Thinking, Memory and Parkinson’s Disease

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I. Defining Terminology
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IV. How does Parkinson’s affect thinking and memory?
V. What can I do to treat or prevent cognitive dysfunction?
VI. What’s in the research pipeline?
I. Terminology

CONFUSION
As long as no one can agree on when you are, no one can complain about where you are or what you're doing.
Clarification of Terms

• Normal Aging: age expected changes in thinking and memory, particularly processing speed
• Mild Cognitive Impairment (MCI): cognitive dysfunction greater than expected for age
• Dementia: cognitive dysfunction in multiple domains of sufficient severity to interfere with self-care
Common Causes of Dementia

• Alzheimer’s Disease
• Lewy Body related disorders (includes PD)
• Vascular/Stroke
• Alcohol
• Medications/iatrogenic
• Vitamin Deficiency, certain infections, tumors, sleep deprivation, chronic pain…
Get Tested
Cognitive Testing

• Montreal Cognitive Assessment (MOCA)
• Neuropsychological Testing
• There are currently NO scans, blood test or spinal fluid test that can diagnose dementia!
Clarification of Terms (cont)

• Parkinson’s Disease Mild Cognitive Impairment

• Dementia with Lewy Bodies (DLB): cognitive impairment within 12 months of symptom onset, may include early visual hallucinations and fluctuations in arousal

• Parkinson’s disease dementia (PDD): cognitive impairment beginning after 12 months of parkinsonism
Cognitive Phenotypes in PD

- Normal
- Mild Cognitive Impairment (amnestic and non-amnestic subtypes)
- Classic Subcortical Dementia
- Cortical Dementia (AD/PD complex)
- Diffuse Lewy Body Dementia (DLBD)
Diffuse Lewy Body Dementia

- Dementia within 12 months of motor onset
- Visual hallucinations
- Episodic lethargy
- Hypersensitivity to neuroleptics
II. What aspects of thinking and memory are affected in PD?
Remember these three words

• BROWN
• TULIP
• HONESTY
Domains of Cognition

- Executive Function (aka frontal)
- Memory
- Visuospatial
- Attention
- Language
- Praxis
Processing Speed
Visuospatial Function
Attention
Language

- Verbal Fluency
- Naming
- Receptive Language
- Prosody
I HAVE A PHOTOGRAPHIC MEMORY.

IT TAKES AT LEAST AN HOUR TO DEVELOP.
Did you remember the three words?

Memory encoding (hippocampus) versus Memory retrieval (frontal)
Executive Function

• Medial Frontal (Anterior Cingulate): motivation
• Orbitofrontal cortex: social cognition
• Dorsolateral prefrontal cortex: complex cognition (set-shifting, multitasking, working memory)
Control of Movement
Praxis

• Control of skilled movements, tool use and recognition of tools
• Left hemisphere dominant network including posterior parietal lobe and supplementary motor area
• When affected suggests alternate diagnosis (corticobasal syndrome)
Mental Fatigue

- Sustained Attention
- Focus and Drive
- Cognitive Fatigability
- Effort
Summary

- Frontal/Executive Function Most commonly affected
- Memory retrieval
- Verbal Fluency
III. Why is this important?
Significance of Cognition in PD

• James Parkinson (1817) described “the senses and intellects being uninjured.”
• 30-40% of PD patients have cognitive impairment at disease onset
• Dementia is the leading cause of nursing home placement in PD
• By 20 years disease duration, up to 75% of PD patients have dementia
Thinking and Memory Affects:

- Fall Risk
- Medication Compliance
- Hallucinations
- Disability
- Caregivers and Family
- Quality of Life
- Feelings about the future
Dementia: Public Enemy #1

WANTED
IN 5 STATES

JOHN DILLINGER
PUBLIC ENEMY NUMBER ONE!
The Attorney General of the U.S. has authorized a
$20,000 REWARD!
for information leading to the arrest of John Dillinger,
Stretch Break
IV. How does PD affect thinking and memory?
The Lewy Body
The Substantia Nigra
Basal Ganglia
Motor Symptoms of PD

