

# NIA ADC Clinical Task Force UDS Neuropsychology Work Group April 2011

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Progress

# 1) Response to comments from ADC's

2) Two Stage Strategy

1) Recommended measures and rationale



• Costs should not be a consideration if the current battery is useful and productive

### Work Group Response

- Cost was only one of the many reasons for which change is being considered. More important are control of dissemination of the battery and concerns about its usefulness in preclinical disease. More useful and more productive e-mail and post
- Also, tests are old, no longer published and costs are still increasing and we are at the mercy of the publishers who have not been receptive to reducing the costs.



• There is a mismatch between what we are doing now and how the field has been moving. We need to keep up with the field and this will require change.

#### Work Group Response

• We are in agreement with this view, and have been exploring instruments with promise of biomarker validation and computerized instruments that might allow more sensitive measurements, including reaction time.



• The Work Group should provide a rationale and existing data in support of the recommended measures.

#### Work Group Response

• We are collecting this evidence which is in the form of published studies (MINT, BCFT,FNAME) and laboratory data (STORIES, DIGIT SPAN).



• Change in longitudinal data collection is disruptive; risks losing continuity in data

#### Work Group Response

• We are devoting a session in the NACC Data Methods meeting to address this very reasonable concern. We invited experts on these methodological issues to contribute to the discussion. Whatever changes occur (paper and pencil or computer) will require such methods.



• Comments about specific tests- notably concerns about dropping the MMSE- it is common currency for many studies, clinical trials, etc.

#### Work Group Response

• We are sensitive to this concern but can also see another perspective, namely, that repetitive use of the MMSE for many purposes means that it could be administered more than once a year. It may be advantageous to replace MMSE for the UDS.



- Develop separate batteries for different subject groups
- Focus on normal cognitive group
- Reduce frequency of follow up testing
- Shorten battery
- Reduce ceiling effects
- Field testing is needed for new instruments
- Tests with biomarker validation
- Diagnostic battery is not necessary
- There are many computerized measures to choose from
- Develop specific research questions and design battery to answer them
- Revisions should not be restricted to the cognitive battery



# Two Stage Strategy

#### **Stage 1. Paper- and pencil replacements**

- a. Use existing test constructs but replace with novel items taken from published papers or available laboratory data. A stopgap measure.
- b. Add new or missing elements:
  - i. biomarker validated test- episodic mem-difficult
  - ii. test of visuospatial functions and non verbal memory

## Stage 2. Computerized instrument Introduce state-of-the-art computerized battery, especially for normal, preclinical and MCI (Toolbox, other)

# WHY COMPUTERIZED TESTING?

- Permits greater stimulus control
- Measures of reaction time to increase data yield
- Improve sensitivity to detect very early changes over time
- Ease of data handling, summaries
- Ever improving technology offers unprecedented opportunities for test design and adaptations to accommodate new developments in the field



# Domains

## EXISTING

# MISSING

- Processing speed
- Attention
- Episodic Memory-Story Recall
- Language
- Executive Function

- Visual Processing
- Non Verbal Memory



DOMAIN: GENERAL COGNITIVE MEASURE CONSTRUCT: DEMENTIA SEVERITY		
CURRENT MEASURES	SCORES (Total score)	PROPOSED
MMSE	Total correct (30) Total orientation items (10)	Replace with MoCA Total items correct (30) (6 orientation items overlap)



DOMAIN: PROCESSING SPEED	
CONSTRUCT: PSYCHOMOTOR SPEED	

CURRENT MEASURES	SCORES (Total score)	PROPOSED
WAIS-R Digit Symbol	Number of items completed in 90 secs (93)	DROP
Trail Making Part A	Time to complete, up to 150" Number correct lines (24) Number commission errors (40)	KEEP (15 (17) (21) (16) (19) (16) (17) (21) (19) (19) (16) (17) (19) (19) (19) (19) (19) (19) (19) (19) (19)
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#### DOMAIN: ATTENTION CONSTRUCT: SPAN, WORKING MEMORY

