LANGUAGE AND LEARNING IN BOYS WITH FRAGILE X SYNDROME: SYNTACTIC PROCESSING AND THE ROLE OF PHONOLOGICAL MEMORY

by

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Dedication

In loving memory of my father

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Table of Contents

Abstract......vi

CHAPTER 1

Language learning processes in neurodevelopmental disorders

Introduction......1
Aims......21

List of Figures
Figure 1: Framework for research on language in fragile X syndrome......22

CHAPTER 2: STUDY 1

Syntactic comprehension in boys with fragile X syndrome or autism spectrum disorder

Introduction......23
Method......34
Results......44
Discussion......54

List of Tables
Table 1: Schematic of syntactic comprehension stimuli......63
Table 2: Sentence ratings by adults grouped by verb......64
Table 3: Participant characteristics: Reversible task......65
Table 4: Participant performance: Reversible task......66
Table 5: Reaction time by group and condition......67
Table 6: Participant characteristics: Nonreversible task......68
Table 7: Participant performance: Nonreversible task......69

List of Figures
Figure 1: Reversible noun comprehension......70
Figure 2: Reversible active and passive sentence comprehension......71
Figure 3: Nonreversible noun comprehension......72

Figure 4: Nonreversible active sentence comprehension....73
Figure 5: Nonreversible passive sentence comprehension....74

Appendices

Appendix 2A: Audio stimuli for Study 1....75
Appendix 2B: Visual stimuli for Study 1....76

CHAPTER 3: STUDY 2

Extensions of syntactic knowledge in fragile X syndrome and autism spectrum disorder

Introduction....79
Method....88
Results....94
Discussion....102

List of Tables

Table 1: Example stimuli for word order cues....112
Table 2: Example stimuli for transitivity cues....113
Table 3: Sample novel verb stimuli with accompanying novel actions....114
Table 4: Number of participants with at least two valid trials by condition....115
Table 5: Participant characteristics: Active condition....116
Table 6: Participant characteristics: Passive condition....117
Table 7: Participant characteristics: Transitive condition....118
Table 8: Participant characteristics: Intransitive condition....119

List of Figures

Figure 1: Task performance for word order....120
Figure 2: Task performance for transitivity....121

Appendix

Appendix 3A: Auditory stimuli for Study 2....122

CHAPTER 4: STUDY 3

Phonological memory and variability in the fragile X syndrome linguistic phenotype

Introduction 123
Method 133
Results 137
Discussion 140

List of Tables
Table 1: Participant characteristics and cognitive processing performance 145
Table 2: Partial correlations for phonological memory 146
Table 3: Mediation analysis for boys with FXS 147
Table 4: Mediation analysis for boys with typical development 148
Table 5: Mediation analysis for boys with ASD 149
Table 6: Predicting standardized test performance 150
Table 7: Variability in FXS 151

List of Figures
Figure 1: Hypothesis 1: The impact of phonological memory 152
Figure 2: Hypothesis 2: Contributions to language outcomes 153
Figure 3: Exploratory predictors of language ability 154

CHAPTER 5

Advancing the study of linguistic phenotypes

General Discussion 155
Future Directions 158

References 159

Abstract

Fragile X syndrome is the leading inherited cause of intellectual disability. Most boys with fragile X syndrome have impaired cognition and language deficits, with significant within-syndrome variability. Syntax may be especially delayed relative to nonverbal cognition; however, little is known about the specificity of delay, the sources of that difficulty, or the impact of those delays on other aspects of language development. Comparisons among boys with fragile X syndrome, idiopathic autism spectrum disorder, and typical development were made to assess syntactic comprehension, the extension of syntactic knowledge to novel verbs, and distinct cognitive abilities that might predict language ability and learning in three studies.

In Study 1, comprehension of nouns, active sentences, and passive sentences was assessed with a looking-while-listening task. Boys with fragile X syndrome demonstrated comprehension of active, but not passive sentences. Study 2 assessed extensions of syntactic knowledge for interpreting sentences containing novel verbs in an infrared eye-tracking preferential looking task. Boys with fragile X syndrome showed a somewhat different pattern of performance than boys with ASD. Study 3 was designed to examine variability in language development in terms of individual cognitive and biological characteristics, with an emphasis on the role of phonological memory. Cognitive processing abilities were found to be significant predictors of language outcomes. Results are discussed with reference to the theoretical importance of language learning mechanisms in differentiating linguistic phenotypes associated with neurodevelopmental disorders.

Chapter 1

Introduction: Language Learning Processes in Neurodevelopmental Disorders

Typically, children acquire language rapidly and with little effort or direct teaching. This feat is far from trivial. During the first two years of life, a child has learned to segment the speech stream, attach meaning to words, combine words in grammatical ways, and use these formal language abilities in social, communicative ways. These tasks rely crucially on learning that results from the interaction of experience with rich input from the environment and the elaborate cognitive machinery with which a child is equipped. Considering language learning from multiple levels of analysis – from biology to behavior – is essential because the development of the brain and the cognitive processing directed at the available language input are ultimately rooted in genetics. A multi-level approach to research on language can inform an understanding of development in both typical cases and cases in which language is impaired.

Neurodevelopmental disorders are associated with an array of developmental sequelae, including impairments in cognition and language. Language development is an important focus of research in neurodevelopmental disorders because of the need for effective interventions and because these disorders provide the opportunity to disentangle the contributions of genes and the environment. For neurodevelopmental disorders resulting from genetic anomalies, phenotypic profiles can provide insight into the genetic bases of the cognitive processes that support the development of language more generally.

Fragile X syndrome (FXS), a single-gene disorder, occurs in approximately 1 / 2,500 males and females and is the leading cause of inherited intellectual disability (Fernandez-Carvajal et al., 2009; Hagerman, 2008a). The cognitive phenotype associated with FXS includes a syndrome-specific profile of learning difficulties, which is also accompanied by considerable within-syndrome variation related to gender, level of functioning, and the presence of challenging behaviors (Abbeduto, Brady, & Kover, 2007). Because it is a single-gene disorder, FXS is an ideal disorder from which to consider cognitive processes as they relate to biology, brain, and behavior, and research on FXS in these domains has flourished in recent years (Belmonte & Bourgeron, 2006; Cornish, Turk, & Hagerman, 2008; Reiss & Dant, 2003).

Research on language in FXS, however, to date has focused on “achieved levels” of language ability. Although assessing language outcomes, such as the number of vocabulary words acquired by a certain age, provides useful benchmarks of delay, it fails to reveal information about the cognitive, linguistic, or social-pragmatic factors that account for language delays (see Swensen, Kelley, Fein, & Naigles, 2007 for a brief discussion of this issue with respect to autism). Even with advances in describing language outcomes in children with FXS, little is known about the ways in which they learn language. For example, fast mapping, the process by which the meaning of a novel word is inferred using the context in which the word occurs (Carey, 1978), has been long established as a word-learning mechanism in typical development, but has been largely ignored in children with FXS.

Fast mapping is an important developmental process to understand in children with language delays and neurodevelopmental disorders because vocabulary learning is a fundamental aspect of language development upon which other linguistic abilities are built. These quick label-referent mappings are sometimes made after only a single exposure to the novel word when there is only one possible object referent (Dollaghan, 1985). This learning mechanism can operate to distinguish between possible referents with the addition of various cues, such as a linguistic contrast between an unfamiliar word and a familiar one (e.g., "The chartreuse one, not the red one,"; Heibeck & Markman, 1987). Fast mapping is also supported by syntactic cues from the sentence frame, or grammatical construction, in which the unfamiliar word appears. The term “syntactic bootstrapping” refers to this use of syntactic cues to support word learning (e.g., the transitive structure of the sentence, "The bunny is gorping the duck," hints at a causative meaning for the novel verb; Gleitman, 1990; Naigles, 1990).

Research on fast mapping in children with other neurodevelopmental disorders can inform research questions about language learning in individuals with FXS. In children with language impairments without intellectual disability (e.g., specific language impairment), some aspects of fast mapping, such as the use of syntactic cues, appear to be more impaired than others (Dollaghan, 1987; Johnson & de Villiers, 2009). Mechanisms of language learning that are weak in language-impaired children who do not have severe cognitive delays might be precisely the mechanisms most susceptible to disruption and most likely to have pervasive effects across development for those with cognitive delays.

Consistent with this claim, the few studies on fast mapping in adolescents with Down syndrome (Chapman, Kay-Raining Bird, & Schwartz, 1990; McDuffie, Sindberg, Hesketh, & Chapman, 2007) and young children with autism (Luyster & Lord, 2009) have been fruitful in refining questions about the loci of language impairments associated with various phenotypes. Studying aspects of learning mechanisms, language abilities that support them, and other cognitive processes relevant to language development will begin to fulfill the need to move beyond descriptive research and toward questions that address processes of language learning in FXS and other neurodevelopmental disorders.

In this dissertation, several aspects of language processing and learning were explored. With FXS as a model neurodevelopmental disorder, this work considers the interrelated consequences of biology and behavior for the cognitive processes underlying important aspects of language development; namely, the comprehension of syntactic forms and the use of syntactic knowledge as a springboard for word learning. These aspects of language development were selected both because there is reason to believe they are particularly impaired in boys with FXS and because they are areas of difficulty in other populations of children with impaired language.

Theoretical Perspectives on Language Development

Research on language in neurodevelopmental disorders has focused largely on the products rather than the processes of development. Description of static linguistic outcomes was a sensible first step because little was known about language in specific populations. Addressing what is learned before how it is learned is a logical sequence of inquiry, mirroring the field of developmental psychology in which typical linguistic accomplishments were described before mechanisms of change were tackled (Saffran, 2009). Another contributing factor was the fact that early theoretical perspectives discounted processes of learning.

One example of these prominent theories is nativism. Nativist theories have favored innate knowledge and modular linguistic systems (Chomsky, 1965; Fodor, 1983). In Chomsky's view, the child is primed with language learning capacity in the form of a universal grammar, requiring only minimal input (Chomsky, 1993; Smith, 1999). With this language-acquisition device, language is hypothesized to be acquired in the same way by all children without reliance on other aspects of cognition (Chomsky, 1959). Given what is now known about the role of input, learning processes, and related cognitive abilities, this claim has fallen out of favor.

More recent empiricist theories incorporate the role of input and cognitive processes that support language learning. For example, interactionist theories emphasize the role of the linguistic environment (e.g., parental interaction style, amount of input), the child's desire to interact, and the mutual interactions between language and other cognitive domains as supporting language development (Abbeduto, Keller-Bell, Richmond, & Murphy, 2006; Chapman, 2000). Like interactionist theories, emergentist theories acknowledge the factors that support development in terms of the child's cognitive ability and the environment in which he or she develops. The emergentist view holds that general abilities related to processing linguistic regularities combine with appropriate learning contexts to yield learning about multiple aspects of language over the course of development, with influences of both prior learning and current knowledge (Marchman, 1997). Emergentism takes into account cognitive processes that are not specific to language, but that serve language acquisition through complex interactions between biology and the environment (Bates et al., 1998). Interactionist and emergentist approaches more adequately account for the language abilities of children with neurodevelopmental disorders compared to nativist theories (e.g., Abbeduto & Chapman, 2005; Evans, 2001).

Neuroconstructivism is another alternative to nativist approaches that applies aspects of empiricist theories and has been fruitfully extended to studies of atypical development. Karmiloff-Smith (1998) suggests that the impairments that define the behavioral phenotypes of any neurodevelopmental disorder are attributable to subtle abnormalities in domain-relevant cognition that interact with the environment over time. In neuroconstructivism, profiles of strengths and weaknesses are viewed as originating from biases in learning processes (Thomas & Karmiloff-Smith, 2005). This perspective has been applied to Williams syndrome, which results from a microdeletion on chromosome 7 and is characterized by impaired nonverbal cognition, especially in the visual-spatial domain, but relatively stronger language (Bellugi, Marks, Bihrle, & Sabo, 1988; Dykens, Hodapp, & Finucane, 2000). Although vocabulary is a relative strength in children with Williams syndrome, early processing differences might result in atypical lexical learning (Stevens & Karmiloff-Smith, 1997). For example, young children with Williams syndrome are delayed in their ability to segment the speech stream into words, which likely leads to delays in vocabulary learning or the use of alternate strategies for language learning (Nazzi, Paterson, & Karmiloff-Smith, 2003). Thus, language impairment is hypothesized to emerge from genetic anomalies and their influences on brain development by way of cognitive processing (Karmiloff-Smith, 1998). The current research thus examines specific aspects of cognitive abilities as they relate to language processing and how those abilities might affect future language learning in individuals with FXS.

Language Learning in Typical Development

Although the cognitive processes related to language learning have not been fleshed out in any detail for most neurodevelopmental disorders, processes of language learning in typically developing children have received considerable attention (Saffran, 2009). Reflecting theoretical shifts by highlighting the role of input and the child's cognitive capacity, statistical learning is one mechanism of language acquisition that has been extensively studied in typical development. Statistical learning is intimately related to implicit learning (or learning without awareness) and refers to the process of extracting patterns from input by "tracking" regularities among units (Perruchet & Pacton, 2006). These patterns include probabilities that one unit will be followed by another in a given distribution and adjacent and nonadjacent conditional dependencies in forwards and backwards directions (Pacton & Perruchet, 2008; Pelucchi, Hay, & Saffran, 2009a). Although these learning processes have primarily been studied with respect to language development, they are thought to be general cognitive processes that can be applied to many types of input and bidirectionally affected by other cognitive domains, in contrast to modular accounts (Marchman, 1997). Processes of statistical learning are thought to contribute to phonological learning, speech segmentation, word learning, and the acquisition of syntax

(Gomez & Gerken, 1999; Graf Estes, Evans, Alibali, & Saffran, 2007; Saffran, Aslin, & Newport, 1996; Saffran & Thiessen, 2003; Thompson & Newport, 2007).

Transitional probabilities are one type of regularity extracted by language learners. In the speech stream, the likelihood that a particular syllable follows another is greater for those that occur together within words than for those that are adjacent but belong to different words. As such, the transitional probability for syllables within a word is higher than the transitional probability of syllables that occur sequentially but across words (Aslin, Saffran, & Newport, 1998). Saffran, Aslin, & Newport (1996) provide a classic example from natural language with the phrase, “pretty baby,” illustrating that “pre” is more likely to be followed by “tty” than “tty” is to be followed by “ba” because “pre-tty” comprises a word, whereas “tty-ba” does not. Saffran and colleagues showed that the peaks and dips of high and low transitional probabilities can be used as cues to segment continuous speech into words by typical language learners.

In their seminal study on statistical speech segmentation, Saffran et al. (1996) exposed eight-month-old infants to two minutes of auditory input from an artificial language composed of four trisyllablic “words,” such as “pabiku” and “tibudo”. Infants were later able to distinguish words from unfamiliar nonwords (e.g., “dapiku“) and from partial words (e.g., “kutibu”) comprised of syllables that they had heard during the familiarization phase. Crucially, partial words had lower transitional probabilities among syllables than did words, but there were no intonational or other cues as to how to segment the continuous speech stream. This study highlighted the role of experience and learning in language development and encouraged an explosion of work on language learning processes (Bates & Elman, 1996). Lending ecological validity to statistical learning in artificial languages, recent evidence has demonstrated that these processes can be applied to natural languages (Pelucchi, Hay, & Saffran, 2009b).

Although transitional probabilities are computed over individual tokens, predictive dependencies can refer more generally to the conditional probabilities among categories. For example, phrases are composed of words that belong to nested categories, with a word from one category (e.g., a determiner) predicting the presence of a subsequent word from another category (e.g., a noun), as in the way a determiner predicts noun *the cat* in English (Saffran, 2001). Using predictive dependencies among adjacent units, adults and children can incidentally acquire the basic phrase structure of an artificial language (Saffran, 2001; Saffran, 2002). This type of statistical learning can be leveraged by infants as young as 12 months of age if the number of units per category is small enough (Saffran et al., 2008). In natural language, hierarchical relationships lead to adjacent and nonadjacent regularities (Hauser, Chomsky, & Fitch, 2002). Predictive dependencies may facilitate the efficiency with which relationships among elements in grammar are processed by meaningfully grouping input (Saffran, 2002; Saffran et al., 2008).

Statistical learning extends to domains of processing outside of language. For example, the phrase structure from an artificial "language" composed of computer alert sounds can be learned with predictive dependencies (Saffran, 2002). Adults and infants are also capable of extracting transitional probabilities from visual displays, such as streams of shapes (Fiser & Aslin, 2001; Kirkham, Slemmer, & Johnson, 2002; Turk-Browne, Junge, & Scholl, 2005). Thus, statistical regularities support learning in nonlinguistic auditory and visual input, reinforcing the notion that these are not language-specific processes. Understanding the ways in which input is processed by learners will be pivotal for research on neurodevelopmental disorders.

Extensions of statistical learning. Patterns in linguistic input that are conceptualized as sequences of probabilities among units can also be thought of as rules. In fact, because language is rich with overlapping cues, statistical regularities and regularities that appear to embody rules can refer to the same phenomena and are difficult to disentangle (Seidenberg, MacDonald, & Saffran, 2002). Marcus, Vihayan, Bandi Rao, and Vishton (1999) conceptualized infant learning of ABA and ABB grammars (e.g., "ga ti ga" and "ta la la") as evidence of infants' ability to extract and generalize representations of algebraic rules. Hypotheses about learning rules from patterns suggest that the child abstracts a representation away from the input in some form or another (Gomez & Gerken, 1999, 2000). The child's task of extracting and generalizing rules in linguistic input is thought to involve abstract representations of categories; however, other types of processing might account for the same outcomes (Perruchet & Pacton, 2006). Thus, statistical learning and rule learning often reflect two perspectives on the same phenomenon, with different emphases on aspects of the learning task and how the child succeeds in it. Although the boundaries between statistical learning and rule learning are unclear, the ability of language learners to make use of rule-like patterns in input has implications for the development of syntax.

Whether conceptualized as distributional cues or rules, the grammatical structures of sentences reflect regularities that provide a reliable source of information for language learners (Gleitman, 1990). The regularities of sentence structure provide the basis for syntax. Once mastered, competence with the syntactic regularities in a child's native language is likely to support further learning in domains such as vocabulary (Moyle, Ellis Weismer, Evans, & Lindstrom, 2007). For example, in the case of syntactic bootstrapping, toddlers can make use of a number of grammatical regularities, including transitivity (i.e., that transitive structures imply causality) and word order, to infer meanings for verbs (Gertner, Fisher, & Eisengart, 2006; Naigles, 1990; Yuan & Fisher, 2009). Research on the relation between syntactic knowledge and lexical acquisition in children with neurodevelopmental disorders would illuminate processes by which profiles of impairment emerge and how interventions might remediate them.

Complementary aspects of language processing. Extracting information from linguistic input for the purpose of learning typically occurs without conscious effort, instruction, or feedback. Such processing can be indexed in a variety of ways, including eye gaze measures of a child's accuracy and speed (e.g., Swingley, Pinto, & Fernald, 1999). Individual differences in accuracy and speed of processing during infancy have been shown to predict language outcomes years later. Speech perception assessed in terms of accuracy and speed in vowel discrimination at six months of age predicts individual differences in receptive and expressive vocabulary at two years of age (Tsao, Liu, & Kuhl, 2004). Further, the speed with which 25-month-old toddlers recognize familiar words predicts the rate of expressive vocabulary development during the second year of life (Fernald, Perfors, & Marchman, 2006) and expressive language at the age of 8 years (Marchman & Fernald, 2008). The ability to process linguistic input accurately and quickly thus relates to further language development, in the expressive as well as the receptive domain.

In summary, processing statistical regularities and using those regularities to acquire meanings for novel words are hypothesized to facilitate further language development for more developmentally advanced aspects of language. This suggestion is supported by studies in which successful linguistic processing is related to both concurrent vocabulary acquisition and later language ability in the domains of vocabulary and syntax (Graf Estes et al., 2007; Newman, Ratner, Jusczyk, Jusczyk, & Dow, 2006). Given this evidence, variability in the cognitive processes related to early language learning will have consequences for later language outcomes. Thus, understanding the interactions between input and cognition is likely to elucidate the mechanisms of language acquisition in neurodevelopmental disorders, such as FXS.

Language Learning in Neurodevelopmental Disorders

Research on language processing and learning in typical development highlights the characteristics of the language input and the cognitive processes on which learning relies. Features of the input, such as statistical regularities, provide critical information for language learners, and the integrity of the cognitive processes the child brings to the learning situation will affect his or her ability to exploit those regularities and thus, the linguistic outcome. This research fits squarely with interactionist, emergentist, and neuroconstructivist perspectives by emphasizing the relevance of the language input and its dynamic interactions with the cognitive processes put into motion by genetics (Bates et al., 1998; Chapman, 2000; Karmiloff-Smith, 1998). Drawing on these perspectives will not only ground hypotheses on the role of biology, brain, and behavior for language development in neurodevelopmental disorders, but also inform theories of typical development. An understanding of the impairments of children with neurodevelopmental disorders will provide insights into the cognitive processes all language learners use to capitalize on the information in input from the linguistic environment.

The ways in which language learning processes operate in atypical development are largely unexplored. Although limited in number and scope, studies on specific language impairment (SLI) and Williams syndrome exhibit the utility of studying these processes in neurodevelopmental disorders. For example, Evans, Saffran, and Robe-Torres (2009) found that children 6 to 14 years of age with SLI required twice as much input as typically developing children to make use of transitional probabilities for word segmentation. Together with other documentation of impaired implicit learning in SLI, this study provides evidence that inefficient processing and difficulty tracking regularities in sequential input contribute to the linguistic profile of SLI (Tomblin, Mainela-Arnold, & Zhang, 2007). Likewise, impaired performance of young children with Williams syndrome on speech segmentation and recognition of English words provides evidence of difficulty with distributional cues and phonological processing that results in atypical language learning (Nazzi et al., 2003). Furthermore, these studies demonstrate the utility of testing hypotheses about processing and learning in neurodevelopmental disorders using paradigms established for typically developing children.

The paucity of research on learning mechanisms in neurodevelopmental disorder leaves open the door for studies on language processing and the use of distributional cues in these populations. Given the limited research on these aspects of language development in neurodevelopmental disorders, what is known about language profiles in well-described disorders can serve as a guide for those with overlapping characteristics. For example, the syntactic deficits characterized in children with SLI have been fruitful areas of investigation for other neurodevelopmental disorders, such as Down syndrome and autism (e.g., Kjelgaard & Tager-Flusberg, 2001; Laws & Bishop, 2003). Some lines of research have helped to delineate shared and unique features of language impairment across neurodevelopmental disorders by making a direct comparison to children with SLI (e.g., Loucas, Charman, Pickles, Chandler, et al., 2008), whereas others have simply examined known aspects of language impairment in SLI in other populations (e.g., grammatical morphology in children with autism; Roberts, Rice, & Tager-Flusberg, 2004). Using related disorders as a point of reference helps to reveal underlying cognitive processes and to address the syndrome-specificity of impairments. Such comparisons will help to achieve the goal of understanding how individuals with neurodevelopmental disorders, such as those with FXS, process language and use the regularities in input.

Fragile X Syndrome from Genes to Behavior

Fragile X syndrome results from a mutation in a single gene and is reliably identifiable through molecular DNA testing. It is an ideal disorder for gaining insights into the biological substrates of cognitive processes relevant to language because our understanding of its genetic basis is relatively advanced, allowing the possibility that the neurobiological mechanisms connecting genotype and phenotype will eventually be understood. The mutation that causes FXS is an expansion of the CGG (cytosine guanine guanine) trinucleotide sequence on the Fragile X Mental Retardation-1 (*FMR1*) gene, located on the X chromosome at Xq27.3 (Verkerk et al., 1991). A CGG expansion of 55 - 200 repeats is called the premutation and is associated with behavioral and emotional difficulties, as well as premature ovarian insufficiency in females and fragile X-associated tremor/ataxia syndrome in males and some females (Hagerman, Ono, & Hagerman, 2005). If repeats fall in the full mutation range (i.e., more than 200), the *FMR1* promoter region is typically methylated, blocking transcription into mRNA and production of the gene's protein, Fragile X Mental Retardation Protein (FMRP; Oostra & Willemsen, 2003). The full mutation and its resulting neurobiological effects – along with the influence of background genes yet to be identified – contribute to the FXS phenotype (Bureau, Shepherd, & Svoboda, 2008; Reiss & Dant, 2003). In at least one third of males with FXS, mosaicism can occur due to methylation status or the presence of premutation expansions, contributing to variability in the phenotype (Nolin, Glicksman, Houck, Brown, & Dobkin, 1994), although background genes and environment no doubt also contribute (Belmonte & Bourgeron, 2006).

