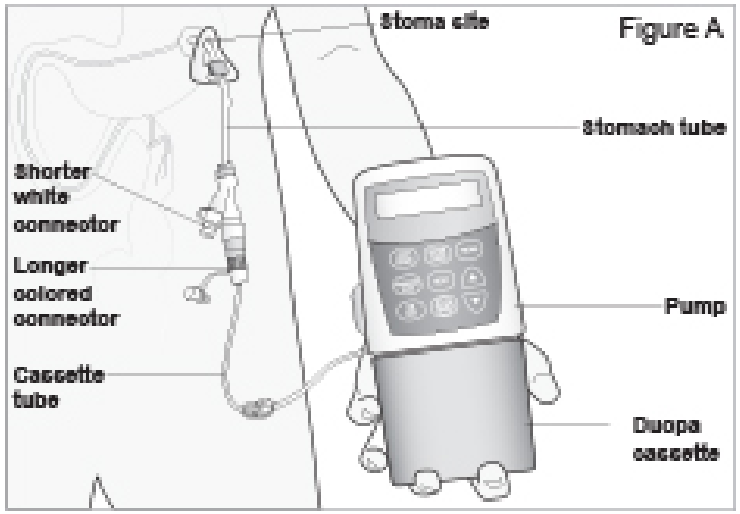
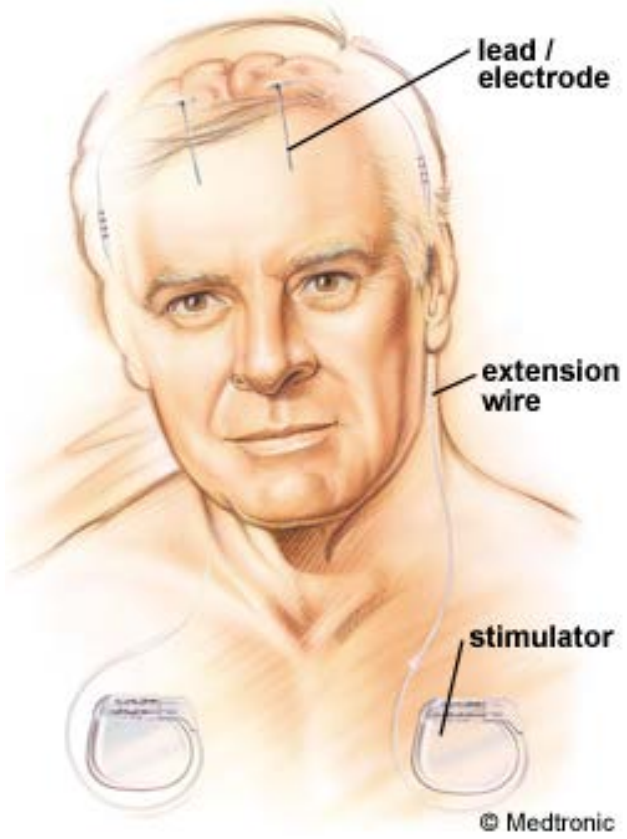


Figure A
Stoma site
Stomach tube
Shorter white connector
Longer colored connector
Cassette tube
Pump
Duopa cassette

DBS


lead / electrode
extension wire
stimulator
© Medtronic

Atypical Parkinsonism

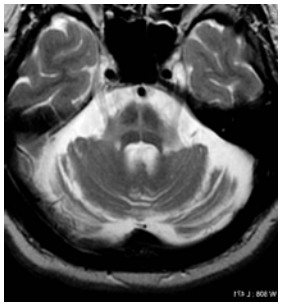
Red flags

- Early cognitive impairment
- Early falls
- Early freezing of gait
- Early swallowing difficulties
- Axial rigidity
- Autonomic dysfunction
- Poor levodopa response
- Rapid progression and worse prognosis
- Sleep problems

DLB (Dementia of Lewy Body)

