



Mass General Brigham

Neuropsychological Evaluation in Neuropsychiatry

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HARVARD
MEDICAL SCHOOL

Disclosures : none

Neither I nor my partner have any relevant financial relationship with a commercial interest to disclose.



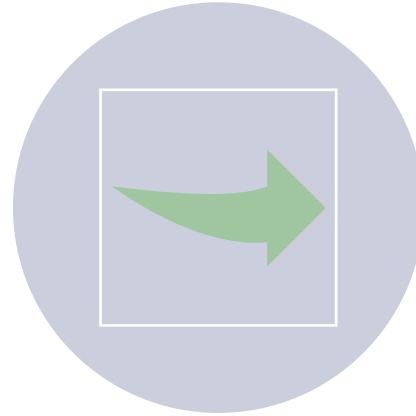
Outline

- Role of neuropsychology
- Components and procedures of neuropsychological evaluation
- Case presentation

Neuropsychology role



MEASURE/
UNDERSTAND



ETIOLOGY/
CONTRIBUTING
FACTORS



RECOMMENDATIONS/
PLAN

Neuropsychology role

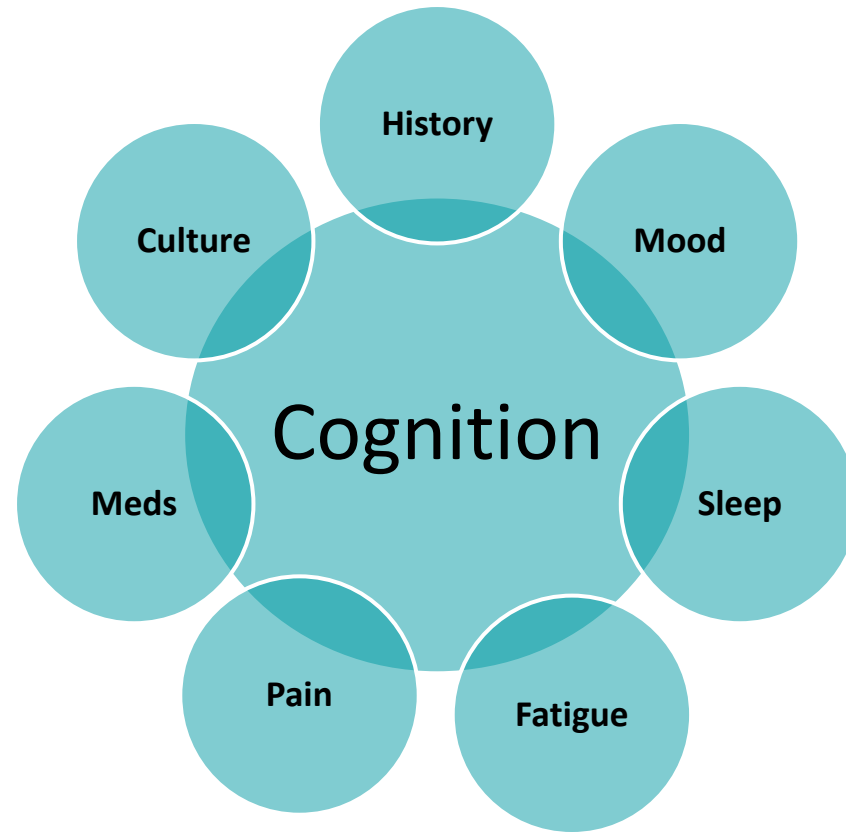
- Quantify cognition by standardized testing
- Profile summary of cognitive strengths and weaknesses
- Characterize cognitive/functional outcome of known brain injury or illness, (e.g., TBI, stroke)
 - Validation for patients and family to better understand deficits
 - Inform functioning (work, home, relationship)
- Inform treatment recommendations (e.g., cognitive rehab)
- Track recovery



Neuropsychology role

- Establish baseline and monitor intervention outcomes
 - e.g., epilepsy, deep brain stimulation, tumor resection
- Differential diagnosis
 - e.g. subjective cognitive decline vs MCI;
 - distinguish among neurodegenerative disorders

Potential factors impacting cognition and testing performance



Components of a neuropsychological evaluation

Record review

Clinical interview

Behavioral observations

Standardized testing

Interpretation/integration

Impressions

Recommendations & feedback



Clinical interview

Early development

Education and occupation

Language & culture

Psychosocial context

Medical & psychiatric history

Patient's goals for the assessment

Patient's concerns

Collateral informant



Test selection

- Base test selection on history, presentation, performance as testing proceeds, i.e., hypothesis testing
- Fixed approach: same comprehensive battery to all patients
- Most (over 80%) use flexible approach, aka fixed-flexible (Sweet et al., 2015)
 - Core battery with flexibility to add/modify tests to fit referral question, patient presentation
 - More patient-centered, prioritizing patient's time, stamina, financial cost



Test selection

- Ability level
 - Vision/hearing loss affect stimuli presentation
 - Motor impairment/aphasia may limit patient's ability to respond
- Culture & language
 - Ideally by a provider fluent in their native language
 - Cultural confounds to testing environment
 - Tests developed and/or normed on sample as similar to patient as possible (e.g., Spanish speakers from Central America vs Spain)



Domains assessed:

Global cognition/cognitive screening measures

- MMSE, MOCA, ACE
- Pros:
 - Items sample/tap various domains
 - Quick snapshot of cognitive functioning
- Cons:
 - Can over/underestimate cognition vs a comprehensive battery
 - This is particularly the case for high functioning individuals, because these screening measures are not sensitive to subtle changes

Domains assessed:

