Published in final edited form as:

J Atten Disord. 2019 January ; 23(2): 181–188. doi:10.1177/1087054715571739.

The Influence of Hyperactivity, Impulsivity, and Attention Problems on Social Functioning in Adolescents and Young Adults With Fragile X Syndrome

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Abstract

Objective—Individuals with fragile X syndrome (FXS) present primarily with cognitive and social deficits in addition to symptoms of ADHD. The relationship between symptoms of ADHD, cognitive functioning, and social skills has never been explicitly studied.

Method—Here, we analyzed both longitudinal ($n = 70$; Time 1: ages 6–18; Time 2: ages 15–26) and cross-sectional ($n = 73$; Time 2 only) data using hierarchical linear regression to assess how global intellectual functioning (IQ) and symptoms of ADHD influence social functioning in individuals with FXS.

Results—We found that ADHD symptoms at Times 1 and 2 consistently predict social functioning in both males and females with FXS at Time 2.

Conclusion—Our results suggest that addressing ADHD symptoms in childhood may have positive, long-term effects on the social functioning of adolescents and young adults with FXS.

Keywords

neurodevelopmental disorders; fragile X syndrome; ADHD; impulsivity; inattention

Introduction

Individuals with fragile X syndrome (FXS) are at increased risk of a wide range of dysfunctional social behaviors (Gabis, Baruch, Jokel, & Raz, 2011; Mazzocco et al., 2006). These include heightened social anxiety, lower levels of social relatedness, problems with social perception, abnormal communication patterns and dysfunctional nonverbal

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

communication, deficits in interacting with peers, gaze aversion, overt discomfort in and withdrawal from social situations, and social phobia (Gabis et al., 2011; Hartley et al., 2011; Hessler, Glaser, Dyer-Friedman, & Reiss, 2006; Mazzocco et al., 2006; Roberts, Weisenfeld, Hatton, Heath, & Kaufmann, 2007). Among these, social avoidance and withdrawal have been suggested to be the most prevalent and disabling behavioral features of the condition (Roberts et al., 2007). Although other genetically based neurodevelopmental disorders confer increased risk of impairment in communication and social abilities, these impairments seem to occur at a greater rate and severity in FXS and may not be solely attributable to co-occurring diagnoses such as autism spectrum disorders or intellectual disability (Gabis et al., 2011; Mazzocco et al., 2006; Oliver, Berg, Moss, Arron, & Burbidge, 2011; Roberts et al., 2007).

Individuals with FXS are also known to have increased rates of hyperactivity, impulsivity, and inattention. Estimates of the prevalence of borderline or clinically significant ADHD in individuals with FXS range from 36% to 93% (Hartley et al., 2011; Sullivan et al., 2006). This prevalence is significant enough that some researchers have suggested that these deficits are part of the core FXS behavioral phenotype and may constitute the most common behavioral problems associated with the disorder (Gabis et al., 2011; Hessler et al., 2006; Sullivan et al., 2006). There have been conflicting findings as to whether ADHD occurs at the same or a higher rate in individuals with FXS compared with IQ and mental age-matched children with non-fragile X associated disability, but evidence suggests that hyperactivity is more common in FXS than in other genetic disorders (Oliver et al., 2011; Sullivan et al., 2006).

Several studies have reported a link between ADHD symptoms and problems with social function. Although children with ADHD show a diverse range of difficulties, social impairments can be severe (De Boo & Prins, 2007; Greene et al., 2001). Children with ADHD are prone to social rejection from early childhood and are perceived more negatively by peers than children with other behavioral disorders (De Boo & Prins, 2007; Diamantopoulou, Rydell, Thorell, & Bohlin, 2007; Karustis, Power, Rescorla, Eiraldi, & Gallagher, 2000). Children and adolescents with ADHD experience more peer rejection (Erhardt & Hinshaw, 1994; Hoza et al., 2005; Mrug et al., 2012) and are less popular than peers without ADHD (Elkins, Malone, Keyes, Iacono, & McGue, 2011). They also exhibit social withdrawal (Hodgens, Cole, & Boldizar, 2000). The primary symptoms of ADHD, namely hyperactivity, impulsivity, and inattention, are considered to be at the root of social difficulties in children with the disorder (De Boo & Prins, 2007; Diamantopoulou et al., 2007; Solanto, Pope-Boyd, Tryon, & Stepak, 2009). Furthermore, individuals with ADHD can display rapid jumps in conversation, failure to attend to others during conversations, repeated intrusions and interruptions, and attempts to converse at unacceptable times, which interfere with the formation and maintenance of social relationships (De Boo & Prins, 2007).

