



Movement Disorders and Cognitive Decline

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DISCLOSURES

None relevant to this talk

FINANCIAL CONFLICTS OF INTEREST

None relevant to this talk

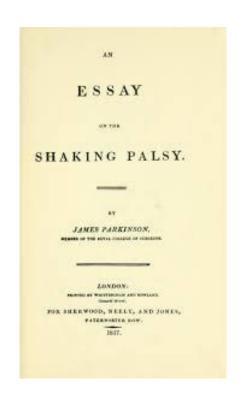
OUTLINE

- Introduction
- Neuroanatomic and neuropathology substrate/link between cognition
 & movement disorders
- DDx of movement disorders with "prominent" cognitive phenomenon
- Cognitive decline in parkinsonism

Early descriptions of MDs

"....the sense and intellect being uninjured'

Unlike PD, Earliest description of HD included cognitive dysfunction





THE MEDICAL AND SURGICAL REPORTER

PHILADELPHIA, APRIL 13, 1874.

ORIGINAL DEPARTMENT.

Communications.

ON CHOREA.

By Gassa Hustractus, M. D., Million Street, Street

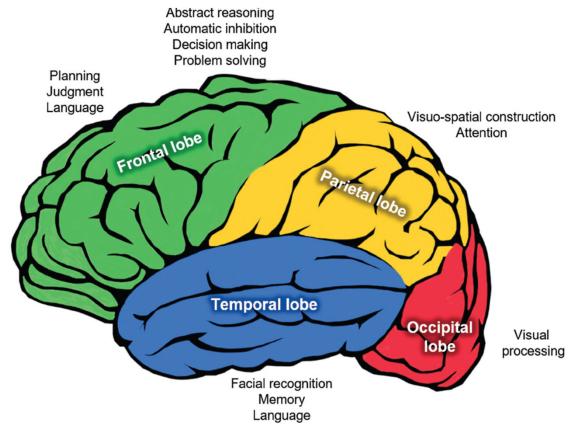
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cognition \neq memory.

And when talking about cognitive decline, all DOMAINS of cognition must be interrogated and evaluated.

Fig. 1 Brain regions and their most commonly associated cognitive functions.

Abdelnour C, Poston KL. Cognitive Impairment in Neurodegenerative Movement Disorders. Semin Neurol. 2023;43(1):81-94.

Why cognitive decline in movement disorders?

- Substantially adds to disease burden
- Negatively impacts QoL
- Contributes to caregiver burden
- Major challenge in management
- One of the unmet needs

Interplay Between Cognition & Movement

- Striatum key contributor in the intersection of motor function, cognition, and emotion.
- Cognitive processes control movement including;
 - OPlans for movement
 - Motor learning
 - O Habit-formation
 - Goal-directed learning
 - Detection of errors

Goldman JG, Holden SK. Cognitive Syndromes Associated With Movement Disorders. Continuum (Minneap Minn). 2022;28(3):726-749.

Movement disorders + prominent cognitive profile

Common

- Parkinson's disease
- Atypical parkinsonism
 - DLB
 - PSP
 - CBD
 - MSA
- Huntington's disease

Less Common

- Chorea-acanthocytosis
- HDL-2
- NBIA (PKAN)
- DRPLA
- Wilson's disease
- Aceruloplasminaemia
- Niemann-Pick disease
- FXTAS

Profile of Cognitive Dysfunction in Movement Disorders

Domain	PD	DLB	CBD	PSP	HD
Memory	+	++			++
Language		+	+	+	
Visuospatial function	++	+++		+	++
Attention		+++		+	
Apraxia		++	+++		
Executive function	+++	+++	++	++++	+++
Social cognition			++		+

Spectrum of cognitive decline in PD

Subjective PD-MCI PDD

Subjective cognitive dysfunction: presence of cognitive complaints in pts with objective normal cognitive performance on standardized neuropsychological evaluation/tests & preserved ability to carry out their ADLs. Important because it predicts future progression to PD-MCI or PDD

