Movement Disorders-
Parkinson’s Disease

Fahed Saada, MD
March 8th, 2019
48th Family Medicine Refresher Course
St. Joseph’s Health
Disclosure

• ACADIA Pharmaceuticals
Objectives

- Review the classification of tremors
- Provide videos of common tremors
- Treatment option
- Discuss Parkinson’s Disease
- Name the tremor
Tremor

• Involuntary, rhythmic, oscillatory movement of a body part
  • Axis I: Clinical Features
    • Isolated tremor syndrome
    • Combined tremor syndrome
  • Axis II:
    • Etiology

Bhatia et al, Movement Disorder, 2017
Tremor

Axis 1: Clinical features

- Historical features
  - Age at onset
  - Temporal onset and evolution
  - Past medical history
  - Family history
  - Alcohol and drug sensitivity

- Tremor characteristics
  - Body distribution
  - Activation conditions
  - Tremor frequency

- Associated signs
  - Signs of systemic illness
  - Neurologic signs
  - Soft signs

- Additional laboratory tests
  - Electrophysiological tests
  - Structural imaging
  - Receptor imaging
  - Serum and tissue biomarkers

Bhatia et al, Movement Disorder, 2017
Tremor

Axis 2: etiology

- Acquired
- Genetically defined
- Idiopathic
  - Familial
  - Sporadic

Bhatia et al, Movement Disorder, 2017
Action Tremor

• Posture tremor

• Kinetic tremor
  • Simple
  • Task-specific
  • Intention
  • Isometric
Physiologic Tremor

- Low amplitude, high frequency
  8-12 Hz
- May be enhanced (more visible)
  - Emotional states
  - Muscle fatigue and exercise
  - Medical condition
  - Alcohol intoxication, alcohol and BDZ withdrawal
  - Drugs (i.e. cocaine)
  - Medications (i.e., VPA, SSRIs, Lithium)
<table>
<thead>
<tr>
<th>DRUG CATEGORY</th>
<th>EXAMPLES</th>
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</thead>
<tbody>
<tr>
<td>β-adrenergic agonists</td>
<td>Albuterol, isoproterenol, theophylline</td>
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<td>Amphetamines/ stimulants</td>
<td>Dextroamphetamine/amphetamine, methylphenidate</td>
</tr>
<tr>
<td>Anti-epileptic drugs</td>
<td>Carbamazepine, valproate sodium</td>
</tr>
<tr>
<td>Chemotherapeutic agents</td>
<td>Cisplatin, thalidomide, tamoxifen, vincristine</td>
</tr>
<tr>
<td>Hormone therapy</td>
<td>Levothyroxine</td>
</tr>
<tr>
<td>Lithium</td>
<td></td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>Haloperidol, olanzapine, risperidone</td>
</tr>
<tr>
<td>Serotonin selective reuptake inhibitors</td>
<td>Paroxetine, fluvoxamine</td>
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</table>
Physiologic Tremor
Essential Tremor

• New Classification- Syndromes
  • ET: $\geq 3$ years of isolated tremor with b/l tremor in upper extremities
  • ET plus: tremor + other movement/neurological signs
  • Isolated posture/kinetic tremor: <3 years

• Exclusion criteria
  • Isolated focal voice/head tremor
  • $>12$ Hz orthostatic tremor
  • Task and position specific tremors
  • Sudden onset, step-wise progression
Essential Tremor Syndromes

• Bilateral action (Kinetic +/- postural)
  • Involves hands and forearms
  • Mild asymmetry often present
  • 4-10 Hz

• Insidious onset, slowly progressive
  • Increase amplitude, decreased frequency (Hellwig, 2009)
  • Intention tremor increases with disease duration
  • Spread to neck (titubation) and voice
Essential Tremor

• Neck: Present in ~ 50% of ET patients with disease >20 years (Whaley, 2007)
  • More common in women- 6x more likely (Handesty, 2004)
  • Less common in children (Tan, 2006)
  • “yes-yes” or ”no-no”
  • Agnosia to tremor ~ 49% (Louis, 2016)
  • May be induced with phonation (Wright, 2013)
  • “Head snap” (Sternberg, 2013)