ADHD symptomatology in children has been shown to predict future social functioning levels in childhood and adolescence, independent of global cognitive abilities (De Boo & Prins, 2007; Diamantopoulou et al., 2007; Solanto et al., 2009). Moreover, ADHD symptoms can be associated with problems such as anxiety and depression, which can further worsen social skills and can reduce opportunities for developing better social skills

(Solanto et al., 2009). Social skill deficits in childhood increase risk of a wide range of social, familial, educational, and vocational difficulties during adolescence and adulthood, indicating that heightened rates of ADHD symptoms can have wide-ranging impacts on quality of life mediated by social functioning deficits (De Boo & Prins, 2007; Solanto et al., 2009).

Although the presence of both social deficits and ADHD symptoms is well-documented in individuals with FXS, the nature of the relationship between these two elements in the FXS population is still unknown, as no study has explicitly addressed this issue. Given that social difficulties are known to be associated with core ADHD symptoms, it is appropriate to explore if some social difficulties occurring in individuals with FXS can be similarly linked to ADHD symptomology. Considering that early deficits in social competence are associated with difficulties that can persist into adolescence and adulthood, and that competence in interpersonal interaction is one of the most important factors in determining independence in adulthood, clarifying the role of ADHD symptoms in social functioning in individuals with FXS could provide clinically important new information. In particular, such information could be used to design or modify specific intervention programs targeting ADHD symptoms or social skills for individual with FXS, thereby improving long-term outcome and quality of life (De Boo & Prins, 2007; Hartley et al., 2011; Solanto et al., 2009).

We conducted a prospective cohort study to investigate the relationship between symptoms typically associated with ADHD (hyperactivity, impulsivity, and inattention) and social functioning in individuals with FXS. We first examined this relationship within a group of participants in the adolescent and young adult age range, and then assessed the predictive value of early ADHD symptoms on later social abilities. We hypothesized that the severity of ADHD symptoms would predict later and current social functioning demonstrated by individuals with FXS. We also predicted that ADHD symptoms would be associated with social functioning after controlling for the effect of global level of cognitive function.

Method

Participants

The sample comprised 73 participants with FXS (33 females) between 15 and 25 years of age (Time 2, $M = 20.40$, $SD = 2.937$) enrolled in a longitudinal study focusing on social, cognitive, and behavioral development in FXS. Seventy of these participants were part of an earlier phase of the study when they were between the ages of 6 and 18 (Time 1, $M = 12.252$, $SD = 2.697$). Participants were recruited via public announcements, websites, word of mouth, and a database of past participants. FXS diagnosis was confirmed by DNA Southern blot analysis (Kimball Genetics, Inc.). Exclusion criteria included having a known genetic disorder in addition to FXS or being unable to travel to our research center (at Time 2). Written consent and assent were obtained from participants and parents as appropriate according to participant age and functioning level. All study procedures and protocols were approved by the university institutional review board.

Procedure

The assessments were part of an extensive experimental protocol including a battery of cognitive and behavioral testing as well as neuroimaging tasks for some of the participants that took approximately 6 to 12 hours distributed over a 2-day period. Participants were assessed at our center or in their homes at Time 1 and at our center at Time 2. Parent interviews were performed in person or were performed by phone if the participant traveled to the research center unaccompanied.

Assessments and Measures

These tests and questionnaires were selected on the basis of their wide use in research, their clinical relevance, and their content and face validity to tap constructs of interest. Test administration was completed by qualified experimenters following standard administration procedures as outlined in the published product manuals; we used age-normed scaled scores for the analyses when appropriate. Several parent reports were chosen to obtain information about how the participants interact with others in their typical environment rather than in an artificial laboratory setting. Given the age range of the participants, parents were chosen over other informants because other informants were not consistently available for all participants (i.e., teachers would not have been appropriate given that many participants were beyond school age). Descriptive statistics for the variables considered in the study are given in Table 1.

Cognitive Functioning

Depending on the participant's age, the *Wechsler Abbreviated Scale of Intelligence* (WASI; Wechsler, 1999) or the *Wechsler Intelligence Scale for Children, Third Edition* (WISC-III; Wechsler, 1991) was used at Time 2 to produce Full-Scale Intelligence Quotient (FSIQ) scores, a global measure of intellectual functioning. The WISC-III is an extensive cognitive battery for children below the age of 17. The WISC-III was used for longitudinal consistency with Time 1. These data were collected as part of a prospective longitudinal study spanning several years, and the WISC-III was the edition in use at Time 1. The WASI is a short cognitive battery that assesses intelligence in children and adults and was administered to participants who were 17 or older.

