Neuropsychiatric Symptoms and Management

J. Vincent Filoteo, Ph.D.
Professor
Department of Psychiatry
University of California, San Diego

Neuropsychologist and Research Psychologist
VASDHS

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Allied Team Training for Parkinson’s Disease (ATTP)

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Disclosures

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- National Institute of Health
- Parkinson’s Association of San Diego
Objectives

Describe the following:

- The diagnostic criteria for Parkinson’s Disease-Mild Cognitive Impairment (PD-MCI) and Dementia (PDD).
- The areas of cognition often impaired in patients with PD-MCI or PDD.
- How PDD differs from other dementias (Alzheimer’s disease) neuropsychologically.
- Working with the cognitive deficits in patients with PD.
- Common psychiatric conditions in PD.
- The risk factors for cognitive decline in PD.
- Questions that can be answered by a neuropsychological evaluation.

Neuropsychological Functioning

Normal cognition

↓

Parkinson’s Disease-Mild Cognitive Impairment (PD-MCI)

↓

Parkinson’s Disease Dementia (PDD)
Why Is This Important?
Many if not most patients with PD develop Parkinson’s Disease Dementia (Mindham, 1999).

Why Is This Important?
At the individual patient level.
What is Parkinson's Disease Mild Cognitive Impairment?

- Thought to be a transition state from normal cognition to dementia
- Cognitive deficits in at least one domain
- Represents a decline from previous level of function
- Does not result in significant problems performing activities of daily living

How Frequent is PD-MCI?

- Prevalence ranges from 18.9 - 38.2% with an average of 26.7% (Litvan et al., 2011)
- Frequency increases with age, disease duration, and disease severity.
- Even in newly diagnosed de novo PD patients, 25% can display mild deficits in two or more domains.
Why Diagnose PD-MCI?

• Most optimal time to implement interventions that can improve current and future cognitive decline.

• Implications for performing instrumental activities of daily living.

• Cognitive difficulties are often under-reported by PD patients and their families, but yet they can have a greater impact on quality of life than motor symptoms.

How Do You Diagnose PD-MCI?

• Formal criteria has been developed by the Movement Disorders Society (Litvan et al., 2012).

• Diagnosis is based on either cognitive screening tools or detailed neuropsychological testing, with a preference for the latter.

• With detailed neuropsychological testing, five domains should be sampled.
Cognitive Domains Assessed for Level II PD-MCI Diagnosis

- Executive Functioning: Problem solving, abstract reasoning, cognitive set shifting, multi-tasking, inhibition
- Attention/Working Memory: Focus or divide attention; maintain information in short term memory
- Language: Production, comprehension, word finding
- Memory: Encode, consolidate, retrieve
- Visual Cognition: Spatial judgment, object recognition, visuoconstruction
How Do You Diagnose PD-MCI?

I. Inclusion criteria
- Diagnosis of Parkinson’s disease as based on the UK PD Brain Bank Criteria
- Gradual decline, in the context of established PD, in cognitive ability reported by either the patient or informant, or observed by the clinician
- Cognitive deficits on either formal neuropsychological testing or a scale of global cognitive abilities (detailed in section II)
- Cognitive deficits are not sufficient to interfere significantly with functional independence, although subtle difficulties on complex functional tasks may be present

II. Exclusion criteria
- Diagnosis of PD dementia based on MDS Task Force proposed criteria
- Other primary explanations for cognitive impairment (e.g., delirium, stroke, major depression, metabolic abnormalities, adverse effects of medication, or head trauma)
- Other PD-associated comorbid conditions (e.g., motor impairment or severe anxiety, depression, excessive daytime sleepiness, or psychosis) that, in the opinion of the clinician, significantly influence cognitive testing

III. Specific guidelines for PD-MCI level I and level II categories
A. Level I (abbreviated assessment)
- Impairment on a scale of global cognitive abilities validated for use in PD
- Impairment on at least two tests, when a limited battery of neuropsychological tests is performed (i.e., the battery includes less than two tests within each of the five cognitive domains, or less than five cognitive domains are assessed)

B. Level II (comprehensive assessment)
- Neuropsychological testing that includes two tests within each of the five cognitive domains (i.e., attention and working memory, executive language, memory, and visuospatial)
- Impairment on at least two neuropsychological tests, represented by either two impaired tests in one cognitive domain or one impaired test in two different cognitive domains
- Impairment on neuropsychological tests may be demonstrated by:
  - Performance approximately 1 to 2 SDs below appropriate norms or
  - Significant decline demonstrated on serial cognitive testing or
  - Significant decline from estimated premorbid levels
How Do You Diagnose PD-MCI? (Level II Summary)

Impaired in the following:

- Two tests within a single domain, or
- One test in two different domains

Represents a decline from previous level of functioning.

