Sentence Comprehension and Phonological Memory in Boys with Fragile X Syndrome and Autism Spectrum Disorder

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Abstract

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Fragile X syndrome (FXS) and autism spectrum disorder (ASD) are prevalent neurodevelopmental disorders that share overlapping characteristics, including deficits in language abilities. The current study examined delays in sentence comprehension in school-age boys with FXS (ages 5 – 12 years), school-age boys with ASD (ages 6 – 12 years), and younger boys with typical development (ages 3 – 7 years) in terms of (1) the extent of delay experienced by boys with FXS relative to cognitive- or vocabulary-level expectations and (2) the relationship between sentence comprehension and phonological memory abilities among boys with FXS or typical development. Further, this study considered the contribution of autism symptom severity to sentence comprehension among boys with FXS or ASD, as well as syntactic complexity by examining the relationship between phonological memory and sentence comprehension for both simple and complex sentence structures. Sentence comprehension was measured using a norm-referenced assessment of receptive syntax. Phonological memory skills were assessed using word recall and digit recall tasks. Findings showed that school-age boys with FXS had lower sentences comprehension abilities than younger typical developing boys who were matched on nonverbal cognitive ability or receptive vocabulary. This study adds to what is known about cognitive factors that contribute to language abilities in boys with FXS and points to a
relationship between phonological memory and sentence comprehension abilities in individuals with and without neurodevelopmental disorders.
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Introduction

Fragile X syndrome (FXS) and autism spectrum disorder (ASD) are two distinct neurodevelopmental disorders with many overlapping characteristics and features. For example, symptoms of ASD have been shown to frequently co-occur in individuals with FXS. Research suggests that approximately 90% of boys with FXS will exhibit symptoms congruent with an ASD diagnosis (McDuffie, Kover, Hagerman, & Abbeduto, 2013). Furthermore, these symptoms are severe enough in 60% of this population to warrant a comorbid diagnosis of ASD (Bailey, et. al, 2006). In addition to problems with social interaction, challenges with language and cognition occur in both individuals with FXS and those with ASD—with important implications for social, academic, and daily functioning.

In typically developing children and children with other sources of language impairment, phonological memory has been shown to be an important source of variability in language learning. However, little research has addressed the relationship between language comprehension and phonological memory in individuals with FXS. Examining sentence comprehension and memory among children with neurodevelopmental disorders will inform our understanding of the development of language abilities, their interaction with cognitive abilities, and ultimately, how targeted interventions may be improved. Therefore, the focus of the current study was on sentence comprehension and phonological memory in boys with FXS or ASD, with younger typically developing boys serving as a point of comparison.

Fragile X Syndrome

Fragile X syndrome (FXS) is a genetic disorder with a distinct phenotype that includes many features shared with ASD (Klueck, Martin, & Losh, 2014). FXS is the most common inherited cause of intellectual disability resulting from a mutation on the FMR1 gene of the X-
chromosome (Mazzocco, 2000). FXS is characterized by deficits in cognition, social interaction, and language (Abbeduto et al., 2003; Sudhalter, Scarborough, & Cohen, 1991). Boys with FXS usually present more severely in phenotype than girls with the same genotype given the syndrome’s X-linked pattern of inheritance (Price, Roberts, Hennon, Berni, & Anderson, 2014). Indeed, boys with FXS often have more severe deficits in language and intellectual disability than girls (Price et al., 2014) and are, therefore, the focus of the present research.

Difficulties in language are characteristic of children with FXS. Behaviors often seen in the subset of children with FXS and ASD include perseverative and noncontingent speech (e.g., the repetition of a phrase that does not fit the given context; Martin, Losh, Estigarribia, Sideris, & Roberts, 2014). Furthermore, boys with FXS and comorbid ASD have lower overall language abilities than those with FXS alone (Estigarribia, Martin, & Roberts, 2012a; Roberts, Martin, et al., 2007). More generally, a majority of boys with FXS have delays in language in the areas of vocabulary, grammar, and pragmatic language (Roberts, Martin, et al., 2007). However, research on these language domains in the FXS phenotype is still relatively sparse. Research in the area of grammar development in children with FXS is particularly limited and would greatly expand on our understanding of language development in children with FXS.

On average, delays in both expressive and receptive language are present relative to or commensurate with nonverbal mental age in children with FXS (Abbeduto, Brady, & Kover, 2007; Price, Roberts, Vandergrift, & Martin, 2007). Among children with FXS, receptive and expressive vocabulary skills have been shown to be a relative strength for children (Abbeduto et al., 2003). However, according to a review by Finestack and colleagues (2009), when compared to children with typically developing language and younger chronological age, children with FXS generally show significantly lower receptive vocabularies than their cognition-matched
peers. Although language deficits are characteristic of individuals FXS in ways that may impact the individual both academically and socially, research on abilities in specific language domains or addressing specific language constructs is limited.

A majority of children with FXS have a delay in syntactic ability when compared to younger peers matched for mental age (Roberts, Price, et al., 2007). However, while this has been seen in most boys with FXS, there is still a large amount of variability within the population (Estigarribia et al., 2012a). Across the literature, there is little consensus on receptive syntax when compared to expressive syntactic abilities. Children with FXS tend to use fewer complex utterances and have a shorter mean length of utterance (MLU) in spoken language than their typically developing peers (Roberts, Martin, et al., 2007). Based on their review, Abbeduto and Hagerman (1997) concluded that boys with FXS show significant delays in developing morphosyntactic skills compared to boys of the same chronological age. Morphosyntactic skills refer to a child’s ability to combine smaller units of language in larger meaningful structures such as sentences. More specifically, receptive morphosyntax may be commensurate with a child’s mental rather than their chronological age (Abbeduto et al., 2007).

Recent work has specifically addressed receptive syntax in adolescents with FXS. A study by Oakes, Kover, and Abbeduto (2013) found that young adolescents with FXS (ages 10 – 16 years, $M = 12.8$) matched on nonverbal cognition, using Leiter-R growth scores, to peers with typical development had deficits in receptive syntax as measured by the Test for Reception of Grammar (TROG-2; Bishop, 2003). However, earlier research by Abbeduto et al. (2003) found that there was no difference in ability in syntactic comprehension on measures of the Test of Auditory Comprehension of Language- Revised (TACL-R) when examining older adolescents and adults with FXS. This discrepancy in findings may be explained in part by the trajectory of
receptive language development in FXS. Some evidence suggests that, over time, receptive language skills in syntax and morphology improve with development (Finestack et al., 2009). That is, receptive language abilities may be more delayed during childhood and the early school-age years, with a reduction in the extent of the deficit later in adolescence. This could explain the differing literature findings on receptive abilities in the FXS phenotype. Nonetheless, given the need for growth in clinical knowledge concerning language deficits in FXS and the difference in findings across existing literature, further research is warranted in these areas.

**Autism Spectrum Disorder**

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social interaction skills, communication skills, as well as the presence of stereotyped and repetitive behavior, interests, and activities (Lord, Cook, Leventhal, & Amaral, 2000). Unlike FXS, which is definitively identified with a blood test, a diagnosis of ASD is based primarily on behavioral observation and developmental history. While deficits in language are often present in individuals with ASD, this feature is widely varied in presentation and severity across the disorder (Tager-Flusberg, 1996) – somewhat like in the case of FXS.

