**Title:** Respiratory Sinus Arrhythmia Predicts Fear Longitudinally in Both Children with Fragile X Syndrome and Typically Developing Controls

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**Introduction:** Fragile X syndrome (FXS) is a neurodevelopmental disorder that affects 1 in 5000 males and 1 in 8000 females (CDC, 2011). Typically, it presents with intellectual disability, attention problems, and increased likelihood of comorbid conditions (Bailey et al., 2008). Specifically, there are high rates of comorbid anxiety disorders in individuals with FXS (Cordeiro, 2010), but the emergent signs of anxiety in infants and young children with FXS are not yet well understood. In very young typically developing children, atypical respiratory sinus arrhythmia (RSA) – an index of parasympathetic nervous system function – and elevated fear are known to predict later anxiety (Chalmers et al., 2014; Viana et al., 2017). However, the relationship of early RSA and fear with later anxiety in children with FXS has not been examined. The objective of the present study is to examine whether baseline RSA predicts fear across early childhood in young children with FXS and typically developing (TD) controls. Further, we aim to determine whether the relationship between RSA and fear is different between children with FXS and TD controls.

**Method:** Participants were recruited as part of a larger longitudinal study exploring the emergence and stability of anxiety symptoms in FXS. Participants included 36 children with FXS (10, 27.8% female) and 37 TD children (7, 18.9% female) with no family history of ASD or related disorders. Participants were tested at several timepoints between 4 and 105 months of age. This resulted in a total of 247 observations (FXS: n = 116; TD: = 131). Baseline RSA was measured using an Alive Wireless Heart Monitor (Alive Technologies, Copyright 2005-2009) or an Actiwave Cardio Monitor (CamNtech Ltd., Cambridge, UK) during a baseline video. Respiratory sinus arrhythmia was extracted using CardioBatch software (Brain-Body Center, University of Illinois at Chicago). Fear was measured via parent report using the Fear subscales from the IBQ-R (<18 months), ECBQ (18-36 months), and the CBQ (>36 months) (Gartstein & Rothbart, 2003; Putnam, Gartstein, & Rothbart, 2006; Rothbart, Ahadi, Hershey, & Fisher, 2001; specifically). The IBQ, CBQ, and ECBQ are used to measure temperament characteristics across development.

**Results:** Univariate analysis of covariance (ANCOVA) controlling for age and sex revealed no difference between the FXS and TD groups for parent-reported fear (F(1,242) = 0.22, p = .641); however, there was a trend suggesting lower RSA in the FXS group on baseline RSA (F(1,242) = 3.55, p = .061). To examine the relationship between RSA and fear across early childhood, a linear mixed model was employed with baseline RSA, age, group, and an RSA by group interaction entered as predictors of fear. There were significant main effects of age (F(1,242) = 14.07, B = -0.15, p < .001) and baseline RSA (F(1,242) = 6.24, B = -0.22, p = .013). The main effect of group (F(1,242) = 1.93, B = -0.82, p = .166) and the RSA by group interaction (F(1,142) = 1.349, B = 0.13, p = .247) were both non-significant.

**Discussion:** These results suggest that higher baseline RSA is related to lower fear in children across both groups. These findings extend the literature to better understand the relationship between physiology and behavior, which could inform interventions targeting RSA to help ameliorate fear responses in children. Given that we observed the same relationship between reduced RSA and elevated fear in FXS and TD groups, interventions shown to be effective to reduce fear and subsequent anxiety in TD groups could be applied to FXS. Future studies should explore the long-term impacts of RSA and fear to determine if early lower baseline RSA and higher fear predict later anxiety diagnoses in children with FXS.
References/Citations: