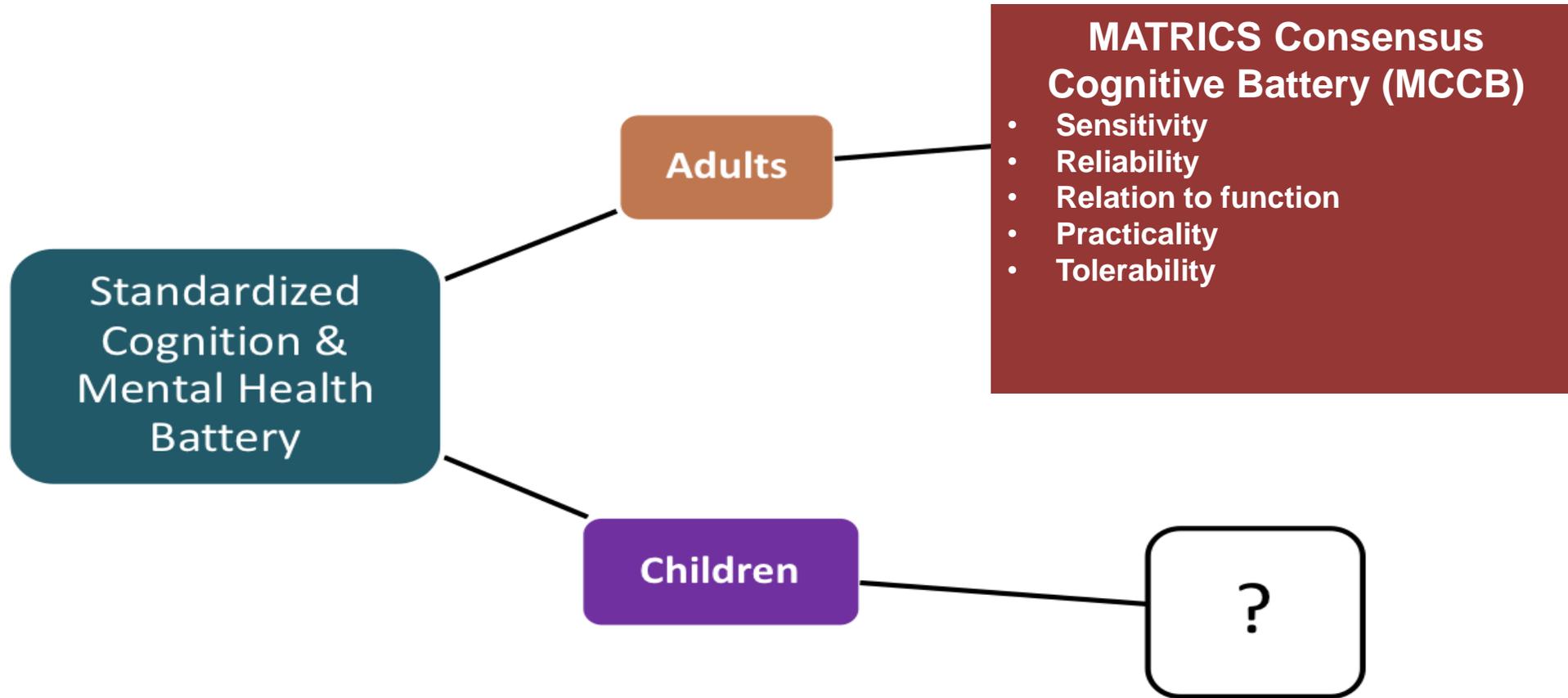


Measurement of Cognition and Behavior in Pediatrics: How Do We Measure a Moving Target?



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No Conflicts to Report



MATRICES: Measurement and Treatment
Research to Improve Cognition in Schizophrenia

Aims

- Review challenges of assessing cognitive and behavioral outcomes in clinical trials with children
- Provide perspective on these assessments based on experience as pediatric neuropsychologist and co-investigator on clinical trials
- Offer recommendations for types of measures to include in clinical trials and point to potential future directions

Why Measure Cognition and Behavior?