Neurodevelopment in fragile X syndrome. When FMRP is absent or reduced, other proteins relevant to synaptic structure (e.g., dendritic spine size and shape) and plasticity are upregulated, affecting memory and learning (Willemsen, Oostra, Bassell, & Dictenberg, 2004).

One upregulated protein is metabotropic glutamate receptor 5 (mGluR5). The increased presence of mGluR5 affects neural functioning by way of increased hippocampal and cerebellar long-term depression (LTD) – a mechanism important for synaptic elimination, as opposed to long-term potentiation, which retains synapses (Bear, Huber, & Warren, 2004). Although LTD processes vary across development, Bear and colleagues hypothesize that the lack of FMRP dysregulates mRNA translation of mGluR, resulting in elongated dendritic spines and cognitive impairments. In FMR1 knockout mice, mGluR5 has been tied to anxiety, autistic-like behaviors, and other symptoms related to FXS (Bear et al., 2004).

The FXS phenotype is associated with abnormalities in size and asymmetry of several brain regions; however, overall brain volume does not seem to be affected (Gothelf et al., 2008; Kates, Folley, Lanham, Capone, & Kaufmann, 2002). FXS is characterized by asymmetry of the frontal lobes and reduced volume of the amygdala compared to same-age typically developing individuals (Gothelf et al., 2008). Structures with abnormal size in young boys and adolescent males and females with FXS include enlarged caudate nucleus and thalamus and reduced superior temporal gyrus, amygdala, and posterior vermis relative to those with autism or typical development (Gothelf et al., 2008; Hazlett et al., 2009; Kates et al., 2002; Reiss & Dant, 2003). Importantly, the superior temporal gyrus (i.e., auditory cortex and Wernicke's area) is related to language, attention, and executive function and accounts for variance in IQ in adolescents with FXS; the caudate nucleus may also be related to stereotyped behaviors and executive function (Gothelf et al., 2008). Given the extent of these neurobiological differences, it would be expected that behavioral consequences would be pervasive across domains of functioning.

The behavioral phenotype of fragile X syndrome. Approximately 85% of males and 25% or more of females have IQs in the range of intellectual disability (Hagerman, 2008b).

Because FXS is an X-linked disorder, males and females are differentially affected due to X-activation ratio in females (Reiss & Dant, 2003; Tassone, Hagerman, Chamberlain, & Hagerman, 2000). However, disparities between genders appear to be largely quantitative, not qualitative, in nature (Abbeduto et al., 2007; Keysor & Mazzocco, 2002). On average, individuals with FXS are thought to have especially severe impairments in executive function, attention regulation, and sequential processing, but relative strengths in long-term memory and simultaneous processing, although even these latter areas are less mature than age-expectations (Dykens, Hodapp, & Leckman, 1987; Freund & Reiss, 1991; Munir, Cornish, & Wilding, 2000b; Roberts, Hatton, Long, Anello, & Colombo, 2011). Given this overall pattern of cognitive strengths and weaknesses, one would expect the aspects of language development dependent on long-term memory, such as high-frequency, concrete vocabulary to be relatively strong. In contrast, aspects of language development dependent on processing features of linguistic input, such as syntactic comprehension and the language learning it supports, might be relatively weak.

Variability in the FXS phenotype. The general profile of abilities associated with the FXS phenotype is displayed in individuals to different degrees, with variability along several dimensions of behavior, cognition, and neurobiology. Autism symptoms are prevalent in those with FXS, with about 25 – 50% having symptoms severe enough to warrant a diagnosis of autism (Bailey et al., 1998; Hagerman, Jackson, Levitas, Rimland, & Braden, 1986; Rogers, Wehner, & Hagerman, 2001). Despite the shared symptomatology, differences between idiopathic autism and FXS are apparent. For example, gaze avoidance in FXS is thought to be more related to anxiety and hyperarousal than to social “indifference” as in idiopathic autism (Cornish, Sudhalter, & Turk, 2004). Deficits in theory of mind, which are extensive in autism, are present in FXS but appear to be the result of working memory deficits rather than being specific to social cognition (Grant, Apperly, & Oliver, 2007). Nevertheless, symptoms of autism seem to have developmental impacts on children and adolescents with FXS. Children with both FXS and autism are, in general, likely to have less positive developmental outcomes (e.g., lower IQs) than those with FXS who do not meet criteria for autism (Bailey, Hatton, Skinner, & Mesibov, 2001; Kaufmann et al., 2004; Rogers et al., 2001). Individuals with FXS and autism also have greater language impairments, particularly in the receptive domain (Bailey et al., 2001; Lewis et al., 2006; Philofsky, Hepburn, Hayes, Hagerman, & Rogers, 2004).

Up to half of boys with FXS meet diagnostic criteria for attention-deficit/hyperactivity disorder (ADHD; Sullivan et al., 2006). Difficulties in this domain seem to match the inattentive variant of ADHD with impulsive tendencies, inattentiveness, and restlessness causing the most disruption (Turk, 1998). Even infants with FXS as young as 12 months of age demonstrate atypical visual attention to objects (i.e., prolonged looking and longer latency to disengage) and psychophysiological functioning (i.e., less heart rate variability and less deceleration) relative to typical development (Roberts et al., 2011). In older individuals, selective attention, working memory, and executive function impairments have been reported for tasks that require switching between responses, inhibiting a prepotent response, or regulating behavior (Cornish, Swainson, et al., 2004; Kirk, Mazzocco, & Kover, 2005; Loesch, Bui, et al., 2003; Menon, Leroux, White, & Reiss, 2004). Thus, level of impairment in cognition in FXS might be linked to attention and sequential processing (Cornish, Turk, et al., 2004). Above and beyond nonverbal cognition, memory, attention, and executive function are of particular interest with respect to syntactic development and learning because of their potential impact on processing linguistic input.

Neurobiological factors are another source of within-syndrome variability. Levels of FMRP in peripheral blood, assessed as the percentage of sampled cells testing positive for

FMRP, are related to levels of cognitive functioning (Loesch, Huggins, & Hagerman, 2004). Higher FMRP levels are usually accompanied by better cognitive and behavioral outcomes in individuals with FXS (Bailey et al., 2001; Cornish et al., 2008; Moore et al., 2004). Autism symptoms and FMRP are inversely related in both males and females with FXS (Hatton et al., 2006); however, the relationship between autism and FMRP may be mediated by nonverbal cognitive ability (Bailey et al., 2004; McDuffie et al., 2010). In another sample of males and females with FXS, caudate nucleus volume was positively correlated with autism symptoms, but negatively correlated with FMRP and IQ (Gothelf et al., 2007). Aspects of attention, memory, and executive function are also inversely related to FMRP (Loesch, Bui, et al., 2003; Menon et al., 2004). Although correlational, these studies suggest that FMRP expression might be an important contributor to variability in the FXS phenotype, including language ability.

Language development in fragile X syndrome. The FXS phenotype is associated with significant delays in language, with some children remaining nonverbal and others developing language consistent with their abilities in other cognitive domains (Abbeduto et al., 2007). In adolescent males and females with at least phrase speech, receptive vocabulary and syntax seem to be on par with nonverbal cognition, but are relative weaknesses in younger boys (Abbeduto et al., 2003; Price, Roberts, Vandergrift, & Martin, 2007). In young males with FXS, spontaneous expressive vocabulary and syntax are also delayed beyond cognitive-level expectations, although expressive vocabulary is commensurate with cognition in some standardized testing contexts (Roberts, Price, Barnes, et al., 2007; Roberts, Hennon, et al., 2007). Language use in FXS is characterized by a quick rate, repetitions (e.g., perseveration, echolalia), and noncontingent talk (Murphy & Abbeduto, 2007; Roberts, Martin, et al., 2007; Sudhalter & Belser, 2001).

Strong conclusions from studies on language abilities in individuals with FXS are difficult to draw, however, because samples have been small, and have included participants with wide ranges of developmental levels. Given the individual variability among children with FXS, large sample sizes may be necessary to accurately discern developmental patterns. Because the development of language abilities may not be strictly linear, including children in vastly different stages of language development could obscure patterns of development that would be apparent if age were carefully considered as a variable relevant to development. The use of small samples with large age-ranges also brings into question whether results might vary across studies because the chosen assessments were not well-suited for some of the participants with lower developmental levels. Much work remains to be done, particularly in the domain of syntax.

The development of syntax in boys with FXS is an important topic of research for several reasons. First, many boys with FXS are severely impaired in the domain of syntax, both in comprehension and production. In the expressive domain, some boys may not produce complex language until adolescence or later (Abbeduto et al., 2007). In the receptive domain, syntactic comprehension is delayed beyond nonverbal cognition when assessed with standardized measures (Price et al., 2007). Challenges with understanding syntactic constructions could have significant impacts on daily functioning, further language learning, and academic achievement. Second, syntactic delays are present in children with SLI and other neurodevelopmental disorders, such as autism. Because the syntactic abilities of boys with FXS have not been well described, it is uncertain whether their delays are distinct from those associated with other neurodevelopmental disorders. Third, the generative nature of syntax is a hallmark of natural language. Mastering proficiency with the syntactic regularities of a native language is a challenging cognitive task, but one that is taken in stride by typically developing children. Thus, understanding the precise nature and specificity of the syntactic deficits experienced by boys with FXS will speak to the cognitive processes underlying language acquisition.

Directions for Research on Language Learning in Fragile X Syndrome

Given what is known about FXS, hypotheses can be made about the connections among the genetic underpinnings of the disorder, brain function, and language. For example, it has been suggested that reduced FMRP causes deficits in behavioral control and attention that unfurl over development, resulting in higher-order cognitive difficulties (e.g., conversational language, mathematics; Cornish, Turk, et al., 2004). According to Cornish, Sudhalter, and Turk (2004), deficits in attention, inhibitory control, and hyperarousal, resulting from interactions among genes, brain, and behavior, may be at the root of the tangential, repetitive, and perseverative speech that is characteristic of FXS. Unfortunately, however, little explanation of difficulties acquiring linguistic knowledge, such as syntax and vocabulary, has been offered.

Research on language development in individuals with FXS should acknowledge that biological factors will interact with environmental input and language learning processes over time (see Figure 1). Patterns of atypical brain development (i.e., reduced superior temporal gyrus, enlarged caudate nucleus) might lead one to suspect that cognition that relies upon those regions will be impaired or inefficient, including processing of linguistic input. Early processing differences would have implications for the course of development by affecting the accuracy and speed with which children with FXS segment the speech stream, acquire vocabulary, and extract grammatical patterns. Behavioral support for these hypotheses comes from evidence of weakness in sequential processing in individuals with FXS (e.g., Dykens et al., 1987; Freund & Reiss, 1991), which could be a source of difficulty for tracking distributional regularities in language. These early processing difficulties could ultimately result in the linguistic profile of especially severe syntactic weaknesses in the FXS phenotype.

This theory-driven framework applies what is known about development across levels of analysis to language learning processes. Importantly, it can also illuminate features of syndrome-specificity and within-syndrome variability in syntactic deficits. It is yet unclear how phenotypic features of FXS, such as impaired memory, attention, and executive function, relate to the foundational processes of language acquisition. Because working memory and attention support syntactic processing and learning based on distributional cues (Ludden & Gupta, 2000), impairments in memory and attention are likely to be prime sources of variability for language learning in neurodevelopmental disorders.

With a focus on the cognitive processes related to language acquisition, findings on FXS will provide insight into other neurodevelopmental disorders as well. Many brain anomalies found in FXS are shared with other disorders; for example, dendritic spine abnormalities are also common in Down syndrome and Rett syndrome (Willemsen et al., 2004), reduced volume of temporal lobes is found in Down syndrome and in individuals with developmental language delay (Kates et al., 2002), and reduced frontal lobe asymmetry has been reported in children with SLI (Friederici, 2006). There is also considerable overlap in the behavioral characteristics of children with FXS and those with autism (Hagerman, 1999). Thus, findings about genes, brain, and behavior in FXS may have implications for other neurodevelopmental disorders.

Clinically, understanding the processes associated with language learning in FXS has implications for developing interventions specific to infants and children with FXS, including indicating the need for syndrome-specific therapies. With pharmacological treatments on the horizon (e.g., minocycline for dendritic maturation and improved cognition; Bilousova et al., 2009), it will be important to consider how amelioration of targeted symptoms, such as memory, will improve language learning. Understanding the effects of memory, attention, and executive function on language in FXS will be informative for other neurodevelopmental disorders, as well (Cornish et al., 2008). Because the relationship between autism and FXS is still being delineated, comparisons between these disorders will contribute to an understanding of the impact of autism symptoms on language development.

Aims

The purpose of this dissertation was to examine areas of language not well understood in boys with FXS; namely, processing syntactic information during comprehension and extending syntactic knowledge to sentences containing novel verbs. Study 1 was designed to clarify the extent and specificity of the delay in syntax by assessing the comprehension of active and passive reversible transitive sentences using a looking-while-listening paradigm, yielding data on accuracy and speed of processing. Using an infrared eye-tracking preferential looking paradigm, Study 2 was designed to characterize one aspect of novel verb interpretation using (syntactic) distributional cues: word order and transitivity. Study 3 was designed to address cognitive and biological correlates of within-syndrome variability in language and learning by focusing on phonological memory, attention, executive function, and FMRP.

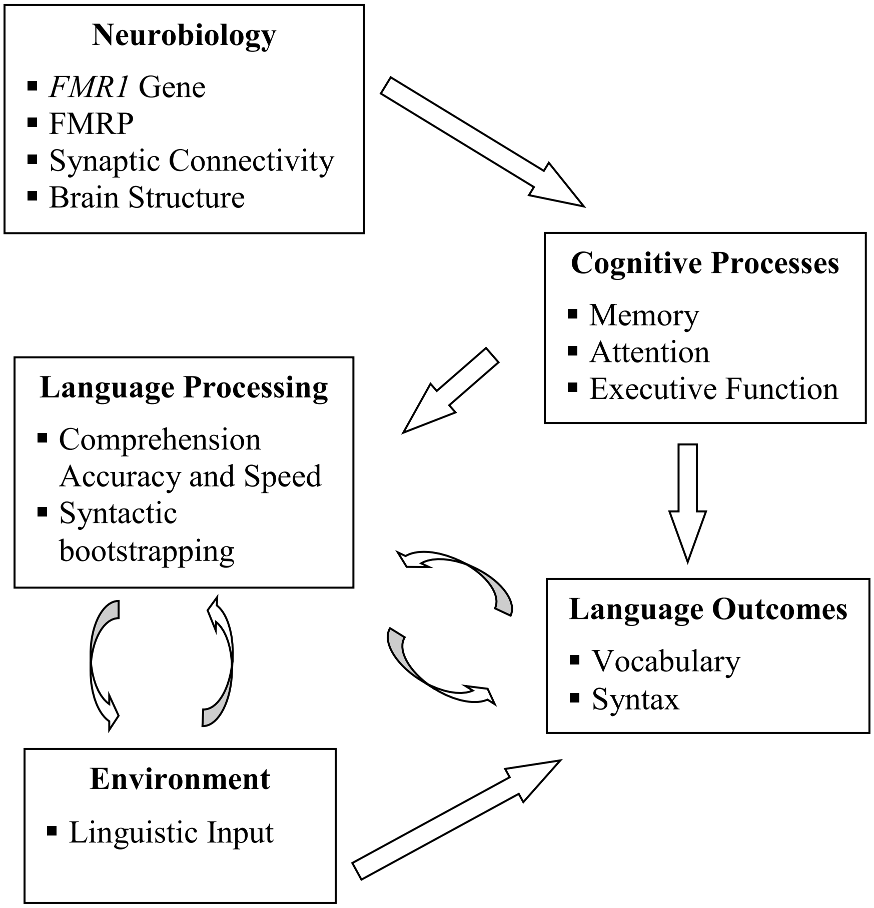

Figure 1. Framework for research on language in fragile X syndrome. The effects of fragile X syndrome at biological, brain, and behavioral levels on language processing and learning across development are highlighted.

Chapter 2

Study 1: Syntactic Comprehension in Boys with Fragile X Syndrome or Autism Spectrum Disorder

Fragile X syndrome (FXS) is a single-gene disorder and leading inherited cause of intellectual disability. The FXS behavioral phenotype includes significant language impairments ranging from mild delays in individuals with average cognitive functioning to profound language difficulties, with some individuals remaining nonverbal into adolescence and beyond (Abbeduto et al., 2007). Since definitive identification of the *FMR1* gene by Verkerk and colleagues (1991), research has made considerable progress in describing language outcomes of children and adolescents with FXS (Abbeduto et al., 2003; Roberts, Mirrett, & Burchinal, 2001; Roberts, Price, Barnes, et al., 2007). Receptive syntax (i.e., the comprehension of grammatical forms) is severely delayed in boys with FXS (Price et al., 2007); however, our knowledge about syntactic development in FXS has many gaps. Wide variability in sample characteristics and limitations of available measures have led to inconsistent findings across studies. The current study builds upon previous research by applying a more sensitive methodology than used to date to assess comprehension in boys with FXS. Two carefully chosen comparison groups aid interpretation of their performance: boys with typical development or autism spectrum disorder (ASD).

Disruption of Syntactic Comprehension

Syntactic comprehension is an area of weakness in many neurodevelopmental disorders. In and of itself, mastery of receptive syntax is important for comprehending language in daily interactions. Beyond this, comprehension precedes production, even in children with autism (Swensen et al., 2007), and receptive syntax serves as a foundation for future learning, including lexical acquisition (McDuffie et al., 2007; Naigles, 2002).

Competence in the domain of receptive syntax is typically attained gradually with age and in a particular sequence, with different strategies for interpreting sentences favored at different points in childhood. Simple transitive sentences with subject-verb-object (SVO) constructions (e.g., “The boy pushes the cup,”) can be correctly interpreted by very young children. For children under the age of two years, successful comprehension of these sentences likely depends in part on contextual information (but see Hirsch-Pasek & Golinkoff, 1996), although even 19-month-old infants have expectations about SVO sentence structures (Franck, Millotte, Posada, & Rizzi, in press). Children between ages two and three years might rely upon probable-event strategies for comprehension (e.g., *The mom feeds the boy*), and only between three and four years of age show comprehension of neutral (e.g., *The boy pushes the girl*) or improbable (e.g., *The cup pushes the boy*) events (Paul, 2007, pp. 280, 343; Paul, Fischer, & Cohen, 1988). Knowledge about word order is necessary to interpret these neutral and improbable event sentences when contextual information is unavailable. These types of grammatical constructions are considered to be reversible because the subject and the object are both candidate actors in the sentence; only their position in the sentence distinguishes them. As such, comprehension of reversible forms relies entirely on syntactic cues because semantic cues (e.g., animacy) cannot disambiguate their meanings; merely understanding the constituent elements of a reversible sentence is not sufficient for understanding.

Without using syntax (i.e., word order in English) as a guide, reversible sentences cannot be interpreted accurately without an unambiguous visual context or other semantic cues. Thus, comprehension of reversible sentences about events with neutral probability can be particularly informative with respect to receptive syntactic abilities because these sentences heavily tax syntactic processing and remove the effects of contextual or semantic strategies. Children who are asked either to act out reversible sentences with toys or to choose the target picture over a grammatical foil (i.e., a girl pushing a boy) might do poorly if they have inadequate syntactic knowledge or fail to access syntactic knowledge due to the processing demands of the task (Evans, 2002). Reversible constructions, including active transitive sentences, may be especially sensitive to a child's syntactic impairments because of the demands they place on syntactic processing relative to nonreversible constructions. Such impairments could present as reduced accuracy or increased latency because of additional time needed to process the linguistic information (Slobin, 1966; van der Lely & Harris, 1990).

Passive reversible sentences, which violate the typical SVO English word order, provide an even greater challenge than do active reversible sentences, both for typically developing children and children with language impairments, in terms of accuracy and speed (Dick, Wulfeck, Krupa-Kwiatkowski, & Bates, 2004; Slobin, 1966). Between two and five years of age, children might identify agents in sentences first by using animacy cues, then with SVO word order, and only later master the word order conventions of English for passive, OVS, sentences (Bates et al., 1984).

Boys with FXS have especially severe deficits in some aspects of cognitive processing and relative strength with semantic information (Dykens et al., 1987; Freund & Reiss, 1991). Delays in receptive syntax, therefore, might be driven by the demands of comprehension that are not supported by contextual or semantic cues. These demands could be specific to syntax or to processing sequential information more generally. Understanding the nature and sources of difficulty in the domain of receptive syntax would allow for targeted interventions and a better understanding of FXS linguistic phenotype. Deficits experienced by other children with language impairments yield further insight into abilities underlying syntactic comprehension.

Specific language impairment. Children with specific language impairment (SLI) have nonverbal IQs in the normal or low-normal range and difficulty with language comprehension, including weak strategies for sentence interpretation (Evans, 2002). In particular, especially impaired comprehension of reversible transitive sentences has been noted in school-age children with SLI (van der Lely & Harris, 1990). Van der Lely and Harris compared 14 children with SLI, ages 4;10 to 7;10, to two groups of typically developing children: one matched on chronological age and a younger group matched on receptive vocabulary age-equivalents, which ranged from 2;6 to 6;0. With a set of toys, children were asked to act out sentences, which included reversible active and passive transitive sentences (e.g., *The boy pushes the girl*, *The girl is pushed by the boy*). The children with SLI were less likely than the language-matched children to meet the criterion of correctly reenacting five out of six of the reversible active and passive transitive sentences. A picture-pointing task also revealed greater impairment in the SLI group with the passive sentences, but the difference between groups failed to reach significance for the active sentences. Van der Lely and Harris suggested that processing of reversible transitive sentences can be problematic for children with SLI, especially in the passive voice.

Other studies confirm that reversible passive sentences pose a specific challenge for children with SLI. Dick and colleagues (2004) found that 7- to 15-year-old children with SLI were less accurate than 5-year-old typically developing children in choosing the correct interpretation of the agent in passive sentences from two choices with a button press. In a study of 6- to 12-year-old children with SLI, comprehension of complex sentences (e.g., reversible passives, reflexives) was impaired relative to a chronological age-matched group (Montgomery & Evans, 2009). No difference between groups was found for active transitive sentences (e.g., *The clown is hugging the tiny white elephant*) in the Montgomery and Evans study; however, the foils for active transitive sentences differed from the targets only semantically (i.e., in terms of the color or size of the agent or patient) and as such, the results might have differed with syntactic foils. Nevertheless, these studies demonstrate that receptive syntax is impaired for children with SLI, with some areas more compromised than others.

In summary, reversible transitive sentence comprehension is an area of weakness in children with SLI. Reversible passive sentences pose an additional challenge over and above that of reversible active sentences. Extending research on syntactic comprehension to other neurodevelopmental disabilities could lend insight into the specificity of the profile of deficits displayed by children with SLI and the language learning processes underlying those deficits.

Autism spectrum disorder. The comprehension difficulties of children with SLI with reversible syntactic constructions could have implications for other neurodevelopmental disorders. There has been some suggestion that SLI and autism might be associated with similar linguistic impairments despite differing etiologies and phenotypes (Kjelgaard & Tager-Flusberg, 2001; Tager-Flusberg, 2004). Language delays are common in children with ASD in both the receptive and expressive domains and often lag behind nonverbal cognitive abilities (Ellis Weismer, Lord, & Esler, 2010). Even high functioning children with ASD have language difficulties that continue into adulthood (Mawhood, Howlin, & Rutter, 2000). In some individuals, only semantic and pragmatic difficulties are present, but many others have delays in syntax and phonological processing (Rapin & Dunn, 2003). Although not always aligned with the SLI profile of impairments, recent research has provided evidence of particular areas of weakness in structural aspects of language in children with ASD.

Only a few studies have specifically examined the domain of syntax in children with ASD. Eigsti, Bennetto, & Dadlani (2007) examined the expressive language of 16 high-functioning children with autism relative to children with developmental delays or typical development matched on nonverbal IQ, gender, and receptive vocabulary. The children with autism displayed less syntactically complex expressive language than the other groups, indicating that syntax was impaired beyond nonverbal IQ and single-word receptive vocabulary. In a subsequent study, Eigsti and Bennetto (2009) found that 9- to 17-year-old high-functioning individuals with autism made poorer grammaticality judgments than typically developing children matched on age, IQ, and receptive vocabulary. Together, these studies indicate that syntax is a relative weakness in children with ASD.

