Real world challenges in developing digital cognitive tools: Two recent examples

Case 1. Creating a technology-assisted version of a traditional cognitive battery

Case 2. Adapting a technology-based functional assessment for use in a new indication

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Case 1: Creating a technology-assisted version of the Brief Assessment of Cognition

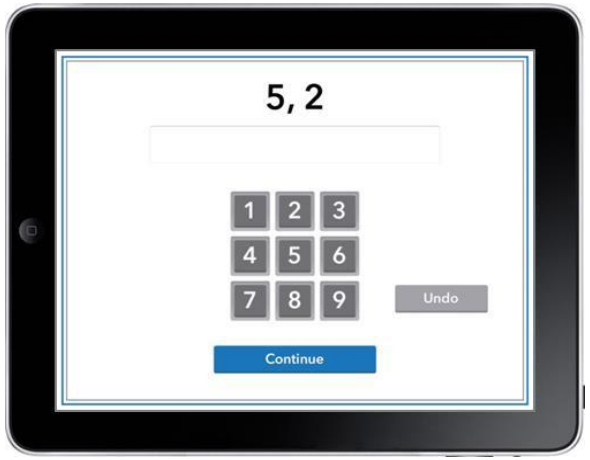
- Original BACS: A brief (30min) cognitive battery comprised of six pen-and-paper subtests that are sensitive to cognitive impairment across a variety of clinical populations. Cognitive domains assessed: verbal memory and learning, working memory, motor function, processing speed, and reasoning/problem solving.
- A tablet-based version of the BAC, the BAC App, was developed to allow standardized presentation of task instructions and stimuli, audio-recording of responses, and automatized scoring and data management

Key challenges:

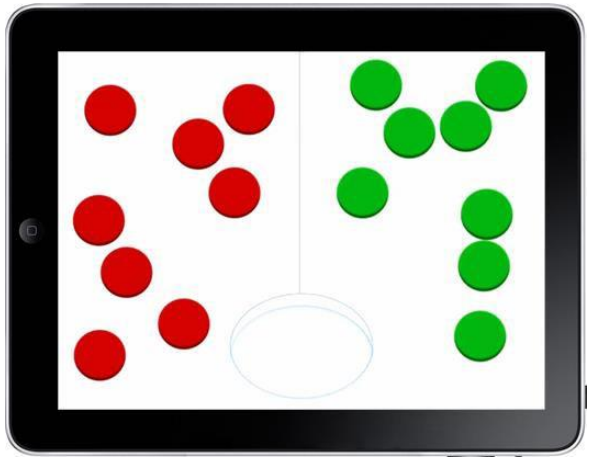
- Demonstrating (rather than assuming) equivalence of the adapted measure
  - Requires clinical validation of the adapted instrument; demonstration of psychometric reliability; collection of normative data
- Ensuring compliance with regulatory guidance and data standards
  - Requires development of 21Part11 and CDISC compliant back-end and computer system validation of the new instrument, including formal requirements, comprehensive testing and maintenance

