Movement Disorders & Dementia

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Disclosures

- Boston Scientific, Inc – Education Faculty, Consulting

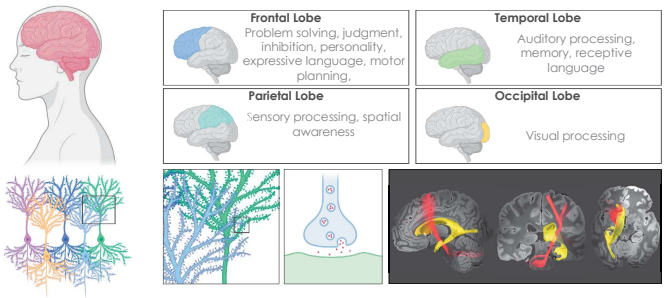
Outline

- Review relevant terminology of cognitive impairment
- Provide an overview of brain structure as it pertains to cognitive function
- Examine clinical scenarios of cognitive impairment associated with different movement phenomena

Cognitive Impairment

- Mild neurocognitive disorder
  - formerly *mild cognitive impairment*
  - A modest decline in cognitive function that **DOES NOT** significantly interfere with daily life, though it may require increased effort or compensatory strategies.
- Major neurocognitive disorder
  - Formerly *dementia*
  - *Substantial decline in cognitive function that* ***DOES*** *interfere with daily life.*
  - **Dementia has a cause**

Structure & Function



Shaking

- A 65-year-old right-handed female with a pertinent history of hypertension and sleep apnea presents with 1 year of shaking in the right hand with trouble focusing and concentrating. Symptoms are not interfering with activities of daily living. The patient's husband reports that she has fallen out of bed and even punched him when sleeping.
- Family history: father diagnosed with Alzheimer disease in his 80's.
- Examination:
  - MoCA 25/30 (visuospatial/executive -2, attention -1, delayed recall -2, MIS 12/15)
  - Flat facial affect, rest tremor (RUE), mild slowed/dampened alternating motion rates (R>L), decreased right arm swing

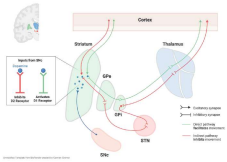
Clinical Diagnosis of Parkinson disease

- MDS Diagnostic Criteria
  - **Parkinsonism**
    - Bradykinesia with rest tremor and/or rigidity
  - Clinically established Parkinson disease
    - Parkinsonism and
      - ≥2 supportive criteria
      - Absence of absolute exclusion criteria
      - No red flags
  - Clinically probable Parkinson disease
    - Parkinsonism and
      - Absence of absolute exclusion criteria
      - Presence of red flags counterbalanced by supportive criteria

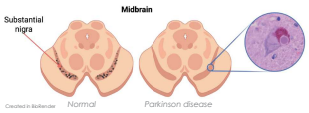
Supportive Criteria

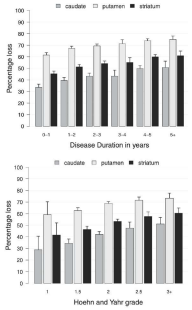
1. Robust clinical improvement with levodopa
2. Levodopa-induced dyskinesias
3. Rest tremor of a limb
4. Olfactory loss or cardiac sympathetic denervation on MIBG scintigraphy

Brain Changes in PD

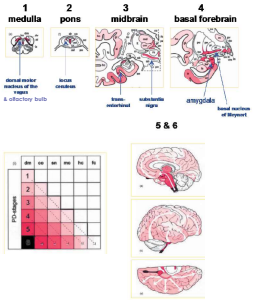


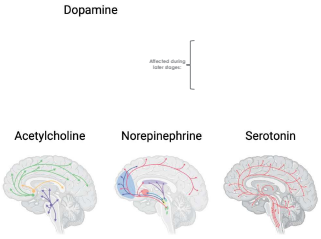
A significant proportion of striatal cells, **~35-45%**, have already been lost at the onset of motor symptoms.





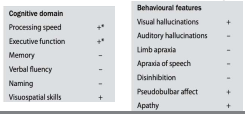
"PD is a Movement Disorder?"