Research on receptive syntax in children with ASD is surprisingly sparse. Early work on the syntactic comprehension of children with ASD with intellectual disability, however, pointed to impairment in transitive sentence comprehension. Prior and Hall (1979) assessed twelve 7- to 15-year-old children with autism who were matched on receptive vocabulary to those with Down syndrome or typical development. Overall comprehension on 24 transitive and 16 intransitive sentences was poorer in the children with autism relative to the comparison groups. This was true even though these sentences were not reversible and comprehension did not hinge on word order. In addition, Prior and Hall found that more errors were made in the transitive condition across the groups. The results of this study suggest that syntactic comprehension might be an area of particular impairment for children with ASD, even when syntactic processing demands are not high and semantic information should provide support. For passive constructions, it is reasonable to suppose that children with ASD will be even more challenged.

Two studies have examined both active and passive sentence comprehension in young children with ASD. Tager-Flusberg (1981) compared sentence comprehension in high-functioning children with autism (ages 3;11 to 11;10) to typically developing three- and four-year-olds, who were matched on receptive vocabulary and nonverbal cognitive ability. Participants acted out active and passive sentences that described probable, neutral, or improbable events. Children with autism demonstrated significantly poorer comprehension than the comparison groups, and at least some children with autism showed use of word order as a comprehension strategy. In a similar study, Paul, Fischer, and Cohen (1988) assessed comprehension in six 4- to 9-year-old children with autism with average to low IQs relative to children with SLI and typically developing 2- and 3-year olds. Again, participants acted out reversible active and passive sentences that described probable, neutral, and improbable events. Overall, performance was better on active than passive sentences, and the best performance was for probable sentences. The three-year-olds had marginally better performance than the children with autism or SLI. Examination of the means reveals that performance on improbable active sentences and all passive sentences – especially the neutral and improbable sentences - was poor for those with autism or SLI. Further investigation of these sentence constructions is warranted.

Recently, Swenson et al. (2007) used an intermodal preferential looking paradigm to test the comprehension of six verbs in reversible transitive sentences in 10 boys with ASD with a mean age of 33 months and 13 typically developing children with a mean age of 21 months, matched on expressive language. Both groups of children successfully interpreted the SVO sentences, indicated by looking more to the target movie during test than control trials. In this study, only one type of sentence construction (e.g., “The boy is tickling the girl”) was tested. Furthermore, the groups were not equated on nonverbal cognitive abilities and nonverbal cognition was not statistically controlled in the analyses. This limits the interpretation of these findings because nonverbal cognitive ability is an important predictor of language abilities in young children with ASD (Ellis Weismer et al., 2010).

In summary, receptive syntax is an intriguing area of study in children with ASD. Despite the primacy of social reciprocity deficits in ASD, evidence for delays in aspects of receptive syntax is mounting. Semantic and conceptual deficits, rather than syntactic knowledge, have been hypothesized as the underlying impairment in comprehension (Tager-Flusberg, 1981). However, this research has largely included very small samples or higher-functioning children who are able to complete demanding testing batteries. The field will benefit from further use of sensitive methodologies appropriate for children with neurodevelopmental disorders that allow comprehension of reversible sentences and sentences with semantic cues to be tested.

Receptive Syntax in Fragile X Syndrome

The extent and sources of receptive syntactic delays in FXS are unclear. Early studies of older males with FXS have indicated that receptive language is commensurate with nonverbal mental age (NVMA; Paul, Cohen, Breg, Watson, & Herman, 1984; Paul et al., 1987). Consistent with this finding, Abbeduto et al. (2003) found that male and female adolescents with FXS did not differ from cognitive level-expectations on receptive vocabulary or receptive syntax based on the Test for Auditory Comprehension of Language-Revised (TACL; Carrow-Woolfolk, 1999b), a conceptually demanding test requiring that the child point to a picture of what is said.

This pattern of results, however, does not seem to hold in younger boys with FXS or in older males with comorbid autism — approximately 25% of children with FXS also meet diagnostic criteria for autism (Bailey et al., 2001; Rogers et al., 2001). A lag in receptive vocabulary and syntax relative to NVMA in males with FXS appears to be particularly pronounced in adolescents with comorbid autism (Lewis et al., 2006). Examining childhood, Price et al. (2007) found that 3- to 16-year-old boys with FXS performed with less success than typically developing children on the same vocabulary and syntax subtests of the TACL after controlling for NVMA and maternal education, regardless of comorbid autism diagnosis.

The specificity of the receptive syntax delay in individuals with FXS remains unclear; however, a recent study suggests that some aspects of syntactic comprehension may be particularly impaired (Oakes, Kover, & Abbeduto, in preparation). Comprehension was assessed with the Test for Reception of Grammar, 2nd edition (TROG-2; Bishop, 2003), in which the examiner reads a sentence exemplifying a syntactic form and the child points to the one drawing of four that matches it. Despite limitations, the TROG-2 has benefits over other measures of comprehension in that it assesses each of 20 constructions separately in four-item blocks. Controlling for nonverbal cognitive ability, adolescents with FXS had poorer comprehension than younger typically developing children on items testing reversible SVO, such as transitive sentences (e.g., *The girl pushes the boy* vs. *The boy pushes the girl*). Because comprehension of reversible syntactic constructions is delayed in other populations, there is reason to more closely examine whether interpretation of such forms is differentially impaired. Research assessing syntax with greater precision and with a less demanding paradigm is required.

Measuring Language Learning in Neurodevelopmental Disorders

Standardized language measures, such as the TACL or TROG-2, are often poorly suited to assessing children with FXS or other neurodevelopmental disabilities. These measures lack the sensitivity to differentiate among children with different ability levels who fall at the lower end of the distribution (Mervis & Robinson, 2005). On the TROG-2, many boys with FXS score near floor, leaving the results difficult to interpret. Moreover, poor performance could arise either because of impairments in understanding syntactic forms or impairments in memory and attention that impact performance due to task demands (Robinson, Mervis, & Robinson, 2003).

Given the memory deficits of children with FXS (Ornstein et al., 2008), these measures of receptive language might not provide valid estimates of syntactic ability. The current study was designed to assess syntactic processing while minimizing non-syntactic demands.

In addition, standardized assessments tend to treat syntactic comprehension as a unitary construct and yield only a gross summary score, without distinguishing among grammatical constructions. As such, research on specific syntactic structures in FXS has been scarce. Understanding syntactic competence at a fine-grained level will allow investigation of the challenges caused by particular constructions, sources of that processing difficulty, and their potential impact on other domains of language, such as vocabulary. Furthermore, there has been great debate about the extent and profile of the receptive language delay in children with ASD, for whom such sensitive paradigms would also be useful (Ellis Weismer et al., 2010).

In contrast to standardized assessments, “on-line measures” of language ability have great potential for examining syntactic comprehension in terms of accuracy and efficiency in children with neurodevelopmental disorders. Looking-while-listening, a type of preferential looking paradigm, has been used extensively to assess comprehension in typically developing infants and toddlers (Fernald, Zangl, Portillo, & Marchman, 2008). In this paradigm, the child views two pictures side-by-side on a screen while listening to an auditory stimulus. Accuracy is defined as the proportion of time spent looking to the target picture rather than the distractor during a window of time after the onset of a key word. Speed of processing is defined as the milliseconds needed to switch from looking to the target picture from the distractor after the onset of the stimulus for the subset of trials in which the child was initially looking at the distractor.

In addition to enabling precise measurement of two distinct aspects of comprehension (i.e., accuracy and speed), looking-while-listening paradigms provide several advantages over traditional assessments. First, these paradigms are developmentally appropriate for a wide range of children with neurodevelopmental disorders across levels of cognitive and language ability. In fact, their utility has been demonstrated in studies of typically developing preschoolers, children with Williams syndrome, and children and adolescents with autism from 2 to 20 years of age (Nazzi et al., 2003; Roseberry, Hirsch-Pasek, Parish-Morris, & Golinkoff, 2009; Swensen et al., 2007; Walker-Andrews, Haviland, Huffman, & Toci, 1994). Secondly, the incidental nature of the tasks places negligible response demands on the individual, which is particularly important for children who are stressed by or unlikely to comply with overt commands. Lastly, the effects of impulsivity and disinhibition seen in young children and in some with neurodevelopmental disabilities, including those with FXS, may be reduced in these testing settings. As compared to standardized testing contexts, the child must simply view an array of two pictures rather than coordinate a planned motor response toward a picture in an array of four. With negligible demands, these paradigms should maximize insight into comprehension.

Processing Speed during Comprehension

Speed, one aspect of language processing performed over the input, is likely to be an informative construct for understanding receptive language in children with neurodevelopmental disorders because learning crucially relies upon efficient processing of linguistic input. In both typically and atypically developing children, processing speed may also relate to later language outcomes (Rose, Feldman, & Jankowski, 2009). The efficiency with which 25-month-olds process familiar vocabulary (i.e., speed and accuracy) relates to expressive vocabulary development between 12 and 25 months of age (Fernald et al., 2006). In older individuals, speed of processing also relates to language abilities and can differentiate performance of children with typical development and language impairments (Dick et al., 2004; Leonard et al., 2007). These studies demonstrate the precision with which processing speed can be measured and emphasize that efficiency of language processing can support successful outcomes. In the current study, both accuracy and speed were considered indicators of competence with the goal of yielding additional insights into the syntactic processing of individuals with FXS or ASD.

Research Questions and Hypotheses

The present research was designed to test the hypothesis that comprehension is more impaired for some constructions than others in boys with FXS. Comprehension of reversible and nonreversible transitive active and passive sentences was assessed with a looking-while-listening paradigm, yielding data on accuracy and processing speed. Reversible sentences were targeted because comprehension of these forms relies entirely upon syntactic competence (i.e., semantic cues do not disambiguate them). Assessing the active and passive voice allowed distinction between difficulty with reversible forms in general from difficulty with complex structures (i.e., passive sentences). Assumed to be less challenging, nonreversible sentences were tested to allow the development of more specific hypotheses about relative challenges with syntactic complexity (i.e., voice: active vs. passive) and the use of semantic cues (i.e., nonreversible probable event sentences can be interpreted without word order by using animacy) for boys with FXS or ASD. Noun comprehension was also tested so that lexical processing might serve as a baseline measure of comprehension and task engagement.

Boys with FXS were hypothesized to have poorer comprehension for reversible active and passive sentences, reflected in accuracy and speed, than typically developing boys with similar nonverbal cognitive skills. Boys with ASD were hypothesized to exhibit poorer comprehension than the boys with typical development, but primarily for passive sentences.

Method

Participants

Participants (*N* = 84) included the following groups: typically developing boys (*n* = 31; ages 2 to 7), boys with FXS (*n* = 25; ages 5 to 12), boys with ASD (*n* = 17; ages 4 to 12), and 11 adult males and females, who validated the experimental tasks. One additional boy with FXS declined to enter the looking-while-listening room. The developmental levels of these boys generally fall in line with those who have just acquired or are acquiring the syntactic forms of interest in typical development. The comparison to typically developing boys speaks to the extent of the delay in FXS relative to nonverbal cognitive level-expectations; the comparison to boys with ASD distinguishes effects of developmental delay from those particular to the FXS phenotype (i.e., syndrome-specificity). This comparison is particularly interesting because of the overlap in behavioral symptoms in FXS and ASD along with hypothesized differences in causal mechanisms. Although receptive language is thought to be a weakness in children with ASD (Ellis Weismer et al., 2010; Loucas, Charman, Pickles, Chandler, et al., 2008; but see Swensen et al., 2007), such a comparison seeks to disentangle underlying features of these disorders.

Participants were primarily enrolled in, and recruited from, a larger ongoing project on word learning from social cues (NIH R01 HD054764; PI: Abbeduto). The majority of these boys (17 with typical development; 19 with FXS; 10 with ASD) were participating in a two-session or one-day follow-up visit 18 months after their initial visit. A few boys (5 with typical development; 2 with FXS; 1 with ASD) participated immediately following their initial assessment, comprised of three sessions for typically developing boys and 2 ½ days of testing for boys with FXS or ASD. The remaining participants were recruited through brochures and fliers posted in public places and through a university research registry. Six sibling pairs participated. The study was approved by a UW-Madison IRB and informed consent was obtained.

Boys enrolled in the larger project (1) were native English speakers, (2) lived with the biological mother, (3) had no uncorrected sensory or physical impairment that would limit performance according to parent report, and (4) used speech as the primary mode of communication (i.e., words without prompting, at least ten per month as per parent report). Boys with FXS entered the larger study having provided a previous molecular genetic diagnosis of an *FMR1* full mutation. Boys with ASD entered the larger study having received a community diagnosis and gave evidence that FXS was ruled out through genetic testing.

Boys not recruited through the larger project (8 with typical development; 2 with FXS; 6 with ASD) provided verbal parental report of the child's diagnosis. All participants were native English speakers who lacked uncorrected sensory or physical challenges that would prevent meaningful completion of the tasks according to parent report, with the exception of one boy with ASD who had been exposed to a language other than English during early development.

Standardized assessments. Nonverbal cognitive abilities were assessed with the Leiter International Performance Scale-Revised Brief IQ subtests (Leiter-R; Roid & Miller, 1997). The Brief IQ subtests (Figure Ground, Form Completion, Sequential Order, and Repeated Patterns) are administered through gesture and other nonverbal cues. The child's responses are also nonverbal. In cases in which the child could not provide a response with only nonverbal cues, simple verbal prompts indicated what the child was supposed to do (e.g., "Point"), as has been done in studies on similar populations (Kuschner, Bennetto, & Yost, 2007). The Leiter-R Brief IQ subtests yield raw scores, nonverbal IQ standard scores, age-equivalents, and growth scores. Participants in the larger study also completed the Peabody Picture Vocabulary Test, Fourth Edition (Dunn & Dunn, 2007) and the TROG-2, for descriptive and comparative purposes.

Autism diagnosis. During their son's initial assessment of the larger study, mothers of typically developing boys completed the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003), which is a screener for autism symptoms. Boys at or above the ASD cut-off of 15 were to be excluded; however, the highest score in the sample was 12. Boys with FXS or ASD completed the Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore, & Risi, 1999), administered by a research-reliable examiner at the initial visit (23 boys with FXS; 10 boys with ASD) and at the second visit (15 boys with FXS), as time allowed. The ADOS is a gold-standard assessment of current autism symptoms involving semi-structured activities designed to elicit social interaction, communication, and play or creativity. Autism severity scores were calculated based on published algorithms (Gotham, Pickles, & Lord, 2009; Gotham, Risi, Pickles, & Lord, 2007). Boys with FXS who met study criteria for ASD were not excluded; autism severity is analyzed explicitly in Chapter 4.

Apparatus and Procedures

The experimental tasks were conducted in a sound-attenuated booth with draped walls in the Infant Learning Lab (PI: Dr. Saffran). The child sat in a chair at a distance from the wall-mounted screen that allowed his eyes to be captured by a video camera. The examiner observed and video recorded from outside the booth. Stimuli were presented with Habit software (Cohen, Atkinson, & Chaput). A secondary examiner was seated behind or next to the child on the floor. This examiner was instructed to wear headphones playing masking music and to look at the floor so as to discourage initiations from the child. Only when necessary did this examiner provide a nonverbal cue to remain seated (e.g., by placing a hand on his shoulder) or other sensory input, as indicated by the parent. In some cases (approximately seven), the primary examiner or the parent also accompanied the child into the booth. When present, the caregiver was asked to listen to masking music, preventing cuing of the child's response.

Several strategies were employed to ensure a maximally positive experience. The child was prepared for the task with pictures of the room, the chair, and the screen and told that their job was to sit in the chair, listen carefully, and watch the screen. The secondary examiner helped the child complete a visual schedule by placing a sticker on the page after each block of the task.

Experimental Measures of Syntactic Comprehension

The primary experimental task assessed accuracy and processing speed for the comprehension of active and passive reversible grammatical constructions. In addition to the reversible task testing neutral active and passive sentences, a subset of participants also completed a nonreversible task, with animacy providing semantic cues to comprehension, yielding probable and improbable sentences. In both tasks, comprehension of animal names was assessed as a baseline. The reversible task always preceded the nonreversible task, usually with at least thirty minutes of other activities between them.

The four types of transitive grammatical constructions are shown in Table 1: (1) active reversible SVO (e.g., *the cat chases the bear*), (2) reversible passive (e.g., *the bear is chased by the cat*), (3) nonreversible active (e.g., *the dog kicks the pan*), and (b) nonreversible passive sentences (e.g., *the pan is kicked by the dog*). All nouns and verbs were monosyllabic and drawn from those likely to be familiar to boys as young as 2;0: bear, cat, dog, mouse; chase, kick, push, touch; book, cup, pan, soap. Scenes were depicted with stuffed animal puppets and small objects. Appendix 2A shows the auditory stimuli; Appendix 2B shows the visual stimuli.

Adult ratings of stimuli. To verify that the stimuli would be interpreted as intended, 10 adults provided ratings on (1) the extent to which the picture of each animal represented a suitable exemplar and (2) the extent to which the picture of each scene depicted the intended reversible sentence. These questionnaires were completed prior to looking-while-listening.

Average ratings, on a scale of 1 to 5, with 5 being a clear example of the specified animal, ranged from 4.20 ($SD = .92$) for *mouse* to 5.00 ($SD = .00$) for *dog*. *Cat* and *bear* each received a mean rating of 4.40 ($SD = .70$). Because *dog* received a rating of 5 from each participant, its ratings were significantly higher than *cat*, *mouse*, and *bear*, $t(9) = 2.71$, $p = .024$, $t(9) = 2.75$, $p = .022$, and $t(9) = 2.71$, $p = .024$, respectively.

Sentence ratings were collapsed across items depicting the same verbs and compared. As seen in Table 2, ratings were generally positive, although *kicking* and *touching* were rated as better depictions than *pushing* and *chasing*, which did not differ from each other. Only the ratings for *chasing* were not significantly greater than neutral (i.e., 3), $t(9) = 1.28$, $p = .117$, one-tailed. It is likely that the verb *chasing* fared less well in adult ratings because the visual stimuli were still-images and *chasing* was the only verb without the benefit of direct contact between the animals to depict the meaning. Based on these ratings, the possibility of verb effects was examined in the primary experimental task.

Experimental task structure. The experimental tasks were based on a looking-while-listening paradigm, measuring fixation of a visual stimulus in response to a sentence. The paradigm is similar to intermodal preferential looking, which has been used to measure comprehension in toddlers and children at various levels of development (Hirsch-Pasek & Golinkoff, 1996), but is more sensitive because it yields latency (i.e., speed) and accuracy.

Auditory stimuli were paired with yoked duos of digital pictures side-by-side on the screen. Sentences were recorded by a female who was not the primary examiner. For all noun trials, the target picture matched the spoken animal (e.g., *Look at my bear!*). In the reversible task, the distractor was one of the three remaining non-target animals; in the nonreversible task, the distractor was an inanimate object (e.g., pan). For active and passive sentence trials in both tasks, the target picture matched the spoken sentence (e.g., *The dog touches the mouse*), and the distractor was a grammatical foil that differed from the target by a single grammatical contrast, namely word order (e.g., a *mouse* touching a *dog*). Because nonreversible sentences only contain one animate noun (e.g., *the book is touched by the mouse*), the grammatical foil was an event unlikely to occur (e.g., *the mouse is touched by the book*; an improbable event). Despite this, grammatical foils were used for both the reversible and nonreversible tasks, maintaining the greatest consistency across tasks. Furthermore, the use of grammatical foils allowed interpretation of performance in terms of comprehension strategies (i.e., word order or animacy).

Trial duration was 5500 ms. In noun trials, the onset of the sentence (e.g., *Look at my bear!*) occurred at 1667 ms with duration of 1500 ms, leaving 3167 ms of silence for interpretation. Noun onset occurred 1000 ms after sentence onset and thus, 2667 ms after trial onset. For trials testing active and passive sentences, auditory onset occurred at 1000 ms with a cue that the sentence was about to begin (*Look!*) with duration of 500ms. Sentence onset occurred at 2000 ms with duration of 2000 ms, leaving 1500 ms of silence for interpretation. The verb of active and passive sentences occurred at 667 ms after sentence onset and thus, 2667 ms after trial onset. As such, for all trial types, the disambiguating word occurred at 2667 ms.

In both the reversible and nonreversible tasks, the noun, active, and passive sentence conditions were comprised of 16 trials each. For the noun condition, each of the 4 animals was tested 4 times. For the active and passive sentence conditions, each of 8 sentences was tested twice, once with the target on the right and once on the left, with each picture appearing as the target and the distractor with equal frequency. In the nonreversible task, 8 active and 8 passive trials were probable; 8 active and 8 passive trials were improbable.

Trials were counterbalanced into two blocks (A and B) for each task; the order of the two halves was randomly assigned to participants. A break was given between blocks to minimize fatigue and to offer reinforcement. Each block was comprised of 28 trials, including four interspersed attention-getter/reinforcement trials (e.g., *You're doing a great job watching and listening!*). The first four trials of each block were noun trials, providing an introduction. Following an attention-getter, five test trials continued, with the middle trial being a noun trial to reinforce task engagement. Total administration time for each task was less than seven minutes.

For the reversible task, 42 of 84 participants received block A first (15 typically developing boys; 11 boys with FXS; 12 with ASD). For the nonreversible task, 16 of 26 participants received block A first (3 typically developing boys; 4 with FXS; 5 with ASD). Order of block presentation had no effect on accuracy, reaction time, or number of valid trials for any group for the reversible task, *p*s > .175, or the nonreversible task, *p*s > .275, with the exception of the number of valid trials from boys with ASD, who contributed more valid nonreversible trials from the A order than the B order, $t(7) = 2.66$, $p = .032$. The preponderance of probable items (all but 5) occurred in block A; most improbable items occurred in block B.

In addition to possible effects of counterbalancing order, effects of fatigue were examined. There were no significant differences between performance in the first and second blocks in the reversible task, *p*s > .15, for overall accuracy, reaction time, or number of valid trials with the exception of the number of valid trials contributed by typically developing boys, which was greater in the first block than the second, $t(28) = 5.11$, $p < .001$. For the nonreversible task, no effects of fatigue were significant for adults, boys with FXS, or boys with ASD, *p*s >

.39, with the exception of accuracy for boys with ASD, whose performance was marginally better during the second block than the first, *t*(7) = -2.08, *p* = .076. For typically developing boys, more valid trials were obtained in the first block than the second, *t*(5) = 4.05, *p* = .010, and reaction times were marginally longer in the second block than the first, *t*(4) = -2.47, *p* = .069.

Finally, the possibility of effects driven by particular animals in the noun condition or particular verbs in the active and passive conditions was examined for the reversible task. No pairwise differences in accuracy emerged in any group for animals, *p*s > .165, with the exception of marginally better performance for *dog* than *cat* for boys with ASD, *p* = .073. Adults showed higher accuracy for *kicking* than *chasing*, *p* = .078, and *pushing*, *p* = .018; typically developing boys had higher accuracy for *pushing* than *touching*, *p* = .028. Because these effects were relatively minimal and not present in the target group, they were not handled further.

Coding and reliability. Trained coders, blind to child's diagnosis and trial content, coded shifts in eye-gaze (i.e., left, right, shift, off-task) frame-by-frame (33 ms intervals), using light onset and offset as a guide for trial timing whenever possible (Fernald et al., 2008). Pointing was ignored, unless it obscured the child's eyes, in which case looking was coded as off-task. A subset of videos (approximately 10%) was coded for reliability by a second trained coder. Average reliability was high (i.e., 98% for frame agreement; 97% for shift agreement).

Trial selection criteria. Trials with prescreening notes (e.g., parent interfering; eyes not visible) were excluded. Trials with technical malfunctions (i.e., one block for a typically developing boy; one trial each for two boys with ASD; one block for another boy with ASD) were also excluded. Valid trials were defined as those for which the child attended to the target and/or distractor from the onset of the disambiguating word to the end of the trial (i.e., 0 ms to 2833 ms after word onset), allowing no more than 15 consecutive frames off-task.

Looking-while-listening analyses are traditionally conducted using only trials in which the participant is looking at either the target or distractor at the instant of onset of the disambiguating word, thereby excluding trials in which the participant is looking elsewhere at that moment (i.e., off-task trials). The result is that off-task trials are discarded, regardless of whether the child reengaged by looking at the target and/or distractor for the remainder of the trial. In the current study, up to three frames were “back-filled” to avoid excluding trials in which the child was merely shifting at the time of verb onset, as is typically done. Given the characteristics of boys with FXS, an additional step was taken to minimize data loss from those prone to attention difficulties: accuracy analyses were repeated including *all* trials (even off-task trials) that met the validity criteria (i.e., no more than 15 consecutive off-task frames), with the goal of increasing the number of participants in the analyses of interest.