BAC App

Verbal Memory

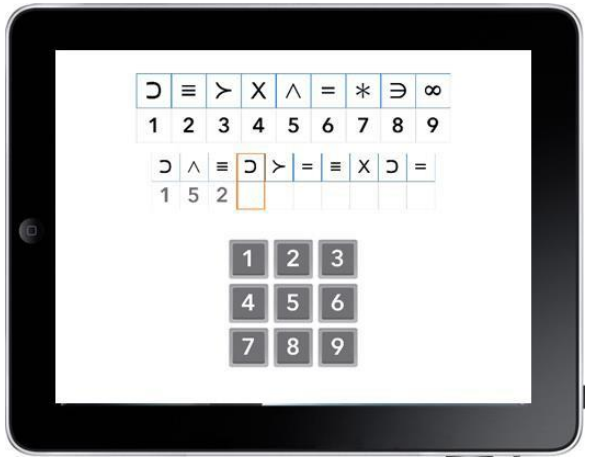


Digit Sequencing

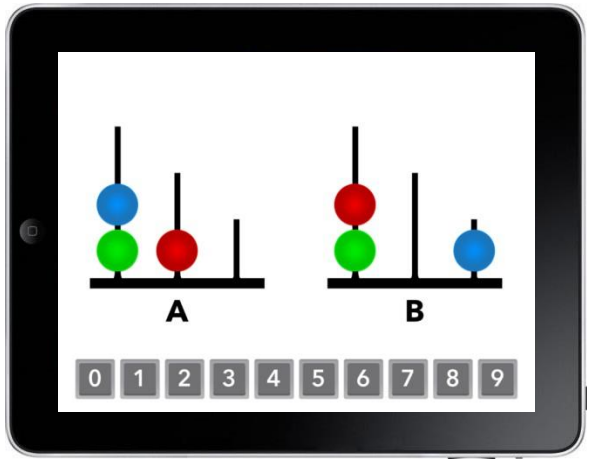


Token Motor

Semantic & Letter Fluency

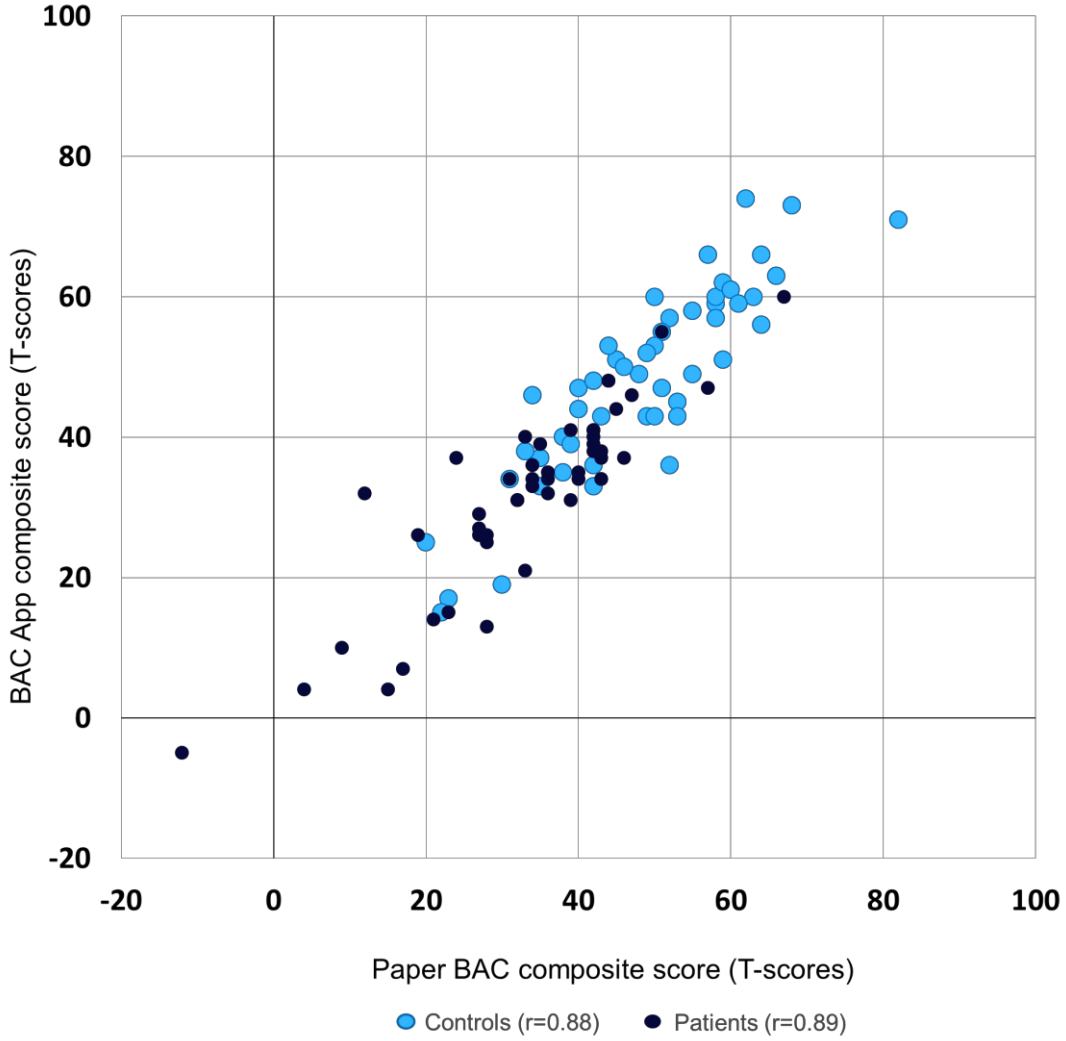


Symbol Coding



Tower of London

BAC App Validation: Sensitivity & Test Equivalence



Atkins et al., 2016 Schiz Res

