Penn State College of Medicine
Continuing Education

Neurology for the Non-Neurologist

Friday, March 6, 2026

Handouts are intended for use by participants of this conference.
Unauthorized distribution or use is prohibited.

Any names or ages used on the upcoming slides are fictitious and not referring to an actual patient.

PennState College of Medicine

1

Recognize & Treat. Refer?

A Practical Guide to
Parkinson's Disease & Essential Tremor

Joseph Seemiller MD

Assistant Professor of Neurology | Movement Disorders Division
Penn State Health Milton S. Hershey Medical Center

2

Disclosures

The speaker has no relevant financial disclosures or conflicts of interest.

3

Learning Objectives

1. **Diagnose**

   Identify idiopathic **Parkinson's disease & essential tremor** by their clinical presentation.
   Name ancillary tests that can be used to help in diagnosis.

2. **Treat**

   Implement evidence-based **management strategies** for PD and ET.

3. **Refer**

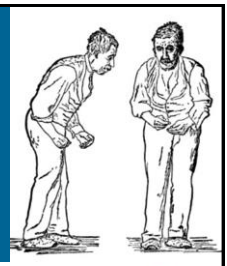
   Review the spectrum of **advanced therapeutics** with attention to **deep brain stimulation & MRI guided focused ultrasound & subcutaneous dopamine** — and know when to refer.

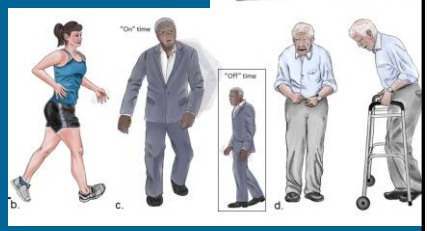
4

01

Parkinson's Disease

Recognition & Diagnosis





Source: Armstrong MJ, Okun MS. JAMA Neurol. 2020;77(11):1345-1346.

5

Part 1

Rest

6

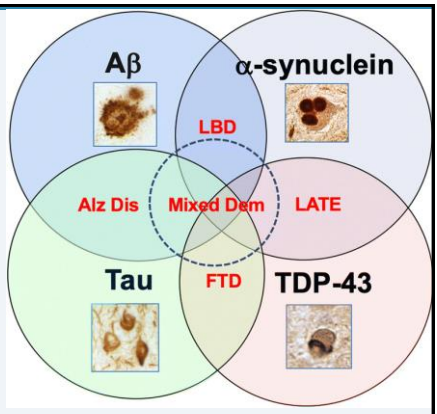
7

Proteinopathies

Alpha-Synuclein
Substrate of **DLB and PD and MSA**

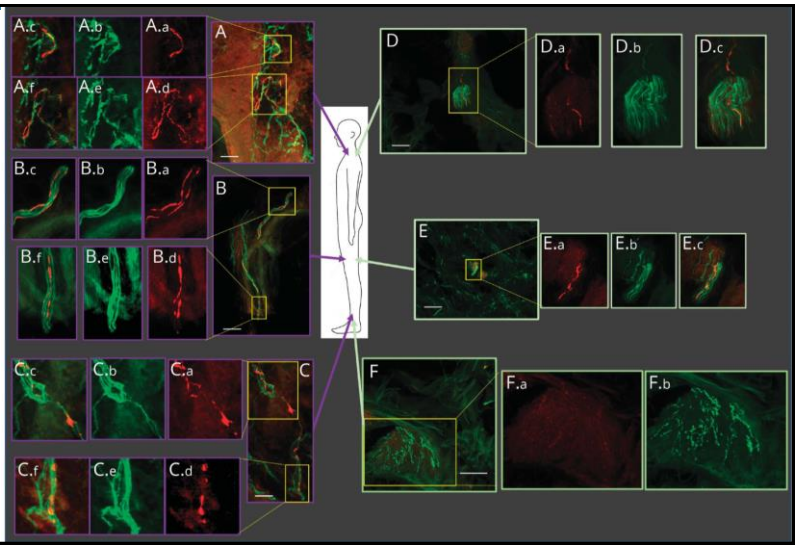
Co-Pathology
Commonly identifiable as amnestic impairment:
- PD + AD
- DLB + AD

AD co-path is more common in DLB than PD



Source: Kwon et al. Neurotherapeutics. 2020;17(3):935-954.