Data reduction and test window selection. Accuracy was calculated as the proportion of looking to the target relative to looking to the target or the distractor during the test window for valid trials in a condition. Latency was averaged across valid trials from a given condition in which the participant was looking at the distractor before shifting to the target, allowing 200 ms for a planned saccade and including shifts until the end of the trial (Trueswell, 2008). Two valid trials was the minimum for a participant’s inclusion in analyses for a given condition.

The a priori test window was defined as 200 ms after the onset of the disambiguating word (i.e., the noun in the noun condition; the verb in active and passive conditions) to the end of the trial, 2833 ms after word onset. Relative to the 300 - 1800 ms window in vocabulary studies on toddlers (e.g., Fernald et al., 2006), this longer window was selected due to the syntactic processing demands of the task, the developmental delays of the participants, and the complex nature of the visual scenes (Meints, Plunkett, Harris, & Dimmock, 2002). In addition, shifting attention for some types of visual orienting might be delayed in individuals with FXS (Flanagan et al., 2007), further justifying the need for a longer test window and a baseline condition (i.e., nouns). Exploratory test windows were (1) a short window comparable to previous studies (200 to 1800 ms), (2) a late, short window to capture slow, but successful processing (1833 to 2833 ms), and (3) a window with a longer allowance for saccade planning (300 to 2833 ms).

Analysis Strategy

Looking to the target by each group was tested against chance (i.e., .5) in each condition. Two-tailed *p*-values are reported. Repeated measures analyses comparing performance across conditions within groups utilized Greenhouse-Geisser corrections. Group comparisons among boys with typical development, FXS, and ASD were tested with one-way ANOVAs within condition. Finally, exploratory correlations between task performance, age, nonverbal cognition, PPVT-4, and TROG-2 scores were calculated.

Results

Results for the reversible task are presented prior to the nonreversible task. In each case, the performance of adults is described separately from that of children.

Reversible Task

Adult performance. Eleven adults completed the reversible syntactic comprehension task and all participants contributed at least two valid trials per condition. Results with exploratory windows were substantively identical for adults.

Noun comprehension. Data loss was minimal for adults with an average of 15.45 trials out of 16 contributed. Adults looked more to the target noun than expected by chance during the test window (i.e., 200 to 2833 ms after noun onset), $t(10) = 77.63$, $p < .001$, $d = 23.47$.

Active sentences. Data loss was minimal with an average of 15.36 trials contributed by each participant. Adults looked more to the target scene than expected by chance during the test window (i.e., 200 to 2833 ms after verb onset), $t(10) = 18.95$, $p < .001$, $d = 5.71$.

Passive sentences. Data loss was minimal with an average of 15.91 trials contributed. Adults looked more to the target scene than expected by chance during the test window (i.e., 200 to 2833 ms after verb onset), $t(10) = 13.32$, $p < .001$, $d = 4.02$.

Comparison of conditions and summary. For the 11 adults, accuracy significantly differed across conditions, $F(2, 20) = 36.14$, $p < .001$, partial $\eta^2 = .78$, such that performance for nouns ($M = .98$, $SD = .02$) was higher than for active ($M = .89$, $SD = .07$) sentences, $p < .001$, $d = 1.69$, and performance for active sentences was higher than for passive ($M = .82$, $SD = .08$) sentences, $p = .002$, $d = 1.24$. Differences across conditions were also examined for reaction times for the seven adults with two valid reaction time trials in all three conditions. There was a significant effect of condition, $F(2, 12) = 26.20$, $p = .001$, partial $\eta^2 =.81$, with shorter reaction times for nouns ($M = 359.11$, $SD = 101.91$) than active ($M = 569.31$, $SD =146.35$) sentences, $p = .006$, $d = -1.55$, and marginally shorter latency for active sentences than passive ($M = 702.21$, $SD = 157.01$) sentences, $p = .065$, $d = -.85$. Overall, the eye gaze performance of adults validates the reversible task for tapping comprehension of nouns, active sentences, and passive sentences.

Child performance. Of the 73 child participants who were exposed to the reversible syntactic comprehension task, not all contributed data to the analyses of interest. One participant with FXS was excluded because he failed to engage in the task. The videos of all other participants' looking-while-listening sessions were coded. After coding, one participant with ASD was excluded due to a side bias. The remaining 71 child participants contributed at least one valid trial to some condition, although many were excluded due to too few trials in certain conditions, as described below. Included in these 71 participants are two participants with FXS for whom only one block was coded due to inattentiveness and one participant with typical development and one with FXS who chose to participate for only one block.

Participant characteristics are shown in Table 3 for those with at least two valid trials in a given condition, maximally 31 boys with typical development, 18 with FXS, and 14 with ASD.

Noun comprehension. Participants with two or more valid noun trials were 31 boys with typical development, 16 boys with FXS, and 13 boys with ASD. Performance is shown in Table 4 and depicted in Figure 1. Typically developing boys and boys with ASD looked more to the target than expected by chance during the test window (i.e., 200 to 2833 ms after noun onset), $t(30) = 6.49$, $p < .001$, $d = 1.17$, and $t(12) = 4.38$, $p = .001$, $d = 1.21$, respectively. Boys with FXS did not reliably look to the target animal, $t(15) = 1.27$, $p = .225$, $d = .32$.

Results did not substantively differ with test windows allowing more time for saccades (i.e., 300 to 2833 ms), or for the early (i.e., 200 to 1800 ms) or late (i.e., 1833 to 2833 ms) window for any group. However, including otherwise valid off-task trials increased the sample of boys with FXS from 16 to 20, leading to better-than-chance noun comprehension ($M = .61$, $SD = .20$), $t(19) = 2.43$, $p = .025$, $d = .54$. Conversely, limiting the analysis to the 14 boys with FXS with at least three valid non-off-task trials ($M = .59$, $SD = .18$) resulted in only marginal success, $t(13) = 1.86$, $p = .086$, $d = .50$.

Active sentences. Participants with two or more valid noun trials were 30 typically developing boys, 18 boys with FXS, and 14 boys with ASD. Performance is depicted in the top panel of Figure 2. All participant groups looked more to the target scene than chance during the test window (i.e., 200 to 2833 ms after verb onset), $t(29) = 3.50$, $p = .002$, $d = .64$ for typical development; $t(17) = 2.34$, $p = .032$, $d = .55$ for FXS; $t(13) = 3.12$, $p = .008$, $d = .83$ for ASD.

Results did not substantively differ for exploratory test windows, except performance of boys with FXS was no longer reliable during the early, $t(17) = 1.49$, $p = .154$, $d = .35$, or late windows, $t(17) = 1.75$, $p = .099$, $d = .41$. However, including otherwise valid off-task trials increased the sample of boys with FXS from 18 to 20, leading to unreliable active sentence performance ($M = .56$, $SD = .17$), $t(19) = 1.61$, $p = .125$, $d = .36$. Limiting the sample to the 11 boys with FXS with three valid non-off-task trials ($M = .58$, $SD = .15$) also produced a non-significant result, $t(10) = 1.81$, $p = .101$, $d = .54$.

Passive sentences. Participants with two or more valid noun trials were 30 boys with typical development, 14 with FXS, and 12 with ASD. Performance is depicted the bottom panel of Figure 2. Looking to the target scene during the test window (i.e., 200 to 2833 ms after verb onset) did not differ from chance for any group, $t(29) = 1.08$, $p = .291$, $d = .20$ for typical development; $t(13) = -.31$, $p = .761$, $d = .08$ for FXS; $t(11) = -.73$, $p = .484$, $d = .21$ for ASD.

Results differed for typically developing boys using a late test window (i.e., 1833 to 2833 ms after verb onset), revealing comprehension of passive sentences, $t(29) = 2.98$, $p = .006$, $d = .54$. Results with early or late windows did not differ for other groups, although participants with ASD showed a trend towards SVO interpretation during the early window (i.e., 200 to 1800 ms), $t(11) = -1.74$, $p = .110$, $d = .50$, as did typically developing boys, $t(29) = -1.50$, $p = .145$, $d = .27$. Including valid off-task trials increased samples to 16 boys with FXS and 13 with ASD, but results did not differ; all boys with at least two valid non-off-task passive trials had three.

Comparisons across conditions. Performance of participants with at least two valid trials in each condition (30 typically developing boys; 12 with FXS; 12 with ASD) was also examined. Before describing those results, it should be noted that bias due to excluding data from participants without two valid trials in a given condition cannot be ruled out. Boys with ASD who met this criterion had significantly higher nonverbal IQ scores than the five boys with ASD who did not, $t(15) = -2.60$, $p = .020$, $d = .63$. The 12 boys with FXS had marginally higher IQs than the 13 who did not meet the criterion, $t(23) = -1.81$, $p = .084$, $d = .36$.

For participants with two valid trials in each condition, there was a main effect of condition, $F(2, 102) = 28.64$, $p < .001$, partial $\eta^2 = .36$ (all pairwise *p*s < .002), but no effect of group, $F(2, 51) = .39$, $p = .682$, partial $\eta^2 = .02$, and no Group X Condition interaction, $F(4, 102) = 1.55$, $p = .201$, partial $\eta^2 = .057$. Utilizing the late test window (i.e., 1833 to 2833 ms), the Group X Condition interaction just failed to reach significance, $F(4, 102) = 2.40$, $p = .055$, partial $\eta^2 = .086$: typically developing boys achieved more comparable performance in all three conditions, whereas boys with ASD and FXS had lower performance in the passive condition, and boys with ASD had higher performance in the noun condition.

Comparisons across groups. Considering those with two valid noun trials (31 typically developing boys; 16 with FXS; 13 with ASD), groups did not differ on Leiter-R growth scores, $F(2, 55) = 2.11$, $p = .131$, but did differ on number of valid trials contributed, $F(2, 57) = 19.97$, $p < .001$, all pairwise *p*s < .05. Groups also differed on noun accuracy, $F(2, 57) = 3.66$, $p = .032$. Boys with FXS performed with less success than boys with typical development, $p = .023$, $d = .34$, and boys with ASD, $p = .019$, $d = .45$. Boys with typical development and ASD did not differ, $p = .580$, $d = .08$. However, the group difference was not significant after controlling for Leiter-R growth scores, $F(2, 54) = 1.77$, $p = .180$, partial $\eta^2 = .06$; only a trend remained for higher accuracy by boys with ASD than FXS, $p = .095$, $d = .32$. The weakness for boys with FXS was also no longer significant when controlling for number of valid trials, $p = .354$. Results were not substantively different limiting comparisons to those with three or more trials.

Considering those with two valid active trials (30 typically developing boys; 18 with FXS; 14 with ASD), groups did not differ on Leiter-R growth scores, $F(2, 57) = 1.81$, $p = .173$, but did differ on number of valid trials contributed, $F(2, 59) = 20.69$, $p < .001$, all pairwise *p*s < .05. Groups did not differ on the accuracy for active sentences, $F(2, 59) = .16$, $p = .852$, which did not change when controlling for Leiter-R growth scores, $F(2, 56) = .32$, $p = .726$, partial $\eta^2 =.01$, or noun accuracy, $F(2, 55) = 1.81$, $p = .174$, partial $\eta^2 =.06$, (FXS vs. TD, $p = .063$, $d = .28$). The group difference was also non-significant when controlling for valid trials, $p = .417$. Results were not substantively different when considering only those with three valid trials.

Considering those with two valid passive trials (30 typically developing boys; 14 with FXS; 12 with ASD), the groups did not differ on Leiter-R growth scores, $F(2, 51) = 1.97$, $p = .150$, but did differ on number of valid trials contributed, $F(2, 53) = 17.57$, $p < .001$, all pairwise *p*s < .05. Groups did not differ on the accuracy for passive sentences, $F(2, 53) = .87$, $p = .423$, which did not change when controlling for Leiter-R growth scores, $F(2, 50) = 1.94$, $p = .154$, partial $\eta^2 =.07$, (typical development vs. ASD, $p = .056$, $d= .31$) or active accuracy, $F(2, 52) = 1.39$, $p = .258$, partial $\eta^2 =.05$, (typical development vs. ASD, $p = .104$, $d = .25$). The group difference was also non-significant when controlling for valid trials, $p = .437$.

Speed of processing. Reaction time was examined for those participants who contributed two valid trials with a shift from the distractor to the target between 200 and 2833 ms. For all child participants combined, there was a main effect of condition, $F(2, 60) = 12.76$, $p < .001$, partial $\eta^2 =.298$, such that processing was faster for nouns than active sentences, $p = .002$, $d = .60$, and somewhat faster for active than passive sentences, $p = .148$, $d = .26$. The complexity of passive sentences likely elicited more shifting between images than other conditions.

Reaction times are shown in Table 5. For noun trials, boys with FXS were slower, but also more variable, than typically developing boys and those with ASD, and thus, not significantly so, $F(2, 43) = .52$, $p = .600$. The pattern of means differed for active trials: boys with FXS or typical development were slower than those with ASD, although not significantly, $F(2, 45) = 1.05$, $p = .357$. Groups did not differ for passive latency, $F(2, 42) = 1.72$, $p = .191$.

Exploratory correlations. Pearson's correlations were calculated within groups for accuracy and latency with age, nonverbal cognition, receptive vocabulary, receptive syntax, and valid trials. Only significant two-tailed ($p < .05$) correlations are reported. For typically developing boys, noun latency was negatively correlated with age, $r = - .37$, Leiter-R growth scores, $r = - .42$, and TROG-2 items passed, $r = -.58$. For boys with ASD, noun accuracy was predicted by valid trials, $r = .55$. For boys with FXS, noun accuracy was predicted by Leiter-R growth scores, $r = .74$, PPVT-4 growth scores, $r = .79$, TROG-2 items passed, $r = .81$, and valid trials, $r = .63$. For the active condition, typically developing boys' accuracy was predicted by Leiter-R growth scores, $r = .53$, TROG-2 items passed, $r = .44$, and noun accuracy, $r = .63$, whereas latency was predicted by age, $r = -.40$, and Leiter-R growth scores, $r = - .44$. For boys with ASD, active accuracy was correlated with noun accuracy, $r = .60$. For boys with FXS, TROG-2 items, $r = -.67$, was correlated with active reaction time. For typically developing boys, passive accuracy was correlated with age, $r = .49$, Leiter-R scores, $r =.51$, PPVT-4 scores, $r = .62$, TROG-2 items, $r = .68$, active accuracy, $r = .45$, and valid trials, $r = .61$; passive reaction time was correlated with age, $r = -.40$, TROG-2 items, $r = -.45$, active latency, $r = .41$, and valid trials, $r = -.40$. For boys with ASD, age, $r = .59$, and Leiter-R scores, $r = .74$, correlated with passive accuracy. For boys with FXS, age correlated with passive latency, $r = -.72$.

Summary. Overall, the performance of children was more variable than that of adults; however, accuracy was generally high for nouns and active sentences for typically developing boys and those with ASD. Typically developing boys showed successful, but slow comprehension of passive sentences and they, as well as boys with ASD, tended to adopt an early SVO interpretation. Group differences failed to emerge when controlling for nonverbal cognitive ability or valid trials contributed. Patterns of correlations differed across groups.

Nonreversible Task

Adult performance.

All four adults contributed at least two valid trials per condition.

Noun comprehension. Data loss was minimal with an average of 15.75 trials out of 16 contributed by each participant. Adults looked more to the target noun than expected by chance during the test window (i.e., 200 to 2833 ms after noun onset), $t(3) = 119.34$, $p < .001$, $d = 59.67$.

Active sentences. Data loss was minimal with an average of 7.75 probable and improbable trials out of 8 contributed. Adults looked more to the target than chance during the test window (i.e., 200 to 2833 ms after verb onset) for probable active, $t(3) = 10.09$, $p = .002$, $d = 5.05$, and improbable active trials, $t(3) = 7.47$, $p = .005$, $d = 3.74$. As expected, accuracy was somewhat lower for improbable than probable trials, $t(3) = -1.92$, $p = .150$, $d = .96$.

Passive sentences. All 8 probable and 8 improbable passive trials were valid for each adult. Looking to the target was greater than chance in the test window (i.e., 200 to 2833 ms after verb onset), for probable, $t(3) = 20.67$, $p < .001$, $d = 10.33$, and improbable passive trials, $t(3) = 19.50$, $p < .001$, $d = 9.75$. As expected, accuracy was somewhat lower for improbable than probable sentences, $t(3) = -2.63$, $p = .078$, $d = 1.32$.

Summary. For four adults, accuracy for nouns ($M = .98$, $SD = .01$) was high, with accuracy in other conditions accordingly lower: probable active ($M = .87$, $SD = .07$), improbable active (*M* = .84, *SD* = .09), probable passive (*M* = .87, *SD* = .04), and improbable passive (*M* = .82, *SD* = .03) sentences. Very few participants had two valid reaction time trials in a given condition: one for nouns (216.75); three for probable and improbable active (*M* = 686.17, *SD* =355.05; *M* = 791.50, *SD* =406.75, respectively); and four for probable and improbable passive (*M* = 613.72; *SD* = 53.39; *M* = 685.42, *SD* = 225.39, respectively) sentences. Adult performance was generally in accordance with expectations for comprehension with semantic (animacy) cues.

Child performance. Participants who completed the nonreversible task, shown in Table 6, were 6 typically developing boys, 5 with FXS, and 11 with ASD. One boy with ASD was excluded after coding due to a side bias. Two participants with ASD did not receive exposure to the entire task. One boy with FXS contributed no valid trials to any condition and one participant with ASD failed to provide two valid trials for any given condition.

Noun comprehension. Boys with two valid noun trials were 6 typically developing boys, 4 with FXS, and 9 with ASD. Performance is shown in Table 7 and depicted in Figure 3. Boys with typical development looked reliably less to the target noun than expected by chance, *t*(5) = -2.89, *p* = .034, *d* = 1.18, presumably due to novelty of the distractor inanimate objects. Boys with FXS and ASD looked more to the target, but not significantly so, *t*(3) = 2.01, *p* = .138, *d* = 1.00, and *t*(8) = 1.83, *p* = .104, *d* = .61, respectively.

Active sentences. Two valid probable active trials were obtained from 6 typically developing boys, 2 with FXS, and 8 with ASD; two valid improbable trials were obtained from 5 boys with typical development, 1 with FXS, and 6 boys with ASD. Performance is shown in Figure 4. For probable trials, neither boys with typical development nor ASD demonstrated reliable performance, *t*(5) = 1.08, *p* = .330, *d* = .42, and, *t*(7) = 1.52, *p* = .172, *d* = .54, respectively. Boys with ASD looked reliably to the target in improbable active trials, *t*(5) = 3.01, *p* = .030, *d* = 1.23; typically developing boys did not, *t*(4) = -.48, *p* = .66, *d* = .21.

Passive sentences. Two probable passive and two improbable passive trials were obtained from 6 typically developing boys, 1 with FXS, and 7 with ASD. See Figure 5. Typically developing boys did not show comprehension of probable passive sentences, *t*(5) = .50, *p* = .637, *d* = .20; boys with ASD reliably looked to the distractor, *t*(6) = -2.58, *p* = .042, *d* = .97. Neither group demonstrated reliable improbable passive sentence comprehension, *t*(5) = -1.10, *p* = .323, *d* = .45, and, *t*(8) = -.35, *p* = .733, *d* = .12, respectively.

Speed of processing. No analyses were performed for nonreversible latency given the small sample sizes. Descriptive results are shown in the bottom panel of Table 5.

Exploratory correlations. Pearson's correlations were computed for typically developing boys and those with ASD. Only significant correlations are reported. Nonreversible noun accuracy was correlated with reversible noun accuracy for boys with ASD, *r* = .73. For boys with ASD, improbable active accuracy was correlated with Leiter-R growth scores, *r* = .86. For typically developing boys, probable passive accuracy was negatively related to Leiter-R scores, *r* = -.85; for typically developing boys, improbable passive accuracy was correlated with age, *r* = .97, and Leiter-R scores, *r* = .85. For boys with ASD, probable passive accuracy correlated with valid trials, *r* = .78; improbable passive accuracy correlated with TROG-2 items, *r* = .99.

Summary. Performance of children was more variable than that of adults. Differences between probable and improbable trials were not significant for participants with typical development or ASD, *p*s > .125. Group comparisons were not tested due to limited sample sizes.

Discussion

The current study examined accuracy and speed of processing of comprehension in boys with FXS, ASD, and typical development. Despite significant delays in receptive language and weaknesses in receptive syntax, little is known about the aspects of comprehension that pose the greatest challenge for children with FXS or ASD. A principal contribution of the current work was examination of the specificity of those weaknesses using a minimally-demanding paradigm. To that end, the primary experimental looking-while-listening task assessed reversible transitive constructions in the active and passive voice. Reversible constructions provide a strict test of syntactic knowledge because semantic information cannot disambiguate them. Preliminary data from nonreversible probable and improbable syntactic constructions were also collected.

Adults served to validate the experimental tasks for tapping comprehension of nouns, active sentences, and passive sentences. Their near-ceiling performance fell in line with expectations. Accuracy and latency were most efficient for nouns. Differences between active and passive sentences were more subtle, with somewhat slower passive processing.

The primary hypothesis was that typically developing boys would demonstrate comprehension of nouns, active sentences, and passive sentences, whereas boys with FXS or ASD would have success in some conditions, but not others. Given the FXS phenotype and the susceptibility of reversible forms to impairment, boys with FXS were expected to have poorer accuracy and speed relative to both comparison groups on reversible sentences, with greatest impairment on passive forms. Boys with ASD were expected to show weakness with passive sentences. Lastly, given the semantic impairments thought to underlie comprehension difficulties in ASD, boys with ASD were thought to benefit less than expected from semantic cues (i.e., that an animate entity is likely to be an agent) in probable nonreversible sentences.

Hypotheses were partially supported, although analyses did not always reach statistical significance. Results for typically developing boys were the most consistent, with evidence of competence for nouns, active sentences, and passive sentences. Of note is that the sample size for typically developing boys was largest and typically developing boys contributed more valid trials on average than boys with FXS or ASD. Even so, boys with FXS or ASD demonstrated above-chance accuracy for some conditions, with evidence of weaknesses in others.

Lexical Processing

Noun comprehension trials served as a baseline of comprehension and engagement with the looking-while-listening tasks. Four nouns were tested: bear, cat, dog, and mouse. In the reversible task, the distractor picture was one of the remaining animals; in the nonreversible task, the distractor was one of four inanimate objects. All boys were expected to succeed.

In the reversible task, typically developing boys and boys with ASD showed convincing understanding of the nouns. Boys with FXS showed less reliable lexical comprehension, which was significantly greater than chance only when bolstering the sample size to 20 by including trials that were otherwise valid, but in which the child was off-task at noun onset. Certainly, boys with FXS in this developmental range would be expected to understand the target words. The results suggest, however, that processing of familiar nouns might be less robust in boys with FXS than for those with typical development or ASD, the latter of whom had superior noun comprehension and generally higher nonverbal cognitive abilities. Boys with FXS had lower accuracy than boys with typical development and ASD, although the differences were no longer significant after controlling for nonverbal cognition or the number of valid trials completed.

Interestingly, accuracy of noun comprehension was significantly correlated with nonverbal cognitive ability, vocabulary ability and syntactic comprehension assessed with standardized measures, and the number of valid noun trials for boys with FXS. For boys with ASD, only the number of valid trials correlated with performance. No significant correlations emerged for typically developing boys. It is possible that, relative to the other conditions tested in this paradigm, noun comprehension was the most useful in pulling apart meaningful variability in language ability among boys with FXS because of their developmental levels.

Children reliably processed nouns faster than active sentences in the reversible task. Reaction time data suggest that noun latency did not differentiate the groups, although analyses were based on smaller sample sizes. Descriptively, the boys with FXS tended to be slower processors, albeit with large variability among individuals. In contrast, boys with ASD, who were older than, and on average as cognitively advanced as, the typically developing boys, appeared to have the fastest lexical processing.

For noun comprehension in the nonreversible task, sample sizes were too small to compare reaction times across groups. Furthermore, typically developing boys in the nonreversible task unexpectedly looked reliably at the distractor object. These data likely reflect fatigue, given that typically developing boys demonstrated comprehension of the animals in the reversible task and were probably drawn to the novelty of the inanimate distractors.

Syntactic Processing

Syntactic comprehension of reversible forms is a demanding task for individuals with language impairments, even in cases of normal-range cognitive abilities (Evans, 2002; van der Lely & Harris, 1990). These challenges are thought to extend to individuals with ASD, although findings have been somewhat mixed, with wide variability in ages, sample sizes, and assessment methods (Paul et al., 1988; Swensen et al., 2007). Given the behavioral and linguistic phenotype of individuals with FXS, weakness in reversible sentence processing was expected to be particularly apparent, resulting in impaired accuracy and speed of syntactic comprehension.

