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Early Gesture Use in Fragile X Syndrome

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Abstract

Background—Emerging evidence suggests that children with fragile X syndrome (FXS) exhibit abnormal gesture use early in development, though few studies have investigated the emergence of gesture use in this population or the impact of autism spectrum disorder (ASD) features on these behaviours. The present study examined the longitudinal development of gesture use in infants with FXS relative to low-risk controls and infant siblings of children with ASD (high-risk siblings), with the goal of establishing potentially unique patterns of gesture development in infants with FXS and understanding the relative impact of ASD symptom severity on these patterns.

Method—Participants included 86 infant males (39 FXS, 27 high-risk siblings, 20 low-risk infants) assessed at 9, 12 and 24 months of age. Multilevel modelling was used to assess differences in number of gestures used and rates of gesture use across groups, as well as the relative impact of ASD symptom severity and nonverbal skills on these patterns.

Results—Infants with FXS used fewer gestures than high-risk siblings and low-risk infants, with this difference being primarily accounted for by the effect of low nonverbal abilities in the FXS group. Furthermore, although higher ASD symptom severity was associated with the use of fewer gestures in both the FXS and high-risk sibling groups, a significant amount of variance was shared between ASD symptom severity and nonverbal skills in FXS, but not in high-risk siblings.

Conclusions—This study presents the first longitudinal analysis of early gesture development in FXS using a multi-group design, clarifying the relative roles of cognitive deficits and ASD symptom severity in the development of gesture use in FXS. These findings offer novel evidence

that early gesture use in FXS may reflect broader features of the FXS phenotype rather than predicting later social-communicative deficits characteristic of comorbid ASD.

Keywords

Autism; Communication; Fragile X; Intellectual Disability; Behavioural Phenotypes; Gesture; Infant

Individuals with fragile X syndrome (FXS) experience numerous social and developmental difficulties, with deficits in social communication representing a particularly limiting aspect of the phenotype. In typical development, nonverbal behaviours, such as gestures, emerge early in infancy and precede the development of verbal social communication (Parladé & Iverson 2011). These early nonverbal skills become the building blocks for the infant to acquire more complex social communication skills, such as words and language (Tomasello *et al.* 2007). Disruptions in this developmental process can therefore impair an individual's ability to communicate with others and navigate social situations effectively.

Emerging evidence suggests that children with neurodevelopmental disorders such as FXS exhibit abnormal gesture use early in development. Atypical gesture use is also a hallmark feature of young children with autism spectrum disorder (ASD), a neurodevelopmental disorder characterised by social communication impairments and repetitive behaviours (APA 2013) that occurs in approximately 50–67% of males with FXS (García-Nonell *et al.* 2008; Klusek *et al.* 2014). However, few studies have investigated the nature of abnormal gesture use in very young children with FXS and the impact of ASD features on these behaviours. The present study addresses this need by examining the longitudinal development of gesture use in infants with FXS relative to low-risk controls and infant siblings of children with ASD. By examining the prospective emergence of gestures in FXS relative to other high- and low-risk groups, we sought to (1) establish potentially unique patterns of gesture development in infants with FXS and (2) determine the relative impact of ASD symptom severity on gesture development in FXS, with the ultimate goal of improving early characterisation and treatment targets that may optimise outcomes in this population.

The Development of Gesture Use in Infants

Appropriate gesture use in early development is a critical tool for preverbal infants to engage in their environment. Simple gestures typically emerge in infants around 9–13 months of age (Crais *et al.* 2004) and almost always emerge before the infant begins to use words (Goldin-Meadow & Butcher 2003; Guidetti & Nicoladis 2008). Given gesture use is predictive of later language abilities in typical development (Iverson & Goldin-Meadow 2005), accurately characterising early gesture use is a fundamental step in understanding the development of social communication, potentially uncovering points in development where intervention may optimise development and combat language delays.

Populations with Impaired Gesture Use

Fragile X Syndrome.

