# Response Evaluation In Neurofibromatosis Schwannomatosis
## INTERNATIONAL COLLABORATION

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# REiNS Neurocognitive Update

- Preschool Subcommittee Update: Measures of Attention (Klein-Tasman)
- Broader Committee Update: Measures of Social Skills (Janusz)

REiNS Meeting
CTF Neurofibromatosis Conference
September 2019

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# Preschool Neurocognitive Subcommittee Update

REiNS Meeting
CTF Neurofibromatosis Conference
September 2019

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Response Evaluation In Neurofibromatosis & Schwannomatosis
INTERNATIONAL COLLABORATION

# Preschool Neurocognitive Subcommittee Members

## Chair:

- Bonnie Klein-Tasman
  *University of Wisconsin-Milwaukee*

## Members:

- Peter de Blank, *Cincinnati Children's Hospital*
- Kelly Janke, *Children's Hospital of Philadelphia*
- Jennifer Janusz, *Children's Hospital Colorado*
- Kristin Lee, *University of Wisconsin-Milwaukee*
- Sara Pardej, *University of Wisconsin-Milwaukee*
- Jonathan Payne, *Murdoch Children's Research Institute*
- Heather Thompson, *California State University, Sacramento*
- Karin Walsh, *Children's National Medical Center*

# Preschool Subcommittee Approach

- Concentrate first on measures for children ages 3;0 through 5;11 (later consider 6 and 7 year olds, and then possibly younger children)
- Review measures of neurocognitive functioning appropriate for young children
- Consider guidance for best practices in inclusion of young children in clinical trials (e.g., training of staff, structure of assessment)
- Consider other design recommendations given that this is a period of rapid growth
- Maintain some parallelism with the work of the broader group

# Measure Review Work to Date

- Clinic-based attention measures (e.g., digits forward task)
- Computerized assessments of attention and emerging executive functioning, including continuous performance test measures
- Questionnaire measures related to attention

# COGRate Form Description

**Cog**nitive Outcomes **R**ating **A**cceptance **T**ool for **E**ndpoints

1. Patient characteristics (age range, normative groups)
2. Used in published studies (descriptive, clinical trials)
3. Test appropriateness for clinical trials endpoint (specificity/purity, reasonable endpoint)
4. Scores available (raw, standardized, gaps in normative data)
5. Psychometric Data (reliability, validity, practice effects)
6. Feasibility (cost, expertise needed)

Each domain is rated as follows:

3=Solid data and published information supporting its use in NF
2=Good preliminary data and relevant information but needs more work
1=Limited data but information suggests potential
0=No/poor data/information
*Half ratings (.5, 1.5, 2.5) can be used if needed

*To maintain consistency with Walsh et al., 2016, mean ratings prioritize items 1, 5, and 6 in this review*

# Ratings of Computerized Measures

** There are more recent published studies using the NIH Toolbox – the group will be revisiting the ratings

| Measure | Age range | Pros | Cons | Mean Rating |
|---|---|---|---|---|
| K-CPT | 4-5 for K-CPT<br>4-7 for K-CPT-II | Psychometrics good, used in published research (including NF1), switch to CPT-3 for older children | Only English, no published studies using current version (K-CPT-II) | 2.48 |
| NIH Toolbox** (Flanker, DCCS) | 3 through adulthood | Easy administration, good psychometrics, covers wide age range | Costly, normative data mostly for typically developing populations, limited use in clinical trials | 2.33 |
| CogState (Identification, 1-back) | 4 through adulthood | Developed for repeated use, being used in ongoing NF1 research with young children (though no publications yet) | Only small amount of work with preschoolers; normative data for preschoolers a little weak | 2.36 |
| TOVA | 4 through adulthood | Psychometrics strong | Very long, only small amount of work in preschoolers | 2.37 |
| Gordon | 4-16 | | Prone to experimenter error, no standard scores, very old norms | 1.86 |

