How will Parkinson’s Disease Affect Me?

*The Non-Motor Manifestations of Parkinson’s Disease*

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# Introduction

## Features of Parkinson's Disease

<table>
<thead>
<tr>
<th>Motor</th>
</tr>
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<tbody>
<tr>
<td>Bradykinesia</td>
</tr>
<tr>
<td>Rigidity</td>
</tr>
<tr>
<td>Tremor</td>
</tr>
<tr>
<td>Postural Instability</td>
</tr>
</tbody>
</table>

*Chaudhuri K. et al, Lancet, 2006*
## Introduction

<table>
<thead>
<tr>
<th>Motor</th>
<th>Non-Motor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradykinesia</td>
<td>Alteration in memory, mood, and thinking (neuropsychiatric)</td>
</tr>
<tr>
<td>Rigidity</td>
<td>Sleep Disorders</td>
</tr>
<tr>
<td>Tremor</td>
<td>Autonomic Symptoms</td>
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<td>Gastrointestinal Symptoms</td>
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*Chaudhuri K. et al, Lancet, 2006*
Why are we talking about the Non-Motor Symptoms?

- They are not commonly addressed by general neurologists but...
  1. These symptoms can impact your quality of life and can be overlooked
  2. Education can be empowering
     - These symptoms can be treated if addressed!
Prevalence of Non-Motor Symptoms

- Studies have established that Non-Motor Symptoms (NMS) occur in over 90% of patients across all stages of disease
  - Not just a sign of “normal aging”

Chaudhury K, et al. Mov Disord, 2006
Most Common Nonmotor Symptoms

<table>
<thead>
<tr>
<th>NMS</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dribbling of saliva</td>
<td>41.5%</td>
</tr>
<tr>
<td>Constipation</td>
<td>52.5%</td>
</tr>
<tr>
<td>Urgency</td>
<td>55.8%</td>
</tr>
<tr>
<td>Nocturia</td>
<td>61.9%</td>
</tr>
<tr>
<td>Memory</td>
<td>44.9%</td>
</tr>
<tr>
<td>Concentration</td>
<td>45.7%</td>
</tr>
<tr>
<td>Depression</td>
<td>50.1%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>45.3%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>45.7%</td>
</tr>
</tbody>
</table>

Adapted from Martinez-Martin P, et al. Mov Disord, 2007
Prevalence of NMS increases with disease stage and duration

<table>
<thead>
<tr>
<th>Disease Duration (y)</th>
<th>Mean NMSQ-T</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5</td>
<td>8.5</td>
</tr>
<tr>
<td>5-9</td>
<td>10.6</td>
</tr>
<tr>
<td>10-14</td>
<td>11.9</td>
</tr>
<tr>
<td>≥ 15</td>
<td>12.8</td>
</tr>
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</table>
Progression and Natural History

• Studies to define the progression rate of non-motor symptoms are few

• Some symptoms such as excessive daytime sleepiness are thought to progress, other symptoms such as loss of smell and dream enactment behavior may remain static or improve

Gender Differences

**Women**
- Fatigue
- Anxiety
- Depression
- Constipation
- Restless Legs
- Pain

**Men**
- Excessive daytime sleepiness
- Drooling
- Sexual dysfunction

*Martinex-Martin, et al. Movement Disorders, 2013*
Impact of Non-Motor Symptoms

- Non-motor symptoms must be considered when treating Parkinson’s disease
  - In fact, in a survey of 163 patients, most patients rated their non-motor symptoms to be more troubling than their motor symptoms

Martin et al. Mov Disorders, 2011
Presentation of Non-Motor Symptoms

- Non-motor symptoms can precede the motor manifestations of Parkinson’s disease
  - Problems with smell
  - Constipation
  - Depression
  - Sleep disorders

Age | Loss of smell | Constipation | Depression | Sleep | Motor
--- | --- | --- | --- | --- | ---
40  | 45  | 50  | 55  | 60  |
What are the Non-Motor Symptoms?

- Neuropsychiatric Symptoms
- Autonomic Symptoms
- Gastrointestinal Symptoms
- Sleep Disorders
- Sensory symptoms
What are the Non-Motor Symptoms?

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What are Neuropsychiatric Symptoms?

- Loss of pleasure/apathy
- Anxiety
- Attention deficit
- Hallucinations/Psychosis/Delusions
- Obsessive behavior
- Dementia
- Depression
Dementia

AN ESSAY ON THE SHAKING PALSY.

CHAPTER I.
DEFINITION–HISTORY–ILLUSTRATIVE CASES.

SHAKING PALSY. (Paralysis Agitans.)
Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from a walking to a running pace; the being uninjured.

... the senses and intellects being uninjured.
Can we treat the dementia?