- Changes in cognition and behavior often targeted by drug (goal of treatment, or “fit for purpose”)
- Way to characterize how children are affected (child-specific efficacy and safety; information needed to support use)
- Certain measures of cognition or behavior may be highly sensitive to drug effects (biomarkers)
- Inform us of how drug affects functional capacity (how child learns and behaves in everyday life)
- May shed light on mechanisms of effect

The “Moving Target”



Infant-Toddler
Period:
Birth-2 years

Early
Childhood:
3-5 years

Middle
Childhood:
6-10 years

Adolescence:
11-17 years

Emerging
Adulthood:
18-25 years

Different Approaches to Testing Required for Younger and Older Children

Infants/Toddlers



Older Children & Adolescents



Young Children



Special Issues in Child Assessment

- Measures typically apply to limited age range
- Child motivation and engagement not a given; examiners need to know how to work with children
- More complex administration procedures may require special expertise and preclude large scale multi-center testing (training and fidelity important)
- Abilities may advance from pre to post treatment in longer trials

Types of Clinical Outcome Assessments (Richardson et al., *Ther Innov Regul Sci*, 2018)

- Performance outcome: based on standardized task administered to child by trained individual
- Observer-reported outcome: parent or teacher ratings, interview involving only recording of response and not professional judgment
- Clinician-reported outcome: clinician observes child and makes professional judgment
- Patient-reported outcome: self-report (younger children may lack insight)

Two Common Types of Assessment in Pediatric Studies

Performance-based Cognitive Tests

- Objective if tester blinded
- Highly structured, constructs clearly defined; goal is to obtain child's best performance
- May be more sensitive to subtle changes in ability
- Change may not be immediately observed in everyday behavior



Observed-reported Behavior Ratings

- Subjective, open to bias
- Behavior being measured less well specified; goal is to assess child's typical level of functioning
- Provides measure of behavior in context
- Contextual demands may obscure drug effects but may also provide greater challenge



Psychometric Properties to Consider in Selecting Cognitive Tests

- Relevant to both adults and children
 - Sensitive to types of changes targeted by drug and to potential side effects
 - Reliable, repeatable, limited practice effects
 - Predict effects outside of test setting
- Especially relevant to children
 - Applicable to multiple ages & wide range of abilities; no floor and ceiling effects
 - Easily administered and engaging