• Voice: ~ 10-25% of ET patients
  • More common in women
  • May cause fluctuations in voice
Essential Tremor Syndromes

• Younger onset
  • Most likely to have family history
    • 50% of adults have a family history
    • ~90% of children have a family history
  • More likely to improve with alcohol consumption

• Neurodegenerative?
Essential Tremor
Essential Tremor Video:
## Treatment of ET

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>10–320 mg/d</td>
</tr>
<tr>
<td>Primidone</td>
<td>25–750 mg/d</td>
</tr>
<tr>
<td>Topiramate</td>
<td>25–300 mg/d</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>100–1800 mg/d</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>0.125–3 mg/d</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>0.5–4 mg/d</td>
</tr>
</tbody>
</table>
Tremors in Dystonia
Definition of Dystonia

• Sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both
• Typically patterned, twisting, and may be tremulous
• Can be worse with voluntary action and associated with overflow muscle activation

Albanese, et al. Mov Disord. 2013
Nomenclature by Distribution

- Focal dystonia
  - Blepharospasm
  - Oromandibular dystonia
  - Spasmodic dysphonia
  - Cervical dystonia
  - Brachial dystonia
  - Foot dystonia
Nomenclature by Distribution

Segmental dystonia
- Craniocervical dystonia
- Hemi-dystonia
Signs suggestive of dystonia

- Starts focally and may progress to other regions
- Activation of distant muscle groups
- Sensory tricks (geste antagoniste)
- Abnormal postures
- Directionality (most common in dystonia)
Sensory trick in Cervical Dystonia
Tremor in Parkinson’s Disease
Parkinson’s disease (PD)

• Age of onset
  • Typically > 50 years

• Tremor is present in the majority of idiopathic PD

• Tremulous PD may be associated with a milder course

• Male to female ratio
  • 2:1
Many people are suffering
Parkinson’s Disease

• Diagnostic Criteria- Validated Clinical Criteria
  • Bradykinesia
  • Muscle Rigidity
  • Resting tremor
  • Postural instability
PD Tremor: Writing sample

Parkinson’s disease
Rest Tremor
PD: Supportive Diagnostic Criteria

- Excellent levodopa response
- Unilateral Onset
- Persistent asymmetry
- Rest tremor
- Progressive disorder
- Levodopa response for at least five years
- Levodopa induced chorea/dyskinesia
- At least 10 years of disease
- Olfactory changes

PD Tremor

- 4-6 Hz resting tremor
- “Pill Rolling” may only have finger tremor
- “Re-emergent” tremor
- Lip, jaw, tongue, tremor seen mostly with PD
- Decrease in amplitude during target directed movements
The Atypical Parkinsonian Syndromes

- These rare conditions constitute a minority of the patients
- Tremor is infrequent in these disorders
- Tremor may have varying amplitudes, frequencies, and associated findings (myoclonus)
- A classic 4-6 Hz tremor is not common in the atypical parkinsonian syndromes
Tremor and Parkinsonism

- **Vascular Parkinsonism** (Kalra, 2010)
  - Postural tremor most common tremor type
- **DLB** (Onofrj, 2013)
  - Head and face tremor more frequent than PD
  - Rest tremor “mixed” postural and action tremor
  - Standing and walking can elicit hand tremor
  - Diffusion of tremor into legs upon standing
Tremor and Parkinsonism

• PSP
  • PSP-P most common 20% classic resting tremor
  • Early gait and balance
  • Supranuclear palsy
  • Imaging
    • “Hummingbird Sign”

Tremor and Parkinsonism

• MSA:
  • < 10% pill rolling tremor
  • Dystonia and myoclonus may resemble tremor
  • Dysautonomia
  • Ataxia
  • Imaging
    • “Hot-crossed bun sign”