Hyperactivity, Impulsivity, and Inattention

ADHD Test (ADHD-T)—The ADHD-T is an informant questionnaire that assesses the extent to which an individual displays symptoms of inattention, impulsivity, and hyperactivity (Gilliam, 1995). Informants rate the frequency of behaviors associated with these symptoms. In this study, a parent completed the questionnaire about his or her child. The ADHD-T is normed to a group of 3- to 23-year-old individuals who met the *Diagnostic and Statistical Manual for Mental Disorders* (4th ed.; *DSM-IV*; American Psychiatric Association, 1994) diagnosis for ADHD. Standardized scores for participants older than 23 in this study ($n = 17$) were calculated with the norms for 23-year-olds. Higher scores indicate more severe symptoms. This measure was used at Time 2 only.

The Hyperactivity Scale of the Aberrant Behavior Checklist–Community

Version (ABC-C)—The ABC-C is a parent questionnaire designed to assess the extent and severity of problem behaviors demonstrated by individuals 6 to 54 years of age at school and in the community. The Hyperactivity scale is a raw subscore of the assessment that reflects the frequency and severity of behaviors reflective of hyper-activity and impulsivity. Higher scores indicate greater impairment. Although the ADHD-T covers an extensive range of symptoms and may be a more comprehensive measure, the ABC-C Hyperactivity scale was also used because data were available for this measure at both time points and because the ABC-C was specifically designed to measure behavioral symptoms in individuals with intellectual disability (Aman, Burrow, & Wolford, 1995).

Social Measures

Three complementary measures of social behavior were used as outcome measures.

The Reciprocal Social Interaction Scale of the Autism Diagnostic Observation Schedule (ADOS)

—The ADOS (Lord, Rutter, DiLavore, & Risi, 1999) was used to assess social interaction abilities at Time 2. The ADOS is a clinical assessment to determine whether an individual meets the diagnostic criteria for autism spectrum disorders. The ADOS is commonly used to assess social functioning of individuals with FXS because up to two thirds of individuals with FXS meet criteria for an autism spectrum disorder (Harris et al., 2008; Loesch et al., 2007). The instrument is administered in a controlled setting by a trained professional. Numerous criteria are assigned a rating based on the individual's interactions with the examiner. The Reciprocal Social Interaction scale focuses on the social interactions between the examiner and the participant, including items such as quality of rapport, nonverbal communication, and insight and empathy. Higher scores indicate more symptoms of autism.

The Socialization Scale of the Vineland Adaptive Behavior Scales and Vineland Adaptive Behavior Scales II

—The Vineland Adaptive Behavior Scale (Vineland) is a semi-structured parent interview designed to assess an individual's level of functioning. The assessment is valid from birth to 90 years of age. A trained interviewer asks an informant (in this case, the parent) about different behavioral skills and rates the extent to which the individual is reported to display these skills. The Socialization scale focuses on interactions between the participant and other people. The Vineland II is the second edition of the Vineland and was used at Time 2 because it provides information based on more current norms (Sparrow, Cicchetti, & Balla, 2006). The Vineland I was used at Time 1 because it was the current version at that time (Sparrow, Cicchetti, & Balla, 1984). Higher scores indicate better adaptive functioning.

The Social Problems Scale of the Achenbach Child Behavior Checklist (CBCL)

—The CBCL is a parent questionnaire assessing a wide range of behaviors (Achenbach, 1991). The assessment is designed for children aged 4 to 18. The Social Problems scale assesses the extent to which a participant has difficulties in his or her peer interactions, such as being disliked, ignored, or teased by peers. Participants who were above 18 years old

received the standardized score that would be received by an 18-year-old based on the participant's raw score. This measure was used at Time 2.

Statistical Analysis

Data were entered into SPSS statistical software Version 18.0 and coded to ensure anonymity prior to analysis. We excluded all data for participants that were outliers, at least two *SD* from the group mean, on two or more assessments ($n = 2$). If a participant was an outlier on a single assessment, the datum for that assessment only was removed ($n = 1$).

Two sets of hierarchical linear regressions were performed. The first set examined cross-sectional data during the most recent phase of the study (Time 2). The second set analyzed the longitudinal relationship between data from an earlier phase of the study (Time 1) and social outcomes at Time 2.

