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Behavioral Phenotype of Fragile X Syndrome in Adolescence and Adulthood

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Abstract

The present study explored the behavioral profile of individuals with fragile X syndrome during adolescence and adulthood. Individuals with both fragile X syndrome and autism ($n = 30$) were compared with (a) individuals diagnosed with fragile X syndrome (but not autism; $n = 106$) and (b) individuals diagnosed with autism (but not fragile X syndrome; $n = 135$) on measures of autism symptoms, adaptive functioning, behavior problems, and psychological symptoms. Results indicated that individuals dually diagnosed with fragile X syndrome and autism displayed greater communication and social reciprocity impairments than individuals with fragile X syndrome only. Individuals in the dually diagnosed group also exhibited higher levels of repetitive and challenging behaviors than either comparison group, suggesting a unique profile of vulnerability for those diagnosed with both fragile X syndrome and autism.

Keywords

fragile X syndrome; autism; adolescence; adulthood

Fragile X syndrome is the leading known inherited cause of intellectual disability, affecting as many as 1 in 4,000 males and 1 in 8,000 females (Crawford, Acuna, & Sherman, 2001), with recent studies suggesting even higher rates (up to 1 in 2,500; Fernandez-Carvajal et al., 2009; Hagerman, 2008). It has been estimated that as many as 50% of individuals with fragile X syndrome have co-occurring autism (Demark, Feldman, & Holden, 2003; Kaufmann et al., 2004; Philofsky, Hepburn, Hayes, Hagerman, & Rogers, 2004). Past research on young children with fragile X syndrome has indicated that children dually diagnosed with fragile X syndrome and autism have behavioral difficulties similar to children with idiopathic autism (Kauffman et al., 2004; Rogers, Wehner, & Hagerman, 2001). However, less is known about the behavioral profile of individuals with fragile X syndrome during adolescence and adulthood and whether behavior problems and symptoms may differ between individuals who are and are not diagnosed with autism at these points in the life course. In the present study, we addressed this gap by examining the behavioral phenotype of adolescents and adults with fragile X syndrome. Individuals dually diagnosed with both fragile X syndrome and autism were compared with (a) individuals diagnosed with fragile X syndrome (but not autism) and (b) individuals diagnosed with autism (but not fragile X syndrome) on multiple measures of autism symptoms, adaptive functioning, behavior problems, and psychological symptoms.

Prior research exploring autism symptomatology in children with fragile X syndrome has indicated that individuals dually diagnosed with fragile X syndrome and autism often have a profile of symptoms similar to individuals with autism without fragile X syndrome. For example, in a study of preschool-aged children (Rogers et al., 2001), children with fragile X syndrome and autism had profiles of scores that were virtually identical to a well-matched sample of children diagnosed with autism without fragile X syndrome on standard autism instruments, including the Autism Diagnostic Interview—Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994) and the Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore, & Risi, 1999). Similarly, Demark et al. (2003) found that children diagnosed with both fragile X syndrome and autism were similar to children with autism without fragile X syndrome in terms of autism symptoms using the Reiss Autism subscale (Reiss & Valentin-Hein, 1990). Demark et al. subsequently hypothesized that having an *FMR1* gene mutation may increase an individual's genetic susceptibility for autism (Demark et al., 2003). A study by Hatton et al. (2006) found that a higher level of fragile X mental retardation protein (FMRP) was related to a lower level of autism symptoms but not to change in symptoms over time. However, these studies used small samples of children, leaving unaddressed questions regarding the phenotype later in the life course. More generally, researchers are unsure whether autism in individuals with fragile X syndrome is qualitatively similar to or different than idiopathic autism (Bailey et al., 2004); thus, this unanswered question remains a controversial aspect of the fragile X syndrome behavioral phenotype.

Although adolescents and adults dually diagnosed with fragile X syndrome and autism have not been systematically compared with their age peers with idiopathic autism on measures of autism symptoms, Abbeduto and colleagues have conducted two within-group investigations of autism symptoms in adolescents and adults with fragile X syndrome. In one of these studies (Lewis et al., 2006), 10 adolescents and adults diagnosed with fragile X syndrome and autism were compared with 44 individuals with fragile X syndrome without autism. This investigation reported that individuals with fragile X syndrome and autism had more serious impairments in cognition, receptive language, and theory of mind than individuals with fragile X syndrome alone and had an asynchronous developmental profile similar to what has been found in individuals with idiopathic autism, with receptive language and theory of mind being more impaired than more general cognitive abilities. In the other study, McDuffie et al. (2010) found differences between individuals with comorbid fragile X syndrome and autism, and fragile X syndrome alone, after controlling for differences in IQ, with respect to communication and repetitive behaviors as measured by the ADI-R (Lord et al., 1994). However, there were no differences between the groups in social reciprocity symptoms, highlighting the importance of examining specific domains of symptoms and behavior problems for a more nuanced understanding of the phenotype.

To date, other characteristics of adolescents and adults with fragile X syndrome, such as adaptive functioning and psychiatric problems, have received limited attention in the research literature. Adaptive behavior is a key predictor of adult functioning for individuals with developmental disabilities, and those who have a diagnosis of an autism spectrum disorder often have poor adaptive functioning (Esbensen, Bishop, Seltzer, Greenberg, & Taylor, 2010). Fisch, Simensen, and Schroer (2002) found that children and adolescents with fragile X syndrome only had higher adaptive behavior scores than children with autism only. Kaufmann et al. (2004) similarly documented lower adaptive behavior scores for children dually diagnosed with fragile X syndrome and autism compared with children with fragile X syndrome alone, with adaptive socialization continuing to differentiate the two groups of children over time (Hernandez et al., 2009). It is notable that these studies did not include a comparison group of children with idiopathic autism. Furthermore, the presence of other co-occurring mental health conditions (including autism) has been associated with less independence during adulthood in individuals with fragile X syndrome (Hartley et al.,

2011). However, to our knowledge, no studies have specifically examined differences in adaptive behavior for adolescents and adults with fragile X syndrome with and without a diagnosis of autism.

Also understudied are the potential phenotypic similarities in behavior problems and psychological symptoms between adolescents and adults dually diagnosed with fragile X syndrome and autism and individuals with idiopathic autism. Similar to studies of individuals with autism, research has indicated that children with fragile X syndrome have heightened levels of compulsive and self-injurious behavior (Hall et al., 2008), and adults with fragile X syndrome have higher levels of psychiatric problems (Sabaratnam et al., 2003) than national norms. However, other studies indicate that preschool children with fragile X syndrome do not have elevated levels of anger or sadness (Shanahan, Roberts, Hatton, Reznick, & Goldsmith, 2008), and adults with fragile X syndrome have fewer emotional and behavioral problems than individuals with Prader-Willi syndrome or Williams syndrome when controlling for severity of intellectual disability, age, and gender (Einfeld et al., 1999). In the present study, we extended this work by examining the behavioral phenotype of fragile X syndrome in adolescence and adulthood among those with and without comorbid autism and comparing them to individuals with autism without fragile X syndrome, with respect to autism symptoms, adaptive behavior, behavior problems, and psychological symptoms.

