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Language Performance in Preschool-Aged Boys with Nonsyndromic Autism Spectrum Disorder or Fragile X syndrome

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Abstract

In the present study, language performance on standardized assessments (e.g., overall verbal performance, receptive and expressive vocabulary) and spontaneous language produced in play was compared between preschool-aged boys with autism spectrum disorder ($_{n}$ASD, $n = 25$) and boys with fragile X syndrome (FXS, $n = 16$). At the group-level, we observed weaknesses in the language skills of boys with $_{n}$ASD relative to those with FXS (e.g., when considering raw score performance, standard score performance relative to nonverbal cognitive skills, frequency of talk in play), after controlling for nonverbal IQ and ASD symptom severity. Moreover, although individually most children in both groups demonstrated language delays relative to CA-expectations, language delays relative to nonverbal level-expectations were more common in boys with $_{n}$ASD.

Keywords

Autism Spectrum Disorder; Fragile X Syndrome; Language/Communication

INTRODUCTION

Current estimates indicate that autism spectrum disorder (ASD) affects 1 in 59 children in the United States, making it one of the most commonly occurring neurodevelopmental disorders (Baio et al., 2018). Importantly, ASD is characterized by considerable heterogeneity at every level of description, likely reflecting a complex interplay of both biological and environmental risk factors (Pelphrey, Shultz, Hudac, & Vander Wyk, 2011; Uljarević, Baranek, Vivanti, Hedley, Hundry, & Lane, 2017). Although ASD arises predominantly from unknown causes (Baio, 2012), recent work has led to the identification of multiple etiological and pathophysiological substrates underling this disorder, with an estimated 10 – 20% of individuals with ASD having an identified genetic etiology (e.g., Betancur, 2011; Abrams & Geschwind, 2008; Jeste & Geschwind, 2014). In terms of

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phenotypic presentation, there is tremendous variation among individuals with ASD in the areas of adaptive functioning skills, cognitive and linguistic levels, and presence/severity of psychiatric comorbidities (e.g., Jones & Klin, 2009).

Moreover, considerable heterogeneity is observed across individuals with ASD in the characteristics considered core to the ASD phenotype. Consider, for instance, the fact that only a proportion of the behaviors implicated in the Diagnostic and Statistical Manual of Mental Disorders – 5th edition (DSM-5; APA, 2013) are required to meet ASD criteria in the restricted, repetitive behavior domain (APA, 2013). As another example, "abnormalities in eye contact," as well as "a total lack of facial expressions and nonverbal communication," are direct examples from the DSM-5 indicating the range of ways in which a person can present with a "deficit in nonverbal communicative behaviors used for social interaction (APA, 2013)." Research focused on characterizing this phenotypic variation associated with the ASD phenotype is vital to elucidate how best to maximize a child's potential for cognitive and functional success.

In the present study, we explored the similarities and differences in the language skills of boys with ASD, for whom a specific genetic etiology has not been identified (herein referred to as nonsyndromic ASD ($_{n}$ASD), and boys with fragile X syndrome (FXS), the most common monogenetic cause of ASD, during the preschool years. Because development reflects complex interactions across multiple factors, direct comparisons between the phenotypes of neurodevelopmental disorders with similar behavioral features will provide insight into common and different mechanisms shaping children's development. Thus, direct comparisons of the $_{n}$ASD and FXS phenotypes can be used to clarify the nature of language difficulties observed in individuals with these disorders and provide insight into the vulnerabilities associated with language development more generally. Additionally, these types of comparisons will contribute critical information for intervention planning for both groups of children and will provide additional insight into the similarities and differences between the $_{n}$ASD and FXS phenotypes more generally.

Language Difficulties Associated with $_{n}$ASD

Using the diagnostic criteria presented in the DSM-5, individuals diagnosed with $_{n}$ASD demonstrate two fundamental features: (1) clinically significant and persistent impairments in social communication and social interaction skills and (2) a tendency to engage in restricted, repetitive patterns of behavior, interests, or activities (APA, 2013). One of the major changes in the DSM-5 (APA, 2013), relative to its predecessor the DSM-IV-TR (APA, 2000), involved removing "language and communication" difficulties as a primary, independent domain and instead, integrating social interaction difficulties and communication difficulties into a single, conjoined area of difficulty. Indeed, it is true that language difficulties are closely intertwined with social difficulties; however, this does not mean these skills reflect the same construct or negate the importance of investigations of language development in children with $_{n}$ASD. Although there are some individuals with $_{n}$ASD who demonstrate structural language skills (e.g., semantics, syntax) that are consistent with their chronological age (CA) expectations, most individuals with $_{n}$ASD have difficulty acquiring language (e.g., Boucher, 2012; Kjelgaard & Tager-Flusberg, 2001; Klinger et al.,

2002; Weismer, Lord, & Esler, 2010). Moreover, the nature of language difficulties in children with $_{n}$ASD extend beyond a difficulty in using language for social purposes.

It is currently estimated that at least half of children with $_{n}$ASD who acquire spoken language demonstrate difficulties relative to CA- and /or nonverbal cognitive level expectations in structural language skills such as vocabulary and grammar during the school-age years or later (e.g., Boucher, 2012; Kjelgaard & Tager-Flusberg, 2001; Klinger et al., 2002). Furthermore, it is currently estimated that around 30% of children with $_{n}$ASD still demonstrate limited spoken language skills by the time they reach the school-age years (e.g., Tager-Flusberg & Kasari, 2013). Indeed, even though there is considerable variation in the development of language among children with $_{n}$ASD, language delays are often the first recognizable symptom of developmental difficulties for children with $_{n}$ASD (e.g., Boucher, 2012; Tager-Flusberg et al., 2009; Talbott et al., 2015). To this regard, results from retrospective studies have identified weaknesses in language and gesture use as early as 12 months of age (e.g., Colgan et al., 2006; Werner et al., 2000). For children with $_{n}$ASD who acquire functional speech, first words emerge around 24 months of age or later (versus 12 months for TD children) and phrases emerge around 48 months of age or later (versus 18 – 23 months for TD children; Mitchell et al., 2006; Rose et al., 2016; Tager-Flusberg, Paul, & Lord, 2005; Weismer & Kover, 2015). Finally, prospective studies of infants at high risk for $_{n}$ASD (i.e., infants who have an older sibling with an $_{n}$ASD diagnosis) have documented language delays apparent within the first year of life for infant siblings who are later diagnosed with $_{n}$ASD themselves (e.g., Mitchell et al., 2006; Ozonoff et al., 2010; Paul et al., 2011; Rozga et al., 2011).

There is a paucity of work considering structural language performance in $_{n}$ASD relative to children with other neurodevelopmental disorders or developmental delays. Multiple investigators have reported a subgroup of children with $_{n}$ASD as having language difficulties resembling those observed for children with specific language impairment (SLI). This has led some researchers to posit shared underpinnings between these two disorders (e.g., Tager-Flusberg & Joseph, 2003; Tomblin, 2011); however, this hypothesis remains controversial, with other researchers noting linguistic differences across the two conditions and arguing that the similarities observed are superficial (e.g., Taylor et al., 2014; Williams et al., 2008). In addition, results from early research considering the language skills of children with $_{n}$ASD relative to children with other developmental delays suggest more severe language difficulties in $_{n}$ASD relative to other populations (e.g., Lord, Pickles, DiLavore, & Shulman, 1996; Sigman & Ruskin, 1999; Weismer, Lord, & Esler, 2010). For example, Weismer, Lord, & Esler (2010), considered the early language patterns of toddlers with $_{n}$ASD (n = 257) to toddlers with developmental delay (n = 69). Although considerable variability was observed, toddlers with $_{n}$ASD were found to demonstrate significant delays in language performance based on CA-level expectations. Furthermore, with respect to nonverbal cognitive level, language in toddlers with $_{n}$ASD was significantly delayed. In contrast, the toddlers with DD demonstrated language skills that were roughly commensurate with their nonverbal cognitive levels.

