Published in final edited form as:
Int J Dev Disabil. 2013 July 1; 59(2): 67–79. doi:10.1179/2047387713Y.0000000016.

The Development of Adaptive Behavior in Toddlers and Preschoolers with Fragile X versus Autism

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Abstract

Although there is extensive research in the early detection of autism, no study has compared the adaptive behavior of young children with fragile X syndrome (FXS) and children with autism across ages. We investigated the cross-sectional development of adaptive behavior in children with FXS and children with autism between 18 and 83 months of age. Analyses revealed a significant relationship between age and adaptive behavior standard scores for children with FXS, with decreased performance across ages. Analyses also revealed that children with FXS had a relatively flat performance across domains while children with autism are typically more variable with lower scores in the communication domain relative to other domains. Delays in adaptive behavior were evident for children with FXS and children with autism at 24 months of age as reported in previous literature. Implications and future directions are discussed.

Keywords

Autism; fragile X syndrome; adaptive behavior; development

Introduction

Fragile X syndrome (FXS) is the most common inherited cause of developmental disabilities affecting approximately 1 in 3,600 individuals (Hagerman et al. 2009). The syndrome is diagnosed through genetic testing and is a single gene disorder associated with a CGG trinucleotide repeat expansion on the 5′ UTR of the fragile X mental retardation gene (*FMR*1), which results in reduced *FMR*1 protein (FMRP). The largest expansion of the CGG region, greater than 200 repeats, is termed full mutation and, corresponds to FXS. Individuals with the *FMR*1 premutation have a CGG expansion ranging from 55–200. Individuals with FXS typically exhibit characteristic cognitive deficits, social anxiety and communication delays (Roberts et al. 2009; Rogers et al. 2001). Comorbid FXS and autism is common, with 30–50% of individuals with FXS meeting the DSM-IV-TR criteria for autism and 60–74% meeting criteria for an autism spectrum disorder (Bailey et al. 2000; Philofsky et al. 2004). Fragile X syndrome is the most common single gene cause of autism, accounting for 2–6% of all cases (McLennan et al. 2011).

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Autism is the most severe form of a spectrum of related developmental disorders referred to as autism spectrum disorders (ASDs) diagnosed through behavioral testing. Individuals with autism have characteristic impairments in social interaction, verbal and non-verbal communication, and stereotypical, repetitive patterns of behavior, interests, and activities. Autism is thought to be due to multifactorial conditions caused by multiple genes in addition to non-genetic environmental factors. Evidence for genetic risk is demonstrated by the increased risk for siblings of children with autism to develop autism themselves, which occurs in approximately 15% of all cases (Landa & Garrett-Mayer 2006; Rice et al. 2007).

Early detection is critical to track developmental outcomes of children with FXS or autism and to provide access to early intervention services. A child with autism or FXS is able to access services beginning at the age of diagnosis, which in the case of children with FXS, is feasible prenatally. Children without a formal diagnosis of FXS may qualify for services as a child with a non-specific developmental delay. Currently, both autism and FXS are not typically diagnosed until three years of age despite stability of diagnosis after two years of age (Lord & Spence 2006, Shattuck & Grosse 2007).

Early development in FXS

To improve outcomes and further early identification efforts, greater understanding of early developmental features is imperative. Moreover, understanding similarities and differences of early developmental patterns among high-risk groups is critical. Language delays may complicate the developmental outcomes seen in early childhood because language delay is often the first developmental disruption associated with autism and is the area of greatest initial delay in FXS (Landa & Garrett-Mayer 2006; Roberts et al. 2009). Children who are diagnosed with both FXS and autism may exhibit a different behavioral profile than children diagnosed with FXS or autism alone. While there is considerable research on the development of FXS and autism separately in early childhood, few studies draw direct comparisons across the two groups which is critical for differential diagnosis of these two disorders.

