The Medical Treatment of Parkinson's disease

Dr. Anne-Louise Lafontaine
Associate Professor
Dept of Neurology and Neurosurgery
McGill University

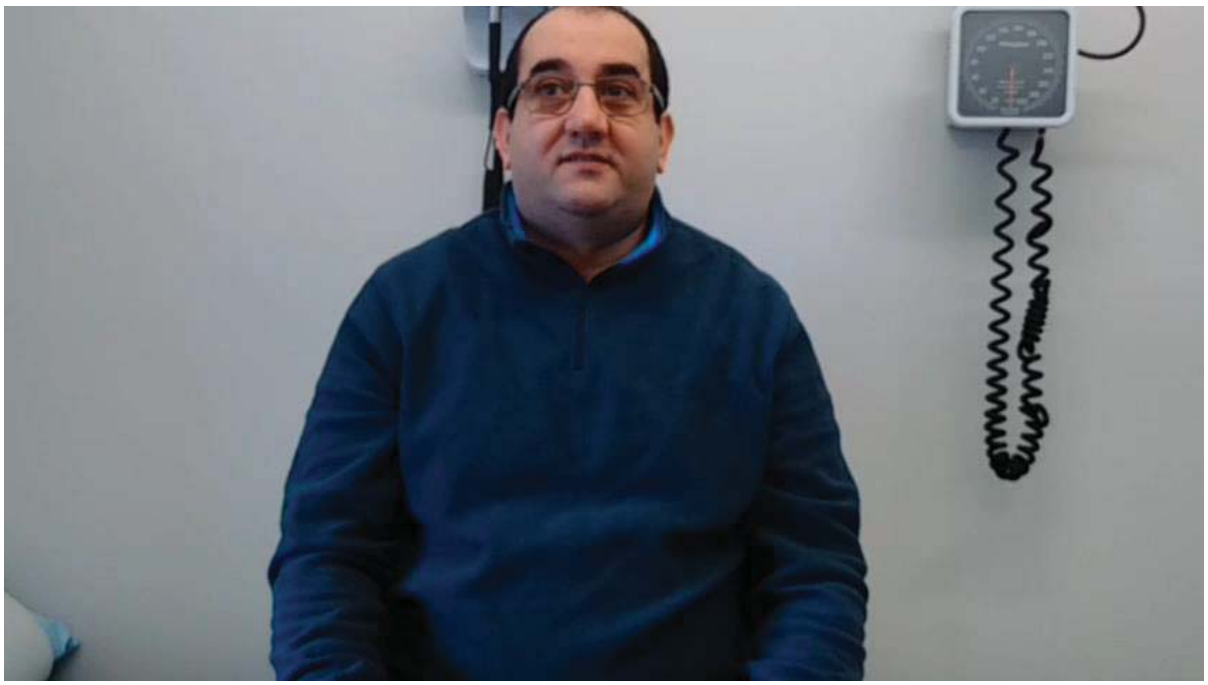
Disclaimer

- I have received honoraria for attending advisory boards: Sunovion, Paladin, Merz
- I have participated in clinical trials: Biogen, Novartis, UCB pharma

Objectives

- Review diagnostic criteria for Parkinson's
- Review the key treatment strategies for early disease
- Learn new therapies for advanced disease

