Cognitive and other non-motor behaviors and how to cope with their manifestations

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- Off-label use of medications will be discussed

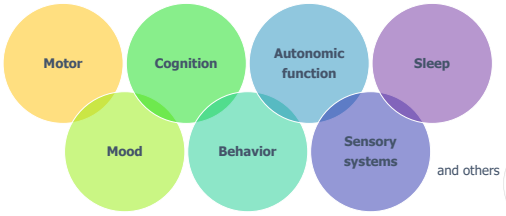
Objectives for today's talk

- Clinical features, concepts and management related to cognitive and non-motor behavioral changes in Parkinson's disease (PD)
- Top 10 "life hacks"

#1.

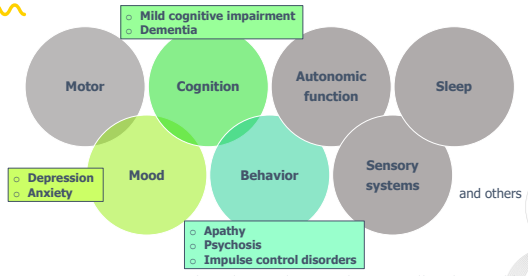
Know the symptoms

Parkinson's disease (PD) symptoms



Schapira et al., LancetNeurol 2017; Seppi et al., Mov Dis 2019; Goldman and Guerra Neurol Clinics 2020

Parkinson's disease (PD) symptoms



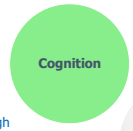
Schapira et al., LancetNeurol 2017; Seppi et al., Mov Dis 2019; Goldman and Guerra Neurol Clinics 2020

But first, a few immediate take away messages

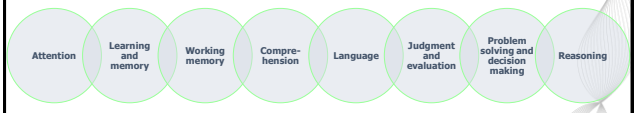
- Not everyone with PD will have cognitive or behavioral symptoms
- These topics can be difficult to talk about or hear about
- Accurate definitions and information are important
- Management strategies, team care, and research can make a difference

"Knowledge is power"
Scientia potentia est

What is cognition?



- From Latin root *cognoscere*, "to know"
- Mental action or process of acquiring knowledge and understanding through thought, experience, and the senses
- Does NOT equal memory
- Rather, includes many different cognitive processes



Cognitive symptoms and domains

COMMON SYMPTOMS	COGNITIVE DOMAINS	AREAS OF THE BRAIN INVOLVED
• Trouble concentrating • Difficulty keeping track of info in one's mind	Attention and working memory	Frontal lobe including DLPFC, parietal lobe, basal ganglia
• Problems with planning, organizing, or initiating activities • Difficulty with multi-tasking • Trouble stopping and starting tasks	Executive function	Prefrontal cortex, basal ganglia
• Difficulty finding words or naming • Reduced fluency of speech	Language	Temporal lobe
• Problems learning new tasks, recalling facts or events • Difficulty performing learned tasks	Memory	Temporal lobe, hippocampus (declarative memory), basal ganglia (procedural memory)
• Impaired sense of direction • Difficulty drawing objects	Visuospatial function	Parietal and occipital lobes

Cognitive changes in PD

- Frequency estimates in literature vary
- Mild cognitive impairment may occur in about 20-50% of PD patients
- Mild deficits may be present at diagnosis or in early stage PD
- About 40% develop more severe deficits (dementia), which may increase with more advanced PD
- **Note - not every person with PD develops cognitive impairment or dementia**

Goldman et al., Mov Dis 2014; Mov Dis 2016

Depression

- Common, prevalence ~40%
- Pre-motor or prodromal phase of PD
- Intrinsic to PD and/or reactive to PD changes
- Common symptoms
  - Sadness
  - Decreased interest (anhedonia)
  - Anxiety
- Can have motor, somatic, and cognitive components

Anxiety

- Common in PD and under recognized…
- Prevalence range: 5-40%
- About 1/3 of PwP have 2 or more anxiety disorders
- Contexts:
  - Depression
  - Generalized anxiety disorder**
  - Panic disorder
  - Phobias (social, agoraphobia)**
  - Obsessive-compulsive disorder
  - Non-motor fluctuations, particularly in the "off" state

Broen et al., Mov Dis 2016

Apathy

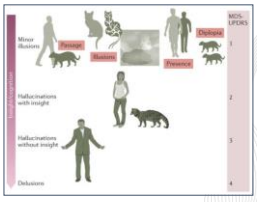
Behavior

- Primary loss of motivation
- Behavioral, cognitive, affective components
- Prevalence 15-70%
- Distinct from depression but can overlap
- Associated with decreased functional independence
- Reduced initiative or participation in activities
- Often more troublesome to caregiver
- Affects quality of life and relationships

