Controlling Involuntary Tremors

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Essential Tremor (ET)

- Tremor is a regular oscillation of hand or head
- Occurs with sustained postures and movements
- It does not occur at rest and goes away during sleep
- There may be a family history of tremor
- Can start at any age but more common with age

ET

- Often increased during times of stress
- The hands and head are most commonly effected
- Stimulants will increase the tremor and some medications may as well
- Alcohol usually decreases the tremor
- It gets slowly worse with time

ET

- Diagnosis is made predominantly based on the clinical characteristics
- Rule out other causes like medications or thyroid disease
- Imaging is not usually necessary
- Basic laboratory tests are appropriate
- Rarely is a precursor to Parkinson’s disease but much better prognosis
ET Treatment

- Medication
  - Propranolol, primidone, gabapentin, topiramate, alprazolam, nimodipine, Botox
- Nonpharmacologic treatment
  - Stress reduction, weights
- Surgery
  - Deep Brain Stimulation

Parkinson’s Disease (PD)

- Tremor is present in most patients and usually one side predominant
- The tremor is at rest and less prominent with activity or posture compared to ET
- Rigidity
- Slowness of movement (bradykinesia)
- Gait disorder
  - Decreased arm swing, stooped posture and shuffling gait

PD

- Not usually inherited
- Onset is usually after age 40
- Progressive disorder with challenges over time
- Other features of the disease may include change in sense of smell; impaired sleep and dementia or cognitive impairment

PD

- Diagnosis is predominantly based on the clinical features of the disease
- Most blood tests are normal
- Brain imaging is usually not needed in classic cases
- DaT scans can suggest the condition but does not separate the different types of Parkinsonian syndromes
- Disease is due to loss of dopamine production in the brain
PD treatment

- Medications
  - Dopamine with carbidopa (Sinemet)
  - Drugs that act like dopamine (Mirapex)
  - Drugs that prolong the effect of dopamine
  - Anticholinergic drugs

PD treatment (2)

- Nonpharmacologic
  - Physical therapy, Speech therapy, Occupational therapy (LSVT big)
  - Exercise
  - Surgery with Deep Brain Stimulation (DBS)

DBS

- Approved Indications for DBS Therapy
- DBS Therapy for Essential Tremor
- DBS Therapy for Parkinson’s Disease
- DBS Surgical Overview
- Resources
- Questions

Current U.S. Approvals

- Parkinson’s Disease – updated 2015 (initial FDA approval 2002)
- Dystonia (Humanitarian Device Exemption: HDE)
- Obsessive Compulsive Disorder (HDE)

135,000+ patients worldwide have received DBS Therapy
Essential Tremor (ET)

- Essential tremor is the most common movement disorder.\(^1\)
- Estimated prevalence of ET is 0.4%-3.9% with even higher prevalence (4.6%) in people over the age of 65.\(^1\)
- A family history of ET is commonly reported by patients with ET.\(^2\)
- ET symptoms often cause embarrassment and can potentially lead to serious disability in a subset of ET patients.\(^1\)
- Up to 75% of patients will note tremor improvement with alcohol intake.\(^3\)

\(^1\) Chopra A., Klassen B., Stead, M. Current clinical application of deep-brain stimulation for essential tremor. Neuropsychiatric Disease and Treatment. 2013, 1859-1865.
When should DBS Therapy be considered?

DBS should be considered when the ET patient, despite use of medical therapy, reaches a stage where the tremor remains disabling.

Definition of Disable
- Restrict somebody in some activities
- To make somebody unable to perform the activities needed to earn a living or carry out the basic tasks of daily life without difficulty

“Disabling” is a subjective term and, thus, should be uniquely defined for each individual.
- Consider DBS earlier in patients with occupations that depend on fine motor tasks or patients experiencing intolerable medication side effects.

DBS Therapy Efficacy for Essential Tremor

- The US Tremor Trial showed significant improvement in tremor score over time for patients receiving DBS Therapy.
- Significant improvement also occurred in activities of daily living in 7 scales.
- No cognitive effects were reported during the study that related to DBS Therapy.
- In the U.S. clinical study, a maximum of 28% of ET patients experienced rebound* lasting for a mean duration of 22 minutes.
  - The exaggerated tremor generally returns to normal within approximately 30 minutes.

*Rebound is a phenomenon in which a patient’s tremor appears clinically exaggerated (compared to baseline tremor) after turning off the stimulator.