Video 1



Video 2

REVIEW

CME

MDS Clinical Diagnostic Criteria for Parkinson's Disease

Slow passive movement "leadpipe" resistance that is velocity independent

Rigidity

Bradykinesia

AND

OR

Tremor

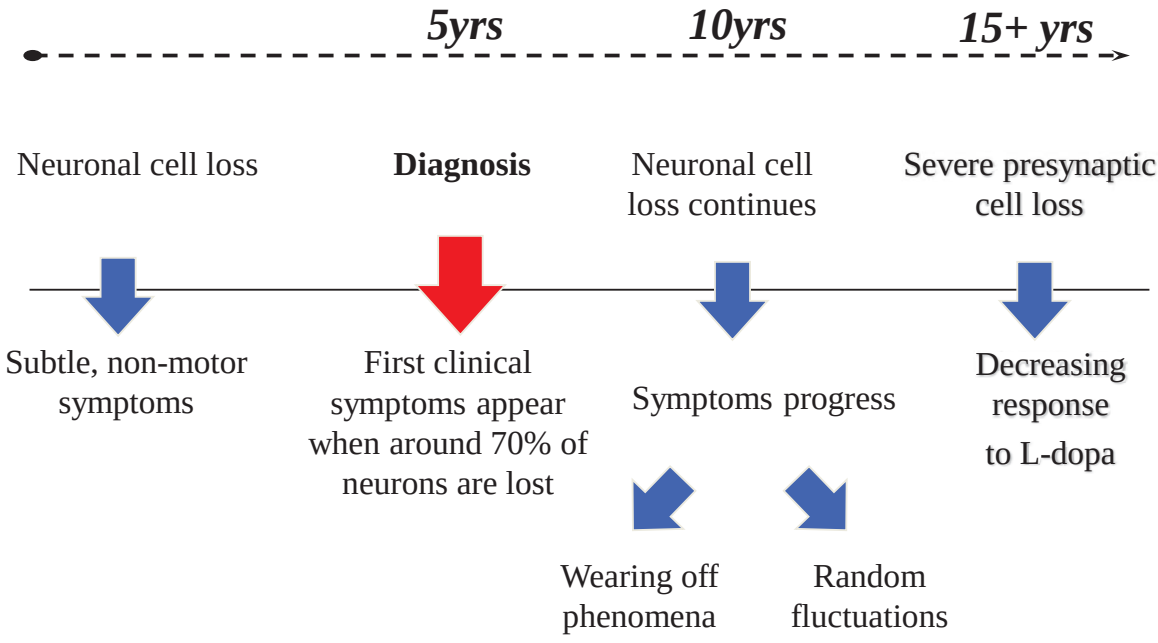
Slowness of movement AND Decrement in amplitude or progressive halts

4 to 6 Hz tremor in the fully resting limb and suppressed during action

Helpful Clinical Findings for Diagnosis

- Masked facies, reduced eye blink
- Change in voice
- Trouble arising from chair
- Difficulty turning in bed
- Trouble buttoning shirt
- Flexed posture with loss of arm swing
- Sialorrhea
- Change in handwriting

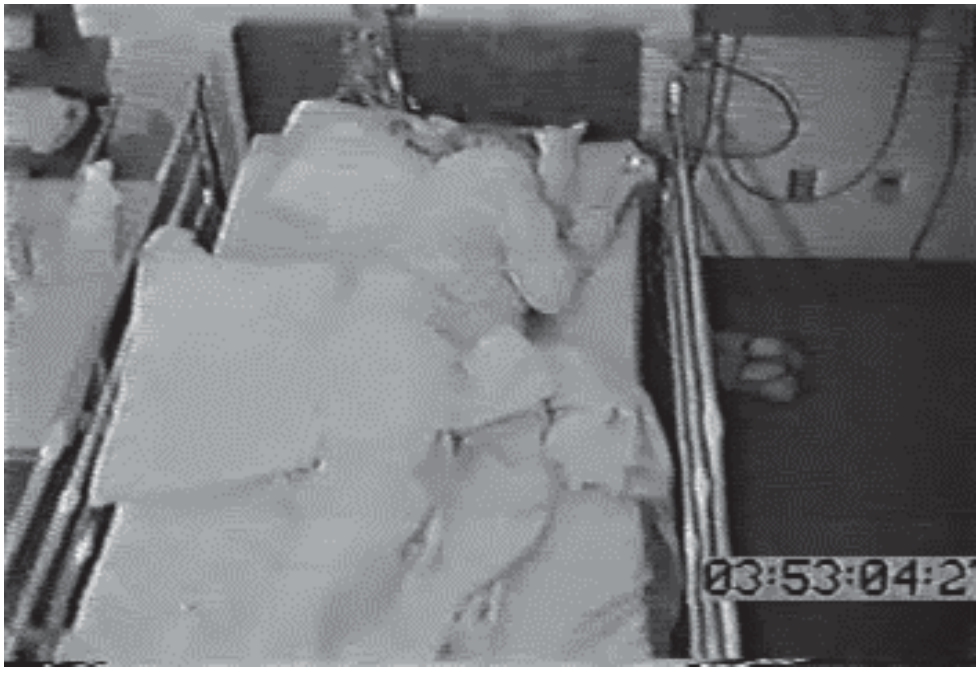
Clinical and Pathological correlation



‘Premotor’ Symptoms of PD

- Hyposmia
- REM sleep behaviour disorder
- Excessive daytime sleepiness
- Anxiety or depression
- Constipation
- Erectile dysfunction

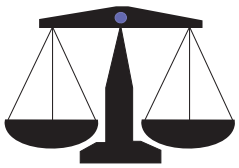
RBD video 3



When do we initiate therapy?