Time 2 cross-sectional data were analyzed to determine whether symptoms of hyperactivity, impulsivity, and inattention predicted ratings on social measures after controlling for FSIQ. Six separate regressions were performed for each sex, first entering FSIQ and age and then either (a) ADHD-T quotient score or (b) ABC-C Hyperactivity sub-scale as predictors of (a) Social Problems subscale of the CBCL, (b) Socialization score on the Vineland II, or (c) Reciprocal Social Interaction subscale of the ADOS. Analyses were conducted separately for males and females because, as expected, IQ was significantly different between sexes, $t(73) = 6.687$ $p < .001$.

We also performed three hierarchical linear regressions on the longitudinal data for each sex to determine whether hyperactivity ratings predict social skills later in life. We entered FSIQ into the model first, Time 1 Vineland Socialization second, and Time 1 ABC-C Hyperactivity third (as separate steps) to predict one of the following Time 2 variables: (a) CBCL Social Problems, (b) Vineland II Socialization, or (c) ADOS Reciprocal Social Interaction.

Results

For females, ADHD-T quotient and ABC-C Hyperactivity, but not IQ, significantly contributed to higher CBCL Social Problems. Both IQ and either ADHD-T quotient or ABC-C Hyperactivity contributed to lower Vineland II Socialization scores. For males, ADHD-T quotient, but not IQ, significantly contributed to higher CBCL Social Problems and lower Vineland II Socialization. ABC-C Hyperactivity and IQ significantly contributed to CBCL Social Problems, with higher IQ predicting lower scores and higher ABC-C Hyperactivity predicting higher scores. No other models reached significance. See Table 2.

For females, only Time 1 ABC-C Hyperactivity predicted higher Time 2 CBCL Social Problems. Time 1 Vineland Socialization was the only significant predictor of higher Time 2 Vineland II Socialization. None of the variables significantly predicted Time 2 ADOS Reciprocal Social Interaction scores. For males, Time 1 Vineland Socialization and Time 1 ABC-C Hyperactivity significantly contributed to Time 2 Vineland II Socialization, with higher Time 1 Vineland Socialization predicting higher Time 2 Vineland II Socialization

scores and higher Time 1 ABC-C Hyperactivity predicting lower Time 2 Vineland II Socialization scores. No other models reached significance. See Table 3.

Discussion

This study examined the role of ADHD symptoms and IQ in predicting social functioning in individuals with FXS. Specifically, we measured social problems with the CBCL, socialization skills with the Vineland II, and social interaction with the ADOS. Our results reveal that ADHD symptoms associated with FXS are associated with different aspects of social functioning including social problems and socialization skills. For our cross-sectional data, ADHD symptoms alone were associated with *social problems* for females with FXS. For one of our two ADHD measures (ABC-C), global intellectual function, as presented by IQ, was also associated with social problems for males. ADHD symptoms, but not intellectual functioning, were predictive of *socialization skills* for males and females with FXS. These results indicate that, overall, ADHD symptoms may be as critical as intellectual level in influencing social functioning in individuals with FXS. Results from our longitudinal data further support this notion and show that early hyperactivity has predictive value for social problems later in life for females with FXS, even after controlling for intellectual function and early socialization skills. For males with FXS, early social skills and hyperactivity predict social skills later in life. Together, results from our cross-sectional and longitudinal analysis suggest that early diagnosis and treatment of ADHD symptoms may play a role in improving both concurrent and long-term social functioning. Furthermore, interventions that reduce ADHD symptoms may improve the social functioning of individuals with FXS, regardless of their level of cognitive functioning.

Although our results indicate that inattention, impulsivity, and hyperactivity are strongly associated with social skills and behaviors in adolescents and young adults with FXS, different results were obtained using three measures that assess different aspects of social functioning. The CBCL Social Problems scale provides information about how social deficits affect everyday life of individuals with FXS. The CBCL measures whether individuals are able to effectively interact with peers in a social setting without provoking negative reactions or rejection. This ability is clearly necessary to form effective social relationships. Having social relationships is important for preventing isolation and its negative emotional correlates, particularly in adolescence and young adulthood.

Higher levels of ADHD symptoms predicted both heightened levels of social problems and decreased levels of socialization skills in our female group. Previous research has indicated that (non-FXS) females who display disruptive behavioral disorders, including ADHD, have increased social problems and are more disliked by peers compared with males with such disorders (Diamantopoulou et al., 2007). This finding in girls without FXS may help explain why symptoms of ADHD correlated with social outcomes for the female group in our study. For females with FXS, both IQ and ADHD symptoms contributed to *socialization skills*, but only ADHD symptoms contributed to *social problems*. Higher IQ may allow females with FXS to develop more advanced socialization skills, but ADHD symptoms still have an impact on the level of skills demonstrated. Independent of IQ, lower levels of ADHD symptoms allow females with FXS to avoid social problems such as rejection by their peers.

