

Cognitive Challenges in Parkinson's and What to Do About Them!

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Overview of cognitive impairment in Parkinson's

Mild Cognitive Impairment in Parkinson's

- Gradual decline in select cognitive abilities
- Deficits are not sufficient to interfere significantly with functional independence, but difficulties on complex tasks may be present



Severe Cognitive Impairment in Parkinson's

- Impairment in two or more cognitive domains
- Decline from baseline with deficits that impair daily function

Cognitive functions/domains

- **Executive** – organization, planning, multitasking
- **Processing speed** – how rapidly information is processed
- **Attention** – ability to focus on a task or thought
- **Memory** – ability to store and retrieve new information
- **Visuospatial** – conception of spatial relationships
- **Language** – ability to comprehend and express meaning, usually in words

Impact of cognitive impairment on daily function

- **Memory loss**
- **Difficulty performing familiar tasks**
- **Language deficits**
- **Time and place disorientation**
- **Poor judgment**

Executive dysfunction and slowed mental processing speed

- Deficits in initiation, sequencing, planning and set shifting; impaired mental speed (bradyphrenia)
- Often the earliest detectable cognitive changes in Parkinson's

Attention/Executive dysfunction/processing speed – Influence of task demands in Parkinson's

“Let’s have tea!” study (Rochester et al, Arch Phys Med Rehab, 2004)

- Looked at how attentional demands during an everyday functional activity contributes to functional performance and gait disturbances

Attention/Executive dysfunction/processing speed – Influence of task demands in Parkinson's

Study

- 20 mild to moderate people with Parkinson's, 10 controls
- Four Tasks
 - Simple walking: walk to the kitchen
 - Dual-motor: walk and carry a tray
 - Dual-cognitive: walk and recall a memory
 - Multiple motor-cognitive task: walk, carry tray and recall a memory

Results

- Increased task complexity → ↓ gait speed

Parkinson's and subcortical cognitive impairment

- Early pronounced executive dysfunction, attentional deficits and slowed processing speed
- Language and memory are usually largely intact compared to cortical dementias until later in Parkinson's progression
- Deviation from this pattern, e.g., 'cortical' deficits could indicate comorbidity e.g., Alzheimer's disease, cerebral vascular disease or Lewy bodies in the cortex

File Cabinet Example



Memory Impairment Parkinson's vs. Alzheimer's: retrieval vs. encoding

Encoding = process of putting info into
memory

Retrieval = process of finding the info to
remember

Memory Impairment Parkinson's vs. Alzheimer's: retrieval vs. encoding

Parkinson's memory
impairment
= poor retrieval

Alzheimer's memory
impairment
= impaired encoding

	Alzheimer's	Parkinson's
Recognition memory	↓↓	-
Free recall memory	↓↓	↓
Benefit for cueing	no	yes

Evidence based treatments for cognitive issues in Parkinson's

Treatments for mild (non-dementia) cognitive impairment in Parkinson's

Drug	Efficacy	Safety	Practice implications
Rivastigmine	Insufficient evidence	Acceptable risk without specialized monitoring	Investigational
Rasagiline	Insufficient evidence	Acceptable risk without specialized monitoring	Investigational
Transcranial direct current stimulation	Insufficient evidence	Insufficient evidence	Investigational
Cognitive rehabilitation	Insufficient evidence	Insufficient evidence	Investigational

The Holy Grail – Disease modifying treatments



Treatments for severe cognitive impairment (dementia) in Parkinson's

Drug	Efficacy	Safety	Practice implications
Rivastigmine	Efficacious	Acceptable risk without specialized monitoring	Clinically useful
Donepezil	Insufficient evidence	Acceptable risk without specialized monitoring	Possibly useful
Galantamine	Insufficient evidence	Acceptable risk without specialized monitoring	Possibly useful
Memantine	Insufficient evidence	Acceptable risk without specialized monitoring	Investigational

