Parkinson’s Disease: Non-Motor Symptoms

Katherine Amodeo, MD
Movement Disorders Specialist
Department of Neurology
Westchester Medical Center- MidHudson Regional Hospital
Poughkeepsie, NY

Assistant Professor of Neurology
School of Medicine at New York Medical College
Valhalla, NY

WMC Health | MidHudson Regional Hospital
Westchester Medical Center Health Network

NEW YORK MEDICAL COLLEGE
A MEMBER OF THE TOURO COLLEGE AND UNIVERSITY SYSTEM
School of Medicine

Disclosures

- My fellowship training was funded by the Edmond J. Safra MJFF Fellowship.
- I serve and have served as PI and Co-I for clinical trials funded by Aptinyx, ROCHE, EIP Pharma, MJFF, NIH, Acadia, Biogen
- 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

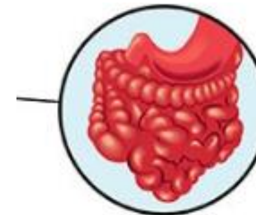
Parkinson's disease: Characterized by Motor and Non-Motor symptoms

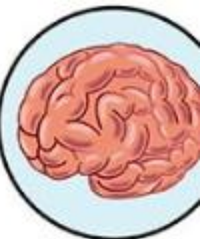
Motor

- Rest tremor
- Bradykinesia
- Rigidity
- Postural Instability

Non-motor

- Constipation
- Anosmia
- Orthostatic hypotension
- Sleep Issues
  - REM Behavior Disorder
- Depression/Anxiety (~40%)
- Cognitive impairment (~30%)





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

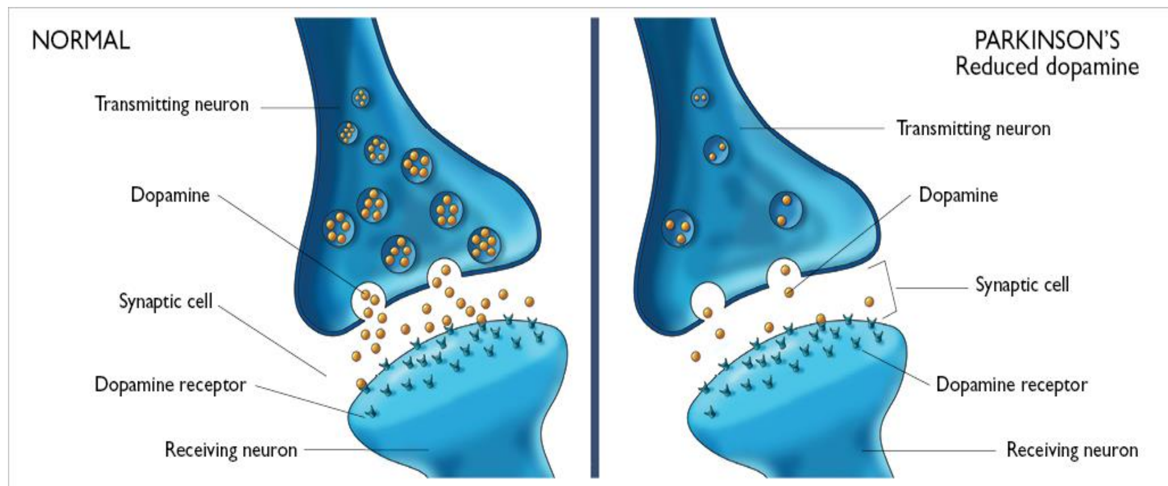


FIGURE 3. Illustration showing low levels of dopamine in a neuron affected by Parkinson's disease (right) and normal levels (left).