Difficulties with language comprehension are often present in children and adolescents with ASD, even when structural language (e.g., phonology, vocabulary) is thought to be developing within typical expectations (Kover et al., 2014; Prior & Hall, 1979). On one measure of syntactic comprehension, the TROG-2, an overall sample of boys with ASD (ages 4 – 11 years) —including a wide range of individuals both with and without intellectual disability (ID) — did not significantly differ in performance from participants with typical development matched on receptive vocabulary (Kover et al., 2014). It is important to note that delays were present relative to chronological age within these school-age boys with ASD, but the overall
comparison groups (ASD vs. typical development) were matched on receptive vocabulary. Prior and Hall (1979) found that children with ASD showed deficits in comprehension of reversible sentences in comparison to typically developing peers matched on verbal mental age and IQ. A functional connectivity study done by Kana et al. (2006) showed that when comprehending sentences, children with ASD often rely more heavily on visual imagery than chronologically matched peers, rather than using linguistic information alone to comprehend the sentence. Together, this work suggests that sentence comprehension may be delayed in at least some samples of children with ASD relative to chronological age, but not necessarily beyond other benchmarks of ability, such as vocabulary comprehension.

However, research has shown specific differences in language ability may be found when participants are categorized by the presence of a comorbid intellectual disability (ID). The American Association on Intellectual and Developmental Disability defines ID as a significant deficit in both intellect and adaptive skills (“American Association on Intellectual and Developmental Disabilities,” 2013). Kover et al. (2014) defined participants with ASD and ID as individuals who scored a 70 or below on the Brief IQ subtest of the Leiter-R (Kover et al., 2014). Deficits in syntax comprehension for school-age boys with ASD differed depending on presentations of the disorder (Kover et al., 2014). That is, this study found that school-age boys with ASD and ID (ages 5 –11 years) had overall deficits in sentence comprehension relative to typically developing boys who were matched on nonverbal cognitive ability. Specifically, the subset of individuals with ASD that also presented with ID performed lower on measures of the TROG-2 (passing fewer blocks, answering fewer items accurately, and incorrectly choosing more lexical foils) than the younger nonverbal cognitive ability-matched comparison group (Kover et al., 2014). These results demonstrated that when ASD co-occurs with ID, there might
be weaknesses in sentence comprehension when compared to nonverbal cognitive abilities. This notion is supported by other research on individuals with ASD with intellectual disability for language and syntax comprehension relative to nonverbal cognition (Boucher, 2012).

For individuals with ASD, research has also illustrated a difference in comprehension ability across sentence types: reversible versus nonreversible sentences. Boys with ASD and intellectual disability were more likely to demonstrate at least one lexical error during reversible sentence comprehension than typically developing boys, but not for nonreversible sentences (Kover et al., 2014). Reversible sentences are those in which the agent and the object can logically be switched (e.g., “the cat chases the dog” or “the dog chases the cat”); in contrast, nonreversible sentences involve inanimate objects (e.g., “the cat chases the leaf”) or other semantic information that aids comprehension (e.g., “the mother rocks the baby”; Kover et al., 2014; Oakes, Kover, & Abbeduto, 2013). Reversible sentences require more use of syntactic knowledge and therefore involve higher process demands on the individual. Therefore, lexical errors may be seen in the comprehension of reversible sentences as children with ASD are challenged by comprehension of these sentence forms (Kover et al., 2014). Based on the presence of lexical errors, the authors concluded that difficulties in sentence comprehension displayed by those with ASD and ID may be attributed to either insufficient lexical knowledge or an inability to effectively use that knowledge; however, that study failed to directly assess memory, which could also have accounted for the pattern of findings (Kover et al., 2014).

In summary, Kover et al. (2014) found that sentence comprehension was delayed in boys with ASD. In particular, these delays were present in the overall sample of boys beyond chronological age expectations, but not receptive vocabulary expectations. In the subgroup of boys with ASD that also had ID, delays in sentence comprehension were more pronounced and
deficits were present beyond nonverbal cognitive expectations. Based on previous research, the profile of sentence comprehension abilities in children with ASD is qualified by other developmental indicators (e.g., nonverbal cognitive ability, presence of ID, receptive vocabulary). To date, phonological memory and severity of autism symptoms have not been considered as predictors of sentence comprehension. Furthermore, examining profiles of ability across sentence types may yield insight into the nature of language impairments in children with neurodevelopmental disorders.

**Memory**

In addition to impaired language, FXS is characterized by deficits in attention, impulsivity, and working memory (Cornish et al., 2009). Significant verbal immediate memory deficits have been observed in boys with FXS (Conners, Moore, Loveall, & Merrill, 2011). Boys with FXS also have difficulties with executive functioning (Van der Molen et al., 2010). Lanfranchi (2009) found that, in individuals with FXS, the ability to perform lower-control tasks involving verbal and visuospatial working memory coincided with mental age; however, performance decreased on higher-control tasks (Lanfranchi et al., 2009). Consistent with these findings, boys with FXS have difficulties in simultaneous processing and storage of verbal information (Conners et al., 2011). Taken together, difficulties with memory for individuals with FXS could have implications for other domains of development, such as language.

Pierpont and colleagues (2011) investigated the contribution of phonological memory to language development in adolescent boys with FXS. They found that phonological memory, measured using a non-word repetition task, was a predictor for gains in vocabulary and syntax over a two-year period (Pierpont et al., 2011). In evaluating the unique contribution of phonological memory, nonverbal cognition, and autism symptomatology, phonological memory
was the only significant predictor of change in syntax (i.e., receptive syntax assessed with the TROG-2 combined in a composite with expressive syntax) over the study period for boys with FXS. Therefore, vocabulary and syntax skills may depend on the ability to maintain phonological representations and manipulate phonological processing online (Pierpont et al., 2011). It is important to note that participants in the Pierpont et al. study were functioning at the level of 4-6 year old typically developing children, a period thought to reflect a strong relationship between phonological memory and vocabulary gains in typical development (Pierpont et al., 2011). This coincides with Baddeley’s argument, described further below, that learning syntactic rules, for example, may depend on maintaining phonological representations with short-term phonological memory for multiword utterances (Baddeley, Gathercole, & Papagno, 1998).

In Baddeley’s model of working memory, attention is controlled in a limited system referred to as the “central executive”, which controls information in two domain-specific components: the “visuospatial sketchpad” and the “phonological loop” (Baddeley, 2003). This phonological loop can be seen as a tool for language learning. Verbal memory is temporarily stored in the phonological store with a rehearsal process. Verbal information is retained by using the rehearsal processes to maintain decaying phonological forms in the store (Baddeley et al., 1998). The construct of the phonological loop illustrates how phonological forms in short-term memory allow for language learning as these forms become represented in long-term memory (Baddeley et al., 1998). The phonological loop facilitates the learning of phonological forms to be stored in the child’s internal lexicon to be applied to the appropriate concept later (Baddeley, 2003). In summary, phonological memory can be thought of as an aspect of short-term memory
that maintains phonological representations during processing – in service of language development.

Impairments in phonological memory are likely to have implications for language development. In children who have deficits in phonological memory, the process of encoding from short-term to long-term memory takes substantial time and may contain errors (Gathercole, Briscoe, Thorn, & Tiffany, 2008). Gathercole (2008) found that children with deficits in short term memory had more difficulty with holding novel words in memory (Gathercole et al., 2008). In these populations, the deficits in phonological memory have also been shown to have specific later effects on language development, including shorter utterance length, delayed syntax, and little diversity in their vocabulary (Gathercole et al., 2008). However, in a study of these effects in children at 8-years-old, Gathercole and colleagues (2005) found that while these deficits have been shown in early ages, effects seemed to diminish in later school ages. Understanding this theoretical construct of phonological memory is important to inform the way we understand and evaluate language and memory development and deficits. Like individuals with FXS, individuals with ASD also have impaired memory abilities, suggesting that considering the link between memory and language will be informative with respect to both populations (Gabig, 2008; Kercood, Grskovic, Banda, & Begeske, 2014).