The novel findings described here have important implications for designing effective interventions for children with FXS. Because hyperactivity and impulsivity have an immediate and a long-term impact on social functioning, early intervention targeting such symptoms may help change the trajectory of social experiences for affected individuals. Targeting social skills may be helpful, yet insufficient when symptoms of hyperactivity, impulsivity, and inattention are present. Interventions that minimize problems with inattention, impulsivity, and hyperactivity may allow individuals a better chance of avoiding social rejection and isolation. Early interventions specifically targeting attention skills (cognitive training interventions) have been proposed to improve long-term outcomes associated with FXS (Cornish, Cole, Longhi, Karmiloff-Smith, & Scerif, 2013). Pharmaceutical intervention with donepezil, an acetylcholinesterase inhibitor, has been associated with reduction of inattention, hyperactivity, and impulsivity of individuals with FXS (Kesler, Lightbody, & Reiss, 2009). Future interventions intended to decrease ADHD symptoms should also measure the impacts of such improvements on socialization.

Some research has suggested that males with FXS become more aware of their social difficulties as they grow older and become more avoidant of social situations as a result (Roberts et al., 2007). Early intervention, focused on both ADHD symptoms and social skills, may protect against social avoidance that decreases opportunities to learn and practice social skills. Because peer relationships have been found to be one of the most important predictors of independence in adulthood (Hartley et al., 2011), this type of targeted early intervention may have substantial widespread impacts on the quality of life individuals with FXS experience in adulthood.

This study has several strengths, including both cross-sectional and longitudinal analyses, and a large sample size that allows separate analyses by sex. However, the study also has limitations. First, two of the social measures were based on parent reports and one was an in-lab assessment with a trained experimenter. To truly understand the social experience of our participants, it may be beneficial and more ecologically valid to make observations in their typical environment. Second, the cognitive measures used were susceptible to floor effects, especially with male participants. However, analyses were performed with raw scores (results not shown), and similar results were obtained, indicating that the floor on the test did not substantially affect the results. Because results were very similar, and a scaled score is more easily interpreted, the analyses with scaled scores were reported. Last, this study did not involve intervention; consequently, it cannot provide information regarding causal links between ADHD symptoms and social functioning.

Future studies should also explore the impact of inattention, hyperactivity, and impulsivity on different aspects of social functioning. For children with ADHD, inattention may be associated with social withdrawal, whereas hyperactivity and impulsivity are more likely to be associated with inappropriate social behaviors including initiating fights and arguments (Hodgens et al., 2000). Individuals with FXS also exhibit social withdrawal (Roberts et al., 2007). Future studies could examine whether social withdrawal in individuals with FXS might also be associated, in part, with inattention rather than hyperactivity and impulsivity.

Future research should also consider observing participants in their natural environment to better understand their social experiences. Ideally, a longitudinal study should be conducted to see how an intervention at a young age that addresses inattention, impulsivity, and hyperactivity affects social skills at a later time, as well as how successful different interventions aimed at reducing ADHD symptomology are with this population.

Acknowledgments

We would like to thank the participants and their families.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This research was supported in part by a grant from the National Institute of Mental Health (MH50047) and Postdoctoral Fellowships to E.M.Q. from the Fonds de Recherche Société et Culture Québec (FRQSC) and to J.F.L. from the Canadian Institutes of Health Research (CIHR).