Pre-morbid intellectual ability

- Helps determine what is “normal” for a particular patient
- Whether scores obtained are in line with expectations or deviant
 - In what areas
 - And to what degree
- Based on a combination of the patient’s education, occupation and “hold” tests tapping crystallized knowledge
 - Word reading tests (Test of Premorbid Functioning)
 - Vocabulary
 - General fund of knowledge
 - Nonverbal tests (Test of Nonverbal Intelligence)



Domains assessed:

Attention and executive functioning

- Basic and complex attention
- Working memory
- Mental flexibility, including establishing, maintaining and shifting mental set
- Cognitive inhibition
- Reasoning and concept formation
- Speed of processing

Domains assessed: Attention and executive functioning

Digit Span Task

Patient repeats digits forward and backward to establish working memory span

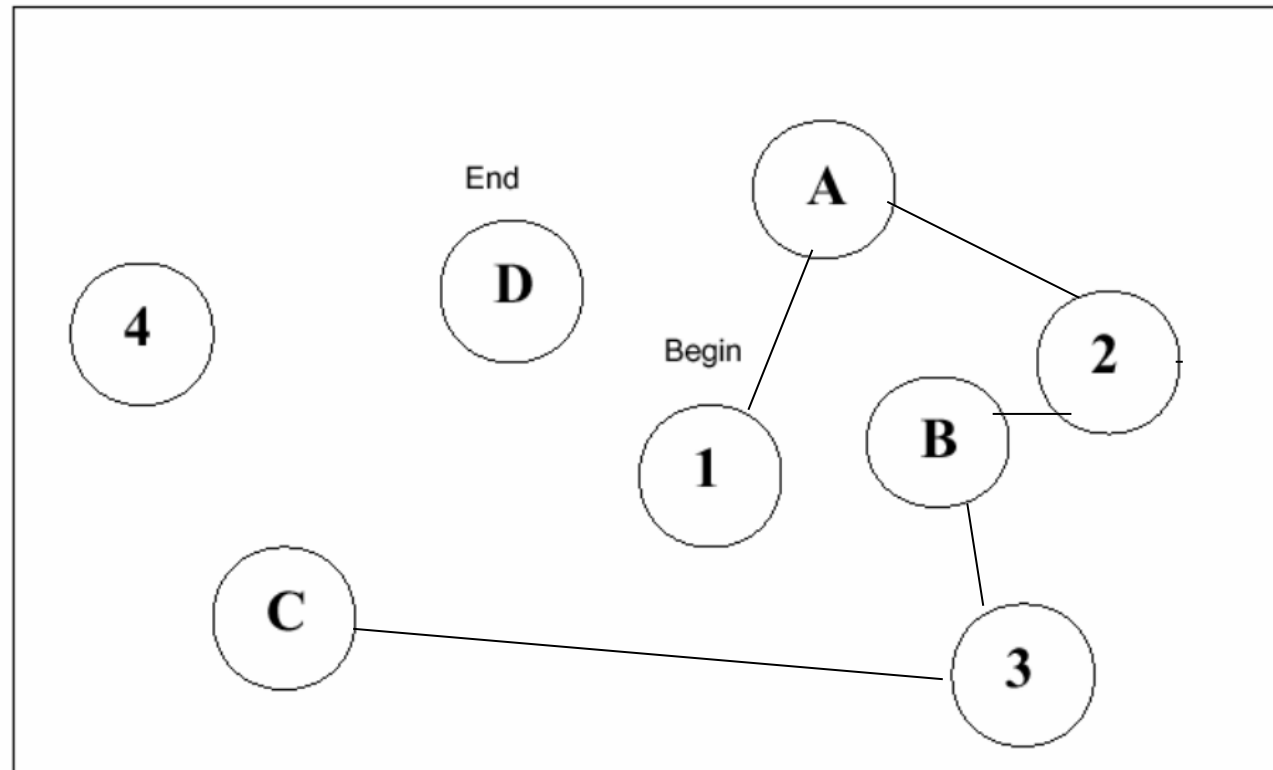
7-9-4-1-5

5-1-4-9-7

Domains assessed: Attention and executive functioning

Trail Making Test B

Alternately sequence numbers and a portion of the alphabet



Domains assessed: Attention and executive functioning

Stroop

Inhibit the automatic reading response to name the color of the ink

Word Reading	Color Naming
Red	XXX
Blue	XXX
Green	XXX
Blue	XXX
Red	XXX
Green	XXX
Blue	XXX

Domains assessed: Attention and executive functioning

Stroop

Inhibit the automatic reading response to name the color of the ink

Word Reading
Red
Blue
Green
Blue
Red
Green
Blue

Color Naming
XXX
XXX
XXX
XXX
XXX
XXX
XXX

Inhibition
Red
Blue
Green
Blue
Red
Green
Red

Domains assessed:

Memory

- Orientation
- Recent personal events / current events
- Remote memory
- Learning/acquisition (encoding, registration)
- Retrieval (recalling information at a later time)
- Storage - ability to hold information over time
 - Assessed by recognition cueing
 - Multiple choice