Cognitive Decline in PD

- 40% Developed MCI over 5 years
- 6.9% annual incidence rate of PD-MC
  - Similar to other studies (~6-9%)
- PD-MCI reverters within 1st 3 yrs of follow-up were at increased risk of PD-D (OR 10.7 95% CI 1.5-78.5, p =0.019)



Cognitive domain	
Processing speed	-*
Executive function	-*
Memory	-
Verbal fluency	-
Naming	-
Visuospatial skills	+

Behavioural features	
Visual hallucinations	+
Auditory hallucinations	-
Limb apraxia	-
Apraxia of speech	-
Disinhibition	-
Pseudobulbar affect	+
Apathy	+

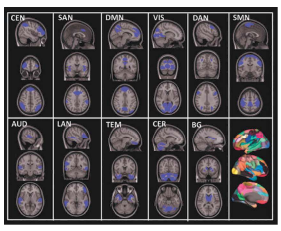
Cognitive Domains Effected in Parkinson's disease

PD-MCI

PD-D

Dual Syndrome Hypothesis

- Two types of cognitive dysfunction in early disease stages
- Frontostriatal executive
  - Common in early disease
  - Did not evolve to dementia over 3.5 years (Williams-Gray et al. 2007)
  - Dopamine dependent "dysexecutive" cognitive syndrome
- Posterior cortically based deficits
  - Visual and memory function
  - Evolved to dementia over 3.5 years (Williams-Gray et al. 2007)
  - Dopamine-independent "posterior cortical" cognitive syndrome
  - More dependent on cholinergic systems



Slowing

- A 65-year-old right-handed female with a pertinent history of hypertension and sleep apnea presents with 2 years of difficulty concentrating and multitasking with ~1 year of a "shuffling" gait and smaller handwriting. Cognition varies from day to day. She is having difficulty parking her car and relies more on GPS. She sees "figures" in her peripheral vision.
- Family history: father diagnosed with Alzheimer disease in his 80's.
- Examination:
  - MoCA 23/30 (visuospatial/executive -3, attention -1, delayed recall -3, MIS 10/15)
  - Flat facial affect, rest tremor (RUE), mild slowed/dampened alternating motion rates (R>L), decreased right arm swing, mildly slowed gait velocity, short stride length.

Dementia with Lewy bodies

- Lewy body disease (DLB) versus Dementia with Lewy bodies (DLB)
- 1 year rule
- DLB mean disease duration is 8.8 years
- Essential to the diagnosis is dementia
- Core clinical features include
  - Cognitive fluctuations
  - Visual hallucinations
  - Parkinsonism (≥1 cardinal feature)
  - R stage sleep disorder
- Clinical heterogeneity

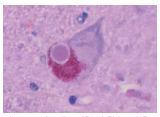


Image used courtesy of Dennis Dickson, M.D.

	PD	DLB
Cognitive domain		
Processing speed	+*	+
Executive function	+*	+
Memory	–	+
Verbal fluency	–	–
Naming	–	–
Visuospatial skills	+	+
Behavioural features		
Visual hallucinations	+	+
Auditory hallucinations	–	–
Limb apraxia	–	–
Apraxia of speech	–	–
Disinhibition	–	–
Pseudobulbar affect	+	+
Apathy	+	–

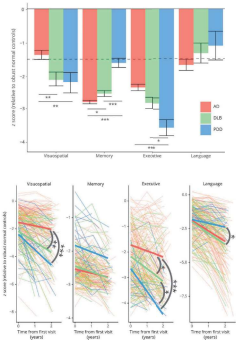
Men: RBD → Cognitive → Fluctuations / Parkinsonism → VH

Women: RBD / Cognitive → VH / Fluctuations / Parkinsonism

Graff-Radford J et al. JAMA Neurology 2017
McKeith et al. Neurology 2017
Tipton PW et al. Neurol Neurochir Pol. 2024;58:8-20.
Choudhury P et al. Alzheimers Dement. 2022 Apr;18(4):591-601.

