Sensory Phenomena in Movement Disorders

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Neurology/Neurosurgery Grand Rounds
KU School of Medicine
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Disclosures

• I have not received any financial, professional or personal benefit from any third-party entity regarding any of the topics I will be discussing today.

• Some of the treatments discussed today are considered off-label usage by the Food and Drug Administration (FDA).
Objectives

• Increase awareness of sensory disturbances found in various movement disorders to offer appropriate treatment.
• Demonstrate familiarity with treatment options of sensory phenomena relevant to movement disorders.
Outline

• Review of somatosensory input
• Feedback from sensory input to motor output
• Examples of sensory disturbance in movement disorders
• Assessment and rating scales
• Treatment of akathisia, tics and restless legs syndrome
Somatosensory Input

- **first order neuron**
  - trigeminal nerve ganglion, dorsal root ganglion of spinal nerve
  - connects peripheral face and body with second order neuron
Somatosensory Input

- **second order neuron**
  - brainstem nuclei, spinal nuclei
  - connects first order neuron with ventral posterior nucleus (VPN) of the thalamus

Courtesy: Clinicalgate.com
Somatosensory Input

- **third order neuron**
  - connects VPN to the post-central gyrus (parietal lobe)

Courtesy: Clinicalgate.com
Sensorimotor Integration

- patients with Parkinson’s disease depend on external sensory cues to initiate and execute movement especially visual and kinesthetic input
- impairment in proprioception likely plays a role in postural instability and limited body awareness in Parkinson’s disease
- when moving both arms simultaneously, there is a tendency for a patient with Parkinson’s disease to overestimate affected limb movement

Sensory Changes in Parkinsonism

- sensory cues can help overcome freezing
- shoulder pain was 21 times more common in Parkinson’s disease patients than controls (small sample of 50 patients)
- shoulder pain can precede motor changes in Parkinson’s disease by several years
- loss of olfactory sense
- endocannabinoids, endorphins and other neuropeptides are found in greater amounts in the basal ganglia

Sensory Changes in Parkinsonism

- akathisia can occur when wearing off from levodopa
- vestibular dysfunction is more common as measured by electronystagmography (ENG) and bithermal caloric tests
- absent or decreased vestibular responses were associated with increased postural instability
- kinesthetic dysfunction especially awareness of dyskinesia
- agraphhesthesia, astereognosia, proprioceptive loss in corticobasal degeneration
- alien limb phenomenon “my arm has a mind of it’s own”

Sensory Changes in Dystonia

- neck pain in cervical dystonia
- photosensitivity/other eye symptoms in blepharospasm
- alleviating maneuvers
  (sensory tricks vs. *geste antagoniste*)
- kinesthetic dysfunction
- abnormal temporal and spatial discrimination
- **peripherally-induced dystonia** vs. parkinsonism
  - controversial
  - associated with increased pain and paresthesias
  - pathogenesis resembles complex regional pain syndrome and phantom limb pain

Sensory Changes in Chorea/Dyskinesia

- visual depth perception and emotional recognition are impaired in Huntington’s disease
- operational, tactical and visuo-integrative impairment correlates with pass-fail driving tests in Huntington’s disease
- many patients with Huntington’s disease are aware of a global movement problem but tend to notice rigidity, gait problems and even bradykinesia more than choreiform movements unless severe
- Parkinson’s disease patients are often unaware of levodopa-induced dyskinesia

Bora E et al. (2016) *Behav Brain Res* 297:131-140.
Sensory Changes in Chorea/Dyskinesia

• oral and genital pain are more commonly found in patients with tardive dyskinesia
• painful/painless legs moving toes syndrome
• painful arms moving fingers syndrome
• pseudoathetosis vs. athetosis
• thought to be related to central processing of peripheral nerve dysfunction although myelopathy has also been implicated
• **phantom dyskinesia** involves perception of involuntary movement in an amputated limb with persistent stump chorea

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Tourette Syndrome

Tourette Syndrome

Akathisia

- a feeling of inner restlessness and a compelling need to be in constant motion
- first described by neuropsychologist and neuropathologist Ladislav Haškovec (1901)
- from Greek \( a \) (not) + \( kathizein \) (to sit)
- unable to sit still
- examples:
  - rocking while standing or sitting
  - lifting the feet (marching in place)
  - tapping the feet
  - fidgeting
  - shifting
  - pacing