8



Source:
Gibbons et al. (2023). Neurology 100(15):e1529-39

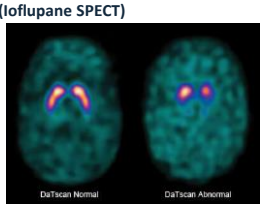
9

The Role of Imaging

DaTscan (Ioflupane SPECT)

Visualizes dopamine transporter density in the striatum.

Identify primary parkinsonism



When to Order

Differentiates PRE-synaptic dopaminergic denervation from:
- **Essential tremor**
- Drug-induced parkinsonism

When NOT to Order

Clear-Cut motor parkinsonism
Prodromals
Should NOT be frequently ordered

MRI

Not diagnostic for PD, but rules out structural causes, vascular parkinsonism, and NPH. Reasonable in workup of new parkinsonism.

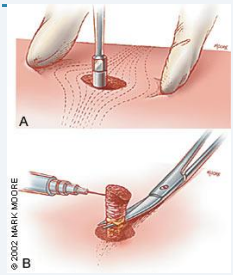
New Tools

CSF alpha-synuclein seed amplification assay (SAA)
Skin biopsy immunoflorescence

Highly sensitive/specific

10

Skin Biopsy



When to Order

–Validate clinical dx of PD, DLB, MSA, PAF

When NOT to Order

–Established disease
–Differentiate PD vs DLB vs MSA vs PAF
–If high likelihood genetic parkinsonism

Where?

3mm x3 punch biopsy:
–Posterior cervical
–Distal leg
–Distal thigh

11

Skin Biopsy

Table 2. Primary Outcomes

Diagnosis	Participants, No.		Proportion of participants positive for P-SYN, % (95% CI)
	P-SYN positive[a]	P-SYN negative[b]	
Synucleinopathy	213	10	95.5 (91.9-97.8)
Parkinson disease	89	7	92.7 (85.6-97.0)
Multiple system atrophy	54	1	98.2 (91.7-99.9)
Dementia with Lewy bodies	48	2	96.0 (86.3-99.5)
Pure autonomic failure	22	0	100 (84.6-100)
No synucleinopathy	4	116	3.3 (1.3-8.0)

Source: Gibbons et al 2024

12

CSF Seed Amplification

Study Reference (First Author, Year, Snippet ID)	Cohort Description	LBD Cases (N)	Control Cases (N, Type)	SAA Method	Overall Sensitivity (%, 95% CI)	Overall Specificity (%, 95% CI)	Sensitivity by LBD Stage/ Distribution
Arnold et al. (2022)	OHSU/UCSD ADRC	66	53 (No LBP)	SYNTap™ / Kinetic SAA (Amprion)	71.2% (59.4-80.7) *Antemortem CSF*	98.1% (90.1-99.9) *Antemortem CSF*	**Antemortem CSF:** Limbic/ Neocortical: 97.8% (44/45); Amygdala-predom: 14.3% (3/21) **Postmortem CSF:** Limbic/Neocortical: 90% (18/20); Amygdala-predom: 60% (6/10)
Samudra et al. (2024)	UCSF NDBB	29	27 (Non-LBD)	SYNTap™ (Amprion)	55.2% (35.7-73.6)	96.3% (81.0-99.9)	Diffuse: 100% (4/4); Transitional: 100% (5/5); Amygdala-predom: 42.8% (6/14); Brainstem-predom: 16.7% (1/6)
Poggiolini et al. (2024)	NP Cohort (Italy)	114	748 (No LBP)	RT-QuIC	Not reported overall; stage-dependent	High (not specified overall)	Limbic/Neocortical (Braak >3): 100%; Braak 3: 73.3%; Braak 1-2: 37.5%; Amygdala-predom: 50%
Leverenz et al. (DLBC prelim.)	US DLBC Autopsy Cohort	25	3 (No LBP)	SYNTap™ (Amprion)	High for Limbic/ Neocortical (22/22 positive)	100% (3/3 negative)	Limbic/Neocortical: 100% (22/22); Amygdala-predom: 1/1 positive; Brainstem/Amygdala-predom (restricted): 0/2 positive (1 Indeterminate)
Metrick et al. (ADNI)	ADNI Autopsy Substudy	78	Controls within ADNI (Specificity calculated vs LBP-)	SAA (Amprion)	79%	97%	Neocortical: 100%; Limbic: 57%; Amygdala-predom: 60%
Hall et al. (2022)	AZSAND / BioFINDER Autopsy Cohorts	LBD (PD/ PDD/DLB) N not specified	Controls/ Non-synucleinopathy N not specified	RT-QuIC	>92% (Clinicopath LBD)	>95%	Performance related to LB stage
Manne et al. (2022)	LRRK2 Autopsy Cohort	9 (LRRK2-PD with LBP)	5 (LRRK2-PD without LBP), 5 (Controls without LBP)	RT-QuIC	100% (for LRRK2-PD with LBP vs controls)	100% (for LRRK2-PD without LBP vs LBP+)	Not applicable (focused on LRRK2)