Fragile X syndrome is a rare genetic disorder and the leading known cause of inherited intellectual disability, occurring in approximately 1 in 7,000 males (Hunter *et al.* 2014). The disorder is caused by a mutation involving an expansion of a cytosine-guanine-guanine (CGG) repeat on the X-linked fragile X mental retardation 1 (*FMR1*) gene (Santoro *et al.* 2012). CGG repeat expansion to more than 200 repeats leads to methylation of the *FMR1* gene, which reduces production of fragile X mental retardation protein (FMRP; Bhakar *et al.* 2012), a protein that is essential to healthy synaptic plasticity and cognitive functioning (Santoro *et al.* 2012). The behavioural FXS phenotype often includes intellectual impairment, attention problems, anxiety, and ASD symptoms (Loesch *et al.* 2004; Hatton *et al.* 2006; Hall *et al.* 2010; Tonnsen *et al.* 2013). Relevant to the present study, the FXS phenotype is also characterised by a number of atypical social communication features, including diminished eye contact and pragmatic language deficits (Hall *et al.* 2006; Klusek *et al.* 2014a).

Gesture Use in FXS.

A growing body of evidence suggests that atypical gesture use may be present early in development in FXS. Overall communication delays were present in a sample of 22 young males with FXS, with particular weaknesses in gesture use relative to other communication skills (Roberts *et al.*, 2002). Furthermore, in a study of 9- to 12-month-old infants with FXS, only 1 of 7 infants was observed to use a gesture in an analysis of retrospective family videos (Marschik *et al.* 2014). Another study of 7–14 month olds showed that infants with FXS used a smaller repertoire of gestures than typically developing infants (Hahn *et al.* 2017). However, given the lack of longitudinal and cross-group studies on gesture use in FXS, it is unclear when these deficits emerge and how they are related to other areas of social functioning. One hypothesis is that gesture use is delayed in concert with broader developmental and adaptive delays that are present as early as 6–9 months of age in FXS and intensify over the first two years of life (Roberts *et al.* 2016; Caravella & Roberts 2017). An alternate hypothesis is that variability in early gesture use within FXS may be related to comorbid conditions associated with FXS, particularly ASD. To date, research exploring the relationship of ASD symptomatology with early social communication in FXS has been limited and results are mixed. One study presented evidence that higher ASD symptomatology is associated with greater early social communication impairment in FXS (Warren *et al.*, 2010), while another study showed wider variety of gestures was *negatively* associated with later language outcomes for children with FXS and high ASD symptomatology (Flenthrope & Brady 2010). Notably, these studies examined samples with wide age ranges spanning from infancy through preschool-age, which may not have captured nuanced developmental patterns of the relationship between gesture use, ASD symptomatology, and later social communication outcomes. Given the variability in findings exploring early gesture deficits in FXS, further research examining early trajectories of gesture development in FXS in contrast to other high-risk populations is needed to disentangle the relative roles of cognitive delay and ASD symptomatology in the development of gesture deficits in FXS.

Gesture Use Associated with ASD Risk.

Atypical gesture use has been identified as one of five “red flags” that emerge during early development in individuals with ASD (Wetherby *et al.* 2007). As with individuals with FXS, language development is often delayed in individuals with ASD (Gernsbacher *et al.* 2015), and there is evidence that abnormal patterns of early gesture use predict later language delays in ASD (Bopp & Mirenda 2011). Recent literature has explored these patterns of impaired gesture use among infant siblings of children with ASD (high-risk siblings), who are at increased risk for developing ASD (Ozonoff *et al.* 2011). There is some evidence that high-risk siblings demonstrate abnormal gesture use relative to low-risk controls, particularly using point and show gestures (Leezenbaum *et al.* 2013). However, these effects may be driven by delays in other areas of development, such as motor skills (LeBarton & Iverson 2016) or by high-risk infants who ultimately receive a diagnosis of ASD (Winder *et al.* 2013). Overall, findings on gesture use in high-risk siblings are inconsistent, possibly reflecting the fact that as a group, high-risk siblings demonstrate a wide range of ASD symptoms regardless of ultimate diagnosis (Messinger *et al.* 2013). Thus, high-risk siblings are a valuable comparison group for characterising gesture use in FXS, as well as determining whether variability in these patterns is driven by emerging ASD symptomatology.

Present Study

While early gesture use is well-studied in typical development and ASD, much less is known about early gesture use in FXS. Though there is emerging evidence that individuals with FXS may demonstrate specific weaknesses in gesture use, it is unclear whether these deficits can be explained by the presence of ASD or if they are driven by broader developmental delays characteristic of the FXS phenotype. Furthermore, no existing studies have examined trajectories of early gesture use related to ASD symptomatology in FXS, or compared these trajectories to those of other high-risk populations. Characterising early social communication in FXS and contrasting it with that of other populations at increased risk for developing ASD allows for the identification of potentially shared or distinct developmental profiles that precede later maladaptive outcomes. The current study aims to inform early trajectories of gesture use in FXS by contrasting profiles to those of high-risk siblings and low-risk infants, and by determining the impact of ASD symptom severity on these profiles of gesture use.