Pagonabarraga et al., Lancet Neurol 2015

Psychosis

- Spectrum
  - Illusions
  - Hallucinations
  - Delusions
- Affect > 50% on chronic PD meds
- Visual hallucinations, most common
- Risk factors
  - Advanced age, longer PD duration, cognitive impairment, sleep disturbances
- Multi-factorial etiology



Ravina et al., Mov Dis 2007; ffytche et al., Nat Rev Neurol 2017

Impulse control disorders

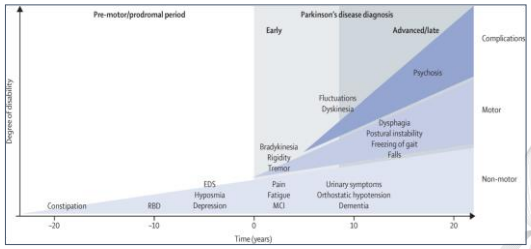
- Range of behaviors
  - Pathological gambling
  - Compulsive shopping
  - Hypersexuality
  - Binge eating
- Prevalence 2-10%
- Repetitive and reward seeking
- Link to dopamine
- Risk factors
  - Psychiatric, addiction history
  - Dopamine agonists
  - Impaired decision making

Weintraub and Claassen Int Rev Neurobiol 2017

#2.

Know that the field of PD is continually evolving

Recognizing pre-motor or prodromal PD



Kalia and Lang Lancet 2015

Redefining PD

Time to Redefine PD? Introductory Statement of the MDS Task Force on the Definition of Parkinson's Disease

MDS Clinical Diagnostic Criteria for Parkinson's Disease

REVIEW

CME

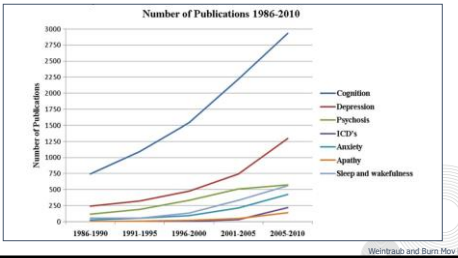
MDS Research Criteria for Prodromal Parkinson's Disease

Berg et al., Mov Dis 2014, 2015; Postuma et al., Mov Dis 2015

REVIEW

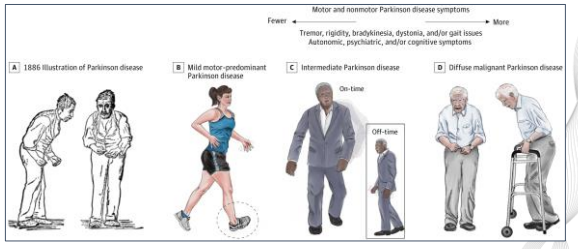
Parkinson's Disease: The Quintessential Neuropsychiatric Disorder

Daniel Weintraub, MD,[1,2]* and David J. Burn, MD[3,4]



Weintraub and Burn Mov Dis 2011

New images of PD



Armstrong and Okun JAMA Neurol 2020

#3.

Recognize your individuality

Individuality

- Each person with PD is unique in his or her journey
- Not everyone will experience the same symptoms
- Differences in progression, genetics, environment, personality, etc.
- Some say, if you've met one person with PD…you've met one person with PD

Cognitive and non-motor behavioral symptoms

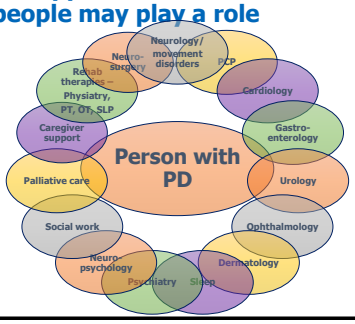
- May be associated with different clinical motor symptoms
  - Postural instability gait disorder vs. tremor
- Gender differences
  - Mood and apathy
- Genetics may play a role
  - Alpha-synuclein, GBA, APOEe4
- Modifiable risk factors?
  - HTN, DM, diet, etc

Martinez-Martin et al., J Neurol 2012; Williams-Gray et al., 2009; Creese et al., 2018

#4.

Build your care team

The team approach – many people may play a role



Why multi-disciplinary care?

- Multiple types of symptoms
- Multiple different perspectives
- Helps manage and assess symptoms over time
- Benefits of team work for patients and their care partners (and other healthcare professionals too)

Eggers et al., J Neurol 2018; Radder et al., Expert Rev Neurother 2019; Jrl Parkinson Dis 2020; Roopan et al., Mov Dis 2020

#5.