- When there is a functional impairment

Rx Options



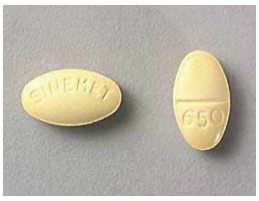
Levodopa

- most effective rx
- rapid onset
- min. side effects
- cheap
- incr. risk of dyskinesias and fluctuations

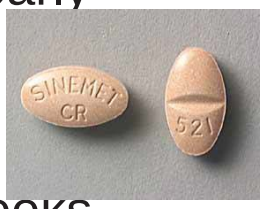
Dopamine Agonist

- decr. risk of dyskinesias and fluctuations
- slower titration
- more side effects
  - Drowsiness
  - Impulse control disorders

How to start levodopa



- Mostly use levodopa/carbidopa IR
  - CR less reliably absorbed (esp. with protein)
  - if you use CR, loose 30% potency
  - CR often used as bedtime dose for early morning off or night time off



- Titrate slowly esp in elderly
  - Sinemet R 100/25 tid by end of 6 weeks
  - In younger patients 100/25 tid by end of 3 weeks

How to use dopamine agonists

- Start low, and go slow (more than Sinemet)

Requip - typical starting dose = 2-3 mg TID
- increase over 6-9 weeks

Mirapex

typical start dose= 0.5 TID
- increase over 3 weeks

Impulse Control Disorders

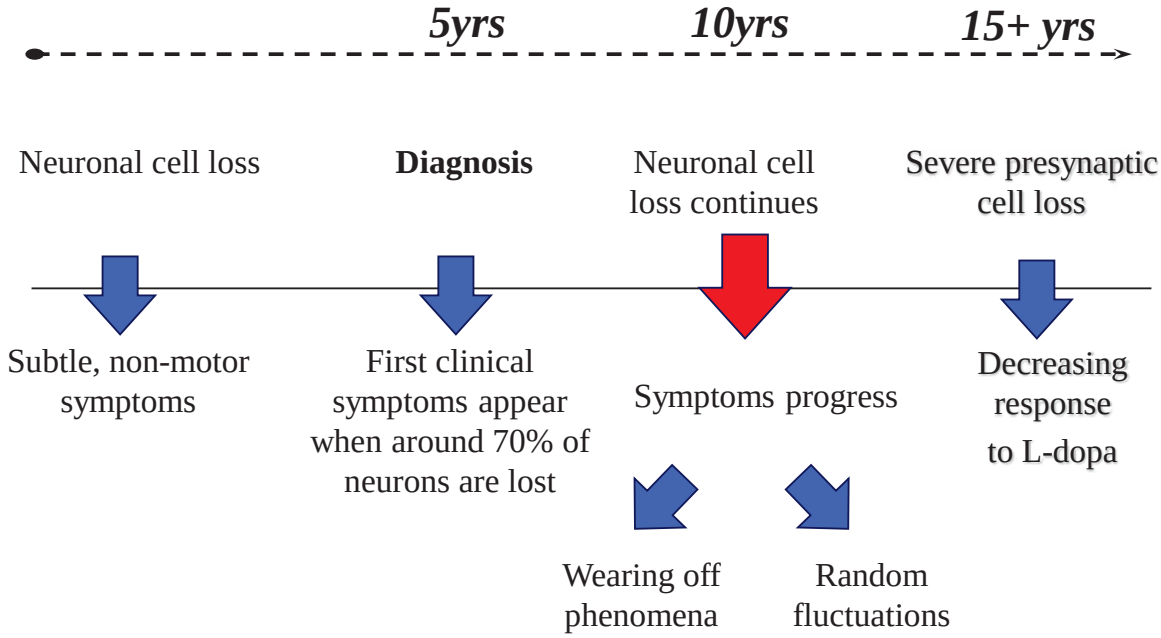
- Affects 13-17% of patients during course of disease
- Highly associated with dopamine agonists
  - Pathological gambling
  - Hypersexuality
  - Compulsive shopping/ shop lifting
  - Compulsive eating
  - Punding

Voon, Neurology, 66,1750-1752.