Present Study

The present study addressed four research questions. First, are there differences among (a) individuals dually diagnosed with fragile X syndrome and autism, (b) individuals with fragile X syndrome but no autism (fragile X syndrome-only), and (c) individuals with a diagnosis of autism but not fragile X syndrome (autism-only) in the three core domains of autism symptoms (social reciprocity, communication, and repetitive behavior) during adolescence and adulthood? Second, do the three groups differ in the level of adaptive functioning? Third, are there differences among the three groups in terms of behavior problems? Fourth, are there differences among the groups in levels of psychological symptoms, including internalizing and externalizing symptoms?

Consistent with past studies (Lewis et al., 2006; Rogers et al., 2001), we hypothesized that individuals dually diagnosed with fragile X syndrome and autism would be more similar to individuals with autism-only than to individuals with fragile X syndrome-only in terms of current autism symptoms. Similar to findings from studies of children (Fisch et al., 2002; Kaufmann et al., 2004), we expected that adolescents and adults with autism (with and without fragile X syndrome) would have lower levels of adaptive functioning than individuals with fragile X syndrome-only. Last, we anticipated that individuals in all three groups would have elevated levels of behavior problems and psychological symptoms relative to national norms, with individuals with autism-only being the most severely affected in this regard (Abbeduto et al., 2004).

Method

Procedure

Fragile X syndrome sample—A total of 136 adolescents and adults with fragile X syndrome were included in the current study. These sample members were drawn from a larger, longitudinal study of family adaptation to fragile X syndrome ($N = 147$), using mothers as primary informants. Study participation required that mothers be the biological parent of a son or daughter with the *FMR1* full mutation, that the son/daughter be 12 years of age or older, and that the son/daughter live in the parental home or have at least weekly

contact with the mother either in person or by phone. Documentation from an appropriate health care professional confirming that the son/daughter had the full mutation of the gene causing fragile X syndrome was also required. Mothers were recruited through service agencies, clinics, and fragile X syndrome foundations across the United States; from a university-based research registry of families having a child with a disability; and from a separate ongoing study of families of children with fragile X syndrome (Abbeduto et al., 2003; McDuffie et al., 2010). Mothers provided data through self-administered, mail-back questionnaires and telephone interviews that typically lasted 1 hr. If a mother had more than one child with fragile X syndrome, she was asked to report on the child that was living in the family home. If there was more than one co-residing child, the mother reported on the child that was, in her opinion, the most severely affected.

For the present study, the sample of adolescents and adults with fragile X syndrome was divided into two groups: those who had a currently valid diagnosis of autistic disorder and those who did not have a diagnosis of autistic disorder. Of the original 147 cases, 7 mothers indicated that their son/daughter with fragile X syndrome had a comorbid diagnosis of pervasive developmental disorder, not otherwise specified or Asperger syndrome; these cases were excluded from the current analyses. We confirmed maternal report of autistic disorder based on a consensus procedure, which included review of medical and educational records provided by the mother as well as reference to lifetime Social Communication Questionnaire scores (SCQ; Rutter et al., 2001) in ambiguous cases. As a result of this record-review process, an additional 4 cases were excluded due to a lack of sufficient evidence to merit an autistic disorder classification, resulting in the final sample for the current study of 136 adolescents and adults with fragile X syndrome ($n = 30$ with an autism diagnosis; $n = 106$ without an autism spectrum disorder diagnosis).

Autism-only comparison sample—A comparison group of 133 mothers of adolescents and adults with autism was drawn from a sample of mothers participating in an ongoing longitudinal study of families of adolescents and adults with autism (Seltzer et al., 2003, 2011). Data from the fifth wave of data collection were used in the current study because these data were collected within a year of the data collected from the mothers of adolescents and adults with fragile X syndrome. Adolescents and adults with a diagnosis of pervasive developmental disorder, not otherwise specified, or Asperger syndrome were excluded from the present analysis. As a requirement of participation in the longitudinal study, sons/daughters had to have received an autism diagnosis from an independent educational or health professional and have had a researcher-administered ADI-R (Lord et al., 1994) profile consistent with this diagnosis. Families of sons/daughters with autism were recruited through service agencies, schools, and clinics. In most families, mothers were the primary caregivers for the sons/daughters with autism, and they provided data through self-administered questionnaires and in-home interviews that typically lasted 2 to 3 hr.

Participants

Mothers in the fragile X syndrome sample resided in 38 U.S. states and 1 Canadian province. Mothers in the autism sample resided in Wisconsin and Massachusetts. The median household income was between \$80,000 and \$89,000 for both fragile X syndrome groups and \$60,000 and \$69,000 for the autism group, but a range in household income was represented in all groups (<\$9,999–\$160,000 or more for all groups). The majority of mothers were White (97% for mothers of children dually diagnosed with fragile X syndrome and autism, 95% for the fragile X syndrome-only group, and 92% for the autism-only group) and currently married (67% for fragile X syndrome and autism, 82% for fragile X syndrome-only, and 68% for autism-only). Means and percentages for child demographic

variables are presented in Table 1. These demographic variables were used as covariates in the analyses comparing the three groups.

Measures

Autism symptoms—Autism symptoms were measured by either the SCQ (Rutter et al., 2001) or the ADI-R (Lord et al., 1994). The SCQ is a screener version of the ADI-R, and there are 24 items in common across the two measures. These measures yield both current and lifetime ratings. It is notable that because this was a study of the behavioral phenotype of adolescents and adults, current scores were used for the present study. Verbal items were excluded so that nonverbal participants would not be lost due to missing data on these items.

Mothers of sons/daughters in the fragile X syndrome sample completed the SCQ and mothers of sons/daughters in the autism sample participated in a standardized ADI-R interview. For the SCQ, items were scored dichotomously (0 = *does not display this behavior* or 1 = *exhibits this behavior*) and summed. For the ADI-R, individual items originally were scored on an ordinal scale, with a code of 0 signifying the *absence* of a given symptom and codes of 1 and 2 indicating the *presence* of impairment characteristic of autism. Some items also used codes of 3, but these are routinely recoded as scores of 2 (Lord et al., 1994). To have a consistent range of possible scores across the two samples, we recoded each ADI-R item to reflect either *absence of impairment* (0; corresponding to an original ADI-R code of 0) or *presence of impairment* (1; corresponding to an original ADI-R code of 1, 2, or 3). This dichotomous coding strategy for the ADI-R has been used in previous studies (Fecteau et al., 2003; Seltzer et al., 2003; Shattuck et al., 2007). For both the SCQ and the ADI-R, higher scores indicated greater severity of impairments in nonverbal communication, social reciprocity, and repetitive behaviors—stereotyped interests. Coefficient alpha values were .84 for the total SCQ and .78 for the total ADI-R.