Memory Processing and Grammatical Constructions

Studies have shown a connection between memory and language learning, specifically in the domain of syntax. Phonological memory has been shown to be a vital component to learning syntax rules in typical language development (Williams & Lovatt, 2005). The role of phonological memory for syntactic mastery is expected to extend to children with neurodevelopmental disorders as well. As described above, Pierpont (2011) found that
phonological memory was a predictor of future syntactic skill in boys with FXS (Pierpont et al., 2011). In a similar vein, Estigarribia et al. (2012b) examined nonverbal cognition, nonword repetition, and maternal education as predictors of expressive syntax in those with FXS and Down syndrome (DS). They found that diagnostic group, nonverbal cognition, and phonological working memory were the best predictors of syntactic ability.

Theoretically, the same processes that Baddeley (1998) proposes in the phonological loop for the acquisition of vocabulary can be applied to the acquisition and storage of syntactic knowledge. In his model, syntactic forms may be learned by temporarily holding phonological forms of these items in the phonological loop (Baddeley et al., 1998). Given this theoretical construct, the relationship between syntax comprehension and phonological working memory should further be examined to give a better understanding of language learning.

This model has been applied to explain language deficits in other neurodevelopmental disorders. Jarrold (1999) applied this construct to explain short-term memory deficits in children with DS. A proposed reason for this deficit is a breakdown of the phonological loop specifically at the level of the phonological store (Jarrold, Baddeley, & Phillips, 1999). Children with DS often have deficits in grammar comprehension and phonological memory (Laws & Gunn, 2004). Phonological memory may also play a major part in grammar learning in children with DS. Laws and Gunn found that, on measures of the TROG, children with DS who had stronger phonological memory skills showed more success in grammar development (Laws & Gunn, 2004). This study further supports the idea of limited phonological store discussed by Jarrold et al. (1999). Chapman (2002) found that along with chronological age, two factors that best predicted syntax comprehension in adolescents with DS were auditory-verbal (i.e., phonological) and visual short-term memory (Chapman, Hesketh, & Kistler, 2002; Miolo, Chapman, &
Sindberg, 2005). Therefore, based these studies, it is plausible that language learning deficits seen in children with DS may stem from a limited memory capacity to store learned information.

The effect of memory on language learning has been further explored in children with specific language impairment (SLI). Children with SLI have been shown to have deficits in verbal short-term (i.e., phonological) memory, which may affect their ability to learn new phonological forms (Archibald & Gathercole, 2006). The evidence supporting the impact of deficits in phonological memory impacting language learning leads to the need for further exploration into the impact of this paradigm on language deficits in children with FXS and ASD, who are known to experience weaknesses in receptive language. In this study, we consider phonological memory as a theoretically motivated predictor of sentence comprehension. In addition, we also consider the putative role of autism symptom severity (i.e., symptoms of autism considered continuously, rather than categorically) as a secondary, exploratory predictors of sentence comprehension ability (see Figure 1). Given the behavioral phenotypes associated with FXS and ASD, it is possible that symptoms of ASD directly impact language comprehension abilities independently of phonological memory abilities.

Figure 1. Framework of Language Comprehension
Syntactic Complexity

Some research has begun to tease apart the relationship between memory and grammatical ability in terms of syntactic complexity in children with neurodevelopmental disorders, including FXS, ASD, SLI, and DS. In the case of FXS, research has found specific differences in syntactic comprehension abilities across grammatical constructions. Oakes et al. (2013) examined comprehension of sentences with varying levels of grammatical complexity and length in adolescents with FXS. For example, reversible subject-verb-object (SVO) sentences were significantly easier than 4-element sentences for adolescents with FXS (Oakes et al., 2013). Adolescents with FXS also made more grammatical errors than lexical errors on these sentences, perhaps due to difficulty with comprehension of syntactically demanding constructions (e.g., the word order of reversible and embedded syntactic form; Oakes, Kover, & Abbeduto, 2013). Interestingly, comprehension of sentences with four syntactic elements and relative clauses were harder for adolescents with FXS than reversible sentences, which may be attributed to the difference in memory load between these two constructs (Oakes et al., 2013). However, the relationship between phonological memory and sentence comprehension has not been directly tested in individuals with FXS when taking into account sentence complexity.

Processing of grammatical constructions has recently been studied in adolescents with ASD. A study by Durrelman and colleagues (2014) examined comprehension of complex syntax in individuals with ASD with a language delay in comparison to those without language delay. Their results showed a slight deficit in grammatical comprehension regardless of the presence of a language delay (i.e., discrepancy between deficits in grammatical constructs in children with ASD was similar to that of children with typical development; Durrleman et al., 2014). Regardless of language ability, participants with ASD were more likely to show mastery of a
subject- rather than object-relative clause. A subject relative clause is defined as a clause in which the relative pronoun describes the subject of the sentence (e.g., “the dog that is black chased the cat”) while the relative pronoun describes the object in an object relative clause (e.g., “the chased the cat that is black”) (Durrleman et al., 2014). Although individuals with ASD and a language delay demonstrated more difficulty comprehending subject relative clauses than those without a coexisting language delay due to embedding demands of these grammatical structures, nonverbal cognitive ability was also correlated with task performance (Durrleman et al., 2014). This is to say that individuals with lower cognitive abilities also performed lower on language tasks (Durrleman et al., 2014). This work reiterates that deficits in grammatical comprehension may be subtle and variable across syntactic constructions.

Frizelle and Fletcher (2015) investigated the effect of syntactic complexity on phonological and working memory by examining sentence recall, rather than comprehension. This study examined the relationship between phonological short-term memory and increasing complexity of syntactic constructions in children with SLI. Specifically, sentence complexity was determined by relative clause construction for five syntactic roles. Phonological memory abilities were measured by subtests of the Working Memory Test Battery for Children (WMTB; Gathercole & Pickering, 2001): digit recall, word recall, word list matching, and nonword recall. Results illustrated a significant relationship between digit recall and the simplest level of syntactic complexity used as stimuli. It was also shown that children with SLI had more difficulty in recalling sentences of increasing complexity (Frizelle & Fletcher, 2015).

Laws and Bishop (2003) investigated phonological memory and grammar in children with SLI, as well as children with DS. Both groups had an overall impairment in phonological memory and grammar. An error analysis of the TROG suggested that these impairments were
due to difficulty with grammar rather than low vocabulary abilities, supporting the presence of syntactic and phonological memory impairment in these populations (Laws, 2003). These findings further show an important relationship between complexity of syntax and phonological memory abilities in children with a wide range of communication difficulties.

Research Questions

The present thesis examined syntactic comprehension in boys with FXS and ASD, extending previous research through direct assessment of phonological memory and the inclusion of a typically developing comparison group. The following questions were addressed:

1. Research Question 1: Are there diagnostic group differences in sentence comprehension between school-age boys with FXS compared to younger typically developing peers who are matched on nonverbal cognitive ability or receptive language ability?

2. Research Question 2: Is there a relationship between phonological memory ability and sentence comprehension ability in boys with FXS or typically developing peers?
   a. Do phonological memory skills and autism severity each independently predict sentence comprehension abilities among boys with FXS and ASD?

3. Research Question 3: Is there a relationship between phonological memory and comprehension of sentences for both simple and complex forms? That is, does increased sentence complexity affect the relationship between phonological memory and sentence comprehension in school-age boys with FXS or typically developing boys?