Rinne JO. Et al Ann Neurol. 1995
Pearls for distinguishing ET vs PD

• Tremor
  • Arm
    • Re-emergence in PD
    • Intention tremor in ET
    • Kinetic amplitude > posture in ET, posture > Kinetic in PD
  • Leg- PD
  • Jaw
    • Predominately PD
    • In ET, more prominent when mouth is moving
• Neck
  • Predominately ET
  • Lie patient down, will persist in PD and dissipate in ET
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Mechanism</th>
<th>Initial Dosage</th>
<th>Maintenance Dosage</th>
<th>Major Side Effects</th>
</tr>
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<tbody>
<tr>
<td>Amantadine</td>
<td>Multiple (N)-methyl-(L)-aspartate (NMDA) receptor antagonist, potentiates dopamine release)</td>
<td>100 mg 2 times a day</td>
<td>100 mg 2 to 3 times a day</td>
<td>Nausea, confusion, hallucinations, leg edema, livedo reticularis</td>
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<td>Benztpmine</td>
<td>Anticholinergic</td>
<td>0.5 mg every night at bedtime</td>
<td>1 mg 2 to 3 times a day</td>
<td>Dry mouth, reduced cognition, urinary retention, hallucinations, blurry vision, constipation</td>
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<td>Bromocriptine</td>
<td>Dopamine agonist (\text{ergot derived)}}</td>
<td>1.25 mg 2 times a day</td>
<td>5-10 mg 2 to 3 times a day</td>
<td>Nausea, impulse control disorders, hallucinations, orthostatic hypotension, fibrosis, sleep attacks</td>
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<td>Carbidopa/levodopa</td>
<td>Aromatic amino acid decarboxylase inhibitor/dopamine precursor</td>
<td>25 mg/100 mg 2 times a day</td>
<td>Variable</td>
<td>Nausea, orthostatic hypotension, confusion, hallucinations, dizziness</td>
</tr>
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<td>Carbidopa/levodopa extended release capsules</td>
<td>Converted to dopamine</td>
<td>23.75 mg/95 mg 3 times a day</td>
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<td>Pramipexole</td>
<td>Dopamine agonist (\text{non-ergot derived)}}</td>
<td>0.125 mg 2 to 3 times a day</td>
<td>0.5-1.5 mg 2 to 3 times a day</td>
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<td>Pramipexole extended release</td>
<td>Dopamine agonist (\text{non-ergot derived)}}</td>
<td>0.375 mg/d</td>
<td>1.5-4.5 mg/d</td>
<td>Nausea, hallucinations, impulse control disorders, orthostatic hypotension, sleep attacks, leg edema</td>
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<td>Rasagiline</td>
<td>Monoamine oxidase type 8 inhibitor</td>
<td>0.5-1 mg/d</td>
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<td>Ropinirole</td>
<td>Dopamine agonist (\text{non-ergot derived)}}</td>
<td>0.25 mg 2 to 3 times a day</td>
<td>2-8 mg 2 to 3 times a day</td>
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<td>Ropinirole extended release</td>
<td>Dopamine agonist (\text{non-ergot derived)}}</td>
<td>2 mg/d</td>
<td>8-24 mg/d</td>
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<td>Rotigotine</td>
<td>Dopamine agonist (\text{non-ergot derived)}}</td>
<td>2 mg/d</td>
<td>6 mg per 24 hours (maximum dose)</td>
<td>Nausea, hallucinations, impulse control disorders, orthostatic hypotension, sleep attacks, leg edema, and may have patch application site reactions</td>
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<td>Selegiline</td>
<td>Monoamine oxidase type B inhibitor</td>
<td>5 mg 1 to 2 times a day</td>
<td>5 mg 2 times a day</td>
<td>Confusion, hallucinations, orthostatic hypotension, insomnia, nausea, benign cardiac arrhythmias</td>
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<tr>
<td>Trifluperidyl</td>
<td>Anticholinergic</td>
<td>2 mg/d</td>
<td>2 mg 2 to 3 times a day</td>
<td>Dry mouth, reduced cognition, urinary retention, hallucinations, blurry vision, constipation</td>
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**Treating the Motor Symptoms of Parkinson Disease**

Morgan, John C.; Fox, Susan H.


doi: 10.1212/CON.0000000000000355
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<td>Class</td>
<td>Dose (daily)</td>
<td>Dose (as needed)</td>
<td>Common Side Effects</td>
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Deep Brain Stimulation

Deep-brain stimulation
Delivering electrical pulses to precisely targeted areas helps the brain maintain motor control lost to Parkinson’s disease. A look at the procedure:

1. Using MRI or computer imaging, a neurosurgeon places wire electrodes in the subthalamic nucleus on both sides of the brain.