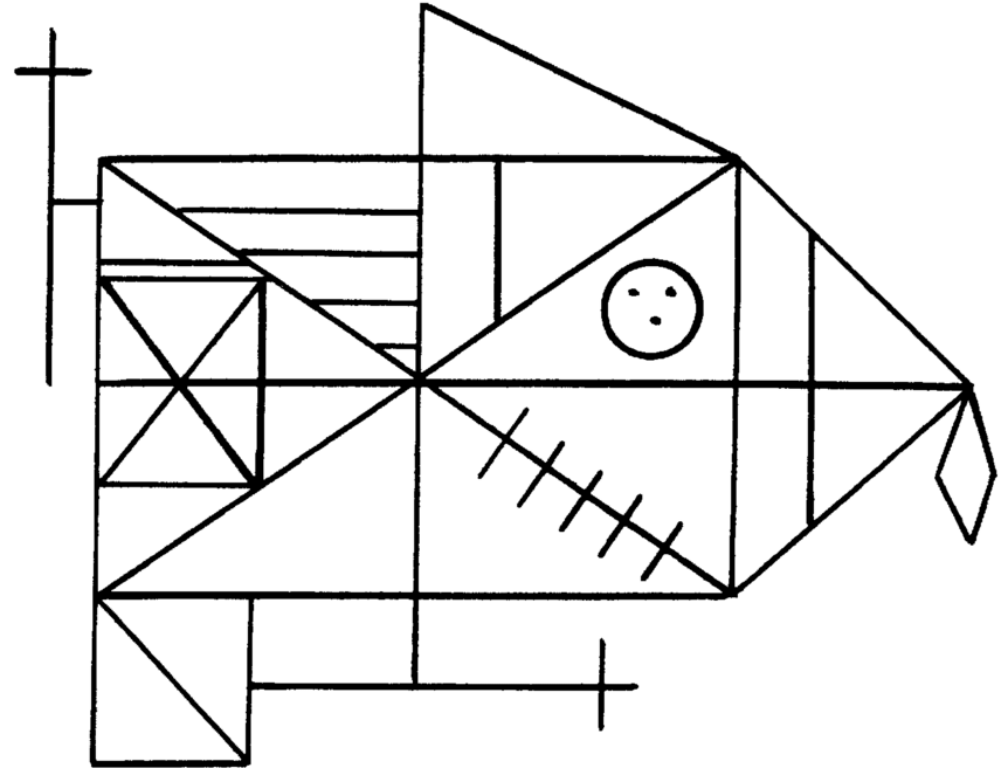
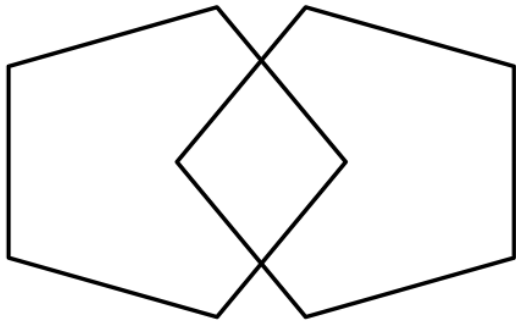
Domains assessed:

Language

- Speech
 - Fluency, grammar, syntax, paraphasias
 - Rate, prosody, volume
- Naming: word finding, object naming
- Comprehension: commands
- Repetition: words and phrases
- Reading, Writing, Spelling
- Calculations

Domains assessed: Visuospatial ability

- Perceptual: matching & discrimination among visual stimuli
- Copying/replication designs
- Nonverbal reasoning



Domains assessed:

Motor

- Captures deficits in manual motor strength, speed, dexterity
- Broader patterns of lateralization

Domains assessed: Mood/behavior/ADLs

- Self-report questionnaires, symptom inventories
 - Beck Depression & Anxiety Inventories
 - Geriatric Depression Inventory
 - PHQ-9/GAD-7
 - Personality Assessment Inventory
 - MMPI
- Collateral informant
 - Frontal Systems Behavior Scale
 - Functional Activities Questionnaire

Domains assessed:

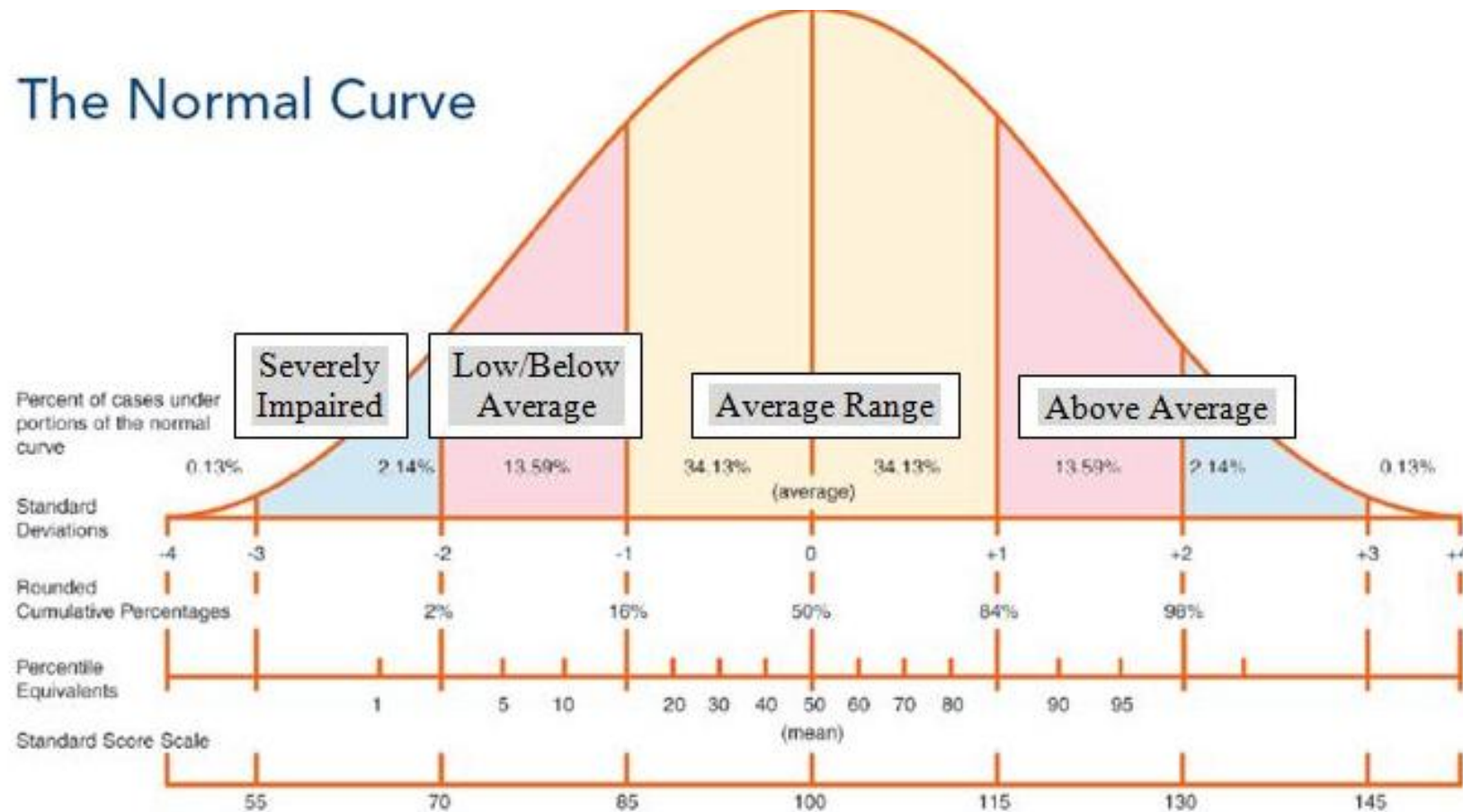
Performance Validity Testing (“PVTs”)