Despite the frequent occurrence of language difficulties, much remains to be understood regarding the development of structural language skills in children with $_{n}$ASD. This is likely,

in part, because the significant heterogeneity in the language skills amongst individuals with $_{n}$ASD increases the complexity of understanding language skills both clinically and theoretically. Disentangling this complexity in language development should be a key focus for current research. Structural language skills facilitate achievements in other developmental domains, such as the abilities to socialize or to develop cognitively (Homer & Tamis-LeMonda, 2005; Vygotsky, 1986; Waxman & Markow, 1995), and are central to a wide range of positive long-term outcomes (e.g., independent living, maintaining employment, establishing and sustaining interpersonal relationships; Clegg, Hollis, Mawhood, & Rutter, 2005; Hartley et al., 2011). Thus, understanding language skills in individuals with $_{n}$ASD not only can elucidate the nature of language development of children, but also can inform treatment planning, which over time can improve adult outcomes. In this study, we use a direct comparison of early language skills in boys with $_{n}$ASD and boys with FXS during the preschool period to help clarify the nature of language difficulties associated with $_{n}$ASD.

The FXS-ASD comorbidity—FXS is a neurodevelopmental disorder resulting from a trinucleotide (CGG) expansion in the *FMR1* gene, which is located on the X chromosome (Oostra & Willemson, 2003). FXS is both the most common single-gene cause of ASD and the leading inherited cause of intellectual disability. The trinucleotide expansion observed in FXS leads to the significant reduction or complete absence of the protein, FMRP (fragile X mental retardation protein), which is known to be involved in experience dependent learning and neural plasticity (Bassell & Warren, 2008). The behavioral features associated with the FXS phenotype are more pronounced in males, because of the protective presence of an unaffected X chromosome, which continues to produce FMRP, and the process of X inactivation in females (Loesch et al., 2004; Tassone et al., 1999; Ligsay & Hagerman, 2016; Stembalska et al., 2016). Most males with FXS present with intellectual disability (Hessl et al., 2009). Not surprisingly, language difficulties are also common in males with FXS. As is observed for most children with $_{n}$ASD, early expressive language is delayed relative to CA-expectations in males with FXS (e.g., Kover, McCary, Ingram, Hatton, & Roberts, 2015; Roberts, Mirrett, & Burchinal, 2001), and estimates suggest that up to 30% of individuals with FXS still demonstrate limited spoken language skills into adolescents (e.g., Levy, Gottesman, Borochowitz, Frydman, & Sagi, 2006). Language delays are also observed relative to achievements in nonverbal cognition, although data suggests that this varies as a function of language domain and the developmental period considered (see Abbeduto et al., 2017 for review).

Research to date has pointed to several behavioral similarities between the $_{n}$ASD and FXS phenotypes. To begin, nearly all males with FXS display behavioral features that are akin to those typically associated with the $_{n}$ASD phenotype. Examples of these behavioral features include perseverative and noncontingent speech (e.g., Belser & Sudhalter, 2001; Martin, Roberts, Helm-Estabrooks, Sideris, Vanderbilt, & Moskowitz, 2012; Sudhalter & Belser, 2001; Murphy& Abbeduto; 2007); restricted and repetitive behaviors, such as hand/finger and other complex mannerisms (e.g., Oakes et al., 2016); and unusual eye contact (e.g., Cohen et al., 1988; Watson et al., 2008). The occurrence of these symptoms is frequent and severe enough to warrant a comorbid diagnosis of ASD in as many as 60% of males with

FXS, when utilizing gold standard diagnostic instruments (e.g., Budimirovic and Kaufmann, 2011; Clifford et al., 2007; Harris et al., 2008; Kaufmann et al., 2004, 2008, 2017; Klusek, Martin, & Losh, 2014; McDuffie et al., 2010). There has been considerable variability, however, in these estimates across studies (Demark, Feldman, & Holden). Other behavioral similarities between the FXS and $_{n}$ASD phenotypes include increased risk of challenging behaviors (Hall, Barnett, & Hustyi, 2016; Chandler et al., 2016), hyperactivity/inattention (e.g., Baumgardner et al., 1995; Thurman et al., 2014), and anxiety (e.g., Cordiero et al., 2011; de Bruin, Ferdinand, Meester, Nijs, & Verheij, 2007; Gevik, Eldevik, Fjæran-Granum, & Sponheim, 2011; Leyfer et al., 2006).

Given these similarities, it seems to follow that neurobiological similarities may also be observed across these phenotypes. To this regard, recent studies (Issofov et al., 2012) have noted that a significant number of the ASD susceptibility genes identified to date are controlled by FMRP, such as SH3 and multiple Ankyrin repeat domains (SHANK) and mammalian target of kinase (PAK). Abnormalities in the GABAergic signaling system have also been implicated in both FXS and $_{n}$ASD (Coghlan et al., 2012), which can interfere with synaptic development and plasticity (e.g., Iossifov et al., 2014; Steinberg & Webber, 2013). Moreover, the actions of many of the ASD susceptibility genes identified to date are controlled by FMRP, further reinforcing the links between FXS and $_{n}$ASD.

In conjunction with these commonalities, developmentally important phenotypic differences have been noted between $_{n}$ASD and FXS (Abbeduto et al., 2014). First, at the group level, the severity of ASD observed in FXS is generally milder than is observed in individuals with $_{n}$ASD, even when only considering children with FXS who meet diagnostic criteria for ASD (e.g., McDuffie et al., 2015; Wolff et al., 2012). Additionally, there is also evidence to suggest between-group differences in the behavioral features correlated with ASD symptom severity (Thurman et al., 2015). Thus, there may be notable differences in the paths by which the similarities observed across these two conditions come to develop. To this regard, there is a growing body of literature suggesting differences in the developmental mechanisms underlying behavioral features commonly observed in both phenotypes but not central to a diagnosis of ASD, such as anxiety and language development (Thurman et al., 2014; Thurman et al., 2015).

Comparisons of Language Skills between Nonsyndromic ASD and Fragile X Syndrome—Early delays in communication are apparent in both children with $_{n}$ASD and children with FXS (Abbeduto et al., 2007; De Giacomo & Fombonne, 1998) and continue to be an area of challenge across the lifespan, at least in individuals with co-occurring intellectual disability (Hartley et al., 2011; Howlin et al., 2014). Moreover, both conditions are characterized by difficulties initiating and responding to the social cues of their interactive partners as well as by increased risk for the presence of maladaptive behaviors that have the potential to negatively impact learning (e.g., Abbeduto, McDuffie, & Thurman, 2014; Thurman, McDuffie, Hagerman, & Abbeduto, 2014).

To date, few studies have been done directly comparing structural skills and/or profiles between children with $_{n}$ASD and children with FXS. In the first study, McDuffie et al. (2013) examined fast-mapping (a word learning process in which children rapidly infer a

correspondence between a novel label and a speaker's intended referent) using a paradigm in which the examiner used a variety of attention-directing cues to direct and maintain the child's attention to the novel object while the examiner was labelling it. The authors found that boys with FXS demonstrated better performance than did boys with $_{n}$ASD, despite having lower levels of nonverbal cognitive ability, when considering the mean number of correct word learning trials and standardized measures of both receptive and expressive vocabulary ability. That said, the number of boys who successfully learned all the target words did not differ across the samples. Finally, for boys with FXS, but not $_{n}$ASD, performance on the word learning task was significantly associated with concurrent receptive and expressive vocabulary performance as well as nonverbal cognitive ability. In general, results from McDuffie et al., provide some insight into lexical skills in both boys with $_{n}$ASD and boys with FXS. However, it is important to note that the ASD severity scores for the boys with FXS were significantly lower than those for the boys with $_{n}$ASD. Because the authors did not factor this difference into the between-group comparisons conducted; it is not clear whether the differences observed reflect word learning difference or just differences in ASD severity levels.

Thurman et al. (2017), in a partially overlapping sample to those reported by McDuffie et al., more explicitly explored the similarities and differences in the lexical and grammatical skill of boys with FXS (n = 51) and boys with $_{n}$ASD (n = 36) between 4 and 10 years of age who presented with nonverbal IQ scores less than or equal to 85. Results from this study identified important differences between the two conditions in terms of both the language profile associated with each condition and the factors associated language performance. More specifically, Thurman et al. observed vocabulary skills to be a strength, relative to nonverbal cognitive level performance, in boys with FXS. For boys with $_{n}$ASD, vocabulary performance was consistent with nonverbal cognitive performance levels. This pattern of performance remained even after restricting the FXS sample to only those participants who also met criteria for a comorbid diagnosis of ASD. Further analyses done revealed a lexical weakness, when using raw-scores (due to floor effects), for boys with $_{n}$ASD, relative to boys with FXS after controlling for the effects of CA, nonverbal IQ, and severity of ASD symptomatology. Moreover, investigators were able to account for a smaller proportion of the variance in lexical performance for boys with $_{n}$ASD than for the boys with FXS. Finally, differences were observed across the two groups in terms of the predictors of language performance. For boys with $_{n}$ASD nonverbal cognition was found to be the strongest predictor of lexical performance; in contrast, CA was the strongest predictor of lexical performance for boys with FXS. In addition, severity of ASD symptomatology was found to be a significant predictor of lexical performance for boys with FXS but not boy with $_{n}$ASD. It remains unclear however, if this difference is observable in younger children. Because research suggests that language acquisition prior to the age of 5 years is associated with better outcomes for individuals with $_{n}$ASD (e.g., Venter, Lord, and Schopler, 1992), this is an important next step to take.