Research Questions

1. Do trajectories of gesture use in FXS differ from those of high-risk siblings and low-risk infants, and what is the association between nonverbal abilities and these trajectories?
2. Is ASD symptom severity differentially associated with trajectories of early gesture use in infants with FXS contrasted to those of high-risk siblings and typical controls, and what is the association between nonverbal ability and these trajectories?

Method

Participants

Participants included 86 infant males: 39 with FXS, 27 high-risk siblings, and 20 low-risk infants. Participants were recruited through an ongoing longitudinal study at the University of South Carolina (USC) aimed at detecting the emergence of ASD in infants and young children with FXS. The FXS group for this paper was supplemented with a subset of male participants ($n=14$) from a similar study completed at the University of North Carolina – Chapel Hill (UNC) with similar goals and methodology, with the exception that the ADOS-T was not completed in the UNC study. Table 1 details the number of participants seen at approximately 9, 12, and 24 months and their actual ages of assessment. Due to the specialised nature of our sample, participants were permitted to enter the study at either 9 or 12 months.

Demographic and descriptive information is summarised in Tables 2 and 3. FXS status was confirmed by genetic report, and high-risk sibling status was confirmed by a community ASD diagnostic report for the older sibling. “Low-risk” was defined as the absence of known or suspected delays, no family history or indicators of ASD, a developmental composite score no more than 1 standard deviation below the mean (i.e., Mullen Early Learning Composite score of 85 or higher) at 24 months, and a Calibrated Severity Score of 3 or less (indicating Little-to-No Concern for ASD). Participants with neurological conditions or gestation less than 37 weeks were excluded from all groups.

Measures

Gesture Use.—The MacArthur-Bates Communicative Development Inventories Words and Gestures form (CDI; Fenson *et al.* 2007) is a parent-report measure used to assess early language skills in children aged 8–18 months, though previous studies have used this form in older populations with known developmental delays (e.g., Yoder *et al.* 2015; Zampini *et al.* 2015). Early gesture use was measured using the Early Gesture summary score, which includes 18 items describing various early-emerging gestures. Parents indicated whether their child demonstrates each gesture “Often,” “Sometimes,” or “Not Yet”. The Early Gestures summary score is calculated by summing all items on which the parent answered “Often” or “Sometimes”. Internal reliability for the Early Gesture scale of the CDI was .88 in Fenson *et al.* (2007). Proportions of participants in each group who achieved ceiling scores at the 24-month assessment were low (FXS: 0 of 27, 0%; high-risk siblings: 3 of 21, 14%; low-risk infants: 2 of 16, 13%).

ASD symptom severity.—The Autism Diagnostic Observation Schedule, Toddler Module (ADOS-T; Lord *et al.* 2012) is a standardised, semi-structured assessment used to assess ASD symptom severity. Ratings are assigned for 41 items, a subset of which are entered into an algorithm that can be converted into a Calibrated Severity Score (CSS) based on the child’s age and language level. The CSS ranges from 1 to 10, with 1 indicating the lowest level of ASD symptomatology (Esler *et al.* 2015). In this study, the CSS was used as a measure of ASD symptom severity. Research reliable examiners administered the ADOS-

T at the 24-month assessment for each participant enrolled in the USC study, and reliability was established for 20% of the ADOS-T administrations (inter-rater reliability 83.3%).

Developmental Level.—The Mullen Scales of Early Learning (MSEL; Mullen 1995) is a standardised developmental assessment which measures a child's developmental abilities in five domains: Gross Motor, Visual Reception, Fine Motor, Receptive Language and Expressive Language. Internal reliability ranges from .75 to .83 for the subscales (Mullen 1995). In this study, a Nonverbal Composite score was calculated by averaging the t-scores from the Visual Reception and Fine Motor domains to obtain a measure of cognitive ability that is independent of language abilities (Munson *et al.* 2008).

