

Advanced Therapies for Parkinson's Disease

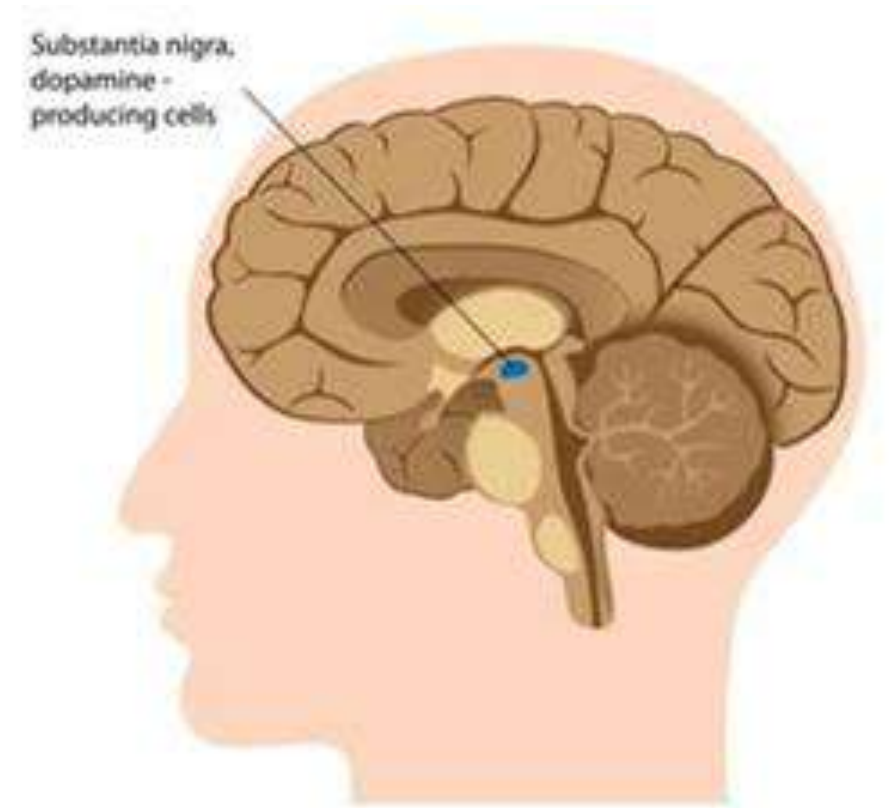
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Review of Parkinson's disease (PD)

- Brain cells makes many different chemicals
- Cells that make dopamine are dying in PD
- This causes motor and non-motor symptoms
- Most treatments aim to replenish the missing dopamine treat the motor symptoms of PD



Treatment vs Cure

- Goal of Parkinson's treatment is to improve *quality of life* and to *reduce symptoms*
- The medications and surgeries currently available do not slow down the progression of the disease
 - *But exercise does!*
- There is no cure available for now

Medications for motor symptoms

- Target: increase the amount of dopamine in the brain's movement circuit
- There are different classes of dopamine-like medications
 - Carbidopa-levodopa (common brand is Sinemet)
 - Other formulations: Rytary, Crexont
 - Dopamine agonists (pramipexole, ropinirole, rotigotine, apomorphine, newest agent recently FDA approved is tavapadone)

Carbidopa-levodopa

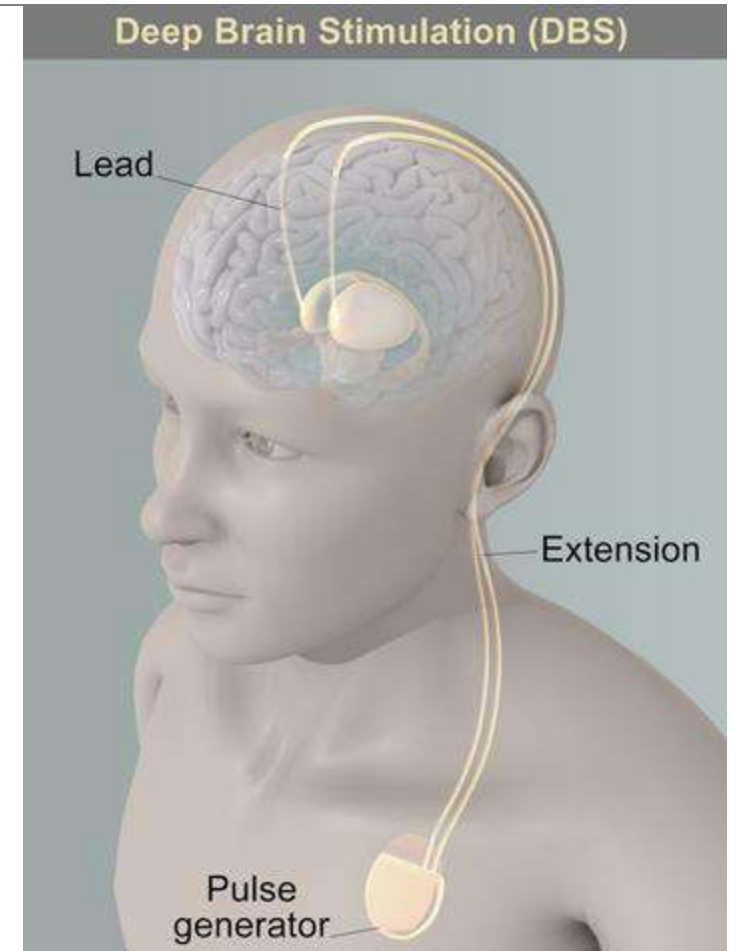
- First medication for Parkinson's disease (developed in 1960s)
- How it works: levodopa is converted to dopamine in the brain
- Carbidopa protects levodopa from getting converted to dopamine in the rest of the body
- Common side effects: nausea, dyskinesia, lower blood pressure
- Short and long-acting versions (IR and CR)
- Many other Parkinson's medications are similar to levodopa or try to extend the effect of levodopa