- BAC App demonstrated equivalent sensitivity to cognitive deficits in schizophrenia – Cohen's d=1.34 for the BAC App, d=1.25 for the pen-and-paper BAC
- Patients (N=48) performed an average of 1-2 SD below healthy controls (N=50) on each BAC App subtest

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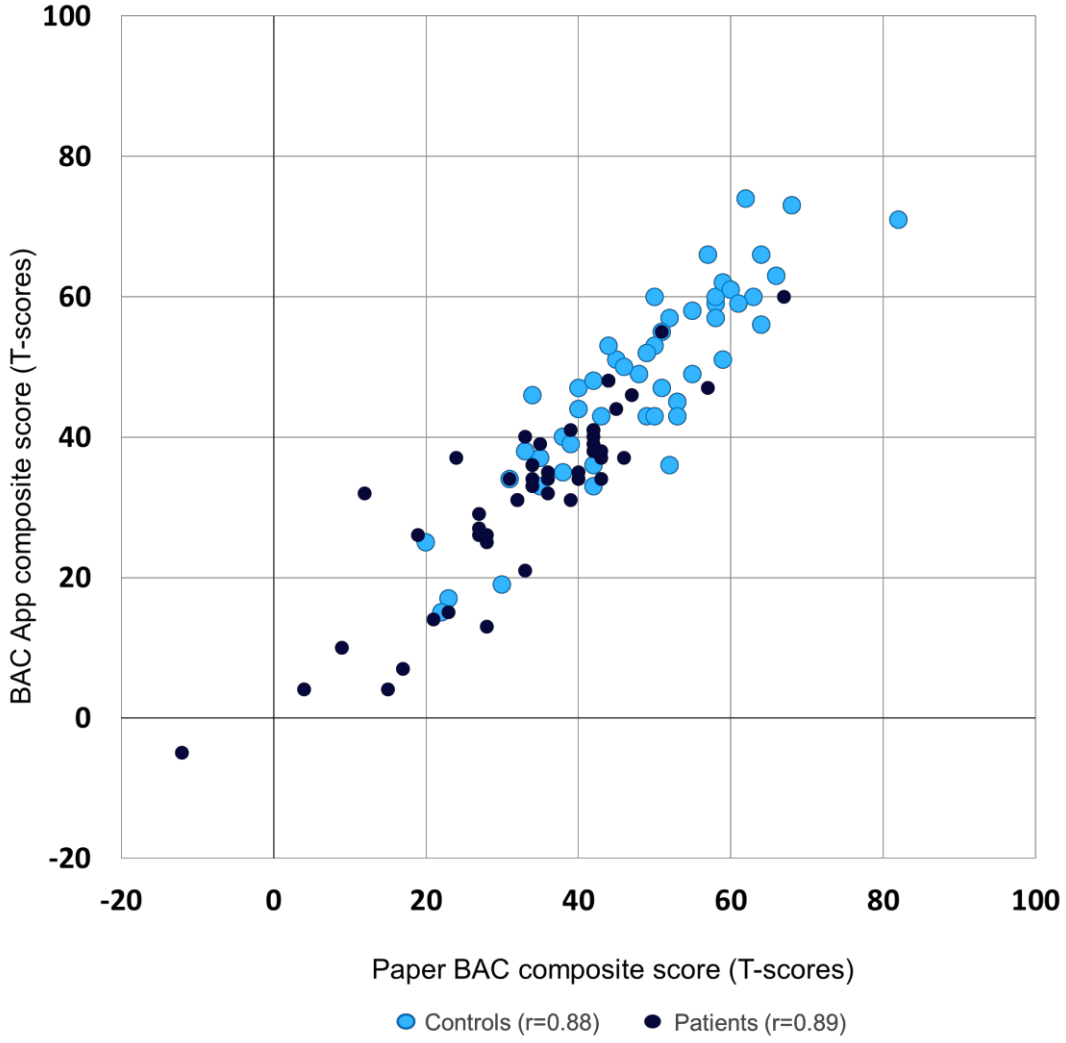