Causes of Akathisia

- acute serotonin syndrome
- can be related to subacute to chronic use of:
  - dopamine antagonists (antipsychotics and anti-emetics)
  - selective serotonin reuptake inhibitors
  - tricyclic antidepressants
  - trazodone
  - mirtazapine
- withdrawal from:
  - barbiturates
  - benzodiazepines
  - cocaine
  - opioids
Restless Legs Syndrome (RLS)

- called Willis-Ekbom disease (WED) as of March 2013 after Sir Thomas Willis (1685) and Karl-Axel Ekbom (1944)
- Theodor Wittmaack – Anxietas tibiarum (1861)
- uncomfortable sensations predominantly in the legs resulting in an urge to move the legs to relieve the sensations
- worse at rest; may occur with sitting or lying down
- may improve with activity (unless severe)
- worse in the evening or at night
- associated with periodic limb movements of sleep (80-90%)

Barnes Akathisia Scale

Barnes Akathisia Rating Scale (BARS)

Instructions: Patient should be observed while they are seated, and then standing while engaged in neutral conversation (for a minimum of two minutes in each position). Symptoms observed in other situations, for example while engaged in activity on the ward, may also be rated. Subsequently, the subjective phenomena should be elicited by direct questioning.

Objective

0  Normal, occasional fidgety movements of the limbs
1  Presence of characteristic restless movements: shuffling or tramping movements of the legs/feet, or swinging of one leg while sitting, and/or rocking from foot to foot or “walking on the spot” when standing, but movements present for less than half the time observed
2  Observed phenomena, as described in (1) above, which are present for at least half the observation period
3  Patient is constantly engaged in characteristic restless movements, and/or has the inability to remain seated or standing without walking or pacing, during the time observed
Barnes Akathisia Scale

Subjective

Awareness of restlessness
0 Absence of inner restlessness
1 Non-specific sense of inner restlessness
2 The patient is aware of an inability to keep the legs still, or a desire to move the legs, and/or complains of inner restlessness aggravated specifically by being required to stand still
3 Awareness of intense compulsion to move most of the time and/or reports strong desire to walk or pace most of the time

Distress related to restlessness
0 No distress
1 Mild
2 Moderate
3 Severe
Barnes Akathisia Scale

Global Clinical Assessment of Akathisia

0  Absent. No evidence of awareness of restlessness. Observation of characteristic movements of akathisia in the absence of a subjective report of inner restlessness or compulsive desire to move the legs should be classified as pseudoakathisia

1  Questionable. Non-specific inner tension and fidgety movements

2  Mild akathisia. Awareness of restlessness in the legs and/or inner restlessness worse when required to stand still. Fidgety movements present, but characteristic restless movements of akathisia not necessarily observed. Condition causes little or no distress.

3  Moderate akathisia. Awareness of restlessness as described for mild akathisia above, combined with characteristic restless movements such as rocking from foot to foot when standing. Patient finds the condition distressing

4  Marked akathisia. Subjective experience of restlessness includes a compulsive desire to walk or pace. However, the patient is able to remain seated for at least five minutes. The condition is obviously distressing.

5  Severe akathisia. The patient reports a strong compulsion to pace up and down most of the time. Unable to sit or lie down for more than a few minutes. Constant restlessness which is associated with intense distress and insomnia.
Other Rating Scales / Limitations

- Abnormal Involuntary Movements Scale (AIMS)
  - does ask about awareness

- Movement Disorder Society Unified Parkinson’s Disease Rating Scale (MDS-UPDRS)
  - inquires about many non-motor symptoms related to sensory disturbance

- Non-Motor Symptom Scale (NMSS) for Parkinson’s disease

- Unified Dystonia Rating Scale (UDRS)

- Unified Dyskinesia Rating Scale (UDysRS)

- Yale Tic Severity Rating Scale (YTSRS)
  - considers ability of tics to interfere with function
### AAN Guidelines for RLS