Adaptive behavior—Independence in activities of daily living was measured by the Revised Adaptive Daily Living Index (Seltzer & Krauss, 1989). Mothers in all three groups rated their son or daughter's level of independence on 17 items covering the domains of personal care, housekeeping, and meal-related activities. Each item was rated on a 3-point scale of independence 0 (*does not perform the task at all*), 1 (*performs the task with help*), or 2 (*performs the task independently*). An average score across all items was computed to create a total adaptive behavior score. An average score was also calculated for each of the three domains to create subscales. Higher scores indicated greater level of functional ability. Coefficient alpha for the total score was .92 for the entire sample.

Behavior problems—Mothers in all three groups completed the Behavior Problems subscale of the Scales of Independent Behaviors—Revised (SIB-R; Bruininks, Woodcock, Weatherman, & Hill, 1996). Note that the SIB-R measures behavior problems frequently exhibited by individuals with intellectual and developmental disabilities. These behaviors are distinct from autism symptoms (as measured by the ADI-R) in both their developmental course (Shattuck et al., 2007) and their impact on parental well-being (Lounds et al., 2007). Mothers indicated whether their son or daughter displayed each of eight behavior problems over the previous 6 months: hurtful to self, unusual or repetitive, withdrawn or inattentive, socially offensive, uncooperative, hurtful to others, disruptive, and destructive of property. Mothers who indicated that their child displayed a given behavior then rated the frequency from 1 (*less than once a month*) to 5 (*1 or more times/hour*) and the severity from 1 (*not serious*) to 5 (*extremely serious*) of the behavior. Standardized algorithms (Bruininks et al., 1996) translate the frequency and severity ratings into a general summary score for maladaptive behavior. Higher scores indicate more severe maladaptive behaviors. Reliability and validity of this measure have been established by Bruininks et al. (1996).

Psychological symptoms—Mothers in all three groups completed the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001) for sons/daughters who were 18.5 years of age or younger and the Adult Behavior Checklist (ABCL; Achenbach & Rescorla, 2001) for sons/daughters who were older than 18.5 years of age. Mothers indicated how true it was that their son/daughter exhibited each of 106 behaviors in the past 6 months. Each item is rated on 3-point scale: 0 (*not true*), 1 (*somewhat or sometimes true*), or 2 (*very true or often true*). Scores for the following subscales were computed: Internalizing Problems, Externalizing Problems, Intrusive, Strengths, Thought Problems, and Attention Problems. Reliability and validity for the CBCL and ABCL are well established (Achenbach & Rescorla, 2001). It is important to note that the Achenbach scales were designed to measure a variety of psychological difficulties such as anxiety and depression in the general population. As such, these scales assess indicators of psychopathology that individuals with and without developmental disabilities may exhibit. This is in contrast to the items from the SIB-R, which assess challenging behaviors that are more unique to individuals with developmental disabilities.

Results

The goal of the current study was to determine whether having a dual diagnosis of autism and fragile X syndrome was associated with a different behavioral phenotype than having fragile X syndrome alone or autism alone. We compared autism symptoms, adaptive living skills, behavior problems, and psychological symptoms, and we used analysis of covariance to compare the three groups, controlling for child age, gender, intellectual disability status, and residential status, with Bonferroni post hoc multiple comparisons to determine the specific differences between the groups.

Autism symptoms

We compared the three groups of adolescents and adults on total autism symptoms scores as well as scores for impairments in Social Reciprocity, Non-Verbal Communication, and Repetitive/Restricted Behaviors sub-scales (see Table 2). Note that higher scores indicate greater impairments.

Consistent with our hypothesis, the fragile X syndrome-only group displayed a significantly lower level of total autism symptoms than either of the other two groups, whereas the fragile X syndrome and autism group and the autism-only group displayed similar levels of overall autism symptoms. The fragile X syndrome-only group had the lowest level of social reciprocity impairments, followed by the fragile X syndrome and autism group, with the autism-only group showing the greatest level of social impairment. Similarly, the fragile X syndrome-only group had the fewest total nonverbal communication impairments, followed by the fragile X syndrome and autism group, and then the autism-only group. These were all statistically significant differences. It is notable that individuals with autism-only exhibited twice as many social reciprocity symptoms and nonverbal communication symptoms as individuals with fragile X syndrome-only.

A different pattern, however, was evident for repetitive–restricted behaviors. The dually diagnosed fragile X syndrome and autism group showed a significantly higher level of impairment than either the fragile X syndrome-only or autism-only groups. The fragile X syndrome-only and autism-only groups did not differ significantly from one another in repetitive and restricted behaviors.

Intellectual disability status was the only statistically significant covariate for overall symptoms and social reciprocity impairments, with having an intellectual disability being associated with greater impairment. Older age and the absence of intellectual disability were

associated significantly with fewer repetitive–restricted behaviors. There were no statistically significant covariates for impairments in nonverbal communication.

For descriptive purposes, data for individual autism symptoms are presented in Table 3, although we do not report statistical tests for these items. The pattern on these individual items is generally similar to the overall patterns described above. However, we note that on the item measuring whether the individual had at least one friend, 57% of individuals with fragile X syndrome-only reported having at least one friend compared with 32% of those with fragile X syndrome and autism and only 7% of those with autism-only.

Adaptive behavior

Next, we hypothesized that adolescents and adults with autism (with and without fragile X syndrome) would display lower levels of adaptive behavior (measured by daily living skills) than individuals with fragile X syndrome alone. This hypothesis was only partially supported. Based on the total adaptive behavior score, individuals with autism-only evidenced a significantly lower level of independence in activities of daily living than either individuals with fragile X syndrome-only or those with fragile X syndrome and autism (see Table 4). Individuals with fragile X syndrome and autism did not differ statistically from those with fragile X syndrome-only on total adaptive behavior. This pattern held for both the Housework and Meal-Related Activities subscales. In terms of the Personal Care subscale, both the autism-only group and the fragile X syndrome and autism group had significantly lower scores than the fragile X syndrome-only group. There was not a statistically significant difference between the fragile X syndrome and autism group and the autism-only group.

Intellectual disability status was a statistically significant covariate for the total score and each of the subscales, with the presence of intellectual disability associated with fewer daily living skills. Older age also was significantly associated with higher scores for overall adaptive behavior, housework, and meal-related activities. There were not statistically significant associations of adaptive behavior with gender or residential placement. Again, for descriptive purposes, we report data for individual adaptive behavior items in Table 5, although we do not present statistical tests.

Behavior problems

We also hypothesized that individuals in all three groups would have elevated levels of behavior problems relative to national norms and that the autism-only group would have higher scores than the two fragile X syndrome groups. To test this hypothesis, we compared the three groups of adolescents and adults on maternal reports of total behavior problems as well as individual item severity ratings (see Table 6). Consistent with our hypothesis, means for all three groups were at or above the clinical cut-off score of 110 on the SIB-R (Bruininks et al., 1996). However, counter to our hypothesis, adolescents and adults in the dually diagnosed fragile X syndrome and autism group evidenced significantly more total behavior problems than the other two groups. Adolescents and adults in the fragile X syndrome-only and autism-only groups did not differ statistically from one another on the total behavior problems score. This pattern held for the socially offensive behavior, withdrawn–inattentive behavior, and uncooperative behavior items.