Recently, Sterling (2018) conducted a comparison of grammar skills between boys with $_{n}$ASD (mean CA = 13.40, SD = 2.00) and boys with FXS with a comorbid diagnosis of ASD (FXS+ASD; mean CA = 12.12 SD = 2.17) who were matched on MLU (ASD: mean = 4.60; FXS+ASD: mean = 3.78; p = .272; d = .37; *variance ratio* = 0.58). Sterling found that boys

with $_{n}$ASD performed significantly better than did boys with FXS+ASD on the norm-referenced assessment of the use of the auxiliary verb “to be.” In addition, consideration of effect sizes demonstrated better performance by the participants with $_{n}$ASD relative to the boys with FXS+ASD on past tense probes on an assessment of sentence imitation skills and on a standardized assessment considering the use of the auxiliary verb “to do.” Importantly, although the two groups were matched on mean length of utterance, nonverbal cognitive skills were significantly stronger for boys with $_{n}$ASD (M = 71.22, SD = 19.88) than for the boys with FXS+ASD (M = 48.89, SD = 8.09). Thus, this data also suggests, broadly, that individuals with FXS may have an advantage in language learning relative to those with $_{n}$ASD relative to their nonverbal cognitive skill level; that is, language abilities seem to fall behind level of nonverbal cognitive ability for those with $_{n}$ASD more so than for those with FXS.

Present Study—In the present study, we sought to expand our understanding of language performance in $_{n}$ASD by considering the similarities and differences in the language skills of boys with $_{n}$ASD and of boys with FXS during the preschool period, a period during which many children with developmental delays are transitioning across the early stages of spoken language development. More specifically, we used multiple analytic approaches to consider whether previous findings of a language weakness in $_{n}$ASD relative to boys with FXS was observable during the preschool years. In addition, we considered children’s language performance on standardized tests that provide an omnibus measure of language ability and measures of both receptive and expressive vocabulary specifically. Moreover, we consider children’s spontaneous use of single-word and multi-word utterances in a less-structured, naturalistic play interaction with a caregiver.

To begin, we conducted preliminary analyses to determine whether prior findings by Thurman et al. (2017) indicating a weakness, at the group-level, in boy with $_{n}$ASD relative to boys with FXS in raw score language performance after controlling for the effects of CA, nonverbal IQ and ASD symptom severity could be replicated during the preschool years. We then considered the following primary aims:

1. To determine whether boys with $_{n}$ASD demonstrated a weakness, at the group-level, relative to boys with FXS in standard score language performance after controlling for the effects of CA, nonverbal IQ and ASD symptom severity. We hypothesized that boys with $_{n}$ASD would indeed demonstrate a weakness in language performance relative to boys with FXS.
2. To determine whether boys with $_{n}$ASD demonstrate a weakness, at the group-level in language performance relative to boys with FXS when considering the amount of difference between standard score performance between the nonverbal cognitive and verbal domains. We hypothesized that boys with $_{n}$ASD would indeed demonstrate a weakness in language performance relative to boys with FXS.
3. To evaluate whether a weakness in language performance, relative to nonverbal cognitive performance or CA, was, at the individual-level, more commonly observed in boys with $_{n}$ASD than in boys with FXS. We hypothesized that a

greater proportion of boys with nASD than boys with FXS would be characterized as having weakness in the language than boys with FXS.

4. To determine whether the correlates of language performance (i.e., CA, NVIQ, and severity of ASD symptomatology in the social affective and restricted and repetitive behavior domains) are similar between boys with nASD and boys with FXS. We hypothesized that there may be differences in the developmental factors predicting language abilities between these two conditions.

METHOD

Participants

Participants were 16 males with FXS and 25 males with nASD between the ages of 3.50 and 5.50 years of age who were drawn from a longitudinal study examining early language abilities in preschoolers with nASD or FXS. Participants were recruited nationally through the help of the [removed for blinding]. Due to the higher prevalence rate, participants with nASD were more likely to reside locally than were those with FXS. Participants were also recruited using parent listservs, social media sites, advertisements by the National Fragile X Foundation, and through clinics and preschools specialized in working with children with neurodevelopmental disorders. The following inclusion criteria, based on parent report, were utilized in the larger project: (a) male aged 36 – 66 months at Time 1, (b) children for whom English is the primary language of exposure; (e) no sensory or physical impairments that would limit participation in project activities; and (f) must have no medical conditions that precludes participation (e.g., severe and frequent seizures) that prevent them from meeting the demands of the testing protocol. In addition, participants reported by parents to be of above average intellectual ability (parent report or prior documentation of IQ greater than 110 or greater) were not included in the present project as nearly all males with FXS demonstrate cognitive skills in the low average to intellectual disability range. Approval from the Institutional Review Board, as well as parental informed consent, was obtained.

Documentation of a diagnosis of *FMR1* full mutation (i.e., >200 CGG repeats, with or without mosaicism) was required and obtained for all participants with FXS. For participants with nASD, families provided documentation of an existing community diagnosis of ASD. This diagnosis was confirmed through administration of the Autism Diagnostic Observation Schedule-2 (ADOS-2; Lord, Rutter, DiLavore, Risi, Gotham, & Bishop, 2012). Project staff who administered the ADOS had completed research reliability training.

Descriptive statistics for the samples are presented in Table 1. Participants with FXS and participants with nASD differed significantly in terms of nonverbal IQ ($U = 94.00$, $z = 2.83$, $p = .004$, $r = .46$, $s^2ratio = 1.41$). Analyses indicated that the two groups did not differ significantly on CA ($U = 183.00$, $z = -0.45$, $p = .65$, $r = .05$, $s^2_{ratio} = 1.09$) or on overall ASD symptom severity ($U = 132.50$, $z = 1.27$, $p = .21$, $r = .24$, $s^2_{ratio} = 0.61$). Direct assessment of ASD symptom severity was available for 14 of the 16 males with FXS; these results indicated that all but 2 of those assessed earned an ASD severity score in the ASD classification range. For participants with FXS, the racial/ethnic composition of the sample was 25% Hispanic, with 6% Black/African American, 67% Caucasian, and 25% Multi-

racial. For the participants with $_{n}$ASD, the racial/ethnic composition of the sample was 32% Hispanic, with 4% Asian, 8% Black/African-American, 64% Caucasian, 20% Multi-racial, and 4% preferring not to answer. Data regarding highest education reported in each household are presented in Table 2.

Measures

Differential Ability Scales – II Upper Level Early Years (DAS-II; Elliott, 2007a, b).—The DAS-II Upper Level Early Years provides an assessment of general intellectual functioning for children aged 3 ½ - 8 years and was designed to provide specific information about an individual's strengths and weaknesses across a wide range of intellectual activities. This battery has six core subtests measures verbal skills (i.e., verbal comprehension and naming vocabulary), nonverbal reasoning skills (i.e., picture similarities and matrices), and nonverbal spatial skills (i.e., pattern construction and copying). The DAS-II yields standard scores (SSs) with a general-population mean of 100, and SD of 15. The DAS-II also yields T-scores for each subtest, with a general-population mean of 50 and SD of 10. The Special Nonverbal Composite, which reflects nonverbal cognition using both nonverbal reasoning and nonverbal spatial subtests was used to assess overall nonverbal IQ. Performance on the verbal subtests as well as the overall Verbal Cluster standard score was also considered in analyses.

Peabody Picture Vocabulary Test – 4th edition (PPVT-4; Dunn & Dunn, 2007).—The PPVT-4 is an individually administered measure of receptive vocabulary for children and adults aged 2 ½ to 90 years and older. The general population mean for the SS is 100, with a SD of 15 and a floor of 20. Administration of the Version A and Version B were alternated across participants in each group; thus, approximately half of the participants in each group received Version A and half of the participants received Version B of this measure.

