

HOW TO MANAGE PD MEDICATIONS FOLLOWING DBS

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Disclosures

- Dr. Pourfar has received prior consultation honoraria from Abbott, Boston Scientific and Medtronic
- This talk will cover approved indications for deep brain stimulation

Note on Vignettes

- All patients have given written consent to share their videos for medical purposes only
- Please do not videotape or share images in any format.

Talk Overview

- Setting expectations before DBS
- Target consideration for post-op medication management
- Special considerations
 - Management of stim-induced dyskinesias
 - Management of worsening gait
- Vignettes
 - VIM, STN, GPI
- Long-term stimulation vs medication adjustments
- Final reflections and recommendations

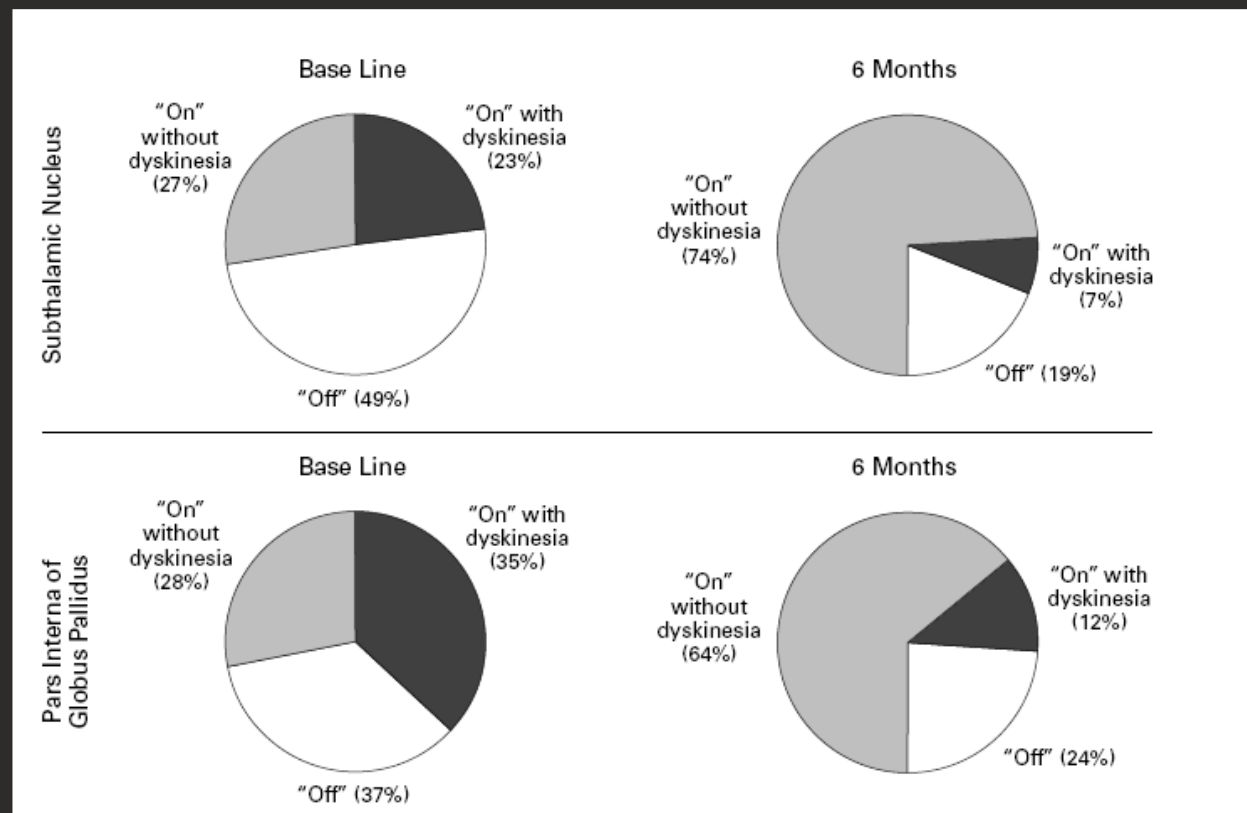
The more things change, the more (or less) they stay the same

- No matter what changes technologically, the principles of successful DBS are the same.