Impairment is not significantly impacting activities of daily living (often evaluated via patient or family member report).

Should specify subtype (e.g., PD-MCI, amnestic).
Level I vs. Level II PD-MCI Diagnosis

Our lab (Pirogovsky et al., 2014) examined the utility of the Mattis Dementia Rating Scale (Level I diagnostic approach) and a comprehensive neuropsychological battery that utilized the MDS PD-MCI criteria (Level II diagnostic approach).

### Discriminant validity of the MDRS total score for detecting PD-MCI

<table>
<thead>
<tr>
<th>Cutoff (≤)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Correctly diagnosed</th>
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Note. MDRS = Mattis Dementia Rating Scale. PPV = positive predictive value. NPV = negative predictive value. Sensitivity, specificity, PPV, and NPV, and patients correctly diagnosed values are all expressed as percentages.

Diagnosis

Screening

In general, there is a low correspondence between Level I and Level II diagnoses.

This most likely has to do with the lower psychometric abilities of the screening measures.

Gold-standard diagnosis is a detailed neuropsychological evaluation that examines the various cognitive domains in the manner proposed by the MDS Study Group.
Progression To Dementia

How Frequent is PDD?

- Point prevalence has been shown to range from 22%-48%.
- Accounts for 3-4% of dementias in the general population.
- Incidence studies indicate that approximately 10% of a PD population will develop PDD per year.
- Cumulative epidemiological prevalence studies have shown that 78% of PD patients will have PDD after an 8 year period.
How Do You Diagnose PDD?

Clinical Diagnostic Criteria for Dementia Associated with Parkinson’s Disease

Murat Erte, MD,1,4* Dag Aarsland, MD,5,23 Richard Brown, PhD,4 David J. Burn, MD,5 Charles Duyckaerts, MD,6 Yoshikino Mizuno, MD,7,8 Gerald Anthony Broc, MD,5,10 Jeffrey Cummings, MD,11 Dennis W. Dickson, MD,12 Serge Gauthier, MD,13 Jennifer Goldman, MD,14 Christopher Goetz, MD,15 Amos Korczyn, MD,15 Andrew Lees, MD,16 Richard Levy, MD, PhD,17 Irene Litvan, MD,18 Ian McKillop, MD,19 Warren Olansky, MD,20 Werner Poeewe, MD,21 Niall Quinn, MD,22 Christina Sampaio, MD, PhD,23 Eduardo Tolosa, MD,24 and Bruno Dabois, MD25

How Do You Diagnose PDD?

I. Core features
1. Diagnosis of Parkinson’s disease according to Queen Square Brain Bank criteria
2. A dementia syndrome with insidious onset and slow progression, developing within the context of established Parkinson’s disease and diagnosed by history, clinical, and mental examination, defined as:
   • Impairment in more than one cognitive domain
   • Representing a decline from premorbid level
   • Deficits severe enough to impair daily life (social, occupational, or personal care), independent of the impairment attributable to motor or autonomic symptoms

11/3/2014
How Do You Diagnose PDD?

II. Associated clinical features:
1. Cognitive features:
   - Attention: Impaired. Impairment in spontaneous and focused attention, poor performance in intentional tasks; performance may fluctuate during the day and from day to day
   - Executive functions: Impaired. Impairment in tasks requiring initiation, planning, conceptual formation, mental flexibility, or set maintenance; impaired mental speed (bradyphrenia)
   - Visual-spatial functions: Impaired. Impairment in tasks requiring visual-spatial orientation, perception, or construction
   - Memory: Impaired. Impairment in free recall of recent events or in tasks requiring learning new material; memory usually improves with cued, recognition is usually better than free recall
   - Language: Core functions largely preserved. Word finding difficulties and impaired comprehension of complex sentences may be present
2. Behavioral features:
   - Apathy: decreased spontaneity, loss of motivation, interest, and effortful behavior
   - Changes in personality and mood including depressive features and anxiety
   - Hallucinations: mostly visual, usually complex, formed visions of people, animals or objects
   - Delusions: usually paranoid, such as nihilism, or phantom-borough (unwelcome guests living in the home) delusions
   - Excessive daytime sleepiness

