Parkinson’s Disease

Spotlight on Parkinson’s Choices – Playing an Active Role in Your Treatment Plan

Welcome and Introductions

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Presentation

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Spotlight on PD Treatment Options: Advocate for Treatment that Works for You

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Goals

- Briefly touch on common side effects of basic treatment options
- What are the other options?
- Discuss options for treatment of non-motor symptoms in PD
Disclosures

• No disclosures that affect this webinar
• Teva (Honorarium)
• Apple, Inc (Consulting)

Basics of Parkinson’s disease

= Dopamine
Initial Treatments

Predominantly treat **MOTOR symptoms**
Tremor, slowness of movement (bradykinesia),
stiffness (rigidity), stooped posture, walking
difficulty

- Carbidopa/Levodopa (Sinemet)
  - *Replaces* dopamine
- Dopamine Agonists
  - Ropinirole (Requip), pramipexole (Mirapex), rotigotine (Neupro patch), apomorphine (Apokyn)
  - *Act like* dopamine

Initial Treatments

**Side Effects**

- Carbidopa/Levodopa (Sinemet)
  - Queasiness/Nausea
  - Lightheadedness
- Dopamine Agonists
  - Sleepiness (including sleep attacks)
  - Cognitive impairment
    - Risk increases with increasing age or pre-existing impairment
  - Nightmares
  - Leg swelling
  - Compulsive or Impulsive Behaviors
What Happens When Meds Stop Working as Well?

• Wearing off
  – Before next dose
  – Overnight
• Just not working enough
• Side effects
  – Dyskinesias
  – Other

Wearing Off

• Adding some extra medication or an extender may help prevent wearing off
Wearing Off

- Adding some extra medication or an extender may help prevent wearing off

ON with dyskinesias

ON

OFF

AM Midday PM Overnight

Wearing Off

- Adding some extra medication or an extender may help prevent wearing off
- Can increase frequency of dosing

ON with dyskinesias

ON

OFF

AM Midday PM Overnight
Other Forms of Carbidopa/Levodopa

- Controlled/Extended release (CR or ER)
- Rytary (IR/ER)
- Duopa

Levodopa “extenders”

- Extend life of levodopa by keeping it around for longer (decrease breakdown of levodopa)
- COMT inhibitors
  - Entacapone (Comtan)
  - Tolcapone (Tasmar)
- MAO-B inhibitors
  - Selegiline (Eldepryl)
  - Rasagiline (Azilect)
Rescue Medication

- For sudden “offs” or dose failures
- Apokyn (apomorphine)

- New drugs being tested
  - Inhaled levodopa
  - Sublingual (under the tongue) apomorphine

Dyskinesias

- Extra movements that typically occur at peak of medication
- Decrease dose/increase frequency
- Agonists may cause less dyskinesias
- Can treat with Amantadine
Dyskinesias

- **ON** with dyskinesias
- **ON**
- **OFF**

<table>
<thead>
<tr>
<th>Time</th>
<th>Symptom Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM</td>
<td>100%</td>
</tr>
<tr>
<td>Midday</td>
<td></td>
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<tr>
<td>PM</td>
<td></td>
</tr>
<tr>
<td>Overnight</td>
<td></td>
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**Will I become “resistant” to meds?**

(commonly asked re: Sinemet)

- **Symptom Control**
- **Time (years)**
Tremor

• Can be quite resistant at times
• If Sinemet or agonists, don’t work...
  − amantadine (Symmetrel)
  − trihexphenidyl (Artane) and (less commonly) benztropine (Cogentin)

Non-motor Symptoms

• Constipation
• Urinary frequency
• Sexual dysfunction
• Cognitive impairment
• Drooling
• Light-headedness/orthostatic hypotension
• Anxiety/depression or other mood disturbances
• Sleep difficulty - insomnia, acting out in sleep
• Psychiatric – hallucinations, delusions, paranoia
**Constipation**

