Neurocognitive Testing

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HIV NEUROBEHAVIORAL RESEARCH PROGRAM

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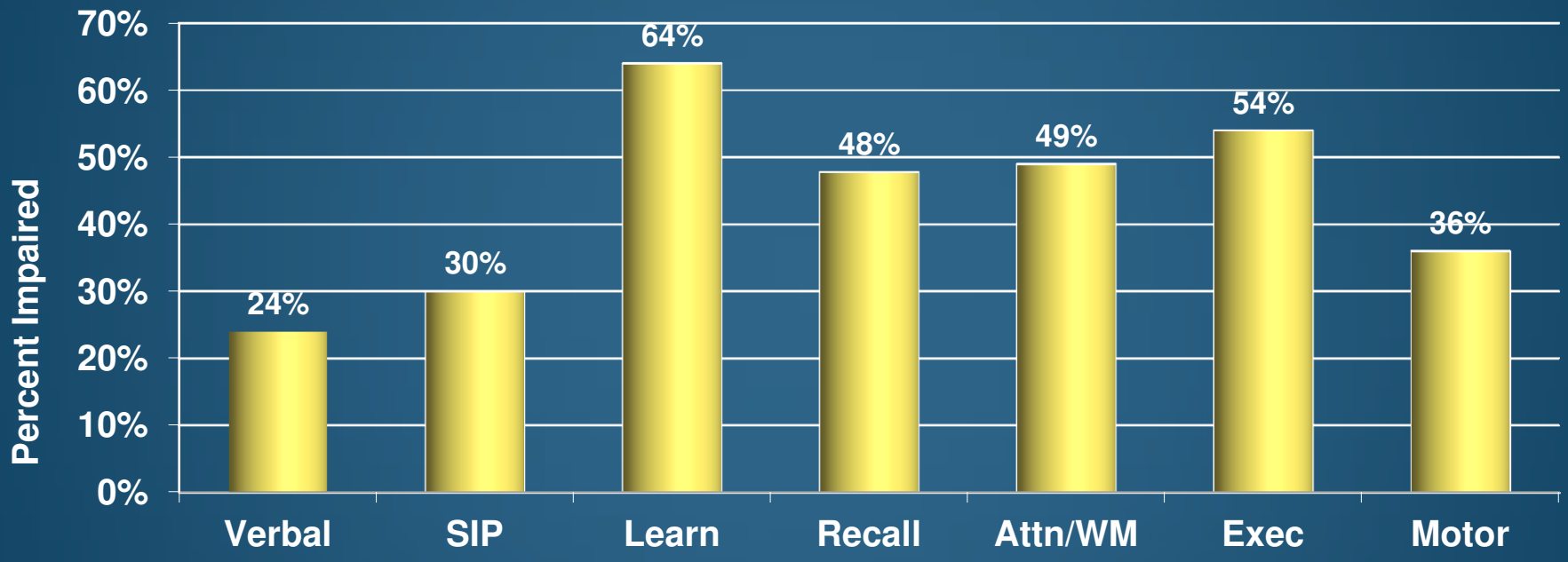
Why Use Neuropsychological Testing?

- HIV-associated neurocognitive disorders (HAND) remain prevalent (30-50%), even in the modern cART era (Heaton et al., 2010)
- Cognitive deficits are more frequently in the mild range
- Unlike HIV-associated dementia (HAD), not readily detectable during a routine clinical evaluation
- Patient self-report of cognitive problems can be affected by mood and lack of insight

Why Use Neuropsychological Testing?

- Neuropsychological testing
  - » Assess many aspects of cognition, important given the “spotty” nature of HAND
  - » Estimate as to whether there has been a decline, or improvement, in cognitive functioning

Impairment by Cognitive Domain (CART era)



Heaton et al. (2011)