Expressive Vocabulary Test – 2nd edition (EVT-2; Williams, 2007).—The EVT-2 is an individually administered measure of expressive vocabulary for children and adults aged 2 ½ to 90 years and older. The mean for the general population SS is 100, with a SD of 15 and a floor of 20 beginning at age 4 years 4 months. The EVT-2 was co-normed with the PPVT-4 to provide a thorough evaluation of both receptive and expressive vocabulary attainment. Administration of the Version A and Version B were alternated across participants in each group; thus, approximately half of the participants in each group received Version A and half of the participants received Version B of this measure.

Play Session - Language Indicator Score (modification of Expressive Communication Indicator reported by Luze et al., 2001).—Children participated in a 20-minute semi-structured play session with a caregiver (Communication Play Protocol; Adamson et al., 2009). These samples were used as the context for coding child communication acts based on the coding procedures outlined by the Expressive Communication Indicator (ECI; Carta et al., 2010). In this coding system, four key communicative elements are considered representing prelinguistic language domain (gestures, vocalizations) and spoken language domain (single word and multiple word

utterances). This method has been shown to be a reliable (reported 90% interobserver agreement) metric for typically developing children from birth to three years of age (Luze et al., 2001). Moreover, this method of assessing communication skills has been found to be significantly associated with both direct and parent report measures of child communicative ability, demonstrates sensitivity to change over time, and has been shown to be a useful method of assessing communication in children with developmental disabilities (e.g., Greenwood, Carta, Walker, Hughes, & Weathers, 2006; Greenwood, Walker, Buzhardt, 2010; Luze et al., 2001; Yoder et al., 2009).

Of primary interest for this report were the two key communicative elements representing the spoken language domain (i.e., occurrence of single word and multiple word utterances). Trained observers coded the Play Sessions using the Behavioral Observation Research Interactive Software (Friard & Gamba, 2016). Coders segmented all participant talk into C-units, which is preferred when assessing spoken language skills as it provides a more objective criteria, relative to utterances, and avoids overestimating language ability(Abbeduto et al., 2014). C-units are defined as an independent clause and any of its modifiers, which can include dependent clauses (Abbeduto et al., 2014). The weighted frequency of single word (1 point) and multiword (2 points) utterances within the play sessions were computed to generate an overall Language Indicator Score, indicative of overall spoken language skills. Intraclass Correlation Coefficient (ICC) estimates and their 95% confidence intervals were computed, for 12% of the sample, based on a mean-rating (k=2), absolute-agreement, 2-way mixed effects model. Results indicate excellent reliability for the language indicator score (ICC = .99; 95% confidence interval, .97 – 1.00), which is the metric considered in analyses.

Autism Diagnostic Observation Schedule-2.—The ADOS-2 (Lord, Rutter, DiLavore, & Risi, 2007) is a semi-structured play-based interaction in which a trained examiner creates specific interactive contexts to observe reciprocal social interaction skills as well as the presence of repetitive behaviors. One of four ADOS modules is administered based upon the participant's expressive language level. In the current project, participants received modules 1 or 2. The Comparison Score, an indicator of overall ASD severity level, as well as the domain severity scores (Hus, Gotham, & Lord, 2014) were utilized in analyses. Within the present study, 28 Module 1s (10 FXS, 17 $_{n}$ASD) and 12 Module 2s (4 FXS, 8 $_{n}$ASD) were administered. Examiners who had achieved standard research reliability training standards on the ADOS-2 administered ADOS-2 sessions in the present project. Ten percent of the administrations were randomly selected to assess reliability. Mean agreement for the algorithm items was 94.30%.

Analysis—Preliminary analyses were conducted to determine if prior findings reported by Thurman et al. (2015) indicating a strength in raw score language performance by the participants with FXS relative to their peers with $_{n}$ASD was observable during the preschool years, after controlling for the effects of CA, nonverbal IQ, and ASD symptom severity. Floor effects prevented the authors from using preferred standard score metrics. To consider the aims of the present study, multiple analytic approaches were then used in the present project to consider the similarities and differences in standard score language performance

between preschool-aged boys with $_{n}$ASD and boys with FXS, with analyses focusing at both the group-level and the individual level.

At the group level, we used two approaches to examine between group differences in standard score language performance and language performance when playing with a caregiver. We predicted that males with FXS would demonstrate a verbal advantage relative to males with nASD; thus, one-tail analyses were conducted. In the first set of analyses (Aim 1), we conducted a series of multiple regression analyses to evaluate whether boys with FXS demonstrated an advantage relative to boys with $_{n}$ASD after controlling for the effects of CA, nonverbal IQ, and overall ASD symptom severity. In the second set of analyses (Aim 2), between-group comparisons were conducted utilizing differences scores representing the Nonverbal IQ standard score performance (DAS-II SNC SS) minus standard score performance on each standardized language measure (i.e., DAS-II Verbal SS, PPVT-4 SS, EVT-2 SS).

At the individual level, we sought to compare the proportion of children in each diagnostic group classified as demonstrating a verbal weakness relative to both CA and to nonverbal cognitive level (Aim 3). To achieve this goal, we computed a difference score representing the differences between children's DAS-II Nonverbal Reasoning standard score and DAS-II Verbal standard score. These values were then compared to the DAS-II norming tables, which specify the magnitude of a between-cluster standard score difference required for statistical significance. Using this information, we identified the children for whom their SS performance on the Verbal domain was significantly weaker than their standard score performance on the Nonverbal Reasoning domain. To consider the delays relative to CA-expectations, the proportion of children in each diagnostic group who earned a SS ≤ 75 on the DAS-II, PPVT-4, and EVT-2 were considered.

Finally, we considered the correlates of within-syndrome variation in language performance for children in both diagnostic groups (Aim 4). For both diagnostic groups, we used Pearson correlation coefficients to consider the concurrent relations between language performance and CA, NVIQ, and ASD symptomatology (i.e., severity of both social affective symptomatology and restricted and repetitive behaviors).

RESULTS

Descriptive statistics for performance on the standardized language measures and for the Play Session - Language Indicator Score were computed and are presented in Table 3.

Preliminary Analyses

Preliminary analyses were conducted to determine if, in our younger sample of boys with $_{n}$ASD or FXS, we could replicate prior findings reported by Thurman et al. (2015) indicating a strength in raw score-level language performance by the participants with FXS relative to their peers with $_{n}$ASD. We considered whether diagnostic group was a significant predictor of raw score level performance on multiple standardized measures of language ability. All regression models were significant with diagnostic group emerging as a significant unique predictor for DAS-II Verbal Comprehension ability score (p = .02,

$\eta^2_{partial}$ = .11), DAS-II Naming Vocabulary ability score (p = .03, $\eta^2_{partial}$ = .10), PPVT-4 growth score (p = .02, $\eta^2_{partial}$ = .13), and EVT-2 growth score (p = .014, $\eta^2_{partial}$ = .09). In all models, scores for boys with FXS were significantly higher than scores for boys with $_n$ASD after controlling for CA, nonverbal IQ, and ASD symptom severity (regression model data not presented here but available from the authors).

Diagnostic Group as a Predictor of Language Performance

First, we conducted a series of multiple regression analyses to evaluate whether preschool-aged boys with $_n$ASD demonstrated a disadvantage relative to boys with FXS in standard score language performance after controlling for the effects of CA, nonverbal IQ, and overall ASD symptom severity (Table 4). The regression models considering performance on the DAS-II Verbal Comprehension subtest, $F(4, 38) = 12.07$, $p < .001$, with an $R^2_{adjusted}$ value of .54, and DAS-II Naming Vocabulary subtests, $F(4, 38) = 10.65$, $p < .001$, with an $R^2_{adjusted}$ value of .50, were significant. Results indicated that boys with FXS earned T-scores that were approximately 5 points higher than boys with $_n$ASD, for both Verbal Comprehension (p = .07, one-tailed) and Naming Vocabulary (p = .09, one-tailed). These numbers suggest that diagnostic group accounted for approximately 5 – 6% of the variance in language performance independently, which was not enough to meet criterion for a significant difference when CA, nonverbal IQ, and ASD symptom severity were held constant. In this, and all other analyses, the same pattern of findings were observed when regression models included only the males with FXS who earned ASD severity scores in the clinical range.

