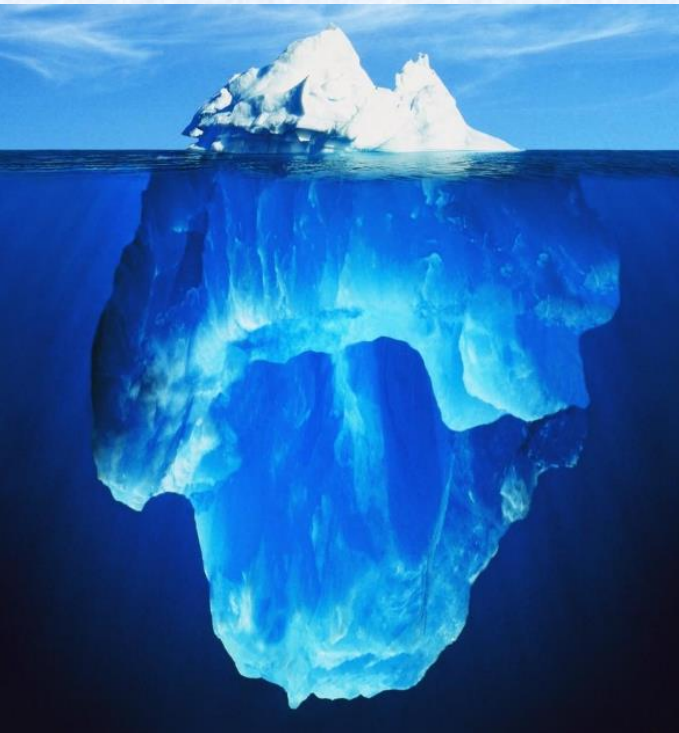


Tip of the iceberg...treating the parkinson's patient



Faculty/Presenter Disclosure

- **Faculty: Anita Madan MD**
- **Relationships with commercial interests:**
 - No disclosures to report

Disclosure of Commercial Support

- This program has **NOT** received financial support other than the support of the MOHLTC
- This program has **NOT** received in-kind support
- Potential for conflict(s) of interest:
None to be disclosed

Mitigating Potential Bias

The information presented in this CME program is based on recent information that is explicitly “evidence-based”.

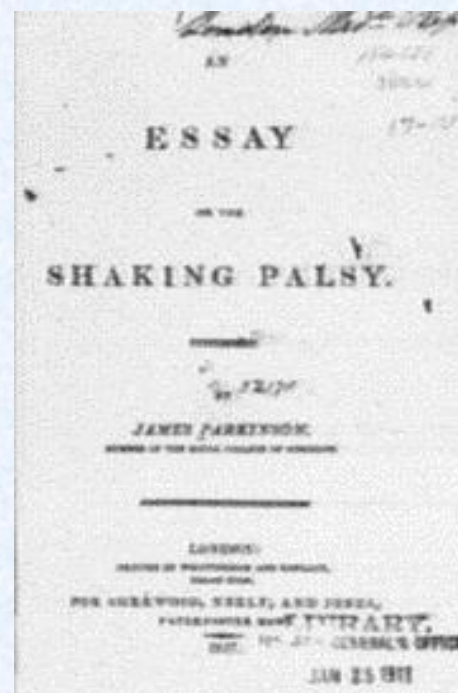
This CME Program and its material is peer reviewed and all the recommendations involving clinical medicine are based on evidence that is accepted within the profession; and all scientific research referred to, reported, or used in the CME/CPD activity in support or justification of patient care recommendations conforms to the generally accepted standards

Objectives

- Review the motor symptoms of parkinson's disease
- Review the non-motor symptoms of parkinson's disease
- Understand the pathology that leads to the above
- Review the diagnosis of Parkinson's disease

Parkinson's disease

- First described by James Parkinson in 1817
 - Essay on the Shaking Palsy
- 2nd most common neurodegenerative disease
 - 1st is Alzheimer's disease
- Men more common than women
- Prevalence of 1-2% in those over 65



Diagnostic criteria: Parkinsonism

- Bradykinesia
 - Slowness of movement
 - Decrease in decrement amplitude or speed (akinesia)
- AND (ONE OR BOTH):
- Tremor
 - Rest tremor
 - Usually 4-6 Hz
- Rigidity
 - Resistance to passive movement
 - Not velocity dependent
 - Not related to failure to relax

Other motor symptoms

- Gait changes
 - Shuffling
 - Festination
 - Short accelerating steps, like running
 - Freezing
 - Getting stuck
 - Decreased arm swing
- Postural instability
 - Present later
 - Inability to correct posture with loss of balance
- Micrographia
- Masked face
 - Lack of facial expression