You need the following:

1. An appropriate candidate
2. Appropriate lead placement
3. Appropriate programming
4. Appropriate expectations

FRAMING EXPECTATIONS



N=96 STN, 36=GPI

NEJM 2001;345:956-963

DBS is a powerful tool that can yield remarkable results but it is not a cure and it does not turn back time.

Discuss realistic medication management BEFORE DBS

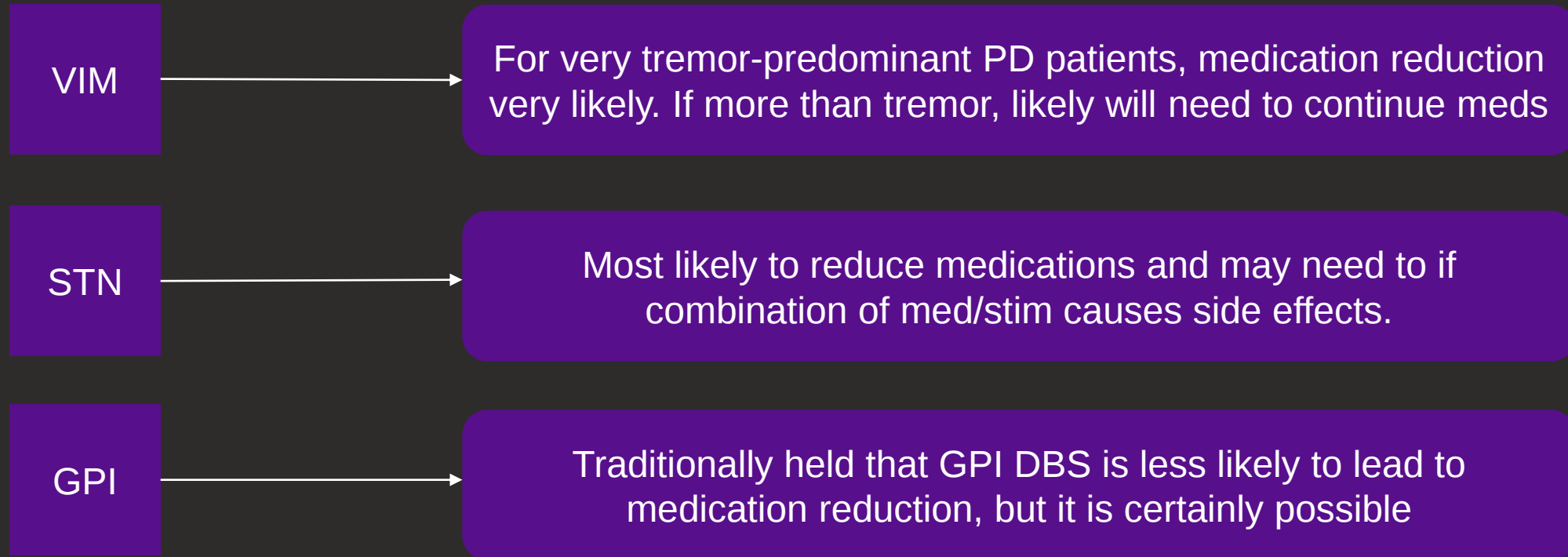
- Many PD patients assume they will drastically reduce their medications after DBS. Except for very tremor-predominant PD patients, this is often not the case.
 - Define what success is likely to look like for a patient but do not have it hinge on a specific dose reduction, or you may transform a success into a perceived failure.
 - Maybe you can reduce or simplify the regimen but emphasize in advance that the main objective is to have them experience more reliable symptom control and that may require continuing to work with a combination of stimulation and medications in ways that are hard to predict.

DBS is complicated. Try to keep it simple!

