

REiNS Neurocognitive Working Group Update

(Emphasis on Preschool Subcommittee)

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Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

Neurocognitive Committee

(*Preschool Subcommittee Members)

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Children's National Medical Center
- Jennifer Janusz (2017-)
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REiNS Neurocognitive Activities

- Examining potential endpoints for clinical trials; recent focus on attention, working memory, and executive functioning
- Attention measures recommendations – lab-based and parent questionnaire (Walsh et al., 2016)
- Currently working on recommendations regarding computerized measures of attention
 - CTF-funded multisite work (Walsh PI) likely to inform these recommendations
- Next steps: Endpoints in other domains, with next area of focus likely on social functioning
- Walsh et al., 2016 recommendation: special consideration of preschool age range measurement



Preschool Subcommittee Plans

- Review measures of neurocognitive functioning appropriate for young children for use in clinical trials
- Concentrate first on measures for children ages 3;0 through 5;11 (later consider 6 and 7 year olds, and then possibly younger 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
- Maintain some parallelism with the work of the broader group



Some 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/development
- Question of feasibility central



Consensus Domains

- Developed a broad list of potentially relevant domains (based on recent preschool NF1 literature)

(e.g., Brei et al., 2014; Casnar et al., 2014; Casnar & Klein-Tasman, 2017; Klein-Tasman et al., 2013, 2014; Legius et al., 1994; Lorenzo et al., 2011, 2013, 2015; Mazzocco, 2001; Oostenbrink et al., 2011; Sangster et al., 2011; Spuijbrok et al., 2011; Thompson et al., 2010)

- Consensus that the following domains may make **particularly important** endpoints for young children*:
 - Overall cognitive functioning
 - Attention/Working Memory/Emerging Executive Functioning
 - Motor functioning
 - Language

**This is not an exhaustive list of domains affected for children with NF1*



Clinical Trials Literature

- Examined literature on **neurocognitive outcomes in clinical trials (especially attention)** with preschoolers without NF1 to see if there is clear consensus
 - Relatively sparse literature (some looks to be in the works)
 - No one lab-based measure that is consistently seen
 - Often parental report, with no one measure consistently used
- Will continue to keep close eye on this developing literature



Attention Measure Review

- Reviewed clinic-based attention measures (e.g., DAS-II digits forward task)
- Reviewed computerized assessments of attention and emerging executive functioning (e.g., Cogstate, NIH Toolbox)
- Review of continuous performance test measures in progress
- Next on the agenda: Questionnaire measures



Future Directions for Preschool Work

- Need for more data about psychometric properties of measures with young children, and especially with children with NF1 (i.e., disease-specific normative data)
 - Test-retest reliability, practice effects (to index reliable change)
 - Sensitivity
 - Validity
- Development of best practice guidelines for including young children with NF1 in clinical trials
- Consideration of measure recommendations in other domains