CURRENT MEASURES	SCORES (Total score)	PROPOSED
WMS-R DIGIT SPAN FORWARD Holding WM	Total number of correct trials (12) Span Length (8)	Retain task paradigm but replace digit strings with novel sequences
WMS-R DIGIT SPAN BACKWARD Manipulation WM	Total number of correct trials (12) Span Length (7)	Retain task paradigm but replace digit strings with novel sequences
	2b. "Here is another: 8-3-9-6."	
	3a. "Here is another: 3-6-9-2-5."	
	3b. "Here is another: 6-9-4-7-1."	
	4a. "Here is another: 9-1-8-4-2-7."	
	4b. "Here is another: 6-3-5-4-8-2."	



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#### DOMAIN: EPISODIC MEMORY CONSTRUCT: Temporal and Spatial Orientation

CURRENT MEASURES	SCORES (Total score)	PROPOSED
MMSE Orientation Items	Total Correct (10) Total Spatial (5) Total Temporal (5)	MoCA Orientation Total (6) Total Spatial (2) Total Temporal (4)

ORIENTATION TO TIME	RESPONSE	SCORE (cir	rcle one)
What is the year?		0	1
season?		0	1
month of the year?		0	1
day of the week?		0	1
date?		0	1



DOMAIN: EPISODIC MEMORY CONSTRUCT: Verbal Learning and Retention		
CURRENT MEASURES	SCORES (Total score)	PROPOSED
WMS-R Logical Memory A Immediate Recall (Learning)	Number of items recalled (25)	Retain task paradigm but replace story with similar narratives
Delayed Recall (Retention)	Number of items recalled (25)	



DOMAIN: EXECUTIVE FUNCTION CONSTRUCT: RESPONSE INHIBITION, SHIFTING		
CURRENT MEASURES	SCORES (Total score)	PROPOSED
Trail Making B	Time to complete, up to 300" Number correct lines (25) Number commission errors (40)	KEEP (13) 9 (1) (1) (10) (13) (13) (13) (13) (13) (13) (13) (13)
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DOMAIN: LANGUAGE CONSTRUCTS: Semantic Memory and Naming		
CURRENT MEASURES	SCORES (Total score)	PROPOSED
Verbal Fluency Category List Generation (Semantic Memory)	Total Animal names generated in 60 seconds Total Vegetable names generated in 60 seconds	KEEP
Boston Naming Test (Object Naming)	Total items correctly named (30)	Multilingual Naming Test 30 items, 3 overlap









PROPOSED SUBDOMAINS	Constructs	PROPOSED MEASURE	Scores
Visuospatial Processing	Constructions	Benson Complex Figure Test* - COPY	Total correctly produced elements (17) (T)
Episodic Memory	Nonverbal Learning/Retention	Benson Complex Figure Test *– Del Recall	Total correctly produced elements (17) (T)
Episodic Memory	Paired Associates Learning	FACE-NAME (FNAME) TEST**	Total Correct Face-Name associations (TBD)

#### \* Incorporated into the NACC FTLD Module (Possin et al, 2011) \*\* Validated against amyloid imaging (Rentz et al, in press)



# Issues For Replacement

TYPE OF VALIDITY	Description
Convergent Validity	New Test scores correlate highly with corresponding measure in old battery
Criterion Validity	New measures discriminate among control, MCI and AD diagnoses
Test-retest reliability	If you give the new test on two occasions no more than weeks apart, you get the same scores



### Issues for Implementation considered by NACC and UDS work group

TYPE OF VALIDITY	Description
Sampling Methods	Stratification, factors (age, ethnicity, gender); how many, which populations?
Distribution of task among centers	Can each center validate a single test? Minimized burden on centers
IRT Methods	Focus on individual items to eventually reduce the test battery
Continuity	Methods for mapping new onto old tests



# Next Steps

- Post responses to ADCs (? NACC website)
- Post supporting materials for recommended measures collected by work group
- Implementation and Timeline
- Assess computer instruments (Toolbox norming will be completed by November; data analyzed and final instrument decisions, Feb 2012)