Parkinson’s Disease

Refuse to Surrender
**Parkinson’s Disease**

- Second most common neurodegenerative disorder, affecting more than 1 million Americans\(^1\)
  - Prevalence of PD is likely to double by 2030\(^2\)

- Progressive neurodegenerative disorder with the cardinal features of:
  - Bradykinesia/akinesia
  - Tremor
  - Rigidity
  - Postural instability

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**Treatments for Parkinson’s**

- Pharmacological treatments

- Supplemental therapies
  - Physical therapy
  - Occupational therapy
  - Speech therapy
  - Exercise
  - Environmental modification

- Surgical interventions
  - DBS Therapy
  - Ablation

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**Changes in Quality of Life as Parkinson’s Disease Progresses**

- PD patients report a significantly worse quality of life compared to the general population.
- Increasing dyskinesia scores on the UPDRS were associated with statistically significant reductions in quality of life scores.

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**Medications initially manage PD well**

- Increasingly troublesome and unpredictable motor fluctuations and dyskinesia begin as early as 2 years following initiation of levodopa therapy.\(^2\)
- Within 4 to 6 years of initiating levodopa treatment, about 40% of Parkinson’s patients experience motor symptoms that impact their quality of life.\(^3\)

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**Diagnosis and Treatment of Parkinson’s Disease**

Bilateral stimulation of the internal globus pallidus (GPI) or the subthalamic nucleus (STN) using DBS Therapy for Parkinson’s Disease is indicated for adjunctive therapy in reducing some of the symptoms of advanced, levodopa-responsive Parkinson’s disease that are not adequately controlled with medication.

Updated labeling - DBS for Parkinson’s disease

**Updated Indication 2015**

Bilateral stimulation of the internal globus pallidus (GPI) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Parkinson's Disease is indicated for adjunctive therapy in reducing some of the symptoms in individuals with levodopa-responsive Parkinson’s disease of at least 4 years’ duration that are not adequately controlled with medication, including individuals with motor complications of recent onset from 4 months to 3 years or with motor complications of longer-standing duration.

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**DBS for Parkinson’s Disease**

- **STN (Subthalamic Nucleus)**
  - Bilateral implant
  - FDA approval 2002

- **GPI (Globus Pallidus Interna)**
  - Bilateral implant
  - FDA approval 2002

**Symptoms that Respond to DBS**

- Dyskinesias
- Bradykinesia
- Tremor
- Rigidity
- Motor fluctuations (Wearing off)

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Level I Clinical Evidence

Primary Clinical Evidence
Recent motor complications
4 months to 3 years


DBS Therapy provided additional hours of “on” time without troublesome dyskinesia each day.1 Motor diary.

- “On” time without troublesome dyskinesias at baseline was 10.3 hours. 1,2
- DBS (STN) patients achieved a 20% significant improvement (2.1 hours from baseline) compared to 2% (0.2 hours) with BMT alone at 24 months follow up. 1,2
- “On” time without troublesome dyskinesias at baseline was only 6.4 hours. 1,3
- DBS patients (STN and GPi) gained up to 5.2 hours each day compared to 0 hours with BMT at 6 months follow-up.1,3
- DBS Therapy had a sustained improvement to 24 months with a 5.0 hour gain for STN and a 5.2 hour gain for GPi. 1,4

73% of patients in a study identified troublesome dyskinesia as a reason for receiving DBS Therapy.5

DBS Therapy reduces time spent in the “off” state. Motor diary.

- DBS Therapy (STN) provided a 39% significant reduction in “off” time (-1.9 hours from baseline) compared to 2% (-0.1 hours) with BMT alone at 24 months, in the study of those with recent-onset of motor complications.
- DBS Therapy (STN and GPi) reduced “off” time by 2.9 hours/day (-49.9%) compared to 0.1 hour/day (-1.3%) reduction with BMT alone. (p<0.001) at 6 months, in the study of those with longer-standing motor complications.

DBS Therapy improves quality of life.

- DBS improved PD-related QoL factors by 27% over BMT alone at 24 months follow up
- DBS improved PD-related QoL factors by 20.6% over BMT alone at 6 months follow up.

DBS Therapy (STN and GPi) improved ADL’s by 28.2% compared to no improvement with BMT alone at 6 months.

MEDTRONIC DBS THERAPY IMPROVES ACTIVITIES OF DAILY LIVING.1 UPDRS II

- DBS Therapy (STN) improved ADL’s by 30% compared to a 12% decline in those receiving BMT alone at 24 months.

1 Medtronic DBS Therapy for Parkinson’s Disease and Essential Tremor Clinical Summary, November 1, 2015
Medtronic DBS Therapy significantly reduces dopaminergic medication used for treatment of PD.\textsuperscript{1}

**DBS showed a 22% significant reduction (STN and GPi) in medication versus a 1.3% increase in dosage in the BMT alone\* group at 6 months.**

- Medication was reduced by 33.6% with STN and by 16.7% with GPi at 24 months.

DBS showed a 39\% statistically significant reduction (STN) in medication versus a 21\% statistically significant increase in dosage in the BMT alone* group at 24 months.

* A reduction in medication would not be expected in the group taking medication alone.