Diagnosis of Parkinson's disease

- Established PD
 - No exclusion criteria
 - 2 supportive
 - NO red flags
- Clinically probably PD
 - No exclusion criteria
 - Red flags (up to two) must be balanced by supportive criteria

Supportive Criteria

- Clear and dramatic response to dopamine
- Levodopa induced dyskinesia
- Rest tremor in a limb
- Olfactory loss or cardiac sympathetic denervation on MIBG scintigraphy

Exclusion Criteria

- Cerebellar abnormalities
- Downward vertical supranuclear gaze palsy (or selective slowing of downward vertical saccades)
- Diagnosis of FTD or PPA
- Parkinsonian features in lower limbs only >3 years
- Treatment with dopamine receptor blocker or dopamine depleting agent at dose/time that could cause drug induced parkinsonism
- No response to levodopa
- Cortical sensory loss
- Normal functional neuroimaging of presynaptic dopaminergic system
- Documentation of another condition that can cause parkinsonism

Red Flags

- Rapid progression of gait impairment
 - Wheelchair in 5 years
- No progression of motor symptoms for 5 years
- Early bulbar dysfunction
- Inspiratory respiratory dysfunction
- Severe autonomic failure in the first 5 years
- Recurrent falls (in first 3 years)
- Disproportionate anterocollis or contractures of hand or feet in first 10 years
- **NOT having the ANY non-motor features after 5 years is a red flag to the diagnosis of parkinson's disease**
- Unexplained pyramidal tract signs
- Bilateral symmetric parkinsonism