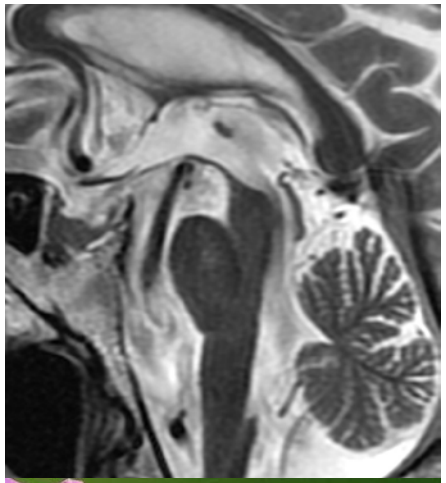
- Cognitive impairment prominent (They have to be demented)
- Fluctuations in cognitive status (unpredictable changes in attention, thinking and alertness)
- Parkinsonism
- RBD
- Visual hallucinations
- Be careful with medications

MSA (Multiple System atrophy)

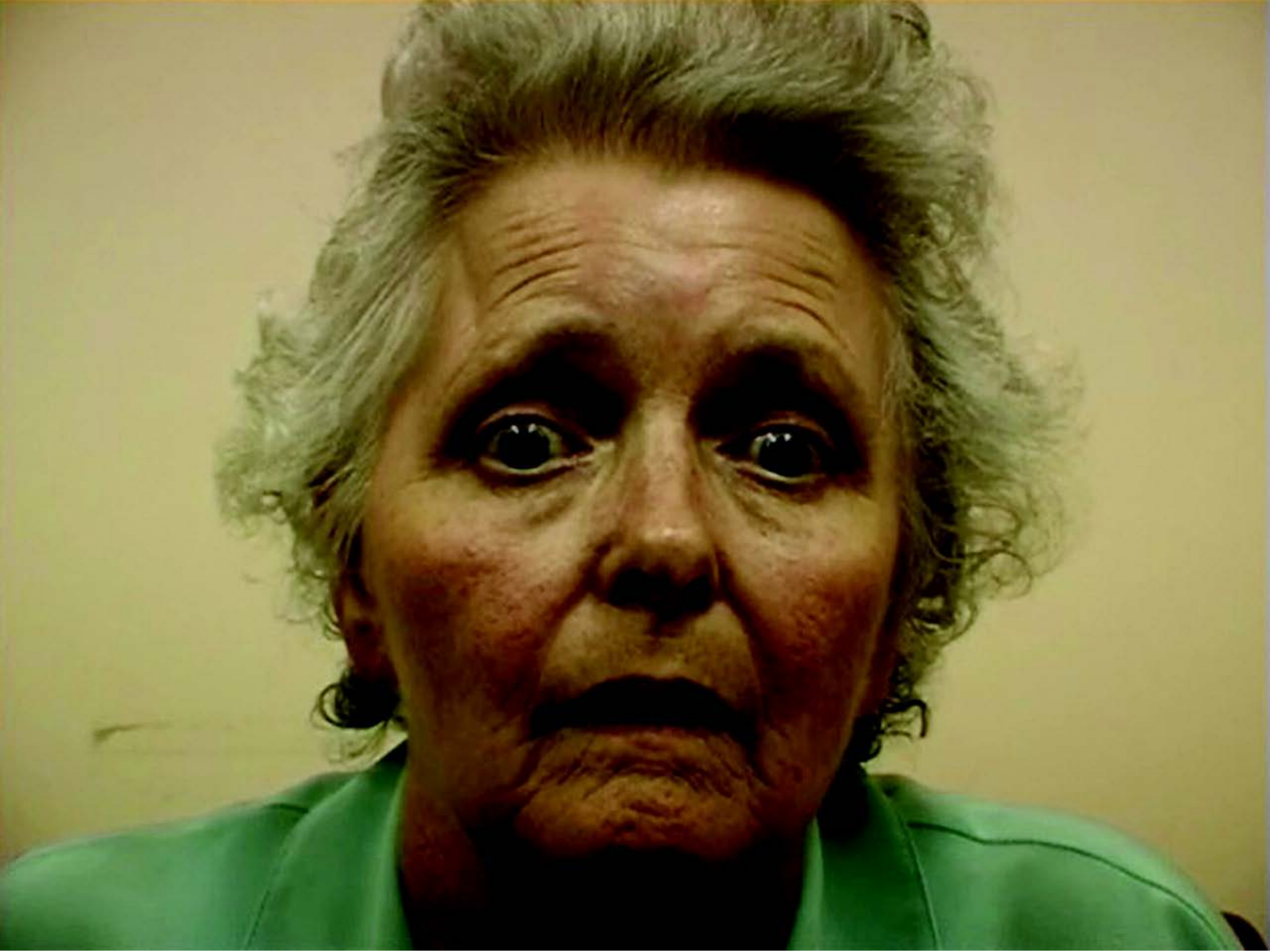


- MSA-C (or OPC atrophy) and MSA-P (or striatonogral degeneration)
- Synucleinopathy (glial rather than neuronal)
- Autonomic dysfunction (orthostatic hypotension, urinary incontinence, sweating problems, erectile dysfunction in men etc..)
- Swallowing difficulties
- Speech problems
- Falls
- Anterocollis
- Cognition remains intact
- Sleep problems (RBD, stridor and even death during sleep, prescribe a CPAP)
- Poor levodopa response(sometimes there are responders)

PSP (Progressive supranuclear palsy)



- This is a tauopathy