Diagnostic Criteria PD MCI

Diagnostic Criteria for Mild Cognitive Impairment in Parkinson's Disease: *Movement* Disorder Society Task Force Guidelines

Irene Litvan, MD, ^{1*} Jennifer G. Goldman, MD, MS, ² Alexander I. Tröster, PhD, ³ Ben A. Schmand, PhD, ⁴ Daniel Weintraub, MD, ⁵ Ronald C. Petersen, MD, PhD, ⁶ Brit Mollenhauer, MD, ⁷ Charles H. Adler, MD, PhD, ⁸ Karen Marder, MD, ⁹ Caroline H. Williams-Gray, MRCP, PhD, ¹⁰ Dag Aarsland, MD, PhD, ¹¹ Jaime Kulisevsky, MD, PhD, ¹² Maria C. Rodriguez-Oroz, MD, PhD, ¹³ David J. Burn, MD, FRCP, ¹⁴ Roger A. Barker, BSc, MBBS, MRCP, PhD, ¹⁰ and Murat Emre, MD, ¹⁵

Inclusion Criteria

- Diagnosis of PD as based on the UK PD Brain Bank Criteria
- Gradual decline, in the context of established PD, in cognitive ability (patient or informant-reported, or observed by clinician)
- Cognitive deficits on either formal neuropsychological testing or a scale of global cognitive abilities
- Cognitive deficits are <u>not sufficient to</u> <u>interfere significantly with functional</u> <u>independence</u>, although subtle difficulties on complex functional tasks may be present

Exclusion criteria

- Diagnosis of PD dementia based on MDS Task Force proposed criteria
- Other explanations for cognitive impairment
- Other PD-associated comorbid conditions that, in the opinion of the clinician, significantly influence cognitive testing (e.g., motor impairment or severe anxiety, depression, excessive daytime sleepiness, or psychosis)

Movement Disorders Vol. 22, No. 12, 2007, pp. 1689-1707 © 2007 Movement Disorder Society

Diagnostic Criteria PDD

1. Core features

- Diagnosis of PD according to Queen Square BBC
- Dementia syndrome developing within the context of established Parkinson's

II. Associated features

- Cognitive: at least 2 of 4 domains
- Behavioural:

Clinical Diagnostic Criteria for Dementia Associated with Parkinson's Disease

Murat Emre, MD, ^{1*} Dag Aarsland, MD, ^{2,3} Richard Brown, PhD, ⁴ David J. Burn, MD, ⁵ Charles Duyckaerts, MD, ⁶ Yoshikino Mizuno, MD, ^{7,8} Gerald Anthony Broe, MD, ^{9,10}

Jeffrey Cummings, MD, ¹¹ Dennis W. Dickson, MD, ¹² Serge Gauthier, MD, ¹³ Jennifer Goldman, MD, ¹⁴ Christopher Goetz, MD, ¹⁴ Amos Korczyn, MD, ¹⁵ Andrew Lees, MD, ¹⁶ Richard Levy, MD, PhD, ¹⁷ Irene Litvan, MD, ¹⁸ Ian McKeith, MD, ¹⁹ Warren Olanow, MD, ²⁰ Werner Poewe, MD, ²¹

Niall Quinn, MD, ²² Christina Sampaio, MD, PhD, ²³ Eduardo Tolosa, MD, ²⁴ and Bruno Dubois, MD²⁵

Probable PD-D

- A. Core features: Both must be present
- B. Associated clinical features:
- Typical profile of cognitive deficits including impairment in at least 2 of the 4 core cognitive domains (attention which may fluctuate, executive functions, visuospatial functions, and memory which usually improves with cueing)
- The presence of at least one behavioral symptom (apathy, depression or anxiety, hallucinations, delusions, EDS) supportive; lack of behavioral symptoms, however, does not exclude the diagnosis