Impulse Control Disorders

- More than 25% had >2 ICDs
- Occurs most often in males with early-onset PD
- Men and women have particular ICDs sex vs shopping

Clinical and Pathological correlation



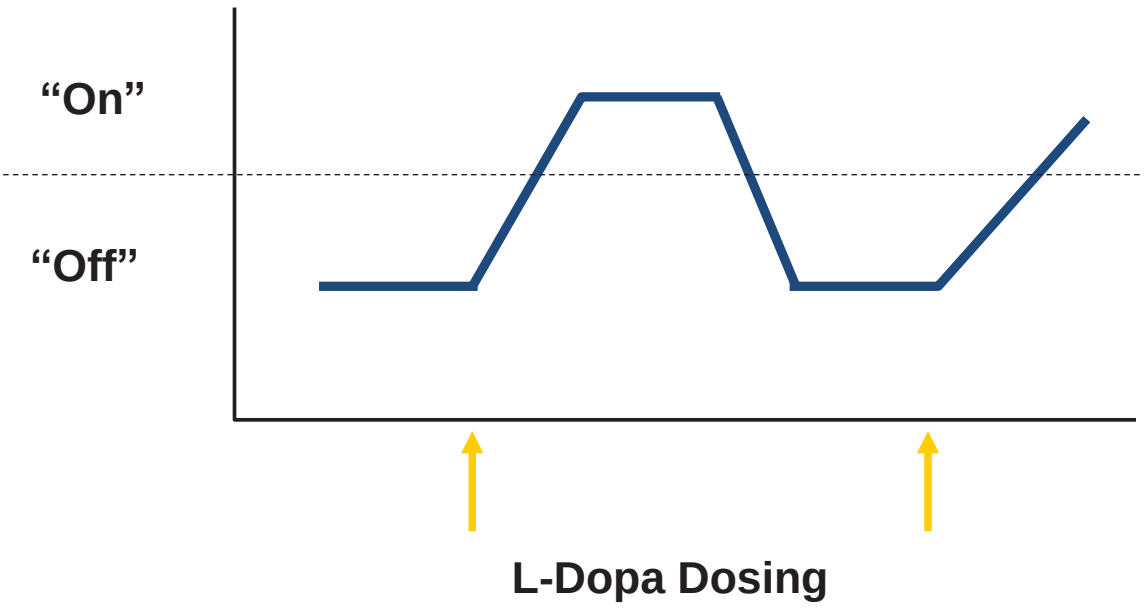
When the Honeymoon is over

- 5 major responses to > 5 years of levodopa therapy:
  - Smooth,good response 25%
  - Troublesome fluctuations 40%
  - Troublesome dyskinesias 25%
  - Toxicity at therapeutic doses 5%
  - Substantial loss of efficacy 5%

Wearing Off

- Regular and predictable decline in response 2-4 hours after LD dose
- Most common motor fluctuation
- Dose adjustments, add-ons:
  - Increase LD frequency
  - Reduce LD, add COMT inhibitor
  - Add MAO-Inhibitor
  - Add Dopamine Agonist

Wearing off



Dyskinesias

- Associated with age (higher in younger: 50% at 5 years)
- Dose of levodopa (higher)
- Disease severity (nigral degeneration)
- Genetic predisposition (polymorphism of the D2 receptor gene)
- Pathogenesis is poorly understood: Chronic pulsatile stimulation of post synaptic receptors may cause potentiation of glutamate receptors

Video 4

Peak Dyskinesias

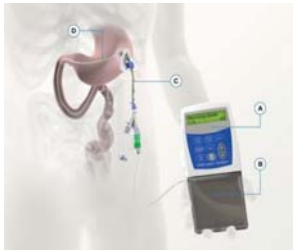
Treatment

- Reduce dose of levodopa
- d/c COMT-inh, MAO-B inh
- Add Amantadine (100-300 mg/day)