- Many phenotypes with variable prognosis depending on the phenotype : classic (Richardson-Steele(PSP-RS), Parkinsonism (PSP-P), cerebellar (PSP-C), akinesia with gait freezing (PSP-PAGF) etc..)
- Oculomotor abnormalities (test saccades)
- Prognosis depends on phenotype and disease duration ranges from 5-7 years (RS) to 20 years (PAGF)
- Early falls and freezing
- A lot of axial rigidity
- Retrocollis
- Vision problems
- Dysphagia
- Poor levodopa response except for PSP-P at higher doses



Tremor

Tremor

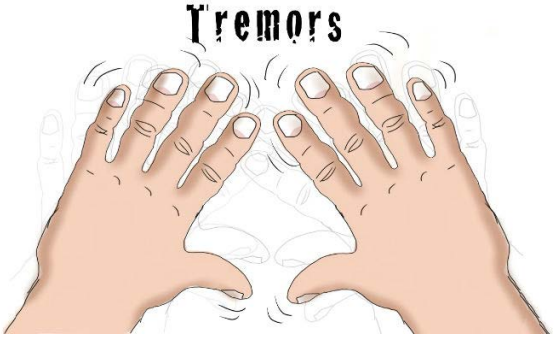
- A rhythmic, oscillation of a body part.
- Classified by *frequency*
- Classified by *presence in* **ACTION** (Postural, Kinetic) vs **REST** vs **TASK SPECIFIC**

Parkinsonian Tremor = 4-6 hz
Essential Tremor = 4-10 hz
Enhanced Physiologic = 8-12 hz

ACTION	REST	TASK SPECIFIC
• Essential Tremor • Physiologic	• Parkinson's Disease	• Primary Writing Tremor