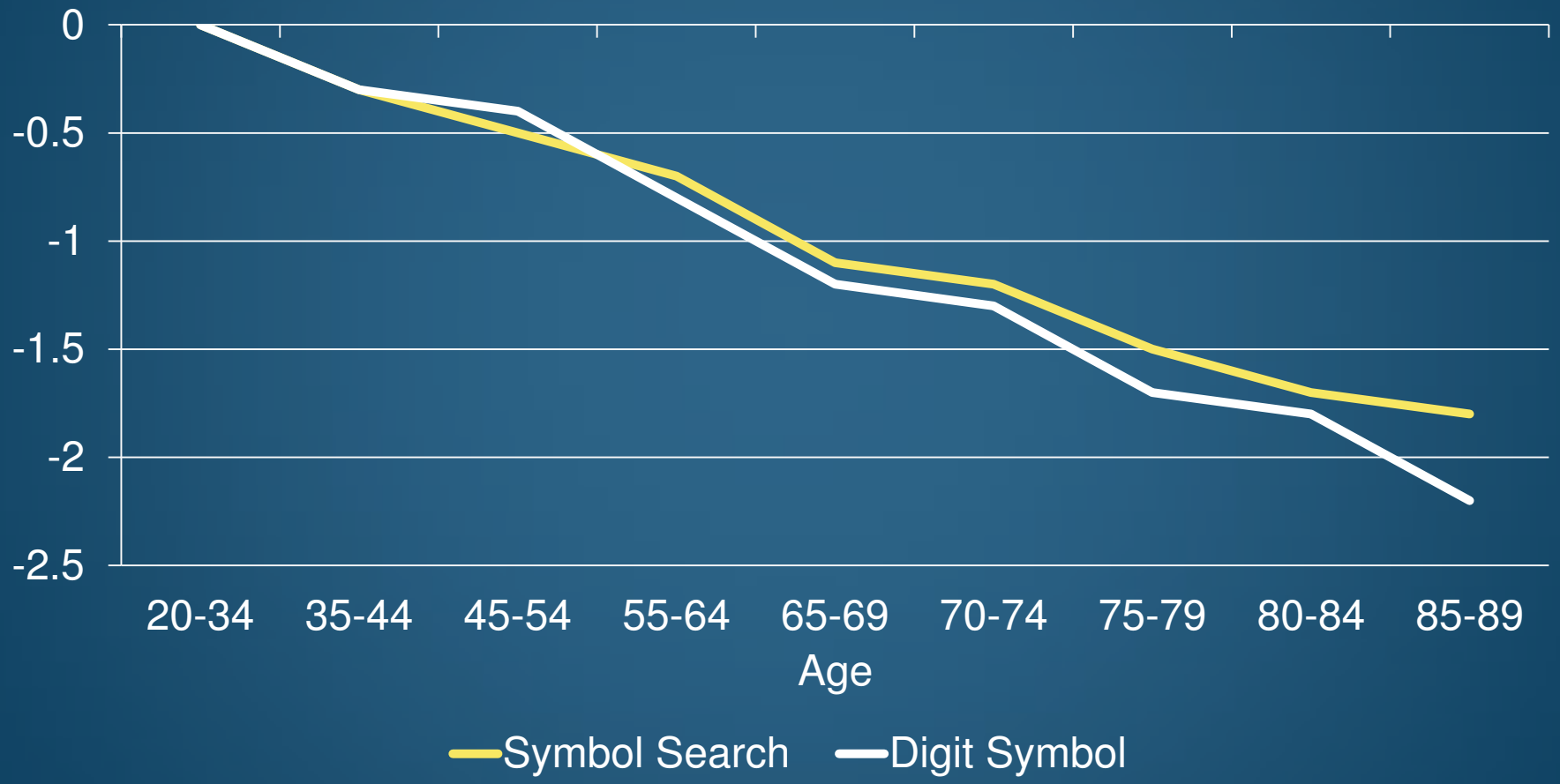
Why Use Neuropsychological Test Norms?