In terms of the hurtful to others item, individuals dually diagnosed with fragile X syndrome and autism had significantly higher levels of aggressive behavior than individuals with fragile X syndrome-only, but the autism-only group did not differ statistically from either fragile X syndrome group (see Table 6). There were no statistically significant differences among the three groups for hurtful to self, destructive to property, or disruptive behavior.

We note that the overall pattern of differences in behavior problems is consistent with the pattern reported above for repetitive behaviors, namely that the dually diagnosed fragile X syndrome and autism group had the greatest level of behavior problems. Furthermore, although there were few statistically significant covariates for most of the individual behavior problems, intellectual disability status and age were statistically significant covariates for total behavior problems, with younger age and the presence of intellectual disability associated with more behavior problems.

Psychological symptoms

We hypothesized that individuals with autism would have the most severe psychological symptoms. In testing this hypothesis, the three groups of adolescents and adults were compared on the following subscales: Internalizing, Externalizing, Intrusive Behaviors, Strengths, Thought Problems, and Attention Problems of the ABCL and CBCL (see Table 7). Counter to our hypothesis, adolescents and adults in the dually diagnosed fragile X syndrome and autism group had the highest total ratings of internalizing and externalizing symptoms; however, their score differed significantly from the fragile X syndrome-only group, but not the autism-only group. The autism-only group did not differ statistically from the fragile X syndrome-only group. Thus, the dually diagnosed fragile X syndrome and autism group was more similar to the autism-only group than the fragile X syndrome-only group on internalizing and externalizing symptoms, consistent with the findings for repetitive behaviors and behavior problems. It is notable that the average score for internalizing problems for the fragile X syndrome and autism group was in the borderline clinical range (scores ranging from 60 to 63; Achenbach & Rescorla, 2001), whereas mean scores for the other two groups were in the normal range.

For the Intrusive Behaviors and Attention Problems subscales, adolescents and adults in the dually diagnosed fragile X syndrome and autism group had significantly higher scores compared with both the fragile X syndrome-only and autism-only groups. On the Thought Problems subscale, the fragile X syndrome-only group had significantly lower scores than either the fragile X syndrome and autism group or the autism-only group. The fragile X syndrome and autism and autism-only groups did not differ significantly on the Thought Problems subscale. It is notable that all groups had means on the Thought Problems and Attention subscales that were elevated enough to merit clinical concern. Last, on the Strengths subscale of the ABCL and CBCL, both groups of adolescents and adults with fragile X syndrome had significantly higher scores than the autism-only group.

There were very few statistically significant covariates for psychological symptoms; however, having an intellectual disability was related to having more internalizing problems and fewer strengths. Age was also as statistically significant covariate for strengths.

Discussion

In this study, adolescents and adults dually diagnosed with fragile X syndrome and autism manifested a behavioral phenotype that overlapped with but was distinct from their age peers with either fragile X syndrome-only or autism-only. To our knowledge, this is the first study to describe how the behavioral phenotype of comorbid fragile X syndrome and autism in adolescence and adulthood differs from these two comparison groups, and the findings show the unique vulnerabilities of the dually diagnosed group. Based on findings from prior research on children with fragile X syndrome (Kaufmann et al., 2004; Rogers et al., 2001), we hypothesized that adolescents and adults dually diagnosed with fragile X syndrome and autism would be more similar to individuals with autism-only than to individuals with fragile X syndrome-only in terms of their autism symptoms. Although this was the case for overall level of autism symptoms, important differences emerged when examining the three

core domains of autism separately. In terms of the scores in the social reciprocity and communication domains, the autism-only group was the most impaired, followed by the dually diagnosed fragile X syndrome and autism group, and then the fragile X syndrome-only group. One notable exception is that both fragile X syndrome groups were much more likely than the autism-only group to have a friend.

In contrast to the findings of similarity between the dually diagnosed fragile X syndrome and autism group and the autism-only group in overall autism symptoms, the dually diagnosed fragile X syndrome and autism group had higher levels of problems in repetitive behaviors and restricted interests than either the autism-only or the fragile X syndrome-only groups. The repetitive behaviors and restricted interests domain has been shown to have the least amount of improvement from childhood to adolescence for individuals with fragile X syndrome (McDuffie et al., 2010). This unique presentation of autism symptoms in individuals dually diagnosed with fragile X syndrome and autism highlights the value of examining specific types of behaviors at multiple points in the life course in addition to global and lifetime ratings for understanding the nuances of the behavioral phenotype of individuals dually diagnosed fragile X syndrome and autism (Demark et al., 2003). In addition, the differences in symptoms between those with fragile X syndrome and autism and those with autism-only underscore the need to study in more depth the pathways leading to autistic traits in individuals with autism of known and unknown etiologies.

As hypothesized, all groups had elevated levels of behavior problems and psychological symptoms relative to national norms. However, counter to our expectation, adolescents and adults dually diagnosed with fragile X syndrome and autism had the highest level of behavior problems and psychological symptoms relative to the other two groups. This pattern held for specific items derived from two well-validated measures, including socially offensive behavior, withdrawn-inattentive behavior, and uncooperative behavior (from the SIB-R) and intrusive behavior and inattention (from the CBCL and ABCL). These findings suggest that for individuals with fragile X syndrome, a profile of especially high externalizing behavior problems, not necessarily autism-specific symptoms, is associated with an additional diagnosis of autistic disorder. However, individuals in the dually diagnosed fragile X syndrome and autism group also displayed greater impairments in social reciprocity and communication than the fragile X syndrome-only group, suggesting that those with fragile X syndrome and autism in this study exhibited a global profile of social communication symptoms consistent with an autism diagnosis. Together, these findings suggest that for individuals with fragile X syndrome, symptoms may be significant enough to meet diagnostic criteria for autism, but the specific behavioral presentation of impairments is different for individuals dually diagnosed with fragile X syndrome and autism than for individuals with autism alone.

We also hypothesized that adolescents and adults with fragile X syndrome-only would have higher levels of adaptive functioning than those in either the fragile X syndrome and autism group or autism-only group. This hypothesis was only partially supported. We found that both fragile X syndrome groups had fewer difficulties in adaptive behavior than the autism-only group. Unlike past studies comparing children with fragile X syndrome-only to children dually diagnosed with fragile X syndrome and autism (Fisch et al., 2002; Hernandez et al., 2009; Kaufmann et al., 2004), there was not a difference between the two groups of adolescents and adults with fragile X syndrome in the present study on overall adaptive behavior scores. It may be that daily living skills are a relative strength for individuals with fragile X syndrome, at least at this later point in development. In addition, both groups with fragile X syndrome had higher scores on the strengths subscale of the CBCL and ABCL than the autism-only group. These findings, as well as those pertaining to friendships, underscore how although individuals dually diagnosed with fragile X syndrome

and autism share many behavioral features in common with or more severe than those with autism alone, the overall profile of strengths and weaknesses for the fragile X syndrome and autism group is unique, at least during adolescence and adulthood. Furthermore, it is important that the elevated levels of behavior problems and autism symptoms in the fragile X syndrome and autism group did not interfere with adaptive functioning in the same way as in the autism-only group.