Procedure

Study procedures were approved by Institutional Review Boards at both participating universities. Participants were assessed at approximately 9 ($M=9.22$, range=7.87–10.39), 12 ($M=12.49$, range=10.62–15.56) and 24 ($M=24.74$, range=22.83–27.92) months of age. At each assessment, trained examiners administered the MSEL, and parents completed the CDI. The ADOS-T was administered to a subset of participants ($n=50$; 15 FXS, 20 high-risk siblings, 15 low-risk infants) who had completed the 24-month assessment in the USC study. Participants from the USC and UNC sites did not differ in age, Early Gesture summary scores or Nonverbal Composite scores at any time point ($p's>.05$), but did differ in number of assessments ($p=.041$). The FXS group was, on average, older than the high-risk sibling group at the 9-month assessment ($p=.024$) and the low-risk group at the 24-month assessment ($p=.018$), and the FXS group had fewer assessments on average than the low-risk group ($p=.023$). The FXS and high-risk sibling groups did not differ significantly in ADOS-T CSS scores, ($p=.107$).

Data Analysis

Statistical analyses were completed using R (R Core Team 2016) and the nlme package (Pinheiro *et al.* 2016). Multilevel modelling was used to analyse the data, as it allows for the analysis of clustered longitudinal data in which some data points are missing. For all models, chronological age in months was centred at 24 months so that the intercept is interpreted as the predicted gesture use at the final time point. Chronological age and an intercept were included as random effects in all models; all other effects were fixed. Raw data did not violate assumptions of shape, normality or homoscedasticity.

To address our first research question, group was entered in the model as the primary predictor of number of gestures used, and the interaction between group and chronological age tested group differences in the rate of gesture development over time. Next, nonverbal ability was tested as a covariate. Given that nonverbal ability fluctuated across time points, measures of both time-invariant nonverbal ability (nonverbal composite score at the final time point) and time-variant nonverbal ability (deviation of nonverbal composite score at each time point from the nonverbal composite score at the final time point) were included as covariates.

To address our second research question, ASD symptom severity was added to the model as a time-invariant predictor of gesture use. The term “predictor” here reflects model structure, not temporal direction. In other words, ASD symptom severity is considered a stable, latent feature in each participant, not a stable, measurable feature over infancy. The interaction between ASD symptom severity and group tested group differences in the association of ASD symptom severity with number of gestures used, while the interaction between all three predictor variables tested group differences in the association of ASD symptom severity with rate of gesture development. We then analysed FXS and high-risk siblings in separate models to explore the association of ASD symptom severity with early gesture use in each group. For each of these models, ASD symptom severity was entered in the model as the primary time-invariant predictor of number of gestures used, and the interaction of ASD symptom severity and chronological age tested group differences in the association of ASD symptom severity with rate of gesture development over time. Time-variant and time-invariant nonverbal ability were then added in as covariates to determine the role of nonverbal ability on these patterns for each group.

To measure effect size, a secondary model was run for each model following the primary analysis, with gesture use standardised within each time point as the dependent variable in the growth model. This approach allows coefficient estimates produced by the growth model (designated as β in Results section) to be interpreted in a metric similar to Cohen’s d , with changes represented in units of standard deviation (Hedges 2007; Schmidt & Hunter 2015).

Results

Gesture Development Across Groups

At 24 months, infants with FXS used on average 4 less gestures than high-risk siblings ($b=4.20$, $SE=1.00$, $p<.001$, $\beta=.95$) and about 6 less gestures than low-risk infants ($b=6.16$, $SE=1.10$, $p<.001$, $\beta=1.39$). The rate at which infants with FXS acquired gestures from 9–24 months did not differ significantly from the rate at which high-risk siblings ($b=0.03$, $SE=0.07$, $p=.666$, $\beta=.01$) or low-risk infants ($b=0.11$, $SE=0.07$, $p=.131$, $\beta=.01$) acquired gestures over timeⁱ. When nonverbal skills were included as a covariate in this model, number of gestures used did not differ between FXS and high-risk siblings ($b=0.98$, $SE=1.14$, $p=.395$, $\beta=.19$) or FXS and low-risk infants ($b=1.97$, $SE=1.50$, $p=.194$, $\beta=.37$). Differences in rate of gesture acquisition remained nonsignificant between FXS and high-risk siblings ($b=-0.04$, $SE=0.07$, $p=.603$, $\beta=.02$) and FXS and low-risk infants ($b=-0.02$, $SE=0.08$, $p=.774$, $\beta=.02$) when nonverbal skills were covaried.

Impact of ASD symptom severity

We next investigated the association of ASD symptom severity with gesture development for the subset of participants that received the ADOS-T at 24 months (15 FXS; 20 high-risk siblings; 15 TD). We addressed this aim first by investigating the differential impact of group on the association of ASD symptom severity with gesture use. In this model, ASD

ⁱBecause some participants were missing MSEL data at the 24-month assessment, models that include nonverbal abilities as a covariate include fewer participants than models that do not include nonverbal abilities. Results using the restricted sample produced identical patterns of results as the full sample, therefore results from the full sample are reported in text.

symptom severity was not associated with differences in number of gestures used at 24 months between FXS and high-risk siblings ($b=0.31$, $SE=0.33$, $p=.363$, $\beta=.06$) or between FXS and low-risk infants ($b=0.03$, $SE=1.06$, $p=.977$, $\beta=.01$). Similarly, ASD symptom severity was not associated with differences in rates of gesture development between FXS and high-risk siblings ($b=0.01$, $SE=0.03$, $p=.754$, $\beta<.01$) or between FXS and low-risk infants ($b=0.09$, $SE=0.08$, $p=.227$, $\beta=.02$). Similar patterns of results were obtained when nonverbal skills were included as a covariate in this model (Figure 1).

We next investigated the association of ASD symptom severity with gesture use in the FXS and high-risk sibling groups individually. In contrast to the previous set of models that examined the differential effect of group on associations between gesture use and ASD symptom severity, these models focused on whether ASD symptom severity moderated within-group trajectories of gesture use (Figure 2). In FXS, higher ASD symptom severity was associated with fewer gestures used at 24 months ($b=-0.82$, $SE=0.31$, $p=.017$, $\beta=.19$), but not the rate at which infants with FXS acquired gestures over time ($b=-0.03$, $SE=0.02$, $p=.146$, $\beta<.01$). Similarly, higher ASD symptom severity was associated with fewer gestures used for high-risk siblings at 24 months ($b=-0.57$, $SE=0.22$, $p=.016$, $\beta=.13$), but not the rate at which high-risk siblings acquired gestures over time ($b=-0.02$, $SE=0.02$, $p=.241$, $\beta=.01$). When nonverbal skills were added as a covariate in these models, the relationship between ASD symptom severity and gesture use at 24 months in FXS was no longer significant ($b=-0.31$, $SE=0.27$, $p=.278$, $\beta=.07$), but this relationship remained significant for high-risk siblings ($b=-0.56$, $SE=0.22$, $p=.022$, $\beta=.13$). In other words, ASD symptom severity was associated with fewer gestures at 24 months in both high-risk groups, with nonverbal skills sharing a significant amount of variance with ASD symptom severity in FXS, but not in the high-risk sibling group.

Discussion

This study presents the first longitudinal analysis of early gesture development in FXS using a multi-group design, clarifying the relative roles of cognitive deficits and ASD symptomatology in the development of gesture use in FXS. We reported two major findings. First, our results showed that infants with FXS used fewer gestures than high-risk siblings and low-risk infants, and that this difference was primarily accounted for by the effect of low nonverbal abilities in the FXS group. Second, although higher ASD symptom severity was associated with the use of fewer gestures in the FXS and high-risk sibling groups, these associations were differentially related to nonverbal skills across groups. These findings offer novel evidence that early gesture use in FXS may reflect broader features of the FXS phenotype, rather than specifically predicting later social-communicative deficits characteristic of comorbid ASD.

Gesture Development

Our findings add to the sparse literature examining early gesture use in FXS, particularly during the period that gestures begin to emerge in typical development (Crais *et al.* 2004) which prospective and longitudinal studies have rarely explored in FXS. Our finding that the FXS group used fewer gestures than high-risk siblings and low-risk infants is consistent with

previous literature indicating that infants with FXS demonstrate deficits in gesture use (Roberts *et al.* 2002; Marschik *et al.* 2014). Furthermore, differences between the three groups were reduced to statistical non-significance when nonverbal abilities were covaried. Importantly, by using a measure of nonverbal ability that is independent of language skills, we can conclude that this finding is not due to the expected association between gesture use and language abilities. These findings suggest that gesture delays in FXS relative to low-risk infants and high-risk siblings may be driven by cognitive deficits typical of the FXS phenotype, as opposed to specific deficits in gesture use. Though previous findings suggest older individuals with FXS ages 21–77 months show a weakness in gesture use relative to other communication skills (Roberts *et al.* 2002), our results may suggest that developmental profiles of specific weaknesses in gesture use observed in older individuals with FXS are less differentiated in very young children.