\textsuperscript{1} Medtronic DBS Therapy for Parkinson's Disease and Essential Tremor Clinical Summary, November 1, 2015

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DBS showed a 22\% significant reduction (STN and GPi) in medication versus a 1.3\% increase in dosage in the BMT alone* at 6 months.

- Medication was reduced by 33.6\% with STN and by 16.7\% with GPi at 24 months.

DBS showed a 61\% statistically significant reduction (STN) compared to a 13\% significant worsening in BMT alone in drug-related complications at 24 months.

- These reductions were sustained in the DBS groups to 24 months: GPi and STN patients had a 46\% and 51\% improvement, respectively.\textsuperscript{3}

DBS showed a 44\% reduction (STN and GPi) and BMT had an 8\% reduction in drug-related complications at 6 months.

In Summary, When to Consider DBS Therapy

- Diagnosis of PD for 4 years
- Levodopa responsive
- Not adequately controlled with medication
- And motor complications (dyskinesias and/or motor fluctuations) for a minimum of 4 months (recent onset) or longer-standing

Goal Oriented Consent

Be sure to discuss:
- Goals
- Expectations
- Family and social considerations
- DBS should only be done on the right patient and for the right reasons!!!
Some Keys to DBS Success for PD

Appropriate Patient Selection*

Some Predictors of Potential Benefit:
- Response to Dopaminergic Therapy Predicts Response to DBS
- Pre-operative ON/OFF evaluation: improvement in motor UPDRS¹

Good Outcomes Follow:
- Appropriate patient selection
- Optimal placement of DBS leads
- Optimal post-operative patient management

Some Predictors of Potential Benefit:
- Response to Dopaminergic Therapy Predicts Response to DBS


Professionals Involved
- Neurology
- Neuropsychology
- Neurosurgeon
- Rehabilitation
- Psychiatry
- Nursing

Emphasis During Evaluation
- Confirm Diagnosis, optimize medications if needed
- Review potential benefit, risks, safety and alternatives
- Review mood, cognition and social support system
- Establish strengths and weaknesses, treat and optimize physical function
- Long term care overview

Evaluation for DBS

DBS Therapy
Product Overview and Surgical Procedure

DBS Therapy: Implantable Components
- Lead wire
- Extension wire
- Neurostimulator* (implantable pulse generator)

External Components

- N’Vision Clinical Programmer
- Activa® DBS Patient Programmer
- Activa® DBS Patient Programmer Antenna

Surgical Technique

- Stereotactic frame placement or frameless stereotaxy
- Targeting
  - Imaging
  - Stereotactic targeting
  - Physiologic targeting (microelectrode recording and stimulation)
- Electrode placement
- Pulse generator implantation

Surgical Technique: Targeting

- Sophisticated imaging and software enables precise targeting for optimal outcomes and minimal risk
- Microelectrode recording (MER) offers additional levels of verification of lead location

Surgical Technique: Microelectrode Recording

- STN
- Border
- Border/STN

Sagittal Section Through the Thalamus
**Surgical Technique: DBS Lead Placement**

- Lead wire placed in motor territory of nucleus
- Lead wire has four electrodes
- Four electrodes allow the clinician to customize stimulation during post-operative programming

**Surgical Technique: Neurostimulator* Placement**

- Typically placed below clavicle
- Neurostimulator attaches to the extension wire that connects to the lead wire

**Medtronic MR Conditional DBS Systems**

*Medtronic DBS systems are MR Conditional and safe in the MR environment as long as certain conditions are met. If the conditions are not met, a significant risk is tissue lesions from component heating, especially at the lead electrodes, resulting in serious and permanent injury including coma, paralysis, or death. Refer to [www.medtronic.com/mri](http://www.medtronic.com/mri) for a complete list of conditions.
Post-Op DBS Management

- Programming of neurostimulator and monitoring of side effects
- Initiate post operative therapy
  - Physical therapy
  - Occupational therapy
  - Speech therapy
- Monitoring hardware integrity and battery status

Device Programming

- Initial device programming: Identifying and programming optimal stimulation parameters during the first several months
- Maintenance device programming: Titrating stimulation as needed over time
- Patient programming is reimbursed

Additional Movement Disorder Treatments

- Physical Therapy
  - Provide feedback to physician on dyskinesia, tremor, rigidity and akinesia
  - Posture and ROM Exercises
  - Strengthening and balance retraining
  - Gait training
- Occupational Therapy
  - Provide feedback about dyskinesia, rigidity and tremor
  - ADLs and need for assistive devices
  - Strengthening
- Speech Language Therapy
  - Optimize speech before and after DBS
  - Monitors swallowing function as needed

Rehab Goals

- Functional mobility (gait, transfers)
- Functional ADLs
- Improve posture and balance
- Improve speech/vocalization
- Improve strength and joint mobility
- Prevent aspiration
- Bowel and bladder continence/function
- Safe Environment
- Patient and family education
- Establish home or community exercise program
Questions

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