The pattern of significant covariates yielded additional insights about the factors that are associated with the behavioral profile of adolescents and adults with these developmental disabilities. Consistent with much past research on the impact of intellectual disability on behavior (Totiska & Hastings, 2009), having an intellectual disability was associated with poorer functioning during adolescence and adulthood in terms of behavior problems, adaptive behavior, and autism symptoms. In addition, child age was significantly associated with multiple aspects of behavioral functioning in the present study. Specifically, being older was related to fewer restricted–repetitive behaviors, better adaptive functioning, and fewer total behavior problems. The findings regarding the association between age and restricted–repetitive behaviors are similar to what has been found in cross-sectional and longitudinal studies of individuals with autism, in that these types of behaviors often partially abate with age (Esbensen, Seltzer, Lam, & Bodfish, 2009; Shattuck et al., 2007). Similarly, adaptive behavior skills have been shown to improve with age for children with fragile X syndrome (Hatton et al., 2003). These findings suggest that there may be continued improvements in several behavioral domains for individuals with fragile X syndrome as they mature into adulthood.

In contrast, gender and residential status were not significant predictors of total scores of behavior in the present analyses, highlighting the possible relative importance of other covariates (e.g., intellectual disability, age) in contributing to behavioral outcomes. Particularly for individuals with fragile X syndrome, factors related to gender (e.g., intellectual disability status) rather than gender itself may be better predictors of symptoms. In a study of children with fragile X syndrome, Hatton et al. (2006) found that girls had fewer autism symptoms than boys, although this relationship was nonsignificant when the level of FMRP was included in the model. Large, longitudinal studies of individuals with varying lengths of CGG repeat and levels of FMRP are needed to further disentangle the relationships among these covariates during adolescence and adulthood.

The present study was not without weaknesses. First, there was a wide range of ages of participants, limiting our ability to understand the phenotype at specific points in the life course. In addition, the autism-only group was considerably older than the fragile X syndrome groups. However, age was statistically controlled in the analyses, and the variability in age made it possible to interpret the effect of age on the behavioral phenotype. Second, the sample had little racial and ethnic diversity; however, the fragile X syndrome sample had excellent geographic representation, with individuals residing in 38 different U.S. states and 1 Canadian province. Third, IQ scores were not available on all sample members, which is why we used intellectual disability status as a control variable instead of a full-scale IQ score. This is a limitation of the current analysis, given that past research has demonstrated that individuals dually diagnosed with fragile X syndrome and autism have lower IQs compared with individuals with fragile X syndrome-only, even in samples including only individuals with intellectual disability (Lewis et al., 2006). Last, it is important to note that autism symptoms were measured using the ADI-R in the autism-only group and using the SCQ in the fragile X syndrome groups. Although the items are identical between the two measures, the ADI-R items were re-coded to reflect absence–presence to match the coding used in the SCQ.

The present study also had several valuable strengths. Studies of individuals with fragile X syndrome often only include males and have small sample sizes, whereas the current study explored the behavioral phenotype in a large sample of males and females with fragile X syndrome. In addition, few prior studies have focused specifically on adolescents, with very few studies examining the behavioral profiles of adults with fragile X syndrome (for a notable exception, see Hartley et al., 2011). In the present study, we addressed this gap by examining the behavioral phenotype of fragile X syndrome in both adolescents and adults. We elaborated on the phenotype by dividing those dually diagnosed with fragile X syndrome and autism from those with fragile X syndrome-only. In addition, as noted above, in the present study we incorporated an analysis of a wide range of positive and negative behaviors (adaptive behaviors and behavior problems) and symptoms (autism symptoms and general psychopathology) and found that not all domains operated the same way, highlighting the value of exploring a variety of behaviors in describing the phenotype.

In conclusion, the present study informs the debate about whether autism in individuals with fragile X syndrome is qualitatively similar to idiopathic autism. The pattern of findings reveals that there is no simple answer to the question posed by Bailey et al. (2004). On the one hand, we found that adolescents and adults dually diagnosed with fragile X syndrome and autism tended to have a presentation of communication and social reciprocity impairments and internalizing symptoms more similar to individuals with autism-only than to those with fragile X syndrome-only. On the other hand, the dually diagnosed individuals exhibited higher levels of repetitive behaviors, restricted interests, and challenging behavior problems than those with either fragile X syndrome-only or autism-only. Therefore, we conclude that autism in individuals with fragile X syndrome is at least as impairing as idiopathic autism and, in some respects (repetitive and challenging behaviors), even more impairing. Counterbalancing this profile of vulnerability is the pattern of greater strengths, more friendships, and better adaptive functioning in individuals dually diagnosed with fragile X syndrome and autism than those with autism-only, which only further complicates the picture.

Nevertheless, the elevated level of behavior problems in the dually diagnosed fragile X syndrome and autism group highlights that individuals with fragile X syndrome and comorbid autism may require additional behavioral and/or pharmacological interventions during adolescence and adulthood. Furthermore, parents of individuals dually diagnosed with fragile X syndrome and autism may need extra supports and services to help address their older children's behavioral needs. It is notable that mothers of adolescents and adults dually diagnosed with fragile X syndrome and autism may be especially vulnerable to the stresses of caregiving due to a heightened level of challenging behaviors and autism symptoms in their children as well as to their own genetic risk as premutation carriers (Bailey et al., 2008; Coffey et al., 2008). This double vulnerability makes the need for adequate family-centered planning and services for families of individuals with fragile X syndrome all the more imperative.