The regression model assessing receptive vocabulary performance as measured by standard scores from the PPVT-4 was also significant (Table 4; $F(4, 37) = 12.72$, $p < .001$, $R^2_{adjusted}$ = .56). In this model, diagnostic group was a significant predictor even when CA, nonverbal IQ, and ASD symptom severity were included in the model (Table 4). Diagnostic group accounted for 9% of the variance in PPVT-4 standard scores uniquely, with boys with FXS having scores approximately 12 points higher than boys with $_n$ASD (p = .04), when CA, nonverbal IQ and ASD symptom severity were held constant. Finally, on the EVT-2 (Table 4), the combination of variables considered in the present project did significant predict standard score performance, $F(4, 38) = 14.84$, $p < .001$, with an $R^2_{adjusted}$ value of .59. We observed that the boys with FXS demonstrating an approximate 9-point standard score advantage, with diagnostic group accounting for 6% of the variance in EVT-2 standard scores uniquely, however this was not enough to meet criterion for a significant difference, when CA, nonverbal IQ, and ASD symptom severity were held constant (p = .07, one-tailed).

In addition, we considered whether preschool-aged boys with FXS demonstrated an advantage relative to boys with $_n$ASD on Play Session-Language Indicator score after controlling for the effects of CA, nonverbal IQ, and overall ASD symptom severity (Table 4). Results demonstrated that the model was indeed significant (Table 4; $F(4, 38) = 9.31$, $p < .001$, $R^2_{adjusted}$ = .47). Moreover, diagnostic group accounted for approximately 20 % of the variance in Play Session-Language Indicator scores uniquely, with boys with FXS demonstrating scores approximately 100 points higher than boys with $_n$ASD (p = .004, one-

tailed) when CA, nonverbal IQ, and ASD symptom severity were held constant. Follow-up analyses were conducted to unpack this finding by considering between-group differences in the production of both single word and multiple word utterances. Results of these analyses demonstrate the same pattern of performance with diagnostic group accounted for 15.84% of the variance in number of single word utterances (unstandardized B = 37.93, SEB = 14.98, β = .41, $\eta^2_{partial}$ =.214, p = .008, one-tailed) and 13.47% of the variance in the number of multiple word utterances produced (unstandardized B = 37.83, SEB = 16.46, β = .37, $\eta^2_{partial}$ =.214, p = .01, one-tailed), when the influences of CA, Nonverbal IQ, and ASD severity were held constant.

Across all models, Nonverbal IQ was consistently observed to be the strongest independent predictor of language performance, accounting for 40 – 50% of the variance in models. CA was observed to be an independent predictor of the Play Session-Language Indicator score and the total number of utterances produced in the play session. ASD severity was not observed to be a significant unique predictor of language performance on any of the models considered.

Diagnostic Group as a Predictor of Nonverbal-Verbal Performance Difference Scores

Between-group comparisons were then conducted utilizing scores representing the differences between overall Nonverbal IQ standard score performance and standard score performance on each standardized language measure (i.e., DAS-II Nonverbal IQ minus DAS-II Verbal SS, DAS-II Nonverbal IQ minus PPVT-4 SS, DAS-II Nonverbal IQ minus EVT-2 SS). For the DAS-II Verbal SS (U = 90.50, z = −2.93, p = .002, one-tailed), the PPVT-4 SS (U = 89.00, z = −2.85, p = .002, one-tailed), and EVT-2 SS (U = 120.00, z = −1.89, p = .03, one-tailed) boys with FXS were observed to demonstrate better language skills relative to overall nonverbal IQ than boys with $_n$ASD. More specifically, as seen in Figure 1, boys with FXS demonstrated a mean Nonverbal IQ SS score that was 6.5 points lower than DAS-II Verbal SS, 10.94 points lower than PPVT-4 SSs, and 6.9 points lower than EVT-2 SSs on average. In contrast, boys with $_n$ASD demonstrated a mean Nonverbal IQ SS that was 6.2 points higher than their mean DAS-II Verbal SS, 4.25 points higher than mean PPVT-4 SSs, and 2.8 points higher than mean EVT-2 SSs on average.

Follow-up analyses were conducted, in the form of a series of multiple regression analyses, to evaluate whether to determine if these between group differences remained after controlling for the effects of overall ASD symptom severity. Models for differences scores utilizing both the DAS-II Verbal SS, F(2,38) = .426, p = .02, r^2_{adj} = .15, and the PPVT-4 SS, F(2,37) = 3.98, p = .03, r^2_{adj} = .14, were significant. Moreover, in both of these models, diagnostic group was a significant predictor even when ASD symptom severity was included in the model. More specifically, for the DAS-II Verbal SS, diagnostic group accounted for 19% of the variance in the difference scores, with boys with FXS a DAS-II Verbal SS advantage of 13.84 points relative to Nonverbal IQ SS performance (represented by a score of −13.84 when computing “Nonverbal IQ SS performance minus DAS-II Verbal SS performance”). For the PPVT-4 SS, diagnostic group accounted for 17% of the variance in the difference scores, with boys with FXS a DAS-II Verbal SS advantage of 14.47 points relative to Nonverbal IQ SS performance (represented by a score of −14.47 when computing

"Nonverbal IQ SS performance minus DAS-II Verbal SS performance"). Finally, for the EVT-2 SS, the overall model did not meet criterion for a significant prediction of language performance, $F(2,38) = 1.65$, $p = .21$, $r^2_{adj} = .03$.

Individual Level Performance as a Function of Diagnostic Group

Language performance for both boys with $_n$ASD and boys with FXS and were also considered at the individual level. First, we considered the proportion of participants in each diagnostic who demonstrated a delay relative to CA-expectations, defined as a standard score ≤ 75. As seen in Figure 2, the proportions varied slightly as a function of assessment, but generally was centered around 50% of the sample for both diagnostic groups.

Finally, using the guidelines provided in the DAS-II norming tables, which allows for the classification of a significant difference between standard score performance on the cluster domains (Verbal, Nonverbal Reasoning, and Spatial). As seen in Figure 3, when comparing the percent of participants classified as having a verbal weakness, a larger proportion of boys with $_n$ASD were classified as demonstrating a verbal weakness, indicated by the SS profile in which Verbal SS performance was significantly lower than Nonverbal Reasoning SS performance, a larger proportion of boys with $_n$ASD were classified as having a verbal weakness. Follow-up analyses were conducted for the boys with $_n$ASD to consider whether those classified as having or not having a language weakness differed from one another on other developmental measures. The two groups did not differ on CA, nonverbal reasoning, or ASD severity (see Table 5).

Correlates of Within-Syndrome Variation in Language Abilities

Finally, we considered the concurrent correlations between language performance and other child characteristics; specifically, CA, NVIQ, and ASD symptomatology. For both boys with $_n$ASD and boys with FXS, NVIQ was significantly correlated with language performance across all measures (see Table 6). In addition, for boys with FXS significant correlations were observed between ASD symptomatology in the form of severity of restricted and repetitive behaviors, and DAS-II Verbal Comprehension ability scores, PPVT-4 raw scores, and EVT-2 raw scores. These associations were not significant for boys with $_n$ASD; in fact, for DAS-II Verbal Comprehension ability scores ($z = -2.63$, $p = .004$) and EVT-2 growth scores ($z = -2.32$, $p = .01$), a significant difference in correlation strength was observed between the two diagnostic groups. Finally, the correlations between CA and ASD symptomatology in the form of social affective symptoms did not reach criterion for a significant association with language performance in either diagnostic group (see Table 6).

DISCUSSION

Although no longer considered a primary, independent symptom domain of ASD, most individuals with $_n$ASD have difficulty acquiring language. Difficulties in structural language skills (e.g., semantics, syntax) can negatively impact achievements in other domains (e.g., nonverbal cognition) as well as a wide range of long-term positive outcomes, such as independent living, maintenance of employment, establishment of interpersonal relationships (e.g., Vygotsky, 1986; Waxman & Markow, 1995; Clegg, Hollis, Mawhood, &

Rutter, 2005; Hartley et al., 2011). In fact, results of longitudinal studies of adult outcomes of $_{n}$ASD have found the most consistent predictor of adult independence to be structural language skills, particularly the development of "meaningful" spoken language before 5 years of age (Billstedt et al., 2007; Eaves & Ho, 2008; Howlin et al., 2004; Lord & Bailey, 2002). Thus, understanding language skills in individuals with $_{n}$ASD, particularly prior to the age of 5 years, not only can elucidate the nature of language development of children, but also can inform treatment planning, which over time can improve adult outcomes.

The specific aims of the present study, therefore, considered comparisons between the language skills of preschool-aged boys with $_{n}$ASD to preschool-aged boys with FXS. Not only are both conditions associated with difficulties acquiring language, they are also both associated with difficulties navigating reciprocal social interactions and at increased risk for behavioral difficulties likely to influence language learning negatively. Thus, direct comparisons of the language skills between $_{n}$ASD and FXS will inform our understanding of the factors shaping language development in these groups, which can be used to inform treatment planning. Moreover, this line of research will elucidate the similarities and differences between the $_{n}$ASD and FXS phenotypes more generally.

