

Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

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Neurocognitive Outcomes Working Group Update

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on behalf of the Neurocognitive Steering Team
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Mission of Neurocognitive Group

- Goal to identify measures of cognition and psychosocial functioning for use in clinical trials
 - Well-designed measures (good psychometrics)
 - Easily administered in clinical trials setting
 - Previous use in clinical trials
 - Previous use with NF1
 - Availability in other languages



Relevant Domains

- Cognition
- Language
- Visual-spatial
- Memory School age measures 2016 Neurology supplement
- Attention
- Executive functions Preschool measures 2021 Neurology supplement
- Adaptive functioning
- Academics
- Psychosocial
- Social skills 2021 Neurology supplement
- Social cognition
- Computerized measures
- Global outcome measures



Measures Defined as Core, Supplemental, or Emerging

- Core
 - Established use in NF1
 - Good Psychometrics
 - Brevity and ease of administration
 - Multiple languages
- Supplemental
 - Specific topics or more in-depth assessment
- Emerging
 - Instruments under development, in the process of validation, or nearing point of published findings with NF1



Academic Measures Reviewed

Academic batteries:

- Wechsler Individual Achievement Test (WIAT)
- Woodcock-Johnson (WJ) Tests of Achievement
- Kaufman Test of Educational Achievement (KTEA)
- Wide Range Achievement Test (WRAT)

Word Reading/Decoding

- Test of Word Reading Efficiency (TOWRE)
- NIH Toolbox Oral Reading Recognition Test

Reading Comprehension

- Gates-MacGinitie Reading Tests (GMRT)
- Gray Silent Reading Test (GSRT)
- ~~Gray Oral Reading Test (GORT)~~
- ~~Test of Everyday Reading Comprehension (TERC)~~



*Subgroup: Kelly Janke (lead), Kristi Hardy, Staci Martin
Deborah Gold, Matt Hocking*

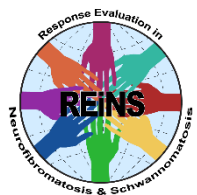
Measures Reviewed

Questionnaires

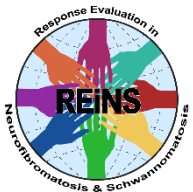
- Child Behavior Checklist (CBCL) School Competence
- Academic Competence Evaluation Scales (ACES)
- ~~Colorado Learning Difficulties Questionnaire~~



Measure	Age	Pros	Cons	Mean Rating
KTEA-3	4-25	Feasibility, range of skills assessed, alternate forms	Less used in research	2.75
WIAT-3/4	4-50	Well established clinical/research measure	No alternate form	2.75
WJ Achievement-4	2-90	Well developed/known battery	Reading & writing subtests less strong, less feasible	2.63
WRAT Reading Composite- 4/5	5-85	Quick screen	Not including in battery comparison d/t limited subtests	2.58
Toolbox Oral Reading	3+	Fast, repeatable CAT, growing research use	Recommended for 7+, administration challenges	2.50
TOWRE-2	6-24	Fast, designed to screen & capture change, used in NF	Only assessing decoding/word recognition	2.76
Gray Silent	7-25	Fast and feasible, mirrors class work, alt form	Old norms, limited use; multiple choice format	2.17
Gates-MacGinitie	Pre-K – adult	Ecological validity, good for monitoring	Lengthy; separate forms by grade level	2.50



Measure	Age	Pros	Cons	Mean Rating
CBCL School Competence	6-18	1 paper reported scores in NF pts, quick to complete	Old norms; very limited items (1-3 rating of class performance and yes/no questions about participation in special classes, grade repetition, and school problems); unlikely to use this option subtest in isolation	2.29
Academic Competence (ACES)	K-12 + college form	Use in clinical trials + couple NF studies. Comprehensive but quick assessment of academic skills (ELA, math, critical thinking) & enablers (e.g., study skills, engagement)	Criterion referenced (1 st edition relies on raw scores and deciles)	2.50



Social Cognition Measures Reviewed

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

- Penn Emotion Recognition Task-40
 - Geneva Emotion Recognition Test
 - Social Problem Solving Inventory
 - Social Information Processing interview
 - Contextual Assessment of Social Skills (CASS)
 - Benton Facial Recognition Task
 - Cartoon Theory of Mind Task
 - Reading the Mind in the Eyes Test
 - Diagnostic Analysis of Nonverbal Accuracy-2
 - Theory of Mind Test
 - Child and Adolescent Social Perception (CASP) Test
 - NEPSY-2: Affect Recognition, Theory of Mind
 - Cambridge Mindreading Face-Voice Battery of Children
 - Pediatric Evaluation of Emotions, Relationships and Socialization (PEERS)
 - TASIT-2
 - CANTAB: Emotion Recognition, Emotional Bias Task
 - ~~Sally Ann Task~~
 - ~~Faux Pas Task~~
 - ~~Hinting Task~~
 - ~~Picture Sequencing Task~~
 - ~~Ekman Faces~~
 - ~~Strange Stories Task~~
- Ruled out in first pass:
- Too experimental
 - Too narrow an age range
 - Minimal-to-no psychometric data