A study by Rogers et al. (2001) with 27 children with autism, 24 children with FXS and 23 children with other developmental delays ranging in age from 21–48 months supported the hypothesis of two trajectories of development for children with FXS. The study predicted that children with FXS displayed a unique pattern of behavior but instead found that there were two distinct subgroups of children with FXS based on autism status. Children with FXS and autism had a similar profile to children with autism with the exception of gross and fine motor development, whereas children with FXS and autism were more severely delayed. The group of children with FXS alone had a similar profile to children with generalized developmental delay. The study by Rogers and colleagues exhibits many of the challenges in accurate diagnosis at an early age due to the overlap in behavioral profiles across children with FXS, autism and developmental delay.

Two large-scale studies of early development in FXS exist. The first is a longitudinal study conducted by Bailey and colleagues (1998). The researchers followed 46 boys with FXS between the ages of 24 and 72 months and measured a range of developmental abilities such as cognition, communication, adaptive behavior, motor skills, and personal-social skills on

the Battelle Development Inventory (Newborg et al. 1984). Results indicated a wide variety of developmental trajectories with differences in both the rate and level of performance across individuals. Overall, boys with FXS were significantly delayed in all areas of development, with an average delay of half the rate expected for typically developing individuals. Across ages, motor and adaptive behavior scores were higher than communication and cognitive scores.

A longitudinal study by Roberts and colleagues (2009) assessed 55 boys with FXS between the ages of 8 and 48 months of age. Roberts and colleagues (2009) found delays in development at 9 months of age in chronological age scores, receptive language scores and expressive language scores. Delays in visual reception and motor functioning could be identified at 10 months and 13 months of age, respectively. The delays identified through developmental assessments had some predictive capacity for boys with FXS at young ages: the level of autistic behavior as measured by the Childhood Autism Rating Scale (CARS) was a stronger predictor of developmental trajectory. While development overall was delayed, approximately 50% of the children in the study did not have a 25% delay in composite scores, indicating they would not likely be eligible for services based on developmental screening using commonly employed eligibility criteria. The results suggest that some boys with FXS are identifiable at 9 months while others do not have developmental delays emerge until 12 months or later, which may be dependent on the severity of autism symptoms. No change or slowing in the rate of developmental was reported as has been reported in previously literature in older children with FXS (Lachiewicz et al. 1987). Roberts and colleagues also examined longitudinal outcomes with a subset of 13 boys with FXS from 9 to 18 months of age and found that infants have atypical visual attention in comparison to typically developing infants as early as 12 months of age (Roberts et al. 2011).

Adaptive Behavior Development

Adaptive behavior describes the functional ways in which an individual typically responds to environmental demands across a variety of situations such as home and school and is dependent on both developmental status and cultural expectations (Dykens et al. 1994; Hatton et al. 2003). The measurement of adaptive behavior includes performance in school, the ability to care for one’s self at home, interactions with peers and adults, and the level of independence in a variety of settings (Hatton et al. 2003). Adaptive behavior has become an important concept in the assessment of individuals with cognitive disabilities and is typically based on interviews with primary care givers. Adaptive behavior has been examined in children with FXS in several studies. Generally, results suggest that individuals with FXS display a relative strength in self-help and daily living skills but a deficit in socialization and communication skills (Hatton et al. 2003). Cohen et al. (1996) suggest that adaptive behavior ratings may more clearly reflect the abilities of individuals with FXS than IQ scores due to social anxiety experienced by those with FXS. Others have suggested that, compared to other developmentally disabled populations, children with FXS have adaptive behavior that is commensurate or superior to their intellectual abilities, suggesting that functional skills may be a strength for these individuals (Hatton et al. 2003).

There has been evidence that adaptive skills decline over time in individuals with FXS and that children with FXS may fall further behind their peers throughout childhood (Cohen et al. 1996; Hatton et al. 2003). It may be either that there is a point in the development of children with FXS when growth in the area of adaptive behavior skills plateaus or that these skills decline with age (Fisch et al. 2002). Together, studies indicate that there are several potential predictors of development in FXS, such as age, genetic status, FMRP, and autism (Cohen et al. 1996; Hatton et al. 2003; Roberts et al. 2009). Cohen et al. (1996) indicated that the rate of adaptive skill development of individuals with mosaicism was two to four times greater than that of individuals with full mutation FXS with no mosaicism. A related finding, Hatton et al. (2003) found that FMRP expression was associated with adaptive behavior domains for males with FXS.