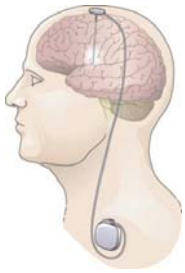
Advanced Therapies

- Apomorphine subcutaneously via single injection, sublingual film

- Duodenal levodopa pump infusion via gastrojejunostomy



- Deep Brain Stimulation



Movapo

- Injectable potent dopamine agonist with affinity for D1,D2,$_{D3}$ receptors
- Indicated for patients with advanced disease with episodic severe “off” periods or delayed “on” periods
- “on” achieved in approx. 7-10 min
- First injection needs close monitoring in clinic to determine the optimal dose and watch for side effects
- Side effects include vomiting and hypotension

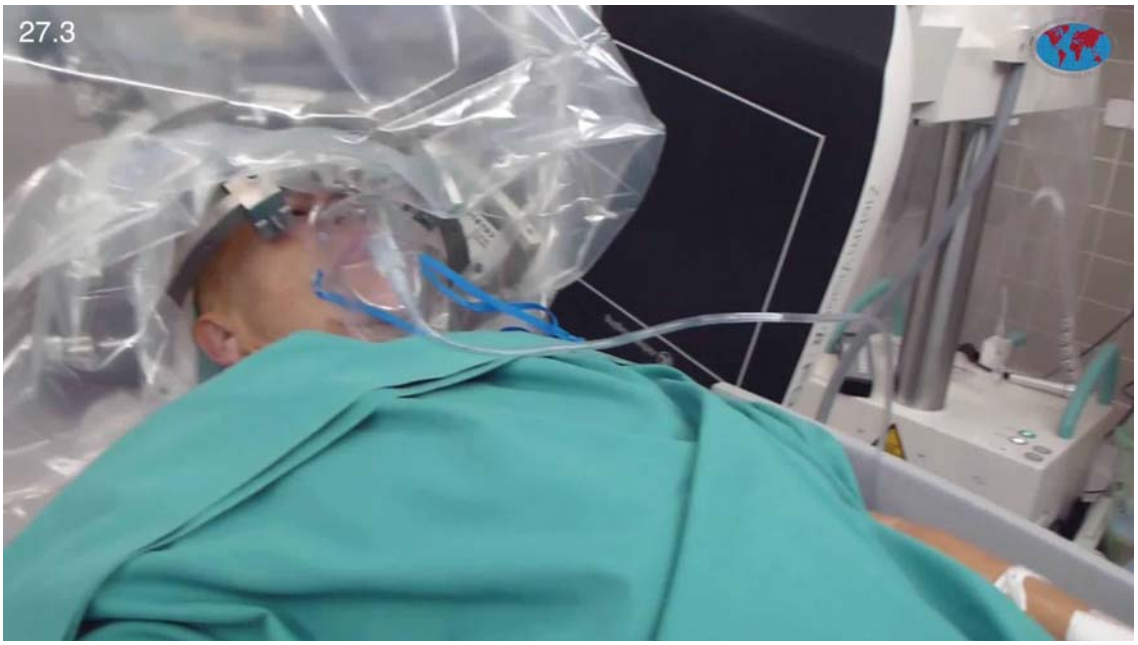
Kynmobi

- Sublingual dopamine agonist
- Same indication as Movapo
- “on” achieved in 15-30 min
- First dose needs monitoring in clinic to determine optimal dose and watch for side effects

Video 5

Indications

- Moderately advanced, **levodopa-responsive** PD
- Unsatisfactory response to oral PD medications
- Severe, disabling motor fluctuations than includes dyskinesia despite optimizing medication
- Cognitive impairment is not strictly contraindicated



Movement Disorders
Official Journal of the International Parkinson and Movement Disorder Society

Article

Core assessment program for surgical interventional therapies in Parkinson's disease (CAPSIT-PD)

- Idiopathic PD >5 years
- *Age under 75*
- Disabling motor symptoms despite optimal medical management
- Clear Levodopa response
  - Levodopa challenge with 33% improvement in UPDRS Part III "on" state
- No severe comorbidities
- No moderate or severe psychiatric issues
- No moderate or severe cognitive issues

Defer GL. Mov Disord. 1999 Jul;14(4):572-84.

Conclusion

- Management of PD can be complex as disease evolves
- Pay attention to non-motor symptoms
- Many therapeutic options for advanced disease
- Disease modifying therapy is hopefully on the horizon