- A randomized double blind placebo controlled trial of 541 patients compared rivastigmine with a placebo drug

Management – Cholinesterase Inhibitors


Change from Baseline in ADAS-cog Score

Rivastigmine (n=329)
Placebo (n=165)

P = 0.002
P < 0.001

Depression

- Affects 10-45% of PD patients\textsuperscript{1}
- Can precede the motor symptoms in approximately 30% of PD patients \textsuperscript{1}
- It has been shown that patients are not depressed just because of Parkinson’s disease, but from Parkinson’s disease\textsuperscript{2}

\textsuperscript{1} Ziemssen H. et al. Parkinsonism and Related Disorders, 2007.
\textsuperscript{2} Schurmann AG. et al Neurology, 2002
Management of Depression

Treat PD

No

Symptom Resolution?

No

Antidepressant & Counseling

Yes

No further treatment
Nonmotor Symptom Complex

- Neuropsychiatric Symptoms
- Autonomic Symptoms
- Gastrointestinal Symptoms
- Sleep Disorders
- Sensory Symptoms
What are Autonomic Symptoms?

- Urination difficulties
- Body temperature dysfunction
- Low blood pressure when standing
- Sexual dysfunction
- Dry eyes
- Constipation
Body Temperature Dysfunction

- During an off period, patients with Parkinson’s disease may have profound sweating.
Blood Pressure Changes

- In Parkinson’s Disease, you may get a drop in blood pressure when you stand.
- This is due to
  - Parkinson’s Disease itself
  - Medications
  - Combination of both
Blood Pressure Changes

- There are treatments for these changes in blood pressure
  - Medication reduction
  - Increase fluid and salt consumption
  - Compression hose
  - Raising the head of bed at night
  - If all this fails, there are medications to increase your blood pressure
Nonmotor Symptom Complex

- Neuropsychiatric Symptoms
- Autonomic Symptoms
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- Sensory Symptoms
Gastrointestinal Symptoms of Parkinson’s Disease

**Mouth**
Pooling of saliva and problems with movements needed to brush teeth can cause dental dysfunction. Motor effects cause jaw tremors.

**Oesophagus**
Symptoms of oesophageal dysphagia include slow oesophageal transit, segmental oesophageal spasm, spontaneous contractions of proximal oesophagus, air trapping, aperistalsis, and gastro-oesophageal influx.

**Salivary glands**
Reduced saliva production, but low swallowing frequency causes drooling.

**Pharynx**
Oropharyngeal dysphagia increases risk of aspiration.

**Stomach**
Impaired gastric emptying (gastroparesis) cause nausea, bloating, early satiety, and weight loss.

**Rectum**
Anorectal dysfunction leads to difficulty with defecation.

**Small intestine**
Dilatation

**Colon**
Colonic dysmotility, constipation, megacolon, volvulus, and bowel perforation.
### Constipation is Common in Parkinson’s Disease

- Occurs in between 20-27% of PD patients
- Presumably due to increased colon transit time

### Management Strategies of Constipation

<table>
<thead>
<tr>
<th>Slow Transit Constipation</th>
<th>Anorectal Dysfunction</th>
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<tbody>
<tr>
<td>Increase fluid and fiber intake</td>
<td>Laxatives generally unhelpful</td>
</tr>
<tr>
<td>Add stool softener (e.g. colace)</td>
<td>Dopaminergic medication if due to “off state”</td>
</tr>
<tr>
<td>Add osmotic laxative or polyethylene glycol (Miralax)</td>
<td>Biofeedback</td>
</tr>
<tr>
<td></td>
<td>Sacral nerve stimulator</td>
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<tr>
<td></td>
<td>Botulinum toxin</td>
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Non-motor Symptom Complex

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- Autonomic Symptoms
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Why am I always so sleepy? (Excessive daytime somnolence)

- What are the causes?
  - Fragmented sleep
    - Restless legs
    - Periodic limb movements
    - Sleep apnea
    - REM Sleep Behavior Disorder
    - Wearing “off” of medications
    - Unable to fall asleep or fall “back asleep”
  - Parkinson’s medications
  - Parkinson’s itself
Sleepiness may be a sign of PD

- Honolulu - Asia Aging study
  - Having EDS was associated with a 3-fold increased risk in development of PD

Abbott RD et al. Neurology, 2005
Managing the Sleepiness

- Get a good night’s sleep
  - Practice good sleep hygiene
  - Treat restless legs or REM sleep behavior disorder
  - Optimize Parkinson’s medication
  - Sleep study
- If associated with administration of medication
  - Consider reduction or switch to another agent
- If no cause is found and no response to change in therapy
  - Consider stimulants (limited by side effects and insurance coverage)
Nonmotor Symptom Complex

- Neuropsychiatric Symptoms
- Autonomic Symptoms
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Sensory Symptoms

- Changes in vision
- Loss of smell
- Pain
  - Sometimes it is unclear whether due to arthritis or Parkinson’s
    - Does it respond to Parkinson’s medications?
Managing Parkinson’s disease means managing more than the tremor
Nonmotor symptoms can have a profound impact on quality of life
Need to be addressed!