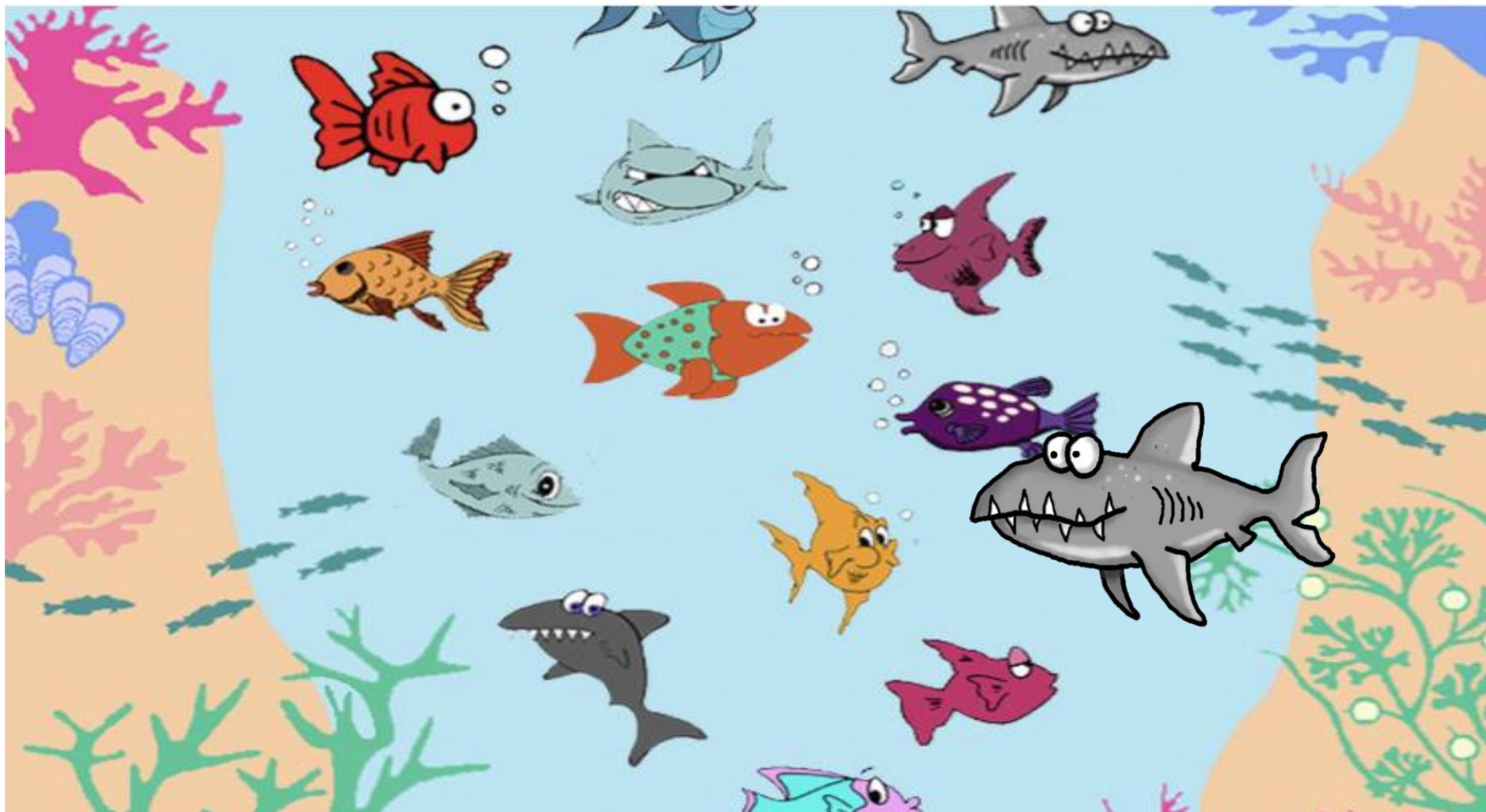
Tests of “Fluid” not “Crystallized” Abilities Best Suited for Pediatric Drug Trials

- Executive function: remaining vigilant and inhibiting responses to distractors (attention regulation), multi-tasking, working memory
- Processing speed
- Memory and learning
- Planning/problem solving
- Perceptual motor skills