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References

- Abbeduto L, Murphy MM, Cawthon SW, Richmond EK, Weissman MD, Karadottir S, O'Brien A. Receptive language skills of adolescents and young adults with Down or fragile X syndrome. *American Journal on Mental Retardation*. 2003; 108:149–160. [PubMed: 12691594]
- Abbeduto L, Seltzer MM, Shattuck P, Krauss MW, Orsmond G, Murphy MM. Psychological well-being and coping in mothers of youths with autism, Down syndrome or fragile X syndrome. *American Journal on Mental Retardation*. 2004; 109:237–254. [PubMed: 15072518]
- Achenbach, TM.; Rescorla, LA. *Manual for ASEBA School-Age Forms & Profiles*. Burlington: University of Vermont, Research Center for Children, Youth, & Families; 2001.
- Bailey DB, Raspa M, Olmsted M, Holiday DB. Co-occurring conditions associated with *FMR1* gene variations: Findings from a national parent survey. *American Journal of Medical Genetics Part A*. 2008; 146A:2060–2069. [PubMed: 18570292]
- Bailey, D.; Roberts, J.; Hooper, S.; Hatton, D.; Mirrett, P.; Roberts, J., et al. Research on fragile X syndrome and autism: Implications for the study of genes, environments, and developmental language disorders. In: Rice, M.; Warren, S., editors. *Developmental language disorders: From phenotypes to etiologies*. Mahwah, NJ: Erlbaum; 2004. p. 121-150.
- Bruininks, RH.; Woodcock, RW.; Weatherman, RF.; Hill, BK. *Scales of Independent Behavior—Revised*. Itasca, IL: Riverside; 1996.
- Coffey SM, Cook K, Tartaglia N, Tassone F, Nguyen DV, Pan R, Hagerman RJ. Expanded clinical phenotype of women with the *FMR1* premutation. *American Journal of Medical Genetics*. 2008; 146:1009–1016. [PubMed: 18348275]
- Crawford DC, Acuna JM, Sherman SL. *FMR1* and the fragile X syndrome: Human genome epidemiology review. *Genetics in Medicine*. 2001; 3:359–371. [PubMed: 11545690]
- Demark JL, Feldman MA, Holden JJA. Behavioral relationship between autism and fragile X syndrome. *American Journal on Mental Retardation*. 2003; 108:314–326. [PubMed: 12901707]
- Dykens EM, Hodapp RM, Ort S, Finucane B, Shapiro LR, Leckman JF. The trajectory of cognitive development in males with fragile X syndrome. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1989; 28:422–426. [PubMed: 2786867]
- Einfeld S, Tonge B, Turner G, Parmenter T, Smith A. Longitudinal course of behavioral and emotional problems of young person with Prader-Willi, fragile X, Williams, and Down syndromes. *Journal of Intellectual & Developmental Disability*. 1999; 24:349–354.
- Esbensen AJ, Bishop S, Seltzer MM, Greenberg JS, Taylor JL. Comparisons between individuals with autism spectrum disorders and individuals with Down syndrome in adulthood. *American Journal on Intellectual and Developmental Disabilities*. 2010; 115:227–290.
- Esbensen AJ, Seltzer MM, Lam KS, Bodfish JW. Age-related differences in restricted repetitive behaviors in the autism spectrum disorder over the lifespan. *Journal of Autism and Developmental Disorders*. 2009; 39:57–66. [PubMed: 18566881]
- Fecteau S, Mottron L, Berthiaume C, Burack JA. Developmental changes of autistic symptoms. *Autism*. 2003; 7:255–268. [PubMed: 14516059]
- Fernandez-Carvajal I, Walichiewicz P, Ziaosen Z, Pan R, Hagerman PJ, Tassone F. Screening for expanded alleles of the *FMR1* gene blood spots from newborn males in a Spanish population. *Journal of Molecular Diagnostics*. 2009; 11:324–329. [PubMed: 19460941]
- Fisch GS, Simensen RJ, Schroer RJ. Longitudinal changes in cognitive and adaptive behavior scores in children and adolescents with the fragile X mutation or autism. *Journal of Autism and Developmental Disorders*. 2002; 32:107–114. [PubMed: 12058838]
- Hagerman PJ. The fragile X prevalence paradox. *Journal of Medical Genetics*. 2008; 45:498–499. [PubMed: 18413371]
- Hall SS, Lightbody AA, Reiss AL. Compulsive, self-injurious, and autistic behavior in children and adolescents with fragile X syndrome. *American Journal on Mental Retardation*. 2008; 113:44–53. [PubMed: 18173299]

- Hartley SL, Seltzer MM, Raspa M, Olmsted MG, Bishop EE, Bailey DB. Exploring the adult life of men and women with fragile X syndrome: Results from a national survey. *American Journal on Intellectual and Developmental Disabilities*. 2011; 116:16–35. [PubMed: 21291308]
- Hatton DD, Sideris J, Skinner M, Mankowski J, Bailey DB, Roberts J, Mirrett P. Autistic behavior in children with fragile X syndrome: Prevalence, stability, and the impact of FMRP. *American Journal of Medical Genetics Part A*. 2006; 140:1804–1813. [PubMed: 16700053]
- Hatton DD, Wheeler AC, Skinner ML, Bailey DB, Sullivan KM, Roberts JE, Clark RD. Adaptive behavior in children with fragile X syndrome. *American Journal on Mental Retardation*. 2003; 108:373–390. [PubMed: 14561110]
- Hernandez RN, Feinberg RL, Vaurio R, Passanante NM, Thompson RE, Kaufmann WE. Autism spectrum disorder in fragile X syndrome: A longitudinal evaluation. *American Journal of Medical Genetics Part A*. 2009; 149:1125–1137. [PubMed: 19441123]
- Kaufmann WE, Cortell R, Kau ASM, Bukelis I, Tierney E, Gray RM, Stanard P. Autism spectrum disorder in fragile X syndrome: Communication, social interaction, and specific behaviors. *American Journal of Medical Genetics*. 2004; 129:225–234. [PubMed: 15326621]
- Lewis P, Abbeduto L, Murphy M, Richmond E, Giles N, Bruno L, Schroeder S. Cognitive, language and social-cognitive skills of individuals with fragile X syndrome with and without autism. *Journal of Intellectual Disability Research*. 2006; 50:532–545. [PubMed: 16774638]
- Lord, C.; Rutter, M.; DiLavore, P.; Risi, S. *Autism Diagnostic Observation Schedule—WPS edition*. Los Angeles: Western Psychological Services; 1999.
- Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview—Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders*. 1994; 24:659–685. [PubMed: 7814313]
- McDuffie A, Abbeduto L, Lewis P, Kim JS, Kover ST, Weber A, Brown WT. Autism spectrum disorder in children and adolescents with fragile X syndrome: Within-syndrome differences and age-related changes. *American Journal on Intellectual and Developmental Disabilities*. 2010; 115:307–327. [PubMed: 20567604]
- Philofsky A, Hepburn SL, Hayes A, Hagerman R, Rogers SJ. Linguistic and cognitive functioning and autism symptoms in young children with fragile X syndrome. *American Journal on Mental Retardation*. 2004; 109:208–218. [PubMed: 15072521]
- Reiss S, Valenti-Hein D. Development of a psychopathology rating scale for children with mental retardation. *Journal of Consulting and Clinical Psychology*. 1990; 62:28–33. [PubMed: 8034825]
- Rogers SJ, Wehner EA, Hagerman R. The behavioral phenotype in fragile X: Symptoms of autism in very young children with fragile X syndrome, idiopathic autism, and other developmental disorders. *Journal of Developmental and Behavioral Pediatrics*. 2001; 22:409–417. [PubMed: 11773805]
- Rutter, M.; Bailey, A.; Lord, C. *Social Communication Questionnaire (SCQ)*. Los Angeles: Western Psychological Services; 2001.
- Sabaratnam M, Murthy NV, Wijeratne A, Buckingham A, Payne S. Autistic-like behavior profile and psychiatric morbidity in fragile X syndrome: A prospective ten-year follow-up study. *European Child and Adolescent Psychiatry*. 2003; 12:172–177. [PubMed: 14505067]
- Seltzer, MM.; Greenberg, JS.; Taylor, JL.; Smith, L.; Orsmond, GI.; Esbensen, A.; Hong, J. Adolescents and adults with autism spectrum disorders. In: Amaral, DG.; Dawson, G.; Geschwind, D., editors. *Autism spectrum disorders*. New York: Oxford University Press; 2011. p. 241-252.
- Seltzer MM, Krauss MW. Aging parents with adult mentally retarded children: Family risk factors and sources of support. *American Journal on Mental Retardation*. 1989; 94:303–312. [PubMed: 2803748]
- Seltzer MM, Krauss MW, Shattuck PT, Orsmond G, Swe A, Lord C. The symptoms of autism spectrum disorders in adolescence and adulthood. *Journal of Autism and Developmental Disorders*. 2003; 33:565–581. [PubMed: 14714927]
- Shanahan M, Roberts J, Hatton D, Reznick J, Goldsmith H. Early temperament and negative reactivity in boys with fragile X syndrome. *Journal of Intellectual Disability Research*. 2008; 52:842–854. [PubMed: 18498331]