PDD vs. DLB

- Visuospatial: PDD declined faster
- Memory: DLB more impaired but declined at similar rate
- Executive: PDD more impaired & declined faster
- Language: similar degree of impairment, but DLB declined faster
- **Visuospatial & executive outcome measures most sensitive in PDD, but memory & language in DLB**



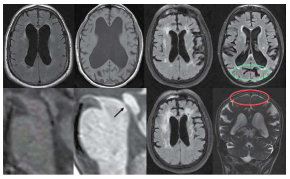
Smirnov et al. 2020 Neurology

Slowing

- A 65-year-old right-handed female with a pertinent history of hypertension, 3 vaginal deliveries, and sleep apnea presents with 2 years of progressive slowing of gait with a couple of falls and more recent mild difficulty concentrating and multitasking without interference of activities of daily living. She has chronic mild urinary when laughing or sneezing but more recently is waking up 2-3 times per night to urinate.
- Family history: father diagnosed with Alzheimer disease in his 80's.
- Examination:
  - MoCA 25/30 (visuospatial/executive -1, attention -3, delayed recall -1, MIS 14/15)
  - Decreased vibration sensation in the distal lower extremities. Gait was mildly slow with short stride length and wide base.

Normal Pressure Hydrocephalus (NPH)

- Incidence: 5.5 per 100,000[1]
- Prevalence
  - 21.9 per 100,000[1]
  - 1.1% of persons >60 years of age
  - 70-79yo: 0.2%, >80yo: 5.9%
- Gait dysfunction
- Cognition
  - No well-defined cognitive dysfunction profile
  - Frontal-executive domain
- Dysuria
  - Detrusor overactivity
  - Hypoperfusion of right frontal gyrus (micturition reflex)
- **Treatable**



Cognitive domain	
Processing speed	+
Executive function	+
Memory	+
Verbal fluency	±
Naming	–
Visuospatial skills	–

Behavioural features	
Visual hallucinations	–
Auditory hallucinations	–
Limb apraxia	–
Apraxia of speech	–
Disinhibition	–
Pseudobulbar affect	–
Apathy	+

Bluett B, et al. Mov Disord Clin Pract. 2021;10:9-16.
Tipton PW. Neurol Neurochir Pol. 2021;55:513-24.
Brean, A., & Eide, P. K. Acta Neurologica Scandinavica. 2008;118(1): 48–53.
Tipton PW et al. Neurol Neurochir Pol. 2024;58:8-20.

NPH Diagnosis

- Temporary cerebrospinal fluid diversion test

Baseline

REVIEW

IDIOPATHIC NORMAL PRESSURE HYDROCEPHALUS REVISITED: THE ROLE OF INTERMITTENCY/VARIABILITY

Standardizing the large-volume "tap test" for evaluating idiopathic normal pressure hydrocephalus: a systematic review

Gait velocity (m/s) = step length (m/step) x cadence (steps/s)

1 Hour after LP

2 Min Walking Trials Metric Comparisons

	Pre	Post1 % Δ	Post2 % Δ
Cadence: R (steps/min)	141.89	-0.61	-6.46
Gait velocity: R (m/s)	0.44	20.45	31.82
Stride length: R (m)	0.39	20.51	35.90

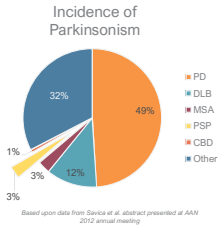
Falls

- A 65-year-old right-handed female with a pertinent history of hypertension, presents with 1 year of progressive walking difficulties now requiring a walker with more recent "slowed thinking", difficulty multitasking, and indifference to things that she once enjoyed. Denies sadness.
- Family history: father diagnosed with Alzheimer disease in his 80's.
- Examination:
  - MoCA 23/30 (visuospatial/executive -2, attention -4, delayed recall -1, MIS 14/15)
  - Slow vertical eye movements. Retropulsion with Romberg. Gait speed was relatively normal but walked with short accelerating steps.