- Whether patient engaged in testing and putting forth adequate effort
- Very easy tasks for most patients – even with serious neurological disorders – with intentionally high specificity to minimize false positives
- Atypically low scores that are inconsistent with their functioning... we must question validity
- Not necessarily intentional
 - PVT’s only tell us that the data are invalid, but not why
- Basing conclusions in invalid data would lead to making or perpetuating inaccurate diagnoses or recommending unnecessary treatment



Test interpretation

Psychometrically-derived scores



Test Interpretation

Boston Process Approach

- Developed by Edith Kaplan and colleagues at VA Boston
- Focus on how the patient arrived at a test score that is meaningful
- Same score of “0” may be earned for very different reasons
 - Perfectionist tinkering and just running out of time
 - Someone who didn’t understand the task
 - Someone who forgot the instructions mid-task



Test Interpretation

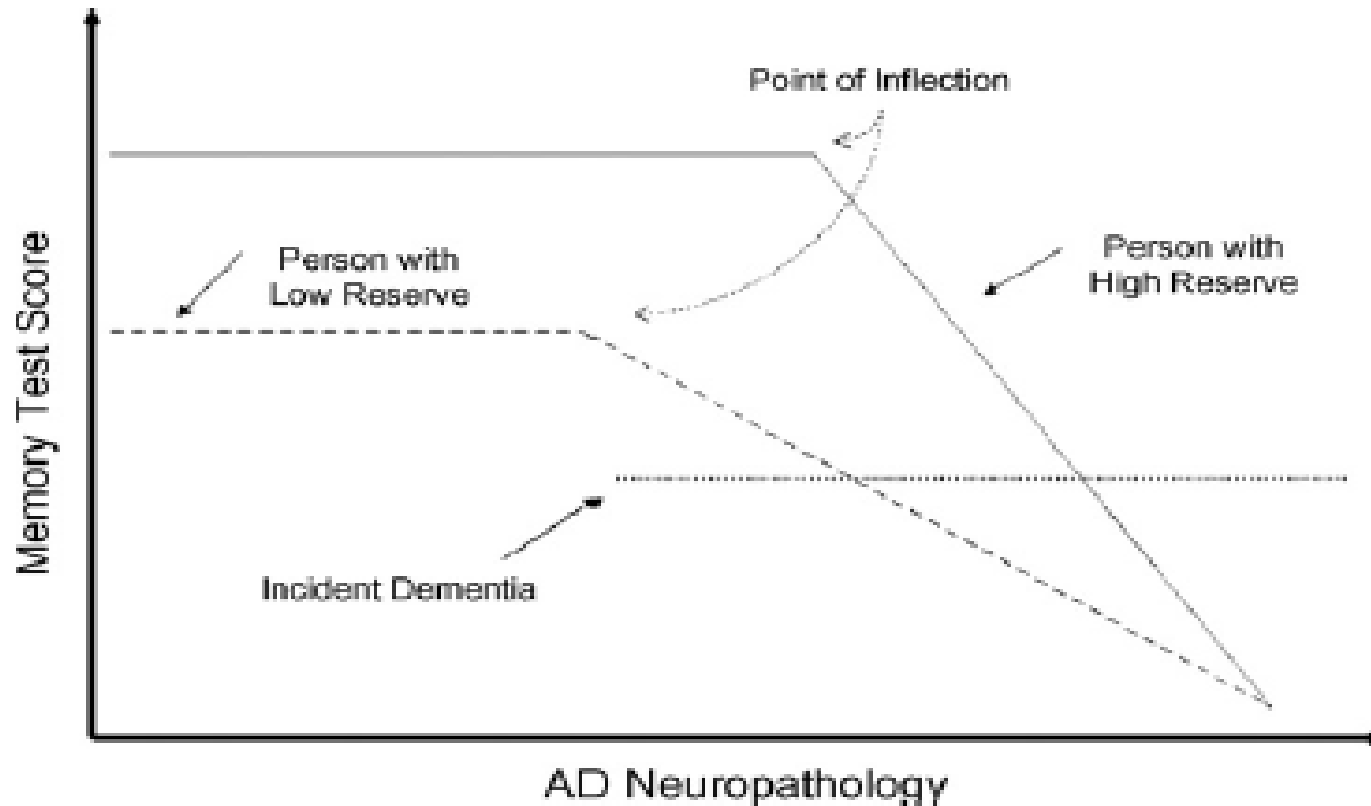
Selecting appropriate norms

- Use of normative/comparison data to aid in test interpretation
 - Test performance differs by age, education, and often by gender
 - Race based norms are proxy for quality of educational experiences
- Main concern when choosing comparison group is with over- or under-pathologizing when determining what is “normal” for an individual