- There is a lot for new DBS patients to process: new charging equipment, programming technology, side effects to monitor and added instructions on top of their already complex medication instructions.
- Remember these are advanced PD patients and can be easily overwhelmed with a multi-step plan so keep it simple to start.
- You cannot fully predict how the medications and stimulation will interact. Be particularly mindful of patients who already have significant dyskinesias as they may be more prone to develop severe med+stim dyskinesias.
- Avoid multiple simultaneous changes

Target selection influences medication expectations

-



There is no “one plan fits all” with DBS

- I like to have a two-step, contingency plan that reduces number of new variables.
 - After initial programming, reduce amplitude from perceived “ideal” to avoid delayed onset dyskinesias, medication-related synergies and overshooting the mark.
 - Tell them to keep medications as is for a couple days and slowly increase the settings toward the target amplitude determined in the office.
 - As they see improvement, give them a simple, single medication adjustment they can try with the option of reverting to the original medication if they feel worse without it.
 - Reducing medications before they sense any improvement from stimulation can lead to the post-DBS blues. Let them know this is a process and not to feel depressed if they don’t feel better in the weeks ahead...it’s a process.

Review the challenges with the current medications

- Dose frequency and complexity
- Cost/Insurance considerations
- Class-related side effects
 - Dopaminergic dysregulation or hallucinations might favor lowering agonists followed by levodopa
 - Constipation, confusion might favor lowering anticholinergics first

Staged versus bilateral DBS medication management

- Some centers perform simultaneous bilateral DBS whereas others stage them.
- If DBS is staged, be mindful about the disconnect between stimulated and non-stimulated side as you adjust medications. Need to proceed gradually unless patient's symptoms are very unilateral.
- Do not expect major improvements with gait or axial symptoms with unilateral DBS
- It can be helpful to get one additional visit in before the second side (depending on timing) to identify challenges with programming or medications.

STN and Dyskinesias: The ecstasy and the agony



- Stim-induced dyskinesias can be immediate or delayed by hours
- Be particularly aware in patients who have significant dyskinesias at baseline
- If you see stim-induced dyskinesias, start low and go slow
- Have a plan in place if patients develop severe dyskinesias
- If severe, have them turn off stimulation and contact you.

Post-GPI Med management for Parkinson's

Medication Approach

- Our center often selects the GPI when patients have low thresholds for dyskinesias.
- Medications may not change as much as with STN but don't rule out the possibility of slow reduction
 - Anticholinergics/Amantadine may not be needed if achieve good dyskinesia control
 - Gentle reductions or simplification of levodopa regimen often possible

GPI for dyskinesias: programming ON Meds



DBS and gait: making it better or making it worse?

