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

H. Gerry Taylor, Ph.D.
Center for Biobehavioral Health
Nationwide Children’s Hospital Research Institute
Department of Pediatrics
The Ohio State University
Columbus, Ohio USA

No Conflicts to Report
MATRICS Consensus Cognitive Battery (MCCB)
- Sensitivity
- Reliability
- Relation to function
- Practicality
- Tolerability

MATRICS: 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

<table>
<thead>
<tr>
<th>Performance-based Cognitive Tests</th>
<th>Observed-reported Behavior Ratings</th>
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<tbody>
<tr>
<td>• Objective if tester blinded</td>
<td>• Subjective, open to bias</td>
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<td>• Highly structured, constructs clearly defined; goal is to obtain child’s best performance</td>
<td>• Behavior being measured less well specified; goal is to assess child’s typical level of functioning</td>
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<td>• May be more sensitive to subtle changes in ability</td>
<td>• Provides measure of behavior in context</td>
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<td>• Change may not be immediately observed in everyday behavior</td>
<td>• Contextual demands may obscure drug effects but may also provide greater challenge</td>
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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 “Crystalized” 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