Take a multi-faceted approach to management

Considerations - cognitive and behavioral issues

- Objective assessments for baseline and serial evaluations
- Exclude other causes, especially if acute
- Review medications (for PD and non-PD reasons)
- Management - medications & non-pharmacological strategies
- Address work, driving, safety, home environment
- Address adjustments and psychosocial impact
- Broaden the care team for person with PD and their care partner

Medication management considerations

- Dementia
  - Rivastigmine, FDA approved
- Mild cognitive impairment
- Depression
  - Antidepressants
- Anxiety
  - Antidepressants, anxiolytics
- Psychosis
  - PD medication adjustments
  - Pimavanserin, FDA approved
- Impulse control disorders
  - PD medication adjustments
- Apathy
  - Dopaminergic medications, antidepressants, cognitive enhancing meds

Always discuss with your medical care team

Cognitive behavioral therapy - depression

- Several trials
- PD depression
- Trials demonstrate reductions in depression

- Can also be done via telephone based CBT
- Telephone CBT outperformed treatment as usual on depression, anxiety and quality of life measures


Telephone-based cognitive behavioral therapy for depression in Parkinson disease

A randomized controlled trial

Dobkin et al., Am J Psych 2011, Neurol 2020

#6.

Exercise!

Physical exercise guidelines

- Regular exercise (150 min/week of moderate intensity exercise)
  - A minimum of moderate intensity aerobic + 2 or more days strengthening

  OR
  - High intensity (75 min/week of vigorous intensity aerobic activity) + 2 or more days strengthening

  OR
  - An equivalent mix of moderate and high intensity aerobic exercise + 2 or more days strengthening

www.cdc.gov, www.health.gov

Exercise, cognition, PD


RESEARCH ARTICLE

Exercise Improves Cognition in Parkinson's Disease: The PRET-PD Randomized, Clinical Trial

Mov Dis 2015

- 51 participants with PD
- No significant cognitive issues
- 2 types of physical exercise
- 38 participants completed trial
- **Both groups had improved cognitive performance for working memory, dealing with cognitive interference and attention.**

Exercise can help mood symptoms

TABLE 1. Exercise interventions for mood in PD

			Intervention	Sample size	Exercise frequency/ duration/setting	Control group	Mood outcome measures	Main results	Limitations
Canning et al., 2015[78]	RCT	71.0	40-60 Minutes of strengthening	231	3×/week for 6 months (in clinic + at home)	Usual care	PANAS	Improved affect in exercise group compared with usual care	No attention control; mood measures included as secondary outcomes
Park et al., 2014[79]	RCT (delayed start)	59.9	60 Minutes of combined aerobic and resistance	31	3×/week for 48 weeks (in clinic)	Delayed start at 24 weeks	BDI	Greater reduction in depression in early-start group compared with late-start group at 48 weeks	Greater social interaction in early-start group relative to late-start group
Shulman et al., 2013[79]	RCT	65.8	3 Exercise groups: (1) 30 minutes of high-intensity treadmill exercise; (2) 50 minutes of low-intensity treadmill exercise; (3) stretching and resistance training	67	3×/week for 3 months (in clinic)	Stretching and resistance exercise (comparative trial)	BDI	No change in depression within any group	No nonexercising comparison condition
Bridgewater and Sharpe, 1998[80]	Pilot RCT	67.3 (EX); 66.5 (CON)	20-30 Minutes of aerobic exercise (+ warm-up calisthenics and cool-down stretching)	26	2×/week for 3 months (in clinic)	Usual care + attendance at "interest talks" once every 3 weeks	LPDQ	Improved mood in exercise group	Small sample size; less social interaction in control group
Dashtipour et al., 2015[81]	Prospective, double-blind, randomized trial	63.4	60 Minutes of combined aerobic and resistance	11	4×/week for 4 weeks (in clinic)	Exercise-based behavioral treatment (LSVT BIG)	BAI, BDI	Reduced depression in combined group	Small sample size; combined data analysis across both groups
Uc et al., 2014[82]	Uncontrolled phase I/II trial	65.5	45 Minutes of aerobic walking	49	3×/week for 6 months (at home)	None	GDS	Reduced depression across all completers	Lack of a control group

BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CON, control group; EX, exercise group; GDS, Geriatric Depression Scale; LPDQ, Levine-Pilowsky Depression Questionnaire; LSVT BIG, Lee Silverman Voice Therapy; PANAS, positive affect subscale of the Positive and Negative Affect Schedule; PD, Parkinson's disease; RCT, randomized, controlled trial.