Atkins et al., 2016 Schiz Res

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- Patients (N=48) performed an average of 1-2 SD below healthy controls (N=50) on each BAC App subtest . . . BUT

Symbol Coding – 10pt shift in distribution for both groups (equal SDs) - initially corrected with a standard raw score correction, normative data now available for 650 healthy individuals

Token Motor – increased variance for tablet-based version - standard correction not appropriate, tablet- based normative data required

CONCLUSION: Demonstrated equivalence for 4 of 6 subtests. 2 subtests require tablet-based norms, which are now available

Case 2: Adapting the Virtual Reality Functional Capacity Assessment Tool (VRFCAT) for use in MCI and Mild AD

- The VRFCAT is *performance-based measure of functional capacity* - initially designed and clinically validated for use in schizophrenia (Keefe et al., 2016); Currently used in schizophrenia and mood disorders

12 tasks (called objectives), presented in an a interactive video-game environment consisting of 4 scenes

1. Exploring a Kitchen
2. Catching a Bus to a Grocery Store
3. Finding/Purchasing Food in a Grocery Store
4. Returning Home on a Bus

VRFCAT Summary Endpoints: Total Adjusted Time; Errors; Forced Progressions

Case 2: Adapting the Virtual Reality Functional Capacity Assessment Tool for use in MCI and Mild AD

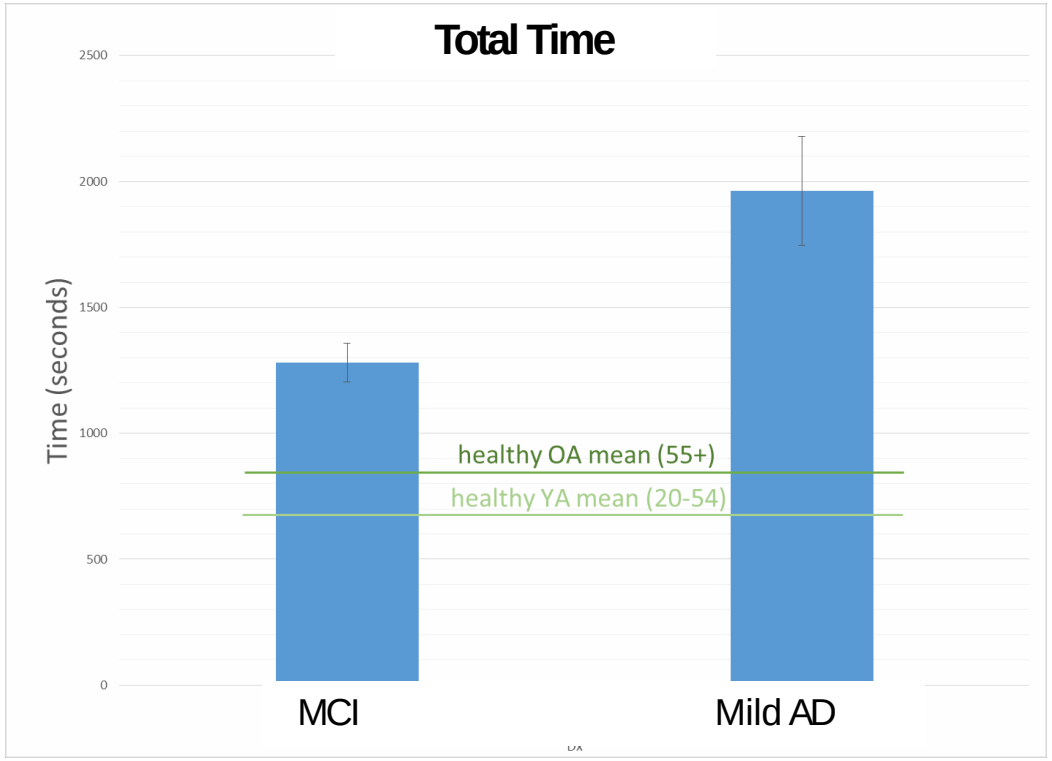
- VRFCAT has demonstrated sensitivity to differences between older adults with and without subjective cognitive decline, as well as strong correlations with cognition (Atkins et al., 2018 JPAD).
- Given the unmet need for improved assessment of function in MCI and early AD, we sought to evaluate the use of the VRFCAT in individuals with MCI and Mild AD