Comparisons of Language Performance between $_{n}$ASD and FXS

Results from the present study demonstrated that, even though structural language difficulties are not considered central to a diagnosis of ASD, preschool-aged boys with $_{n}$ASD demonstrated a weakness in language skills relative to their male peers with FXS. These findings are consistent with prior work considering language skills across these two neurodevelopmental disorders (e.g., Sterling, 2018; Thurman et al., 2017). The prior work done in this area has focused on school-age boys with $_{n}$ASD or FXS, most of whom demonstrating phrase level speech or higher. In contrast, most (70%) of the children in the present study were at an expressive language level consistent with the use of the ADOS-2 Module 1, which is designed for children who have speech abilities ranging from no speech at all up to and including the use of simple, but not consistent, phrases. Thus, the present study was unique in comparing language skills between boys with $_{n}$ASD and boys with FXS in the preschool years, a period of considerable variation in spoken language skills/level.

Preliminary analyses considering DAS-II Verbal Comprehension ability scores, DAS-II Naming Vocabulary ability scores, PPVT-4 growth scores, and EVT-2 growth scores demonstrated a verbal advantage for boys with FXS relative to boys with $_{n}$ASD across all metrics considered after controlling for between-group differences in CA, nonverbal IQ, and ASD symptom severity. Across these models, we found that diagnostic group accounted for 9 – 13% of unique variance in scores for these measures.

Results from primary analyses demonstrate significant differences in PPVT-4 SS performance between the two groups, favoring the FXS sample, and nonsignificant trends for the same pattern of findings on all other standard score measures. It is important to note that with our small sample sizes, we would expect statistical power to be sufficient to detect only large effects; thus, our findings indicating nonsignificant trends would be more likely to reach criterion for a statistical difference in studies with larger samples. Nonetheless, overall, standard scores ranged from 5 – 10 points lower for boys with $_{n}$ASD than boys with

FXS; diagnostic group accounted for 9% of unique variance in PPVT-4 SSs and 6% of unique variance in SSs for all other measures considered. Collectively, we see that during the preschool period, significant differences in raw score performance on standardized measures of language are observed between boys with $_{n}$ASD and boys with FXS, with these between-group raw score differences likely to contribute to small differences in standard score performance.

Moreover, when considering language performance measured during a play session with the caregiver, weighted scores for boys with $_{n}$ASD were 100 points lower than those for boys with FXS, which would be equivalent to producing 100 fewer single-word utterances or 50 fewer multiple-word utterances during the 20-minute sample. With this difference, diagnostic group accounted for approximately 20% of unique variance in language scores collected in the play session. Again, this was found after controlling for the effects of CA, nonverbal IQ, and ASD symptom severity.

Results did show that the standard score profile of language performance relative to nonverbal cognitive skills significantly differed between boys with $_{n}$ASD and boys with FXS. On all three language measures considered, boys with $_{n}$ASD, as a group, demonstrated verbal performance standard scores that lagged nonverbal standard score performance. In contrast, boys with FXS demonstrated the opposite profile, with nonverbal standard score performance lagging verbal standard score performance. Across all analyses the same pattern of findings were observed when the FXS sample was restricted to only boys with ASD severity scores in the clinical range.

We also found that, when considering language performance individually for both groups, most children demonstrated CA-level delays on the DAS-II ($_{n}$ASD: 56% versus FXS: 62.5%), PPVT-4 ($_{n}$ASD: 52% versus 50%), and EVT-2 ($_{n}$ASD: 40% versus 60%). However, our data suggests that boys with $_{n}$ASD are at greater risk than are boys with FXS of having a language weakness relative to their nonverbal cognitive ability, with 45% of our boys with $_{n}$ASD, versus 24% of our boys with FXS, earning a verbal standard score that was significantly lower than their Nonverbal Reasoning standard score on the DAS-II.

Correlates of Language Performance

Finally, we considered the correlates of language performance for both boys with $_{n}$ASD and boys with FXS. It should be acknowledged that the correlations are rather preliminary, given that with the small sample size we would expect statistical power to be sufficient to detect only large effects (see Cohen, 1988 or Looney 2018). That said, our data suggest that there are likely both similarities and differences across the two groups. For both boys with $_{n}$ASD and boys with FXS, despite the between group differences in overall nonverbal cognitive ability, and despite differences the language performance relative to nonverbal cognitive ability, language performance was strongly associated with advancements in nonverbal cognition. In contrast, our data suggests differences in the relation between severity of repetitive behaviors and some areas of language performance between the two groups. In our sample of boys with FXS, but not in boys with $_{n}$ASD, severity of restricted and repetitive behaviors was strongly and negatively associated with multiple measures of language performance. For boys with $_{n}$ASD, no significant associations were observed between the

language measures and severity of restricted and repetitive behaviors. Moreover, we found that the magnitude of the association between repetitive behaviors and language performance when considering raw score performance on the DAS-2 Verbal Comprehension subtest and growth scores on the EVT-2 significantly differed.

Although preliminary, this finding is consistent with prior reports of a between-group difference in the relation between language performance and restricted and repetitive behaviors (Thurman et al., 2015). Importantly, there is literature supporting a negative relationship between repetitive behaviors and language skills in young children with $_{n}$ASD (e.g., Paul, Chawarska, Cicchetti, Volkmar, 2008; Ray-Subramian & Weismer, 2012). Ray-Subramian & Weismer (2012), found that, in toddler with $_{n}$ASD, in addition to a significant relation between language and restricted and repetitive behaviors, gains in language skills predicted decreases in RRBs. The differences observed across projects may be due to the present study's use of the ADOS-2 RRB severity scores, which was specifically designed to limit the influence of developmental characteristics on ASD severity scores (Hus et al., 2014). Thus, it may be that the attempt to limit the influence of developmental characteristics on ADOS-2 severity scores was not generalizable to participants with FXS and/or that the negative association between language skills and severity restricted and repetitive behaviors is much stronger in FXS than it is in $_{n}$ASD.

Clinical Implications

In combination with findings from previous work (e.g., Thurman et al., 2017; Sterling, 2018; Weismer, Lord, & Esler, 2010; Rose, Trembath, Keen, & Paynter, 2016), our findings suggest that children with $_{n}$ASD are at greater risk for delays in language skills relative to their nonverbal cognitive abilities than children with FXS. Moreover, our findings indicate that most preschoolers with $_{n}$ASD demonstrate significant delays in languages skills relative to their CA and/or nonverbal cognitive level and, therefore, will require speech/language intervention to stimulate development in these domains, in addition to the standard recommendations for intervention targeting social communication skills or pragmatic language. For boys with FXS, even though only 24% of the sample was observed to demonstrate a language delay relative to their nonverbal cognitive level, most boys were found to demonstrate delays relative to CA-expectations. Research done by Roberts, Mirrett, & Burchinal (2001) suggested that during early development, for every month in CA, children with FXS gain .39 months in expressive language and .49 months in receptive language. Thus, boys with FXS are also in need of speech/language intervention to stimulate development in these domains.

In addition, our findings are important in demonstrating the need to consider the behavioral similarities and differences observed between the $_{n}$ASD and FXS phenotypes and even across children with the same condition more deeply. Even though neurobiological and behavioral similarities are observed across these two conditions, findings from the present study, and prior work in this area, suggests that there are differences in the factors shaping language development between $_{n}$ASD and FXS. Even though the present study controlled for differences in ASD severity between the two groups, children with $_{n}$ASD may still be disadvantaged relative to those with FXS in terms of reciprocal social interaction skills that

are likely to facilitate and support word learning. For example, McDuffie et al., (2015) found that even when matching individuals with $_{n}$ASD or FXS on overall severity of ASD symptomatology, boys with $_{n}$ASD still tended to demonstrate more severely affected scores on all social affective symptoms considered than did boys with FXS. Though not largely discrepant, these differences over time may still negatively influence word learning opportunities for boys with $_{n}$ASD. In addition, our data and previous work in this area suggests that nonverbal cognition may play a key role in language development for boys with $_{n}$ASD. Thus, identifying the specific cognitive skill and mechanisms supporting successful language learning in nASD may be critical for supporting optimal outcomes for this population.