III. Features which do not exclude PD-D, but make the diagnosis uncertain:
   - Co-existence of any other abnormality which may by itself cause cognitive impairment, but judged not to be the cause of dementia, e.g., presence of relevant vascular disease in imaging
   - Time interval between the development of motor and cognitive symptoms not known

IV. Features suggesting other conditions or diseases as cause of mental impairment, which, when present make it impossible to reliably diagnose PD-D
   - Cognitive and behavioral symptoms appearing solely in the context of other conditions such as:
     - Acute confusion due to a. Systemic diseases or abnormalities
     - b. Drug intoxication
   - Major Depression according to DSM IV
   - Features compatible with "Probable Vascular dementia" criteria according to NINDS-AIREN (dementia in the context of cerebrovascular disease as indicated by focal signs in neurological exam such as hemiparesis, sensory deficits, and evidence of relevant cerebrovascular disease by brain imaging AND a relationship between the two as indicated by the presence of one or more of the following: onset of dementia within 3 months after a recognized stroke, abrupt deterioration in cognitive functions, and fluctuating, stepwise progression of cognitive deficits)
How Do You Diagnose PDD?

Probable PD-D
A. Core features: Both must be present
B. Associated clinical features:
   - Typical profile of cognitive deficits including impairment in at least two of the four core cognitive domains (impaired attention which may fluctuate, impaired executive functions, impairment in visuo-spatial functions, and impaired free recall memory which usually improves with cueing)
   - The presence of at least one behavioral symptom (apathy, depressed or anxious mood, hallucinations, delusions, excessive daytime sleepiness) supports the diagnosis of Probable PD-D, lack of behavioral symptoms, however, does not exclude the diagnosis
C. None of the group III features present
D. None of the group IV features present

Possible PD-D
A. Core features: Both must be present
B. Associated clinical features:
   - Atypical profile of cognitive impairment in one or more domains, such as prominent or receptive-type (fluent) aphasia, or pure storage-failure type amnesia (memory does not improve with cueing or in recognition tasks) with preserved attention
   - Behavioral symptoms may or may not be present
C. One or more of the group III features present
D. None of the group IV features present

How Do You Diagnose PDD? (Summary)

Diagnosis of Parkinson’s disease
Deficit in two or more areas of functioning
Represents a decline from previous level of functioning
Impacts daily functioning above and beyond what is due to the other symptoms associated with Parkinson’s disease

(Emre et al., 2007)
Key Feature Distinguishing PD-MCI and PDD

PDD significantly impacts daily functioning above and beyond what is due to the other symptoms associated with PD, whereas PD-MCI does not.

Often times very difficult to determine what is “significant” and what is not due to other PD symptoms.

Use of Performance-Based Measures of Instrumental Activities of Daily Living in PD

Standardized lab-based measures of medication management and financial management:

- Medication Management Ability Assessment (MMAA; Patterson et al., 2002)
- Financial Skills subscale of UCSD Performance-Based Skills Assessment (UPSA-Finances; Patterson et al, 2001).

Scoring does not emphasize motor functioning deficits.
Use of Performance-Based Measures of Instrumental Activities of Daily Living in PD

Our initial study (Pirogovsky et al., 2013) demonstrated that non-demented PD patients were impaired in finance management but not medication management.

Medication management and finance management not associated with global cognitive functioning or motor severity.

Small association between depressive symptoms and finance management but not medication management.

Medication management and finance management not associated.

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Use of Performance-Based Measures of Instrumental Activities of Daily Living in PD

Our follow-up study (Pirogovsky et al., 2014) compared PD-MCI, PD-normal cognition (PD-NC), and healthy controls (HC) on medication management and finance management.

<table>
<thead>
<tr>
<th>Medication Management</th>
<th>Finance Management</th>
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<tr>
<td>PD-NC = HC</td>
<td>PD-NC = HC</td>
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<tr>
<td>PD-MCI &lt; HC</td>
<td>PD-MCI &lt; HC</td>
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<tr>
<td>PD-MCI &lt; PD-NC</td>
<td>PD-MCI = PD-NC</td>
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PD-MCI patients’ scores on specific cognitive measures were not associated with performance-based skills.
Neuropsychological Profile Often Seen in PD

**Impaired:**

- Executive Functioning: Problem solving, abstract reasoning, cognitive set shifting, multi-tasking, inhibition
- Attention/Working Memory: Focus, divide or sustain attention; maintain information in short term memory
- Memory: Encoding and retrieval
- Visual Cognition: Spatial judgment and visuoconstruction

**Normal/Relative Strength:**

- Language: Simple production, comprehension, word finding
- Visual Cognition: Simple object recognition
Neuropsychological Profile Often Seen in PD

**Impaired:**

**Attention/Working Memory:**

- Focus- Process targeted information while inhibiting distracting information.
- Divide- Attend to more than one target.
- Sustain- Focus or divide attention over extended period.
- Maintain and manipulate- Keep information “on-line” and manipulate in the absence of external cues.