None of the group III features OR 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 OR 1 or > group II features

None of Group IV

Neuropsychological Tests

Global Cognition

- Montreal Cogntive Assessment (MOCA)
- Frontal Assessment Battery
- Mattis Dementia Rating Scale (MDRS)
- Mini-mental State
 Examination (MMSE)

Executive function

- Clock drawing test
- Symbol Digit Modalities
 Test
- Semantic verbal fluency
- Phonemic verbal fluency (F, A, S)
- Wisconsin CST

Attention & Working memory

- Digit span (Forward & backward)
- Trail-making Test
- Stroop test

Memory – HVLTs; Visuospatial – Benton JLO; Language – Boston NT, MINT

REVIEW



Global Scales for Cognitive Screening in Parkinson's Disease: Critique and Recommendations

Matej Skorvanek, MD, PhD,^{1,2*} Jennifer G. Goldman, MD, MS , Marjan Jahanshahi, PhD,⁴ Connie Marras, MD, PhD,⁵ Irena Rektorova, MD, PhD,⁶ Ben Schmand, PhD,⁷ Erik van Duijn, MD, PhD,⁸ Christopher G. Goetz, MD,³ Daniel Weintraub, MD,⁹ Glenn T. Stebbins, PhD,³ Pablo Martinez-Martin, MD, PhD,¹⁰ and the members of the MDS Rating Scales Review Committee

- "Recommended": Montreal Cognitive Assessment, Mattis Dementia Rating Scale 2nd ed, Parkinson's Disease-Cognitive Rating Scale
- "Recommended with caveats": the Mini-Mental Parkinson, Scales for Outcomes in Parkinson's Disease-Cognition
- "Suggested" or "Listed": MMSE, ADAS-Cog, PANDA, CAMCOG-R, PDD-SS, RBANS

Skorvanek M, Goldman JG, Jahanshahi M, et al. Mov Disord. 2018;33(2):208-218.

	GNITIVE ASSESSMI riginal Version	ENT (MO	CA)	Ed	ucation : Sex :		Date of birt DAT		
(S) (B) (B) (B) (B) (B) (B) (B) (B) (B) (B	(B) (2)			Copy	Draw (3 po		Ten past elev	ven)	POINTS
(D)	(4)			[]	[] Conto] mbers	[] Hands	/5
NAMING			1			Y.			/3
MEMORY repeat them. Do 2 trial Do a recall after 5 minu	Read list of words, subject s, even if 1st trial is successful. Ites.	1	FA st trial	CE VEL	VET C	HURCH	DAISY	RED	No points
ATTENTION	Read list of digits (1 digit/		ubject has to republication				[]21 []74	8 5 4 2	_/2
Read list of letters. The	subject must tap with his h	and at each		mil ≥2emms CMNAAJ	KLBAFA	KDEAA	AJAMOF	AAB	_/1
Serial 7 subtraction sta	arting at 100] 93	[] 86 or 5 correct subtra	[];		[] 72 2 pts,1 com		65 ect: 0 pt	_/3
LANGUAGE	Repeat : I only know that The cat always I	John is the c		y.[]	- 800				/2
Fluency / Name	maximum number of words					[]_	(N ≥ 11 v	vords)	_/1
ABSTRACTION	Similarity between e.g. ba	nana - orang	e=fruit [] train – bio	ycle []	watch - ru	uler		_/2
DELAYED RECALL	Has to recall words WITH NO CUE Category cue	FACE []	VELVET []	CHURCH []	DAISY []	RED []	Points for UNCUED recall only		/5
Optional	Multiple choice cue								
ORIENTATION	[] Date []	Month	[] Year	[] [ay [] Place	[]	ity	_/6
© Z.Nasreddine MI Administered by:	D	www.me	ocatest.org	Norm	mal ≥26/3		L Add 1 point if	≤ 12 yr edu	_/30