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

https://www.clinicaladvisor.com/features/link-between-pesticides-and-parkinsons-disease/article/492896/

Associated Non-Motor Features of PD

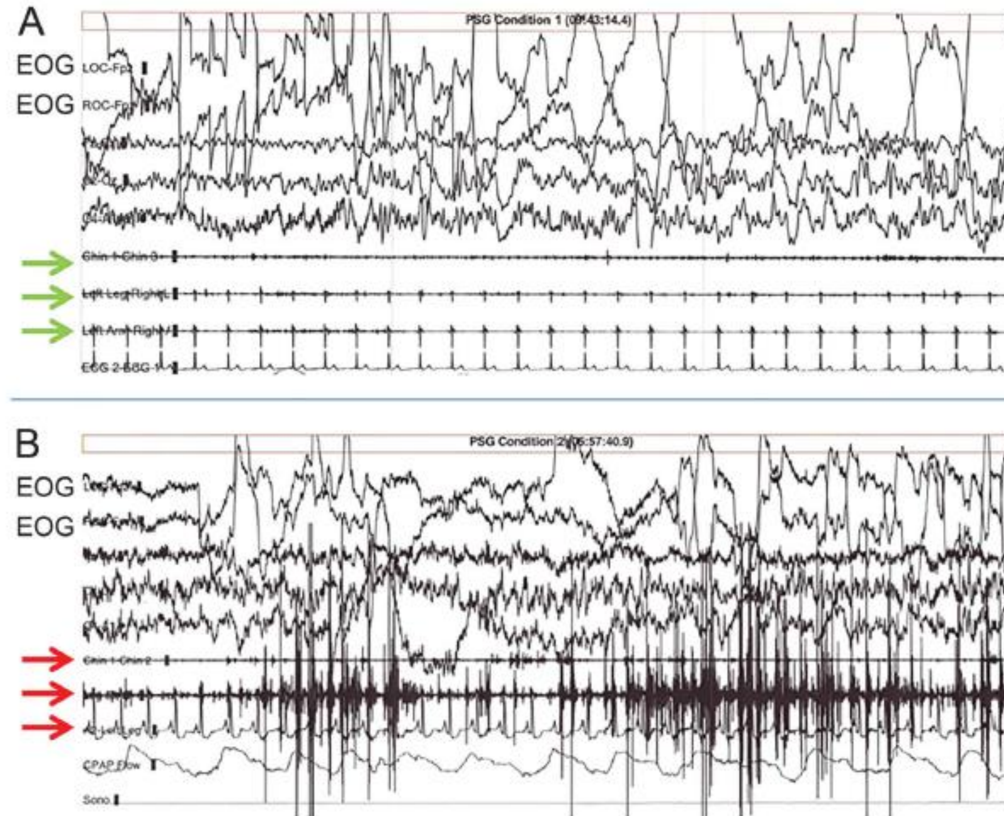
- Premotor features: **RBD**, anosmia, constipation

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

- Autonomic Dysfunction: Constipation; Orthostatic Hypotension

RBD is recognized as key prodromal biomarker

Figure 3 **Polysomnographic (PSG) recordings**



PSG recordings of normal REM sleep (A) and REM sleep without atonia, typical of REM sleep behavior disorder (B). REM are reflected by the high-amplitude, abrupt deviations from baseline in the electro-oculogram (EOG) leads during a 30-second epoch. In (A), note the absence of EMG activity in the submental, leg, and arm leads (green arrows), whereas increased EMG tone is present in the same leads (red arrows) in B, particularly in the middle (arm lead), in this patient.

Therapeutic Approach:

Non- Motor Symptoms

Approach to Treatment

- Two Fold
  - Non-pharmaceutical
  - Pharmaceutical

Interdisciplinary Approach

- Neurologist
- Geriatrician
- Nurse Practitioner/PA
- Psychiatrist
- Psychotherapist
- Cognitive Therapist/Neuropsychologist
- Nutritionist/Health Coach
- ST, PT,OT

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

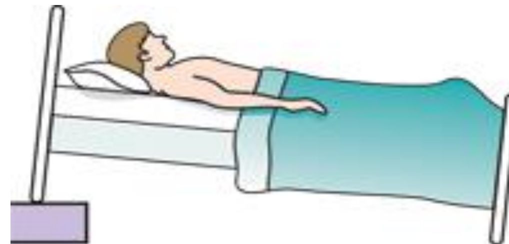
Non-Pharmacologic Approach to Orthostasis

- 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 (ie, 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