Cognitive and Psychiatric Symptoms in Parkinson’s Disease

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Objectives

• What type of thinking problems do patients with PD have?
• How do we diagnose PD-MCI, PDD, DLB?
• What are treatment options for cognitive symptoms in patients with PD?
• What type of psychiatric symptoms are common in PD?
• What are the treatment options for psychiatric symptoms.
James Parkinson’s Observations

- Published in 1817
- Described 6 patients
- Jean Charcot coined term “Parkinson’s disease” in 1877
Cognitive Impairments in PD

- Slowness of Thought Process (Bradyphrenia)
- Impaired Executive Function
- Impaired Recall > Encoding of Memories
- Impaired Working Memory
- Visual-Spatial Perception Problems
- Variable Performance, Inattention, Fluctuations

Cummings, JL, Benson DF. Arch Neurol. 1984;41:874.
Bradyphrenia
Executive Cognitive Function

Decision Making

Problem Solving, Sequencing, Planning, Prioritizing
Memory Impairment

• Retrieval of information most involved
  – Cueing (eg category, multiple choice) helps patient recall information

• New learning remains more intact
  – Better able to learn new things as compared to Alzheimer’s disease patient
Visual Spatial Problems
Cognitive Fluctuations
Mild Cognitive Impairment in PD (PD-MCI)

- Diagnosis of PD
- Gradual decline in cognitive abilities noted by patient, informant or clinician
- Cognitive deficits on cognitive testing (e.g. neuropsychological testing, global cognitive screening test)
- Cognitive deficits are not sufficient to interfere significantly with everyday function

Adapted from Litvan I; et al. Diagnostic Criteria for MCI in PD. Movement Disorders 2012; 27(3):349-356
PD with Dementia (PDD)

• **Diagnosis of Parkinson’s Disease**
  – PD Diagnosis based on UK Brain Bank Criteria
  – Motor symptoms of PD must precede the symptoms of dementia by more than one year, typically many years.

• **Evidence of Dementia**
  – Should have typical features of PD dementia (e.g. attention, subcortical, and visual-spatial deficits may predominate)
  – Dementia not due to other conditions

Dementia with Lewy Bodies (DLB)

- One Year Rule*
- Progressive Dementia
  - Attentional, Subcortical, And Visualspatial Deficits May Predominate
- Core Features (2 of 3 required)
  - Signs of Parkinsonism*
  - Recurrent Visual Hallucinations
  - Fluctuating Cognition

Prevalence of Cognitive Impairment in Patients with PD

Incidence of Dementia in PD

From Hughes, TA. Neurology 2000;54:1596-02.
Risk Factors for PDD

• Age at Onset of Motor Symptoms
  - Older age at onset = increased risk

• Severity of Motor Symptoms
  - Greater severity = increased risk

• Duration of PD
  - Longer duration = increased risk

• Poor Response to Dopamine
  - Poor motor response or psychosis = increased risk

• Additional Risk Factors
  - REM Sleep Behavior Disorder, Orthostatic Hypotension
Pathology in PD & PDD: Lewy Bodies

Lewy Body In Substantia Nigra

Lewy Bodies In Cerebral Cortex
Cortical Lewy Bodies are associated with PDD/DLB

Evaluation of Cognitive Complaints

• Rule out non-PD causes of cognitive problems
  – Vitamin deficiencies, thyroid hormone problems, kidney or liver dysfunction
  – Sleep disorders (e.g. sleep apnea, PLMS, RBD)
  – Depression or Anxiety

• Review medications

• Cognitive testing
  – Consider neuropsychological testing

• Brain Imaging (e.g. brain MRI or head CT)
Medications to Avoid

• Avoids drugs that block acetylcholine
  – Benadryl (diphenhydramine), anti-spasmodics (e.g. Ditropan),

• Avoid opiate pain medications or related narcotics
  – For example: hydrocodone, morphine, Fentanyl

• Avoid sedatives and benzodiazepines during the day
  – For example: Chloral hydrate, primidone, lorazepam
Treatment of Cognitive Impairment in PD

- Keep mentally and physically active, socially connected and eat “heart” healthy diet
- Medications (Cholinesterase inhibitors)
  - Exelon (rivastigmine), Aricept (donepezil), Razadyne (galantamine)
  - Can improve memory, attention and neuropsychiatric symptoms
  - May worsen tremor in PD and can cause with nausea, diarrhea, runny nose, vivid dreams
Exelon (rivastigmine)* for PDD

Cognitive Test - ADAS-Cog (2.5 points better)

Global Impression of Change (CGIC)

* FDA-approved for the treatment of PDD

Psychiatric Symptoms in PD

- Depression
- Apathy
- Anxiety
- Impulse Control Disorder
- Psychosis
Depression in PD

- 20-35% of patients
- Lack of enjoyment, sadness, loss of hope, crying spells, irritability
- Premotor to late stage
- **Risk factors**: severity of motor symptoms, sleep disturbance, history of depression, women
- Several medication classes are effective
Apathy in PD

- 20-40%
- Severe loss of motivation, can be with or without depression
- Can begin in early stages of PD
- Consider rivastigmine, bupropion, modafinil, methylphenidate, if symptoms are severe
Anxiety in PD

• Can affect up to 60% of patients with PD
• Nervous, worried, fearful symptoms
• Risk factors: women, young onset, off periods and/or freezing of gait
• Treatment can include: SSRIs, adjust PD meds, buspirone, CBT, benzodiazepines
Impulse Control Disorder in PD

- Up to 35% of patients
- Symptoms can include compulsive gambling, buying, sexual behavior, and eating
- Risk factors: young age, dopamine agonists, history of alcoholism
- Consider stopping agonist, and/or reduction of dopaminergic therapy
Psychosis in PD

• 22 to 38% of PD patients
• Visual hallucinations most common, but also auditory hallucinations or delusions
• Risk factors: cognitive decline, anti-cholinergic or DA agonist medications
• Treatment includes: adjustment of PD meds, pimavanserin, atypical antipsychotic medications
Nuplazid (pimavanserin)* for PD Psychosis

Figure 3. Primary endpoint of pimavanserin pivotal phase III trial—change in total Scale for the Assessment of Positive Symptoms-Parkinson’s Disease (SAPS-PD) score from baseline.

*FDA approved for the treatment of PD Psychosis

Cognitive and Psychiatric Symptoms in PD

Figure 1: Summary of Parkinson’s disease stage and motor and non-motor symptoms that predominate at each stage\textsuperscript{24}

REM = rapid eye movement. Adapted with permission from Poewe et al., 2017.\textsuperscript{24}