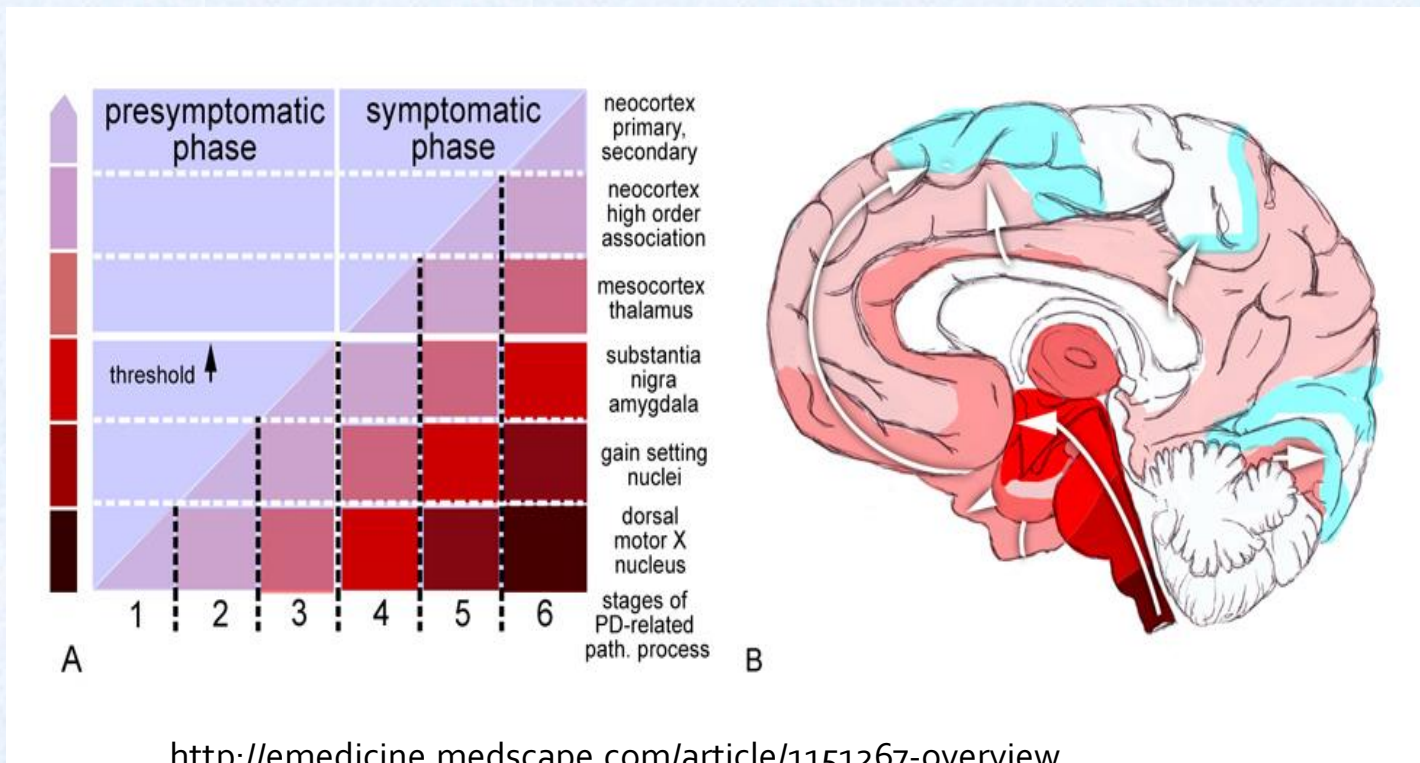
Pathology: Lewy body

- Alpha synuclein is a normal presynaptic protein
- It forms aggregates that cause the disease
- Damage to substantia nigra, pars compacta
 - hallmark of parkinson's disease
- Causes the hallmark motor impairment
- **URNS OUT IT IS MORE COMPLICATED!**



<http://www.urmc.rochester.edu/neuroslides/slide199.html>

Pathology



- The Braak hypothesis suggests PD begins long before motor symptoms appear
- PD begins in the lower brain stem and progresses to other parts of the brain
- Some non-motor symptoms appear before diagnosis

Pathology

Stage 1:

- dorsal motor nucleus of the vagal nerve; anterior olfactory structures

Stage 2:

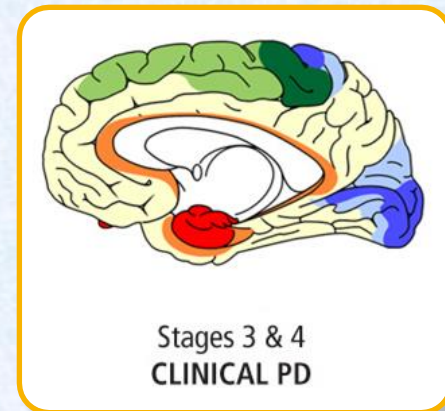
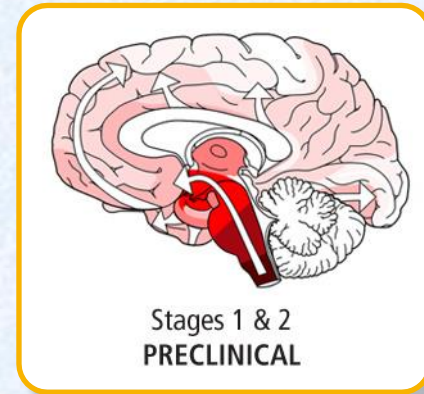
- lower raphe nuclei; locus coeruleus

Stage 3:

- substantia nigra; amygdala; nucleus basalis of Meynert (clinical diagnosis)

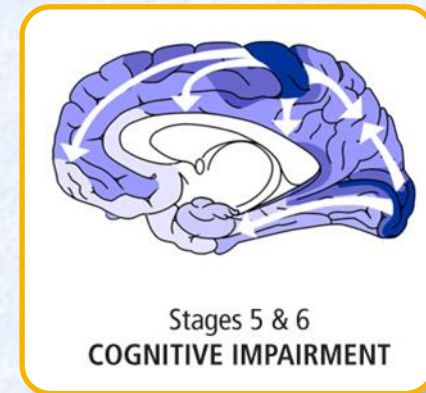
Stage 4:

- temporal mesocortex



Pathology

- Stage 5:
 - temporal neocortex;
sensory association and
premotor areas
- Stage 6:
 - neocortex; primary
sensory and motor areas



Just the tip of the iceberg

- We are really only treating the tip of the iceberg
 - We treat what we can see
 - The symptoms could have been developing for decades
 - Stage 1 and 2
 - We are catching it while it is more advanced
 - Stage 3

The rest of the iceberg

- Thought to start in neurons of the nasal cavity AND the neurons in the gut
 - Spreads from there via olfactory trace and vagal nerve to the CNS
- Preceding the diagnosis
 - Problems with olfaction (loss of smell)
 - Problems with digestive tract (constipation)

Olfactory Loss

- 85% of PD patients have olfactory loss
- Those with olfactory loss have higher risks of developing parkinson's disease

Constipation

- Can occur >15 years prior to diagnosis
- Due to the degeneration of nerve cells
- Increased transit time
- Treatment (not unique to PD)
 - routine
 - Water exercise
 - Fibre
 - Stool softeners (osmotics, stimulants)
 - Constella seems to work well (coverage an issue)

RBD

- Highest PD risk
- 38% developed PD after 5 years
- 81% eventually developed neurodegenerative disease
 - Mild cognitive impairment (MCI)
 - Dementia
 - Synucleinopathy (MSA, PD)

