Neuropsychiatric burden in Parkinson’s disease: insights from a tertiary referral center

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Disclosures

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Objectives

- Be able to outline primary ways in which motor dysfunction causes disability
- Be able to recognize the typical pattern of mild cognitive impairment and dementia in PD
- Be able to identify patterns of psychiatric impairment as related to medical and surgical therapy related to PD as well as PD itself
Pre-lecture questions

1. Motor fluctuations are significantly influenced by:
   a) too much dopaminergic medication
   b) age of onset
   c) fewer remaining dopaminergic neurons as disease advances
   d) all of the above
2. Mild cognitive impairment present at the time of presentation of motor symptoms constitutes a diagnosis of Lewy Body Dementia
   True
   False
Pre-lecture questions

3. Antipsychotic medications are an effective way to treatment impulse control disorders in PD patients
   True
   False
Case

- Ms. G is a 69 year old RH woman who began noticing a right handed resting tremor about 7 years prior
- 6-9 months later a right leg resting tremor developed
- 3 years later, shampooing, buttoning, cutting food becomes more tiresome writing becomes smaller
- Pramipexole 0.25mg twice daily, which helps restless legs symptoms as well as carbidopa/levodopa 25/100 1 tab twice daily- though these are not helpful for above sx's
- Reports vivid dreams, has fallen out of bed once, no hallucinations
Case (continued)

- Her exam shows:
  - normal extraocular movements
  - mild hypophonia
  - mild reduction of facial expression
  - persistent right arm and leg tremor while seated
  - reduction of finger taps on the right
  - reduction of armswing on the right while walking
Case (continued)

- Pramipexole is increased to tid, with modest response
- Later carbidopa/levodopa is increased to 1.5 tabs tid because stiffness and tremor return if doses are not taken precisely every 5 hours
- Two years later, while on carbidopa/levodopa 25/100 1.5 tabs tid and pramipexole, she looks more “restless” but she notices only “twitchiness” in her leg
- Over the years, a combination of adjunct medications are tried with little success
3 years later, she admits to gambling, losing $50,000, and having to apply for a reverse mortgage on her home.

Pramipexole is stopped.

Daughter reports she is less able to keep track of her medications.

She continues to have sudden freezing episodes when she is later for medications.

She more frequently expresses hopelessness and frustration in her visits.
Motor complications

- Wearing off
- Delayed kicking in
- Peak dose involuntary movements - dyskinesias
- Rarely, wearing off dyskinesia or so-called “diphasic dyskinesias”
Video
Figure 1 Chronic levodopa response: narrowing of the therapeutic window

The role of deep brain stimulation

- Deep brain stimulation of the subthalamic nucleus - widely accepted treatment for advanced PD (Weaver et al. 2009, Deuschl et al. 2006)

- Patients can often lower their medications doses

- Some cases of new impulse control disorders or suicide - relationship to surgery??
Correctly understanding disease progression is key to proper use of DBS

Characteristics favoring good outcome following DBS

- Significant impairment from motor fluctuations, tremor, dyskinesia
- Excellent levodopa responsiveness
- No or little significant axial motor impairment
- No cognitive impairment
- No uncontrolled psychiatric disease
Cognitive impairment: how defined?

- Working memory, executive function, processing speed
- Practical assessment includes Montreal Cognitive Assessment (MOCA) score <26
- Mild cognitive impairment is present more often than previously appreciated in early PD
  - 21% in early de novo patients, increasing to 35% by 2 years (de la Riva et al. 2014)
- Can progress to frank dementia with other cortical signs such as amnestic impairment, visuospatial dysfunction
- Neuropsychological testing helpful to assess domains affected and how best to address
Risk factors at baseline

- **age** (Aarsland et al. 2010)
- **greater motor severity, falls and freezing** (Aarsland et al. 2010; Anang et al. 2014)
- **presence of REM behavior disorder** (Barton et al. 2010; Nomura et al. 2013)
- **worse olfaction** (Postuma et al. 2008; Baba et al. 2012)
- ** autonomonic dysfunction** (Kim et al. 2012; Pilleri et al. 2012; Anang et al. 2014)
- **Baseline MCI** (Pederson et al. 2013; Anang et al. 2014)
- **gait dysfunction** (Anang et al. 2014)
Mood disorders