- Need a method to estimate at what level the patient should be performing; has there been a decline from previous levels of functioning?
- We rarely have cognitive test results from pre-infection

Demographically Adjusted T-scores

- Cognitive functioning is often associated with
  - age
  - education
  - gender
  - race/ethnicity
- Use this information to estimate the predicted score

Age Effects on WAIS-III Digit Symbol and Symbol Search (education-corrected, referenced to the 20-34 group)



Demographically adjusted T-scores

Use normative age, education and gender data to determine

- Expected/predicted (meant T score of 50, s.d. of 10), vs.
- Observed (actual T score)

to estimate whether there has likely a decline from premorbid levels

Monitoring Cognition over Time

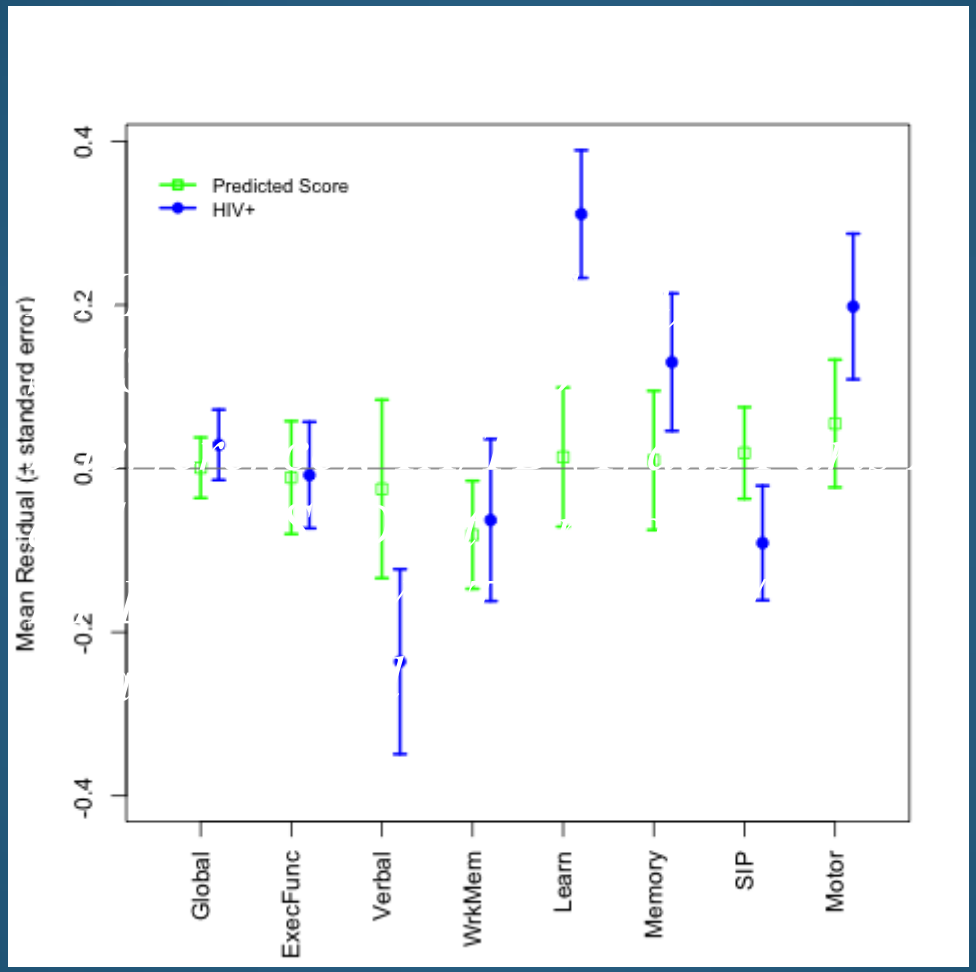
Neuropsychological testing can be used to track changes

but…

Follow-up scores are influenced by

- Baseline performance
  - On the specific test
  - Overall cognitive competence
  - Demographics (occasionally)
- Change scores and norms for change (Cysique et al., 2011)
  - Is the amount of improvement less than would be expected?

Global and domain-specific change at one year for individuals in India starting ART at CD4 < 200



Ghate et al., 2015

Cross-Cultural Neuropsychology: Challenges of Test Translation

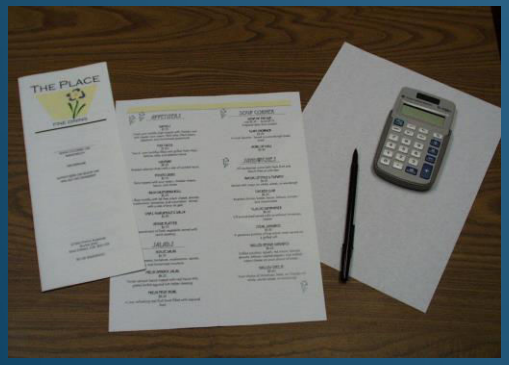
- Multiple languages, dialects, lack of words/familiarity for objects (rhino)
- Approach
  - » Translated by expert with knowledge of culture, language, and NP
  - » Backtranslation into English to confirm meaning is retained
  - » Additional review by other bilinguals (e.g., not all highly-educated)
  - » Pretest on a pilot group and adjust as necessary