Test Interpretation

Cognitive reserve



Innate intelligence

Education/Occupation

Hobbies

Social engagement

Physical activity

Test Interpretation

Rules & caveats

- Relationship between test performance and cognitive function is complex
- Intraindividual variability is the norm
- Neuropsychologists are looking for patterns
- Must base diagnostic inferences on clinically recognizable patterns rather than psychometrics alone (Schretlen et al 2003)
- Limits on ecological validity: test behavior and “real life” behavior are imperfectly correlated

Impressions

- Describes and summarizes pattern of strengths/weaknesses
- Whether change from baseline to warrant a neurocognitive disorder dx
- Etiology, rule outs and contributing factors
- Functional implications (living arrangements; employment)

Potential recommendations

- Individually tailored, considering the patients needs, resources (social, financial), culture
- Additional Referrals – Neurology, Psychiatry, Sleep study
- Safety concerns (falls, driving, Rx)
- Additional behavioral health
- Cognitive rehabilitation
- Social work consult (other services, day program, caregiver burnout)



Potential recommendations

- **Optimization of health habits:** management of medical conditions, exercise, nutrition (Mediterranean diet), sleep, stress management
- Social and cognitive engagement
- Ophthalmology/Hearing evaluation
- Vocational Counseling
- HCP, advanced directives (conversation project), POA
- And ...others tailored specifically to each patient

Neuropsychology's limitations

We may be less helpful when:

- Patients cannot meaningfully engage, e.g., severe psychiatric symptoms
- Diagnostic clarification, relative contributions of multiple comorbidities that have nonspecific cognitive profiles
- Diagnosis of certain neurodevelopmental or psychiatric disorders (e.g., ADHD, autism)
 - Cognitive profiles subtle and nonspecific, testing doesn't provide additive value
 - **Social cognition tests are not diagnostic** (e.g., Reading the Mind in the Eyes) can document theory-of-mind and emotion-recognition problems but discriminative accuracy on the individual level is too low and non-specific
 - Diagnosis based on clinical/developmental history and behavior observations

Case examples:

A tale of two MOCAs



66yo white woman referred for DBS for ET

- Retired teacher with a bachelor's degree
- PMH included h/o thyroid ca s/p thyroidectomy, mild anxiety
- MRI brain scattered WMD
- MOCA with her neurologist 23/30
 - Points lost for memory (-3) and orientation (-1)
 - Registered 5/5, 5/5, recalled 2, +2 with cues and missed last word
 - Along with points lost for abstraction, repetition and attention

66yo white woman referred for DBS for ET

GLOBALLY INTACT

- Estimated baseline: average
- Attention and EF: average to above average
- Language: intact
- Visuospatial: intact
- Memory: intact – average to high average
 - Story memory: 75th percentile
 - List learning (12-word HVLT): 62nd %ile and 100% rate of retention
 - RBANS figure recall: 63rd percentile

66yo white woman referred for DBS for ET

In this case....

Low MOCA score $\neq$ cognitive impairment

Reflected patient's situational anxiety

60yo black woman ref. by neurologist for memory loss

- Pt has associate's degree
- Still working full time as IT manager for large hospital system
- MOCA 16/30



MOCA

16/30

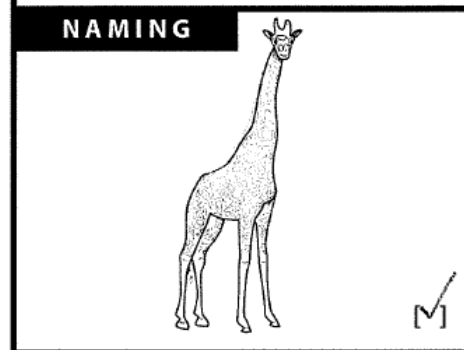
VISUOSPATIAL / EXECUTIVE

Copy rectangle

Draw CLOCK (Five past four)
(3 points)

[✓] Contour [✓] Numbers [✓] Hands

4/5



MEMORY		Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.									
		TRUCK	BANANA	VIOLIN	DESK	GREEN					
1st trial		✓	✓	✓		✓					
2nd trial		✓	✓	✓	✓						
ATTENTION		Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [✓] 3 2 9 6 5									
		Subject has to repeat them in the backward order [X] 8 5 2									
		Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors [✓] FBACMNAAJKLBAFAKDEAAAJAMOF AAB									
		Serial 7 subtraction starting at 90 [X] 83 [X] 76 [X] 69 [X] 62 [X] 55									
		4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt									
LANGUAGE		Repeat: A bird can fly into closed windows when it's dark and windy. [X] X									
		The caring grandmother sent groceries over a week ago. [✓]									
		Fluency / Name maximum number of words in one minute that begin with the letter S [✓] 15 (N ≥ 11 words)									
ABSTRACTION		Similarity between e.g. carrot - potato = vegetable. [✓] diamond - ruby [X] cannon - rifle [X] goat									
DELAYED RECALL		Has to recall words WITH NO CUE [X] [X] [X] [X] [X]									
		Category cue car - chair real									
		Multiple choice cue [✓] apple [✓] bed [✓]									
ORIENTATION		[X] Date [✓] Month [✓] Year [X] Day [✓] Place [✓] City [✓]									
		Adapted by : Z. Nasreddine MD, N. Phillips PhD, H. Chertkow MD									
		© 7 Nasreddine MD www.mocatest.org									
		Normal ≥ 26 / 30					TOTAL 16/30				

Most points lost for memory and executive functioning



60yo black woman ref. by neurologist for memory loss

Would you first order MRI brain, LP, or neuropsychology?