When to Order

–Validate clinical dx of PD, DLB, MSA, PAF
–**Prodromal** (hyposmia or REM behavior disorder)
–If ordering CSF AD testing, it can be added on

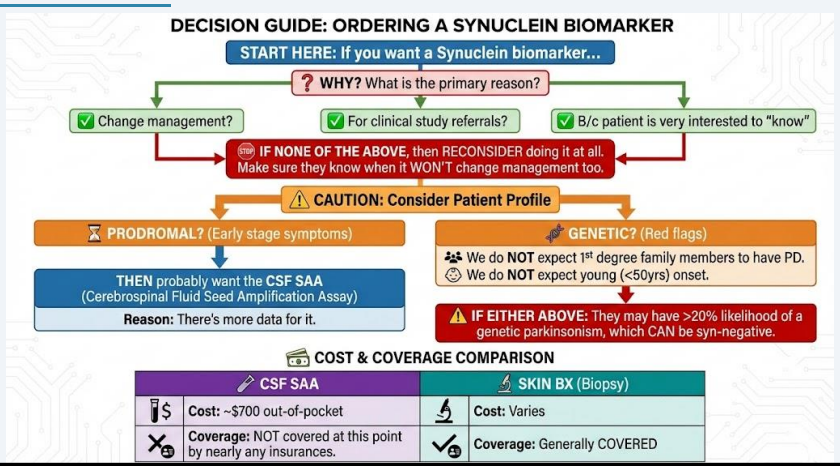
When NOT to Order

–Established disease
–Differentiate PD vs DLB vs MSA vs PAF
–If high likelihood genetic parkinsonism

13

Biomarkers of PD & ET

Image created with AI



14

02

Parkinson's Disease

Treatment & Management

15

When to Start Treatment

Treat When Functionally Bothered/Impaired

Start meds when there are **motor sx** that bother / cause issues
Specifically ask about fine motor: (1) Shoes, (2) Buttons/zippers, (3) writing and typing

No Disease-Modifying Therapy — Yet

Available treatments are **symptomatic only** and not neuro-protective

The "Levodopa-Sparing" Strategy Is Outdated

The historical concern that early levodopa "uses up" its benefit or accelerates dyskinesias has been debunked (LEAP study; NGJM 2019).

There is **no advantage to withholding levodopa** when there are bothersome sx

Exercise IS the Closest to Neuroprotection

Sustained aerobic exercise (SPARX trial data), resistance training, and balance work
Exercise should be encouraged at EVERY visit

16

First-Line Pharmacotherapy: Carbidopa/Levodopa

Carbidopa/Levodopa (Sinemet) remains the gold standard.
Clear kick-in and wear-off allows differentiation of responsive symptoms early in treatment course.

Starting Dose
25/100 mg TID (can start half-tabs for one week, then whole tabs).

Administration
Take 30–60 min before meals or 1 hour after for best absorption. Protein competes for absorption at the gut amino acid transporter. Small carbohydrate snack is OK if nauseous.

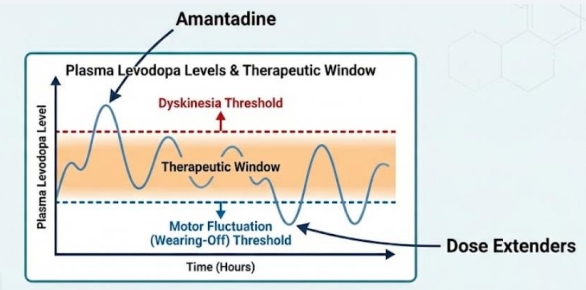
Common Side Effects
Nausea (mitigated by adding extra carbidopa or small carb snack), lightheadedness/orthostasis, somnolence, vivid dreams. Nausea is common early and often self-limited.