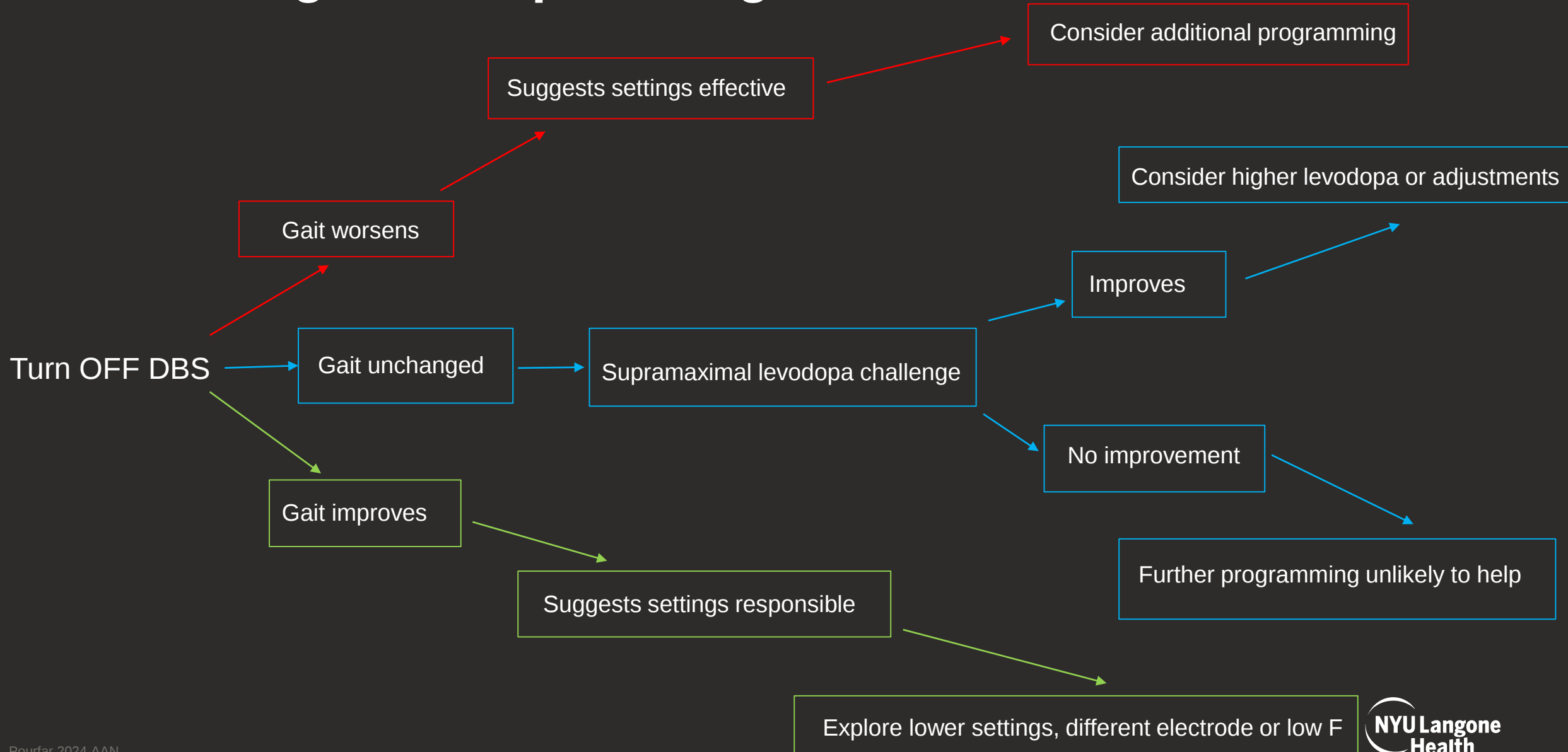
Worsening gait over years (ET)

Worsening gait over months (dystonia)

DBS and PD gait: Responsive or non-responsive?



Assessing DBS impact on gait



Vignette 1

- 76f with PD x 10 years, fluctuations and bothersome dyskinesias, undergoes side 1 Left STN DBS. Initial programming is well-tolerated with mild stimulation-induced dyskinesias.
 - Regimen: Sinemet 25/100 2 – 1.5 – 1.5 – 1 – 1 – 1 (6am/9am/12pm/3pm/6pm/9pm) + Sinemet 50/200 CR around 11pm and middle of night PRN, opicapone, Azilect, pramipexole 0.5 hs (RLS)
 - Optimal initial settings OFF medications: C+2- 2.0mA 60us 130 Hz
- She tells you she has difficulty with the q3 regimen and the opicapone is quite expensive but it was helpful when added. She does not really notice a major difference between the 1.5 tab doses and the 1 tab doses but has been doing it for years.

Management Options for Vignette 1

- Not one right answer but an example of a game plan could be:
 - Start with 1.0mA with same medications and report back at end of week.
 - If develop severe dyskinesias, turn off DBS and report back sooner.
 - If feeling better but more dyskinesias, drop the two 1.5 tabs to 1 tab.
 - Plan to build up the following week, depending on feedback toward 1.5mA and reassess.
 - Monitor impact on non-stimulated side and mood and gait as dropping medications
 - Return to clinic in 3-4 weeks.
 - Step-wise ideas could include phasing out opicapone and further simplifying the LD regimen, potentially revisiting options after pursuing side 2 if staged.

