Title: Predictors of Self-Injurious Behavior Among Individuals with ASD-Associated Disruptive Mutations

Authors: Eva Kurtz-Nelson1, Rachel Earl1, Arianne Wallace1, Evan Eichler1,2, & Raphael Bernier1

Introduction: Self-injurious behavior (SIB) occurs at high rates in several genetic syndromes associated with intellectual and developmental disability (IDD), suggesting that disruptive genetic mutations may contribute to the etiology of SIB in IDD (Shirley et al., 2016). However, the mechanisms by which disruptive mutations promote SIB in IDD are not well understood (Huisman et al., 2018). A number of single gene mutations associated with autism spectrum disorder (ASD) and IDD have been recently identified (Iossifov et al., 2014, and comprehensive phenotyping of individuals with these mutations may elucidate how genetic factors influence SIB in IDD. While case series have reported SIB in some individuals with ASD-associated mutations (e.g., Van Dijck et al., 2019), rates and predictors of SIB have not been systematically examined across studies. Severe gastrointestinal (GI) problems have been reported across multiple ASD-associated mutations (e.g., Bernier et al., 2014), which are predictive of SIB among individuals with ASD (Neuhaus et al., 2018). As such, this study examined predictors and rates of SIB in a cohort of individuals with disruptive mutations to ASD risk genes, with a focus on associations between GI problems and SIB.

Methods: Participants were 112 individuals (mean age = eight years) with a pathogenic or likely pathogenic mutation in one of eight high confidence ASD risk genes. Participants completed a battery of clinical and diagnostic assessments, including the Autism Diagnostic Interview—Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994), the Repetitive Behavior Scale—Revised (RBS-R; Bodfish, Symons, Parker, & Lewis, 2000), the Vineland-II or Vineland-III (Sparrow, Balla, & Cicchetti, 2005; Sparrow, Cicchetti, & Saulnier, 2016), the Social Responsiveness Scale-2 (Constantino & Gruber, 2012), a cognitive assessment, and a comprehensive medical history interview. A dichotomous current SIB variable was created from the ADI-R using procedures described by Dempsey, Dempsey, Guffey, Minard, and Goin-Kochel (2016), while the self-injury subscale score from the RBS-R was used as a continuous measure of SIB severity. Fisher’s exact test and one-way ANOVA were used to compare rates and severity of SIB across mutation groups, and t-tests were used to determine whether IQ, adaptive behavior, and ASD symptoms differed according to the presence of SIB. Logistic regression was used to predict the presence of SIB, while linear regression was used to predict SIB severity; in both models, IQ and adaptive behavior were entered in the first step, while GI problems (constipation, gastroesophageal reflux, and abdominal pain) were entered in the second step.

Results: Across mutation groups, prevalence of current SIB ranged from 0% to 56% (total prevalence = 30%); rates and severity of SIB did not differ significantly across groups. Individuals with SIB had significantly lower IQ (t(69) = 2.13, p = .04) and adaptive behavior (t(88) = 2.27, p = .03) than individuals with no SIB, while differences in ASD symptom severity approached significance (t(78) = -1.69, p = .05). In both the logistic regression model and the linear regression model, the addition of GI problems significantly improved model fit, and final models were statistically significant. The logistic model correctly classified 77% of cases and explained 31% of the variance in SIB. Severe abdominal pain was associated with the presence of SIB (β = 2.15, p = .01), and individuals with severe abdominal pain were 8.58 times more likely to exhibit SIB than individuals without abdominal pain. Severe abdominal pain was also a significant predictor of SIB severity, β = 2.70, p = .01.

Discussion: Severe abdominal pain predicts SIB prevalence and severity among individuals with ASD-associated single gene mutations. This result suggests that for these individuals, associations between genetic risk and SIB may be mediated or moderated by pain experience. Future research should examine pain perception and experiences among individuals with ASD-associated mutations, whether abdominal pain predicts specific functions or topographies of SIB, and how interactions between genetic susceptibility and pain may contribute to challenging behavior in ASD.
References:


\textsuperscript{1} University of Washington, Seattle; \textsuperscript{2} Howard Hughes Medical Institute