Essential Tremor

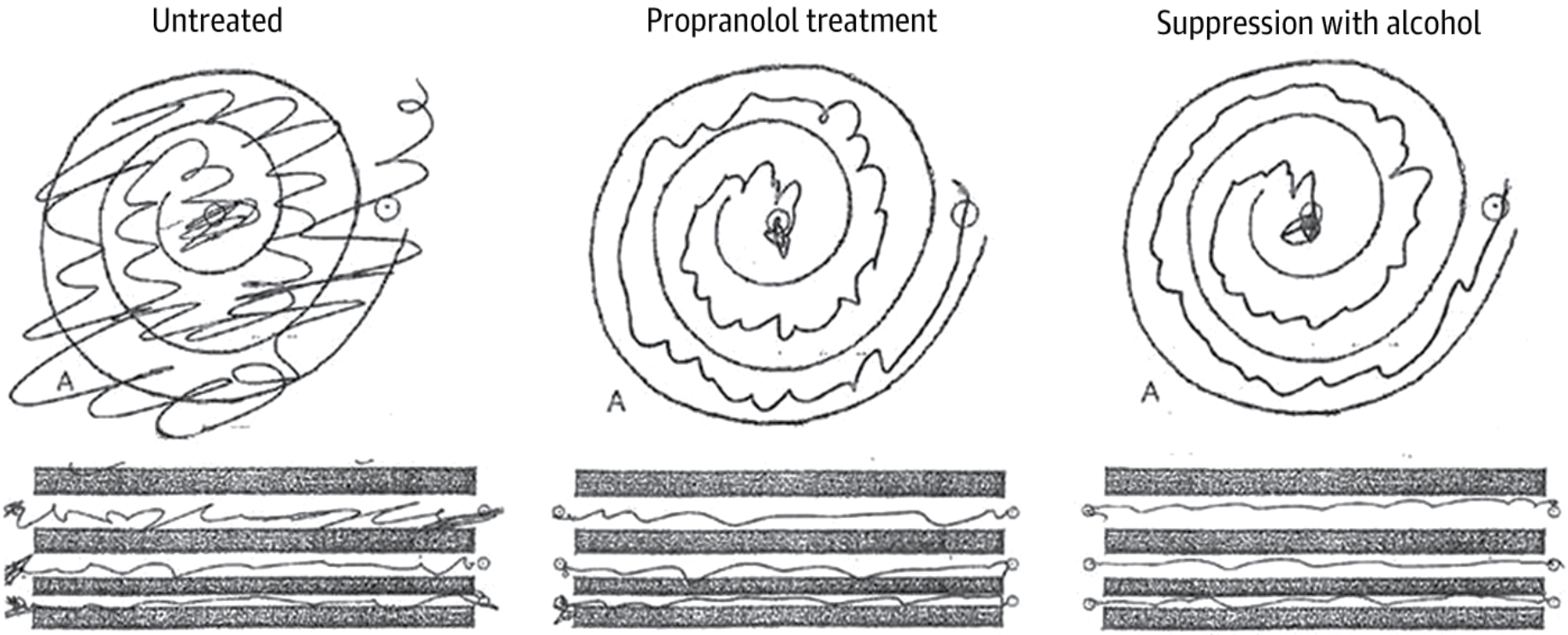
- Bimodal age range – 40yo or less | 60yo or more
- Frequency **4-10 hz**
- Most often symmetric and in the arms
- **Action** tremor (postural and kinetic)
- Approx 50% will have a family history of tremor
- Tends to improve with etoh.. But not always



Treatment

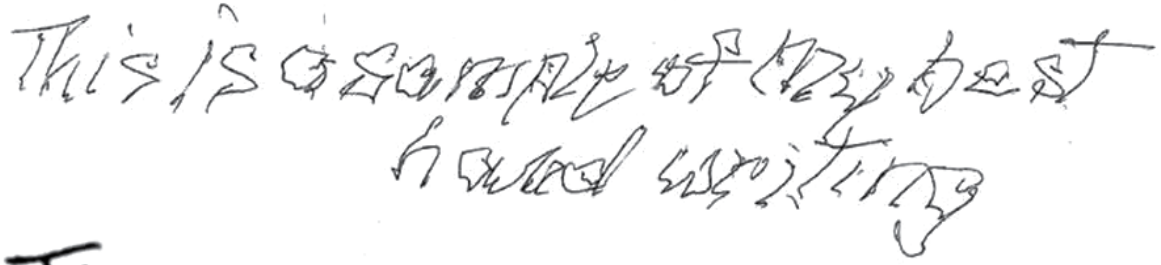
1st line – Propranolol (Inderal) vs Primidone (Mysoline)
2nd line – Combo therapy; Gabapentin (Neurontin), Topirimate (Topamax)
3rd line – Deep Brain Surgery

A Spiral and line drawings by patient with essential tremor (case 1)



B Handwriting samples from case patients

Patient with essential tremor (case 1)



Patient with Parkinson disease (case 2)

Table 1. Distinguishing Features Between Essential Tremor and Parkinson Disease Tremor

Clinical Evaluation	Essential Tremor	Parkinson Disease
History		
Age of onset	Bimodal (adolescence or early adulthood or age ≥65 y)	Incidence increases with age, particularly age ≥60 y
Family history	Common	Rare
Response to alcohol	Common	Never
Tremor assessment		
Phase of movement	Postural and kinetic plus resting if severe; quiesces when walking	Resting; reemerges after sustained posture, prominent when walking
Distribution	Head and voice	Mouth, tongue, and legs
Frequency, Hz	7-12	4-6
Neurological examination		
Handwriting	Sloppy with large, rhythmic strokes	Micrographic, decremental (decreasing size of movements)
Face	Normal expression	Reduced eye blink, masked facies, blunted emotional expression
Voice	Vocal tremor	Hypophonia
Gait	Normal	Stooped posture, shortened stride length and step height, reduced asymmetrical arm swing

Enhanced Physiologic Tremor

- Occurs at any age
- High frequency – **<u>8-14 hz</u>**
- Low amplitude
- Brought on by:
  - Medications (next slide)
  - Drugs (etoh, cocaine, caffiene)
  - Metabolic Disease (hypoglycemia, hyperthyroidism)
  - Stress, Anxiety, Sympathomimetics
  - Insomnia

Drug-induced Tremor

Drugs and Medications

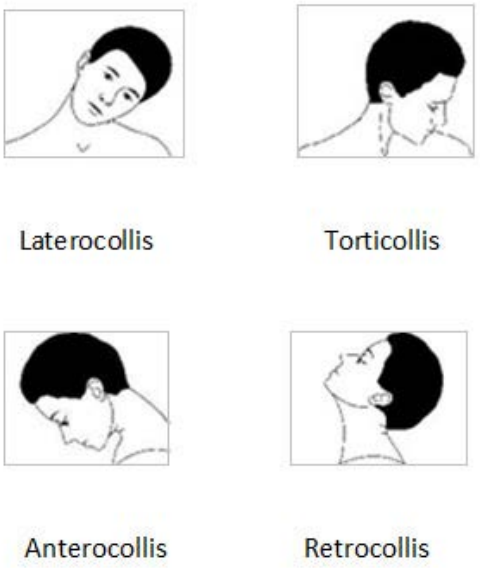
- Neuroleptics
- Metoclopramide (Reglan)
- Antidepressants (esp TCA or serotonergics)
- Lithium
- Cocaine
- EtOH (withdrawal)
- Bronchodilators (albuterol..)
- Caffiene
- Steroids
- Cyclosporine
- Valproic Acid
- Amiodarone
- Procainamide
- Levothyroxine (synthroid)
- Chemo

Dystonia

Dystonia

- Dystonia is an involuntary muscle contraction that causes slow repetitive movements or abnormal postures
- May have a geste antagoniste (sensory trick)
- Classified best *by distribution*: Focal / Segmental / Multifocal / Generalized

*Earlier onset tend to have a genetic mutations.. Ex. DYT 1



Common postures involved in cervical dystonia

According to 1 study of 300 patients[1]:

82% of patients

Torticollis
(rotated)

42% of patients

Laterocollis
(to the side)

25% of patients

Anterocollis
(forward)

29% of patients

Retrocollis
(backward)

66% of cervical dystonia patients present with a combination of postures[1]

Treatment

Medications	Botulinum toxins	DBS
• Anticholinergics • Dopamine (in specific cases) • Benzodiazepines	• Onabotulinum toxin (Botox) • Incobotulinum toxin (Xeomin)	• Target is usually GPI

Myoclonus

Myoclonus

- sudden, involuntary jerking of a muscle or group of muscles. Myoclonic twitches or jerks usually are caused by sudden muscle contractions, called positive myoclonus, or by muscle relaxation, called negative myoclonus (e.g Asterixis)
- Approx 75% is 'symptomatic' or secondary to medical illness (infections, organ failure, prolonged hypoxia) or Rx
- Classified *by presence at* **REST** or with **ACTION**
- Classified *by distribution:* Focal / Segmental / Multifocal / Generalized

Treatment

- Treat underlying cause:
- Medication adjustment
- Improve organ function (Lung, liver, kidney etc..)
- Use benzodiazepines or antiepileptics if needed

Tics

Tics

- Sudden, repetitive, non-rhythmic motor movement or vocalization.
- Maybe accompanied by an urge
- Semivoluntary, maybe Suppressible
- Copralalia (shouting obscenities) not often seen

	SIMPLE	COMPLEX
MOTOR	Blink Grimace Head jerk Shrug	Spitting Jumping Kicking Pelvic thrusting
VOCAL/ PHONIC	Throat clearing Cough Sniff Grunt	Belching Echolalia Palilalia Coprolalia

Tourette Syndrome

1) BOTH motor and phonic tics present
2) Occur many times a day or nearly everyday for 1 year +
3) Tics evolve over time
4) Onset before age 18
5) Unexplained otherwise