Action Items: what you can do to help cognitive function

Action items

- Reduce distractions
- Focus on one task at a time
- Talk to your doctor about depression
- Exercise
- Quality sleep
- Healthy diet
- Cognitive training/rehabilitation
- Social interaction

Overview of psychosis in Parkinson's

Psychosis – a general definition

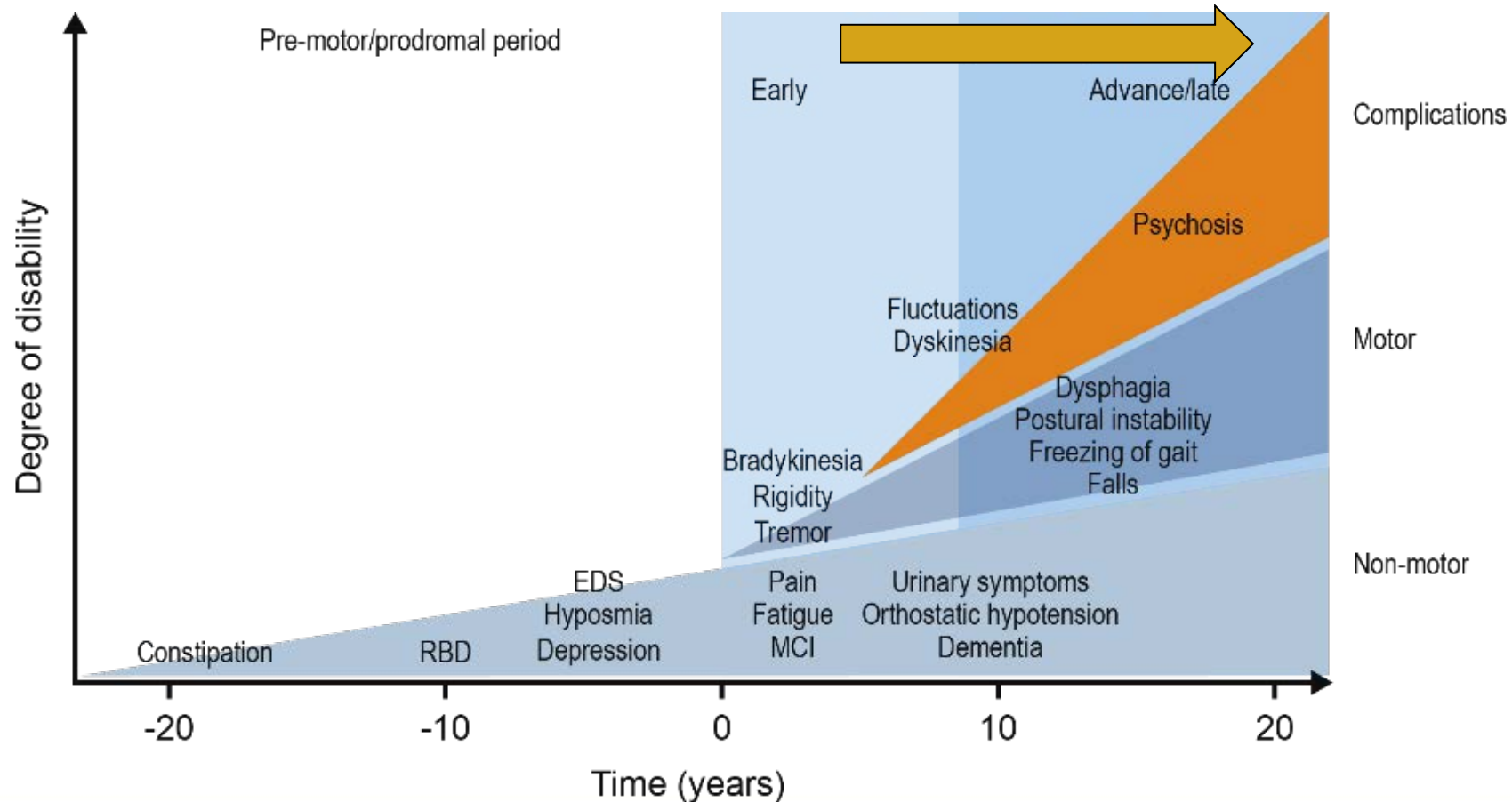
“A severe mental disorder
in which contact is lost
with external reality”