17

A "Dose" of Dopamine

Dose Extenders

- MAO-B Inhibitor
  - Selegiline, Rasagiline
  - Safinamide
- COMT Inhibitor
  - Entacapone
  - Opicapone
- Adenosine A2A Antagonist
  - Istradefylline



Long-Acting Dopamine

- Carbidopa/Levodopa CR
- Rytary®
- Crexont®

Anti Dyskinetic

- Amantadine
  - Amantadine ER (Gocovri®)
- (Long-Acting Dopamine)
- (Advanced Therapies)

Continuous Dopamine

- Duopa™ (c/l enteral suspension)
- Vyalev™ (foslevodopa)
- Onapgo™ (apomorphine)

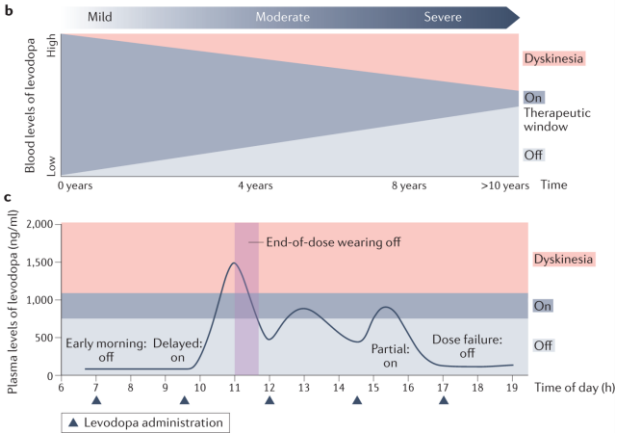
Image generated using AI / LLMs with supervision

18

A "Dose" of Reality

Inconsistency

- Delayed Kick-In
- Partial/Incomplete ON
- Dose Failure



Source:
Teymourian H, Tehrani F, Longardner K, et al. Closing the loop for patients with Parkinson disease: where are we? *Nature Reviews Neurology*. 2022;18(8):497-507.

19

03

Essential Tremor

Recognition & Treatment

20

What Is Essential Tremor?

Epidemiology

Most common movement disorder. Often familial (autosomal dominant with variable penetrance). Prevalence increases with age (~5% over 65). Bimodal onset: late teens/20s and 60s.

Phenomenology

Bilateral action tremor: both postural (arms outstretched) and kinetic (during movement, e.g., pouring, writing). Frequency typically 4–12 Hz. Upper extremities most commonly affected.

Beyond the Hands

Can involve: head tremor ("yes-yes" or "no-no" oscillation), voice tremor (quavering quality), and less commonly legs and trunk.

Progressive & Disabling

"Benign essential tremor" is a misnomer. ET is progressive and can be significantly disabling — impairing writing, eating, drinking, and professional tasks. Social embarrassment is common.

21

What Is Essential Tremor?

	Essential tremor	Dystonic tremor	Parkinson's disease
Handwriting			
Size	Normal or large	Normal	Usually small Variable
Tremor features	Regular amplitude and frequency	Irregular jerky amplitude and frequency	Regular amplitude and frequency
Tremor intrusion in letter sections	Vertical letter strokes; unidirectional axis	All sections of letters; multidirectional axis	Vertical letter strokes; unidirectional axis
Progressive deterioration	No	Yes—shape of letters worsens due to posturing	Sometimes—size of letters may decrement
Pen pressure	Normal	Hard pressure	Normal
Spirals			
Size	Normal	Normal	Small
Spacing of turns	Normal (maybe wider)	Normal (maybe tighter)	Tighter
Tremor axis	Unidirectional	Multidirectional	Unidirectional
Tremor frequency	Regular	Irregular/jerky	Regular
Progressive deterioration	No	Sometimes—more tremor and pressure	No
Straight lines			
Tremor axis	Unidirectional Right: 8–2 o'clock Left: 10–4 o'clock	Multidirectional	Unidirectional Right:8–2 o'clock Left:10–4 o'clock
Tremor frequency	Regular	Irregular	Usually regular
Tremor amplitude	Small, regular	Small, irregular	Small, regular
Symmetry	Symmetrical	Asymmetrical	Asymmetrical

Source: NASA for Doctors. (n.d.). *Dystonic tremor*. In *Movement disorders: Tremor*. https://www.nasafordoctors.co.za/articles.php?cid=4&id=5&aid=76

ET as a Phenotype

- Isolated tremor syndrome of b/l upper limb action tremor
- >3 years duration
- With or without tremor in other locations (head, voice, lower limbs)
- Absence of other neurological signs

Source: Bhatia et al. (2018). Movement Disorders 33(1):75-87.