Cross-Cultural Neuropsychology: Challenges of Test Interpretation

- Interpretation more challenging than test administration
  - » Cultures may vary in emphasis placed on development of certain abilities (e.g., speed vs. accuracy)
  - » Variance in years of education
    - Access
    - Quality
  - » Level of literacy, test-wiseness
- Appropriate norms should be obtained to accurately classify individuals

Cross-Cultural Neuropsychology: Determining Impact on Everyday Functioning (EDF)

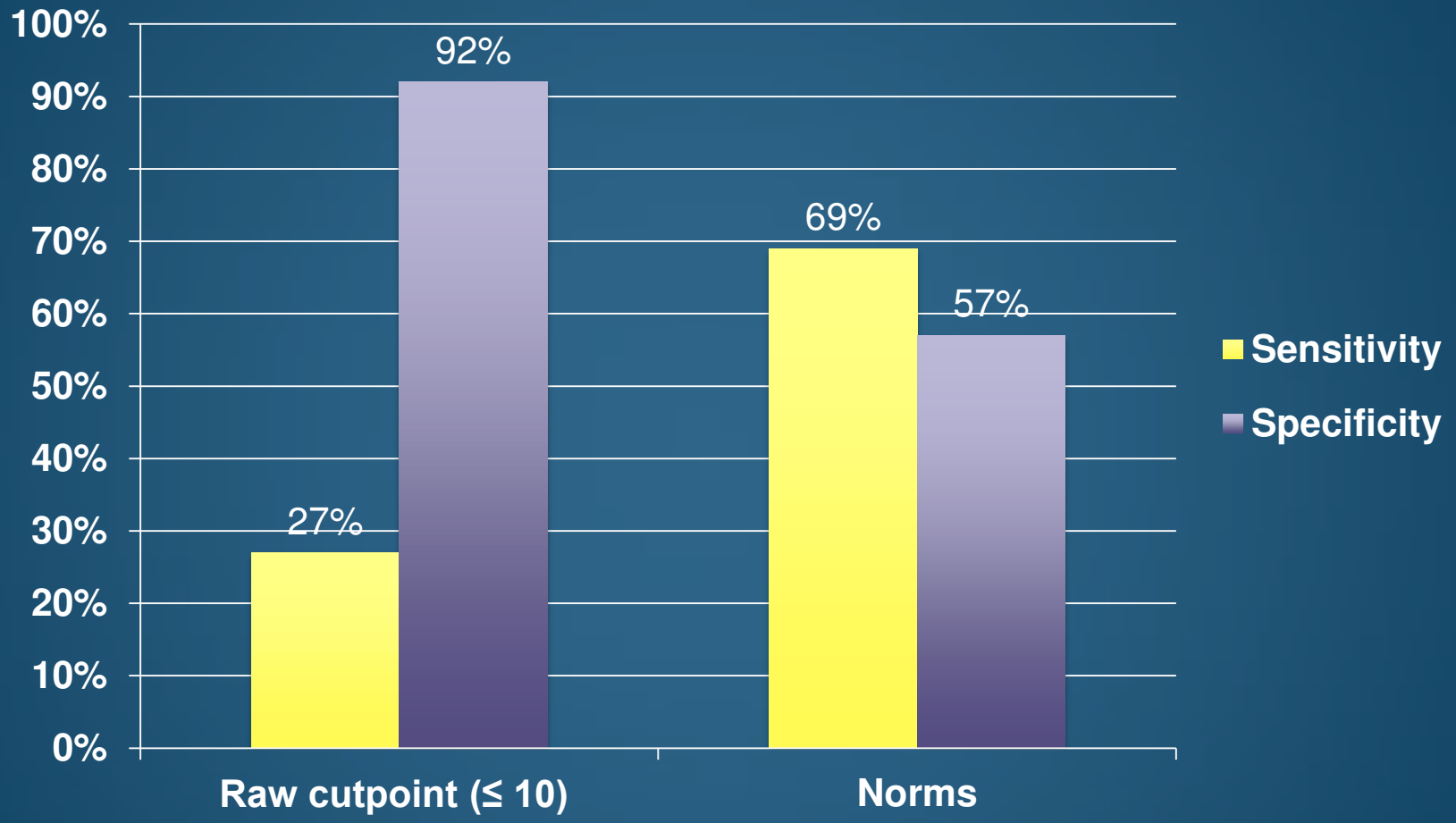
- Mostly self-report inventories (often biased)
- Should be specific for populations of interest
  - » Elderly Thai (Senanarong et al., 2003): hiring a taxi-boat, bicycling, walking to the village
  - » Rural elderly Indian population (Fillenbaum et al., 1999): remember important local festivals, holiday rituals
- Development of performance-based measures