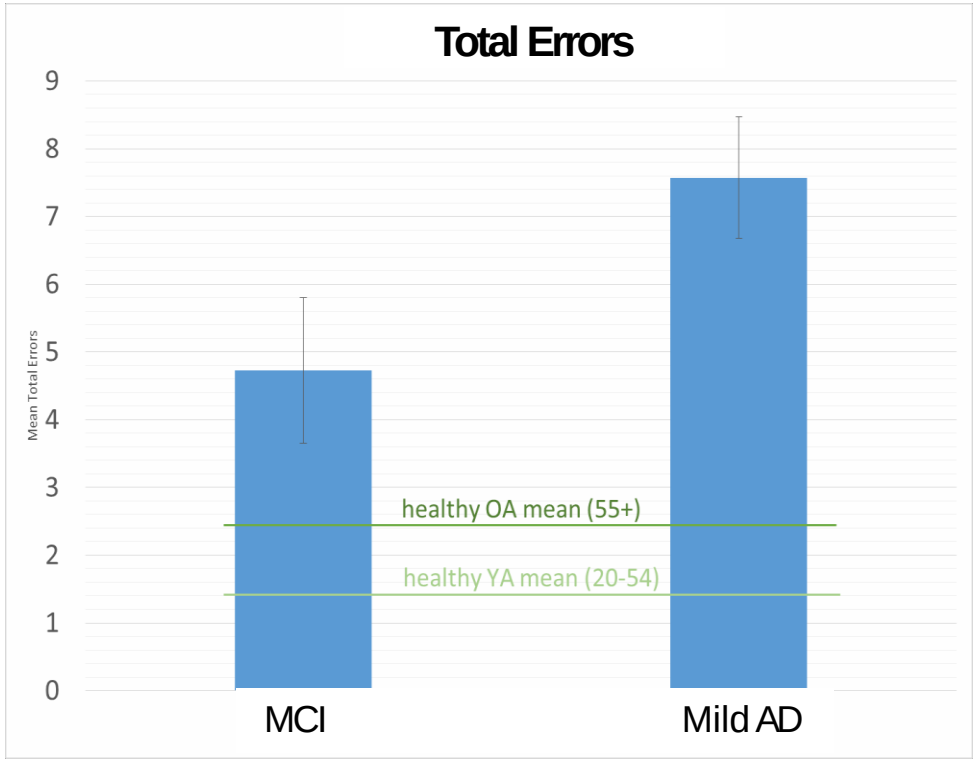
Key challenges:

- Evaluate (rather than assume) appropriateness of the VRFCAT for individuals with MCI and Mild AD
  - ➢ Requires pilot testing of the instrument in the population of interest; Use pilot data to drive conclusions regarding potential revisions

- If needed, modify the VRFCAT to facilitate use in a cognitive declining population
  - ➢ Requires technically intense customization of tasks with attention to the specific needs of the user