Don't Split Hairs

- Can be a spectrum of tremor & dystonia
- Multiple tremor types can be present
- Parkinson:
  - "Parkinson tremor" doesn't exist
  - Can't diagnose PD on tremor alone
  - Can't r/o PD on tremor alone

22

ET - PD

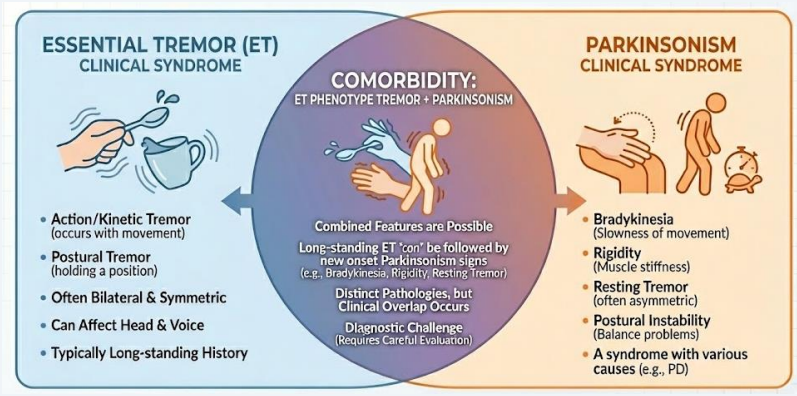


Image generated using AI / LLMs with supervision

23

ET First-Line Treatment

Propranolol

First-line. Non-selective beta-blocker.

Starting dose: 10mg TID → 20mg TID → 60mg/day ER
Titrate as tolerated
Monitor: heart rate, orthostasis

Contraindications: asthma or COPD with respiratory flares, diabetes with hypoglycemic events, heart block

Can be used PRN for performance situations

Primidone

Equally effective first-line. Barbiturate.

Starting dose: 25 mg QHS (even 12.5 mg)
Titrate as tolerated

Can combine propranolol + primidone for additive effect when monotherapy is insufficient.

Second-Line Options

- Topiramate — evidence-based but limited by cognitive side effects and weight loss
- Gabapentin — mild benefit, well tolerated
- Benzodiazepines (alprazolam, clonazepam) — effective but use judiciously due to dependence, sedation, fall risk
- ~50% of ET patients have medically refractory tremor → consider referral for advanced therapies

24

04

Advanced Therapeutics

When to Refer for (1) DBS, (2) MRIgFUS, (3) subcutaneous levodopa infusion

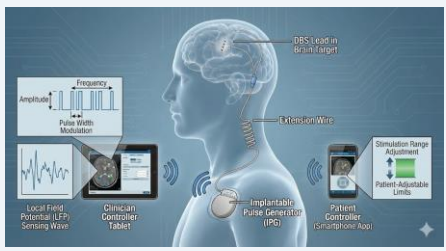
25

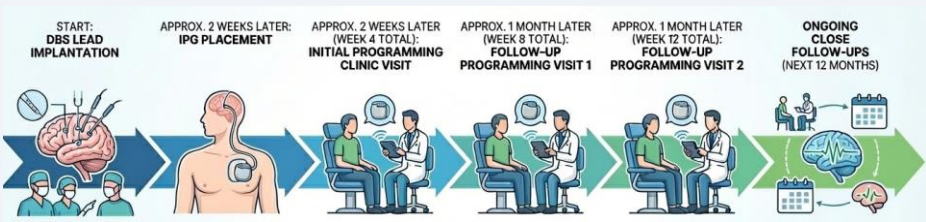
Deep Brain Stimulation (DBS)

Images created using generative AI

How it Works

- Awake (generally)
- Bilateral simultaneous (can be exceptions)



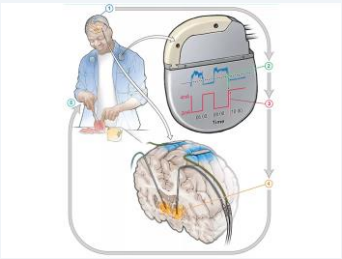


26

DBS Features

Sensing & Adaptive / Closed Loop

- Medtronic
- Deep brain signal (local field potential) sensing:
  - Electrode identification
  - Capture clinical events
  - Adapt in real-time