Early Development in Autism

In children with autism, the adaptive behavior profiles are different than in individuals with FXS. Autistic behavior is associated with lower scores on measures of adaptive behavior relative to intellectual functioning with an increase in this discrepancy over time (Jónsdóttir et al. 2007). This trend remains across levels of intellectual affectedness, as individuals who have higher cognitive abilities make few gains in adaptive skills (Howlin et al. 2000; Mawhood et al. 2000). Studies have demonstrated that, like children with FXS, children with autism show relative deficits in socialization and communication domains, with relative strengths in daily living and motor skills domains (Baghdadli et al. 2012).

A large scale study 318 children (22–72 months) purported to identify an “autism profile” on the Vineland Adaptive Behavior Scales (Perry et al. 2009). This group predicted children diagnosed with autism score highest on the Motor domain, followed by Daily Living, Communication, then Socialization. Perry and colleagues found significant differences between the profiles of children with autism and children with PDD-NOS. The same “autism profile” also applied to children with developmental delays, although children with autism scored significantly lower on Communication and Social domains compared to children with developmental delays (Perry et al. 2009).

The assessment of adaptive behavior is important for treatment planning, progress monitoring, program evaluation, and service delivery (Carter et al. 1998; Sparrow et al. 2005). However, few studies have focused on understanding treatment options for increasing adaptive behavior. Before these interventions can be effectively developed, it is necessary to understand similarities and difference of adaptive behavior profiles across groups, and this is particularly important at young ages. Thus, the aim of the present study was to examine the development of adaptive behavior in boys with FXS and boys with autism. Specifically, we aimed to examine the relationship between adaptive behavior and age for boys based on their diagnosis. We also aimed to identify ages at which potential differences are evident across groups. We hypothesized that group differences will be evident across domains at 24 months of age.

Methods

Data were drawn from three sources. The first source was an ongoing longitudinal study on early indicators of autism in high-risk populations. Data were also collected from an extant database from a study examining family adaptation to FXS. Finally, autism data were drawn from the National Database for Autism Research (NDAR), a collective national database for autism research funded by the National Institutes of Health. A more detailed description of the NDAR database, including all relevant child questionnaires, can be found at http://ndar.nih.gov/. Combining data across studies allowed us to examine development across a range of ages for both groups.

Participants

One hundred and sixty nine boys participated in this study ranging in ages from 18 months to 83 months (mean age = 42 months). Of the 169 participants, 118 boys were diagnosed with FXS and 51 were diagnosed with autism. Children with FXS were diagnosed through genetic testing and all had the full mutation (more than 200 CGG repeats). Children with autism were diagnosed by a licensed clinician. Confirmation of the autism diagnosis was made through either the Autism Diagnostic Observation Schedule (ADOS) or the Childhood Autism Rating Scale (CARS). Parents provided written consent. Participant demographics are listed in Table 1.

Measures

The Vineland Adaptive Behavior Scales, Survey Interview Form (VABS) is a measure of adaptive behavior, or the performance of the daily activities required for personal and social sufficiency (Balboni & Pedrabissi 2001). The VABS is a 265 item parental report administered through a semi-structured interview that can be administered for individuals from birth to adulthood. Each item is scored 0 (never performs the task), 1 (sometimes or partially performs the task), 2 (usually performs the task), or DK if the respondent does not know about the child's ability to perform the task. There are four domains on which the VABS provides standardized scores: Communication (receptive, expressive and written), Daily Living (person, domestic and community), Socialization (interpersonal relationships, play and leisure time and coping skills) and Motor Skills (gross and fine motor skills). The VABS also includes ratings of maladaptive behaviors, which were not included as part of the present study. Based on the results of the above four domains, an Adaptive Behavior Composite (ABC) provides an overall comparison to normative sample of same-aged peers. The results on the Vineland are standardized based on a representative sample with a mean score of 100 and a standard deviation of 15. The Vineland has adequate test-retest reliability ranging from .76 to .93 and inter-rater reliability ranging from .62 to .78 (Rosenbaum et al. 1995). The Vineland is widely used for both research and clinical applications. For this study, the Vineland Adaptive Behavior Scales was completed by the primary caregiver of the child, which was typically the biological mother. Standard scores were used for all analyses.