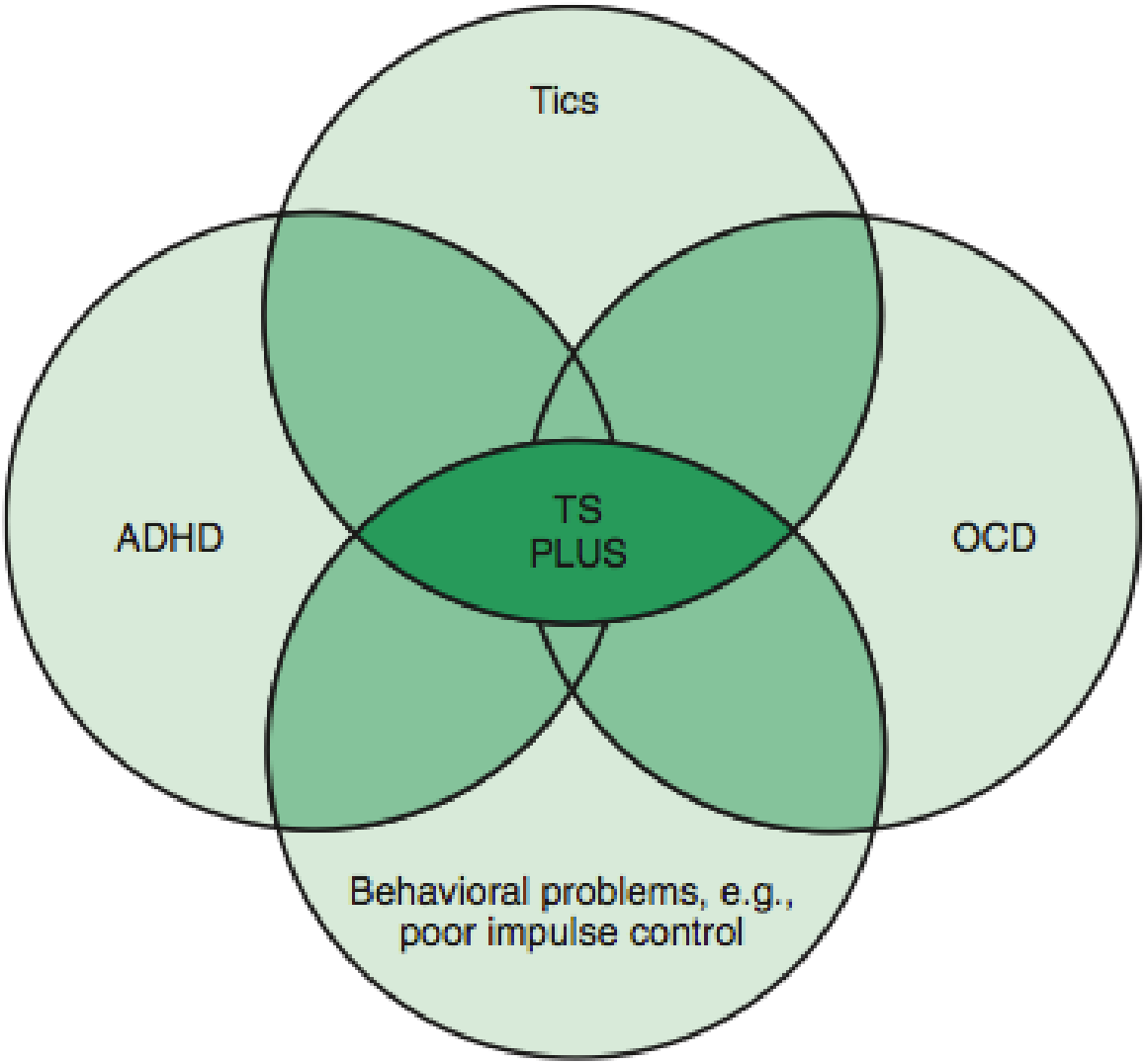


Figure 16.1 An overlap of disorders typically coexisting in patients with TS.
Redrawn from Jankovic J: Tourette's syndrome. N Engl J Med 2001;345:1184–1192.