Methods

Participants

Participants whose data were available for the current study (prior to any matching) were 23 boys with FXS ages 5 to 12 ($M = 9; SD = 2$), 8 boys with ASD ages 6 to 12 ($M = 9; SD = 2$),
and 23 boys with typical development ages 3 to 7 years old ($M = 5; SD = 1$; See Table 1 for descriptive statistics). Participants were drawn from a large longitudinal study on social-affective cues to word learning (NIH R01 HD 054764; PI: L. Abbeduto). Participants were recruited primarily nationally, regionally, and locally (FXS, ASD, and typical development, respectively), and largely through university recruitment services. The current study focuses on the second assessment, which occurred 18 months after the initial visit.

Table 1

| Characteristics of Participants with Data Available from the Larger Study Prior to Matching |
|---------------------------------|---------------------------------|---------------------------------|
|                                 | ASD $(n = 8)$                   | FXS $(n = 23)$                  | TD $(n = 23)$                   |
| Age                             | M = 9.2, SD = 2.3, Range = 6.4-12.4 | M = 9.49, SD = 2, Range = 5.7-12.2 | M = 5.3, SD = 1.2, Range = 3.5-7.4 |
| Leiter-R                        |                                 |                                 |                                |
| Age Equivalent                  | 5.5, 2.2, 3.3-9.0               | 4.5, 0.9, 3.1-6.4               | 6.3, 1.7, 3.9-9.9              |
| Growth Score                    | 465.8, 17.4, 447-494            | 457.8, 9.1, 440-474             | 473.7, 12.6, 453-496           |
| Nonverbal IQ                    | 64.1, 22.6, 36-98               | 50.48, 11.1, 36-71              | 117.5, 15.4, 87-143           |
| PPVT-4                          |                                 |                                 |                                |
| Growth Score                    | 121.8, 35.8, 77-175             | 134.4, 15.1, 103-165            | 151, 17.7, 120-181             |
| Standard Score                  | 62, 28.1, 20-98                 | 68, 12.9, 45-87                 | 122, 12.3, 103-147            |
| WMTB                            |                                 |                                 |                                |
| Digit Recall Score              | 16.6, 11.6, 0-35                | 12.04, 5.4, 0-22                | 23.2, 4.4, 16-30              |
| Digit Recall Standard Score $(n=4)$ | 93.5, 23.3, 73-126            | 64.5, 6.9, 57-75                | 105.3, 12.3, 83-123           |
| Word Recall Score               | 11, 7.2, 0-20                   | 9.22, 4.5, 0-21                 | 16.5, 3.6, 11-24              |
| Word Recall Standard Score $(n=5)$ | 80.8, 20.4, 58-97              | 68, 13, 28-98                   | 105.2, 16.6, 76-129           |


In the larger study, inclusion criteria were English as a native language, with speech as their primary form of communication. Both boys with ASD and FXS were required to have diagnostic documentation of their disorder. Participants with ASD were also required to have ruled out the presence of FXS through genetic testing. To ensure the validity of ASD
classification, participants with a community diagnosis also met criteria on the Autism Diagnostic Interview, Revised (ADI-R; Rutter & LeCouteur, 2003) and the Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, Dilavore, & Risi, 2000). Children with ASD were determined to meet research classification for ASD if they met cut-offs on the ADI-R and had a calibrated severity score of at least 4 on the ADOS. Boys with typical development were also verified to have scored below the cut-off on an ASD symptom screener, the Social Communication Questionnaire (SCQ: Rutter & Bailey, 2003). Participants were only enrolled if parents reported no significant vision or hearing impairments with mild impairments being corrected. Sessions occurred across multiple days and behavioral supports such as visual schedules and breaks were provided.

**Measures**

**Nonverbal Cognition.** The Brief IQ subtests of the Leiter International Performance Scale-Revised (Leiter-R; Roid & Miller, 1997) were used to determine nonverbal IQ. The Leiter-R tests nonverbal cognition by assessing reasoning and visualization skills without requiring a spoken response from the child. Scoring methods yield raw, standard, and growth scores, as well as age-equivalents. The Leiter-R is a valid measure of nonverbal cognition with strong psychometric properties including construct, content, and criterion validity. The Leiter-R is reliable in test-retest and internal reliability.

**Receptive Vocabulary.** The Peabody Picture Vocabulary Test, Fourth Edition (PPVT-4; Dunn & Dunn, 2007) was used a measure for receptive vocabulary. Scores yielded include raw, standard, and growth scores. Children with ASD and FXS began testing based on their current developmental level, while starting points for children with typical development were determined by chronological age. The PPVT-4 shows high internal consistency and was
designed to be paired in administration with the measure of the EVT-2. Tests scores from the PPVT-4 and EVT-2 are positively correlated with a mean of $r = 0.82$ (Dunn & Dunn, 2007).

**Sentence Comprehension.** Sentence comprehension was measured using the Test for Reception of Grammar, Second Edition (TROG-2; Bishop, 2003), a standardized measure of receptive syntax. The TROG-2 tests 20 syntactic constructions organized into blocks of four items per syntactic construction. The child is asked to choose the correct picture out of an array of four when given a sentence. A block is failed when one or more errors are made within the block; a ceiling is reached and testing ceases when five consecutive blocks are failed. Errors in each block can be determined to be either lexical or syntactic in nature given that foils in each array differ by either one lexical element or syntactic element. Scores yielded by performance include the overall number of blocks passed and age equivalent scores. Raw scores based on blocks passed may be converted into standard scores for comparison if the child is older than four-years-old. In addition, the number of total number of items passed (rather than blocks passed) can be used as an indicator of ability (Kover & Ellis Weismer, 2014; McDuffie et al., 2013; Oakes et al., 2013). The TROG-2 shows high internal consistency with a .88 correlation between odd and even blocks. The test also showed moderate levels of concurrent validity with the linguistic concepts subtest of the Clinical Evaluation of Language Fundamentals – Preschool (CELF-P\textsuperscript{UK}) and the Clinical Evaluation of Language Fundamentals – Third Edition (CELF-3\textsuperscript{UK}) concepts and direction subtest. This level of validity shows that the TROG-2 measures many of the same concepts as subtests of the CELF-P and CELF-3. The TROG-2 is shown to be a sensitive measure of deficits in communication.

**Expressive Language.** Although not the focus of the current study, standardized assessments of expressive vocabulary and syntax allow the current analyses to be situated in the
broader literature. The Expressive Vocabulary Test, Second Edition (EVT-2; Williams, 2007) measured expressive vocabulary. The EVT-2 has appropriate content validity. This test measures a child’s expressive language quantified by standard scores based on age, age equivalents, and growth scores. Expressive syntax abilities were measured using the Syntax Construction subtest of the Comprehensive Assessment of Spoken Language (CASL; Carrow-Woolfolk, 1999). This subtest measures the child’s knowledge and their ability use grammatical morphemes and syntax. The CASL yields a variety of scores including age- and standard and age equivalents.

**Phonological Memory.** Phonological memory was measured using the Working Memory Test Battery for Children (WMTB; Gathercole & Pickering, 2001). The WMTB is comprised of nine subtests, some of which test short-term/phonological memory including digit recall, word list matching, word list recall, and nonword list recall, and some of which test working memory including listening recall, counting recall, and backward digit recall. The current study examined two subtests—digit and word list recall—in order to determine phonological memory capacity of each participant. The WMTB is designed for children aged 5 to 15 and assesses memory ability in adolescents and young children, for both short-term and phonological memory. The WMTB has been shown to have test-retest ability as well as inter-tester reliability. This measure also has high internal validity proving to be a good measure in young children and adolescents of short-term memory and the phonological loop.

**Phonological memory composite.** Bivariate correlations between the digit recall and word recall subtests were analyzed to determine if a composite variable would be appropriate. The overall sample of participants ($N=52$; ASD $n=7$; FXS $n=22$; TD $n=23$) showed significant results for both one-tailed Pearson ($r = 0.85, p < .001$) and spearman’s rho ($r_s = 0.87, p < .001$) correlations. Within-group correlations were also examined using Pearson and Spearman’s
coefficients for each of the three groups. Significant positive correlations were found between WMTB subtests for each group: ASD ($r = 0.92, p = .002$; $r_s = 0.96, p = <.001$), FXS ($r = 0.78, p = <.001$; $r_s = 0.76, p = <.001$), and TD ($r = 0.60, p = .001$; $r_s = 0.60, p = .001$). Thus, a phonological memory composite was derived from the sum of z-scores from the Digit Recall and Word Recall subtests of the WMTB within each diagnostic group by creating a standardized z-score for each subtest (Digit Recall and Word Recall) and then adding them together to create a single indicator of relative standing within the group for phonological memory. This composite was utilized in the primary analysis for Research Question 2, which examined phonological memory for carefully selected groups of participants with FXS or typical development.

**Autism Severity.** Autism severity was measured using the ADOS (Lord, Rutter, Dilavore, & Risi, 2000). The ADOS is used to observe symptoms of ASD in children and adults. The assessment is composed of four separate modules to be given individually depending on the language abilities of the individual. The ADOS uses observation of social interactions, prelinguistic skills, communication, and play to assess diagnostic characteristics. Calibrated severity scores were used as an index of symptom severity (Gotham et al., 2009) for boys with FXS or ASD in supplementary Research Question 2a.

**Analysis Plan**

**Preliminary analyses: Group Matching.** A preliminary analysis was conducted to match groups on nonverbal mental age using Leiter-R growth scores or receptive vocabulary based on PPVT-4 growth scores before addressing the primary research questions. Both nonverbal cognition and receptive vocabulary were considered as matching variables because previous literature has suggested that findings related to language comprehension may differ according to the matching metric chosen (e.g., Kover et al., 2014). To assess the adequacy of
group matching, comparisons were made between participants with FXS and typical development using a $t$-test to determine $p$-values and effect sizes. Following Kover and Atwood (2013), we report effect sizes (approaching zero indicates a good match) and variance ratios (approaching one indicates a good match) as an index of the extent of equivalence between groups (Kover & Atwood, 2013).

Individuals were only considered for matching if they had valid data for the primary assessments of interest. Two participants (one boy with ASD and one boy with FXS) were not included due to invalid (zero) scores on the WMTB subtests. After these considerations, 22 boys with FXS, 23 boys with typical development, and 7 boys with ASD were available for matching. Thus, participants with ASD were not included in the group matching process or analyses related to matched groups because of the limited sample size (fewer than 5 participants remaining after matching, depending on the matching metric). As such, participants with ASD were included only in the continuous analysis of autism symptom severity as a predictor of sentence comprehension abilities (Research Question 2a).

**Preliminary analysis: Correlations with language.** A second preliminary analysis examined within-group bivariate correlations for language and memory to help situate the current findings in the context of previous literature (e.g., Pierpont et al., 2011). Within-group correlations were completed for phonological memory and the language variables of interest: receptive vocabulary, expressive vocabulary, receptive syntax, and expressive syntax.

**Primary research questions.** The first research question examined the group difference in sentence comprehension between participants with FXS and typical development. Groups were matched on nonverbal cognition or receptive vocabulary and compared on items passed on the TROG-2. We used a $t$-test to compare these two groups (FXS vs. typical development).
To examine the second primary research question, within-group correlations were calculated for phonological memory and sentence comprehension. Specifically, within-group correlations were determined between the phonological memory composite and items passed on the TROG-2. As previously described, a composite variable of phonological memory was selected as the predictor for this second primary research question because correlations between Word Recall and Digit Recall were significant and the composite variable allows interpretations of within-group relationships for the matched samples (FXS, typical development).

To examine the effect of autism severity (Research Question 2a), a regression analysis was used to predict sentence comprehension on the TROG-2 from phonological memory and autism symptom severity, assessed using ADOS calibrated severity scores (Gotham et al., 2009). Data were taken from the ADOS administration that occurred at participants’ initial visit, given that many participants did not receive the ADOS at the second visit, which was concurrent with the current measures of interest (i.e., the TROG-2 and WMTB). This strategy was adopted to optimize the sample size. This supplementary analysis included 29 participants with FXS \((n = 22)\) or ASD \((n = 7)\), all of whom had valid data on the TROG-2, WMTB, and an ADOS at the initial visit (see Table 2). No matching was done for this supplementary research question. Analyzing data from individuals with FXS and ASD together in terms of autism symptom severity allowed an examination of autism symptoms on sentence comprehension with respect to severity rather than group (i.e., a continuous, rather than categorical approach).

Table 2

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall ((N=29))</th>
<th>FXS ((n=22))</th>
<th>ASD ((n=7))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(M)</td>
<td>SD</td>
<td>Range</td>
</tr>
<tr>
<td>Leiter-R Growth Score</td>
<td>460.6</td>
<td>12.1</td>
<td>440-494</td>
</tr>
<tr>
<td>PPVT-4 Growth Score</td>
<td>133</td>
<td>20.5</td>
<td>80-175</td>
</tr>
</tbody>
</table>
To examine syntactic complexity in terms of the relationship between phonological memory and sentence comprehension (Research Question 3), correlations were determined between the phonological memory composite and (1) the sum of items correct for 3 simple blocks on the TROG-2, and (2) the sum of items correct for 3 complex blocks on the TROG-2. Simple blocks on the TROG-2 were defined as two elements (Block A), negation (Block B), and three element (Block D) sentences. Complex blocks of the TROG-2 were reversible SVO (Block E), four elements (Block F), and relative clause in subject (Block G) sentences. These blocks were selected using information in the TROG-2 Manual and based on previous literature (Bishop, 2003; Oakes et al., 2013). In examining complex blocks, only participants who completed the relevant blocks without first reaching a ceiling on the TROG-2 were included.

Table 4 shows the number of participants in each group (from those with available data, prior to group matching) who completed each block (A-G) on the TROG-2; however, the final number of participants included in each analysis is reported in the Results below. That is, the participants included in the analysis of this final research question were limited both by (1) initial matching procedures for nonverbal cognition or receptive vocabulary and (2) whether or not they have completed each block of interest (i.e., have reached ceiling by failing 5 consecutive blocks prior to reaching the blocks of interest) and thus, results should be interpreted with caution.

Table 3

<table>
<thead>
<tr>
<th>TROG-2 Block</th>
<th>FXS</th>
<th>TD</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Two elements</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>B. Negative</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>C. Reversible <em>in</em> and <em>on</em></td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>D. Three elements</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>E. Reversible SVO</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>F. Four elements</td>
<td>15</td>
<td>23</td>
</tr>
<tr>
<td>G. Relative clause in subject</td>
<td>12</td>
<td>23</td>
</tr>
</tbody>
</table>
Results

Preliminary Analyses

**Group matching.** Again, given that the sample size of boys with ASD was small, the FXS and TD groups were chosen as the primary groups of interest for examination in the study. Two pairs of groups were selected: one pair that was matched on nonverbal cognition using the Leiter-R \((n = 16\) for FXS and \(n = 11\) for TD) and one pair that was matched on receptive vocabulary based on scores on the PPVT-4 \((n = 16\) for FXS and \(n = 14\) for TD). Matching was achieved by eliminating participants with scores at the extreme ends of the distribution (i.e., greater than 475 and less than 450 on the Leiter-R; greater than 159 and less than 119 on the PPVT-4). Based on Leiter-R nonverbal growth scores, the groups were well matched Leiter-R nonverbal growth scores, \(t(25) = .20, p = .840\), effect size = -.08, variance ratio = 1.02 (Kover & Atwood, 2013). See Table 4 for descriptive statistics for Leiter-R matched groups.