**Memory:**

- Encoding- Processing information following initial exposure; transferring information into longer term stores
- Retrieval- Accessing information from longer term stores
Neuropsychological Profile Often Seen in PD

Impaired:

Visual Cognition:

- Spatial judgment: Judging relative orientation between two objects in space (allocentric); judging relative orientation between oneself and objects in space (egocentric).
- Visuoconstruction: Recreating visual objects by drawing

PDD vs. Alzheimer’s Disease (AD)

<table>
<thead>
<tr>
<th></th>
<th>PDD</th>
<th>AD</th>
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<tbody>
<tr>
<td><strong>Executive</strong></td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td><strong>Attention/WM</strong></td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td><strong>Memory</strong></td>
<td>++</td>
<td>++++</td>
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<tr>
<td><strong>Language</strong></td>
<td>+</td>
<td>+++</td>
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<tr>
<td><strong>Visual Cognitive</strong></td>
<td>++</td>
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</table>
PDD vs. Alzheimer’s Disease (AD)

Aarsland et al., 2003

PDD vs. AD: Memory Functioning

Encoding ➔ Consolidation ➔ Retrieval
PDD vs. AD: Memory Functioning

Encoding ➔ Consolidation ➔ Retrieval

AD

PDD vs. AD: Memory Functioning

Encoding ➔ Consolidation ➔ Retrieval

PDD
Risk Factors for Cognitive Impairment in PD

Demographic: Age,

Motor: Rigidity, bradykinesia, postural-instability (falls)

Cognitive: Executive functioning (cognitive set shifting, inhibition, verbal fluency), visuoconstruction

Psychiatric: Depression, anxiety, apathy, psychosis

Specific Strategies for Working with Cognitive Symptoms

Executive Functioning:

• Provide concrete instructions and stay away from abstract constructs.
• Reduce amount of information that must be maintained in working memory.
• Minimize multi-tasking requirements.
Specific Strategies for Working with Cognitive Symptoms

Memory:

- Lessen retrieval requirement for memory by providing choices or cues.
- Provide information with greater context.
- Allow for breaks in between learning new information (if it will take 30 minutes to learn something, break it up in 20 minute intervals with 10 minute breaks in between).
- Use both verbal and visual cues.

Specific Strategies for Working with Cognitive Symptoms

Visual Cognition:

- Reduce amount of external stimuli.
- Allow activities to occur in more open environments.
- Encourage reduction of clutter at home.
Psychiatric Factors in PD

Depression:
- Diagnosed in 20-40% of cross sectional samples
- Great impact on health-related quality of life
- Treatable with both psychotherapy (Cognitive Behavioral Therapy) and medications

Apathy:
- Very common in PD
- Can have apathy alone, apathy and depression, but rarely depression alone
- May be related to involvement of different brain structures
- No treatments identified

Psychosis:
- Diagnosed in 20-40% of cross sectional samples.
- Longitudinal studies indicate that 60% of patients will eventually develop psychotic symptoms.
- Treatments are both typical a-typical antipsychotics.
- MDS task force suggests treatment using a-typical (clozapine)
Neuropsychological Consultation

Questions:

- Does the patient have PD-MCI or PDD?
- What is the nature of the patient's cognitive deficits?
- How impaired is the patient's cognition?
- Is the patient's mood contributing to their cognitive deficits?

Neuropsychological Consultation for Pre-Deep Brain Stimulation Surgery

Additional Questions:

- Does the patient understand the cognitive and mood risks associated with the surgery?
- Does the patient have realistic expectations of the surgical outcome?
- Do family members and friends have an understanding of the cognitive and mood risks associated with the surgery?
- Do family members and friends have realistic expectations?
Very Simplistic Overview of PD

Motor

Cognitive ↔ Mood

Thank You!

vfiloteo@ucsd.edu