# 2021 Gatlinburg Conference Poster Submission

**Title**: Development of Inhibitory Control Across Early Childhood in Males and Females with Fragile X Syndrome

**Authors**: Erin Hunt, Abigail Hogan, & Jane Roberts

University of South Carolina

**Introduction**: Inhibitory control refers to the voluntary ability to restrain, modulate, or redirect inappropriate behavioral responses (Rothbart, Ellis, Rueda, & Posner, 2003). In typically-developing (TD) children, inhibitory control emerges within the first year of life and increases steadily throughout early childhood, concurrent with rapid neural maturation in the prefrontal cortex (Kochanska, Murray, & Harlan, 2000). Inhibitory control is important in the development of social-emotional skills and has been associated with sociability (Dyson, Olino, Durbin, Goldsmith, & Klein, 2012) and social competence (Lengua, 2003). Poor inhibitory control has also been linked with increased incidence of internalizing and externalizing behavior problems in typically-developing children (Lengua, 2003). Fragile X syndrome (FXS) is characterized by significant social impairments, internalizing and externalizing behavioral problems, and elevated rates of ADHD (Baumgardner, Reiss, Freund, & Abrams, 1995; Hatton et al., 2002; Bailey, Raspa, Olmsted, & Holiday, 2008), with males more significantly affected than females across all domains. While some studies have investigated other temperament factors (e.g., attentional control, negative affect) in young children with FXS, (e.g., Hatton et al., 2002; Tonnsen, Wheeler, Hamrick, & Roberts, 2019; Wall et al., 2019), to date the emergence and developmental of inhibitory control has not been characterized in FXS. Given the critical role of inhibitory control in social and behavioral development, a better understanding of inhibitory control in FXS may inform our understanding of the factors contributing to behavioral problems within this population and help identify potential targets for early intervention and treatment.

**Method**: The sample included 163 children with FXS (25 (15.3%) females; *M* age= 47.66 months) and 75 TD children with no family history of FXS, autism, or related disorders (25 (33.3%) females; *M* age= 45.44 months). Participants completed multiple assessments between 16 and 100 months of age, resulting in 501 total observations (FXS: $n = 353$; TD: $n = 148$). Inhibitory control was measured via parent-report using the Inhibitory Control subscale from the Early Childhood Behavior Questionnaire (ECBQ; 18-36 months) and the Child Behavior Questionnaire (CBQ; >36 months) (Putnam, Gartstein, & Rothbart, 2006; Rothbart, Ahadi, Hershey, & Fisher, 2001; respectively). Between-group differences in inhibitory control and change in inhibitory control over age were investigated by fitting a multilevel model (MLM) via PROC MIXED in SAS 9.4. Group, sex, age, and the group*sex*age interaction were included as predictors, with age nested within participant to account for change in inhibitory control over time. A random intercept was included to account for intra-individual differences. An unstructured covariance structure was specified and shown to be the best fitting covariance structure. Follow-up MLM analyses were run to probe the significant group*sex*age interaction (TD males v. FXS males; TD females v. FXS females; and FXS males v. FXS females). Models were centered at the grand mean of 47.00 months.

**Results**: Results from the overall model indicated main effects of group, $F(1,211) = 85.28$, $p < .0001$, and sex, $F(1,211) = 13.14$, $p = .0004$, with a marginal main effect of age, $F(1,179) = 3.59$, $p = .060$. The group*sex*age interaction was also significant, $F(3,179) = 4.93$, $p = .003$. To probe this interaction, a series of post-hoc MLM models were employed. When TD males and FXS males were compared, significant main effects of group, ($F(1,170) = 81.86$, $p < .0001$, $b = -1.18$), and age, ($F(1,136) = 19.67$, $p < .0001$, $b = 0.02$), emerged. Additionally, the group*age interaction was significant, ($F(1,136) = 13.83$, $p = .0003$, $b = -0.02$), indicating that the inhibitory control score increased more with age in TD males than in FXS males. When TD females and FXS females were compared, a main effect of group, ($F(1,40) = 7.76$, $p = .0081$, $b = -0.90$), was observed. The main effect of age, ($F(1,43) = 0.00$, $p = .9501$), and the group*age interaction, ($F(1,43) = 0.54$, $p = .4660$), were not significant. These results suggest that TD females have higher inhibitory control scores than FXS females, but the groups exhibit similar change in inhibitory control across age. When FXS males and females were compared, a main effect of sex, ($F(1,149) = 15.05$, $p = .0002$, $b = 0.58$), emerged. The main effect of age, ($F(1,127) = 2.61$, $p = .1085$), and the sex*age interaction, ($F(1,127) = 0.92$, $p = .339$), were non-significant, suggesting that though FXS females have higher inhibitory control scores than males, both groups exhibit similar rates of change across age.