Table 4

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FXS ((n=16))</th>
<th>TD ((n=11))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(M)</td>
<td>(SD)</td>
</tr>
<tr>
<td>Age</td>
<td>10.12</td>
<td>1.80</td>
</tr>
<tr>
<td>Leiter-R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age Equivalent</td>
<td>4.95</td>
<td>0.71</td>
</tr>
<tr>
<td>Growth Score</td>
<td>462.5</td>
<td>6.27</td>
</tr>
<tr>
<td>Nonverbal IQ</td>
<td>51.25</td>
<td>10.7</td>
</tr>
<tr>
<td>PPVT-4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Growth Score</td>
<td>141.4</td>
<td>11.2</td>
</tr>
<tr>
<td>Standard Score</td>
<td>69.5</td>
<td>11.3</td>
</tr>
<tr>
<td>WMTB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit Recall Score</td>
<td>13.69</td>
<td>4.44</td>
</tr>
<tr>
<td>(n=6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit Recall Standard Score</td>
<td>64.5</td>
<td>6.9</td>
</tr>
<tr>
<td>(n=6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Word Recall</td>
<td>10.69</td>
<td>3.84</td>
</tr>
<tr>
<td>(n=8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Word Recall Standard Score</td>
<td>68.5</td>
<td>14.3</td>
</tr>
<tr>
<td>(n=8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Based on PPVT-4 growth scores, comparison groups were also well matched, $t(28) = 0.22$, $p = .829$, effect size = -.08, variance ratio = .64 (Kover & Atwood, 2013). See Table 5 for descriptive statistics related to these PPVT-4 matched groups.

Table 5
Participant Characteristics for final groups matched on receptive vocabulary

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FXS ($n=16$)</th>
<th>TD ($n=14$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$M$</td>
<td>$SD$</td>
</tr>
<tr>
<td>Age</td>
<td>9.882</td>
<td>1.915</td>
</tr>
<tr>
<td>Leiter-R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age Equivalent</td>
<td>4.75</td>
<td>.71</td>
</tr>
<tr>
<td>Growth Score</td>
<td>460.7</td>
<td>6.88</td>
</tr>
<tr>
<td>Nonverbal IQ</td>
<td>50.19</td>
<td>10.2</td>
</tr>
<tr>
<td>PPVT-4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Growth Score</td>
<td>139.13</td>
<td>9.74</td>
</tr>
<tr>
<td>Standard Score</td>
<td>69.31</td>
<td>11.1</td>
</tr>
<tr>
<td>WMTB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit Recall Score</td>
<td>13.63</td>
<td>4.44</td>
</tr>
<tr>
<td>Digit Recall Standard Score</td>
<td>64.5</td>
<td>6.9</td>
</tr>
<tr>
<td>Word Recall</td>
<td>10.31</td>
<td>3.9</td>
</tr>
<tr>
<td>Word Recall Standard Score</td>
<td>70.0</td>
<td>14.7</td>
</tr>
</tbody>
</table>


**Concurrent correlations among broadly defined aspects of language.** The second set of preliminary analyses examined the extent to which phonological memory generally related to language and cognitive ability in participants with FXS or typical development. Correlations were determined between phonological memory and language measures of interest (receptive vocabulary, expressive vocabulary, receptive syntax, expressive syntax), as well as nonverbal cognition. The phonological memory composite was used as the overall phonological memory variable, calculated separately for each group selected according to each matching variable (i.e., essentially four times: FXS and TD selected for Leiter-R, FXS and TD selected for PPVT-4).
Correlations were significant for all measures using one-tailed tests. See Tables 6 and 7 below.

That is, in this cross-sectional examination, phonological memory positively predicted all aspects of receptive and expressive language (i.e., vocabulary and syntax) for both boys with FXS and boys with typical development. In addition, phonological memory was correlated with nonverbal cognitive ability in both groups.

Table 6
Correlations With Phonological Memory for participants matched on Nonverbal Cognition

<table>
<thead>
<tr>
<th></th>
<th>PPVT-4 Growth Score</th>
<th>EVT Growth Score</th>
<th>CASL Raw Score</th>
<th>TROG-2 Blocks Passed</th>
<th>Leiter-R Growth Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Sample</td>
<td>r .54 p .002</td>
<td>r .54 p .002</td>
<td>r .75 &lt;.001</td>
<td>r .53 p .002</td>
<td>r .45 p .009</td>
</tr>
<tr>
<td>FXS (n=16)</td>
<td>.45 .042</td>
<td>.40 .061</td>
<td>.88 &lt;.001</td>
<td>.66 .003</td>
<td>.47 .035</td>
</tr>
<tr>
<td>TD (n=11)</td>
<td>.69 .010</td>
<td>.88 &lt;.001</td>
<td>.70 .008</td>
<td>.81 .001</td>
<td>.43 .095</td>
</tr>
</tbody>
</table>

Table 7
Correlations With Phonological Memory for participants matched on Receptive Vocabulary

<table>
<thead>
<tr>
<th></th>
<th>PPVT-4 Growth Score</th>
<th>EVT Growth Score</th>
<th>CASL Raw Score</th>
<th>TROG-2 Blocks Passed</th>
<th>Leiter-R Growth Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Sample</td>
<td>r .50 p .003</td>
<td>r .56 p .001</td>
<td>r .62 &lt;.001</td>
<td>r .42 p .011</td>
<td>r .43 .008</td>
</tr>
<tr>
<td>FXS (n=16)</td>
<td>.52 .019</td>
<td>.44 .043</td>
<td>.88 &lt;.001</td>
<td>.68 .002</td>
<td>.50 .025</td>
</tr>
<tr>
<td>TD (n=14)</td>
<td>.49 .038</td>
<td>.73 .001</td>
<td>.51 .030</td>
<td>.60 .012</td>
<td>.48 .042</td>
</tr>
</tbody>
</table>

Research Question 1

The first research question examined group differences between boys with FXS and boys with typical development on the number of items passed on the TROG-2. A t-test was used to analyze differences. Boys with FXS had significantly fewer items correct on the TROG-2 relative to typically developing boys, t(25) = 4.92, p < 0.001, effect size Cohen’s d = -1.93, when matched on nonverbal cognition based on the Leiter-R. Boys with FXS also passed significantly
fewer items on the TROG-2 relative to typically developing boys when matched on receptive vocabulary using the PPVT-4, $t(28) = 6.16, p < 0.001$, Cohen’s $d = -2.25$.

**Research Question 2**

**Phonological memory and sentence comprehension.** This analysis differs from the preliminary correlation because it uses items, rather than blocks passed, on the TROG-2, which is a potentially more sensitive measure of sentence comprehension (McDuffie et al., 2012). Again, because correlations between Word Recall and Digit Recall were positive and significant, we utilized a composite $z$-score in correlations for matched groups of participants with FXS and typical development. That is, the phonological memory composite scores were calculated within groups for each matching variable pair, for each group separately (separately within each of the four groups – FXS and TD matched on Leiter-R or PPVT-4) to capture variability – and individuals’ relative standing - within the group in each diagnostic category.