- Tremor
- Masklike facies
- Stooped posture
- Arms flexed at elbows and wrists
- Rigidity
- Hips and knees slightly flexed
- Short shuffling steps
Non-motor Symptoms of PD

• Cognition
• Fatigue
• Depression
• Anxiety
• Pain
• Constipation
• Sleep
• Hallucinations

• Urinary urgency
• Sexual dysfunction
• Sweating
• Compulsive Behaviors
• Skin Cancer
• Osteoporosis
• Visual dysfunction
The evolution of PD

This figure shows how PD progresses from the earliest symptoms (often non-motor symptoms) to diagnosis and start of treatment through to the early and advanced stages of the condition.

Preclinical PD
- Olfactory loss
- RBD
- Constipation
- Anxiety
- Depression
- Impaired colour vision

Early treated PD (stable)
- Bradykinesia
- Rigidity
- Rest-tremor (+/- non-motor symptoms)

Onset motor symptoms

Advanced PD
- Motor complications
  - Wearing off / Dyskinesias
  - Gait & balance problems
  - Axial deformities
  - Dysarthria / Dysphagia
- Non-motor complications
  - Cognitive decline / Dementia
  - Depression
  - Psychosis
  - Autonomic dysfunction
  - Sleep-awake dysregulation

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Lewy Body Dementia
Figure 1 - Frontal-striatal connections.

DL: dorsolateral; DM: dorsomedial; VL: ventrolateral; VA: ventroanterior; VM: ventromedial.
Epidemiological Observations

- Age is a better predictor of cognition in PD than disease duration
- Cognitive dysfunction is seen most in gait predominant disease > bradykinesia/rigid variant > tremor predominant
- Visual hallucinations and REM behavior disorder are associated with dementia
Neuropathology of PD Dementia

• Cell loss and Lewy Bodies in the Locus Coeruleus and Nucleus Basalis of Meynert
• Also cell loss in Ventral Tegmental Area and Dorsal Raphe Nuclei
• LB in cortex (especially Frontal)
• Less clear association with amyloid pathology although PDD and DLB frequently show AD pathology
Ascending Neurotransmitter Systems Affected by PD

- Dopamine (Substantia Nigra and Ventral Tegmental Area)
- Acetylcholine (nucleus basalis of Meynert, medial septal nuclei)
- Serotonin (dorsal raphe nucleus)
- Norepinephrine (locus coeruleus)
Dopamine and Cognition

• Improves Performance in some areas, particularly set-shifting and working memory
• No affect in most areas.
• Can cause worsening of other areas including reversal learning and gambling tasks
Other neurotransmitters and Cognition

- Acetylcholine: important for memory and arousal
- Norepinephrine: important for attention and signal to noise ratios
- Serotonin: has a role in learning and memory (also mood)
V. What can I do?
Get Tested
Rule Out Other Causes

- Sleep
- Medications
- Pain
- Vitamins, infection, thyroid, tumor...
EXERCISE

• Physical
  – Aerobic
  – Other

• Mental
  – Have fun

• Social
  – Social capital

• Spiritual
  – Meditation
Treatments

• Acetylcholinesterase Inhibitors
  – Aricept, exelon
• Memantine
• Stimulants
• Anti-depressants
• Cognitive Rehabilitation
V. What’s in the research pipeline?
Research Goals

• Better understand the cause(s)
• Develop Biomarkers
  – Diagnostic
  – Predictive
  – Track Progression
• Treatment
• Prevention
In the works

• New medication targets
• Deep Brain Stimulation
• Cognitive Rehabilitation
• Animal Models and genetics
MEG/MRI

- MEG signals
- Magnetic field pattern
- Magnetic source localization images
Brain Stimulation
Questions are guaranteed in life; Answers aren't.