Vignette 2

- 71m with tremor-predominant PD for 5 years has limited response to levodopa but continues it and moderate benefit from trihexyphenidyl but causes constipation and some clouded thinking. Undergoes unilateral VIM DBS
 - Sinemet 25/100 1 tab qid, trihexyphenidyl 2mg tid
 - Initial programming reveals excellent tremor control at higher amplitudes but causes mild speech impact and mild paresthesias.
 - Optimal OFF medication setting: C+1- 3.0 60 130

Management options vignette 2

- Lower DBS to 2.0mA to start and keep medications same for a week to gauge impact
- If trending better, can slowly increase amplitude by 0.1-0.2mA every few days and see if effects speech.
- Once tremor is clearly reduced, begin taper of trihexyphenidyl, going to ½ tablets three times daily for a week and report back. May need to adjust amplitude upward in process.
- Monitor impact on contralateral side during the taper.
- If speech does become an issue may need to bring back for tweaking settings before dealing with medication taper
- Turn attention next to levodopa and whether needed or not, slow taper remembering that rigidity, bradykinesia, gait not likely to be helped with VIM DBS if they emerge.

Vignette 3

- 68f had GPI DBS for her PD with prominent dystonia and dyskinesias. She has had an excellent response in terms of dyskinesias and dystonia but thinks her walking has worsened.
 - Sinemet 25/100 ½ tablet qid (was full tablets pre-DBS), amantadine 100 bid
 - DBS settings: C+1- 2.3mA 90us 160Hz

Management Options for Vignette 3

- Is this a DBS, medication or PD problem?
- Turn off DBS and assess gait. Does it improve?
- If so, may need to revisit initial programming notes to assess other options
- If not, could be that the levodopa was lowered. If re-increased and improves but dyskinesias return, this can be potentially programmed around by performing another monopolar review ON medications.
- GPI DBS may allow for higher doses of levodopa than pre-DBS since it can often target the dyskinesias directly rather than indirectly.

Medication Management: PD and Beyond

Essential Tremor: Most patients undergo DBS because the medications haven't worked so often can slowly taper off as benefit accrues unless unilateral and needed for other side or some residual midline or subtle persistent tremors require a combination. Monitor BP if tapering beta-blockers.

Dystonia: The response to dystonia varies so the reduction of medication is often dependent on the degree of stimulation-related improvement. Typically wait to see if trending better before tapering medications to avoid worsening or confounds. I recommend starting the taper with whichever medication is most problematic or costly

PD: This varies a great deal depending on target and symptoms. Tremor-predominant patients can often reduce more markedly (especially anticholinergics) but gait-predominant or mood-dependent patients may need to maintain higher levels. Make incremental reductions contingent on impact of stimulation changes. Everyone is different. Prioritize reducing medications associated with problems, cost or complexity

Have a simple, step-wise plan with contingencies depending on impact of changing stimulation and/or medications.

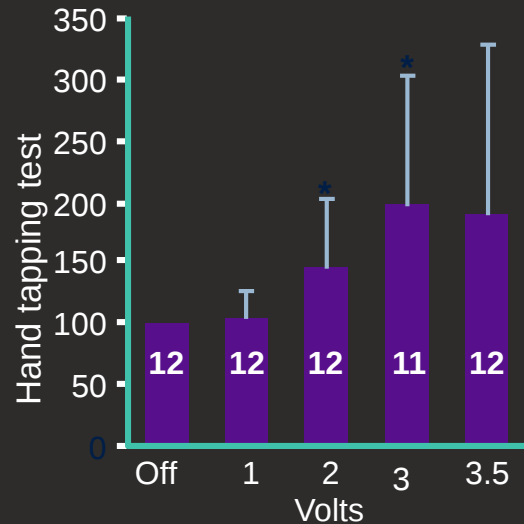
Some important things to remember

- Avoid rapid reduction of any medications but especially dopaminergics
 - Rapid reduction of dopamine can lead to a serious crash of motor and/or mood symptoms and may well have been a factor contributing to increased incidence of suicide in some DBS reports.
 - Advanced PD patients have a great deal of variability from day to day. If someone complains of an issue all the time since programming, it's probably the programming. If it's now and again, it's probably the PD. Changing programs or medications too quickly muddies the waters. When in doubt as to whether the issue relates to meds vs stim vs combo vs just PD, have them turn off the DBS for a little while and reassess.