2. The leads are inserted through holes in the skull. Extension wires are threaded under the skin and down the side of the patient’s head, then connected to a battery pack implanted in the patient’s chest.

3. The battery pack sends more than 100 electrical pulses a second to the brain. The electrical stimulation helps control the tremors and other abnormal movements of Parkinson’s disease and other movement disorders.
The four simple words
• “you have Parkinson’s Disease”
Pearls to Diagnosis

- Spend time when you render a diagnosis
- 1/5 (20%) will not have tremor
- When “on” meds could look normal
- Be careful taking people off meds because you suspect a functional movement disorder
- DAT scans are overused
Does seeing a neurologist matter?

Neurologist-associated reduction in PD-related hospitalizations and health care expenditures

Objective: To investigate the impact of neurologist care on Parkinson disease (PD)-related hospitalizations. Recent data indicate that neurologist treatment in PD may be associated with improved survival, yet is underutilized. Factors contributing to this improved survival remain unknown, but may be due in part to optimal disease treatment or avoidance of disease-related complications.

Methods: This was a retrospective cohort study of Medicare beneficiaries diagnosed with PD in 2002 and still living in 2006. Hospitalization for PD-related (neurodegenerative disease, psychiatric) reasons was the primary outcome measure and the dependent variable in a multivariable logistic regression.

Neurologist care in Parkinson disease

A utilization, outcomes, and survival study

Objective: To investigate the utilization of neurologist providers in the treatment of patients with Parkinson disease (PD) in the United States and determine whether neurologist treatment is associated with improved clinical outcomes.

Methods: This was a retrospective observational cohort study of Medicare beneficiaries with PD in the year 2002. Multivariable logistic regression was used to determine which patient characteristics, including neurologist care, were associated with survival and decreased hospitalization.
Coordination of Care
“Lack of activity destroys the good condition of every human being, while movement and methodical physical exercise save and preserve it.” - Plato
Identify and Treat Impulse Control Disorder

Shopping, gambling, binge eating, hobbyism, others

Patient may “like the behavior” and not have insight

Be careful to have a monitoring plan when start a dopamine agonist

Two studies that suggest the patch (Rotigotine) may have less ICD
Pearl for Primary Care Providers

What affects quality of life more? Motor or Non-motor Parkinson’s Symptoms
Medication

• “The right thing at the wrong time is the wrong thing.” – Joshua Harris
Avoid the Hospital

• Big 3 safe Psychosis Drugs:
  • Clozapine
  • Quetiapine
  • Pimavanserin

3 out of 4 Parkinson’s patients don’t get their medications on time every time.
Last Tremor
Functional Tremor

• Neurologist who MUST diagnose (that’s if you don’t want to diagnose)
• 10-20% cases in movement disorder centers are functional
• More common in women
• May be co-morbid with organic disease (10% cases)
• Red flags:
  • Acute onset, following physical injury, emotional stress
  • Rapid generalization
  • Maximum deficit at onset
  • Periods of remission
  • Other somatic complaints
  • Employment in the health profession

Hellet, Parkinsonism Relat Disorder, 2016.
Functional Tremor

- Tremor at rest, posture, and action are the same
- Variation in amplitude, frequency, and direction
- Selective disability (exam starts in examination room)
- Suggestibility

Treatment:
- Minimize testing
- Cognitive behavior therapy
- Reassurance
Conclusion

• The diagnosis of tremor disorders is challenging
• Approach involves history and careful neurologic examination
• Generating a differential diagnosis (action or rest)
• Arriving at the correct diagnosis is often based on pattern recognition
References

• Bhatia et al, Movement Disorder. 2017
• Hellwig et al, Clin Neuroophysiolog. 2009
• Tan et al, Mov Disord. 2006
• Louis et al, Continuum 2016
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• Rinne JO. Et al, Ann Neurol. 1995