Procedures

For the FXS group, participants were visited in their home by two researchers. The primary examiner interviewed the biological mother using the VABS during the first day of the two-day assessment. Protocols were then scored using the computerized scoring software and checked for reliability by trained research assistants.

For the autism group, data were accessed through NDAR based on specified conditions. We selected only those participants for whom adequate demographic data was available (notably age and gender). Then, we requested access to data for all males with a confirmed diagnosis of autism within our specified age range and of male gender. All cases (51) were able to be analyzed in the current study.

Results

Linear regression models were conducted using PROC REG in SAS 9.3 to investigate the presence of group differences on adaptive behavior on the Vineland Adaptive Behavior Scale. The presence of group difference was first assessed by the Adaptive Behavior Composite (ABC) for boys with FXS and boys with autism. Differences were then examined on four domains of the Vineland: Communication, Daily Living, Socialization, and Motor Skills. In addition to grouping variables, child chronological age and an age by group interaction were included in each regression model to assess whether the association between group and the outcome variables was dependent on child chronological age.

Multiple regression models were also conducted by group to investigate the relationship between age and each outcome variable. For boys with FXS, the relationship between standard scores and age was significant for every outcome variable except for Communication. For boys diagnosed with autism, the relationship between age and Motor and Daily Living Skills standard scores was significant but age was not significant for other domains or the Adaptive Behavior Composite (ABC).

Adaptive Behavior Composite

Results of the regression analyses for the ABC revealed no significant difference by group, F (1,165) = 0.26, p = .61 indicating that the relationship between age and the adaptive behavior composite did not differ by group. Age was only related to the ABC score for the FXS group with the ABC standard score decreasing across ages, indicating that boys with FXS on average receive lower scores across ages. The autism group also showed declines in overall adaptive behavior standard scores; however, these results were not significant. The FXS group had an average adaptive behavior composite score two standard deviations below the mean beginning at 20 months of age while adaptive scores for the autism group did not fall below 70 until 41 months of age. Decreases in ABC standard scores do not indicate that these children are losing developmental skills (as verified by examination of raw scores); rather, the decreases reflect suboptimal growth in adaptive behavior rather than true decline because their trajectory becomes increasingly delayed over time. See Figure 1.

Communication Domain

Results of the regression analyses for the communication domain revealed no significant difference by group, F (1, 165) = 2.46. Age was not significantly related to either groups' scores although the FXS group did approach significance (p = .07). Across ages, communication scores decreased for the FXS group and increased for autism group. At 26 months of age, boys with FXS and boys with autism performed equally on the Communication Domain; however, subsequent scores for boys with autism increased across ages, while scores for boys with FXS decreased across ages. This difference in slope may be due to the fact that children with autism often begin intense Applied Behavior Analysis targeting communication once diagnosed, and increased language skills may be a reflection of these services. See Figure 2.

Daily Living Domain

Results of the regression analyses for the daily living domain revealed a significant difference by group, F (1, 162) = 5.44, p = .02. Age was significantly related to daily living scores for the FXS group (p = .03) and the autism group (p = .002), with scores decreasing across age for both groups. Boys with FXS on average performed two standard deviations below the mean on the daily living domain at 18 months of age while boys with autism did not show significant deficits until 45 months of age. At 58 months of age, boys with autism demonstrated lower Daily Living Skills than the FXS group. See Figure 2.

Socialization Domain

Results of the regression analyses for the socialization domain revealed no significant difference by group, F (1, 165) = .07, p = .79. Age was significantly related to socialization for the FXS group (p = .0003) but not for autism group. Scores decreased across ages for both groups, with a greater decline for the FXS group.

