Title: Rates and predictors of ADHD in Preschoolers with Autism Spectrum Disorder or Fragile X Syndrome

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Introduction: Attention deficit/hyperactivity disorder (ADHD) is the most prevalent disorder in childhood, affecting 11% of the population. ADHD symptomology includes inattention, hyperactivity, and/or impulsivity. Children with fragile X syndrome (FXS), non-syndromic autism spectrum disorder (ASD), or comorbid FXS+ASD show increased symptoms of ADHD (53-84%, 37-85%, respectively). A substantial number of individuals with FXS or non-syndromic ASD also have intellectual disability (ID), which predisposes them to an increased risk for developing ADHD. However, the overlap in symptomology inherent in comorbid diagnoses poses greater complexity in determining co-occurrence of ADHD, in addition to FXS, ASD, and ID. Co-occurring ADHD may lead to negative outcomes beyond those associated with FXS or ASD without ADHD. Thus, it is important to clearly delineate these overlapping symptoms within various disorders to provide more accurate assessment and interventions. This study aims to characterize the rates of ADHD in pre-schoolers with FXS, ASD, and FXS+ASD, per parent interview and clinical assessment, and to determine whether over activity during clinical assessment or ASD severity predict ADHD diagnoses in preschoolers with FXS-only, comorbid FXS+ASD, and children with non-syndromic ASD.

Method: Participants included 25 children with comorbid FXS+ASD, (M CA = 45.97 months, 12% female), 20 children with FXS-only, (M CA = 44.86 months, 45% female), and 37 with non-syndromic ASD (M CA = 44.24, 11% female). Participants were mean matched on chronological age, [F(2,79) = .299, p = .742]. Demographic information was gathered from all the participants including age, risk status, and gender. Each child took part in a full battery assessment where he/she participated in the ADOS-2 and Mullen Scales of Early Learning protocols. Parents of the children were interviewed using the Preschool Age Psychiatric Assessment (PAPA), a semi-structured DSM-based parent interview for children ages 2-6 with limited verbal skills. Clinical Best Estimate (CBE) was used to determine presence of comorbid diagnoses, in participants with FXS, including comorbid ASD or ADHD. For ASD participants, the CBE process was used to confirm an ASD diagnosis and determine presence of additional comorbid diagnoses, such as ADHD. The CBE process involves full review of developmental, adaptive behavior, psychiatric, and autism assessment results by a licensed psychologist, lead assessors, and a third team member trained in assessment. As such, the results of the PAPA clinical parent interview were considered in light of a larger set of information to confirm or refute a diagnosis of ADHD in the groups. These two diagnostic methods were employed given the challenge of determining ADHD in young samples with ID and ASD. Descriptive statistics were used to examine the rates of comorbid ADHD in FXS, FXS+ASD, and ASD across parent interview and clinical assessment measures. Separate logistic regression models were then computed to test predictors of ADHD diagnostic outcomes in each group.

Results: Results indicated an overall rate of 10.53% of comorbid ADHD in the FXS group per clinical parent interview, which was also highly consistent per CBE diagnostics (10.53%). Results in the ASD group indicated an overall rate of 29.73% comorbid ADHD per parent interview, versus 10.81% per CBE diagnostic process. The comorbid FXS+ASD group had an overall rate of comorbid ADHD at 45.83% per parent interview, versus 19.05% per CBE diagnostics. Results from the logistic regression demonstrated that the only significant predictor of ADHD was over activity (coded on the ADOS) for the FXS+ASD group, (p = .0437) with an odds ratio of 10.87. These results indicated that for each unit increase in over activity, there was approximately an 11 times greater likelihood that a participant with comorbid FXS+ASD would receive an ADHD diagnosis. Neither over activity nor ASD severity were significant predictors in any other group.

Discussion: Proportions of ADHD diagnoses are higher using a parent interview alone than using a comprehensive CBE diagnostic process in both comorbid FXS+ASD and non-syndromic ASD groups. The higher rates per clinical interview may be explained by the overlapping symptomatology of ASD and ADHD, such as hyperactivity, inattention, fidgeting, etc. that may be hard for parents to disentangle. Overall, this study shows that the severity of autism symptoms does not have an effect on comorbid diagnosis of ADHD within groups. However, a large discrepancy between parent interview and CBE diagnoses of ADHD was evident only in the two ASD groups suggesting that caution should be taken in ADHD diagnostic determination when considering...
parent interview in isolation of more detailed clinical data particularly for children with ASD, who might over-attribute ADHD symptoms when ASD is also present.

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