- GOAL: 3x/week and easy to go
- Adequate fluid intake
- Have a routine
- Exercise
- Diet
- Fiber
- Miralax
- Colace, Senna
- Dulcolax, Magnesium Citrate (use sparingly)
- Enema

**Stay ahead of the game!**

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**Urinary Frequency, Urgency, Loss of Control**

- May or may not be related to PD
- Reduce liquid after 6pm
- Reduce caffeine later in day
- Take diuretics in AM if possible
- Check for enlarged prostate in men
- Some medications can reduce size of prostate
- Others control overactive bladder
Sexual Dysfunction

- Decreased desire
- Erectile dysfunction
- Difficulty/inability to orgasm
- Social stressors, etc

- Medication side effects
- Treatment options and/or lifestyle changes

Orthostatic Hypotension

- Drop in blood pressure causing light-headedness upon sitting or standing
- Can be due to disease or medications
- Drop antihypertensives
- Take with food
- Extra carbidopa
- Increase salt intake
- Compression hose/abdominal binder
- Meds to increase blood pressure
Drooling

• Not more saliva – less swallowing
• Stooped posture
• Lips parted
• Meds by mouth can dry everything out, cause confusion
• Botulinum toxin injections

Sleep Difficulties

• Trouble falling or staying asleep
• Wearing off
• Vivid dreams/nightmares?
• Sleep apnea
• Sleep hygiene
• Avoid caffeine later in day
• Decrease afternoon fluid intake
• Bed is for two things only!
Anxiety/Depression

- Depression more common in PD than in patients with cancer
- Often more withdrawn, apathetic, less initiative
- Anxiety may be part of wearing off
- Same meds used to tx symptoms in those without PD

Cognitive Impairment

- Tip-of-the-tongue
- Multi-tasking
- Slowed thinking (bradyphrenia)
- Does it interfere with daily activities?
- Could be med side effect
Psychosis/Hallucinations

- Various types
- Hallucinations should only be treated if bothersome
- #1 rule – remove offending agent
  - Dopamine Agonists, Amantadine, Artane, benzodiazepines

Take Home Points

- Ask your doctor about symptoms – they may be related to PD
- Symptoms may be due to disease or side effects from meds
- Educate yourself too! APDA is a great resource
- Talk to other people with PD
Deep Brain Stimulation for Parkinson’s Disease: Using New Device Technologies to Optimize Patient-Centered Outcomes

Harrison C. Walker, M.D.
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APDA Webinar
August 17, 2016
Disclosures

- UAB Bachmann Strauss Dystonia & Parkinson’s Foundation Center of Excellence
- Medtronic Clinical Research Grant
- R01HD068488 PART study (Co-Investigator)

“Off label” investigational and experimental therapies

- I may discuss uses of drugs and or devices for indications not approved by the Food and Drug Administration

Overview

- Summary of DBS components, brain targets, and indications in movement disorders
- Expected outcomes from DBS for Parkinson’s disease: efficacy, battery longevity, and potential adverse events / side effects
- Utilizing unique human resources of patients and caregivers to optimize DBS management
- Using brain physiology to efficiently bring new DBS technologies online for PD patients
- Concluding remarks / Questions
FDA Approved DBS Indications / Targets

<table>
<thead>
<tr>
<th>Indication</th>
<th>Target</th>
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<tr>
<td>Parkinson’s disease</td>
<td>subthalamic nucleus (STN) or globus pallidus interna (Gpi)</td>
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<tr>
<td>Generalized dystonia*</td>
<td>bilateral Gpi</td>
</tr>
<tr>
<td>Essential tremor</td>
<td>unilateral ventral intermediate thalamus (VIM)</td>
</tr>
<tr>
<td>Very severe OCD *</td>
<td>anterior limb of internal capsule</td>
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* FDA Humanitarian Device Exemption

Deuschl et al, NEJM, 2006
Schuurman et al, NEJM, 2000
Kupsch et al, NEJM, 2008
• DBS is superior to medications for motor symptoms of moderate and advanced PD, whether the target is the GPi or the STN
• Lower stimulation intensities and greater medication reduction with STN versus GPi
• A good response to the levodopa (Sinemet/Stalevo) and other dopaminergic medications generally predicts a favorable response to DBS
• Dyskinesias and “wearing off” both improve with DBS and suggest that DBS will help
• Typical tremor from PD responds very well, regardless of the response to medications
• Freezing of gait and imbalance can be more difficult to treat, especially if unresponsive to dopaminergic medications, and over time
• Postoperative medication management is important and sometimes complex

Deuschl et al, NEJM, 2005, Weaver et al, JAMA, 2009
Long-term Adverse Events Following DBS Surgery in 510 Consecutive Cases – Repeat Craniotomy For Any Reason

![Graphs showing probability of DBS electrode revision and probability of surgery for DBS electrode revision over time.](image)

**FIGURE 1.** Probability of DBS electrode revision over time. We separately characterized overall revision, device infection, complete reposition, and repositioning the same DBS electrode without complete electrode replacement. Revision for both infection and repositioning occurred at the highest rate during the first postoperative year but continued to accumulate at a slower rate over the subsequent years. DBS, deep brain stimulation.

**FIGURE 2.** Probability of DBS electrode revision over time for staged bilateral and unilateral DBS surgery. We characterized overall revision between these 2 techniques and show that bilateral DBS is associated with more long-term surgical adverse events than unilateral DBS and that the difference between the unilateral and bilateral DBS electrode repositioning is statistically significant. DBS, deep brain stimulation.

Daxa Patel et al, Neurosurgery 2015

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Post-op Simulator Adjustments Are Critical to the Success of Any DBS Program

- There are **three main goals** in DBS programming:
  - Maximizing symptom relief
  - Maximizing tolerability
  - Good battery usage efficiency

- Although DBS programming is rewarding for patients and clinicians, it can be a time-consuming, trial-and-error process

Volkmann et al 2002 Mov. Disord., Deuschl et al 2006 Mov. Disord.
IPG (battery) Longevity is an Important Patient-centered Outcome: Results From 470 Consecutive IPGs

Reversible Improvement in Severe Freezing of Gait From Parkinson’s Disease With Unilateral Interleaved Subthalamic Brain Stimulation
DBS Adjustments at Home Increase Access to Therapy and Likely Improves Outcomes

• Patients often live far from experienced DBS centers, creating practical management issues
• Although multidisciplinary teams enhance patient access, greater flexibility for stimulator adjustments at home have been helpful
• We increasingly allow patients and their caregivers to tailor their own DBS settings – therapeutic demands can be different at home versus the relatively brief time window in clinic

DBS Adjustment at Home – Personalizing Therapy

• Stimulation parameters are evaluated and selected by clinicians in clinic visits that are snapshot in time
• Clinic adjustments may not address sleep, gait, and other symptoms that relate to function at home
• Patients may not be interested in the symptoms that clinicians typically focus on (“the 90% rule”)
• Home programming likely decreases the need for return to clinic visits, especially for patients who live far away
• Not for everyone
Cortical Physiology During DBS Targeting and Activation

Future Directions: Segmented Leads and Adaptive Stimulation
Conclusions

- DBS is an established therapy for PD and other movement disorders that do not respond to more conventional treatments
- Although DBS therapy is safe overall, it is associated with adverse events that do not occur with oral medications alone
- Patient-driven programming adjustments, in addition to traditional DBS programming in clinic, provides new opportunities to personally tailor symptom management at home
- We need to better understand how DBS works in patients to quickly and effectively implement increasingly complex and versatile DBS technologies
Question & Answer

Jaime Hatcher-Martin, MD, PhD
Harrison Walker, MD

Closing Remarks

Stephanie Paul
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For additional information, answers to your questions, or resources

Please visit our website
www.apdaparkinson.org

Or call us
1-800-223-2732