It is not surprising that there is a growing body of research demonstrating differences in the mechanisms supporting development between boys with $_{n}$ASD and boys with FXS; neurodevelopmental disorders represent multi-system disorders being shaped by a variety of attributes across development. Disentangling this complexity, in the relations between biological, genetic, environmental, and developmental factors, has the potential to inform our understanding of the developmental mechanisms underlying both $_{n}$ASD and FXS, as well as development more generally. More specifically, understanding the mechanisms leading to and from language development in boys with $_{n}$ASD and boys with FXS will likely help us identify the factors predicting treatment response across these conditions.

Limitations and Conclusions

There are certain limitations that are worth noting in the present study. First, although we were able include a more inclusive group of children with $_{n}$ASD than in previous studies (NVIQ up to 110), our $_{n}$ASD sample did not represent the full range of cognitive skills for children with $_{n}$ASD. Thus, there is need for continued examination of the full range of cognitive skills for children with $_{n}$ASD relative other neurodevelopmental disorders. Second, the sample size is relatively small, although it is on par with most other studies in the field of research that includes a sample of participants with FXS. Third, we have included only boys in the present study, due to the higher rates of males affected by both neurodevelopmental disorders and the fact that FXS is an X-linked disorder, affecting girls differently than boys. It is important for this work to be extended to consider the same relations and questions in girls with $_{n}$ASD and FXS. Fourth, the present project utilized a cross-sectional approach during a developmental period associated with considerable language growth. Longitudinal examinations of the similarities and differences in language acquisition processes associated with these neurodevelopmental disorders are needed. Finally, the present project considered a small number of predictors likely to influence language development in these populations. Thus, additional predictors warrant consideration, such as factors known to support language acquisition (e.g., joint attention, imitation) and phenotypic features that potentially interfere with learning (e.g., attention, challenging behaviors).

In conclusion, taken together, the data from the present project provide additional support (1) language is an area of weakness for many children with $_{n}$ASD and (2) that there may be differences in the factors influencing language development between $_{n}$ASD and FXS that are likely to influence either treatment response or the active ingredients needed within the

intervention approach to support optimal language outcomes in these populations. Language delays can create a developmental cascade that has significant long-term implications across multiple domains and levels. For example, language facilitates cognitive development in that it provides a tool that can be used to organize information, refine/clarify categorical boundaries, and efficiently access and use information from others (e.g., Donald, 1991; Vygotsky, 1986; Waxman & Markow, 1995). In addition, language skills by the age of 5 years have been shown to be a strong predictor of long-term success for individuals with $_{n}$ASD. Research has also demonstrated that early language difficulties also shapes the child's surrounding environment. For example, as discussed by Iverson & Wozniak (2016), there is a bi-directional developmental cascade that unfolds across time in the interplay between production of early communicative acts (e.g., use of gaze, production of vocalizations, gestures, spoken language) and the responses of the child's social partners (e.g., caregivers) that supports a child's growth toward increased communicative complexity. Finally, we know that these early difficulties are also shaping, and in turn being shaped by, the child's neurobiological development (e.g., Dawson, 2008). It is therefore vital that we continue assess language skills, relative to both nonverbal cognitive performance and CA and recommend speech/language intervention accordingly.

In addition, information from the present project adds to our understanding of the FXSASD association. A notable number of similarities have been observed across the $_{n}$ASD and FXS phenotypes. That said, there is also a growing body of research suggesting important ASD symptom-level differences and differences in the factors associated with ASD severity. To clarify the nature of the relationship between these two conditions and provide insight into the complex developmental mechanisms leading to their phenotypic weaknesses investigations we must expand the scope of our empirical investigations. More specifically, research is need that both considers more broadly the ways in which the $_{n}$ASD and FXS phenotypes are similar and different. More work is needed, however, that considers these phenotypes across a variety of different domains as well as different developmental periods. In the present project, we see that in addition to differences in ASD symptomatology, it appears that the mechanisms underlying language development may also be different between those with $_{n}$ASD and those with FXS. Such between-group comparisons will likely help clarify the factors influencing heterogeneity within and across both conditions. In addition, as we consider development in both $_{n}$ASD and FXS, it is important that we take a deeper look into the mechanisms underlying the similarities and differences across these conditions. For example, given the findings from the present project, it is important to look deeper into the factors shaping language development in both $_{n}$ASD and FXS and understand how these mechanisms compare across these conditions. This deeper understanding is likely to elucidate the links between biomedical and behavioral attributes, thereby supporting the development of intervention methods that can be used to improve the quality of life outcomes in both $_{n}$ASD and in FXS.

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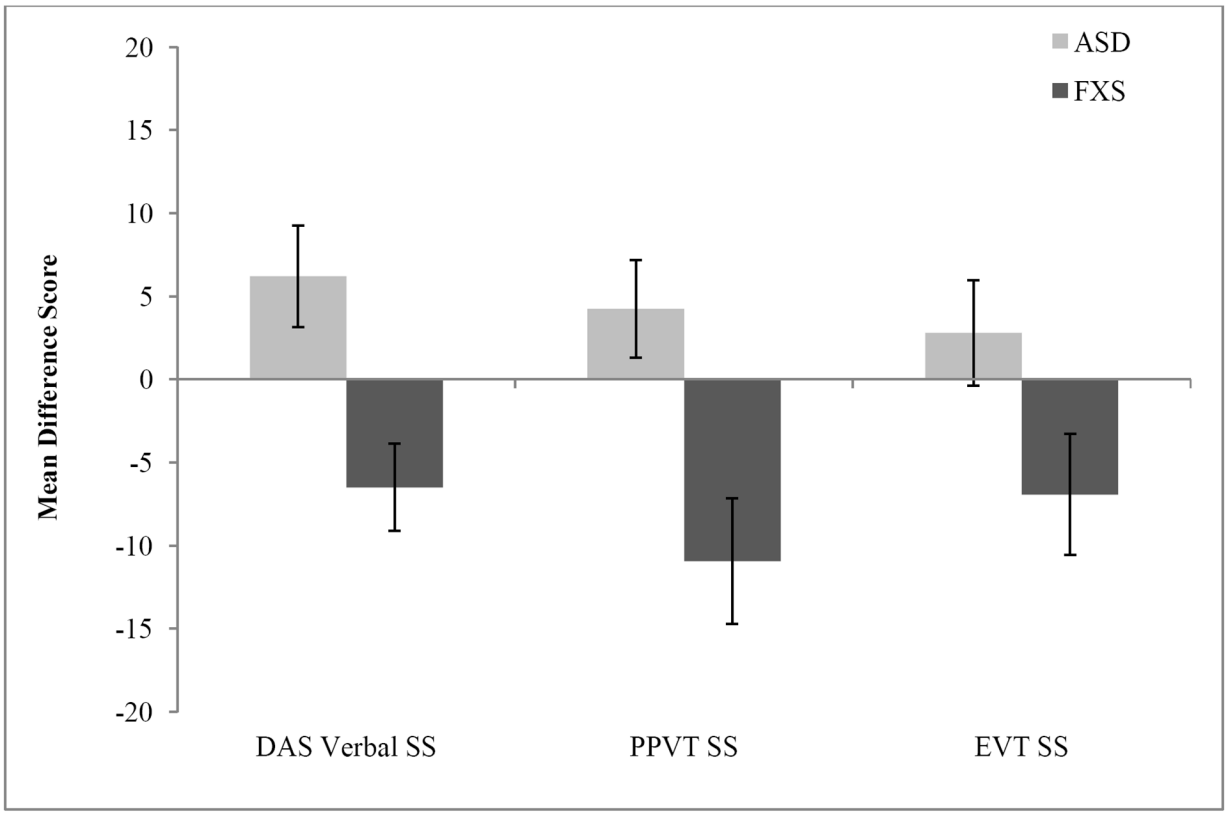

Figure 1.
Differences scores reflecting Nonverbal SS Performance (DAS SNC) minus Verbal SS Performance (DAS Verbal SS, PPVT SS, and EVT SS) as a function of diagnostic group.

