Parkinson’s Disease: Non-Motor Symptoms

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• I serve as Co-chair for the Lewy Body Dementia Association Working Group on Clinical Care and Professional Education.
Outline

• Overview of Non-motor clinical characteristics of Parkinson’s disease

• As we discuss more on the non-motor features, we will discuss current treatment approaches to the Non-motor features of Parkinson’s disease
  • Pharmacologic and Non-pharmacologic
Parkinson’s disease: Characterized by Motor and Non-Motor symptoms

<table>
<thead>
<tr>
<th>Motor</th>
<th>Non-motor</th>
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<tbody>
<tr>
<td>Rest tremor</td>
<td>Constipation</td>
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<tr>
<td>Bradykinesia</td>
<td>Anosmia</td>
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<tr>
<td>Rigidity</td>
<td>Orthostatic hypotension</td>
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<tr>
<td>Postural Instability</td>
<td>Sleep Issues</td>
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<tr>
<td></td>
<td>- REM Behavior Disorder</td>
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<td></td>
<td>- Depression/Anxiety (~40%)</td>
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<td>- Cognitive impairment (~30%)</td>
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Clinical Symptoms: Vary from person to person

- Not all individuals will have all symptoms
- Also vary in timing of onset and rate of progression of symptoms
Role of Dopamine and other Neurotransmitters in Motor and Non-Motor Symptoms

• Cells that produce Dopamine are lost.
  • Increasing Alpha Synuclein burden

• We know that other neurotransmitters, like Norepinephrine, Acetylcholine, and Serotonin are involved as well.

Associated Non-Motor Features of PD

• Premotor features: RBD, anosmia, constipation

• Cognitive and Behavioral disturbances
  • Mood disorders
  • Delusions, Psychosis
  • Fluctuations

• Autonomic Dysfunction: Constipation; Orthostatic Hypotension
RBD is recognized as key prodromal biomarker
Therapeutic Approach:
Non-Motor Symptoms
Approach to Treatment

• Two Fold
  • Non-pharmaceutical
  • Pharmaceutical
**Interdisciplinary Approach**

<table>
<thead>
<tr>
<th>Professional</th>
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<tbody>
<tr>
<td>Neurologist</td>
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<td>Geriatrician</td>
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<tr>
<td>Nurse Practitioner/PA</td>
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<td>Psychiatrist</td>
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<td>Psychotherapist</td>
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<tr>
<td>Cognitive Therapist/Neuropsychologist</td>
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<tr>
<td>Nutritionist/Health Coach</td>
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<td>ST, PT, OT</td>
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Constipation

• HYDRATION and Fiber

• Optimizing levodopa can help
  • Body movement enhances colonic movement

• Regular bowel regimen
Mood symptoms (Depression and anxiety)

• Depression and Anxiety are common (~40% of patients)

• SSRI or SNRI

• Therapy (Talk therapy)

• Socialization

• Exercise
Sleep disturbances

- REM sleep behavior disorder
  - Common in Parkinson’s
  - Melatonin is first-line treatment
  - Clonazepam if melatonin is ineffective

- Increased risk of obstructive sleep apnea in PD
  - Dopamine agonists can also cause daytime sleepiness
  - When in doubt, screen
Non-Pharmacologic Approach to Orthostasis

• Reduce or eliminate medications and other substances that contribute to low blood pressure
  • Diuretics; other antihypertensives
    • Seated BP can be elevated
    • Measure seated and standing BP before deciding
  • Urology meds

• Reinforce hydration; augment salt intake

• Counseling re: common precipitants
  • Dehydration
  • Vasodilation (hot weather; hot tub)
  • Increased vagal tone (bathroom; postprandial; morning)

• Mitigate supine hypertension
  • Contributes to morning orthostasis
  • Elevate head of bed
Pharmacologic therapy to Orthostasis

• Fludricortisone (Florinef)
  • Mineralocorticoid → volume expansion

• Droxidopa (Northera)
  • Norepinephrine precursor

• Midodrine (ProAmatine)
  • Alpha agonist
  • Last resort due to supine hypertension
Cognitive Impairment: Nonmotor feature

• What does it mean?

• “Umbrella term”
  • Multiple domains
    • Executive dysfunction: Multitasking, planning, organizing, problem solving
    • Attention
    • Visuospatial
    • Language
    • Orientation
    • Memory- Recall
    • Abstraction

• “Bradyphrenia”: Slowed thought processing
Cognitive Impairment: Nonmotor feature

• Not acute. Gradual.
  • Acute → Suggests something else (i.e., infection, medication rxn)

• Mild, Moderate, Severe

• Cognitive Impairment is not synonymous with dementia
Non-Pharmacological approach to Cognitive Impairment

• Diet
  • Mediterranean- What are they eating in Tuscany tonight?

• Exercise
  • Physical activity
  • “Brain”  some literature to support “cognitive training”

• Socialization

• Strategies
Strategies to help with Attention/executive function / working memory changes

• Manage other issues that can interfere with attention
  • Hearing problems
  • Sleep problems
  • Depression

• Reduce working memory demands
  • Simplify
    • Eliminate unnecessary items from your space, unnecessary tasks from your agenda
  • Organize
    • Identify specific places for essential items (keys, medications, etc)
  • Write things down
  • Delegate

• Give yourself extra time
Pharmaceutical Therapies

• Recall other neurotransmitters implicated in PD?
  - Reduction in Acetylcholine → associated with dementia risk

• Medications aimed at addressing this deficiency:
  • Rivastigmine (Exelon)
    • FDA approved in PDD
  • Donepezil (Aricept)
Hallucinations and Delusions

• Can occur with or without dopaminergic therapy
• Can occur with or without dementia / cognitive impairment

• Hallucinations (typically visual)
  • Usually well-formed (people or animals)
  • Can be non-threatening or threatening

• Delusions less common
  • Typically paranoid
  • Spousal infidelity (Othello syndrome) is most common
Hallucinations and Delusions: Management

• Acute onset
  • Look for underlying causes & address if possible
    • Infection (UTI)
    • Dehydration
    • Other metabolic issues (thyroid studies)
    • Medications (may include dopaminergic therapy)

• Chronic, persistent
  • Maximize behavioral supports
    • Frequent reorientation
    • Family (staff) education
  • Pharmacologic
    • Acetylcholinesterase inhibitors
    • Second generation antipsychotics
      • Quetiapine, Clozaril, Pimervanserin
Concluding Thoughts
Summary Points

• Non-motor features are increasingly recognized in PD

• There are different strategies to help address the non-motor features in PD
  • (Two fold): Pharmacologic and Non-pharmacologic