The rate of gesture use over time did not differ in FXS versus other groups, suggesting that the pattern of gesture development in infants with FXS is delayed but not characteristically atypical from similarly-aged peers. We found gesture use was generally increasing in FXS from 9–24 months, that infants with FXS acquired gestures at similar rates to high-risk siblings and low-risk infants, and that these findings remained consistent regardless of whether nonverbal abilities were taken into consideration. This provides insight into early developmental processes in FXS, indicating that gestures emerge somewhat later for this group but that they do not fall increasingly behind infants in the other groups. This finding has implications on intervention strategy, as it may suggest that targeting an increase in number of gestures used in FXS early in development may promote a trajectory more closely matched with the one observed in typical development.

Impact of ASD symptom severity

A strength of our study was the integration of cross-group comparisons to determine whether early trajectories of gesture use in FXS were similar to those of high-risk siblings. Very few studies have contrasted FXS with other high-risk populations (Cornish *et al.* 2007), particularly in regard to gesture use and early development (Roberts *et al.* 2016b; Caravella & Roberts 2017; Hahn *et al.* 2017). We found that while both FXS and high-risk sibling populations are at increased risk for ASD, early gesture use was differentially associated with ASD symptom severity in these two groups. For both groups, higher ASD symptom severity was associated with fewer gestures used at 24 months, though a high degree of variability was observed among individuals in each group. However, in the FXS group, it appeared that this effect may be due to the significant variance shared between nonverbal ability and ASD symptom severity. This pattern suggests that delays in gesture use may not be an ASD-specific profile in FXS, but rather the result of the overall cognitive deficits typically observed in this population.

This finding deviates from previous literature indicating that individuals with FXS differ in their trajectories of communicative skills depending on whether they demonstrate low or high ASD symptomatology (Warren *et al.* 2010). While Warren *et al.* (2010) established a differential effect of level of ASD symptomatology on language abilities, our results suggests that gesture development may not be similarly associated with ASD symptom

severity, at least at very young ages. Notably, the relationship between ASD symptom severity and gesture use observed in our high-risk sibling group suggests that gesture use is more directly associated with ASD symptom severity in this group, which is consistent with prior research indicating that delays in gesture use are a “red flag” for later ASD diagnosis (Wetherby *et al.* 2007). Given our small sample size and the fact that these results were unexpected, further investigation is needed to clarify the role of ASD symptom severity in early gesture use in FXS. This information may help identify underlying mechanisms of social communication deficits in FXS, as well as inform ASD research more broadly by identifying shared and unique paths of social communication development.

Limitations

While this study fills a much-needed gap in the FXS social communication literature through its multi-group and early longitudinal design, there are limitations. Given the low-incidence of FXS and challenges of recruiting very young infants, we were limited by small sample sizes. However, effect size estimates indicated that we were able to detect most relationships with small-to-medium effects. Furthermore, our study did not utilise developmentally-matched comparison groups; thus, it is possible that these findings are not specific to FXS and may extend to other developmentally-delayed populations as well. Finally, due to the well-known risk of communication deficits in the FXS and high-risk sibling populations, it is possible that many of these individuals begin receiving intervention services at an early age, and that rates of gesture development are reflecting the effects of intervention as opposed to “natural” rates of gesture development.

The CDI presents some limitations in measurement of early gesture use. While the CDI and ADOS-T measure separate constructs, these measures were correlated ($r = -.32, p < .001$), likely due to the overlap in the content each of these measures assesses. The use of specific gestures listed on the CDI, such as pointing or showing, is also coded directly on the ADOS-T. Likewise, some skills listed on the CDI, such as playing peekaboo and patty cake, require social engagement that many children with ASD lack. Thus, we may have been limited in our ability to measure gesture use and ASD symptomatology independent of each other. Additionally, scores on the CDI Early Gesture scale range from 0 through 18, producing a small range that may have limited our ability to detect true effects on change in early gesture use. Furthermore, although administering the CDI to children outside the suggested age range of 8–18 months has been done previously in developmentally delayed samples (Yoder *et al.* 2015; Zampini *et al.* 2015), this may have impacted our ability to accurately measure language in older children in our sample. However, the proportions of participants who achieved ceiling scores at the 24-month assessment were low, thus it is unlikely our results were substantially impacted by measurement range limitations. Finally, we did not measure ASD symptomatology at each time point, and were therefore unable to capture potential variability in ASD symptoms across time that may have influenced our results.