(obviously, we need more background first....)



60yo black woman ref. by neurologist for memory loss

MRI brain unremarkable:

1. No acute intradural abnormality, mass, or hydrocephalus.
2. Small (6 mm) cystic focus within the left parotid gland. May consider further evaluation with parotid ultrasound.

Case: 60yo black woman ref. by neurologist for memory loss

Med/Psych history

Medical hx:

- chronic migraine, untreated OSA, HTN, HLD, DMII, asthma

Meds:

- Albuterol inhaler, 81mg aspirin, atenolol 25 mg, atorvastatin 40 mg, galcanezumab 120 mg pen, metformin 500 mg, hydrochlorothiazide 25 mg, loratadine 10 mg, losartan 25mg, sumatriptan 6mg/0.5mL, melatonin

Psych hx: situational depression in the 90's. therapy and meds for 1 year

Fam hx: clean – no history of neurodegenerative disorders



Case: 60yo black woman ref. by neurologist for memory loss

Patient's concerns and ROS

- Patient was primarily concerned with migraine and poor sleep
- Her mood is okay
- Her only cognitive concern was diminished attention while reading
- Has been told she's having memory problems

Case: 60yo black woman ref. by neurologist for memory loss

Collateral informant

- Family more concerned about her memory than patient
- The issue became apparent ~5 years ago
 - At that time, she lost both parents to cancer within one week of each other
 - Stopped using CPAP while caring for them and never resumed, amid caregiver burden then grief
- Repetitiveness, retelling stories within minutes, not remembering details, when/where for family gathering
- Forgetful in other iADLs, buys duplicate items, had been forgetting meds, had forgotten to pick up sister on way to eval



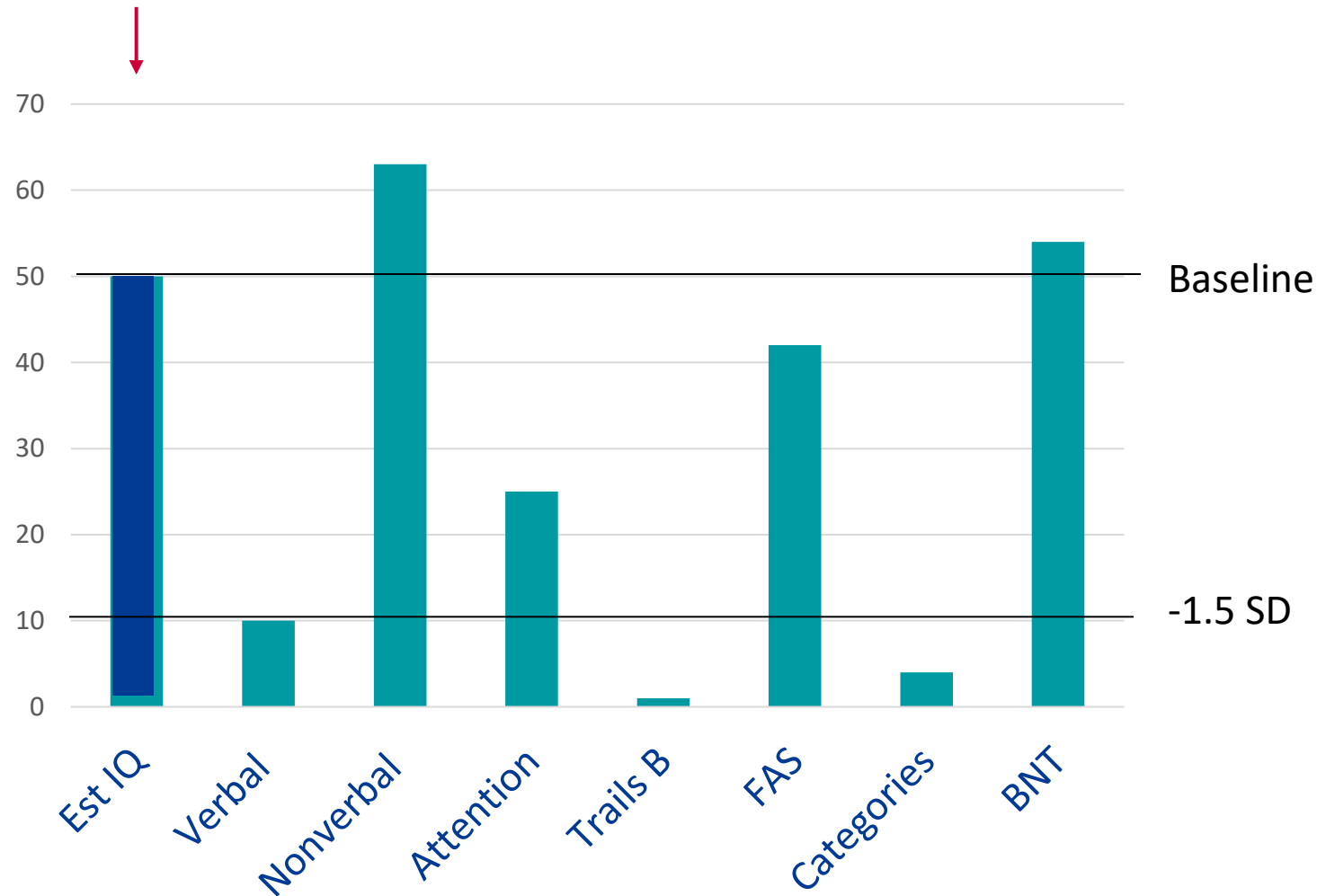
Case: 60yo black woman ref. by neurologist for memory loss