Chorea

Chorea

(dance)

- Involuntary, irregular, purposeless, non-rhythmic and non-sustained movements that seem to flow from one body part to another.
- *athetosis, aka slower, more distal chorea*
- *ballism, is a larger amplitude, proximal flinging chorea movement.*

Table 15.2 Differential diagnosis of inherited and sporadic choreas

Inherited disorders

- HD
- HDL1, HDL2, HDL3
- DRPLA
- Neuroacanthocytosis
- SCA2, 3, 17
- NBIA
  - Pantothenate kinase associated neuodegeneration (PKAN), neuroferritinopathy, aceruloplasminemia, infantile neuroaxonal dystrophy
- Benign hereditary chorea
- Wilson disease
- Mitochondrial disorders
- Ataxia with oculomotor apraxia (types 1 and 2)
- Ataxia telangiectasia

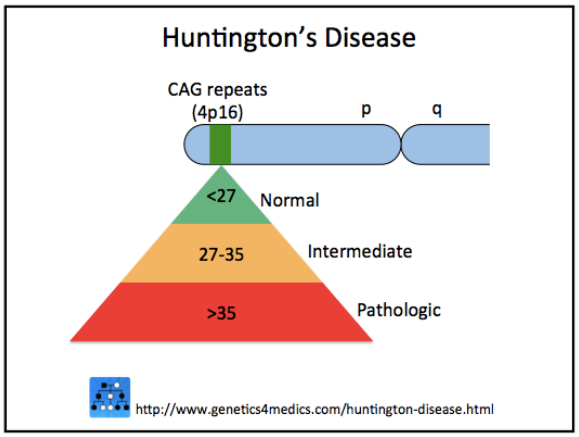
Sporadic disorders

- Static encephalopathy (CP)
- Essential (senile) chorea
- Sydenham chorea
- Vascular chorea
- Polycythemia vera
- Sporadic Creutzfeldt–Jakob disease
- Systemic lupus erythematosus
- Antiphospholipid syndrome
- Hyperthyroidism
- AIDS
- Tardive dyskinesia
- Metabolic encephalopathy
  - Hepatolenticular degeneration
  - Nonketotic hyperglycemia
  - Hypoglycemia
  - Renal failure
  - Ketogenic diet

Huntington's Disease

Huntington's Disease

- Autosomal Dominant, CAG repeat disorder
- Age of onset varies based on # of CAG repeats
- Symptoms include:
  - Chorea
  - Bradykinesia
  - Dystonia
  - Swallowing difficulties, Dysarthria
  - Dementia
  - Psychiatric disease (depression, hallucinations, suicidality***)



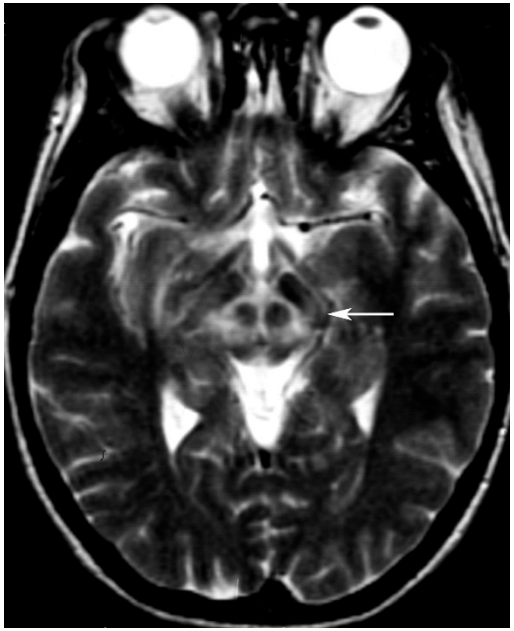
3 M's : Movement | Memory | Mania

Wilson’s Disease

Wilson's Disease

- Autosomal Recessive, often starts in teens or 20s
- Disorder of copper transport → deposition in tissues (liver, brain)
- Symptoms include:
  - Chorea
  - Tremor
  - Dystonia
  - Parkinsonism
  - Dysarthria