Advanced therapies for PD

- Deep brain stimulation (DBS)
- Focused ultrasound (FUS)
- Botulinum toxin injections
- When to consider these:
 - Motor symptoms are poorly controlled with medications
 - Bothersome fluctuations between OFF and ON states
 - Tremor that doesn't respond to levodopa
 - Bothersome side effects with medications

Deep Brain Stimulation

- Invasive brain surgery while awake
- Two electrodes implanted into movement centers of the brain and connected via a wire to a battery in the chest
- Doctor and patient can adjust the electrical stimulation via Bluetooth
- Potential side effects of stimulation: slurred speech, swallowing problems, balance problems



Process at UPMC

- 1) Determine potential candidacy for DBS, typically with an in-person evaluation with DBS specialized doctor
 - Main contraindications to DBS: memory/thinking issues, gait issues, uncontrolled psychiatric problems
- 2) ON OFF evaluation (objective assessment of motor exam on and off medications, determining if there is response to levodopa)
- 3) Neuropsychological evaluation
- 4) Pre-operative MRI
- 5) Consultation with functional neurosurgeon Dr. Andrew Wensel
- 6) Multidisciplinary conference to discuss final recommendation on proceeding with DBS
- 7) Surgery (one major for DBS leads, another more minor procedure for the battery)
- 8) Programming with movement disorders neurologist (2-3 sessions post-op to figure out stimulation settings)

Focused Ultrasound

- A powerful ultrasound beam destroys a small specific spot that contributes to symptoms
- Not technically surgery but still somewhat “invasive”
- Not reversible
- Potential side effects: weakness, numbness, slurred speech, swallowing problems, balance problems
- **Not offered at UPMC. Available at UHS in Binghamton, possibly in Buffalo at UB Neurosurgery



Comparing the two

Deep brain stimulation

Pros:

- Lots of long-term data available
- Can adjust target in real-time
- Reversible
- Adjustable stimulation

Cons:

- More invasive
- Surgical risk

Focused ultrasound

Pros:

- No surgery / less invasive
- Immediate benefit

Cons:

- Not reversible
- May wear off
- Less long-term data available

Botulinum toxin injections

- Botulinum toxin injections are used to treat dystonia and sialorrhea (excessive saliva production/drooling) in some patients with PD when oral medications are insufficient
- Injections are typically performed every 3 months
- Common brand names: Botox, Xeomin, Myobloc, Dysport
- Possible side effects for dystonia muscle injections includes overweakness of the muscles, and additional side effects depending on the sites injected
- Possible side effects for saliva production include dry mouth and difficulty chewing or swallowing

Vyalev

- FDA-approved in October 2024
- Subcutaneous (under the skin) infusion of foslevodopa
- Potential benefits: more consistent levodopa administration, less pills, less OFF time, less dyskinesias, no dietary restrictions



Process for Vyalev at URMC

- 1) Referral from URMC movement disorders specialist
- 2) Initial evaluation with Vyalev-specialized neurologist (Dr. Dave Sell, Dr. Nami Shah)
 - Candidacy: Demonstrate levodopa responsiveness (i.e. ON OFF evaluation), >2.5 hours of OFF time per day, >400mg levodopa per day, no significant skin conditions
- 3) Initiation Visit (setting pump rates)
- 4) 2-3 week follow up adjustment
- 5) 4-6 week follow up adjustment

Thank you!