Title: Early Behavioral and Physiological Risk Markers in Infants with Fragile X Syndrome

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Introduction: Fragile X syndrome (FXS) is a neurodevelopmental disorder that typically presents with intellectual disability and an increased prevalence of maladaptive behaviors (Cornish et al., 2013). FXS has high comorbidities with anxiety disorders which often are not diagnosed until later in development (Cordeiro et al., 2010; Kessler et al., 2005). Given that early features of social anxiety are present before formal diagnoses, prospective studies of infants with FXS provide a unique opportunity to study the earliest predictors of anxiety. In typically developing (TD) infants, elevated fear and atypical physiological regulation (e.g., respiratory sinus arrhythmia, RSA) have been identified as early markers of the later emergence of social anxiety. (Booker et al., 2013). No studies have examined behavioral fear or physiological regulation as risk markers of social anxiety in infants with FXS. The current study uses both physiological and observable indices of fear to investigate differences in social fear responses in 12-month-old infants. We hypothesized that physiological regulation during social interactions is disrupted in FXS, causing them to exhibit a dampened physiological response to a novel social situation. Additionally, we believed that FXS infants would have increased attention towards the novel person, an index of attention bias towards threat, within the social situation in relation to TD infants.

Methods: Participants included 23 infants with FXS (Male: n =15, chronological age: M =13.01 months, SD=1.02) and 37 TD infants (Male: n = 29, chronological age M=12.41 months, SD=0.61). Physiological response to a novel social scenario was measured via heart activity monitor during a baseline period and during the Stranger Task of the LABTAB (Goldsmith & Rothbert, 1996). This task is designed to elicit a social fear response in young children. RSA reactivity was computed as the change in RSA from baseline to stranger task. Further, visual attention was recorded during the entire Stranger Task. The average time spent attending to the stranger was calculated by taking the total time the infant looked at the stranger over amount of independent stranger gaze events.

Results: There was no difference between groups in RSA reactivity F(1,36) = .14, p > 0.05. Paired sample t-tests were conducted between baseline and stranger RSA for each group. The TD group showed a significant decrease from baseline (M = 4.61, SD = 1.03) to stranger task (M = 3.84, SD = .76), t(22) = -3.80, p < .001. The FXS group did not show a difference between baseline (M = 4.49, SD = 1.41) and stranger task (M = 3.79.50, SD = 1.43), t(15) = 2.08, p > .05. Moreover, when looking at average stranger gaze time the FXS group (M=5.99, SD=4.15) shows elevated looking time in comparison to the TD group (M=3.34, SD=1.66), F(1,58)=12.12, p<.001.

Discussion: These results provide intriguing insights into the early physiological and behavioral risk markers of social fear. The blunted RSA response to social fear shows a potential early biomarker of social anxiety. Further, the increased average gaze towards stranger exhibits an early behavioral maker of social anxiety. In conjunction, both a physiological and behavioral maker reflecting prodromal symptomatology could be instrumental to early identification and treatment of social anxiety. Future studies should investigate how both physiological and behavioral markers develop longitudinally.