Subgroup: Jonathan Payne (Lead), Natalie Pride, Kristina Haebich, Annaliese Rossi

Measure	Age	Pros	Cons	Mean Rating
TASIT-2/S	13-75+	Standardized. Large normative sample (~800)	Time; age range	1.59
CASS	16-22	Nil	Age range	0.69
Penn ER-40	Adults	Quick to administer	Age range	1.46
CASP	6-15	<i>Relatively</i> well validated within the social cog literature	Fairly long to administer; a little complicated	1.98
PEERS	5-17	Normed in >800 children; not published, but looks solid	Minimal published data on tool	2.45
Reading eyes	6-adults	Established psychometrics in adults; fairly easy to administer; free	Still fairly experimental; what does it mean?; fairly rudimentary psychometrics in children	1.39
Benton Facial Recognition test	4-16	Nil	Very old test; measures 'lower level' social cognition only	1.08
DANVA-2	6-13	Used in many clinical trials; captures meaningful change	Clunky administration	2.61
CANTAB NEPSY-2	Still to review			

Social Cognitive Measures

Take away messages from subgroup:

- In general, clinical usefulness of social cognitive measures is not well established – what does a low score actually mean in terms of functioning?
- In NF1 – only a handful of studies have reported social cognitive outcomes
- Hard to see a situation when a social cognition measure would be a primary outcome for a trial in NF1
- If testing an intervention for social behavior, social cognitive outcome may be an appropriate secondary outcome

Current recommendations (*may change before final measure reviewed*)

- DANVA-2 would be recommendation for a supplementary outcome
- PEERS* looks like a promising option, but need more data (we will have some NF1 data from key PEERS subtests soon); recommend as an emerging outcome measure



Adaptive Behavior Measures Reviewed

- Scales of Independent Behavior - Revised
- ABAS
- Vineland Scales of Adaptive Behavior – 3rd Edition
- Achenbach Child Behavior Checklist
- Behavior Assessment Scale for Children – 3rd Edition
- ~~Adaptive Behavior Evaluation Scale – Third Edition~~
- ~~Diagnostic Adaptive Behavior Scale~~



Subgroup: Bonnie Klein-Tasman (lead), Danielle Glad, Jennifer Janusz, Pam Wolters, Heather Thompson, Rene Pierpont, Pte Stavinoha, Cynthia Campen, Jo Wallace, Tena Rosser, Connie Sorman

Measure	Age	Pros	Cons	Mean Rating
Vineland Adaptive Behavior Scales – Third Edition	0-90+	Well-standardized and updated norms, widely used in descriptive studies (including NF1) and clinical trials, growth scores available	Can be difficult to administer and score in its traditional interview form, though there is an alternative approach that would be easier	2.71
Adaptive Behavior Assessment System – Third Edition	0-89	Well-standardized, easy to administer/score.	Limited use in NF1 or clinical trials, not a lot of independent assessment of psychometric properties and factor structure. No growth scores	2.53
Scales of Independent Behavior – Revised	0-80+	Original standardization reasonable, used in NF1 research	Out of date content and norms, not used in clinical trials	1.75
Achenbach Child Behavior Checklist Adaptive Scales		Strong reliability	Validity concerns; does not align with typical definitions and models of adaptive behavior	1.01
Behavior Assessment Scales for Children – Third Edition Adaptive Scales	2 - 21	Strong reliability, covers a range of areas of adaptive behavior, easy administration	Different forms at different ages, no adult forms, lack of validity data, no clinical trials	1.96



Adaptive Behavior Measures

Take away messages from subgroup:

- Vineland recommended
- Use the same method of administration across participants
- Recommend use of the interview (with computerized assistance) but understand that feasibility might lead to use of the measure as a checklist
- Vineland checklist recommended over other checklist measures
- Recommend comprehensive over domain level scores as primary outcome measure
- In a clinical trial, would likely benefit from centralized administration for consistency



Next Steps:

Address Additional Domains

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- Psychosocial
- Social skills 2021 Neurology supplement
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Thank you

Chair

Jennifer Janusz

Committee Members

- Cynthia Campen
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- Allison del Castillo
- Shruti Garg
- Dani Glad
- Deborah Gold
- Tamar Green
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* Steering Committee