Active voice. All three participant groups demonstrated comprehension of active reversible SVO sentences. Typically developing children would be expected to understand these structures, given evidence of SVO knowledge by toddlers under the age of two (Gertner et al., 2006). Such competence is also in line with a previous study of young children with ASD, who demonstrated understanding of transitive sentences in an eye gaze task (Swensen et al., 2007). Results of the current study suggest that the use of word order as a comprehension strategy might also be available to boys with ASD who are older, but have significant developmental delays.

For boys with FXS, accuracy was significantly greater than chance for the a priori test window; however, their overall pattern of results suggests that competence in SVO comprehension might be underdeveloped, given that the results did not hold in exploratory windows as it did for the other groups. The inconsistent performance of boys with FXS could be due to increased cognitive effort needed to process reversible constructions due to weak syntactic knowledge. Alternatively, the processing demands of the complex scenes (e.g., visual attention) and syntactic constructions (e.g., auditory attention) could have challenged the boys with FXS. Despite the fact that the looking-while-listening paradigm is designed to place minimal demands on the child, the current study cannot distinguish completely between purely syntactic and task-related processing because they are confounded across conditions. Teasing these apart will be an intriguing area for future research.

No group differences emerged for accuracy or speed of processing for active sentences. It is of course possible that boys who struggle with syntactic comprehension were less likely to contribute valid trials and that weaknesses in SVO processing for boys with FXS or ASD might have been revealed had those participants been adequately assessed. Curiously, accuracy for active sentences correlated with no other measures for boys with FXS. For boys with ASD, active sentence accuracy correlated with noun accuracy; for typically developing boys, active sentence accuracy correlated with noun accuracy, nonverbal cognition, and syntactic comprehension on the TROG-2 for typically developing boys.

Descriptively, boys with FXS appear to process reversible SVO constructions more slowly and with greater variability than boys with ASD, who are their age-mates. For this subset of boys with FXS with at least two valid reaction time trials, speed of processing was negatively correlated with performance on the TROG-2, suggesting that the reversible task did tap aspects of syntactic ability for some boys, perhaps those with better attention. For these school-age boys with FXS, SVO comprehension might not have reached the level of automaticity expected based on their developmental levels, requiring more processing time for those with weaker syntactic knowledge or susceptibility to processing demands.

Passive voice. For children with and without language impairments, passive sentence comprehension is more taxing than SVO comprehension due to the syntactic complexity and lower frequency of the passive voice (Dick et al., 2004; Slobin, 1966). Even if SVO comprehension is intact, individuals with language impairments or typically developing children just acquiring the passive voice might be expected to show variable performance or increased latency for comprehension. This pattern was generally observed in the reversible task, with passive sentences providing the greatest difficulty.

Boys with FXS failed to demonstrate any reliable pattern of looking for passive sentences, suggesting that this complex syntactic construction was perhaps well beyond the ability levels of these boys. Typically developing boys showed reliable passive comprehension only during a late exploratory test window, in line with the expectation that comprehension of the passive voice occurs slowly and with great cognitive effort. Like the boys with FXS, boys with ASD also failed to show comprehension of the passive voice; however, they did tend to initially interpret passive sentences with an SVO word order strategy (i.e., as though the subject of the sentence was the agent). Typically developing boys also tended to initially favor a word order strategy for interpretation, but unlike the boys with ASD, correctly abandoned the SVO interpretation and eventually fixated the target image demonstrating the subject as the patient. The similarity in looking behavior between boys with ASD and typically developing boys suggests the use of overlapping comprehension strategies and, perhaps, emerging syntactic competence. It is conceivable that with more processing time, it would be possible to capture passive sentence comprehension for boys with ASD. If the passive voice is indeed beginning to be acquired by these boys with ASD, success might be detectable only in adolescents or adults.

Accuracy in passive sentence comprehension was correlated with age for both boys with typical development and those with ASD. The passive construction is less frequent than the active construction in spoken English and exposure is therefore likely to be limited for young children or those who are perceived to have low comprehension abilities. Nonverbal cognitive ability was also correlated with passive comprehension for boys with ASD. For the typically developing boys, it appeared that the passive condition highlighted meaningful variability. In addition to age and nonverbal cognition, accuracy was correlated with vocabulary and syntactic comprehension performance from standardized tests, active sentence accuracy, and the number of passive valid trials contributed, with a similar pattern for latency.

Although group differences were not significant, boys with FXS and ASD failed to correctly interpret passive sentences, while younger typically developing boys demonstrated success.   Further research on the comprehension of complex forms and interpretation strategies utilized by children with neurodevelopmental disorders is warranted.

Semantics in Syntactic Processing

The spirit of the nonreversible task was to identify the extent to which boys with FXS or ASD were able to harness semantic information for the benefit of improving efficiency of language processing. Participants were expected to show competence with simple sentence comprehension (i.e., nonreversible, probable active transitive sentences). Relative to the reversible task, it was expected that boys with FXS would show improved processing of probable active and passive sentences, whereas boys with ASD would not. This pattern of results would have suggested that boys with FXS can successfully use animacy as a strategy for comprehension, but struggle to when only syntactic cues are available.

Given the extremely small sample sizes for the nonreversible task, it was not possible to detect the hypothesized effects. It is also likely that fatigue and habituation played a role in the nonreversible task because all participants had recently completed the reversible task, which tested the same constructions with the same verbs and nouns, with the exception of the addition of four inanimate objects. Nonetheless, the mean performance of adults and typically developing boys hints at some benefit of animacy with an advantage for probable over improbable sentences. For boys with ASD, descriptively, it appears that the effects of semantic animacy cues differed: accuracy was lower for probable than improbable trials for boys with ASD, which was the opposite pattern from boys with typical development.

Just as the novelty of inanimate images appeared to drive the performance of typically developing boys in the noun condition, it is possible that the novelty of the improbable images drove performance of the boys with ASD, who looked reliably to the target for improbable active trials and also looked to the improbable event during probable passive sentences. However, high-functioning adults with ASD show sensitivity to animacy and its typical relations to word order (i.e., an animate agent is usually the subject in an active sentence) in constructing active and passive sentences (Lake, Cardy, & Humphreys, 2010). The role of semantic knowledge in language comprehension should certainly be further examined in children with ASD.

Strengths and Limitations

This study was the first to utilize eye gaze to assess lexical or syntactic processing in boys with FXS. The inclusion of a comparison group drawn from a distinct neurodevelopmental disorder provides context to the findings, despite the fact that the groups were not as well-matched on nonverbal cognition as hoped. Larger sample sizes that allow matching on one or more dimensions (e.g., nonverbal cognition, receptive vocabulary) will be desirable in the future.

The experimental tasks were designed to collect maximal information about language processing boys across the range of the FXS and ASD phenotypes. Inclusion of lexical and syntactic items was an aspect of innovation, as was the decision to assess not only SVO constructions, but also more complex passive constructions. Nonetheless, it remains to be seen whether performance would differ with each condition tested in a separate task. For example, one might wonder if boys with ASD would still be led to interpret passive sentences with an SVO framework if active sentences were not intermixed with the passive.

A notable limitation was that relatively few participants with FXS (*n*s= 12 - 18) were included in the primary analyses, given that 25 boys participated and only two valid trials were required in a given condition. This criterion was viewed as a minimum to ensure meaningful estimates of ability and many steps were taken to maximize engagement with the task, including a preparatory picture book, a visual schedule with sticker reinforcement, noun trials distributed throughout the task to promote feelings of success, and the presentation of two complete blocks of stimuli with a break between them. The data regarding the number of valid trials provide many questions for future research, particularly given the differences among groups. It will be important to disentangle the ways in which syntactic demands and general task demands (e.g., attention) relate to task engagement and language comprehension. That is, the extent to which the number of valid trials reflects an artifact or a meaningful indicator of the ways in which a child attends to visual and auditory stimuli in the environment remains to be determined.

Future Directions

Although the focus was on syntactic processing, results regarding comprehension of nouns suggest that lexical processing might tap theoretically important aspects of ability, even in school-age children with neurodevelopmental disorders. Extending established familiar word tasks (e.g., Fernald & Marchman, 2012) to those with FXS or ASD will be a vital next step. Likewise, the role of semantic knowledge could only be examined here in a cursory manner, but these preliminary data can lead the way to well-defined hypotheses regarding semantic and syntactic deficits in language processing, particularly for children with ASD.

Finally, this work demonstrates the utility of eye gaze measures of syntactic processing and improves upon the currently available methods for assessing receptive syntax in neurodevelopmental disorders. The results contribute to a nuanced understanding of the linguistic phenotype of FXS, hinting at the extent and nature of delays in boys with FXS. Research on the accuracy and speed of processing for adolescents and adults with FXS, as well as for females with FXS, who are notoriously understudied, will also be worthwhile. Extensions of these syntactic processing tasks to young typically developing toddlers, school-age children with SLI, or adolescents and adults with ASD would be other natural extensions of this research.

Table 1

Schematic of Syntactic Comprehension Stimuli

	Voice	
	Active	Passive
Reversible	*The dog touches the mouse.*	*The mouse is touched by the dog.*
Nonreversible	*The mouse touches the book.*	*The book is touched by the mouse.*

Note. The reversible and nonreversible tasks were each comprised of 16 noun trials, 16 active trials, and 16 passive trials.

Table 2

Sentence Ratings by Adults Grouped by Verb

Sentence	*M*	(*SD*)	Range
The cat kicks the dog. The dog kicks the cat.	5.00^a	(.00)	5 - 5
The mouse pushes the bear. The bear pushes the mouse.	3.55^b	(.93)	5 - 5
The cat chases the bear. The bear chases the cat.	3.39^b	(.96)	2 - 5
The mouse touches the dog. The dog touches the mouse.	4.93^a	(.17)	4 - 5

Note. Ratings ranged from 1 (the picture depicts the sentence hardly at all) to 5 (the picture depicts the sentence very well).

[a,b]Different superscripts indicate significant differences, $p = .001$.

Table 3

Participant Characteristics: Reversible Task

	Typical Development (*n* = 30)			Fragile X Syndrome (*n* = 18)			ASD (*n* = 14)		
Measure	*M*	(*SD*)	Range	*M*	(*SD*)	Range	*M*	(*SD*)	Range
Age	4.50	(1.62)	2 - 7	9.25	(2.07)	5 - 12	8.08	(2.05)	4 - 12
Nonverbal IQ[a]	116.86	(13.55)	93 - 143	53.22	(11.35)	36 - 71	75.43	(30.07)	40 - 141
Nonverbal AE	5.52	(1.97)	3 - 10	4.53	(.90)	3 - 6	6.18	(3.05)	2 - 12
PPVT-4 SS	121.89	(11.34)	103 - 133	68.00	(13.11)	47 - 87	60.78	(26.07)	28 - 98
PPVT-4 AE[b]	6.63	(2.32)	2 - 11	5.53	(1.20)	4 - 9	4.84	(2.50)	2 - 10
TROG-2 SS	115.50	(20.32)	86 - 145	55.50	(1.41)	55 - 60	70.71	(16.34)	55 - 92
TROG-2 AE[c]	7.19	(3.02)	4 - 12	4.16	(.34)	4 - 5	5.58	(2.14)	4 - 9
Autism severity[d]	-	-	-	6.06	(1.92)	3 - 10	7.63	(1.92)	4 - 10

Note. Nonverbal IQ = Leiter-R Brief IQ; AE = age-equivalent; PPVT-4 = Peabody Picture Vocabulary Test, Fourth Edition; SS = standard score; TROG-2 = Test for Reception of Grammar, 2nd Edition. [a]Two typically developing participants were not assessed with the Leiter-R (*n* = 28). [b]Data reflect 21 typically developing boys, 16 boys with FXS, and 9 boys with ASD. Three additional typically developing boys lacked standard scores because they were younger than the norming sample. [c]Data reflect 21 typically developing boys, 16 boys with FXS, and 7 boys with ASD. Five additional typically developing boys lacked standard scores because they were younger than the norming sample. [d]ADOS severity scores were available for 17 participants with FXS and 8 participants with ASD at initial assessment. Substituting the most recent assessment for 11 participants with FXS yields a mean of 5.94.

Table 4

Participant Performance: Reversible Task Accuracy

	Typical Development (*n* = 30)			Fragile X Syndrome (*n* = 18)			ASD (*n* = 14)		
Condition	*M*	(*SD*)	Range	*M*	(*SD*)	Range	*M*	(*SD*)	Range
Noun[a]	.68	(.15)	.35 - .95	.56	(.19)	.27 - .84	.71	(.17)	.47 - .97
Valid trials	11.39	(3.48)	2 - 16	5.06	(2.79)	2 - 11	9.23	(3.19)	2 - 14
Active	.59	(.14)	.37 - .85	.59	(.16)	.25 - .89	.62	(.14)	.43 - .83
Valid trials	12.47	(3.06)	5 - 16	5.56	(3.87)	2 - 13	8.50	(4.55)	2 - 16
Passive[b]	.52	(.12)	.14 - .71	.49	(.11)	.31 - .66	.47	(.12)	.30 - .71
Valid trials	12.87	(2.50)	5 - 16	6.79	(3.77)	3 - 14	10.08	(4.01)	3 - 16

[a] Noun accuracy included 31 boys with typical development, 16 boys with FXS, and 13 boys with ASD. [b] Passive accuracy included 14 boys with FXS and 12 boys with ASD.

Table 5

Reaction Time by Group and Condition

	Typical Development			Fragile X Syndrome			ASD		
Condition	*n*	*M*	(*SD*)	*n*	*M*	(*SD*)	*n*	*M*	(*SD*)
Reversible									
Noun	29	631.77	(402.68)	9	751.11	(523.72)	8	552.36	(272.61)
Active	28	1013.39	(349.27)	10	1066.27	(423.11)	10	854.33	(256.94)
Passive[a]	27	1162.79	(314.04)	8	908.35	(323.43)	10	1102.04	(417.75)
Nonreversible[b]									
Noun	5	724.62	(358.17)	2	410	(14.14)	3	859.83	(402.34)
Probable active	3	1209.17	(438.26)	-	-	-	3	559.11	(220.65)
Improbable active	3	1142.61	(296.96)	-	-	-	3	470.28	(211.39)
Probable passive	1	-	-	1	-	-	4	870.83	(451.97)
Improbable passive	1	-	-	1	-	-	4	823.08	(482.88)

[a] Results for passive sentences should be interpreted with caution because no participant group demonstrated significant comprehension during the 200 to 2833 ms test window. [b] Results for the nonreversible task should be interpreted with caution given the sample sizes.

Table 6

Participant Characteristics: Nonreversible Task

	Typical Development (*n* = 6)			Fragile X Syndrome (*n* = 4)			ASD (*n* = 9)		
Measure	*M*	(*SD*)	Range	*M*	(*SD*)	Range	*M*	(*SD*)	Range
Age	3.29	(1.11)	2 - 5	8.93	(2.98)	6 - 12	7.37	(1.52)	4 - 10
Nonverbal IQ	116.33	(10.88)	98 - 129	56.50	(12.50)	38 - 65	63.33	(21.42)	42 - 105
Nonverbal AE	4.05	(.86)	3 - 6	4.59	(1.26)	3 - 6	4.55	(1.62)	2 - 8
PPVT-4 SS[a]	-	-	-	66	(22.63)	50 - 82	55.67	(28.95)	28 - 98
PPVT-4 AE	-	-	-	6.88	(2.90)	5 - 9	4.00	(2.05)	2 - 7
TROG-2 SS[b]	-	-	-	55.00	(0)	-	65	(12.54)	55 - 81
TROG-2 AE	-	-	-	4.21	(.30)	-	4.54	(1.09)	4 - 6
Autism severity[c]	-	-	-	5.67	(2.52)	3 - 8	8.17	(1.47)	6 - 10

Note. Nonverbal IQ = Leiter-R Brief IQ; AE = age-equivalent; PPVT-4 = Peabody Picture Vocabulary Test, Fourth Edition; SS = standard score; TROG-2 = Test for Reception of Grammar, 2nd Edition. [a]Data reflect 1 typically developing boy, 2 boys with FXS, and 6 boys with ASD. [b]Data reflect 1 typically developing boy, 2 boys with FXS, and 4 boys with ASD. [c]ADOS severity scores were available for 3 participants with FXS and 6 with ASD.

Table 7

Participant Performance: Nonreversible Task Accuracy

	Typical Development (*n* = 6)			Fragile X Syndrome (*n* = 4)			ASD (*n* = 9)		
Condition	*M*	(*SD*)	Range	*M*	(*SD*)	Range	*M*	(*SD*)	Range
Noun	.42	(.07)	.33 - .50	.61	(.11)	.47 - .74	.64	(.23)	.37 - 1.00
Valid trials	10.67	(3.83)	3 - 13	4.75	(4.27)	2 - 11	8.67	(4.64)	2 - 14
Probable active[a]	.55	(.11)	.37 - .68	.61	(.02)	.60 - .63	.60	(.19)	.34 - .85
Valid trials	6.00	(2.00)	3 - 8	5.50	(3.54)	3 - 8	4.50	(2.33)	2 - 8
Improbable active[b]	.48	(.08)	.40 - .55	-	-	-	.65	(.12)	.46 - .77
Valid trials	4.80	(2.05)	3 - 7	-	-	-	5.00	(1.67)	3 - 7
Probable passive[c]	.52	(.09)	.35 - .63	-	-	-	.37	(.13)	.18 - .54
Valid trials	5.33	(1.37)	3 - 7	-	-	-	5.71	(1.80)	3 - 8
Improbable passive[d]	.42	(.19)	.22 - .71	-	-	-	.49	(.10)	.31 - .61
Valid trials	5.17	(1.72)	3 - 8	-	-	-	4.89	(1.90)	2 - 8

[a] Probable active accuracy is based on 2 boys with FXS and 8 with ASD. [b] Improbable active accuracy is based on 5 typically developing boys, 1 boy with FXS, and 6 with ASD. [c] Probable passive accuracy is based on 1 boy with FXS and 7 with ASD. [d] Improbable passive accuracy is based on 1 boy with FXS and 9 boys with ASD.

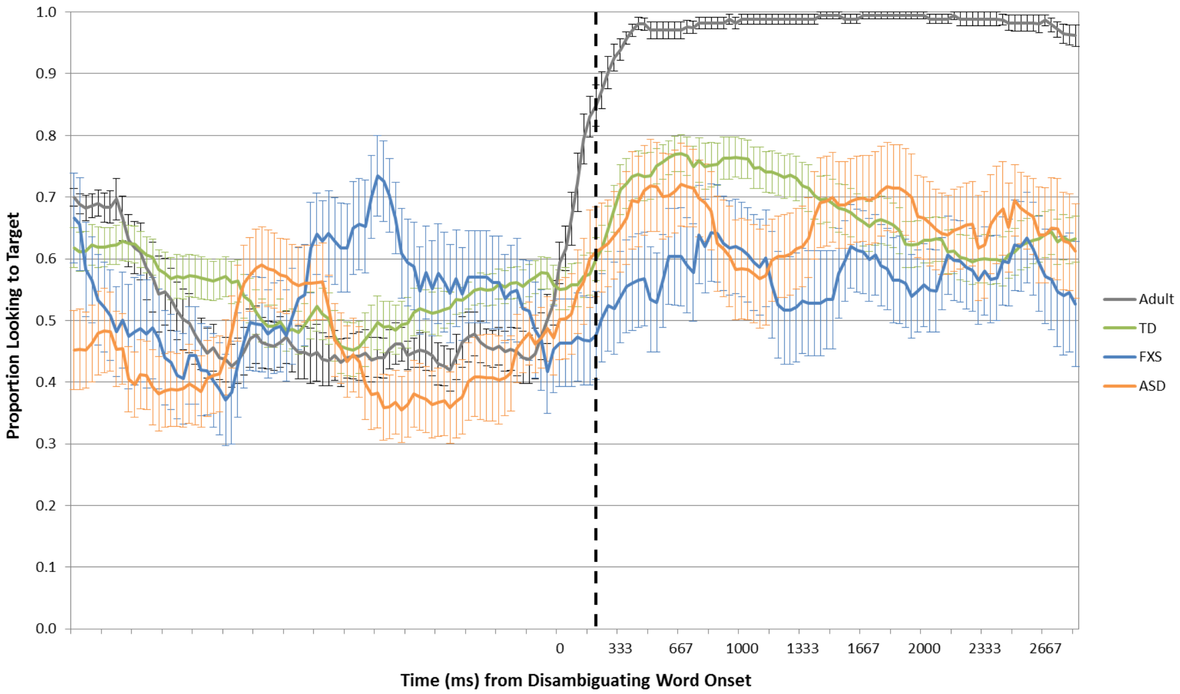

Figure 1. Time course of the mean proportion of looking to the target for the noun condition of the reversible task. Data represent 11 adults, 31 typically developing boys, 16 boys with FXS, and 13 boys with ASD. Error bars show standard errors.

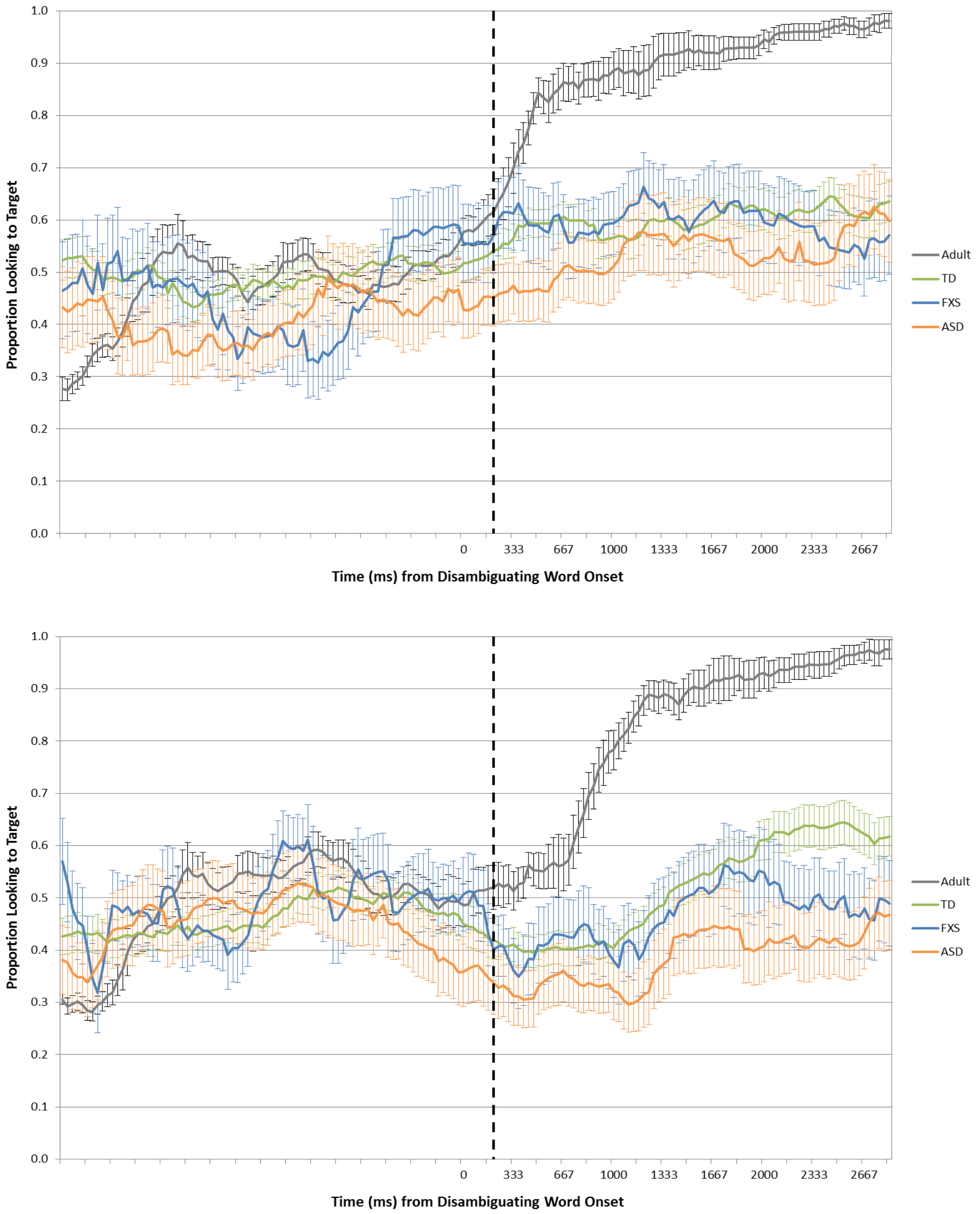

Figure 2. Time course of the mean proportion of looking to the target for the active (top panel) and passive (bottom panel) conditions of the reversible task. Data for the active condition represent 11 adults, 30 typically developing boys, 18 boys with FXS, and 14 boys with ASD. Data for the passive condition represent 11 adults, 30 typically developing boys, 14 boy with FXS, and 12 boys with ASD. Error bars show standard errors.