- Shattuck PT, Seltzer MM, Greenberg JS, Orsmond GI, Bolt D, Kring S, Lord C. Change in autism symptoms and maladaptive behaviors in adolescents and adults with an autism spectrum disorder. *Journal of Autism and Developmental Disorders*. 2007; 37:1735–1747. [PubMed: 17146700]
- Totsika V, Hastings R. Persistent challenging behavior in people with an intellectual disability. *Current Opinion in Psychiatry*. 2009; 22:347–441.

Table 1

Analyses of Variance of Child Demographic Variables

Child variable	Fragile X syndrome and autism (<i>n</i> = 30)		Fragile X syndrome-only (<i>n</i> = 106)		Autism-only (<i>n</i> = 135)		<i>F</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	
Age ^{a,b} (years)	18.47	5.37	21.62	7.57	31.37	10.09	49.84 ^{***}
Percent female	10	0.31	18	0.39	28	0.45	3.29 [*]
Percent with intellectual disability	93	0.25	77	0.42	85	0.37	2.58
Percent living in family home ^{a,b}	93	0.25	86	0.35	41	0.49	42.39 ^{***}

Note. Superscripts indicate that groups differ at $p < .05$ in Bonferroni post hoc multiple comparisons:

^aFragile X syndrome and autism differs from autism-only;

^bFragile X syndrome-only differs from autism-only.

* $p < .05$.

*** $p < .001$.

Table 2

Analysis of Covariance Comparisons of Autism Symptoms, Controlling for Child Age, Residential Status, Sex, and Intellectual Disability Status

Variable	Fragile X syndrome and autism (<i>n</i> = 30)		Fragile X syndrome-only (<i>n</i> = 106)		Autism-only (<i>n</i> = 122)		Covariates (<i>F</i> s)				
	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	Group <i>F</i>	Age	Residential status	Gender	Intellectual disability
Total ^{a,c}	16.25	0.81	9.47	0.43	16.97	0.42	79.74***	0.65	0.34	0.83	15.69***
Social ^d	8.48	0.52	4.40	0.28	10.22	0.27	104.46***	0.10	0.25	0.06	9.19**
Nonverbal communication ^d	2.41	0.24	1.45	0.13	3.21	0.12	43.74***	0.49	0.46	0.20	2.05
Repetitive-restricted behaviors ^{a,b}	5.36	0.34	3.62	0.19	3.54	0.18	11.87***	7.99**	0.02	2.11	13.86***

Note. Adjusted means are reported. Superscripts indicate that groups differ at $p < .05$ in Bonferroni post hoc multiple comparisons:

^a Fragile X syndrome and autism differs from fragile X syndrome-only;

^b Fragile X syndrome and autism differs from autism-only;

^c Fragile X syndrome-only differs from autism-only;

^d All three groups differ.

** $p < .01$.

*** $p < .001$.

Table 3

Autism Symptom Items, Controlling for Child Age, Residential Status, Sex, and Intellectual Disability Status

Variable	Fragile X syndrome and autism (n = 30)		Fragile X syndrome-only (n = 106)		Autism-only (n = 122)	
	M	SE	M	SE	M	SE
Social						
Facial expression usually appropriate (R)	.42	.06	.09	.03	.91	.03
Use your hand like a tool	.66	.09	.33	.05	.77	.05
Friends–best friend (R)	.68	.08	.43	.04	.93	.04
Looks at you directly in the face (R)	.77	.09	.66	.05	.78	.05
Smiles back (R)	.67	.08	.21	.04	.82	.04
Shows you things of interest to him/her (R)	.59	.08	.32	.05	.79	.04
Shares (R)	.84	.08	.44	.04	.90	.04
Join in his/her enjoyment (R)	.62	.09	.31	.05	.42	.05
Comforts you (R)	.64	.09	.35	.05	.69	.05
Looks–gestures to get your attention (R)	.35	.08	.15	.04	.64	.04
Normal range of facial expression (R)	.76	.08	.29	.04	.85	.04
Interested in others (R)	.80	.08	.54	.04	.84	.04
Responds positively when approached (R)	.68	.08	.29	.04	.90	.04
Nonverbal communication						
Spontaneously points (R)	.65	.09	.43	.05	.83	.05
Gestures other than pointing (R)	.57	.08	.44	.04	.88	.04
Nods for “yes” (R)	.60	.09	.32	.05	.75	.05
Shake head for “no” (R)	.59	.09	.27	.05	.75	.05
Repetitive–restricted behaviors						
Has to do things in a very particular way/rituals	.77	.13	.61	.07	.73	.07
Odd interests that preoccupy	.75	.09	.59	.05	.56	.05
More interested in parts of toys	.83	.09	.43	.05	.39	.05
Interests of unusual intensity	.75	.09	.54	.05	.41	.05
Unusual sensory interests	.68	.10	.42	.05	.59	.05
Odd mannerisms (e.g., hand flapping)	.90	.09	.69	.05	.50	.05
Complicated whole-body movements (e.g., spinning)	.68	.09	.36	.05	.36	.05

Note. R = item was reverse coded: 1 (*does not display this behavior*), 0 (*exhibits this behavior*). All other items were coded: 0 (*does not display this behavior*) or 1 (*exhibits this behavior*). Adjusted means are reported.