Cognitive Screens

- Goal: brief but sensitive to HAND (spotty presentation)
- Many have been proposed
  - HIV Dementia Scale (HDS), International HIV Dementia Scale (IHDS), Montreal Cognitive Assessment (MoCA), CogState, Computerized Assessment of Mild Cognitive Impairment (CAMCI), Cognistat, NIH toolbox
- **Limitations**
  - **Lack of sensitivity to mild impairments (false positives)**
  - **Difficult to balance sensitivity and specificity**
  - **No normative adjustments**

Classification Accuracy of the HIV Dementia Scale (HDS)



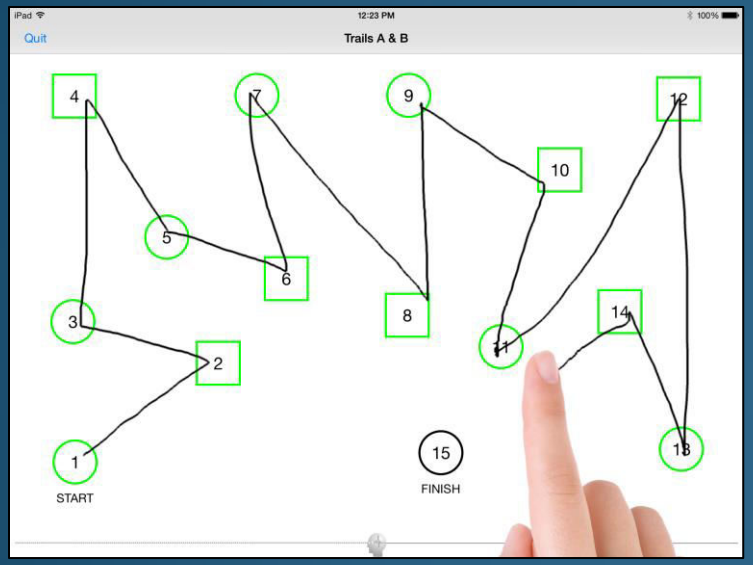
Overall Accuracy: Raw = 57% Norms = 63%
N = 1580

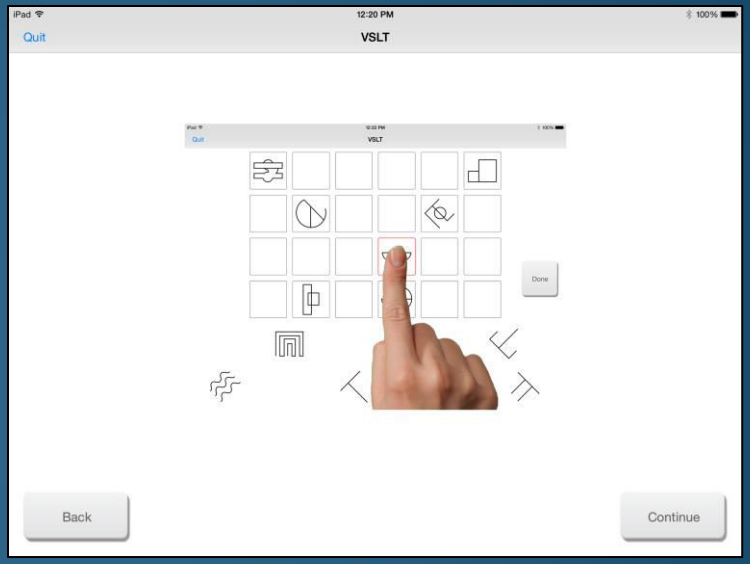
Sakamoto et al. (2013)