**Discussion:** The present study demonstrated that young children with FXS and their TD peers exhibit different profiles of inhibitory control over time. Both males and females with FXS exhibited lower inhibitory control than their TD counterparts, and males with FXS exhibited significantly less increase in inhibitory control with age than TD males. These findings are critical to informing our understanding of risk for the behavioral problems and comorbid disorders often observed in FXS while also identifying a potential target for early intervention.

**References:**

Bailey, D. B., Raspa, M., Olmsted, M., & Holiday, D. B. (2008). Co-occurring conditions associated with FMR1 gene variations: findings from a national parent survey. *American Journal of Medical Genetics. Part A*, *146A*(16), 2060–2069. https://doi.org/10.1002/ajmg.a.32439

Baumgardner, T. L., Reiss, A. L., Freund, L. S., & Abrams, M. T. (1995). Specification of the neurobehavioral phenotype in males with fragile X syndrome. *Pediatrics*, *95*(5), 744–752. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7724315

Dyson, M. W., Olino, T. M., Durbin, C. E., Goldsmith, H. H., & Klein, D. N. (2012). The structure of temperament in preschoolers: A two-stage factor analytic approach. *Emotion*, *12*(1), 44–57. https://doi.org/10.1037/a0025023

Hatton, D. D., Hooper, S. R., Bailey, D. B., Skinner, M. L., Sullivan, K. M., & Wheeler, A. (2002). Problem behavior in boys with fragile X syndrome. *American Journal of Medical Genetics*, *108*(2), 105–116. https://doi.org/10.1002/ajmg.10216

Kochanska, G., Murray, K., & Harlan, E. (2000). Effortful control in early childhood: continuity and change, antecedents, and implications for social development. *Developmental Psychology*, *36*(2), 220–232. Retrieved from http://dx.doi.org/10.1037/0012-1649.36.2.220

Lengua, L. (2003). Associations among emotionality, self-regulation, adjustment problems, and positive adjustment in middle childhood. *Journal of Applied Developmental Psychology*, *24*, 595– 618. https://doi.org/10.1016/j.appdev.2003.08.002

Putnam, S. P., Gartstein, M. A., & Rothbart, M. K. (2006). Measurement of fine-grained aspects of toddler temperament: The Early Childhood Behavior Questionnaire. *Infant Behavior and Development*, *29*(3), 386–401. https://doi.org/10.1016/j.infbeh.2006.01.004

Rothbart, M. K., Ahadi, S. A., Hershey, K. L., & Fisher, P. (2001). Investigations of temperament at three to seven years: The children's behavior questionnaire. *Child Development*, *72*(5), 1394–1408. https://doi.org/10.1111/1467-8624.00355

Rothbart, M. K., Ellis, L. K., Rueda, M. R., & Posner, M. I. (2003). Developing Mechanisms of Temperamental Effortful Control. *Journal of Personality*, *71*(6), 1113–1143. https://doi.org/10.1111/1467-6494.7106009

Tonnsen, B. L., Wheeler, A. C., Hamrick, L. R., & Roberts, J. E. (2019). Infant Temperament in the FMR1 Premutation and Fragile X Syndrome. *Journal of Clinical Child and Adolescent Psychology, 48*(3), 412–422. https://doi.org/10.1080/15374416.2018.1514613

Wall, C. A., Hogan, A. L., Will, E. A., McQuillin, S., Kelleher, B. L., & Roberts, J. E. (2019). Early negative affect in males and females with fragile X syndrome: implications for anxiety and autism. *Journal of Neurodevelopmental Disorders*, *11*(1), 22. https://doi.org/10.1186/s11689-019-9284-y