#### Table: Evidence for Non-prescription Drug Treatment Options

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Strength of Evidence*</th>
<th>Conclusion/Recommendation</th>
<th>Adverse Events (AEs)</th>
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<tbody>
<tr>
<td>Pneumatic compression</td>
<td>Moderate</td>
<td>Pneumatic compression is likely effective in the treatment of patients with primary moderate to severe RLS.</td>
<td>No AEs were reported.</td>
</tr>
<tr>
<td>Near-infrared spectroscopy (NIRS)</td>
<td>Weak</td>
<td>NIRS is possibly effective in the treatment of primary moderate to severe RLS.</td>
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<td>Repetitive transcranial magnetic stimulation (rTMS)</td>
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<td>rTMS is possibly effective in the treatment of primary moderate to severe RLS.</td>
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<td>Vibrating pads</td>
<td></td>
<td>Vibrating pads are possibly ineffective in treating RLS symptoms.</td>
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<tr>
<td>Transcranial direct current stimulation (tDCCS)</td>
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<td>tDCCS is probably ineffective for improving RLS in women who have never taken medication for RLS.</td>
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AAN Guidelines for Tardive Syndromes

Data are insufficient to support or refute use of acetazolamide, bromocriptine, thiamine, baclofen, vitamin E, vitamin B6, selegiline, clozapine, olanzapine, melatonin, nifedipine, fluperlapine, sulpiride, flupenthixol, thiopropazate, haloperidol, levetiracetam, quetiapine, ziprasidone, sertindole, aripiprazole, buspirone, yi-gan san, biperiden discontinuation, botulinum toxin type A, electroconvulsive therapy, α-methyldopa, reserpine, and pallidal deep brain stimulation as TDS treatments (Level U). Data are insufficient to support or refute TDS treatment by withdrawing causative agents or switching from typical to atypical DRBA (Level U).

No AAN Guideline for Tourette Syndrome (yet!)
AAN Guidelines for RLS

In moderate to severe primary restless legs syndrome (RLS), clinicians should consider prescribing a pharmacologic agent to reduce RLS symptoms:

<table>
<thead>
<tr>
<th>Strong Evidence</th>
<th>Pramipexole, rotigotine, cabergoline*, and gabapentin enacarbil (Level A).</th>
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<tr>
<td>Moderate Evidence</td>
<td>Ropinirole, pregabalin, and IV ferric carboxymaltose, and in patients with serum ferritin ≤ 75 mcg/l, ferrous sulfate with vitamin C (Level B).</td>
</tr>
<tr>
<td>Weak Evidence</td>
<td>Levodopa (Level C).</td>
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<td>Cabergoline* instead of levodopa (Level C).</td>
</tr>
<tr>
<td>Insufficient Evidence</td>
<td>Preferential use of pregabalin instead of pramipexole (Level U).</td>
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<td>Gabapentin, IV iron sucrose, oxycodone, clonazepam, bupropion, clonidine, selenium, rifaximin, botulinum neurotoxin, valproic acid, carbamazepine, or valerian in the treatment of RLS (Level U).</td>
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* Cabergoline is rarely used in clinical practice for RLS because of a risk of cardiac valvulopathy at higher doses.

## AAN Guidelines for RLS

**For patients with RLS who have not responded to other treatments:**

| Weak Evidence | Prolonged-release oxycodone/naloxone (where available) *(Level C)*, but potential benefits need to be weighed against known opioid risks. |

**For patients with primary RLS for whom clinicians want to target sleep, clinicians should consider prescribing a pharmacologic agent that improves objective or subjective sleep parameters (or both). Evidence supports agents to different extents for subjective and objective outcomes:**

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<td>Ropinirole, when targeting periodic limb movements of sleep (PLMS), specifically the Periodic Limb Movement Index (PLMI) as measured by polysomnography (PSG) <em>(Level A)</em>.</td>
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<td>Pramipexole, rotigotine, cabergoline*, and pregabalin, when targeting PLMS, specifically the PLMI as measured by PSG <em>(Level B)</em>.</td>
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<td>Ropinirole, gabapentin enacarbil, and pregabalin, for at least some objective sleep measures (e.g., total sleep time [TST], sleep efficiency, sleep latency, and wake after sleep onset [WASO]) <em>(Level B)</em>.</td>
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<td>Pregabalin instead of pramipexole, with regard to subjective sleep outcomes <em>(Level B)</em>.</td>
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<td>Rotigotine, with regard to subjective sleep measures <em>(Levels B and C)</em>.</td>
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Questions/Discussion

• Thank you!