Mood

- Usually just two years prior to diagnosis
- 30% of patients
- Anxiety may be a risk factor for Parkinson's disease

Most common non-motor features:

- NOT having any the after 5 years is a red flag!
- Emerge more as the disease progresses
- Sleep issues
 - Excessive daytime somnolence, RBD
- Autonomic Dysfunction
 - Constipation, daytime urinary urgency, symptomatic orthostasis
- Hyposmia
- Psychiatric dysfunction
 - Depression, anxiety or hallucinations

Other non-motor features:

Psychiatric

- Depression
 - Treat with pramipexole (good evidence)
 - Commonly use antidepressants
- Anxiety
- Apathy
 - Exercise, socialize, psychotherapy, psychiatry
 - Can be medication wearing off
- Hallucinations
 - Can be due to medication
 - Look for triggering factors (like any patient)
- Psychosis
 - Clozapine (good evidence)
 - Commonly also use quetiapine

Other non-motor features:

Cognitive

- Mild cognitive impairment
 - Not all patient reach degree of dementia
 - Treatment not unique to Parkinson's disease, exercise, sleep
- Dementia
 - Commonly use donepezil, galantamine, and memantine

Other non-motor features:

Autonomic

- Salivation
 - Botox injections
- Dysphagia
- Constipation
- Nocturia, Urgency
 - Treatment not unique to PD
 - Diapers, catheter, medication (mirabegron)
- Excessive sweating
 - Can be off phenomenon (adjust PD medications)

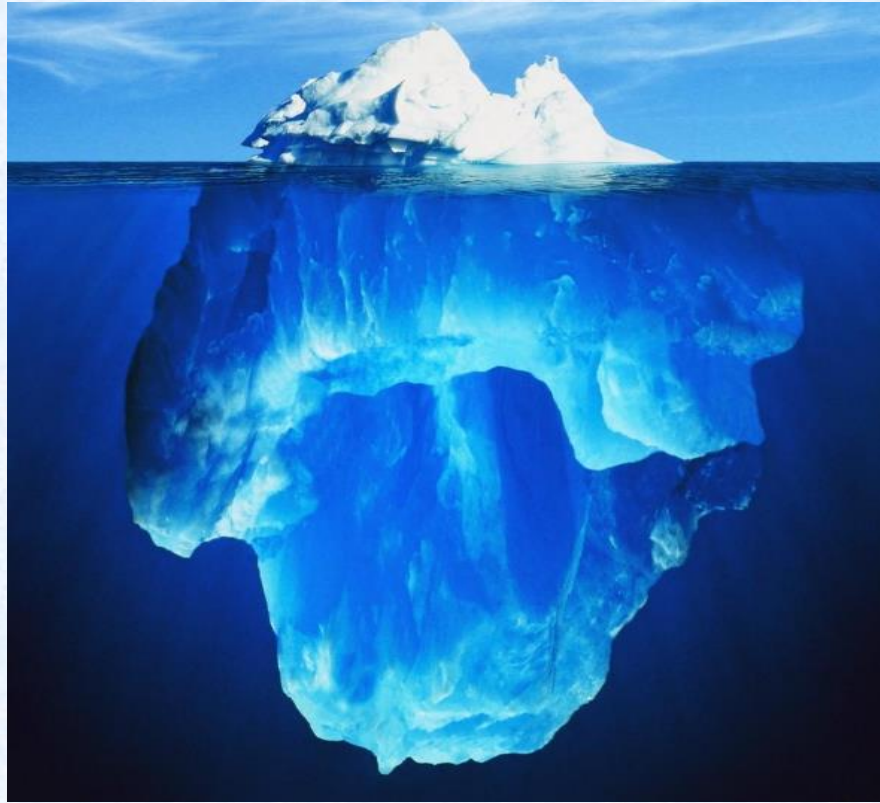
Other non-motor features:

Autonomic

- Sexual dysfunction
 - Again treatment not unique to Parkinson's disease
 - Sildenafil (viagra), tadalafil (cialis), vardenafil (levitra)
- Low blood pressure
 - Compression stockings
 - Increase salt
 - Increase water intake
 - Midodrine or florinef

Other non-motor features: Sleep

- RBD
 - Clonazepam, melatonin.
- Excessive daytime sleepiness
 - Good sleep hygiene
 - Commonly use methylphenidate and modafinil



- Parkinson's disease is a complicated disease
- There is a lot below the surface we still don't understand
- New research is looking further into the non-motor symptoms and how to best address/treat

QUESTIONS?