References

- Achenbach, TM. Manual for the Child Behavior Checklist/4–18. Burlington: University of Vermont, Department of Psychiatry; 1991.
- Aman MG, Burrow WH, Wolford PL. 1995; The Aberrant Behavior Checklist–Community: Factor validity and effect of subject variables for adults in group homes. *American Journal of Mental Retardation*. 100:283–292. [PubMed: 8554775]
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4. Washington, DC: Author; 1994.
- Cornish K, Cole V, Longhi E, Karmiloff-Smith A, Scerif G. 2013; Mapping developmental trajectories of attention and working memory in fragile X syndrome: Developmental freeze or developmental change? *Development and Psychopathology*. 25:365–376. DOI: 10.1017/S0954579412001113 [PubMed: 23627950]
- De Boo GM, Prins PJM. 2007; Social incompetence in children with ADHD: Possible moderators and mediators in social-skills training. *Clinical Psychology Review*. 27:78–97. [PubMed: 16814435]
- Diamantopoulou S, Rydell A, Thorell LB, Bohlin G. 2007; Impact of executive functioning and symptoms of Attention Deficit Hyperactivity Disorder on children's peer relations and school performance. *Developmental Neuropsychology*. 32:521–542. [PubMed: 17650992]
- Elkins IJ, Malone S, Keyes M, Iacono WG, McGue M. 2011; The impact of attention-deficit/hyperactivity disorder on preadolescent adjustment may be greater for girls than for boys. *Journal of Clinical Child & Adolescent Psychology*. 40:532–545. DOI: 10.1080/15374416.2011.581621 [PubMed: 21722026]
- Erhardt D, Hinshaw SP. 1994; Initial sociometric impressions of attention-deficit hyperactivity disorder and comparison boys: Predictions from social behaviors and from nonbehavioral variables. *Journal of Consulting and Clinical Psychology*. 62:833–842. DOI: 10.1037/0022-006X.62.4.833 [PubMed: 7962888]
- Gabis LV, Baruch YK, Jokel A, Raz R. 2011; Psychiatric and autistic comorbidity in fragile X syndrome across ages. *Journal of Child Neurology*. 26:940–948. [PubMed: 21527394]
- Gilliam, JE. Attention-Deficit/Hyperactivity Disorder Test. Austin, TX: Pro-Ed; 1995.
- Greene RW, Biederman J, Faraone SV, Monuteaux MC, Mick E, DuPre EP, ... Goring JC. 2001; Social impairments in girls with ADHD: Patterns, gender comparisons, and correlates. *Journal of the American Academy of Child & Adolescent Psychiatry*. 40:704–710. [PubMed: 11392349]
- Harris SW, Hessel D, Goodlin-Jones B, Ferranti J, Bacalman S, Barbato I, ... Hagerman RJ. 2008; Autism profiles of males with fragile X syndrome. *American Journal of Mental Retardation*. 113:427–438. DOI: 10.1352/2008.113:427-438 [PubMed: 19127654]