Motor Skills Domain

Results of the regression analysis for motor skills domain revealed no significant difference by group, F (1,165) = .05, p = .82. Age was significantly related to motor skills for both the FXS group (p <.0001) and the autism group (p = .03) with scores decreasing across ages for both groups. Children with FXS on average scored two standard deviations below the mean after 29 months of age while boys with autism did not meet this threshold until after 65 months of age.

Discussion

Understanding adaptive behavior development in young children with FXS and those with autism is of critical importance for treatment planning, progress monitoring, program evaluation, and service delivery (Bishop et al. 2008; Carter et al. 1998; Sparrow et al. 2005). Despite this significance, few studies have focused on understanding early development of adaptive behavior in these populations and the comparison among the two groups. Thus, we examined the development of adaptive behavior in boys with FXS and boys with autism in order to understand the relationship between adaptive behavior and age for these two groups and the ages at which potential differences are evident.

Consistent with our hypothesis, age interactions occurred for the FXS group across most domains and age interactions were noted across two domains (Daily Living, Motor Skills) for the autism group. Older boys with FXS were, on average, performing two standard deviations below the mean (average score of less than 70) on every domain and the adaptive behavior composite score. These delays were evident by 30 months of age in the FXS group. Boys in the autism group did not demonstrate the same severity of deficits except for in the communication domain; however, this is in contrast to previous research which suggests young children with autism experience deficits in these adaptive behavior domains that may not be adequately detected with our measurement.

Overall adaptive behavior was delayed for both groups, with both the FXS and autism group displaying declines in adaptive behavior standard scores across ages. Further inspection of raw scores indicated that these declines were not due to a loss of skills, but rather a slowing in the rate of development for both groups. This slowing in the rate of development for the FXS group is inconsistent with some literature (Bailey et al. 1998) that showed no slowing in the rate of development, but consistent with other research (Roberts et al. 2009) which did indicate a slowing in the rate of development. Delays in adaptive behavior reached clinical significance (standard score less than 70) earlier for the FXS group (20 months of age) than the autism group (41 months of age) on average.

In the area of communication, scores decreased across ages for the FXS group but increased across ages for the autism group. Increasing scores for the autism group is inconsistent with previous literature which indicated communication scores being among the lowest for children with autism (Perry et al. 2009). We hypothesize that the increase in communication scores may reflect intensive early intervention efforts that are begun at diagnosis. Declining scores in the FXS group are consistent with previous literature which suggests communication delays may be among the first delays noted in young children with FXS (Bailey et al. 1998).

Patterns for daily living skills changed across ages, with boys with autism showing increased skills in daily living at earlier ages, and decreased skill at later ages compared to the FXS group. Both groups demonstrated significant delays in daily living, with the FXS group showing clinically significant delays very early on (by 18 months of age) and the autism group demonstrating clinically significant delays by 45 months of age. Daily living skills are critical for later success and independence thus may be a targeted area for intervention.

Socialization skills were more impaired for the FXS group than the autism group. Scores decreased across ages for both groups; however socialization skills were more impaired in the FXS group. This is in contrast to previous literature in autism which suggests socialization is one of the areas of greatest impairment (Perry et al. 2009). Again, this contrast may be due to intensive early intervention begun at diagnosis, and may be unique to our sample. Although children with FXS are likely to receive intervention services as well, children with autism may have a longer duration and increased intensity of services provided. Longitudinal data analysis will help elucidate the effects of intervention on

communication and socialization abilities, and help determine whether this is a global characteristic of children.

The current study indicates that FXS and autism are similar in several ways in regard to adaptive behavior development. Both groups demonstrated total and domain score age-related declines although the significance of these differences varies across domain. Thus, the present data suggest that the profiles of FXS and autism change across development. Children with FXS become increasingly delayed in multiple domains across ages. In comparison to children with autism, low scores in motor skills or daily living may suggest a profile of a child with FXS. Children with autism have higher flat profiles of development in motor skills, daily living, and socialization but are more variable in the communication domain. These findings are important as this is the first study to examine adaptive behavior in children this young and comparing both FXS and autism. Further development of the similarities and differences between the profiles of boys with autism and boys with FXS is necessary to aid in differential diagnosis and treatment efforts.