Video courtesy of Dr. Eric Eggenberger

Progressive supranuclear palsy (PSP)

- 1963: First described by Steele, Richardson, and Olszewski
- Most common atypical parkinsonism
- 5-6% presenting with parkinsonism
- Rochester Epidemiology Project
  - Annual incidence rate: 5.3 new cases per 100,000 person-years (Bower et al. 1997)
- Prevalence (age-adjusted): 1.39-4.9 per 100,000 (Nath & Burn 2000)
- Average age of onset 63-66 yrs
- Mean survival time (from dx) = 5-8 yrs



Based upon data from Savica et al. abstract presented at AAN 2012 annual meeting

PSP: Core Features

Levels of Certainty	Ocular Motor Dysfunction	Postural Instability	Akinesia	Cognitive Dysfunction
Level 1	O1: Vertical supranuclear gaze palsy	P1: Repeated unprovoked falls within 3 years	A1: Progressive gait freezing within 3 years	C1: Speech/language disorder, i.e., nonfluert/agrammatic variant of primary progressive aphasia or progressive apraxia of speech
Level 2	O2: Slow velocity of vertical saccades	P2: Tendency to fall on the pull-test within 3 years	A2: Parkinsonism, akinetic-rigid, predominantly axial, and levodopa resistant	C2: Frontal cognitive/behavioral presentation
Level 3	O3: Frequent macro square wave jerks or "eyelid opening apraxia"	P3: More than two steps backward on the pull-test within 3 years	A3: Parkinsonism, with tremor and/or asymmetric and/or levodopa responsive	C3: Corticobasal syndrome

PSP: Gait

- Stiff & broad-based
- Tendency to knee and trunk extension and arms slightly abducted
- Tend to pivot with turns (further compromises balance)
- Akinesia of gait
  - Freezing, motor blocks, festination, disequilibrium with frequent falling
- "Rocket Sign"

Table 2. Gait features of parkinsonian disorders

	PD	DLB	MSA		PSP				CBD	NPH	Vasc.-Park	Med.-Park
			P	C	RS	P	C	CBS				
Gait velocity	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
Stride length	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
Asymmetry	+	–	–	–	–	+	–	+	+	–	±	±
Arm swing	↓	↓	↓	↓	↓	↓	↓	↑↓	↑↓	Nml/↓	Nml/↓	↓
FoG	+*	+	+	±	+	+	+	+	+	+	+	+
Ataxia	–	–	–	+	–	–	+	–	–	–	±	–
Cadence	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑↓	↑	↑↓
Step width	Nml/↓	Nml/↓	Nml/↓	↑	↑	Nml/↓	↑	Nml/↓	Nml/↓	↑	Nml/↓	Nml/↓
Levodopa response	+	+	±	–	±	±	–	–	–	–	+	±

PSP: Cognition/Behavior

- Cognitive slowing
- Dysexecutive syndrome
- Subcortical dementia with deficits in tasks requiring sequential movements
- Conceptual shifts
- Rapid retrieval of verbal knowledge
- **Apathy** ± depression
  - Dysfunction in frontal cortex & associated circuitry

Table 1. Typical cognitive features of parkinsonian disorders

	PD	DLB	MSA		PSP					CBD	NPH	Vasc.-Park	Med.-Park
			P	C	RS	P	C	CBS	SL	FTD				
Cognitive domain													
Processing speed	+*	+	+	+	+	+	+	+	+	+	+	±	±
Executive function	+*	+	+	+*	+*	+	+	+	+	+	+	±	±
Memory	–	+	–	–	–	–	–	–	–	–	+	±	–
Verbal fluency	–	–	+	–	+*	–	–	+*	±	±	+*	±	±	–
Naming	–	–	+	–	–	–	–	±	±	–	–	–	±	–
Visuospatial skills	+	+	+	+	–	–	–	–	+	–	–	–	±	–
Behavioural features														
Visual hallucinations	+	+	±	–	–	–	–	–	–	–	–	–	–	+
Auditory hallucinations	–	–	–	–	–	–	–	–	–	–	–	–	–	+
Limb apraxia	–	–	–	–	–	–	–	+	–	–	+	–	±	–
Apraxia of speech	–	–	–	–	–	–	–	±	±	–	±	–	–	–
Disinhibition	–	–	–	–	–	–	–	–	–	–	±	–	±	±
Pseudobulbar affect	+	+	+	+	+	+	+	±	±	+	±	–	+	–
Apathy	↑				+*	–	–	–	–	–	±	↑	±	±