- Hartley SL, Seltzer MM, Raspa M, Olmstead M, Bishop E, Bailey DB Jr. 2011; Exploring the adult life of men and women with fragile X syndrome: Results from a national survey. *American Journal on Intellectual and Developmental Disabilities*. 116:16–35. [PubMed: 21291308]
- Hessl D, Glaser B, Dyer-Friedman J, Reiss AL. 2006; Social behavior and cortisol reactivity in children with fragile X syndrome. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*. 47:602–610. DOI: 10.1111/j.1469-7610.2005.01556.x
- Hodgens JB, Cole J, Boldizar J. 2000; Peer-based differences among boys with ADHD. *Journal of Clinical Child Psychology*. 29:443–452. DOI: 10.1207/S15374424JCCP2903_15 [PubMed: 10969428]
- Hoza B, Mrug S, Gerdes AC, Hinshaw SP, Bukowski WM, Gold JA, ... Arnold LE. 2005; What aspects of peer relationships are impaired in children with attention-deficit/hyperactivity disorder? *Journal of Consulting and Clinical Psychology*. 73:411–423. DOI: 10.1037/0022-006X.73.3.411 [PubMed: 15982139]
- Karustis JL, Power TJ, Rescorla LA, Eiraldi RB, Gallagher PR. 2000; Anxiety and depression in children with ADHD: Unique associations with academic and social functioning. *Journal of Attention Disorders*. 4:133–149. DOI: 10.1177/108705470000400301
- Kesler SR, Lightbody AA, Reiss AL. 2009; Cholinergic dysfunction in fragile X syndrome and potential intervention: A preliminary 1H MRS study. *American Journal of Medical Genetics Part A*. 149:403–407. DOI: 10.1002/ajmg.a.32697
- Loesch DZ, Bui QM, Dissanayake C, Clifford S, Gould E, Bulhak-Paterson D, ... Huggins RM. 2007; Molecular and cognitive predictors of the continuum of autistic behaviours in fragile X. *Neuroscience & Biobehavioral Reviews*. 31:315–326. DOI: 10.1016/j.neubiorev.2006.09.007 [PubMed: 17097142]
- Lord, C, Rutter, M, DiLavore, P, Rissi, S. *Autism Diagnostic Observation Schedule-WPS (ADOS-WPS)*. Los Angeles, CA: Western Psychological Services; 1999.
- Mazzocco MMM, Thompson L, Sudhalter V, Belser RC, Lesniak-Karpiak K, Ross JL. 2006; Language use in females during brief initial social interactions. *Journal of Developmental and Behavioral Pediatrics*. 27:319–328. [PubMed: 16906008]
- Mrug S, Molina BS, Hoza B, Gerdes AC, Hinshaw SP, Hechtman L, Arnold LE. 2012; Peer rejection and friendships in children with Attention-Deficit/Hyperactivity Disorder: Contributions to long-term outcomes. *Journal of Abnormal Child Psychology*. 40:1013–1026. DOI: 10.1007/s10802-012-9610-2 [PubMed: 22331455]
- Oliver C, Berg K, Moss J, Arron K, Burbidge C. 2011; Delineation of behavioral phenotypes in genetic syndromes: Characteristics of autism spectrum disorder, affect, and hyper-activity. *Journal of Autism and Developmental Disorders*. 41:1019–1032. DOI: 10.1007/s10803-010-1125-5 [PubMed: 21080217]
- Roberts JE, Weisenfeld LAH, Hatton DD, Heath M, Kaufmann WE. 2007; Social approach and autistic behavior in children with fragile X syndrome. *Journal of Autism and Developmental Disorders*. 37:1748–1760. DOI: 10.1007/s10803-006-0305-9 [PubMed: 17180715]
- Solanto MV, Pope-Boyd SA, Tryon WW, Stepak B. 2009; Social functioning in predominately inattentive and combined subtypes of children with ADHD. *Journal of Attention Disorders*. 13:27–35. DOI: 10.1177/1087054708320403 [PubMed: 19372497]
- Sparrow, SS, Cicchetti, DV, Balla, DA. *Vineland Adaptive Behavior Scales (Vineland-I)*. San Antonio, TX: Pearson Assessments; 1984.
- Sparrow, SS, Cicchetti, DV, Balla, DA. *Vineland Adaptive Behavior Scales, Second Edition (Vineland-II)*. San Antonio, TX: Pearson Assessments; 2006.
- Sullivan K, Hatton D, Hammer J, Sideris J, Hooper S, Ornstein P, Bailey D Jr. 2006; ADHD symptoms in children with FXS. *American Journal of Medical Genetics Part A*. 140A:2275–2288.
- Wechsler, D. *Wechsler Intelligence Scale for Children*. 3. San Antonio, TX: The Psychological Corporation; 1991.
- Wechsler, D. *The Wechsler Abbreviated Scale of Intelligence*. San Antonio, TX: The Psychological Corporation; 1999.

Biographies

Lindsay C. Chromik is a research assistant in the Center for Interdisciplinary Brain Sciences Research at Stanford University. Her primary research and clinical interests include understanding the causes of ADHD to better develop treatments, especially in early childhood. She holds a master of science in counseling psychology.

Eve-Marie Quintin is a clinical child and adolescent neuropsychologist and assistant professor in the Educational and Counselling Psychology Department at McGill University. Her research is designed to understand variability in cognitive, socio-emotional, and brain development throughout the life span. Her work focuses on neurodevelopmental disorders of childhood and adolescence including autism spectrum disorders and fragile X syndrome..

Jean-François Lepage is a clinical neuropsychologist whose main research endeavors focus on the role of genetic influences on brain development. He is currently a postdoctoral fellow at Spaulding Rehabilitation Hospital and a lecturer at Université du Québec à Trois-Rivières.

Kristin M. Hustyi is a board certified behavior analyst. Her clinical interests include understanding the pathogenesis of aberrant behavior and behavioral intervention for individuals with autism spectrum disorders and genetic disorders.

Amy A. Lightbody is a senior research scholar in the Center for Interdisciplinary Brain Sciences Research at Stanford University. Since 1996, she has been involved in research on fragile X syndrome and related disorders including autism, idiopathic developmental delay, and ADHD. She has extensive experience in clinical work with patients with a broad range of behavioral phenotypes as well as complex research project implementation. Her research interests include understanding the trajectory of cognition, language, and behavior in individuals with genetic disorders.

Allan L. Reiss has personally conducted research focused on FXS since 1982. His lab, the Center for Interdisciplinary Brain Sciences Research at Stanford University, is designed to investigate how specific genetic and environmental factors are associated with variations in brain development and behavioral function in children with specific genetic risk factors such as FXS. In this work, he integrates genetic, neuroimaging, cognitive, and behavioral measures as well as specific metrics of the environment, using state-of-the-art methods to advance our knowledge of mechanisms associated with variation in developmental and behavioral outcome.