Table 4

Analysis of Covariance Comparisons of Adaptive Behavior, Controlling for Child Age, Residential Status, Sex, and Intellectual Disability Status

Variable	Fragile X syndrome and autism (<i>n</i> = 30)		Fragile X syndrome-only (<i>n</i> = 106)		Autism-only (<i>n</i> = 133)			Covariates (<i>F</i> s)		
	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>Group F</i>	Age	Residential status	Gender
Total ^{a,c}	1.33	.07	1.48	.04	1.06	.04	27.66***	8.44**	.07	.34
Housework ^{b,c}	1.07	.09	1.20	.05	.74	.05	21.54***	12.90***	.09	.02
Personal care ^{a,c}	1.42	.08	1.67	.04	1.27	.04	19.90***	2.97	.34	.32
Meal-related activities ^{b,c}	1.46	.07	1.56	.04	1.13	.04	27.14***	5.88*	.21	1.17

Note. Adjusted means are reported. Superscripts indicate that groups differ at *p* < .05 in Bonferroni post hoc multiple comparisons:

^a Fragile X syndrome and autism differs from fragile X syndrome-only;

^b Fragile X syndrome and autism differs from autism-only;

^c Fragile X syndrome-only differs from autism-only.

* *p* < .05.

** *p* < .01.

*** *p* < .001.

Table 5
Adaptive Behavior Items, Controlling for Child Age, Residential Status, Sex, and Intellectual Disability Status

Variable	Fragile X syndrome and autism (n = 30)		Fragile X syndrome-only (n = 106)		Autism-only (n = 133)	
	M	SE	M	SE	M	SE
Housework						
Making own bed	1.47	0.14	1.60	0.08	0.97	0.07
Doing household tasks	1.47	0.12	1.59	0.06	1.01	0.06
Doing errands	0.90	0.12	0.97	0.06	0.70	0.06
Doing home repairs	0.55	0.14	0.73	0.08	0.33	0.07
Doing laundry	0.97	0.13	1.13	0.07	0.67	0.07
Personal care						
Washing—bathing	1.33	0.11	1.74	0.06	1.24	0.05
Grooming	1.36	0.11	1.61	0.06	1.22	0.06
Dressing—undressing	1.73	0.09	1.93	0.05	1.52	0.04
Toileting	1.59	0.10	1.75	0.05	1.59	0.05
Taking own medication	1.01	0.15	1.17	0.09	0.80	0.07
Meal-related activities						
Preparing simple foods	1.39	0.13	1.74	0.07	1.12	0.07
Cooking simple foods	1.19	0.13	1.29	0.07	0.66	0.07
Preparing complete meal	0.70	0.12	0.70	0.06	0.30	0.06
Setting—clearing table	1.58	0.12	1.77	0.06	1.19	0.06
Drinking from cup	2.01	0.05	1.99	0.02	1.93	0.02
Eating from plate	1.95	0.05	1.98	0.03	1.93	0.02
Washing dishes	1.41	0.13	1.45	0.07	0.79	0.07

Note. Adjusted means are reported. Scoring was as follows: 0 = does not perform the task at all, 1 = can perform the task with help, or 2 = performs the task independently.

Table 6

Analysis of Covariance Comparisons of Scales of Independent Behaviors—Revised Behavior Problems, Controlling for Child Age, Residential Status, Sex, and Intellectual Disability Status

Variable	Fragile X syndrome and autism (<i>n</i> = 30)			Fragile X syndrome-only (<i>n</i> = 106)			Autism-only (<i>n</i> = 133)			Covariates (<i>F</i> s)			
	<i>M</i>	<i>SE</i>		<i>M</i>	<i>SE</i>		<i>M</i>	<i>SE</i>		Age	Residential status	Gender	Intellectual disability
Total ^{a,b}	118.44	1.80		109.76	0.97		111.76	0.94		9.95***	5.08*	0.19	0.08
Hurtful to self	0.83	0.23		0.62	0.12		0.85	0.11		0.94	0.07	0.24	1.71
Hurtful to others ^a	1.32	0.24		0.57	0.13		0.77	0.12		4.48*	5.80*	2.37	0.22
Destructive to property	1.03	0.22		0.66	0.12		0.62	0.11		1.43	0.97	0.12	1.84
Disruptive behavior	1.30	0.22		0.76	0.12		0.82	0.11		2.65	3.41	1.70	0.13
Unusual habits	1.93	0.25		1.38	0.13		1.59	0.13		2.25	0.65	0.50	0.17
Socially offensive behavior ^{a,b}	1.95	0.25		1.02	0.13		1.04	0.12		6.42**	1.63	0.47	6.07*
Withdrawn-inattentive ^{a,b}	2.36	0.25		1.31	0.14		1.50	0.13		7.24**	0.73	5.12*	0.05
Uncooperative behavior ^{a,b}	2.18	0.25		1.23	0.13		0.90	0.13		9.62***	0.11	0.24	0.03

Note. Scales of Independent Behaviors—Revised (Bruininks, Woodcock, Weatherman, & Hill, 1996). Adjusted means are reported. Superscripts indicate that groups differ at $p < .05$ in Bonferroni post hoc multiple comparisons:

^aFragile X syndrome and autism differs from fragile X syndrome-only;

^bFragile X syndrome and autism differs from autism-only.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

Table 7

Analysis of Covariance Comparisons of Child Behavior Checklist and Adult Behavior Checklist Psychopathology t Scores, Controlling for Child Age, Residential Status, Sex, and Intellectual Disability Status

Variable	Fragile X syndrome and autism (<i>n</i> = 34)		Fragile X syndrome-only (<i>n</i> = 106)		Autism-only (<i>n</i> = 123)			Covariates (<i>F</i> s)			
	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	Group <i>F</i>	Age	Residential status	Gender	Intellectual disability
Internalizing ^a	62.20	1.67	56.63	0.89	58.70	0.87	5.12**	.00	1.79	.00	4.64*
Externalizing ^a	59.07	1.56	53.69	0.83	55.87	0.81	5.64**	2.77	0.03	1.38	0.01
Intrusive ^{a,b}	59.78	1.12	55.47	0.60	54.97	0.59	7.30**	1.18	0.07	4.99*	0.12
Strengths ^{b,c}	51.62	2.06	47.32	1.11	36.79	1.07	25.71***	10.33**	0.10	0.57	11.68**
Thought problems ^{a,c}	64.83	1.37	61.18	0.74	67.10	0.72	14.79***	0.03	1.99	0.48	0.10
Attention problems ^{a,b}	67.05	1.37	61.92	0.74	61.92	0.72	6.32**	0.33	3.20	0.03	0.01

Note. Child Behavior Checklist (Achenbach & Rescorla, 2001); Adult Behavior Checklist (Achenbach & Rescorla, 2001). Adjusted means are reported. Superscripts indicate that groups differ at $p < .05$ in Bonferroni post hoc multiple comparisons:

^aFragile X syndrome and autism differs from fragile X syndrome-only;

^bFragile X syndrome and autism differs from autism-only;

^cFragile X syndrome-only differs from autism-only.

* $p < .05$.

** $p < .01$.

*** $p < .001$.