- Depression is frequently cited as affected $\frac{1}{2}$ of all PD patients

- Rate of depression in early de novo untreated patients about 14%, increasing to 19% after 2 years (de la Riva et al. 2014)
  - Over 2/3 of patients with depression were not being treated

- Presence of depression/anxiety correlated with quality of life (Duncan et al. 2014)

- TCA possibly more efficacious than SSRI (Menza et al. 2009)
Other behavioral aspects

- Impulse control disorders
- Compulsive behaviors
- Dopamine dysregulation syndrome
Impulse control disorders
What is an impulse control disorder?

- The irresistible and uncontrollable drive or temptation to perform an action

- Examples include:
  - hypersexuality
  - excessive gambling
  - excessive spending
  - eating disorder
A conversation

“Do you gamble?”

“Never, doctor, gambling is the work of the devil!”

“Do you purchase lottery tickets?”

“All the time.”

“How many do you buy?”

“Several hundred dollars a week— it’s like a magnet and I can’t resist it.”
ICD: Prevalence and manifestations

- A large 46-center study in North America, n=3,090 (Weintraub et al. 2010)

- 1 in 7 patients with PD on dopamine replacement therapy

- Fairly equally divided among gambling, spending, sexual activity and excessive eating (4-5% each)

- Compare to 1% in general population
Risk factors

- Taking a dopamine agonist (2-3x risk)
  - Pramipexole (mirapex), ropinirole (requip), rotigotine (neupro) all are potent D2/D3 agonists
  - Possible difference in rates of ICD with rotigotine transdermal (Garcia-Ruiz et al. 2014)

- Being younger
- Being unmarried
- Having a family history of gambling problems
- Current smoker
Compulsive behaviors
Compulsive behaviors

- **Punding**
  - Intense, time-consuming preoccupation with seemingly aimless activities
    - assembling and reassembling doorknobs
    - lining up pebbles
More compulsive behaviors

- **Hobbyism**
  - Intense, time-consuming preoccupation with specific hobbies

- **Walkabout**
  - Aimless walking or driving

- Possibly more common with levodopa
Dopamine dysregulation syndrome (DDS)
DDS features

- Rare phenomenon of taking increasing quantities of dopamine replacement therapy (usually levodopa) despite:
  - Increasingly severe dyskinesias and more than adequate dosing to control their motor symptoms
  - Cyclical mood disorder or manic state
  - Development of a withdrawal like state
  - Signs of pathological use: drug hoarding, unwillingness to reduce medications
  - Interference in social and work life
Treatment and management

- Education and prevention
- Open communication with physician
- Removal of the offending drug
- May require referral to a psychiatrist or behavioral health specialist
- Depending upon the persistence of the problem, consider support groups (i.e. Gamblers Anonymous, Overeaters Anonymous, etc.)
Take-home points

- “On-off” motor fluctuations are more often a key driver of PD-related quality of life than treatment-related dyskinesias.

- Mild cognitive impairment can be present in early Parkinson’s disease, while frank dementia is not uncommon in advanced PD.

- Impulse control disorders affects up to 1 in 7 PD patients on dopamine agonists.
1. Motor fluctuations are significantly influenced by:
   a) too much dopaminergic medication
   b) age of onset
   c) fewer remaining dopaminergic neurons as disease advances
   d) all of the above
2. Mild cognitive impairment present at the time of presentation of motor symptoms constitutes a diagnosis of Lewy Body Dementia

True

False

MCI is seen in up to 20% of de novo PD patients
Post-lecture questions

3. Antipsychotic medications are an effective way to treat impulse control disorders in PD patients
   - True
   - False

Removal of the offending agent
Antipsychotics are most useful for management of psychosis