Behavioral observations

- Very personable, warm demeanor
- Appears attentive & engaged
- No sensory/motor issues
- Speech and language unremarkable to observation
- Tired, “raging” headache during eval
- Repeats herself without awareness throughout interview and testing

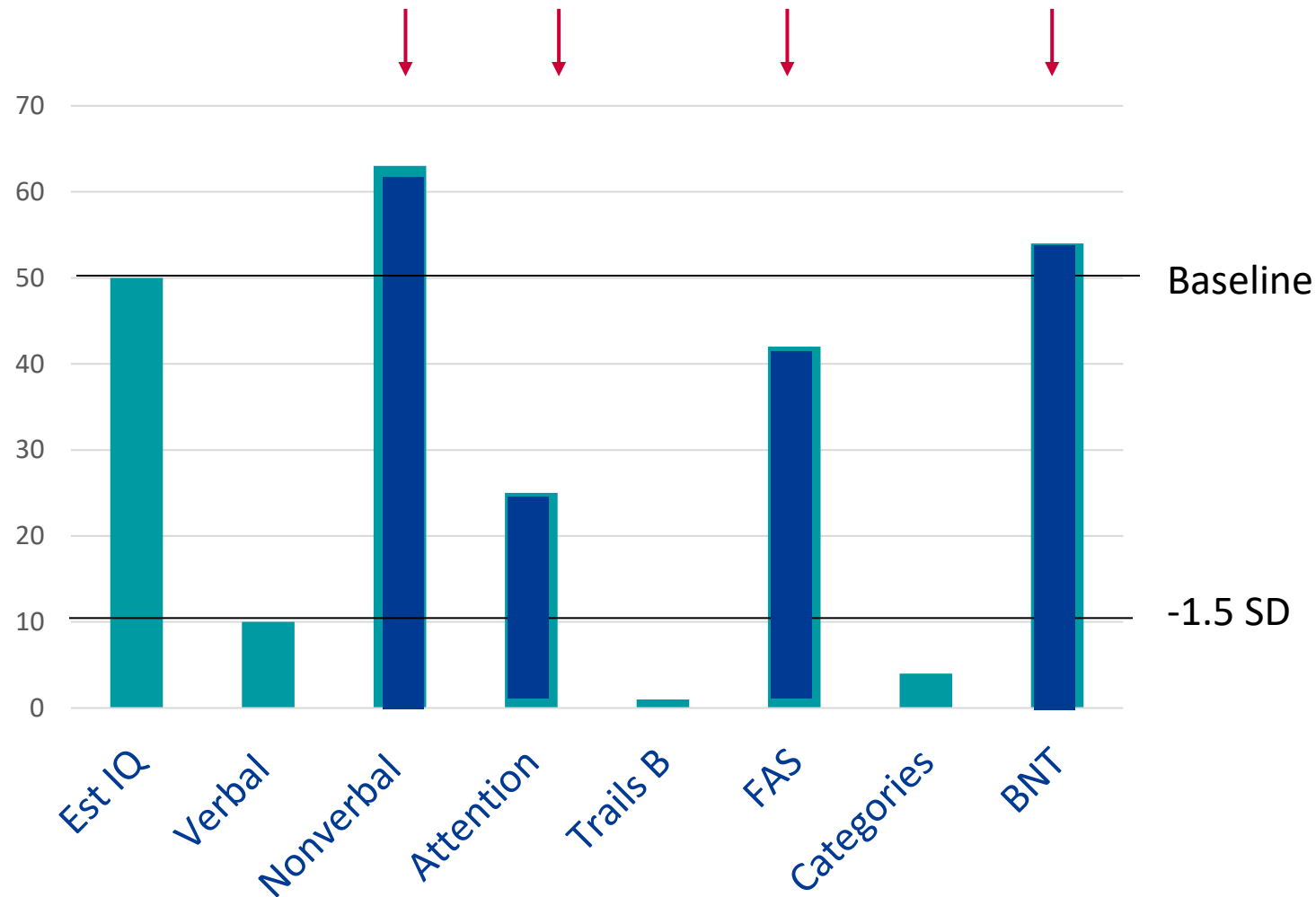
Case: 60yo black woman ref. by neurologist for memory loss