** will be re-reviewing given updated literature

# Practical Issues when Using Computerized Measures with Young Children

- Need personnel with experience working with young children
- Need clear guidelines about how much support and assistance should be provided (e.g., criteria during training to move forward with the task, extent of reminders to stick with the task)
- Need a sense of whether the data yielded for each child is “valid”
- Need to be careful to avoid measures where floor performance is likely

# Consensus of the Group To Date: Computerized Measures

- Most clinical trials are not yet using computerized measures (or Continuous Performance Tests) as an outcome with preschoolers
- Consensus that the following measures are NOT likely to be useful: Gordon (norms much too old and not really computerized), TOVA (length, lack of use with preschoolers)
- We really need more data about the feasibility, test-retest reliability, and utility of K-CPT-II, Cogstate, and Toolbox measures in preschoolers with NF1
- We also need to be thinking about WHICH of the indices produced by these measures are most suitable as primary outcomes

# Ratings of Questionnaire Measures

| Measure | Age range | Pros | Cons | Mean Rating |
|---|---|---|---|---|
| Achenbach Child Behavior Checklist (CBCL 1 ½ to 5) | 1 ½ to 5<br>6 to 18<br>YABCL 18+ | Availability in many languages, widely used in developmental studies | Participant burden; small number of questions assessing attention within a broad measure; may not be as sensitive to attention in NF1 as a more targeted measure<br>, | 2.58 |
| Behavior Assessment Scale for Children – 3rd Edition (BASC-3 2 to 5) | 2 to 5<br>6 to 11<br>12 to 21 | Used in NF1 literature, and broadly in the literature | Participant burden; small number of questions assessing attention within a broad measure; may not be as sensitive to attention in NF1 as a more targeted measure, most published data on BASC-2 (32% of items changed) | 2.75 |
| Behavior Rating Inventory of Executive Functioning – Preschool (BRIEF-P) | BRIEF-P: 2 to 5<br>BRIEF-2: 5 to 18 | Used in NF1 in preschoolers (with published data) | Not a pure attention measure – more broadly reflects emerging executive functioning which includes attention<br>Unclear if sensitive to change in clinical trials | 2.78 |
| Conners Parent Rating Scale – Short Form (CPRS) | 3 to 17 | Widely used in descriptive and clinical trials<br>Good continuity across development | No longer in print; last norms in 1997 | 2.83 |
| ADHD Rating Scale – Preschool (ARS-P) | 3 to 5 (Prechool form)<br>5 to 17 (ADHD RS) | Widely used in descriptive and clinical trials<br>Good continuity across development, available in Spanish, good normative data, strong reflection of DSM | Raw scores, mean and SD available, but not standard scores | 2.83 |

# Consensus of the Group To Date: Questionnaire Measures

- Concern about the use of a small number of items from a broad measure (e.g., BASC, CBCL) as they may be less likely to capture change and there is evidence that elevations on these measures are very mild in the preschool years

- While the BRIEF-P shows some promise, concern that it is not a pure measure of attention problems or ADHD symptoms but rather reflects the overlapping construct of emerging executive functioning

- The CPRS is promising and has been used in NF1, but it is no longer published

- The ARS-P is promising as it is fairly widely used outside of NF1 in attention trials, but there are no published data in children with NF1

# Some Developmental Themes

- Context of “emerging skills” in the preschool years
- Period of relatively rapid development (e.g., early 3 may be quite different than late 3)
  - Timeframe of measurement
  - Reliable change estimates
- Priorities about balance of sensitivity and specificity in younger children may be different given expected variability in normative functioning
- Question of feasibility central
- Continuity with measures with older children

# Change in Forms/Versions with Age

- This causes challenges!
- What to do when a child ages out of one form and into another?
  - Stay with the original measure and use raw scores to assess change
  - Move to the age-appropriate measure and use standard scores
  - ➔ The “correct” answer may depend on the length of time between the assessment points
- It would be helpful for test publishers to overlap their normative data collection some to demonstrate what happens with scores when you move from one form to another (i.e., give parents of both 5 and 6 year olds both the BRIEF-2 and BRIEF-P to see how they correspond)
- **This is less of a challenge if we are interested in raw score changes <u>and</u> have a control group**