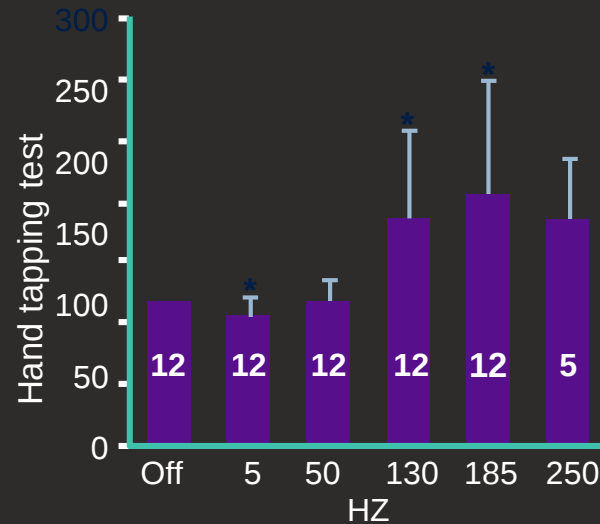
“Turn up the juice, doc”

- Many patients who have experienced dramatic improvement assume that more stimulation will make them even better.
- If you keep raising the settings to appease them, you will eventually stimulate beyond the target and only bring on side effects: worsening gait, speech, pulling, etc.
 - Explain that stimulation is like medication, too little is ineffective and too much causes side effects
- Before adjusting the parameters on a patient who has been doing well for many visits, ask yourself is the complaint typically DBS-responsive or resistant and did the issue relate to a recent reduction in medications or simply progression-related?

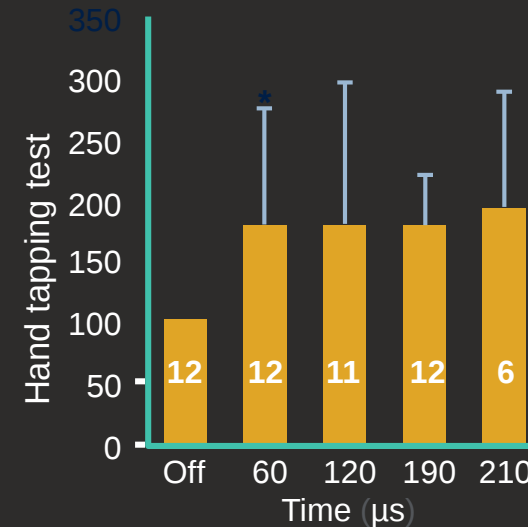
Effects of parameter adjustment on bradykinesia in DBS



Amplitude ↑
Frequency constant
PW constant



Amplitude constant
Frequency ↑
PW constant



Amplitude constant
Frequency constant
PW ↑

* p<0.05, compared with baseline

- Improvement is not a continuously linear phenomenon

Some Final Recommendations

Don't

- Don't Overcomplicate (at least to start)
- Don't Over-program (more is not better)
- Don't Over-promise (DBS is not a cure)
- Don't overwhelm (yourself or the patient)

Do

- Do prepare in advance (save everyone time)
- Do have patience
- Do have a clear, simple but contingent plan
- Do have some fun

THANK YOU!

- Dr. Alon Mogilner, Dr. Dennis London, Elizabeth Kohan NP, Lisa Lin NP
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 - Steve Frucht, Un Kang, Patrick Drummond, , Rebecca Gilbert, Xavier Paradis, Betsy Thomas
- All the DBS patients who have entrusted us with their care

Thank you for your time and attention!



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