Telehealth DBS

- Abbott: NeuroSphere™ Virtual Clinic
- Program DBS remotely

27

MRI Guided Focused Ultrasound (MRIgFUS)

New at HMC

Our first case was in 2026 (Dr. Pratik Talati)

How it Works

Converging ultrasound beams → Thermal energy

Sub-Therapeutic energy → Test the lesion
Increased energy → Make permanent ablation

History

Essential Tremor:
–Approved 2016 (unilateral)
–Bilateral approval in 2023

Skull Density Ratio (SDR): Too much density makes not a candidate

28

DBS vs MRIgFUS

	DBS	MRIgFUS
Invasive	Craniotomy w/ lead & IPG placement	Lesioning (still permanent).
Anesthesia	Monitored anesthesia; awake or asleep	Awake (need to give feedback on side effects)
Laterality	Bilateral can be done same time	Unilateral initially; contralateral side possible as staged
Adjustability	Programmable (clinician & user)	None
Durability	Sustained effect (with programming adjustments)	Benefit may wane
Non-Motor Symptoms	No coverage (motor only)	No coverage (motor only)
Approval	ET & PD & dystonia	ET only (PD could be cash-pay)
Ideal Candidate (my opinion)	Younger Less surgical risk	Older Higher surgical risk

DBS = Deep brain stimulation
MRIgFUS = MRI guided focused ultrasound

29

When to refer for advanced therapies?

Essential Tremor

(1) First line meds (**primidone & propranolol**) are inadequate at max tolerated doses **together**
Or contraindicated

(1) Consider:
- (a) Trial of 2nd line meds: Gabapentin, topiramate, clonazepam
- (b) Occupational therapy assessment
- (c) Devices (i.e. CALA kIQ with TAPS)

Parkinson's Disease

(1) Response to Sinemet (at least bradykinesia responds)
(2) One of the below:

One of:
-**Motor fluctuation** despite long-acting dopamine
-**Dyskinesia** despite long-acting dopamine and amantadine
-Difficulty sustaining consistent **good ON-time** d/t poor fluctuation/dyskinesia, failed doses, etc.
-Severe resting tremor (i.e. tremor predominant phenotypes)

Everyone has different standards of acceptable

Nobody has to be "bad enough" for advanced therapies

30

Candidacy: DBS & MRIgFUS

Good Candidates

(1) We know what they have

(1) Their goals are reasonable

(1) Their exam fits their goals

(1) No red flags (esp. on neuropsychological screening)
i.e. dementia, unstable psychiatric disease

DBS Doesn't work for:

- Poorly levodopa responsive sx
- Gait freezing
- Speech and swallowing
- Cognitive symptoms
- Axial symptoms
- Postural instability (levodopa-unresponsive)

In PD: **DBS improves what levodopa improves**

Help purely with **motor** symptoms

Picking the right candidate

Diagnoses MUST be clear to ensure **benefits >>> risks**

Goals / expectations must be reasonable to **estimate benefits**
Neuropsychiatric profile must be clear to **estimate risks**

31

Subcutaneous Infusion

Available as VYALEV™ and ONAPGO™
Vyalev = foscarbidopa/foslevodopa
Onapgo = apomorphine hydrochloride

Advantages

– Avoid medication dynamics (No fluctuations or dyskinesia)
– Avoid failed / delayed oral doses
– Low invasive! (only skin site rotations)

Caution

– Have to carry around device on-person
– Support / caregiver to help with device (esp. if motor-OFF)
– Requires frequent site exchanges

Image from: VYALEV delivery system. (n.d.). AbbVie Inc. Retrieved March 1, 2026, from https://www.vyalev.com/delivery-system

32

What happens when you refer for “DBS”?

Multi-Disciplinary Clinic

Evaluated by:

1. Movement disorders subspecialist
   Sol De Jesus, MD; or Joseph Seemiller, MD
2. Neuropsychologist
   Elana Farace, PhD
3. Neurosurgeon
   James McInerney, MD; or Pratik Talati, MD
4. Physical therapist
   Jackie Bentlage-Brown, MSPT

Discussion

- Group discussion after full neuropsychological eval
- Outcome:
  - Good idea / Offer procedure
  - Relative contraindication / Decline candidacy
  - Not optimized / recommend steps

Thank you!
Thank you for your referrals!
We welcome personal communication (email too) if desired

33

Questions?

Joseph Seemiller, MD

Movement Disorders Division | Penn State Health

Email:
jseemiller@pennstatehealth.psu.edu

34