New UCSD iPad Brief Screen Project

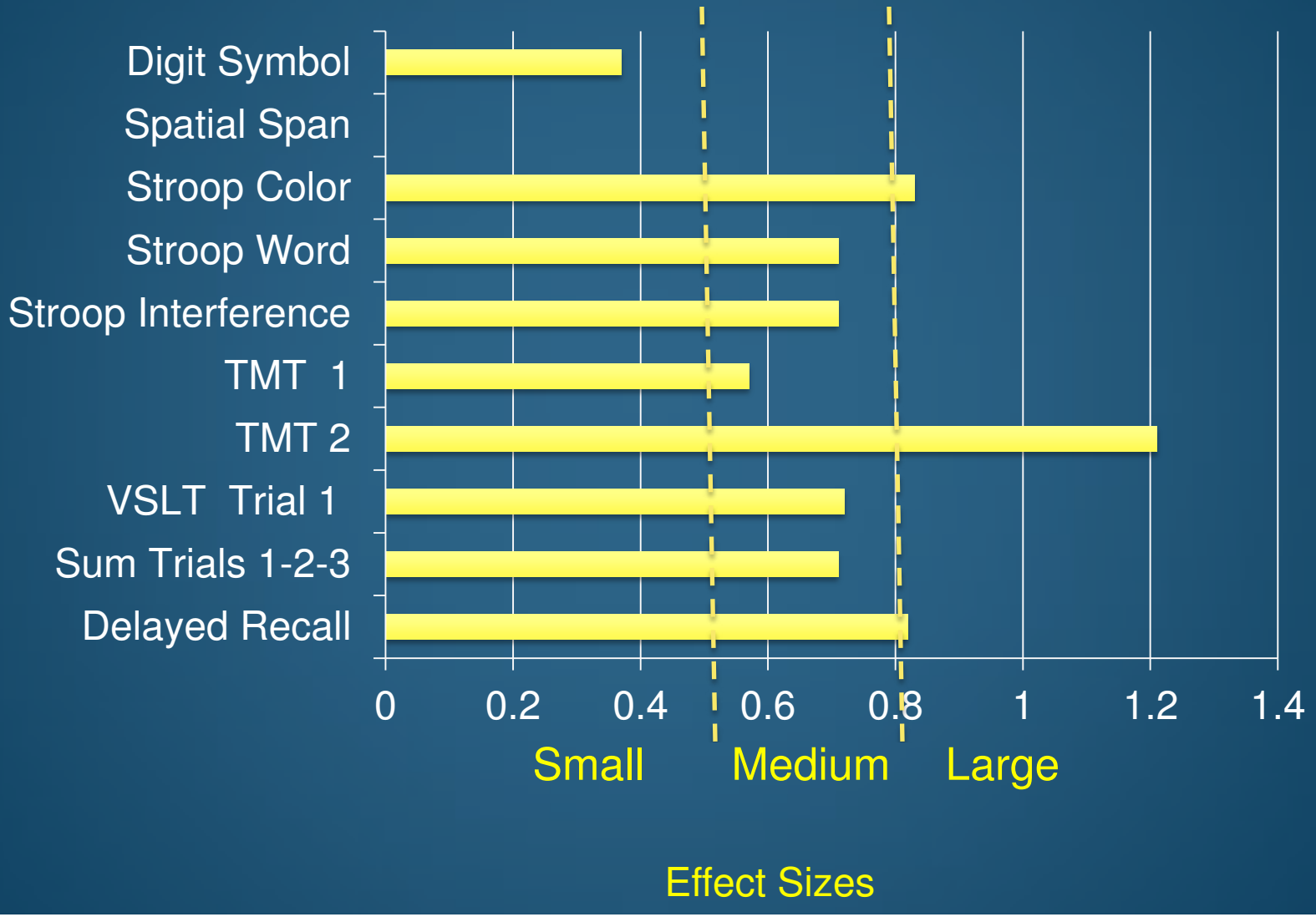
- Goals
  - Brief tool
  - Intuitive (using touchscreen interface)
  - Self-administered
  - Assesses multiple cognitive domains
  - Automated scoring and data aggregation
  - Uses locally-generated norms
  - Real-time preliminary determination of cognitive impairment