Slurring

- A 65-year-old right-handed female with a pertinent history of hypertension presents with 2 years of progressive slowing of gait with a couple of falls and more recent mild difficulty concentrating and multitasking without interference of activities of daily living.
- Family history: father had slurred speech and imbalance beginning in his 60's
- Examination:
  - MoCA 24/30 (visuospatial/executive -3, language -2, delayed recall -1, MIS 14/15)
  - Ataxic dysarthria and unable to maintain balance with Romberg. Velocity dependent hypertonia in the legs. Gait was slow with short stride length, wide base, and irregular cadence.

Cerebellar Syndromes

- Cerebellar cognitive affective syndrome (CCAS)
  - Impaired executive function, language, visuospatial abilities, verbal memory
  - Neuropsychiatric symptoms, e.g., affect dysregulation
  - "Dysmetria of thought"
- >40 genetic SCAs
  - Clinically heterogeneous with overlapping phenotypes
  - Most are autosomal dominant
  - Diagnosis is with genetic testing
  - Most often associated with cognitive symptoms are SCA1, SCA2, SCA3, SCA7, SCA8, SCA10, SCA27B, SPG7.
- Friedreich's ataxia (most common autosomal recessive form)
  - Slowed processing, impaired conceptual thinking, impulsivity

Petit E et al. Neurology. 2025 Sep 9;105(5):e213980.
Hoche F et al. Brain. 2018 Jan 1;141(1):248-270.

Swinging

- A 45-year-old right-handed female with a pertinent history of hypertension presents with 2 years of progressive irritability, difficulty multitasking, and more recent development of involuntary arm movements
- Family history: father had similar "weird" movements and died from suicide in his early 40s.
- Examination:
  - MoCA 24/30 (visuospatial/executive -4, delayed recall -2, MIS 10/15)
  - Involuntary wiggling movements of the R>L arm.

Huntington disease (HD)

- HD is an autosomal dominant neurodegenerative condition caused by CAG repeat expansion in the *HTT* gene on chr 4.
- Average age of onset is 40 years, although anticipation occurs.
- Movement, cognitive, and psychiatric symptoms
  - 51.8% of patients present with all three
  - 25% with movement and cognitive
  - 14.3% with movement and psychiatric
  - 8.9% with isolated movement manifestations.
- Deficits in psychomotor and executive skills, memory, emotion recognition, and social cognition.
- Neuropsychiatric symptoms (eg, apathy, irritability, and executive dysfunction) are common in premanifest stages of HD.
- Atrophy of caudate head seen on brain MRI
- Diagnose with genetic testing (if negative, consider phenocopies)

Vinther-Jensen T et al. Orphanet J Rare Dis 2014; 9:114.
Martinez-Horta S et al. Parkinsonism Relat Disord 2016;25:58-64.
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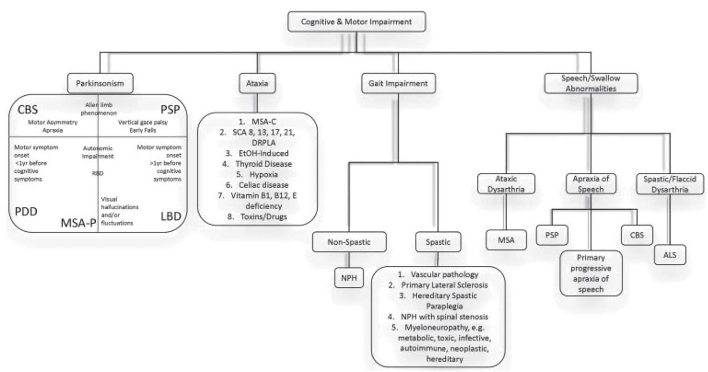

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