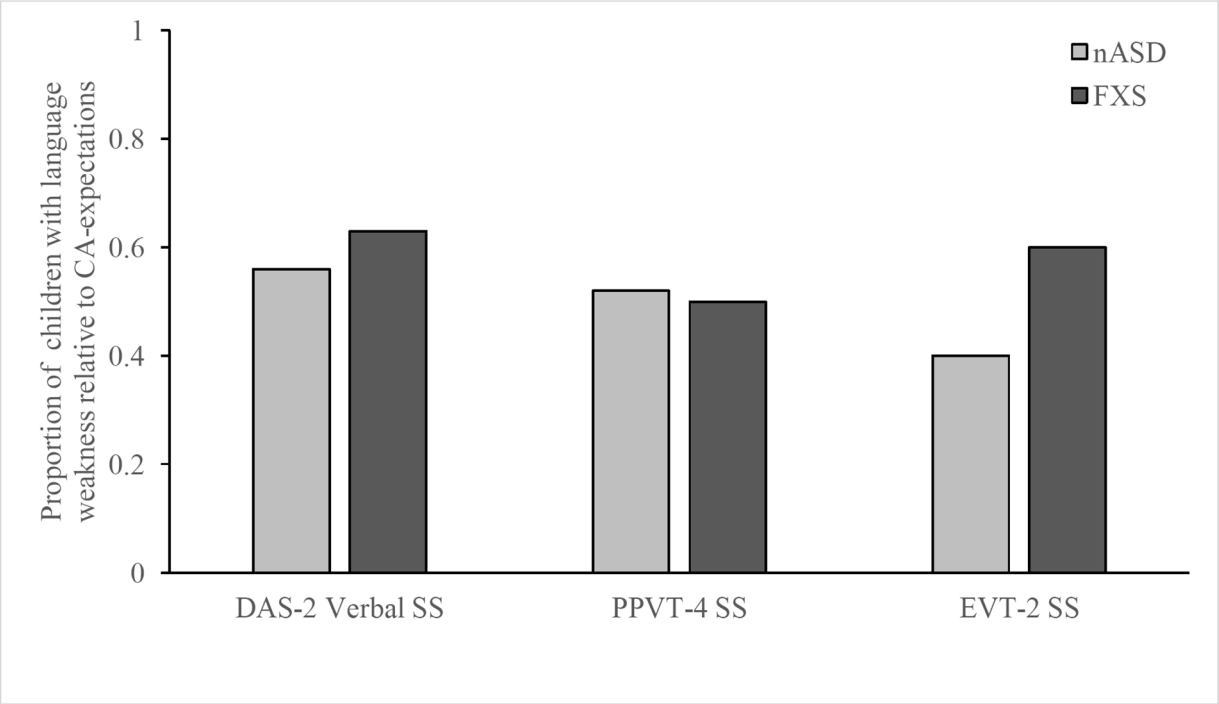

Figure 2.
Proportion of children, as a function of diagnostic group, for whom language scores were 2 or more standard deviations (70 +/−5) below norming sample mean (100).

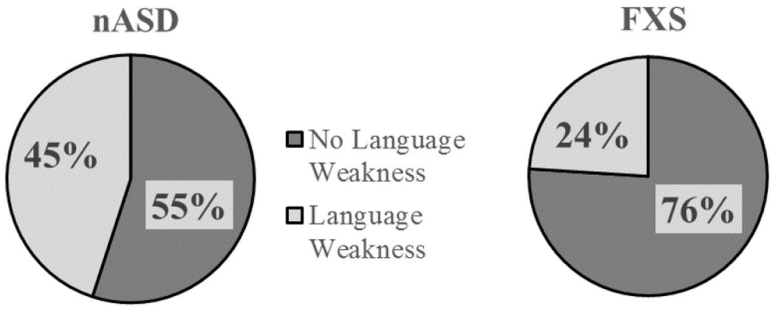

Figure 3.

DAS-II profile performance demonstrating percent of sample, as a function of diagnostic group, for whom DAS-II Verbal SS performance was statistically weaker than DAS-II Nonverbal Reasoning SS.

Table 1

Descriptive statistics (Mean, Standard Deviation, and Range) for participant groups

	Fragile X Syndrome (*n* = 16)	**Nonsyndromic ASD (*n* = 25)**
Chronological Age	4.53 (0.17,3.82–5.50)	4.60 (0.14,3.50–5.56)
Nonverbal IQ[1]	56.63 (17.29,30–91)	76.12 (20.55,30–113)
Autism Symptom Severity[2]	5.86 (2.21, 2–9) [3]	6.84 (1.72,4–10)

[1]Differential Ability Scales –2nd Edition, Special Nonverbal Composite,

[2]Autism Diagnostic Observation Schedule −2 Comparison Score,

[3]ADOS-2 data missing for 2 participants with FXS.

Table 2

Descriptive statistics regarding highest caregiver education level as a function of diagnostic group.

	Fragile X Syndrome (*n* = 16)	Nonsyndromic ASD (*n* = 25)
Prefer Not to Answer	12.5%	20%
Graduated high school/GED	0%	4%
Some college/technical school	18.8%	8%
Graduated – Associates/technical college degree	12.5%	20%
Graduated – B.A./B.S.	0%	20%
Some graduate work completed	6.3%	8%
Graduated – M.A/M.S. or higher graduate degree	50%	20%

Table 3

Descriptive statistics (Mean, Standard Deviation, and Range) for language measures as a function participant group

	Fragile X Syndrome (*n* = 16)	**Nonsyndromic ASD (*n* = 25)**
DAS-II Verbal SS	63.13 (20.84,30–92)	69.92 (20.52,30–100)
PPVT-4 SS[1]	67.56 (23.66, 25 – 101)	73.00 (22.97, 20 – 105)
EVT-2 SS[2]	62.93 (24.19,20–92)	73.32 (25.17,20–110)
ECI-LI	170.44 (152.95,0–540)	156.12 (111.78,0–362)

[1]PPVT-4 data missing for 1 participant with ASD,

[2]EVT-2 data missing for 1 participant with FXS

Table 4

Linear regression analyses evaluating between-group differences in language performance

	B (unstandardized)	SEB	β	*p* value	η^2 partial
DAS-II Verbal Comprehension T score					
Chronological Age	−0.27	1.94	−0.15	0.89	.001
Nonverbal IQ	0.43	0.08	0.79	<.001*	.479*
Autism Symptom Severity	−0.58	0.79	−0.09	0.47	.015
Diagnostic Group	4.97	3.35	0.20	0.07	.061
DAS-II Naming Vocabulary T score					
Chronological Age	−1.58	2.24	−0.08	0.49	.014
Nonverbal IQ	.50	0.09	0.83	<0.001*	.489*
Autism Symptom Severity	0.70	0.91	0.10	0.45	.017
Diagnostic Group	5.28	3.86	0.20	0.09	.052
PPVT-4 Standard Score					
Chronological Age	0.49	3.85	0.01	0.90	.000
Nonverbal IQ	0.92	0.16	0.85	<0.001*	.508*
Autism Symptom Severity	−0.45	1.57	−0.37	0.77	.002
Diagnostic Group	12.29	6.81	0.26	0.04*	.090*
EVT-2 Standard Score					
Chronological Age	1.11	3.90	0.03	0.78	.002
Nonverbal IQ	1.01	0.15	0.87	<0.001	.561*
Autism Symptom Severity	0.13	1.59	0.01	0.94	.000
Diagnostic Group	9.88	6.72	0.19	0.08	.060
Play Session - Language Indicator Score					
Chronological Age	45.69	22.83	.24	.05	.105
Nonverbal IQ	4.66	0.90	.78	<0.001*	.441*
Autism Symptom Severity	−1.44	9.30	−.022	.88	.001
Diagnostic Group	113.59	39.34	.427	.004*	.197*

*$p < .05$

Table 5

Descriptive statistics for boys with nASD as a function of verbal weakness classification.

	nASD − No Verbal Weakness (M, SD)	nASD + Verbal Weakness (M, SD, Range)
CA	4.71 (0.67)	4.43 (0.74)
Nonverbal Reasoning	75.40 (22.61)	77.20 (18.11)
ASD Severity	7.13 (1.77)	6.40 (1.65)

Table 6

Pearson correlation coefficients considering correlates of language performance as a function of diagnostic group

	CA	NVIQ	SA severity	RRB Severity
		nASD		
DAS-II Verbal Comprehension raw score	.02	.68**	−.20	−.01
DAS II Naming Vocabulary raw score	.09	71**	−.22	−.10
PPVT-4 growth score	.17	.76**	−.21	−.28
EVT-2 growth score	.23	74**	−.06	−.07
Play Session - Language Indicator score	.16	.68**	−.18	−.28
		FXS		
DAS-II Verbal Comprehension raw score	.32	72**	−.41	. 73**
DAS II Naming Vocabulary raw score	.08	75**	−.25	−.37
PPVT-4 growth score	.18	72**	−.40	57**
EVT-2 growth score	.39	.69**	−.41	−.75**
Play Session - Language Indicator score	.14	72**	−.29	−.45