Visit www.mocatest.org/training-certification

IDEA COGNITION SCREENING INSTRUMENT

Please note the total time taken to complete the entire questionnaire (including the preparation for Question 5)

STEP 1: Preparation for ten-word list item (Question 5)

Interviewer instructions:

- · Read out the instructions to the participant.
- . There are 3 attempts in all.
- For each attempt, let the participant know that you will require him/her to repeat the words after you.
- . Tick the words the participant remembers on the grid at each attempt.
- · After completing these attempts, move to Step 2 (completion of the IDEA instrument)

Interviewer to participant: I am going to read out a list of words. Please listen carefully and I will ask you to repeat them back to me once I have finished (Read out the words slowly).

- 1. First attempt: Now tell me all the words you can remember (Tick the words remembered)
- Second attempt: Now I will read out the words again. Listen carefully and I will ask you to repeat as many as you can. (Read out the words slowly). Now tell me all the words you can remember (Tick the words remembered)
- Third attempt: Now I will read out the words one last time. Listen carefully and I will ask you to repeat as many as you can. (Read out the words slowly). Now tell me all the words you can remember (Tick the words remembered)

		Vernacular word list	First attempt	Second attempt	Third attempt
1	Butter				
2	Arm				
3	Letter			(2)	
4	Queen				
5	Ticket				
6	Grass				
7	Corner				
8	Stone				
9	Book				
10	Stick				

IDEA SCREENING INSTRUMENT QUESTIONS

ITEM	INSTRUCTION	SCORE
I will tell you the name of some want you to describe what it is. bridge? (correct answer: som goes across a river, canyon or re	. What is a ething that road) 2 if correct	/2
2 I want you to name as many animals as you can in one minu		/2
3 Who is the chief/head/leade village?	er of this 0 if incorrect; 1 if correct	/1
4 What day of the week is it?	0 if incorrect; 2 if correct	
5 Can you tell me the ten words a earlier? Try to remember as ma can.		/5
6 Can you make the design show using these four matchsticks. I vyou once and then you have to exactly (* The examiner should make the first using the matchsticks and spoint out to the person that the the matchsticks all need to poin way. Once the examiner has mishape, collect up the matchstich bunch and place them in front operson being interviewed and the person to make the same si	that is performed correctly the design specifically heads of the ks in a of the hen ask that is performed correctly 1 Middle two matchstick head pointing same way 1 Outside two matchstick pointing at an angle and the correctly	5
	TOTAL SCORE/1	
Interviewer	Date:	
Approximate time taken to complete the test (including preparation for Q 5)		Minutes

Cognitive dysfunction is common in PD

- Pooled PD MCI prevalence: 40% (n=7053 pwPD) (95% CI 36–44)
- Point prevalence of PDD: 30%
 - After 5 years: 15 20%; After 10 years: 46%; At 20 years: 80%
- Incidence of PDD: 24.3/1000 per year
- Risk of dementia 5 6x normal aging population
- Moderated by stage of PD
- Associations (PD MCI): older age, lower education, longer PD duration, higher LEDD, more severe motor symptoms, PIGD motor subtype, poorer quality of life, higher apathy, depression.
- Associations (PDD): older age, more severe parkinsonism (particular rigidity, PIGD),
 MCI at baseline

Baiano C, Barone P, Trojano L, Santangelo G. *Mov Disord*. 2020;35(1):45-54; Litvan, I et al. *Mov Disord*. 2011;26(10);1814-24; Aarsland D, Kurz MW. *Brain Pathol*. 2010;20(3):633-9.

Take-home points

- Movement disorders are heterogenous syndromes reflecting degeneration in multiple circuits & neurotransmitters systems
- Neurodegenerative movement disorders are not just motor syndromes
- Cognitive dysfunction accompanies parkinsonism PD, DLB and common in PD where it predicts QoL
- Testing at initial presentation and periodically important
- Choice of screenin and neuropsychological tests important (consider level of education; is the test culturally appropriate?)

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