A brief update on the diagnosis and management of tremor disorders

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Plan

• Diagnosis of upper limb tremor
  Review:  Clinical diagnosis of tremor
  What’s new:  DATscan

• Management of essential tremor
  Review:  Drugs and non-pharmacological treatments
  What’s new:  Deep brain stimulation
Tremor

- Involuntary oscillating movement of a body part
- Produced by rhythmic contraction of opposing groups of muscles
Videos of different tremors
How to distinguish essential tremor from Parkinson’s disease clinically

<table>
<thead>
<tr>
<th>Parkinson’s disease</th>
<th>Essential tremor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest tremor</td>
<td>Postural/kinetic tremor</td>
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<tr>
<td>Postural/re-emergent</td>
<td></td>
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<tr>
<td>Typically unilateral/asymmetric</td>
<td>Typically bilateral</td>
</tr>
<tr>
<td>Leg, jaw, lip tremor</td>
<td>Head, voice tremor</td>
</tr>
<tr>
<td>Other signs PD</td>
<td>No extrapyramidal or cerebellar features</td>
</tr>
<tr>
<td>L-DOPA responsive</td>
<td>EtOH, propanolol responsive</td>
</tr>
</tbody>
</table>
DATscan

- Ioflupane – $^{123}\text{I}$-labeled ligand for dopamine transporter found on dopaminergic terminals in striatum
- $^{123}\text{I}$ is a gamma-emitting isotope that can be imaged with a gamma camera
- Loss of the striatal DATscan signal is indicative of degeneration of dopaminergic terminals
- FDA approved to assist in evaluation of adult patients with suspected Parkinsonism, Jan 2011
Drugs that interfere with DATscan

- Drugs that bind to the dopamine transporter with high affinity may interfere with imaging:
  - Amphetamine, methamphetamine
  - Benztropine
  - Bupropion
  - Buspirone
  - Cocaine
  - Methylphenidate
  - Selegiline
  - Sertraline

- Other SSRIs may increase or decrease binding

- The impact of dopamine agonists and antagonists upon DATscan imaging results has not been established
DATscan pitfalls: negative scan early in course of Parkinson’s disease

- Subjects without evidence of dopaminergic deficit “SWEDDs”
- 16 patients with asymmetric arm tremor and normal scan
- 5 year follow up
- 2/16 (12.5%) had abnormal scan

Batla et al Movement Disorders 2014
Summary: DATscan

• May be useful in diagnosing unusual tremors

• My experience so far (small numbers) suggests DATscan may be providing the same information as the presence of bradykinesia or rigidity on the examination

• Some patients are helped by a confirmatory test that makes it easier for them to accept the diagnosis

• A negative scan does not exclude Parkinson’s disease, but makes it less likely
Treatment of essential tremor

- Withdraw caffeine or drugs exacerbating tremor
- Consider mechanical aids
- Consider drugs to suppress tremor
- Consider DBS
Drugs that cause tremor

- Caffeine, stimulants
- β2 agonists
- Antidepressants (SSRI, TCA, lithium)
- Antiepileptics (especially valproate*)
- Cardiac drugs (nifedipine, amiodarone*)
- Neuroleptics*
- Antiemetics (metoclopramide*, prochlorperazine*)
- Immunosuppressants (cyclosporin, tacrolimus)
- Drug withdrawal (BDZ, EtOH)

* may also cause Parkinsonism
AAN recommendation levels

- **A** = Established as effective, ineffective or harmful.
- **B** = Probably effective, ineffective or harmful.
- **C** = Possibly effective, ineffective or harmful.
- **U** = Data inadequate or conflicting; given current knowledge, treatment is unproven.
Treatment of essential tremor:
(AAN practice parameter)

(Level A)
- Propranolol
- Primidone

(Level B)
- Atenolol, nadolol, sotalol
- Gabapentin, topiramate
- Nimodipine
- Clonazepam, alprazolam
- Botulinum toxin

Probably equally efficacious (Level B)
AAN essential tremor management – changes between 2005 and 2014

• Levetiracetam and 3,4-diaminopyrididine should not be considered for treatment of limb tremor in ET (Level B).

• Clinicians may choose not to consider flunarizine for treatment of limb tremor in ET (Level C).

• The evidence is insufficient to make recommendations regarding the use of pregabalin, zonisamide, or clozapine (Level U).
Indications and contraindications for deep brain stimulation in essential tremor

**Indications:**
- Definite clinical diagnosis of ET
- Refractory to medication and/or limiting drug side effects
- Normal MRI
- Normal neuropsychological status

**Contraindications:**
- Dementia (MCI is considered on case-by-case basis)
- Other illness/not fit for surgery

*Slide courtesy of: Mark Richardson MD PhD (Department of Neurosurgery)*
Outcomes from deep brain stimulation for essential tremor

Expected benefits:
• Multiple studies have demonstrated an average of 80% improvement in upper extremity tremor
• Unlike drug treatments, head and voice tremor often also improve

Risks:
• Intracerebral hemorrhage  1% per side
• Infection  5%
• Cognitive/affective changes  5%

Slide courtesy of: Mark Richardson MD PhD (Department of Neurosurgery)
AAN recommendations

• DBS of the VIM thalamic nucleus may be used to treat medically refractory limb tremor in ET (Level C).

• There is insufficient evidence to make recommendations regarding the use of thalamic DBS for head or voice tremor (Level U).
Summary of DBS in essential tremor

• Can be highly effective in patients refractory to medical therapy
• Fairly low surgical risk in otherwise healthy subjects
• Can be a ‘game-changer’ in patients whose lives are made miserable by severe tremor