The research reported in the present study has several limitations. The study utilized cross-sectional data to examine broad patterns of the development of adaptive behavior. In the future, longitudinal studies following the same children over time would have more direct implications for screening and diagnosis of FXS and autism. We did not rule out autism in the children with FXS for these analyses, so it is possible that there may be different patterns for those individuals with FXS and those with comorbid FXS and autism as reported in other studies (Hatton et al. 2003). Inclusion of a developmental delay group to account for non-specific delays is warranted. Female children should be included in future studies.

In future research, studies on adaptive behavior may consider multiple outcome measures due to potential strengths and weaknesses of each measure. Previous researchers have proposed that the VABS may not reflect the full variability in the performance of children with autism because basal and ceiling cutoffs may make inaccurate assumptions about their performance. The method of scoring on the Vineland may also limit the detectability of small changes in behavior (Cunningham 2012). Cornish and colleagues (2007) propose that the delays in communication and socialization of children with FXS and children with autism are fundamentally different: children with FXS may exhibit autistic-like behaviors due to hyperarousal and social anxiety while children with autism may exhibit the same behaviors due to a lack of understanding of the social situation. Measures such as Vineland may not reflect subtle differences in communication, which may help to differentiate between FXS and autism. Additional measures would provide more detail on the scores in the broad domains of the Vineland.

Acknowledgments

This research was supported in part by grants from the Office of Special Education Programs, US Department of Education (H023B70035) and the National Institute of Mental Health (R01MH0901194-01A1).

This study was supported by funding from the Office of Special Education Programs, US Department of Education H023B70035 (PI: Baily) and the National Institute of Mental Health; R01MH0901194-01A1 (PI: Roberts).

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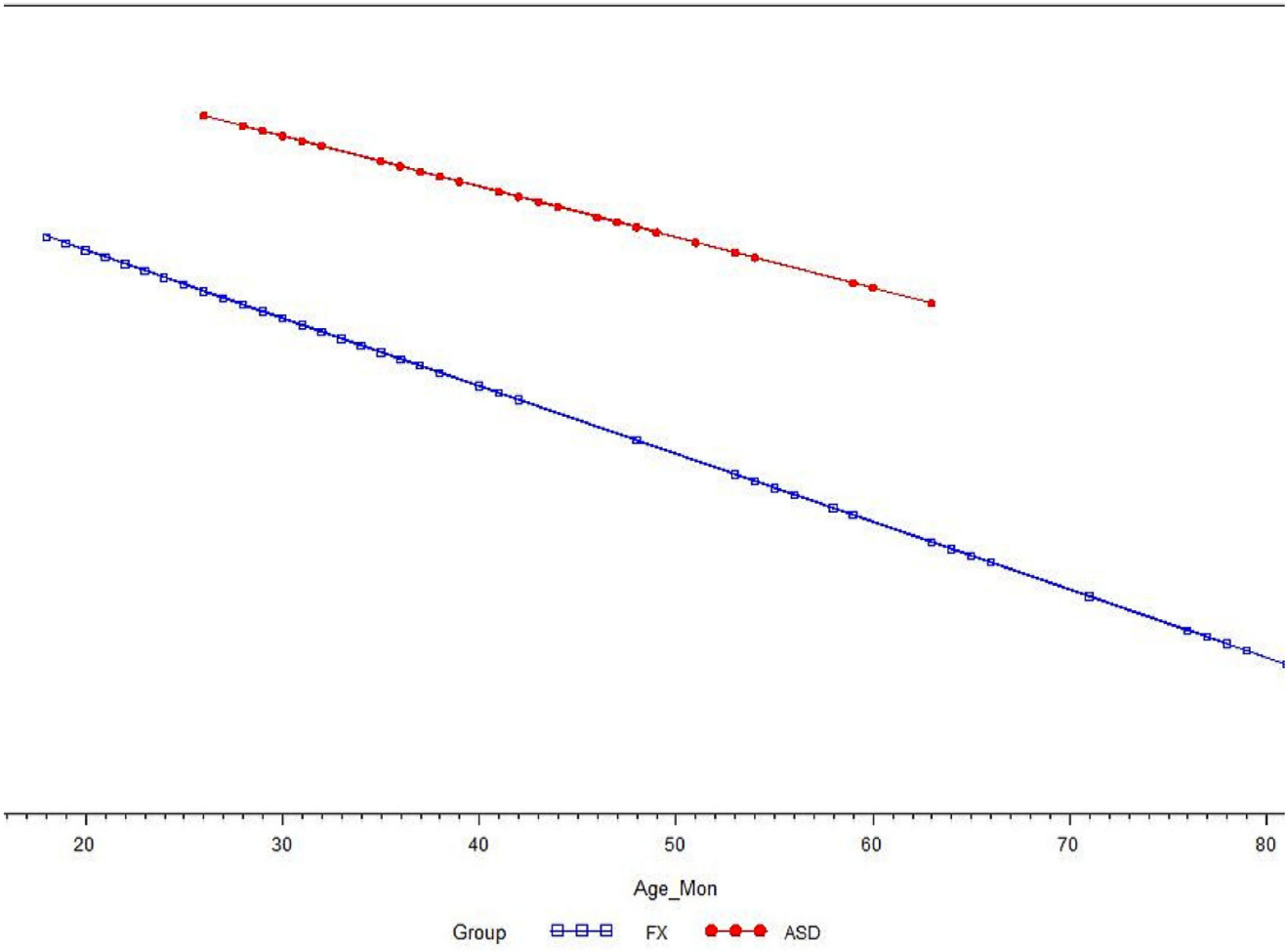