Conclusion

In conclusion, our findings offer new information to the emerging body of research aimed at characterising early gesture use in FXS. We build on the literature suggesting that early gesture use in infants with FXS is impaired, and provide new evidence that global

developmental delays characteristic of the FXS phenotype play a significant role in explaining these impairments. This can inform our understanding of shared and unique pathways of social communication development in populations at increased risk for developing ASD. Results from this study can be used to inform intervention strategies for FXS, suggesting that targeting gesture use early in intervention may provide individuals with FXS the best chance at approaching an optimal trajectory of gesture development.

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Early Gesture Use Over Time Not Covarying Nonverbal Ability

Early Gesture Use Over Time Covarying Nonverbal Ability

Figure 1.

Predicted number of gestures used in each group across age in months. Regression lines indicating average rates of gesture development for each group are shown. The top plot shows regression lines for average rates of development before nonverbal skills were added into the model. In this model, FXS used fewer gestures at 24 months than both high-risk siblings and low-risk controls, though the rate of gesture development (slope) was not significantly different between groups. The bottom plot shows regression lines for the average rate of gesture development when nonverbal skills were added to the model as a covariate. In this model, neither the number of gestures used at 24 months nor the rate of gesture development were different across groups.

Figure 2. Spaghetti plots of number of gestures used by FXS and high-risk siblings, divided into those with low ASD symptomatology (CSS ≤ 3) and high ASD symptomatology (CSS > 3). Each line represents number of gestures used by one participant across available time points.

Table 1

Average Age of Participants and Number of Assessments at Each Time Point

	Age in Months <i>M(SD)</i>	FXS <i>n</i> = 39	High-Risk Siblings <i>n</i> = 27	Low-Risk Infants <i>n</i> = 20	Total <i>n</i> = 86
9 Month Assessment	9.22 (0.56)	24	20	20	64
12 Month Assessment	12.49 (0.98)	29	23	17	69
24 Month Assessment	24.74 (0.99)	27	21	16	64

Table 2

Demographic Information

Race	FXS (n = 39)	High-Risk Sibling (n = 27)	Low-Risk Infants (n = 20)
White	26 (67%)	24 (89%)	15 (75%)
Black or African American	2 (5%)	2 (7%)	3 (15%)
More than One Race	7 (18%)	1 (4%)	0 (0%)
Not Reported	4 (10%)	0 (0%)	2 (10%)
Household Income			
\$0 – \$15,000	1 (3%)	2 (7%)	1 (5%)
\$15,001 – \$35,000	4 (10%)	4 (15%)	4 (20%)
\$35,001 – \$75,000	12 (31%)	5 (18%)	4 (20%)
\$75,001 – \$150,000	9 (23%)	7 (26%)	7 (35%)
Over \$150,000	6 (15%)	1 (4%)	2 (10%)
Not Reported	7 (18%)	8 (30%)	2 (10%)
Maternal Education Level			
Less Than High School	2 (5%)	0 (0%)	0 (0%)
High School Degree	2 (5%)	4 (15%)	0 (0%)
Associates Degree	2 (5%)	2 (7%)	4 (20%)
Some College	6 (15%)	6 (22%)	0 (0%)
Bachelor's Degree	10 (26%)	6 (22%)	6 (30%)
More Than Bachelor's Degree	14 (36%)	9 (33%)	10 (50%)
Not Reported	3 (8%)	0 (0%)	0 (0%)

Table 3

Participant Descriptive Information at 24 Month Assessment

	FXS <i>n</i> = 15	High-Risk Siblings <i>n</i> = 20	Low-Risk Infants <i>n</i> = 15
Nonverbal Composite	25.26 (5.61)	44.99 (8.04)	49.60 (7.41)
ADOS-T CSS	5.93 (3.15)	4.05 (2.76)	1.53 (0.74)

Note. ADOS-T CSS = Autism Diagnostic Observation Schedule, Toddler Module Calibrated Severity Scores. Nonverbal Composite score is calculated by averaging the MSEL Visual Reception and Fine Motor domains, and has a $M = 50$ and $SD = 10$. ADOS-T CSS ranges from 1–10, with low scores indicating low ASD symptomatology and high scores indicating severe ASD symptomatology.