Reynold et al., Mov Dis 2016

JAMA Neurology | Original Investigation

Effects of Mindfulness Yoga vs Stretching and Resistance Training Exercises on Anxiety and Depression for People With Parkinson Disease
A Randomized Clinical Trial

Jojo Y. Y. Kwok, PhD, MPH, RN, RN; Jackie C. Y. Kwan, MSocSc, PDAH, BSW, RSW; M. Auyeung, MB(ChB); Vincent C. T. Mok, MD, MBBS; Carrie K. Y. Lau, MSc, RN, APN; K. C. Choi, BSc, PhD; Helen Y. L. Chan, PhD, RSN, RN

- Randomized Controlled Trial, 8 weeks
- Mindfulness yoga vs. stretching and resistance training (SRTE)
- 138 mild-moderate PD
- HADS (anxiety and depression scale)
- Effective and safe
- Yoga better than SRTE ($p<0.001$)
  - Anxiety and depression
  - Perceived hardship
  - Health-related quality of life

Kwok et al., JAMANeurol 2019

#7.

Maximize function and quality of life

Maximize function and quality of life

- Look at your everyday activities
  - Self-care, leisure, household, work-related activities
- Plan your day, energy conservation strategies

- Role of occupational therapy (OT) – *and others too*
- Need for greater awareness and referrals from physicians
  - UK survey – 13-25% patients referred to OT
  - Dutch survey – 9%
  - U.S. data – Referrals for PT >> OT > SLP

- Evidence from several studies that OT can support better functioning of people with PD in their daily activities

Clarke et al., 2009; Sturkenboom et al., 2013, 2014; Ramig et al., 2018

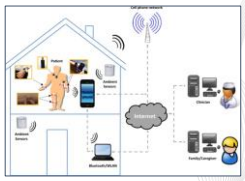
Tips and tricks

- Harness technology – but don't forget the "simple"

- Gizmos, gadgets, apps

- Medication reminders
- Adaptive equipment
- Augmentive technology/communication

- Wearable sensors
- Real-time monitoring of falls and alert systems



Espay et al., 2016; Lonini et al., 2018

#8.

It takes two (or more) to tango

Relationships and more

- Recognize the potential for caregiver stress
- More common with advanced PD, greater motor symptoms, neuropsychiatric issues
- However, need to address across all stages of PD

- Considerations
  - Changes in roles
  - Adjusting to a new "normal"
  - The whole family – not only spouse/significant other
  - Planning ahead

- Maintain healthy coping skills
- Don't be afraid to ask for help!

Schrag et al., 2004; Tan et al., 2012; Berger et al., 2019

Find resources and ways to connect

- There are many ways and resources

- PD team – physician, nurse, social worker, psychologist, counselor, spiritual, etc.
- Support groups
- Community networks
- Parkinson's disease foundations

Coping strategies to help take control

- Make checklists for specific tasks – medications, meals, exercise
- Use notes as reminders around your home
- Keep assistive devices within your line of vision so you remember to use them
- Use cueing and memory strategies
- Ask for help – human reminders
- Create a routine
- Get adequate sleep
- Be kind to yourself
- Practice gratitude

Thoughts for caregivers

- Take time for yourself – and be kind to yourself too
- Build in breaks
- Create your support system
- Express your feelings – caregiver support groups, friends, therapists
- Recognize that sometimes it is the disease talking, NOT YOUR LOVED ONE
- Education and support
- Cherish certain moments and practice gratitude

#9.

Participate in research, if interested

Research resources

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Examples of engagement in research process

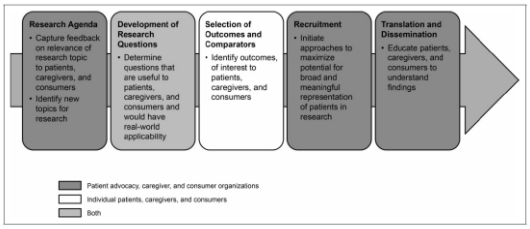


Figure 2. Patient engagement in the R&D process. Reproduced with permission from the National Health Council.[44]

Hoos et al., 2015

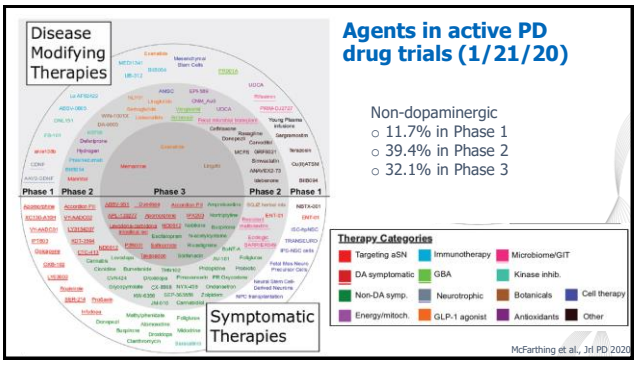
Participatory medicine

- Core principles (Rogers, 1957)
- Basis for the reciprocal cultural change of patient as an active collaborator involved in partnership with clinicians and researchers
- Applicable to individuals or organizations in promoting growth and well-being

Williams et al., 2017

#10.

Keep up hope!



No matter where someone is in their journey

Thank you



Shirley Ryan Abilitylab

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