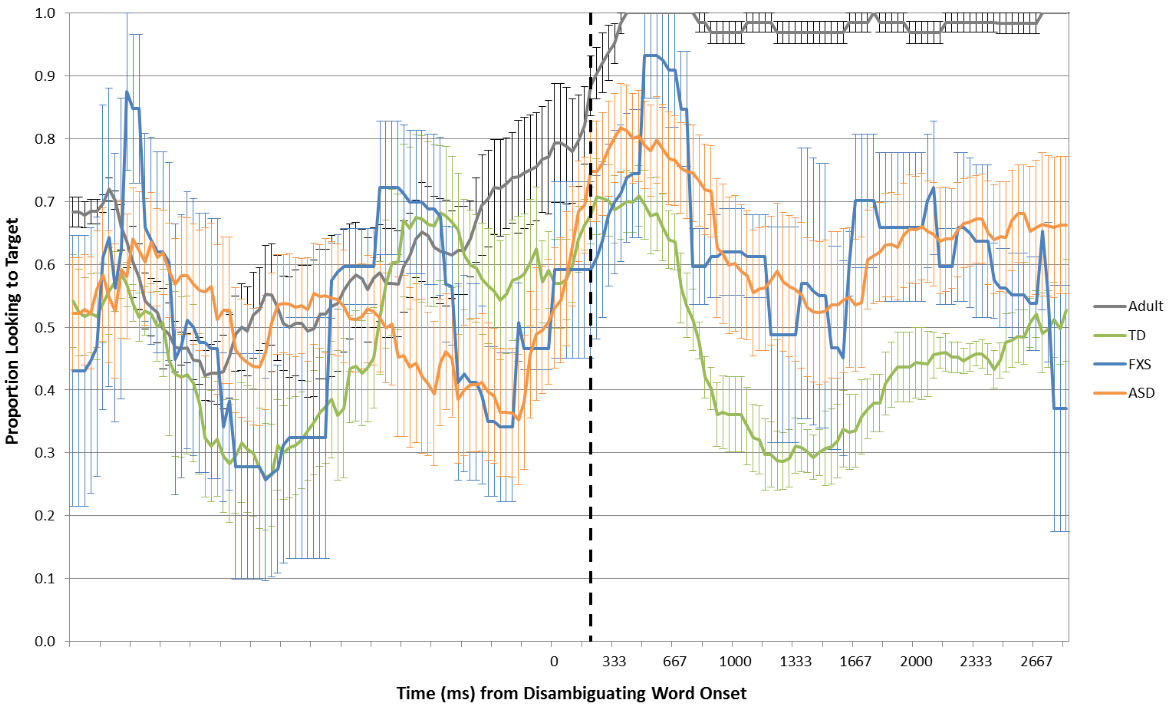

Figure 3. Time course of the mean proportion of looking to the target for the noun condition of the nonreversible task. Data represent 4 adults, 6 typically developing boys, 4 boys with FXS, and 9 boys with ASD. Error bars show standard errors.

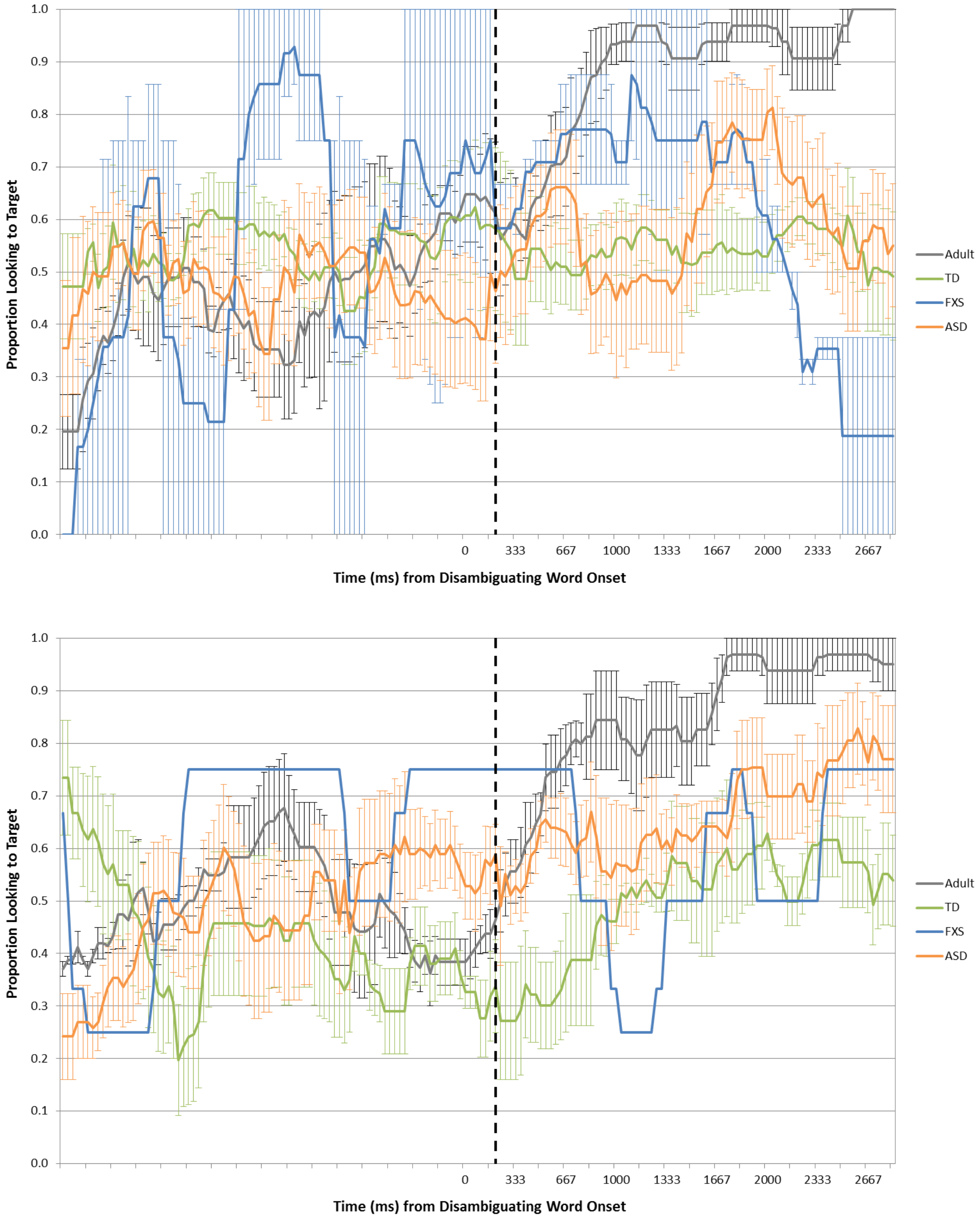

Figure 4. Time course of the mean proportion of looking to the target for the probable active (top panel) and improbable active (bottom panel) conditions of the nonreversible task. Data for the probable condition represent 4 adults, 6 typically developing boys, 2 boys with FXS, and 8 boys with ASD. Data for the improbable condition represent 4 adults, 5 typically developing boys, 1 boy with FXS, and 6 boys with ASD. Error bars show standard errors.

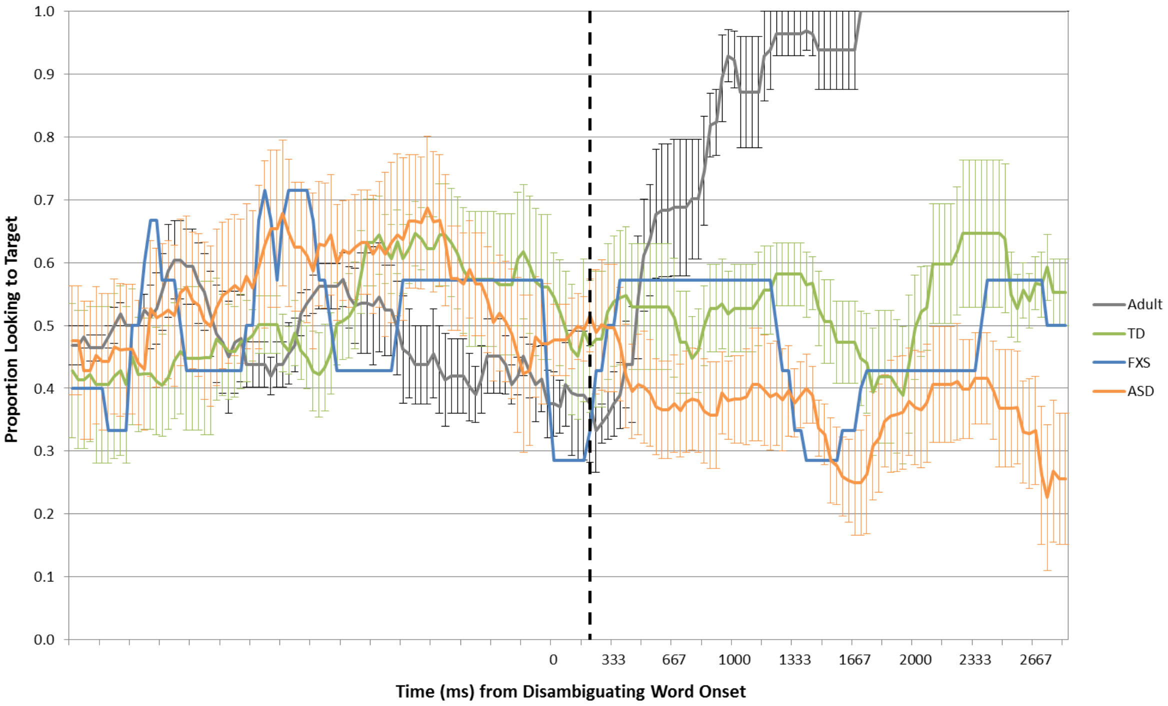

Figure 5. Time course of the mean proportion of looking to the target for the probable passive (top panel) and improbable passive (bottom panel) conditions of the nonreversible task. Data for the probable condition represent 4 adults, 6 typically developing boys, 1 boy with FXS, and 7 boys with ASD. Data for the improbable condition represent 4 adults, 6 typically developing boys, 1 with FXS, and 9 with ASD. Error bars show standard errors.

Appendix 2A: Auditory Stimuli for Study 1

Noun

	Look at my bear!
	Look at my cat!
	Look at my dog!
	Look at my mouse!

Reversible Task

Active	The bear chases the cat.
	The cat chases the bear.
	The cat kicks the dog.
	The dog kicks the cat.
	The bear pushes the mouse.
	The mouse pushes the bear.
	The dog touches the mouse.
	The mouse touches the dog.
Passive	The cat is chased by the bear.
	The bear is chased by the cat.
	The dog is kicked by the cat.
	The cat is kicked by the dog.
	The mouse is pushed by the bear.
	The bear is pushed by the mouse.
	The mouse is touched by the dog.
	The dog is touched by the mouse.

Nonreversible Task

Active	The cat chases the soap.
	The soap chases the cat.
	The dog kicks the pan.
	The pan kicks the dog.
	The bear pushes the cup.
	The cup pushes the bear.
	The mouse touches the book.
	The book touches the mouse.
Passive	The soap is chased by the cat.
	The cat is chased by the soap.
	The pan is kicked by the dog.
	The dog is kicked by the pan.
	The cup is pushed by the bear.
	The bear is pushed by the cup.
	The book is touched by the mouse.
	The mouse is touched by the mouse.

Appendix 2B: Visual Stimuli for Study 1

Target Noun Stimuli: Bear, Cat, Dog, and Mouse

Reversible Task Active and Passive Stimuli: Chase, Kick, Push, and Touch

Nonreversible Task Active and Passive Stimuli: Chase, Kick, Push, Touch

(Here, probable events are shown on the left; improbable events are on the right.)

Chapter 3

Study 2: Extensions of Syntactic Knowledge in Fragile X Syndrome and Autism Spectrum Disorder

Statistical learning – the use of distributional cues among units – contributes to a variety of developmental accomplishments, from speech segmentation and word learning to syntactic acquisition (Graf Estes et al., 2007; Newman et al., 2006). Word order can be thought of as one type of distributional cue in language input that scaffolds comprehension and further language learning. For example, word order can be used to at least partly interpret the meaning of a novel verb given a referential context and the syntactic construction in which it appears (e.g., The duck is gorping the bunny!; Gertner et al., 2006). Typically developing children have been shown to further extend knowledge about such grammatical cues through syntactic bootstrapping, a learning mechanism that contributes to lexical acquisition by allowing inferences about the referent or meaning of a novel word from word order and other syntactic cues.

It is unclear whether children with neurodevelopmental disorders make use of statistical learning and the learning mechanisms that build on it in the same ways as do typically developing children, as noted by Swensen, Kelley, Fein, and Naigles (2007). Given what is known about cognition and brain functioning in neurodevelopmental disorders, there are reasons to believe that difficulties in language development are due to altered or inefficient learning processes. However, the extension of syntactic knowledge has yet to be explored in boys with fragile X syndrome (FXS) or boys with autism spectrum disorder (ASD). If learning based on distributional cues is less established in these populations, interpretation of novel verbs using word order may be impaired. Likewise, if syntactic-semantic links are not well developed, syntactic bootstrapping could be negatively impacted. The current study was designed to assess the ability of boys with FXS or ASD to extend syntactic knowledge to interpret scenes with novel actions using a preferential looking task. The hypothesis was that the extension of specific syntactic knowledge (i.e., word order and transitivity) to interpret sentences with novel words is especially impaired in boys with FXS or ASD.

Vocabulary and Syntax in Fragile X Syndrome and Autism Spectrum Disorder

Beginning early in life, boys with FXS and children with ASD have language delays that are more severe than expected for chronological age or even developmental level (Ellis Weismer et al., 2010; Roberts et al., 2001). Bodies of research on levels of vocabulary and syntax development in these populations are building and hint at candidate language learning processes for the sources of those impairments.

Fragile X syndrome. Some studies have indicated that receptive vocabulary is a relative strength of boys with FXS or that it at least keeps pace with the development of nonverbal cognition (Abbeduto et al., 2003; Roberts, Price, Nelson, et al., 2007). These studies have utilized the PPVT or samples of older adolescents that have included girls. In contrast, studies using conceptually challenging measures of vocabulary, such as the lexical subtest of the TACL, have shown that vocabulary may lag behind developmental level in the receptive domain (Price et al., 2007). Discrepancies in conclusions regarding extent of delay between measures such as the PPVT and the TACL have been found in neurodevelopmental disorders such as Down syndrome, as well (Miolo, Chapman, & Sindberg, 2005). It is likely that differences in the emphases on concrete nouns or abstract concepts and verbs across measures contribute to differences between assessments. In sum, it is premature to conclude that vocabulary keeps pace with nonverbal cognition for boys with FXS, especially in terms of more complex learning tasks;

however, assigning meaning to words might not be impaired to the same extent as other aspects of language for boys with FXS (McDuffie, Kover, Hagerman, & Abbeduto, under review).

Syntactic development, on the other hand, may be especially challenging for boys with FXS. Receptive syntax is delayed relative to typically developing children after controlling for nonverbal cognitive ability, as evidenced by performance of 3- to 14-year-old boys with FXS on the Grammatical Morphemes and Elaborated Phrases and Sentences subtests of the TACL (Price et al., 2007). Delays in receptive syntax may be particularly severe in boys with comorbid FXS and ASD, although results on this matter have been mixed (Lewis et al., 2006; Price et al., 2007). Despite the extent of delay in receptive syntax, previous research has failed to examine specific aspects of syntactic processing (e.g., comprehension of constructions of varying complexity) or the use of syntactic knowledge as a springboard for further language learning.

Autism spectrum disorder. In general, receptive language is an area of challenge for children with ASD. Many youth with ASD have greater impairments in receptive language than children with SLI and greater impairments in receptive language than expressive language (Hudry et al., 2010; Loucas, Charman, Pickles, Simonoff, et al., 2008). Results from research on syntactic comprehension have been somewhat mixed. Several studies have utilized acting-out tests of active and passive sentence comprehension in small samples of children. These studies have generally shown impaired comprehension for the children with autism relative to comparison groups matched on receptive vocabulary or nonverbal cognitive ability (Paul et al., 1988; Prior & Hall, 1979; Tager-Flusberg, 1981). In addition, performance for passive sentences has been shown to be poorer than active sentences across studies and participant groups.

A subset of studies has suggested that difficulties in sentence comprehension may be the result of semantics rather than syntactic impairments per se in children with autism (Paul et al., 1988; Tager-Flusberg, 1981). One study examined the use of syntactic structures to interpret familiar verbs that appeared in ungrammatical sentences in a sample of so-called optimal-outcome children, who were no longer on the autism spectrum (Kelley, Paul, Fein, & Naigles, 2006). Even these children demonstrated some delays in their strategy use for sentence interpretation (e.g., over-reliance on the sentence frame rather than on the lexical verb). The notion that word-order use may be less impaired than the use of semantic cues is also supported by a recent study demonstrating that young children with autism successfully utilize SVO word order to understand transitive sentences (Swensen et al., 2007). With the exception of the study by Swensen and colleagues, however, this research has been limited to very small samples, large age ranges of participants, and generally higher-functioning children with autism who are able to complete demanding tasks that require acting out sentences with a set of toys or pointing to a picture. Thus, these results might not generalize to children with lower levels of receptive vocabulary or nonverbal cognitive ability. Further investigation into the relationship between syntactic knowledge and lexical development in children with ASD is needed.

Research on how delays in one aspect of receptive language could impact delays in another has been almost nonexistent in children with FXS or ASD. As described below, there is ample evidence of bootstrapping in language development for typical children. Understanding the processes involved in syntactic bootstrapping – and their disruptions – will help to reveal the underlying causes and specificity of the language phenotypes associated with FXS and ASD.

Processes Underlying Verb Learning

Reciprocal domains. Across the course of typical language development, language learning builds upon itself. For example, Fernald, Perfors, & Marchman (2006) provide evidence of reciprocal development, with speed of comprehension supporting expressive vocabulary. Such reciprocity has also been described between vocabulary and syntax; however, reciprocal syntactic and lexical development might be disrupted in children with language impairments (Moyle et al., 2007). For example, in children with Williams syndrome and typically developing children, receptive vocabulary and receptive syntax are correlated (Robinson et al., 2003). In language learners with other neurodevelopmental disorders, such as Down syndrome, it has been hypothesized that grammatical deficits could impact verb learning by making it more difficult to extract the syntactic patterns that aid semantic interpretation of verbs (Grela, 2002; Hesketh & Chapman, 1998). Indeed, adolescents with Down syndrome have at least as much difficulty using grammatical cues to learn nouns and verbs as do much younger typically developing children (McDuffie et al., 2007). Studies such as these suggest that the positive links between vocabulary and syntax may be weak in children with some neurodevelopmental disorders and that strengthening one domain could benefit others.

Bootstrapping and abstracting syntactic knowledge in typical development. Bootstrapping processes account for many aspects of language acquisition (e.g., Christiansen, Onnis, & Hockema, 2009; Naigles, 2002). Syntactic bootstrapping is a mechanism that involves combining knowledge about the syntactic regularities of language with the available learning contexts for novel words to interpret nouns, verbs, and spatial prepositions (Fisher, Klinger, & Song, 2006; Gleitman, 1990). Verbs, however, are at the heart of syntactic development and are difficult to acquire, and thus, they are the focus of the present study.

In a seminal study, Naigles (1990) demonstrated how knowledge of transitivity can inform the verb learning of children ages 1;11 to 2;3. In this study, children watched a video of two actors simultaneously performing different novel actions. One action was causative, with one actor doing something to the other. The other action was non-causative, performed simultaneously by both actors. The novel verb was then either presented in a transitive (e.g., *The duck is gorping the bunny*) or intransitive (e.g., *The duck and the bunny are gorping*) frame. The test trials showed side-by-side movies, each demonstrating one of the two actions. The children who heard the transitive frame looked longer at the causative action; likewise, children who heard the intransitive frame looked longer at the non-causative action. This study established that young children could interpret novel scenes by using syntactic cues and their semantic implications (i.e., the correlation between transitivity and causation in English).

Gertner, Fisher, and Eisengart (2006) found that toddlers extend another aspect of syntactic knowledge about reversible transitive sentences – word order – to novel verbs. While listening to transitive sentences (e.g., *The duck is gorping the bunny!*), 21- and 25-month olds watched side-by-side videos of a duck acting on a bunny and a bunny acting on a duck. They looked longer to a video in which the agent was the subject of the sentence (e.g., a duck acting on a bunny) than the reverse (e.g., a bunny acting on a duck). This study demonstrates that young children are able to use word order (i.e., a representation of a transitive sentence, according to Gertner and colleagues) to interpret novel verbs.

In perhaps an even stronger test of the abstraction and use of SVO word order, Franck, Millotte, Posada, & Rizzi (in press) demonstrated that 19 month-old French infants preferred a causative scene to a scene with the same action performed reflexively when presented with an SVO sentence containing a novel verb. Importantly, their findings cannot be accounted for by lexical training during the initial phase of the task or by a general preference for SVO sentences or causative scenes. Given how early such syntactic knowledge is demonstrated in typical development, it is of theoretical and practical value to know whether boys with FXS or ASD use distributional regularities from input, such as word order or transitivity, for language learning.

Bootstrapping in SLI. Verb learning is a challenge for children with SLI, as is the use of syntactic bootstrapping for that learning, relative to age and general comprehension levels (O'Hara & Johnston, 1997; Oetting, 1999). For example, Riches, Tomasello, and Conti-Ramsden (2005) found that children with SLI show poorer retention of novel verbs than younger typically developing children. A handful of studies have pointed to deficits in syntactic bootstrapping for various types of lexical acquisition, but especially verbs (e.g., O'Hara & Johnston, 1997; Rice, Cleave, & Oetting, 2000).

Oetting (1999) compared the interpretation and retention of novel verbs in six-year-old children with SLI to chronological-age and language-age matched typically developing children. In their task, novel labels were paired with two scenes, each of which contained either a causative action or the two actors simultaneously performing a non-causative action. The children with SLI were less successful than their age-mates. Additionally, children with SLI retained the label-action pairing with less success than either comparison group. This study suggests that such bootstrapping is impaired in children with SLI, even into the school-age years.

More recently, Johnson and de Villiers (2009) examined syntactic bootstrapping in a large sample of four- to nine-year-old children with language impairment and those with typical language. The children with language impairment had significant difficulty relative to the typical children using syntactic bootstrapping to interpret novel verbs using multiple sentence structures, including intransitive, transitive, and dative sentences. In summary, syntactic bootstrapping is an area of weakness for children with language impairment and this deficit extends to multiple syntactic constructions.

Syntactic bootstrapping in neurodevelopmental disorders. No studies have assessed syntactic bootstrapping by boys with FXS and only two studies have focused on syntactic bootstrapping in ASD. Shulman and Guberman (2007) assessed knowledge about transitivity for verb learning in Hebrew-speaking children with autism, ages 3;10 to 7;0, children with SLI, ages 3;7 to 6;0, and children with typical development, ages 1;11 to 4;7. The groups were matched on language ability. The syntactic bootstrapping task was modeled after Naigles (1990). Interestingly, the children with autism outperformed the children with SLI and did not differ from the typically developing children. Unfortunately, the nonverbal cognitive abilities of the participants were not reported; however, it can be assumed that these children were likely to be high functioning, as they were matched to the children with SLI of approximately the same age and language ability. As such, these results are difficult to interpret and further research on children with ASD is warranted.

More recently, Naigles, Kelty, Jaffery, and Fein (2011) found that young children with autism (*n* = 17; mean age = 41 months) did not perform differently than typically developing toddlers (mean age = 28 months) in a preferential looking task assessing the ability to map novel transitive verbs to causative actions using SVO sentences. This study followed the Naigles (1990) study more closely than did Shulman and Guberman. Interestingly, Naigles et al. found that vocabulary and sentence-processing (SVO sentence comprehnesion with familiar verbs) predicted syntactic bootstrapping performance. One limitation of the Naigles et al. study was a failure to test intransitive verbs, which would provide a more complete picture of syntactic-semantic links in children with ASD.