Psychosis – definitions

- **Hallucinations** – false sensory perceptions in the absence of external stimuli
- **Illusions** – misperception of actual stimuli
- **Passage hallucinations** – indefinite object passing through the peripheral visual field
- **Sense of presence hallucination** – a ‘feeling’ (or idea) of someone close by (leibhatige Bewussheit from Jaspers)
- **Delusions** – false, fixed, idiosyncratic belief

Parkinson's disease psychosis (PDP) typically occurs in more advanced stages of Parkinson's



Evidence based treatments for psychosis in Parkinson's

Management Strategies

- Treatment of underlying medical illness, if needed
- Discontinuation of medications that may exacerbate psychosis (eg, pain, bladder and CNS-acting medications)
- Reduction of Parkinson's medications
- Use of antipsychotic therapy
- Treatment with cholinesterase inhibitors
- Nonpharmacologic techniques to address PDP

Antipsychotic Treatments for Parkinson's disease psychosis

Treatment		Efficacy	Safety	Practice Implications
MDS review designation (2019) ¹	Clozapine	Efficacious	Acceptable risk with specialized monitoring	Clinically useful†
	Quetiapine	Insufficient evidence	Acceptable risk without specialized monitoring	Possibly useful†
FDA approved for PDP (2016) ²	Pimavanserin	Efficacious ³	No impairment of motor function ³ ; increase in QT interval	Clinically useful

† Black box warning for typical and atypical APs in elderly patients who have dementia-related psychosis⁴

1. Seppi K, et al. *Mov Disord*. 2019;34:2 2. US Food and Drug Administration Web site. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm498442.htm>. Published April 29, 2016. Accessed October 27, 2016. 3. Cummings J, et al. *Lancet*. 2014;383(9916):533-540. 4. US Food and Drug Administration Web site. <http://www.fda.gov/Drugs/DrugSafety/ucm124830.htm>. Published June 16, 2008. Accessed November 5, 2016.

Action Items: what you can do for psychosis in Parkinson's

Action items - Strategies for psychosis in Parkinson's

Talk to your doctor!

- Home modifications (e.g. night lights), stimulation/structured environment
- Coping strategies
 - visual techniques
 - cognitive techniques
 - interactive techniques
- Discussion, education

Selected References

Calleo, J. , Burrows, C. , Levin, H. , Marsh, L. , Lai, E. , & York, M. K. (2012). Cognitive rehabilitation for executive dysfunction in Parkinson's disease: application and current directions. *Parkinson's Disease, 2012*.

Ffytche DH, Creese B, Politis M, Chaudhuri KR, Weintraub D, Ballard C, et al. The psychosis spectrum in Parkinson disease. *Nat Rev Neurol.* 2017 Feb;13(2):81–95.

Goldman, J. G. , Vernaleo, B. A. , Camicioli, R. , Dahodwala, N. , Dobkin, R. D. , Ellis, T. , . . . & Golden, R. (2018). Cognitive impairment in Parkinson's disease: A report from a multidisciplinary symposium on unmet needs and future directions to maintain cognitive health. *npj Parkinson's Disease, 4*(1), 19.

Litvan I, Aarsland D, Adler CH, Goldman JG, Kulisevsky J, Mollenhauer B, et al. MDS Task Force on mild cognitive impairment in Parkinson's disease: critical review of PD-MCI. *Mov Disord.* 2011 Aug 15;26(10):1814–24.

Seppi K, Ray Chaudhuri K, Coelho M, et al. Update on treatments for nonmotor symptoms of parkinson's disease-an evidence-based medicine review. *Mov Disord.* 2019;34(2):180-198.