Figure 1.
Adaptive Behavior Composite Scores Across Age

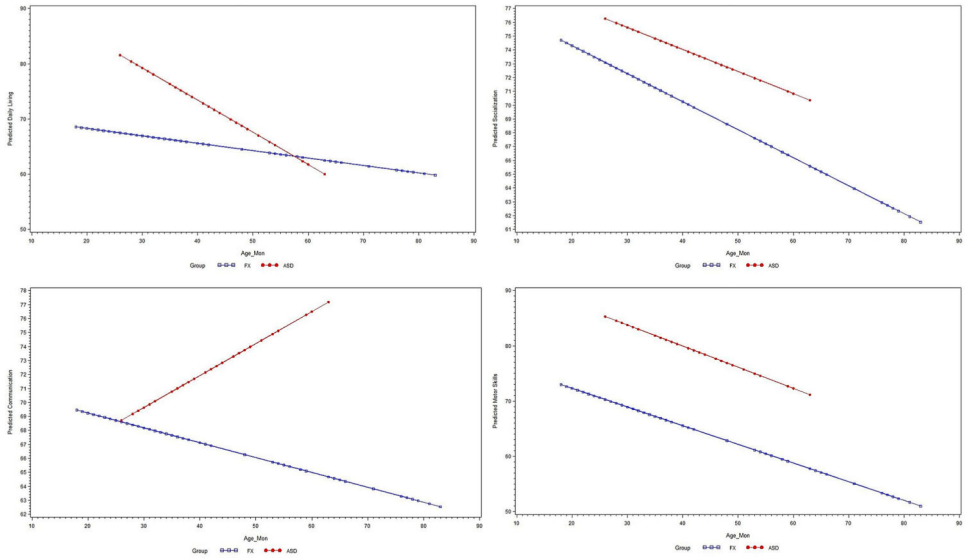

Figure 2.
Communication, Daily Living, Socialization, and Motor Standard Scores Across Age

Table 1

Participant Demographics

	M	*SD*
Age		
Fragile X syndrome	43	17.2
Autism	40	9.4
Adaptive Behavior Composite		
Fragile X syndrome	60	11.5
Autism	71	12.5
Communication Domain		
Fragile X syndrome	66	11.1
Autism	72	17.5
Daily Living Skills Domain		
Fragile X syndrome	65	12.1
Autism	73	13.2
Socialization Domain		
Fragile X syndrome	69	10.6
Autism	73	11.7
Motor Skills Domain		
Fragile X syndrome	64	13.6
Autism	79	12.4