Syntactic bootstrapping is an important new area of research in FXS and ASD because it is unknown whether children with these disorders extend various aspects of syntax to novel verbs to constrain interpretation in support of lexical learning. In children with ASD, first steps have been taken in identifying some circumstances under which small samples of children with ASD can correctly comprehend specific syntactic forms (i.e., SVO structures) or apply knowledge about transitivity (i.e., causation). However, the use of word order by boys with ASD to interpret scenes with novel verbs has been considered neither in isolation, nor in relation to another neurodevelopmental disorder. Furthermore, the use of syntactic structures other than the active voice (e.g., the later-acquired passive voice) has not been examined in boys with either ASD or FXS. Examining the use of word order and transitivity, as done for typical acquisition by Gertner et al. (2006) and Naigles (1990), is an important starting point for both boys with FXS and ASD because these cues can be utilized early in typical development, and they reflect pervasive patterns of English that could bolster future learning. The current research assessed these types of syntactic cues using a paradigm appropriate to these populations.

Research Questions and Hypotheses

This study was designed to assess the use of syntactic cues (i.e., word order in active and passive sentences) and the use of the link between syntactic patterns and semantics (i.e., transitivity and causation) to interpret novel verbs. Although not testing verb learning in terms of retention, this study examined one aspect of the lexical acquisition of verbs – the use of syntactic cues to interpret scenes with novel actions – in a preferential looking task. If areas of syntactic knowledge are weak, then bootstrapping from those syntactic forms would be limited. It was expected that participants with FXS or ASD would perform with less success than younger typically developing children with similar nonverbal cognitive ability. For participants with FXS, this weakness was expected to be most pronounced in the use of word order, particularly for passive sentences, which rely more heavily on syntactic knowledge. For participants with ASD, for whom syntactic-semantic links may be least developed, this weakness was expected to be most pronounced in the use of transitivity as a cue to causation.

Method

Participants

As described further in Chapter 2, participants (*N* = 80) were drawn in part from a longitudinal study on the use of social cues to word learning in boys with FXS and ASD, and otherwise recruited using similar methods. A total of 30 typically developing boys, 24 boys with FXS, and 15 boys with ASD completed part or all of the experimental tasks for the present study. Eleven adults completed the experimental tasks as a point of comparison.

Most participants in the current study (all but three adults and one boy with FXS) also completed Study 1. Of participants who completed Study 1, two adults, one boy with typical development, two boys with FXS, and two boys with ASD did not complete the current tasks of interest. The samples from Study 1 and Study 2 are not completely overlapping due to time restrictions, scheduling conflicts, or a participant's choice not to complete one or more activities. Those who completed both studies completed Study 1 prior to Study 2. Appropriate informed consent was obtained and the study was approved by a UW-Madison IRB.

All child participants were native English speakers free of uncorrected sensory or physical limitations that would prevent meaningful participation in the tasks, according to parental report. Families of boys with FXS from the larger study provided proof of a positive molecular genetic test for the *FMR1* full mutation; boys with ASD from the larger study had a community, educational, or medical diagnosis of ASD and their parent provided proof of a negative molecular genetic test for the *FMR1* full mutation. Boys with typical development from the larger study fell below the SCQ screening cut-off and only one participant met a conservative cut-off of 12 (Corsello et al., 2007). Several children (seven with typical development, two with

FXS, and six with ASD) did not participate in the larger study; these boys' parents provided verbal confirmation of the child's diagnosis.

Autism symptom severity. Participants with FXS or ASD enrolled in the larger project completed the appropriate module of the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999) with a research reliable examiner. These participants were assigned a severity score based on the revised algorithm (Gotham et al., 2007) and the severity score metric (Gotham et al., 2009), which ranges from 1 to 10, with 4 or more indicating ASD or autism. The ADOS was completed either concurrently with the experimental tasks (*n* = 13, all of whom had FXS) or 18 months prior. Boys with FXS, regardless of autism severity, were included provided that they completed the tasks of interest; excluding boys with FXS and comorbid ASD would have limited the generalizability of the study findings, given the high comorbidity of the two conditions.

Apparatus and Procedures

The experimental tasks were designed to assess, via preferential looking, interpretation of sentences containing novel verbs with respect to two related aspects of reversible syntactic constructions: word order and transitivity. The tasks were presented on either a Tobii 2150 infrared eye-tracker with 21 inch display and 50 Hz refresh rate (*n* = 38) or a Tobii T60 XL infrared eye-tracker with 60 Hz refresh rate (*n* = 42). The word order and transitivity tasks were administered in separate consecutive blocks (with the exception of one participant, for whom the tasks were presented on consecutive days). Task order was randomized among participants (39 participants completed the word order task first: 4 adults, 19 boys with typical development, 9 with FXS, and 7 with ASD). Order of presentation had no effect on performance for any group for any condition in the word order or transitivity task, *p*s > .220.

Participants were seated approximately 24 inches from the monitor in a chair or, rarely, in his caregiver's lap (approximately three cases). Standard automatic calibration provided by ClearView (Tobii Technology, 2006) or Studio (Tobii Technology, 2010) software was completed immediately preceding the task. ClearView or Studio software was also used to present the dynamic stimuli, created from AVI movies, and to collect gaze data.

Measures

The word order and transitivity tasks were each comprised of 20 total test trials with 4 additional trials interspersed as attention-getters. Each test trial had a duration of 7000 ms with two movies played simultaneously side-by-side. Each trial contained a verbal cue (*Look!*; 500 ms duration) at 1000 ms after trial onset, followed by 1000 ms of silence to allow ample time for visual processing of the novel actions. At 2500 ms, a sentence containing a novel verb played. Sentence duration was 2500 ms. From sentence offset at 5000 ms until the end of the trial, no auditory stimuli were presented. All auditory stimuli were recorded by a female who was not the primary examiner. The onset of the disambiguating verb was 667 ms into the sentence, or 3167 ms into the trial. Thus, the baseline portion of the trial was considered to be from 0 to 3100 ms and the test portion began at 3200ms and continued to the end of the trial at 7000 ms.

The target movie matched the sentence (described further below); movies appeared equally as frequently as target and distractor and the side of the target movie was also balanced. Of the 20 test trials, the first 4 provided an introduction to the structure of the task with familiar verbs. All sentences were depicted with four familiar characters (bear, cat, dog, and mouse) that were paired within each task. Novel actions were roughly equated in timing for the completion of one cycle of the action. Two novel verbs were included in each task and were tested with eight trials each, as described further below. Auditory stimuli are listed in Appendix 3A.

Knowledge of word order. The word order task was designed to assess the application of word order knowledge to the interpretation of transitive sentences with novel verbs in the active and passive voice. Use of simple SVO word order leads to success in the active condition, but overextension leads to erroneous interpretation in the passive condition if the subject is incorrectly interpreted as the agent. In addition to including a passive condition, this task differed from that of Gertner et al. (2006) in that (1) the target and distractor depicted the same novel action, akin to Franck et al. (in press), (2) the test phase was embedded in the exposure phase to reduce memory demands, and (3) the novel verb was presented only once in each trial.

The four introductory trials tested interpretation of two active (*The cat is squeezing the mouse*, *The mouse is squeezing the cat*) and two passive (*The dog is kissed by the bear*, *The bear is kissed by the dog*) sentences, with the agent and patient reversed in each pair of scenes.

Two novel verbs were tested with four active and four passive trials each, yielding eight total trials in both the active and passive condition. As seen in Table 1, the mouse and dog depicted *foping* and the cat and bear depicted *pugging*. For example, one active item tested *The dog is foping the mouse,* in which the target movie showed the dog pushing the mouse's nose down with its paw and the distractor movie showed the mouse pushing the dog's nose down with its paw. One passive trial tested *The cat is pugged by the bear*, with the target movie showing the bear nudging the cat's chin up with its head and the distractor movie showed the cat nudging the bear's chin up with its head. Although no semantic bootstrapping is necessary because the target and distractor contain the same novel action, success in this condition can be unambiguously attributed to abstract knowledge about word order because no semantic information is available to disambiguate the scenes. The passive condition places the highest demands on syntactic knowledge because reliance on the simple SVO word order strategy would result in poor performance. Success in the passive condition would be evidence of processing a lower-frequency structure in conjunction with a "by" phrase, signaling the passive construction.

Knowledge of transitivity. Trials testing the transitivity cue assessed the extension of the understanding that a transitive sentence structure marks a causal relation between the agent and patient to novel verbs. Although modeled after Naigles (1990), the current task differed from that study in that (1) the test phase was embedded in the exposure phase to avoid unnecessary memory demands and (2) the novel verb was presented only once in each trial.

The four introductory trials tested interpretation of two transitive (*The cat is squeezing the mouse*, *The mouse is squeezing the cat*) and two intransitive (*The cat is sitting with the mouse*, *The mouse is sitting with the cat*) sentences.

The two novel verbs (one transitive, one intransitive) were tested in eight trials each, yielding eight trials in both the transitive and intransitive conditions. Each animal appeared as the subject of the sentence with each verb twice. The bear was paired with the mouse and the dog was paired with the cat. As seen in Table 2, for example, one transitive sentence tested *The dog is kabing the cat* in which the target movie depicted the dog rotating the cat's arm and the distractor movie depicted the dog and cat swaying. One intransitive trial tested *The dog is yooking with the cat*, with the target movie depicting the dog and cat swaying and the distractor movie depicting the dog rotating the cat's arm. Success in this condition relies upon the understanding that transitive sentences, but not intransitive, cue a causative relation between the agent and patient of a sentence. Table 3 allows comparison of the stimuli from each condition.

Analysis Strategy

Sampled gaze data were collapsed into 100 ms bins to allow data from both eye trackers to be combined. Bins were classified as either (1) primarily containing gaze to the target or to the distractor (ties were awarded to the target), or (2) containing no gaze to either the target or the distractor. Invalid trials were defined as those in which the participant failed to look at either the target or distractor movie for a consecutive 1000 ms period after verb onset (i.e., during the test window of 3200 ms to 7000 ms).

Only participants who completed a successful calibration and had valid data were considered for inclusion in analyses. Of the participants who attempted the experimental tasks, it was not possible to properly calibrate the eye tracker for three (one adult, one child with FXS, and one child with ASD). The number participants who were successfully calibrated and completed at least one valid trial were 10 adults, 30 typically developing children, 19 boys with FXS, and 14 boys with ASD (note that 4 boys with FXS contributed no valid trials during either the word order or transitivity tasks).

Out of this reduced pool of participants (*N* = 73), participants who contributed two valid trials in a given condition were included in analyses for that condition, allowing the estimation of average proportion of gaze to the target per condition. Although having more trials per participant would be desirable, such a criterion would limit sample sizes further and constrain the generalizability of the findings and reduce power. The number of participants who met the two trial criterion for each condition is presented in Table 4. Characteristics of the child participants who met this criterion for each condition are described in Tables 5 - 8, including autism symptom severity, nonverbal cognitive ability assessed with the Leiter International Performance Scales-Revised (Roid & Miller, 1997), receptive vocabulary ability assessed with the Peabody Picture Vocabulary Test, Fourth Edition (Dunn & Dunn, 2007), and the number of valid trials that served as the basis of their estimated performance in the experimental tasks.

For each condition, the dependent measure for the primary analysis was the average proportion of gaze to the target movie relative to gaze to either the target or distractor movie. Gaze during the baseline and test windows was analyzed. Tests of looking behavior during the baseline window were two-tailed because no baseline differences were expected. To glean evidence of the use of word order or transitivity cues for sentence interpretation, one-tailed t-tests were used to determine that the proportion of looking to the target was greater than expected by chance during the test window and that looking to the target was greater during the test window than the baseline window.

Results

Results for each task are presented separately. In each case, the performance of adults is described before that of children.

Word Order Task

Adult performance. Due to equipment malfunction, introduction trials for the word order task were not analyzed for one adult; analyses for all other conditions reflect 10 adults.

Familiar verbs. Active and passive trials were not distinguished for introductory trials because only two of each were presented. Adults demonstrated no preference for either movie during the baseline window, $t(8) = .02, p = .985, d = .01$. As expected, adults showed comprehension of the familiar verbs with greater looking to the target than chance, $t(8) = 11.00$, $p < .001, d = 3.66$. Adults' gaze to the target was significantly greater during the test window relative to the baseline window, $t(8) = -5.97, p < .001, d = -1.99$.

Active condition. Adults showed no preference during the baseline window of active trials, $t(9) = -.51, p = .624, d = -.16$. Adults did look more to the target than expected by chance during the test window, $t(9) = 9.58$, $p < .001$, $d = 3.03$. Looking to the target was significantly greater in the test window than the baseline window, $t(9) = -6.64$, $p < .001$, $d = -2.10$.

Passive condition. Adults showed no preference during the baseline window of passive trials, $t(9) = -1.01$, $p = .339$, $d = -.32$. Adults looked more to the target than expected by chance during the test window, $t(9) = 19.47$, $p < .001$, $d = 6.61$. Looking to the target was significantly greater in the test window than the baseline window, $t(9) = -8.72$, $p < .001$, $d = -2.76$.

Summary. Because condition was crossed with verb in the word order task, the possibility of verb effects was also examined. Adults showed no preference during the baseline window of *foping* or *pugging* trials, *p*s > .55. Looking to the target during the test window did not differ between verbs, $p = .758$. Adults looked more at the target during the test window than the baseline window for both *foping* and *pugging*, *p*s < .001, $d = 4.41$ and $d = 4.26$, respectively.

Overall, adult performance validates the experimental task for tapping syntactic cues, at least ones available to highly experienced language learners, for interpreting novel verbs.

Child performance. Performance of participants with typical development, FXS, or ASD is described in Tables 5 and 6.

Familiar verbs. For the word order task, participants with at least two valid introductory trials included 23 boys with typical development, 12 with FXS, and 9 with ASD. Unexpectedly, looking to the target during baseline was significantly greater than chance for typically developing participants, $t(22) = 2.61$, $p = .016$, $d = .54$, but not the other groups, *p*s > .50. Looking to the target during the test window was greater than chance for participants with typical development, $t(22) = 2.87$, $p = .005$, $d = .60$, and participants with ASD, $t(8) = 2.00$, $p = .041$, $d = .66$, but not participants with FXS, $t(11) = -2.13$, $p = .943$, $d = -.61$. Looking behavior between the baseline and test window did not differ significantly for any group, *p*s > .225, which might not be unexpected given that only four trials, two in the passive voice, were presented.

Active condition. As seen in Table 5, 22 boys with typical development, 12 boys with FXS, and 10 boys with ASD had at least two valid active trials. Baseline looking to the target did not differ from chance in any group, *p*s > .40 for boys with typical development and FXS, and *t*(9) = 1.65, *p* = .134, *d* = .52, for boys with ASD. See Figure 1. Boys with typical development looked significantly more than chance at the target during the test window, *t*(21) = 2.24, *p* = .018, *d* = .48. Boys with FXS did not look to the target more than expected by chance during the test window, *t*(11) = .284, *p* = .391, *d* = .08. Boys with ASD also did not look significantly more to the target than chance during the test window, although the effect size was medium, *t*(9) = 1.35, *p* = .106, *d* = .43. For no group did test and baseline window looking to the target significantly differ, *p*s > .310 for boys with ASD and FXS, and *t*(21) = -1.41, *p* = .087, *d* = -.30, for boys with typical development.

Passive condition. As seen in Table 6, results for passive trials include 20 boys with typical development, 10 boys with FXS, and 8 boys with ASD. Baseline looking to the target did not differ from chance in any group, *p*s > .60 for boys with typical development and FXS, and *t*(7) = -1.67, *p* = .139, *d* = -.59, for boys with ASD. During the test window, boys with typical development looked more than expected by chance at the target, *t*(19) = 1.84, *p* = .041, *d* = .41, as did boys with ASD, *t*(7) = 2.08, *p* = .038, *d* = .73. Boys with FXS did not have looking behavior that differed from chance during the test window, *t*(9) = -.17, *p* = .872, *d* = -.05. Looking to the target during the test window was greater than baseline for boys with typical development, *t*(19) = -1.96, *p* = .033, *d* = -.44, and ASD, *t*(7) = -2.56, *p* = .019, *d* = -.90, but not for boys with FXS, *t*(9) = 1.08, *p* = .979, *d* = .03.

Summary. Performance for the two verbs was examined separately (combining active and passive trials) for participants with at least two valid *foping* and two valid *pugging* trials. No looking behavior during baseline differed from chance for any group, *p*s > .275, with the exception of typically developing boys, who looked more to the target during the *foping* baseline window than expected, *t*(19) = 1.97, *p* = .032, *d* = .44. During the test window, typically developing boys looked at the target more than chance for *foping*, *t*(19) = 2.84, *p* = .005, *d* = .63, but not *pugging*, *t*(19) = .43, *p* = .335, *d* = .10. In contrast, boys with ASD looked more than chance at the target for *pugging*, *t*(8) = 2.94, *p* = .010, *d* = .98, but not *foping*, *t*(8) = 1.20, *p* = .133, *d* = .40. In fact, boys with ASD looked significantly more to the target for *pugging* during the test window than during baseline, *t*(8) = -2.94, *p* = .010, *d* = -.98, whereas no other groups demonstrated per verb success, *p*s > .22. Boys with FXS showed no effects by verb, *p*s > .85. Together, the findings suggest that *foping* was perhaps more ambiguous or difficult to interpret.

Overall, performance of child participants was less clear than that of adults; however, typically developing boys showed a general pattern of interpreting sentences with novel verbs using word order in both active and passive trials. Boys with FXS did not demonstrate this ability, whereas boys with ASD did, albeit most convincingly for the passive condition.

Transitivity Task

Adult performance. All ten adults contributed to analyses for each transitivity condition.

Familiar verbs. Transitive and intransitive sentences were not distinguished given the small number of introductory trials (i.e., two each). Adults showed a preference for the target during both the baseline, *t*(9) = 2.42, *p* = .039, *d* = .76, and test windows, *t*(9) = 12.95, *p* < .001, *d* = 4.09. Nonetheless, adults demonstrated comprehension of familiar verbs with greater looking to the target during the test than baseline window, *t*(9) = -12.17, *p* < .001, *d* = -3.85.

Transitive condition. Adults showed no preference during the baseline window of transitive trials, *t*(9) = 1.14, *p* = .283, *d* = .36. Adults looked more to the target than expected by chance during the test window, *t*(9) = 9.22, *p* < .001, *d* = 2.92. Looking to the target was significantly greater during test than baseline windows, *t*(9) = -6.76, *p* < .001, *d* = -2.14.

Intransitive condition. During the baseline window, adults looked more to the causative (i.e., distractor) scenes during intransitive trials, *t*(9) = -2.40, *p* = .040, *d* = -.76. Adults looked more to the target than expected by chance during the test window, *t*(9) = 6.97, *p* < .001, *d* = 2.20. Looking to the target was significantly greater during test than baseline windows, *t*(9) = -6.88, *p* < .001, *d* = -2.18.

Summary. Verb and condition were not crossed due to the semantic nature of the task: verb effects were redundant with condition. Overall, adult performance validates the task for successful interpretation of scenes with novel transitive and intransitive verbs.

Child performance. Performance of boys with typical development, FXS, and ASD is described in Table 7 and Table 8.

Familiar verbs. For the transitivity task, 20 participants with typical development, 12 with FXS, and 10 with ASD had at least two valid introductory trials. Typically developing boys looked to the target during the baseline window, *t*(19) = 2.03, *p* = .057, *d* = .47. Neither boys with FXS nor ASD showed this preference during the baseline window, *p*s > .5. Both typically developing boys and boys with FXS looked more to the target than expected by chance during the test window, *t*(19) = 4.45, *p* < .001, *d* = .99, and *t*(11) = 1.98, *p* = .037, *d* = .57, respectively. The effect was of medium size for boys with ASD, but failed to reach significance, *t*(9) = 1.59, *p* = .073, *d* = .50. Typically developing participants showed significantly greater looking to the target during the test window relative to the baseline window, *t*(19) = -2.25, *p* = .018, *d* = -.50.

Participants with FXS or ASD did not show this effect reliably, *t*(11) = -.93, *p* = .186, *d* = -.27 and *t*(9) = -1.07, *p* = .157, *d* = -.34, respectively.

Transitive condition. As seen in Table 7, 22 boys with typical development, 7 boys with FXS, and 12 boys with ASD contributed at least two valid transitive trials. For transitive trials, looking to the target during the baseline window did not differ from chance for any group, *p*s > .45 for boys with FXS and ASD, and *p* = .150, *d* = -.32, for boys with typical development. As in the case of Naigles et al. (in press), this trend was towards a preference for the simultaneous action. For typically developing boys, looking to the target during the test window was greater than chance, *t*(21) = 3.64, *p* = .001, *d* = .78. For boys with FXS, the effect failed to reach significance, but was in the expected direction, *t*(6) = .22, *p* = .416, *d* = .08. For boys with ASD, the observed difference was in the opposite direction, but also not significant, *t*(11) = -1.22, *p* = .125, *d* = -.35. In terms of looking to the target during the test window relative to during the baseline window, the difference was significant for typically developing boys, *t*(21) = -5.11, *p* < .001, *d* = .-1.09, but not boys with FXS or ASD, *p*s > .30, *d*s < .15.

Intransitive condition. As seen in Table 8, participants who contributed at least two valid intransitive trials were 18 boys with typical development, 9 with FXS, and 11 with ASD. Baseline looking to the target was different than chance for boys with ASD, *t*(10) = 4.29, *p* = .002, *d* = 1.29, who looked more to the target (i.e., the simultaneous action). Baseline looking behavior did not differ from chance for boys with FXS, *t*(8) = -.86, *p* = .414, *d* = -.29, or boys with typical development, *t*(17) = .48, *p* = .634, *d* = .11. Looking to the target during the test window was greater than chance for typically developing boys, *t*(17) = 1.76, *p* = .048, *d* = .42. Looking to the target during in the test window did not differ from chance for boys with FXS, *t*(8) = .91, *p* = .194, *d* = .30, or boys with ASD, *t*(10) = .27, *p* = .273, *d* = .08. Looking to the target significantly differed between baseline and test window for participants with FXS, for whom the effect was in the expected direction, *t*(8) = -4.98, *p* = .001, *d* = -1.66, and for those with ASD, for whom the effect was in the opposite direction, *t*(10) = 2.36, *p* = .020, *d* = .71. The effect was not significant for typically developing boys, *t*(17) = -1.15, *p* = .134, *d* = -.27.

Summary. Again, the performance of children was less clear than that of adults. Typically developing boys, however, looked reliably to the target for both transitive and intransitive verbs. Boys with FXS showed reliable interpretation of the intransitive verb. Boys with ASD, in contrast, showed inconsistent test performance with preference for simultaneous actions at baseline, but looking behavior in the unexpected direction for the intransitive verb.

Exploratory Analyses

Several avenues of exploratory analyses were pursued. First, instead of the a priori test window, a test window based on the gaze performance of pilot participants was set to 4800 to 7000 ms. Results were largely comparable, with the following exceptions. For the active condition of the word order task, boys with ASD demonstrated significantly more gaze to the target than expected by chance, *t*(9) = 1.87, *p* = .047, *d* = .59. For the introductory trials of the transitivity task, boys with FXS no longer looked significantly toward the target during test, *p* = .085. In the intransitive condition, typically developing boys looked significantly more to the target during the test than baseline window, *t*(17) = -2.05, *p* = .028, *d* = -.48. For boys with FXS and ASD in the intransitive condition, the difference between baseline and test window looking to the target no longer reached significance, *t*(8) = -1.39, *p* = .102, *d* = -.46, and *t*(10) = 1.65, *p* = .065, *d* = .50, respectively.

Second, it was confirmed that results would not have differed having required three, rather than two, valid trials per participant per condition. Results were not substantively different when limiting analyses to participants with three or more valid trials, with the following exceptions. In the word order task, typically developing boys looked more to the target during test than baseline windows in the active condition, *t*(20) = -1.78, *p* = .045, *d* = -.39. In the passive condition for typically developing boys, performance was no longer greater than chance in the test window, *t*(13) = .74, *p* = .238, *d* = .20, and baseline and test looking no longer differed, *t*(13) = -1.14, *p* = .138, *d* = -.30. In the transitive condition, typically developing boys displayed a baseline preference for the simultaneous actions, *t*(15) = -2.25, *p* = .040, *d* = -.56. In the transitive condition, boys with FXS looked longer to the target during test than baseline window, *t*(2) = -13.05, *p* = .003, *d* = -7.54, although this reflects the performance of only three boys. In the intransitive condition, boys with FXS showed a baseline preference for the causative action, *t*(5) = -2.72, *p* = .042, *d* = -1.11, an effect opposite to that observed for boys with ASD, but in line with that observed for adults.

