Title: Autism Symptomatology and Prevalence in Preschool Age Children with Fragile X Syndrome

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Introduction: Autism spectrum disorder (ASD) is one of the most common co-morbid conditions occurring in individuals with fragile X syndrome (FXS), with between 60-75% of males, and 25% of females meeting criteria for ASD (Harris et al., 2008; Klusek, Martin, & Losh, 2014). In preschool aged children with FXS, reported rates have been lower, approximately 30% met criteria for ASD (Hazlett et al., 2009; Rogers, Wehner, & Hagerman, 2001). No studies, however, have characterized the early developmental trajectories of autism symptomatology in young children with FXS, and how they may differ from those with non-syndromic ASD. The present study has two primary aims. First, to present the prevalence of ASD in pre-school age children with FXS using a clinical best estimate diagnostic procedure. Second, to examine the change in autism symptomatology across time in toddlers with FXS and co-morbid ASD (FXS+ASD) compared to a sample of FXS toddlers without ASD, and a sample of toddlers with non-syndromic ASD.

Method: All FXS participants (46 total: 13 females, 33 males) in the study were evaluated longitudinally between the ages of 2 and 7 years old, for at least 2 time points. The Autism Diagnostic Observation Schedule-2 (ADOS-2) was administered at each time point. A clinical best estimate diagnosis was given to each participant after considering ADOS-2 scores plus other available information (e.g., clinical judgement, cognitive level, adaptive functioning). To collect data for the second aim, the Brief Observation of Social Communication Change (BOSCC) was coded from video clips from the videotaped ADOS-2 administrations (Grzadzinski et al., 2016). The BOSCC contains 15 behavioral codes, with scores ranging from 0-5 points on each item. Higher scores on the BOSCC indicate greater autism symptomatology. Coding of data for aim 2 is currently underway, with a pilot sample of 6 are available presently. A total of 25 participants (15 with FXS, and 10 with non-syndromic ASD) will be available by conference presentation.

Results: Best estimate diagnosis was taken from the first time point available in the study for each participant. Average age of the participants were 36 months and 28 months respectively for males and females. In the sample of females, 23% met criteria for ASD, 31% evidenced no clinical features, and 46% evidenced a developmental delay. In the sample of males, 80% met criteria for ASD and 20% evidenced a developmental delay. Pilot results are available for the BOSCC data over time (see figure). The figure suggests that participants with FXS+ASD evidence higher initial scores on the BOSCC, however may show varying change over time. Participants with non-syndromic ASD evidence more stable BOSCC scores over time, while participants with FXS without ASD evidence decreasing scores over time.

Discussion: Diagnostic prevalence of ASD in preschoolers with FXS appears consistent with existing reports in older samples, however higher than previous studies conducted in toddlers. A primary difference between the procedures in this study and previous studies in preschool age children with FXS is the use of the Autism Diagnostic Interview-Revised (ADI-R) in previous studies as part of the criteria for being categorized as having ASD. This study did not require the ADI-R. This study also employed the ADOS Toddler module with children under the age of 30 months, which was not available when the previous studies were published. Additionally, both previous studies relied on DSM-IV criteria for Autistic Disorder to determine their ASD groups, while the present study used DSM-5 criteria for ASD. BOSCC scores suggest that toddlers with FXS +ASD may show more impoverished social communication skills and greater restricted and repetitive behaviors at 24 months of
age than participants with non-syndromic ASD, however the trajectories of these skills may be more variable than individuals with non-syndromic ASD. Individuals with FXS without ASD appear to show lower levels of initial BOSCC scores, with decreasing scores over time evidencing the development of increasing social communication skills.

References/Citations: