



Cognitive Outcome Measures for Rett Syndrome: Assessment of Reliability and Stability

Susan Rose, PhD

Montefiore Health System, Albert Einstein College of Medicine

\$149,912.00

Because of the inability of Rett syndrome (RTT) patients to speak and use their hands purposely, most standard neuropsychological testing is precluded. Consequently, the cognitive phenotype associated with RTT is largely unknown. As a result, there is an absence of objective behavioral outcome measures for use in assessing the effects of therapeutic interventions. At the Rett Center at Montefiore we have begun to overcome this problem in pioneering work that uses eye tracking technology. To date, we have identified specific deficits and atypicalities in RTT in three areas: memory, anticipation (an executive function), and attention. The deficits we found are clinically meaningful hallmarks of intellectual delay that have real-world implications. The measures which revealed these deficits show promise for use in clinical trials because (a) the methods have proven feasible with RTT, and (b) the measures themselves have proven sensitive to change after treatment with Glatiramer Acetate (Copaxone) and Lovastatin (Mevacor). Thus they satisfy two important characteristics of an optimal outcome measure: feasibility and sensitivity. Now we seek to accomplish the critical next step -- namely, establish their reliability and stability. For this proposal, 45 females with genetically confirmed RTT will be assessed on the following cognitive functions: Scanning (characterized by the duration, number, and dispersion of fixations, with poorer scanning linked to less looking to key target areas and poorer information processing); Recognition Memory (memory for faces, emotional expression, and patterns -- assessed by pairing familiar with novel targets, and indexed by differential looking to the novel one); Anticipation (shifting attention to the location of an upcoming target in expectation of its appearance); Sustained attention (maintaining attentional focus on a target -- a butterfly that 'flies' across the screen -- while ignoring distracters); Selective Attention (finding a target in an array of distracters) and Disengagement of Attention (shifting attention from one location to another while ignoring competing information -- shifting to a peripheral target when the central stimulus remains on the screen). Measures will include scanning (obtained from the familiarization phase of recognition memory), reaction time (from a number of tasks), novelty scores (recognition memory), time spent engaging with the task (sustained attention) and number of correct responses (search and disengagement tasks). Analyses will focus on reliability (primarily Cronbach's alpha) and stability over the 3-6 month test-retest interval (Pearson r or Spearman ρ , as appropriate). Additionally, to examine performance within the RTT population, two subgroups will be created, based on the severity of symptoms associated with the child's genetic mutation, and performance on each task will be compared across the two testing sessions (test and retest) to determine whether there is differential impairment across cognitive functions. Finally, performance will be correlated with phenotypic characteristics, the Rett Syndrome Severity Scale, age at testing, and age at regression to assess the degree to which cognitive performance is related to these factors.