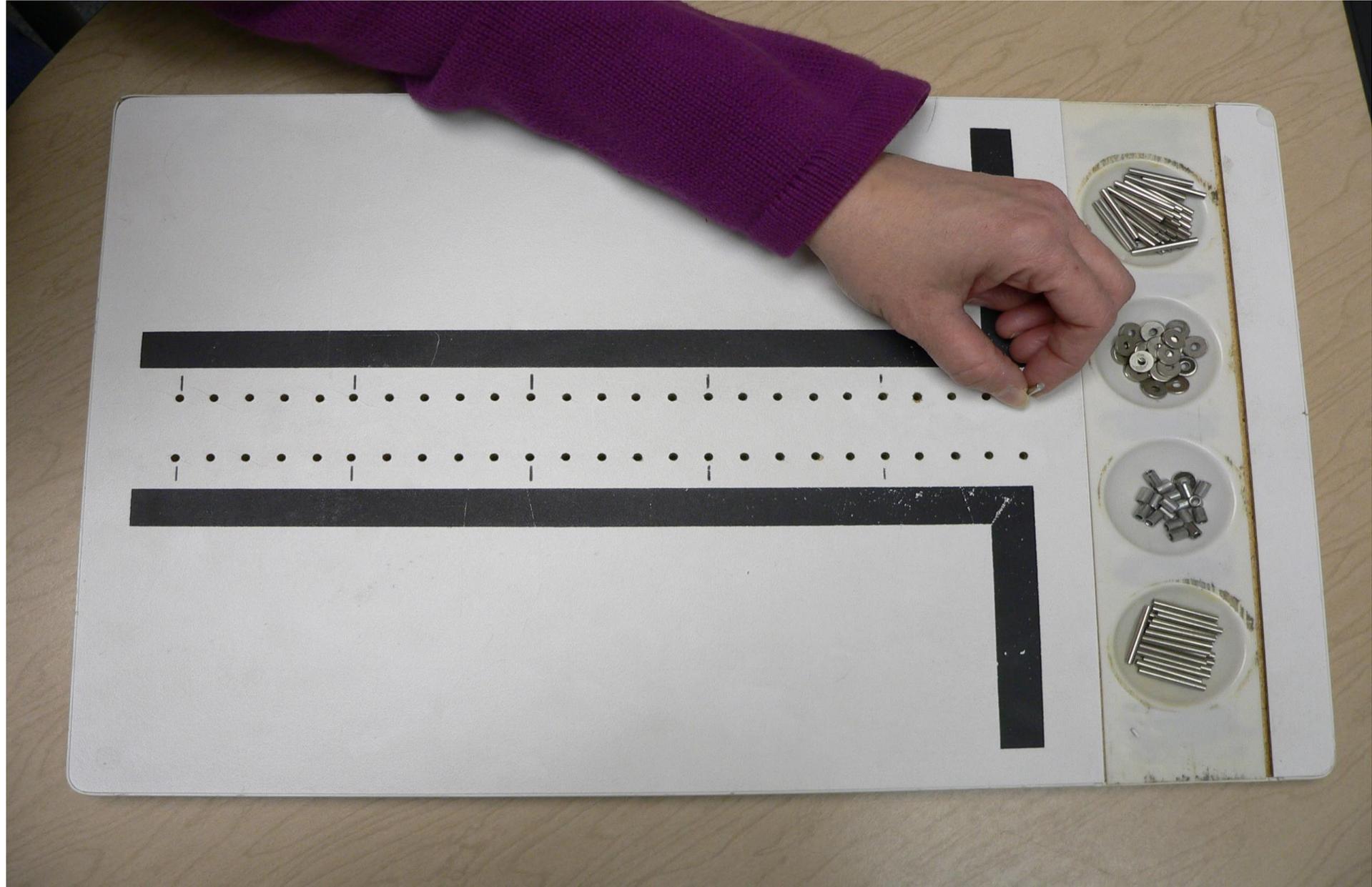
Computerized Testing



Computer Go No-Go Attention Task



Purdue Pegboard



Status of Cognitive Testing in Drug Trials

- Many standardized computerized or paper and pencil measures are available to assess drug effects in children, including tests of:
 - Attention (continuous performance tests)
 - Executive function (verbal fluency, NIH Toolbox Cognition Battery, digit and picture span tests)
 - Processing speed
 - Fine motor dexterity

- However, there are also some challenges:
 - Several standardized computerized neuropsychological tests of concussion effects have limited reliability or sensitivity
 - Adaptations of standardized tests may be needed for special populations, and more "experimental" tasks may have advantages
 - Functional significance of tests is uncertain
 - Little apparent consensus across drug trials

Measures of Behavior and Functional Capacity

- Typically entail ratings or interviews with parent or teacher ratings to obtain impressions of child behavior problems or functional capacities
- Many measures available to assess different types of behavior or psychiatric disorders, or problems in areas such as attention, executive function, memory
- Tests of functional capacity are possible but infrequently used in pediatric trials (e.g., observations of behavior at home/school, videos of child interactions, performance on laboratory versions simulating real-life demands)

Parent and Teacher Behavior Ratings

Behavior at Home



Behavior at School



Functional Capacity as Assessed by the Map Task (McLaughlin et al., *Schiz Bull*, 2016)



Recommended Future Directions

- Establish consensus regarding existing (standardized) measures best suited to drug trials with children
- Examine psychometric properties of these measures to determine their applicability and potential utility for different ages and special populations
- Consider alternative non-standardized (experimental) or modified procedures that might be more optimally suited to drug trials with children
- Develop performance measures of functional capacity

Conclusions

- Measures of cognition and behavior serve several purposes in drug trials
- Children pose special challenges in conducting these assessments
- Both performance-based tests of cognition and functional capacity and more subjective measures of behavior are needed and complementary
- Multiple measures are currently available but further research required to examine their utility, search for even better methods for assessing drug effects, and achieve greater consensus across drug trials