Sample instruction screens from iPad brief cognitive screen

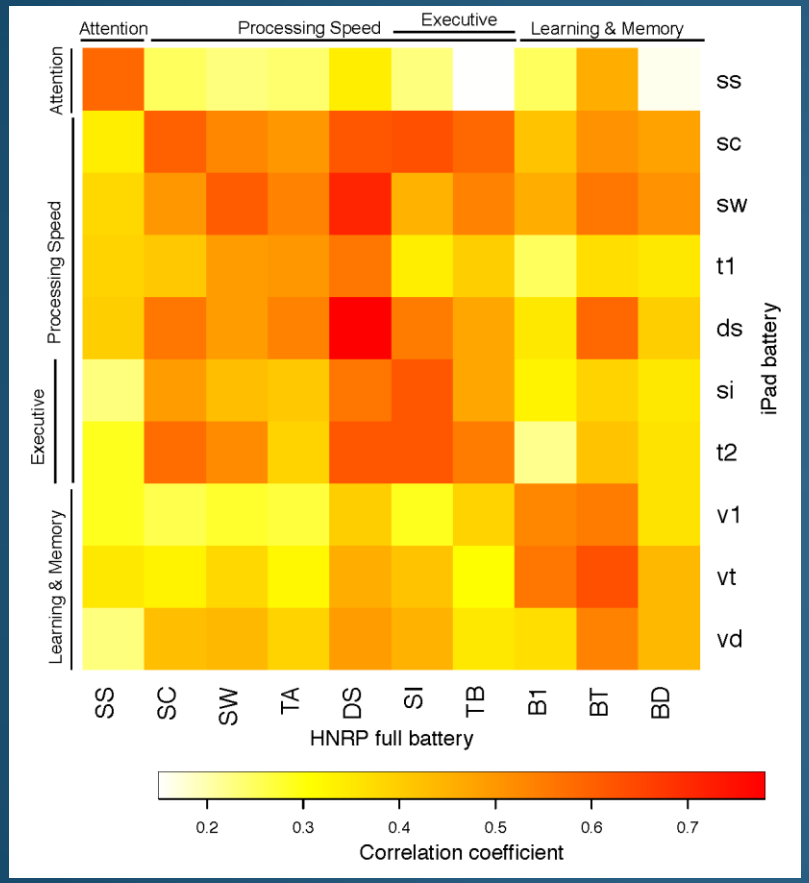




Effect sizes between HIV+ impaired and unimpaired participants



Correlations between iPad tests and similar full neuropsychologal paper-and-pencil tests



iPad

ss	Spatial span
sc/sw/si	Stroop color-word- Interference
t1/t2	Trails 1 and 2
ss	Digit symbol
v1/vt/vd	VSLT trial 1/Total Trials 1-3, delayed trial

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SS	Spatial Span	SC/SW/SI	Stroop Color/Word/Interference
DS	Digit Symbol	B1/BT/BD	BVMT-R Trial 1/Total Trials 1-3, Delay Trial

Classification Accuracy: Recursive Partitioning with 5-fold Cross-validaton

Six-Minute Screen:

1. Stroop Color (Processing Speed)
2. VSLT Trial 1 (Visual Learning)
3. Trailmaking I (Processing Speed)
4. Trailmaking II (Executive Functioning)

Actual	Predicted: Impaired	Predicted: Normal	
Impaired	13	4	17
Normal	3	16	19
	16	20	36
Sensitivity	13/17	76.5%	
Specificity	16/19	84.2%	
PPV	13/16	81.2%	
NPV	17/29	80.0%	

Summary

- NP testing provides an important method for the baseline determination of HAND, as well as tracking of cognitive change
- Adapting current cognitive measures to new regions involves careful consideration of both translation and interpretation
- The search for an effective cognitive screen continues; new technologies may provide enhanced methods for clinic-based screening

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