When participants were matched on nonverbal cognition based, Pearson’s parametric correlations revealed that phonological memory was significantly correlated with total items correct on the TROG-2 for both boys with FXS, $r(14) = .68, p = .002$, and boys with typical development, $r(9) = .74, p = .005$. Conclusions based on nonparametric correlations did not differ from those reported above. See Figure 2.
When participants were matched based on receptive vocabulary, phonological memory and total items on the TROG-2 were also significantly correlated for both boys with FXS, $r(14) = .70$, $p = .001$, and boys with typical development, $r(12) = .64$, $p = .007$. Results reveal that for participants with FXS or TD, sentence comprehension and phonological memory were correlated using both parametric and nonparametric procedures. See Figure 3.
Research Question 2a. A linear regression was performed with the sum of total items on the TROG-2 as the dependent variable. The predictors included in the model were autism symptom severity based on the ADOS, as well as phonological memory as indexed by digits and words. Raw scores, rather than the phonological composite score, were used because conclusions were not being compared across groups. Participants included in this analysis ($N = 29$) were both those with FXS ($n = 22$) and those with ASD ($n = 7$). The model predicting TROG-2 items passed performance based on autism severity and digit and word recall was significant, $F(3,25) = 20.57, p < .001$. Each of the three predictors uniquely predicted items passed on the TROG-2. Symptoms of ASD were a significant negative predictor for sentence comprehension when controlling phonological memory for words and digits. Trials correct for Word Recall was an independent positive predictor of performance on the TROG-2, as was the number of trials correct for Digit Recall.

Table 8

Regression coefficients predicting TROG-2 items passed from Autism Severity at initial assessment and phonological memory at second assessment for participants with FXS and ASD

<table>
<thead>
<tr>
<th></th>
<th>Unstandardized B</th>
<th>Standard Error</th>
<th>Semi-partial Correlation</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autism symptom severity</td>
<td>-3.42</td>
<td>1.22</td>
<td>-.301</td>
<td>-2.80</td>
<td>.010</td>
</tr>
<tr>
<td>Digit recall trials correct</td>
<td>1.203</td>
<td>.540</td>
<td>.239</td>
<td>2.28</td>
<td>.035</td>
</tr>
<tr>
<td>Word recall trials correct</td>
<td>1.718</td>
<td>.781</td>
<td>.236</td>
<td>2.20</td>
<td>.037</td>
</tr>
</tbody>
</table>

Research Question 3

Correlations were determined between the phonological memory composite and total sum of items correct for blocks A, B, and D (simple blocks), as well as total sums for blocks E, F, and G (complex blocks) of the TROG-2. When matched on nonverbal cognition, for typically
developing boys, phonological memory was correlated with sentence comprehension for both simple, \( r(9) = .79, p = .002 \), and complex, \( r(9) = .59, p = .027 \), items of the TROG-2. However, for boys with FXS, phonological memory was only correlated with sentence comprehension for simple items, \( r(14) = .75, p < .001 \), not for complex items, \( r(10) = .39, p = .104 \), based on parametric correlations. Note that fewer participants were included in the correlation analysis for complex blocks due to the ceiling rule of the TROG-2. The lack of significance for complex blocks may be related to a power issue resulting from the small sample size. Results for nonparametric correlations were the same, except the relationship between complex performance and phonological memory was significant for boys with FXS, \( r(10) = .53, p = .039 \).

**Figure 4.** Complex sentences and phonological memory for participants matched on nonverbal cognition

When groups were matched based on receptive vocabulary based on PPVT-4 growth scores, phonological memory in boys with typical development was significantly correlated with sentence comprehension of both simple, \( r(12) = .58, p = .015 \), and complex blocks, \( r(12) = .52, p = .029 \) of the TROG-2. For boys with FXS, phonological memory was significantly correlated with simple items of the TROG-2, \( r(14) = .76, p < .001 \); however, the result for complex blocks
was not significant, $r(9) = .45, p = .081$. When utilizing nonparametric analysis, phonological memory and complex items passed were correlated for boys with FXS, $r(9) = .62, p = .022$.

In summary, for boys with typical development phonological memory predicted sentence comprehension of simple and complex items in every case; phonological memory predicted sentence comprehension of simple sentences for boys with FXS, but the relationship was less robust for complex sentences.

**Discussion**

The purpose of this study was to examine the extent of delay in syntactic comprehension in boys with FXS, as well as the relationship between phonological memory abilities and sentence comprehension in boys with FXS and boys with typical development. Furthermore, we aimed to examine the impact of sentence complexity on the relationship between sentence comprehension and phonological memory. The current study extends the work of Oakes et al. (2013) and Pierpont et al. (2011) by examining the extent of delay in syntactic comprehension in a younger sample of boys with FXS in comparison to those with typical development, as well as the role of phonological memory as a source of individual variability, both overall and with respect to simple and complex structures.

**Sentence Comprehension**

Individuals with FXS experience deficits in cognition, social interaction, and language (Abbeduto et al., 2007). Syntax is a domain of weakness in individuals with FXS; however, there is wide individual variability (Estigarribia et al., 2012a; Roberts, Price, et al., 2007) and the evidence for the extent of delay for school-age boys with FXS has been mixed (Abbeduto et al., 2003; Finestack et al., 2009). Based on the TROG-2, recent evidence suggests that adolescents with FXS have poorer syntactic comprehension than typically developing boys matched on
nonverbal cognitive ability (Oakes et al., 2013). Results from the current study build upon these findings. Indeed, the current analyses suggest that younger school-age boys with FXS have significantly lower syntactic comprehension abilities than boys with typical development when matched either on receptive vocabulary or nonverbal cognition. Thus, the current findings extend what is known about delays in syntactic comprehension in individuals with FXS in several ways. First, this study contributes to current evidence that sentence comprehension is an area of particular weakness for boys with FXS, even during the early school-age years. Second, it suggests that sentence comprehension is weak relative to both general developmental level (i.e., nonverbal cognitive ability), but also other domains of language ability (i.e., vocabulary comprehension). In line with other studies of young individuals with FXS (Oakes et al., 2013), sentence comprehension is an area that might warrant extra support for boys with FXS.

In previous work by Kover et al. (2014), the profile of delay in sentence comprehension on the TROG-2 in boys with ASD differed for groups matched on receptive vocabulary and groups matched on nonverbal cognition. In that study, no differences were found in TROG-2 performance for groups matched on receptive vocabulary, but a weakness in sentence comprehension was found when considering the participants with ASD (with ID) matched on nonverbal cognitive ability to younger typically developing children. In contrast, in the current study, boys with FXS had poorer performance than the typically developing comparison groups regardless of which matching metric was used. This could relate to the presence of ID in boys with FXS and/or suggest that sentence comprehension is an area of particular weakness during middle childhood in children with the FXS phenotype.

**Phonological Memory**
The current findings suggest that phonological memory is a potentially important predictor of variability among school-age boys with FXS. In line with Baddeley et al. (1998), phonological memory may be useful for understanding individual differences in sentence comprehension abilities in children with developmental disabilities. In the current study, when matched on either nonverbal cognition or receptive vocabulary, correlations were seen between measures of phonological memory and total items passed on the TROG-2. For both groups, results revealed that based on both parametric and nonparametric measures, phonological memory was correlated with sentence comprehension ability. This further builds on Baddeley’s model, extending what we know about language development, specifically in receptive syntax.

