Neuromotor Outcome Measures for Clinical Trials in Fragile X Syndrome

And Strategies/Supports for Successful Testing

Tracy M. Stackhouse, Nicole Tartaglia, Lisa Cordeiro, and Jamie McGrew

Developmental FX- Fragile X Resource Centre, Denver, CO

University of Colorado, Denver- Department of Pediatrics, Aurora, CO

STUDY PURPOSE

With the promise of targeted treatments leading to improved outcomes in Fragile X Syndrome (FXS) there is a critical need to identify outcome measures for use in clinical trials. Neuromotor deficits are an important part of the early presentation and ongoing deficits requiring treatment in FXS. However, there are currently no well tested measures of neuromotor functioning that have been validated in FXS.

In the context of a larger study examining the feasibility, reliability and validity of neuromotor measures in FXS, we also sought to develop recommendations for successful testing of individuals with a range of abilities.

The ability to successfully collect a variety of measures from individuals with FXS is more important than ever. Recent targeted treatment studies indicate that medications may be most efficacious in those with the fully methylated allele [1], who also have the most clinical involvement.

AIMS

- Identify neuromotor outcome measures for use in clinical trials in FXS, and to examine feasibility, reliability and validity of neuromotor outcome measures when testing this population
- Document challenges to testing including behavior, skills and length of testing
- Identify supports and strategies that are useful with all patients during testing
- Provide helpful tips to professionals related to the understanding of FXS
- Develop recommendations for clinical trials related to study design and personnel expertise

METHODS

- 2 occupational therapists administering neuromotor test measures: each with extensive pediatric clinical experience, 1 new to the field of FXS
- 2 study sites: hospital clinic (Children's Hospital Colorado), private therapy center (Developmental FX)

- Neuromotor Measures: PANESS, QNST-2, MABC-2, BOT-2, MAND, Berg Balance Scale, CATSYS Zurich Neuromotor Assessment and Grooved Pegboard
- IQ: Stanford Binet- Fifth Edition, Abbreviated IQ (ABIQ)
- Adaptive Skills: Vineland Adaptive Behavior Scales, Second Edition

CHALLENGES TO TESTING IN FXS

As documented in literature, patients with lower functional abilities are more likely to have more challenging behaviors [2,3]. However, patients with higher functional abilities also struggle with anxiety [4], sensory defensiveness and poor self-regulation [5].

As is widely reported in FXS, the most common challenges to testing found in our study were:

- Anxiety (often to new examiners, new environments and unknown task demands)
- Low cognitive abilities
- Low adaptive functioning abilities
- Attention/Hyperactivity problems
- Poor self-regulation abilities
- Low motivation and persistence to try challenging motor tasks
- Sensory defensiveness
- Gaze aversion (which impacts attending to modeling during testing)
- Language delays (following multi-step directions often required in standardized testing)

STRATEGIES AND SUPPORTS THAT ARE VITAL FOR TESTING IN FXS

There are specific supports and accommodations that can increase the ability to obtain accurate results on patients across all functional levels. The examiner will benefit from using a variety strategies in order to complete testing. The following were used consistently in the study:

- Create a positive social connection and provide positive feedback frequently
- Use highly motivating topics/objects for the patient throughout and for breaks
- Provide a visual schedule or checklist
- Provide movement and/or down time breaks

- Create a simple and consistent routine and stick to it (i.e. work, work, take a walk etc)
- Always ask before touching a patient, whether for a task or trying to help calm/soothe
- Be attentive to signs of anxiety or stress. Change your approach and provide breaks accordingly
- Be aware and set up the environment to fit the patient's sensory profile (i.e. visual distractions in room, background noise, voice volume, temperature, size of room, etc)
- Simplify language and break down directions into small steps when possible
- Use imitation and modeling of motor tasks when possible to increase participation and success
- Be aware of and adjust your own eye contact and body language given the patient's level of anxiety or sensory defensiveness

RESULTS

- Those patients with lower functional abilities consistently need a higher level of supports and strategies
- There are specific supports and strategies that should be used with all patients across all functional levels
- Those patients with higher functional abilities need and are more responsive to extra cueing
- The variability in percentages of strategies needed between functional levels follows a developmental curve which is non-linear as we would expect. Each person has his/her own strengths and weaknesses. Therefore, the type, amount and frequency of supports /strategies needed are unique to the individual.

THE IMPORTANCE OF FXS KNOWLEDGE FOR TESTING IN CLINICAL TRIALS

Successful testing of patients with FXS requires knowledge and understanding of the behavioral features of FXS. An examiner can be well versed in administration and scoring of neuromotor assessments, but working with patients with FXS requires an additional level of expertise. In addition to clinical reasoning, it requires flexibility, quick thinking, and patience. Data collected through this study indicates that all individuals, regardless of ability level, need supports for successful testing. Not only is knowledge of FXS important, but experience working with a range individuals with FXS is essential to successful testing. The tester will need to anticipate core challenges and will benefit from utilization of strategies as suggested above.

REFERENCES

[1] Jacquemont S, Curie A, des Portes V, Torrioli MG, Berry-Kravis E, Hagerman RJ, et al. (2011). Epigenetic modification of the FMR1 gene in fragile X syndrome is associated with differential response to the mGluR5 antagonist AFQ056. *Sci Transl Med*.*3*, 64ra1.

[2] Bailey, D.B., Jr., Hatton, D.D. and Skinner, M. (1998). Early developmental trajectories of males with fragile X syndrome. *Am J Ment Retard*, *103*(1), p. 29-39.

[3] Bailey, D.B., Jr., Hatton, D.D., Tassone, F., et al. (2001). Variability in FMRP and early development in males with fragile X syndrome. *Am J Ment Retard. 106*(1): p. 16-27.

[4] Cordeiro, L., Ballinger, E., Hagerman, R.J., and Hessl, D. (2011). Clinical assessment of DSM-IV anxiety disorders in fragile X syndrome: prevalence and characterization. *Journal of Neurodevelopmental Disorders, 3*, p. 57-67.

[5] Stackhouse, T.M. (1994 March) Sensory Integration Concepts and Fragile X Syndrome. Sensory Integration Special Interest Section Newsletter 17, 2-6.