Test Scores



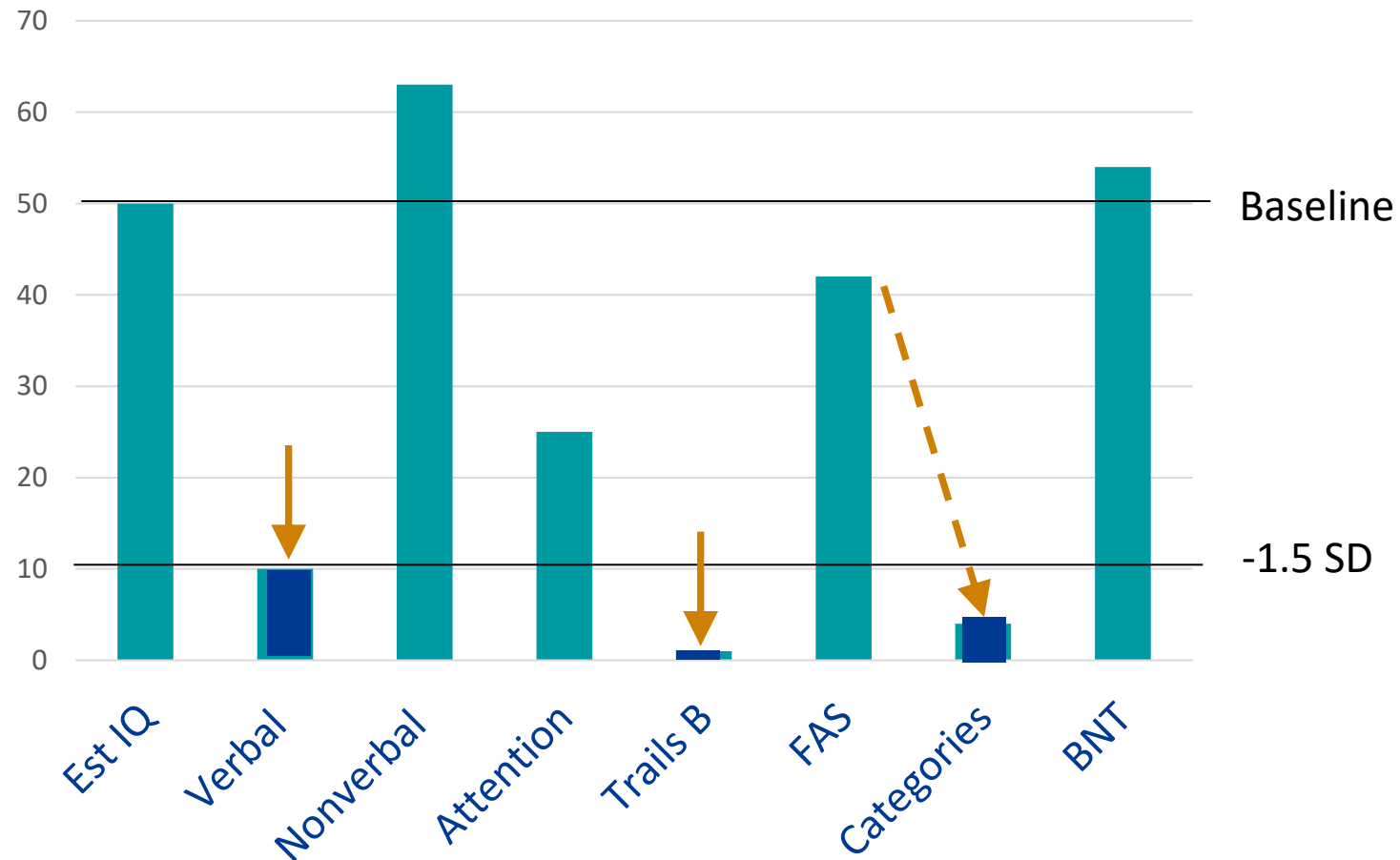
Case: 60yo black woman ref. by neurologist for memory loss

Test Scores



Case: 60yo black woman ref. by neurologist for memory loss

Test Scores



Case: 60yo black woman ref. by neurologist for memory loss

Memory profile

- Very limited encoding, flat curve
- Loss of information at the delay
- Not helped by cues/recognition format

CVLT (short) 9-word list read to her 4x

She recalled 4 words each time

0 words at the delay, +intrusions when cued

Positive response bias, 7 hits & 7 false positives

Case: 60yo black woman ref. by neurologist for memory loss

Summary of test findings

- Amnestic (encoding/storage deficit) + multi-domain impairment
 - Semantic retrieval below expectations
 - Executive functioning – variable decline, impaired set-shifting, working memory
- Basic attention and visuospatial skills reasonably preserved
- Mild mood issues on self-reports driven by poor sleep and fatigue

Case: 60yo black woman ref. by neurologist for memory loss Impressions

Major Neurocognitive Disorder

- Profile not explained by known med/psych history, e.g., vascular risks, migraine, OSA
- Patient's amnesia, behavior (repetition) and lack of insight are concerning for neurodegenerative disorder impacting MTL + broader cortical

Case: 60yo black woman ref. by neurologist for memory loss

Recommendations

- F/u with neurology and lumbar puncture
- Bring trusted friend/family to appointments
- Neurology social work for support, education
- Also connecting to Alzheimer's Association
- Consider applying for medical disability
- Memory support strategies (external, environmental structure & support)
- Optimize health habits (CPAP)
- Opportunities for research



Case: 60yo black woman ref. by neurologist for memory loss
After the evaluation...

Abeta42 **702** (range >1,026)

Total-Tau **480** (range <=237)

p-Tau181 **51.4** (range <=21.7)

p-Tau/Abeta42 **0.073** (range <.023)

CSF consistent with Alzheimer's pathology



Case: 60yo black woman ref. by neurologist for memory loss After the evaluation...

- Connected with social work for ongoing support/adjustment to diagnosis and future planning
- Family involved in RENEW caregiver support group
- On donepezil
- Considered for Lecanemab

Case: 60yo black woman ref. by neurologist for memory loss After the evaluation...

Repeat MRI brain 1.5 years after initial scan:

“Brain Parenchyma: No evidence of acute infarct, mass lesion, or hemorrhage. No significant parenchymal signal abnormality. **No significant parenchymal volume loss to suggest a specific neurodegenerative disorder.**”

Case highlights integration of info from the history, collateral, test data and observations to arrive at most likely dx of likely Alzheimer's - despite normal imaging, young age and apparent high level of functioning



The takeaway...

- The relationship between test performance and cognition is complex
- Requires thoughtful approach to information gathering, considering the myriad variables that can impact each patient
- Appropriate selection of tests and norms
- Integrated with observations of patient behavior
- To accurately characterize cognitive function, contributing factors and inform treatment planning



Thank you