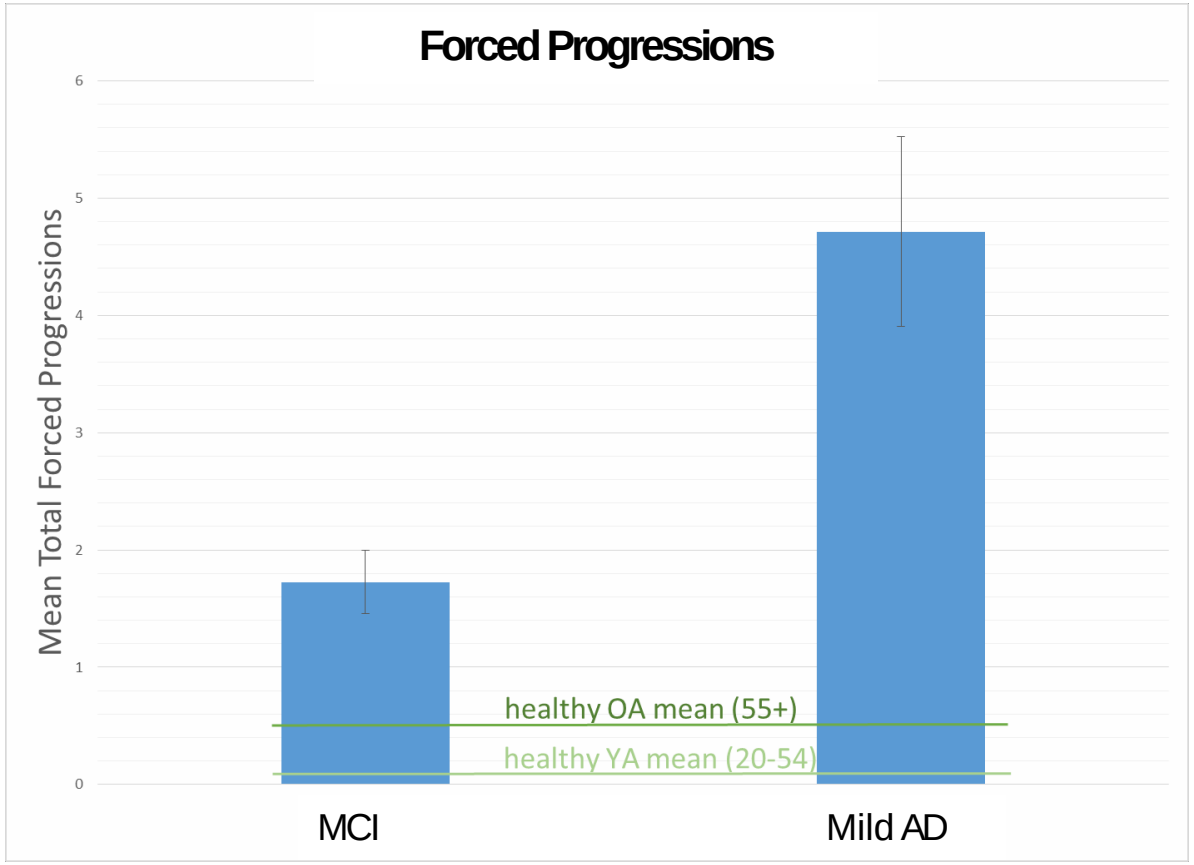
Pilot Testing in MCI and Mild AD





- Participants with MCI (N=11) and Mild AD (N=7) performed significantly worse than normative controls on all VRFCAT endpoints including total adjusted time, errors and forced progressions ($p<.001$ for all) **AND**
- Strong correlations between the VRFCAT and the CDR-SB ($r=.53$, $p<.05$) and partner reported ADL functioning ($r=.64$, $p<.01$) . . . BUT

Pilot Testing in MCI and Mild AD



. . . Participants in the Mild AD group were forced progressed, indicating floor-level performance, on an average of 5/12 VRFCAT objectives

CONCLUSION: Although the VRFCAT is sensitive to differences, task customization is required to avoid floor effects in more impaired patient groups

- A simplified VRFCAT for neurodegenerative diseases will reduce task complexity and include an interactive tutorial to provide addition instruction and reminders
- Full clinical validation planned for Q1 2019

Conclusions

- Both cases emphasize that there are no good “shortcuts” in the development of valid digital assessments.
- The efficiency gained in standardized data collection and endpoint precision is real and worthwhile . . . BUT development and validation of these instruments requires a scientifically rigorous approach that includes cycles of technological development, validation and testing

Thank you!

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