Table 1

Descriptive Statistics of Study Variables.

Assessment	<i>n</i>	Minimum	Maximum	<i>M</i>	<i>SD</i>
Time 2 data					
Age	73	15.3	25.68	20.40	2.937
Full-scale IQ	73	40	116	66.26	19.411
ADHD-T quotient	68	57	109	77.24	13.940
ABC-C hyperactivity	71	0	30	6.61	7.176
CBCL social problems	68	50	81	61.15	8.008
Vineland II socialization	73	35	103	69.66	16.190
ADOS reciprocal social interaction	69	0	14	5.59	3.832
Time 1 data					
ABC-C hyperactivity	70	0	34	10.84	8.982
Vineland socialization	66	21	108	66.91	20.045

Note. ABC-C = Aberrant Behavior Checklist–Community; CBCL = Child Behavior Checklist; ADOS = Autism Diagnostic Observation Schedule.

Table 2

Time 2 Cross-Sectional Data.

Outcome variable	Predictor	Model <i>p</i> value	<i>R</i> ²	<i>R</i> ^{2a}	<i>F</i>	<i>df</i>	Age		IQ		Predictor	
							<i>p</i> value	Beta	<i>p</i> value	Beta	<i>p</i> value	Beta
Females												
CBCL social problems	ADHD-T quotient	<.001	.516	.235	8.524	27	.030	0.895	.137	−0.097	.002	0.352
	ABC-C hyperactivity	<.001	.596	.444	12.789	29	.007	0.989	.166	−0.082	<.001	1.117
Vineland II socialization	ADHD-T quotient	.001	.499	.098	8.303	28	.003	−2.798	.010	0.401	.036	−0.440
	ABC-C hyperactivity	<.001	.541	.362	11.021	31	<.001	2.975	.007	0.367	.009	−1.304
ADOS reciprocal social interaction	ADHD-T quotient	.234	.166	.080	1.528	26	.603	−0.086	.378	−0.026	.152	0.057
	ABC-C hyperactivity	.185	.167	.051	1.731	29	.682	0.065	.236	−0.033	.262	0.111
Males												
CBCL social problems	ADHD-T quotient	.001	.369	.309	6.614	37	.547	−0.251	.069	0.266	<.001	0.341
	ABC-C hyperactivity	<.001	.408	.348	7.795	37	.651	1.182	.042	0.291	<.001	0.576
Vineland II socialization	ADHD-T quotient	.009	.278	.185	4.500	38	.090	−1.196	.490	0.163	.005	−0.411
	ABC-C hyperactivity	.090	.167	.166	2.337	38	.075	1.347	.582	0.140	.086	−0.416
ADOS reciprocal social interaction	ADHD-T quotient	.238	.119	.007	1.480	36	.453	0.152	.051	−0.137	.613	−0.020
	ABC-C hyperactivity	.257	.114	.016	1.411	36	.495	0.138	.054	−0.136	.785	0.018

Note. CBCL = Child Behavior Checklist; ABC-C = Aberrant Behavior Checklist-Community; ADOS = Autism Diagnostic Observation Schedule.

^aFrom previous model with only age and IQ to the reported model generated by the addition of the predictor.

Table 3

Time 1 to Time 2 Longitudinal Data.

Outcome variable	Model <i>p</i> value	<i>R</i> ²	<i>R</i> ^{2a}	<i>F</i>	<i>df</i>	IQ		T1 Vineland Socialization		T1 ABC-C Hyperactivity	
						<i>p</i> value	Beta	<i>p</i> value	Beta	<i>p</i> value	Beta
Females											
CBCL social problems	.011	.390	.187	4.693	25	.470	−0.057	.439	−0.078	.016	0.498
Vineland II socialization	.010	.359	.002	4.657	28	.106	0.246	.038	0.417	.826	−0.072
ADOS social	.019	.346	.022	4.051	26	.136	−0.033	.077	−0.051	.388	0.042
Males											
CBCL social problems	.104	.173	.084	2.229	35	.071	0.318	.456	−0.053	.080	0.290
Vineland II socialization	<.001	.466	.088	9.603	36	.826	−0.044	<.001	0.397	.026	−0.439
ADOS reciprocal social interaction	.386	.092	.002	1.046	34	.130	−0.112	.456	−0.022	.810	−0.017

Note. ABC-C = Aberrant Behavior Checklist–Community; CBCL = Child Behavior Checklist; ADOS = Autism Diagnostic Observation Schedule.