  Mixed
- Panda Sign on MRI



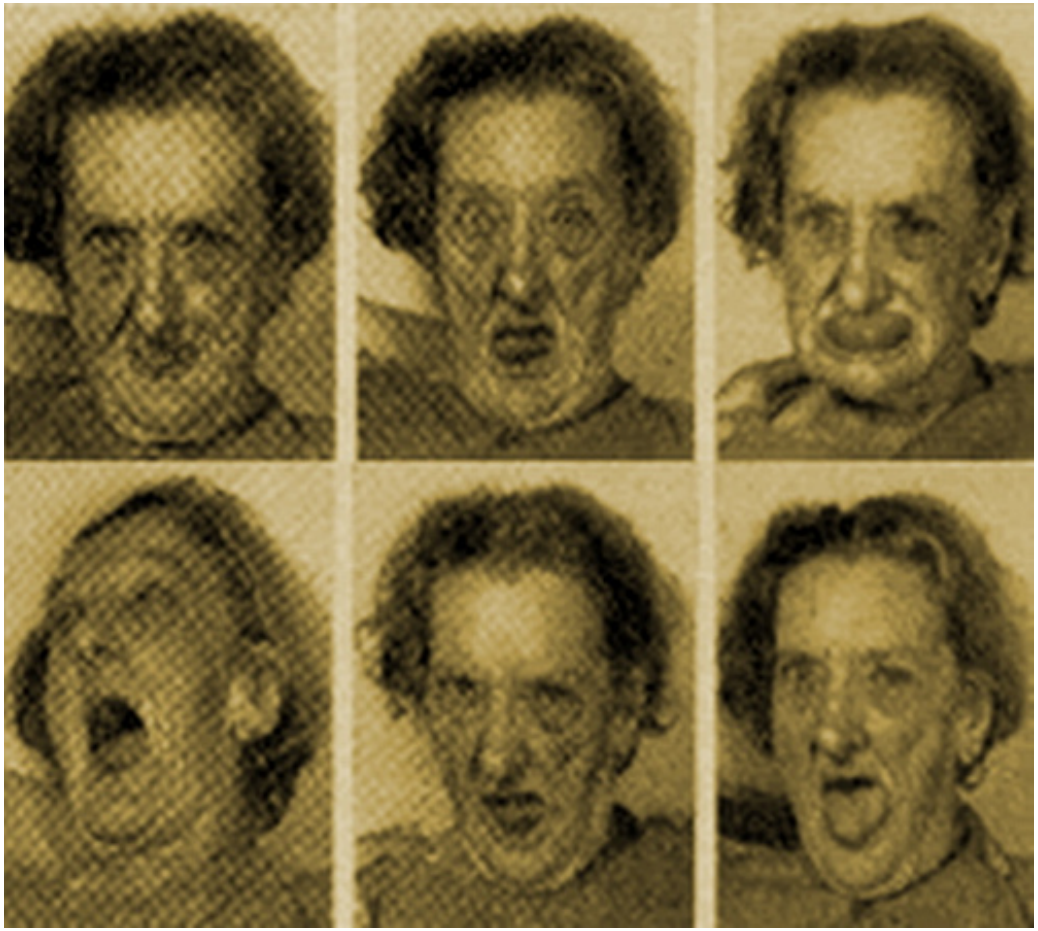
Diagnosis: Ceruloplasim, 24hr Urine Cu

Treatment: Zinc, Penicillamine

Tardive Symptoms

Tardive Dyskinesia

(Tardive = late or after)



Tardive Dyskinesia

- Involuntary movements, often induced by medication (*dopamine blockers*)
- Faster than dystonia, not as flowing as chorea.
- Most commonly involves mouth (*lip smacking*) and neck (*retrocollis*).
- Treatment may be challenging without full reversal.
- Offending agents:
  - Typical > Atypical Antipsychotics
  - Metaclopramide (reglan), Prochlorperazine (Compazine), Promethazine (Phenergan)

Restless Legs Syndrome

Restless Legs Syndrome

1) Urge to move legs +/- accompanying unpleasant sensation
2) Occurs or worsens during rest or inactivity
3) Partially or totally relieved by movement
4) Evening-Night > Day

Evaluation: PSG, Iron Studies (*replete!*)
Treatment:

- First line – Pramipexole (Mirapex), Ropinerole (Requip)
- Second line – Gabepentin (Neurontin), Pregabalin (Lyrica)
- Third line – Opiates [tramadol, methadone]

Interested in observing at the Movement Center?

Shuri.Pass@neurology.ufl.edu