# Next Steps

- Consider any recent data and revisit ratings as needed
- Discuss with the broad group whether a separate preschool review of the Social measures is needed
- Consideration of measure recommendations in other domains – will likely look at general cognitive functioning next
- Examine measures that may be appropriate for even younger children

# Social Skills Outcomes Measures

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Neurocognitive Outcomes Working Group

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# Neurocognitive Committee

Chair
Jennifer Janusz

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- Pete de Blank
- Allison de Castillo
- Deborah Gold
- Kristina Haebich
- Kristi Hardy
- Matt Hocking
- Kelly Janke
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- Staci Martin
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- Jonathan Payne
- Tena Rosser
- Heather Thompson
- Karin Walsh
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- Connie Sorman
- Melissa White
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# Identifying Appropriate Measures- What do we look for?

- Measure areas we are interested in
  - Communication and social cognition
- Well-designed measures (good psychometrics)
- Easily administered in clinical trials setting
  - Focused on parent questionnaires
- Previously used in clinical trials where social skills are an outcome measure
- Broad social skills and social behaviors related to ASD

# Measures Reviewed

After comprehensive literature review, the following measures were identified as relevant:

- Social Skills Questionnaire
- Social Skills Checklist
- Social Competence Inventory
- Social Communication Questionnaire
- Autism Social Skills Profile
- Profile of Social Difficulty
- Socialization scale, Vineland Adaptive Behavior Scales- 3
- Social Skills scale, Adaptive Behavior Assessment System- 2/3
- Aberrant Behavior Checklist
- Social Skills Rating System/ Social Skills Improvement System
- Social Responsiveness Scale-2
- Children's Communication Checklist-2

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- Social Responsiveness Scale-2
- Children's Communication Checklist-2

| Measure | Age | Pros | Cons | Mean Rating |
|---|---|---|---|---|
| Profile of Social Difficulty | 6-11 | | Primarily used for therapy objectives | .81 |
| Autism Social Skills Profile | 6-17 | Good psychometrics | No use in clinical trials; no norms | 1.91 |
| Social Communication Questionnaire | 4-40 | | Limited normative group; narrow focus on ASD symptoms | 1.62 |
| Aberrant Behavior Checklist | 5-adult | Developed for use in clinical trials | Focus on ASD and ID | 2.32 |
| Vineland Adaptive Behavior Scales-2/3 | 0-adult | Extensive use in research | Must administer in entirety; limited languages | 2.17 |
| Adaptive Behavior Assessment System-2/3 | 0-89 | Use in clinical trials; electronic version | Must administer in entirety; limited languages | 2.44 |
| Children's Communication Checklist-2 | 4-16 | Use in clinical trials; good psychometrics | Primary focus on language and pragmatics | 2.52 |
| Social Skills Improvement System | 3-18 | Use in many clinical trials; long history of research, incl. NF | | 2.61 |
| Social Responsiveness Scale | 2.5-adult | Use in many clinical trials; long history of research, incl. NF | | 2.66 |

## Social Skills Improvement System

- Social Skills
  - Communication
  - Cooperation
  - Assertion
  - Responsibility
  - Empathy
  - Engagement
  - Self-control
- Problems Behaviors
  - Externalizing
  - Bullying
  - Hyperactivity/Inattention
  - Internalizing
  - Autism Spectrum

## Social Responsiveness Scale

- Social Awareness
- Social Cognition
- Social Communication
- Social Motivation
- Restricted Interests and Repetitive Behaviors

# What's Next?

- Reviewing measures of executive function
  - Paper and pencil
  - Computerized

- Reviewing measures of emotional functioning for children and adults
  - Easier (?); frequently an outcome measure for intervention studies