Previous literature has established the effect of phonological memory in other developmental disability and language impairment populations using Baddely’s model (Laws, 2003). Findings of lower sentence comprehension abilities, in conjunction with the relationship between sentence comprehension and phonological memory, in children with FXS further add to our understanding of language development and impairment in children with communication disorders. To interpret these results we may use the idea of a breakdown in the phonological loop proposed by Jarrold et al. (1999). Given that correlations were seen between phonological memory and lower sentence comprehension abilities, these findings support the theory of lower phonological memory capacity in children with communication disorders (Jarrold et al., 1999). Overall these findings contribute to current knowledge of the contribution of phonological memory to language learning.

The current study extends what is known about sentence comprehension and autism severity. Kover et. al (2014) found that when ASD occurred with ID, there was a significant deficit in sentence comprehension relative to nonverbal cognition. Results from the current
study showed that autism severity was a negative predictor of sentence comprehension among individuals with ASD and FXS. Given that many individuals with FXS present with a concomitant diagnosis of ASD, examining the effect of ASD severity on sentence comprehension is particularly meaningful. Combining participants with ASD and FXS using a continuous, rather than a categorical approach to quantifying autism symptoms allowed an examination of autism severity as a putative predictors of sentence comprehension alongside the specific cognitive skill of phonological memory. Both autism symptom severity and phonological memory independently predicted sentence comprehension abilities, suggesting that the ability to hold phonological representations in mind, along with difficulties in social communication and interaction and restricted and repetitive behaviors and interests might contribute to poor syntactic comprehension in individuals with FXS or ASD. More broadly, the language comprehension of individuals with neurodevelopmental disorders is likely to relate to specific cognitive abilities, such as phonological memory, as well as social-communicative behaviors and skills that have important consequences for language across development.

**Syntactic Complexity**

Among school-age boys with FXS and young typically developing boys, phonological memory predicted syntactic comprehension skills on the TROG-2, which is the same measure that has been used to examine differences in ability across syntactic ability in adolescents with FXS or DS (Oakes et al., 2013). The relationship between syntactic comprehension and memory would be predicted by current models of short-term memory (Baddeley et al., 1998). Frizelle and Fletcher (2015) also looked measures of the WMTB to examine the role of sentence complexity and phonological memory in language development for children with SLI. They found that there was a significant relationship between phonological memory and simple
sentences. Findings showed that children with SLI had difficulty with sentences of increasing complexity (Frizelle & Fletcher, 2015).

Lastly, findings speak to the role of phonological memory as a predictor of comprehension for both simple and complex sentence structures. In the current sample, phonological memory predicted simple and complex sentence comprehension for boys with typical development, but only simple sentence comprehension for boys with FXS was consistently related to phonological memory. One hypothesis to account for these findings is that the complex sentences were outside the developmental range of participants with FXS, and therefore, provided less meaningful information about their syntactic comprehension abilities. This could also be interpreted in the context of Pierpont et al. (2011). They found a relationship between phonological memory and receptive syntax for boys with FXS function in the developmental range of 4 – 6 years, but not for girls who were functioning at more advanced levels. As such, phonological memory may be most supportive of earlier aspects of language ability, such as the comprehension of simple sentences. The current findings would align with this, given that the boys with FXS had developmental levels similar to or slightly lower than those in the Pierpont et al. study and that the correlations with simple sentences were robust. Nonetheless, these findings support the need for further research on the relationship between phonological memory and language development in individuals with FXS – especially given that both simple and complex sentence comprehension were related to phonological memory for typically developing boys.

**Distinctions between other types of memory.** One factor in interpreting the effect of phonological memory on sentence comprehension is making a distinction between declarative and procedural memory. Declarative memory includes both semantic and episodic memory
(Boucher, Mayes, & Bigham, 2008; Kover et al., 2014). Kover (2014) discussed the possible influence of declarative memory deficits on sentences comprehension, specifically in children with ASD and ID. It was shown that children with ASD may rely heavily on syntactic knowledge to support comprehension (Kover et al., 2014). Boucher (2008) hypothesized that children with ASD and ID show a deficit in sentence comprehension due to deficits in declarative memory (Boucher et al., 2008).

The current results showed a relationship between phonological memory abilities and sentence comprehension for simple and complex sentence constructions. These findings can be understood in the context of deficits in declarative memory. This is in line with Boucher (2008) findings that impaired comprehension and semantic knowledge may be due to limited word knowledge stemming from these deficits (Boucher et al., 2008). Therefore, declarative memory deficits may contribute to limitations in sentence comprehension when challenged by vocabulary items or concepts. It is worth noting, however, that the TROG-2 was specifically designed to utilize simple and familiar vocabulary. An error analysis that examined whether incorrect selections were syntactic or semantic foils could speak to the issue of weaknesses in declarative memory in school-age boys with FXS and would be an interesting area of future research.

Limitations and Future Directions

Findings from the current study contribute to our understanding of language and phonological memory in individuals with FXS in both a clinical and theoretical framework in terms of the cognitive factors that contribute to individual variability in the language development of boys with FXS. A better understanding of the impact of phonological memory on syntactic complexity may be gained by expanding upon current research regarding the extent of syntactic impairments for individuals with FXS—especially in light of the limitations of the
current study. One limitation is that only boys were included. Boys are more severely affected in individuals with FXS (Price et al., 2014). However, given that FXS and ASD affect both boys and girls, future studies would benefit from extending findings to girls with FXS or ASD. Including boys and girls with FXS and ASD would allow for a broader picture of sentence comprehension and phonological memory in these populations. This would further allow for comparisons between genders within groups to expand on knowledge of gender differences.

It should be noted that fewer boys with FXS were included in the analysis for complex sentences given more limited availability of data for advanced items on the TROG-2. Therefore, a smaller sample size could have impacted the power to detect a significant relationship for complex sentences. Indeed, many of the analyses were focused on FXS given the small number of participants with ASD. Future studies may increase the sample size likely increasing the availability of valid data for analysis. An increase in the availability of data would allow for a more expansive comparison between diagnostic groups, ASD and FXS.

Due to the small sample size, it was not possible to include other predictors of sentence comprehension simultaneously in the analyses. For example, phonological memory was examined as a predictor of sentence comprehension in groups matched on nonverbal cognitive ability, but nonverbal cognitive ability was not controlled (e.g., using partial correlations). It would be expected that nonverbal cognitive ability would also predict sentence comprehension and controlling for this would establish the unique contribution of phonological memory over and above that broad ability level. Likewise, in examining autism symptom severity as a predictor alongside phonological memory, it may be helpful to simultaneously consider the role of nonverbal cognitive ability. Although phonological memory was selected for theoretically
motivated reasons, failing to analyze the role of general developmental level does make interpretation more challenging.

Future studies may examine the effect of anxiety on phonological memory and language learning. Anxiety presents as a common psychosocial characteristic in ASD and FXS (Frolli, Piscopo, & Conson, 2015; Selles et al., 2015). Anxiety may affect sentence comprehension given stress related to social interactions during standardized testing. Anxiety relating to social interactions may add to cognitive demands (Frolli et al., 2015). This increase to cognitive load could further add to the limited comprehension abilities found in this study.

**Conclusion**

The current study expands on current theories of phonological memory and its role in language development. Results reveal that individuals with FXS have significantly lower sentence comprehension abilities than their typically developing peers, relative to both nonverbal cognition and receptive vocabulary. This study also expands upon the relationship between phonological memory and sentence comprehension, with both syntactic complexity and autism severity predicting the comprehension abilities of boys with FXS or ASD. This study has important implications for what is known about language development in boys with FXS and ASD; however, future research is needed to expand upon these results and improve our understanding of language development and impairment within these populations.
References