Third, nonverbal cognitive ability and receptive vocabulary were considered as concurrent predictors of eye gaze performance in each condition for all child participants combined, with two-tailed *p*-values. Regressions predicting looking to the target during the test window indicated that Leiter-R growth scores were positively related to performance in the active condition, *t*(31) = 2.35, *p* = .025, semipartial *r* = .39, but only when controlling for PPVT-4 raw scores. Looking to the target during the test window in the passive condition was predicted by Leiter-R growth scores, even when controlling for PPVT-4 scores, *t*(28) = 2.31, *p* = .029, semipartial *r* = .39. In the transitive condition, looking to the target during the test window was related to Leiter-R growth scores, *t*(28) = 4.34, *p* < .001, semipartial *r* = .63, but not when controlling for vocabulary scores, *p* = .627; however vocabulary scores, with Leiter-R growth scores in the model, predicted transitive performance, *t*(27) = 2.65, *p* = .013, semipartial *r* = .35.

For target looking during the test window of intransitive trials, nonverbal cognition was a predictor when controlling for vocabulary, and the regression containing cognition, vocabulary, and group was also significant, with a positive relationship with Leiter-R scores, $t(24) = 4.00$, $p = .001$, semipartial $r = .54$. In addition, participants with ASD scored lower than those with typical development, $t(24) = -3.60$, $p = .001$, semipartial $r = -.48$. An unexpected negative relationship with PPVT-4 scores was detected, $t(24) = -5.16$, $p < .001$, semipartial $r = -.69$.

Lastly, group differences were tested, despite the mismatch in cognitive abilities, with one-tailed *p*-values. For the active condition, there were no significant differences in looking to the target during the test window, *p*s > .175, for all comparisons, except $p = .095$ for the advantage of typical development over FXS. For the passive condition, no group differences were found: FXS relative to typical development, $p = .095$; FXS relative to ASD, $p = .115$; ASD relative to typical development, $p = .440$. For the transitive condition, looking to the target by boys with typical development during the test window differed from boys with ASD, $p = .002$, but not those with FXS, $p = .055$, whose performance fell between the other two groups. No group differences emerged during the intransitive test window, *p*s > .30, for all comparisons, except $p = .189$ for typical development relative to ASD.

Discussion

In light of the challenges with language development experienced by boys with FXS or ASD, the current study examined extensions of syntactic knowledge that might serve as platforms for future language learning. The use of two types of distributional cues was assessed in the interpretation of sentences and scenes containing novel verbs: word order and transitivity.

Adult performance served as a point of comparison for the experimental word order and transitivity tasks. As expected, adults correctly interpreted sentences containing novel verbs on the basis of word order for active SVO sentences (e.g., *The dog is foping the mouse*) and sentences in the passive voice (e.g., *The cat is pugged by the bear*). Adults also correctly interpreted sentences containing a transitive verb (e.g., *The bear is kabing the mouse*) or an intransitive verb (e.g., *The dog is yooking with the cat*).

The primary hypothesis was that typically developing boys would also demonstrate success in interpreting these sentences with novel verbs, even in cases in which older boys with FXS and ASD would not. Specifically, weakness with syntax was hypothesized to lead to poor performance for boys with FXS when interpretation was based on purely syntactic cues (i.e., word order in the active and passive voice). Weakness with semantics was hypothesized to lead to poor performance for boys with ASD when interpretation was based on syntactic-semantic links (i.e., transitivity and causation). Likewise, relative strength with vocabulary in boys with FXS was thought to lead to some success in sentence interpretation with transitivity cues, whereas relatively intact syntactic knowledge was thought to allow boys with ASD to succeed in interpreting sentences using word order cues.

These hypotheses were partially supported. Typically developing boys generally succeeded in using both word order and transitivity cues, although not every analysis reached significance. The performance of boys with FXS or ASD was more variable, although both groups of boys showed evidence of successful interpretation of sentences with novel verbs using some aspect of syntactic knowledge.

Word Order in the Active and Passive Voice

In the word order task, target and foil movies depicted the same novel action with the same characters. The scenes were distinguished only in the role of the characters, akin to Franck et al. (in press). For active transitive sentences, novel verbs are interpreted with the English

SVO word order cue that the agent, the subject of the sentence, acts on the patient. In the case of passive transitive sentences, the sentences had to be interpreted with a lower-frequency word order, in which the agent is not the subject of the sentence. Thus, targets for active sentences served as foils for passive sentences and vice versa.

Boys with FXS demonstrated no evidence of looking behavior that was guided by the active or passive sentences they heard. In contrast, the boys with ASD correctly interpret the scenes using active SVO word order (but only when considering a shorter, later test window) and sentences using the passive voice. Interestingly, successful performance was most reliable during passive trials for boys with ASD. Passive sentences are generally thought to be acquired only later during the course of language acquisition and are more challenging for children with language impairments than active sentences (Montgomery & Evans, 2009). Passive sentences violate the more frequent SVO word order but include a salient "*by the* agent" clause, which might draw attention to the agent in such a way as to aid interpretation of sentences with novel verbs. It is possible that the advanced age and accompanying increased exposure to the passive voice for the boys with ASD supported their success in this task; however, boys with FXS were no younger and did not demonstrate successful interpretation of scenes using the passive voice.

The conclusion that boys with ASD can successfully interpret scenes with novel verbs using word order supports and extends the findings from Swensen et al. (2007), who presented children with ASD with a test of transitive SVO sentence interpretation with familiar verbs. The current findings demonstrate that boys with ASD are able to abstract SVO word order and apply it to novel verbs to allow interpretation of scenes with novel actions, with some evidence of extending this to both the active and passive voice.

Because participants with FXS failed to show evidence of sentence interpretation using syntactic cues based on word order, word order may be a distributional cue that is challenging for boys with FXS to harness in the face of increased processing demands associated with novel words. These difficulties are not unexpected given what is known about the cognitive phenotype associated with FXS. Syntactic comprehension is thought to be a weakness for boys with FXS (Price et al., 2007). Other cognitive abilities, including phonological memory, are also impaired in boys with FXS (Ornstein et al., 2008). These limitations may together make the task of extending syntactic knowledge about sentence constructions to novel actions and verbs quite difficult for boys with FXS. If replicated, these findings would suggest that syntactic knowledge is a rather weak platform for learning for boys with FXS and should be targeted for intervention.

It is striking that participants with FXS did not show successful performance on the word order task in light of the successful performance by much younger typically developing children and same-age children with ASD. Extension of SVO word order to novel verbs has been demonstrated in typically developing toddlers as young as 19 months of age (Dittmar, Abbot-Smith, Lieven, & Tomasello, 2011; Franck et al., in press; Gertner et al., 2006). Using highly similar stimuli (i.e., videos in which the actions are identical in the target and distractor movies, with only the agent and patient reversed), Dittmar et al. (2011) demonstrated that 31-month-olds could indicate use of the knowledge of agent and patient roles in relationship to word order in active sentences containing novel verbs in a forced-choice pointing paradigm. Thus, the knowledge being tested in the present study should be developmentally appropriate for children with neurodevelopmental disorders with this level of nonverbal cognitive ability.

It has been suggested that the presence of nouns in training trials that are later used in test trials might support interpretation of SVO word order when such an ability is emerging, but not yet established (Dittmar, Abbot-Smith, Lieven, & Tomasello, 2008). The current study contained four introductory trials with the same characters that appeared in test trials for the word order task (only two of the four nouns were introduced with familiar verbs in the transitivity task) and this should be taken into account when interpreting the results. However, even with this "support," boys with FXS still failed to demonstrate abstract knowledge about word order in active or passive sentences.

Transitivity and the Link between Syntax and Semantics

In the transitivity task, one novel causative action and one novel simultaneous action were performed side-by-side by the same characters. The causative action was described with a novel transitive verb and thus, a transitive sentence. The simultaneous action was described with an intransitive verb and thus, an intransitive sentence. The target for transitive trials served as the distractor for intransitive trials and vice versa. In contrast to the Naigles (1990) paradigm, the current experimental tasks did not require retention of the novel actions or the novel verb and thus limited memory and attention demands.

It was expected that harnessing syntactic-semantic links for interpreting novel verbs would be challenging for children with ASD. This pattern of results falls in line with the semantic impairments reported for children with ASD and mounting evidence that, in some cases, structural aspects of language, such as phonological form, may be more salient than aspects of meaning for children with ASD (Norbury, Griffiths, & Nation, 2010).

The findings from the current study, however, contrast with previous findings that children with ASD are able to successfully engage in syntactic bootstrapping for transitive verbs. The work by Naigles et al. (2011) demonstrated that 41-month-old children with ASD were able to map transitive verbs to causative actions, as were 28-month-old typically developing children.

Their task was directly modeled after Naigles (1990), with six exposures for each of two novel verbs presented in transitive sentences. Naigles et al. found that young children with ASD showed a preference for non-causative actions during baseline trials, although they were able to shift their attention to the causative actions during transitive test trials. In the current study, boys with ASD never showed reliable looking to the causative action. It is possible that increased time to process the visual scenes and the novel verb benefited performance in the Naigles task. Even so, the pattern of results for boys with ASD is surprising in that the current sample of boys was much older than the sample reported by Naigles and colleagues. The performance of adult participants suggests that extending syntactic knowledge to novel verbs remains possible, even when linguistic knowledge is firmly established. Further research on processing strategies utilized by children with ASD is warranted.

In contrast to the case of ASD, it was expected that boys with FXS would be able to leverage information about syntactic-semantic links to achieve success in the transitivity task. Although not every statistical test of the use of knowledge about transitivity reached significance, the pattern of results suggests that boys with FXS appreciate the link between syntax and semantics in that transitive sentences generally refer to causative actions, whereas intransitive sentences refer to non-causative or simultaneous actions. In line with this, there is some evidence that semantic ability is not a weakness in boys with FXS (Roberts, Price, Barnes, et al., 2007) and that some aspects of linking novel labels and referents might not be as challenging for boys with FXS as for boys with other neurodevelopmental disorders, such as ASD (McDuffie et al., under review). From a clinical standpoint, drawing the child's attention to the links between form and meaning might support stronger syntactic knowledge and ultimately improve comprehension, production, and further learning in boys with FXS.

Indeed, the implications of the feat of linking meaning and form in the course of language development, even without cognitive impairments, has not been overlooked (Naigles, 2002). For ASD, it has been suggested that language acquisition might be driven by a protracted developmental pattern such that biases or mechanisms for learning come into play later than would be expected based on typical development or nonverbal cognitive levels (Eigsti, de Marchena, Schuh, & Kelley, 2011). The current findings suggest that syntactic-semantic links might be weak for at least some children with ASD and might limit the extent to which syntactic knowledge serves as a jumping-off point for some aspects of future language learning.

Strengths and Limitations

This is the first study to utilize eye gaze to assess abstract syntactic knowledge in boys with FXS. The presence of a group of boys with ASD, a distinct but overlapping neurodevelopmental disorder, strengthens the interpretation of the findings from boys with FXS. Unfortunately, the boys with FXS tended score lower on measures of nonverbal cognitive ability than both the boys with typical development and those with ASD. Having sample sizes large enough to allow careful matching and thus, group comparisons that can be unambiguously interpreted would be desirable, but was not possible in the current study.

Indeed, the primary analyses were based on a small sample of participants in each group and a small number of trials (i.e., a minimum of two out of eight trials in each condition). Although 80 participants attempted the experimental tasks, the number of participants to contribute two valid trials to any given condition per group was small, with the worst instance being the transitive condition, for which only seven boys with FXS met the two-trial criterion. Despite these small samples and variability within groups, effect sizes were generally medium or large, suggesting that eye gaze paradigms designed to assess language processing might be ideally suited to children with neurodevelopmental disorders.

Likewise, the number of trials excluded due to inattention or a failure to capture the child's gaze was not trivial. While adults completed on average over seven valid trials per condition, child participants contributed an average of two (boys with FXS, for transitive trials) to five (boys with ASD, for active trials) trials per condition. Fatigue could be one explanation for the amount of data loss, especially given that the word order and transitivity tasks were presented consecutively and introduced a total of four novel verbs. Fatigue has been noted as a factor in similar studies, even for typically developing children, for whom these eye gaze paradigms were developed. Dittmar and colleagues (2011) found that only under certain conditions avoiding fatigue were 25-month-olds able to demonstrate knowledge about SVO word order. The current analyses did not differentiate between invalid trials due to failure to maintain an accurate track on the participant's eyes or instances in which the child was disengaged from the task. Future research should begin to pull apart attention deficits that make auditory and visual processing difficult in real-world learning contexts from those that make assessment challenging. These will be intertwined, but important to quantify nonetheless.

No previous studies have examined the interpretation of passive sentences with novel verbs and thus, the inclusion of the passive condition brings a more complex sentence structure to bear on the literature regarding the abstraction of word order patterns in English. However, because the passive voice is previously unexplored, it is unclear what effect intermixing active and passive sentences might have on sentence processing. Active sentences are more common than passive sentences in spoken English, whereas they occurred with equal frequency in the word order task. It is possible that performance would have differed had the active and passive conditions been blocked or presented on separate days.

Finally, there was differential performance across verbs for child participants in the word order task. It is possible that ambiguity in the agency of scenes depicting *foping* led to poorer performance than desired. Other studies have reported findings for sentence processing that varied by item, including for familiar verbs (Swensen et al., 2007). Future research will seek to replicate the current findings using the tried-and-true stimuli developed by Gertner et al. (2006) and Naigles (1990). In those studies, the novel verb was presented multiple times per trial, as opposed to once per trial in the current tasks, which might make knowledge easier to detect.

Future Directions

Only one other study has utilized eye-tracking to examine early syntactic processing (Franck et al., in press). One advantage of eye tracking is the ability to assess a child's fixations within a given scene rather than simply distinguishing between gaze to one scene or the other. Future studies might maximize the utility of this paradigm by determining which aspects of distractor scenes held the visual attention of boys with FXS or ASD in cases of misinterpretation. Such a line of research has the potential to inform an understanding of individual differences in learning and outcomes for both boys with FXS and ASD.

Some of the effects of interest (e.g., performance for active SVO word order by boys with ASD) were only detected in a post hoc test window that was later and shorter than the a priori test window. This suggests that children with neurodevelopmental disorders may require more time for processing linguistic stimuli and has implications for future research and interventions that strive to support comprehension and learning.

The current study did not assess syntactic bootstrapping or verb learning per se, but merely the extension of syntactic or syntactic-semantic knowledge to sentences and scenes containing novel actions and verbs. This represents only a starting point for verb learning processes. Future research should examine the retention of verbs learned with the support of syntactic cues, perhaps using separate exposure and test phases to distinguish challenges in interpreting the meaning of a novel verb from challenges retaining a novel label-action pairing.

There are many developmental questions that remain unanswered. Studies of this nature in boys with FXS younger than six years of age will be invaluable for addressing them, as will longitudinal studies of children with FXS, ASD, and even typical development. The relationship between extending syntactic and syntactic-semantic knowledge to novel words and later language outcomes has yet to be established in these populations, although there is emerging evidence that sentence comprehension supports syntactic bootstrapping (Naigles et al., 2011).

Conclusions

Little is known about the integrity of language learning mechanisms for children with neurodevelopmental disorders. The current study contributes to an understanding of the processes through which boys with FXS or ASD learn language and sets the stage for further research examining the potential impact of syntactic delays on other aspects of development.

Table 1

Example Stimuli for Word Order Cues

Condition	Stimulus	Target	Distractor
Active	*The dog is foping the mouse.*	Agent (subject) acts on patient (object)	Patient acts on agent
Passive	*The cat is pugged by the bear.*	Agent (theme) acts on patient (subject)	Patient acts on agent

Table 2

Example Stimuli for Transitivity Cues

Condition	Stimulus	Target	Foil
Transitive	*The cat is kabing the dog.*	Causative	Non-causative
Intransitive	*The cat is yooking with the dog.*	Non-causative	Causative

Table 3

Sample Novel Verb Stimuli with Accompanying Novel Actions

Item	Target Movie	Foil Movie
Word Order		
Active		
The dog is foping the mouse.	Dog pushes mouse's head	Mouse pushes dog's head
The cat is pugging the bear.	Cat nudges bear's chin	Bear nudges cat's chin
Passive		
The dog is foped by the mouse.	Mouse pushes dog's head	Dog pushes mouse's head
The cat is pugged by the bear.	Bear nudges cat's chin	Cat nudges bear's chin
Transitivity		
Transitive		
The bear is kabing the mouse.	Bear rotates mouse's arm	Bear and mouse sway
The dog is kabing the cat.	Dog rotates cat's arm	Dog and cat sway
Intransitive		
The bear is yooking with the mouse.	Bear and mouse sway	Bear rotates mouse's arm
The dog is yooking with the cat	Dog and cat sway	Dog rotates cat's arm

Note. All items were presented twice, once with the target on the left and once on the right.

Table 4

Number of Participants with at Least Two Valid Trials by Condition

Condition	Adults	Typical Development	Fragile X Syndrome	ASD
Word Order				
Introduction	9	23	12	9
Active	10	22	12	10
Passive	10	20	10	8
Transitivity				
Introduction	10	20	12	10
Transitive	10	22	7	12
Intransitive	10	18	9	11

Note. A total of 10 adults, 30 boys with typical development, 19 boys with FXS, and 14 boys with ASD were calibrated and completed at least one valid trial in any condition (i.e., were eligible to contribute data to the analyses described).

Table 5

Participant Characteristics: Active Condition

	Typical Development (*n* = 22)			Fragile X Syndrome (*n* = 12)			ASD (*n* = 10)		
Measure	*M*	(*SD*)	Range	*M*	(*SD*)	Range	*M*	(*SD*)	Range
Age	4.50	(1.51)	2 - 7	8.92	(2.03)	6 - 12	9.48	(2.16)	6 - 12
Nonverbal IQ[a]	118.40	(12.98)	93-141	55.17	(8.84)	40 - 65	73.00	(34.07)	36-141
Nonverbal AE	5.59	(1.94)	3 - 10	4.72	(1.05)	3 - 6	6.68	(3.25)	3 - 12
PPVT-4 SS	122.79	(10.50)	103 - 133	70.27	(10.80)	52 - 87	55.43	(27.42)	20 - 86
PPVT-4 AE[b]	6.61	(2.26)	3 - 10	5.67	(1.49)	3 - 8	4.80	(2.80)	2 - 10
Autism severity[c]	-	-	-	6.17	(2.08)	3 - 10	7.00	(1.83)	4 - 9
Valid trials	4.82	(1.84)	2 - 8	4.92	(1.44)	2 - 8	5.50	(1.96)	3 - 8
Target baseline	.49	(.19)	.16 - .91	0.52	(0.10)	.34 - .65	.58	(.15)	.44 - .83
Target test	.58	(.17)	.25 - .86	0.51	(0.11)	.32 - .73	.57	(.15)	.30 - .82

Note. Nonverbal IQ = Leiter-R Brief IQ; AE = age-equivalent score; PPVT-4 = Peabody Picture Vocabulary Test, Fourth Edition; SS = standard score.

[a] Two typically developing participants were not assessed with the Leiter-R (*n* = 20). [b] Data reflect 11 boys with FXS, 7 boys with ASD, and 14 typically developing boys. Two additional boys with typical development lacked standard scores because they were younger than the norming sample. [c] ADOS symptom severity scores were only available for seven participants with ASD.

Table 6

Participant Characteristics: Passive Condition

	Typical Development (*n* = 20)			Fragile X Syndrome (*n* = 10)			ASD (*n* = 8)		
Measure	*M*	(*SD*)	Range	*M*	(*SD*)	Range	*M*	(*SD*)	Range
Age	4.57	(1.61)	2 - 7	9.40	(2.06)	6 - 12	9.03	(2.17)	6 - 12
Nonverbal IQ[a]	117.67	(13.93)	93-143	52.30	(10.70)	36 - 65	68.25	(35.18)	36-141
Nonverbal AE	5.72	(2.13)	3 - 10	4.68	(1.13)	3 - 6	5.76	(2.76)	3 - 11
PPVT-4 SS[b]	122.92	(10.91)	103 - 133	67.00	(13.07)	47 - 87	50.33	(36.15)	20 - 85
PPVT-4 AE	6.58	(2.38)	2 - 10	5.48	(1.39)	3 - 9	4.00	(2.02)	2 - 7
Autism severity[c]	-	-	-	6.50	(1.78)	3 - 10	7.50	(1.38)	6 - 9
Valid trials	5.00	(2.32)	2 - 8	4.30	(1.83)	2 - 7	4.88	(1.46)	3 - 7
Target baseline	.51	(.10)	.31 - .75	.50	(.15)	.32 - .85	.42	(.14)	.23 - .58
Target test	.57	(.18)	.14 - .81	.49	(.13)	.25 - .67	.58	(.11)	.50 - .84

Note. Nonverbal IQ = Leiter-R Brief IQ; AE = age-equivalent score; PPVT-4 = Peabody Picture Vocabulary Test, Fourth Edition; SS = standard score.

[a] Two typically developing participants were not assessed with the Leiter-R (*n* = 18). [b] Two participants with ASD and five typically developing participants were not assessed with the PPVT-4. Three boys with typical development were younger than the norming sample. [c] ADOS symptom severity scores were only available for six participants with ASD.

Table 7

Participant Characteristics: Transitive Condition

	Typical Development (*n* = 22)			Fragile X Syndrome (*n* = 7)			ASD (*n* = 12)		
Measure	*M*	(*SD*)	Range	*M*	(*SD*)	Range	*M*	(*SD*)	Range
Age	4.80	(1.55)	2 - 7	8.64	(2.10)	6 - 12	8.50	(2.35)	4 - 12
Nonverbal IQ[a]	117.80	(15.05)	93-143	54.00	(9.22)	40 - 65	71.75	(32.29)	36-141
Nonverbal AE	5.92	(1.96)	3 - 10	4.48	(.91)	3 - 6	5.91	(3.17)	2 - 12
PPVT-4 SS[b]	124.71	(9.58)	103 - 133	68.50	(7.09)	61 - 78	56.25	(27.80)	20 - 98
PPVT-4 AE	7.06	(2.38)	2 - 11	5.38	(1.52)	3 - 8	4.23	(1.90)	2 - 7
Autism severity[c]	-	-	-	6.00	(1.92)	3 - 8	7.88	(1.46)	6 - 10
Valid trials	4.95	(2.34)	2 - 8	3.00	(1.53)	2 - 6	3.92	(2.20)	2 - 8
Target baseline	.42	(.24)	0 - .98	.49	(.13)	.34 - .66	.46	(.17)	.16 - .73
Target test	.65	(.19)	.15 - 1	.52	(.20)	.22 - .77	.44	(.17)	.24 - .74

Note. Nonverbal IQ = Leiter-R Brief IQ; AE = age-equivalent score; PPVT-4 = Peabody Picture Vocabulary Test, Fourth Edition; SS = standard score.

[a] Two typically developing participants were not assessed with the Leiter-R (*n* = 20). [b] Six boys with typical development, one boy with FXS, and four boys with ASD were not assessed with the PPVT-4. Two typically developing boys were younger than the norming sample. [c] ADOS symptom severity scores were only available eight participants with ASD.

Table 8

Participant Characteristics: Intransitive Condition

	Typical Development (*n* = 18)			Fragile X Syndrome (*n* = 9)			ASD (*n* = 11)		
Measure	*M*	(*SD*)	Range	*M*	(*SD*)	Range	*M*	(*SD*)	Range
Age	4.97	(1.52)	2 - 7	8.68	(2.12)	6 - 12	8.93	(2.65)	4 - 12
Nonverbal IQ[a]	118.38	(14.09)	93 - 141	56.11	(8.71)	40 - 65	75.82	(32.02)	36-141
Nonverbal AE	6.20	(1.98)	3 - 10	4.67	(1.02)	3 - 6	6.51	(3.23)	2 - 12
PPVT-4 SS[b]	123.92	(9.91)	103 - 133	70.88	(9.92)	61 - 87	65.43	(28.49)	20 - 98
PPVT-4 AE	7.24	(1.95)	3 - 10	5.57	(1.31)	3 - 8	5.40	(2.55)	2 - 10
Autism severity[c]	-	-	-	6.33	(1.50)	3 - 8	7.14	(2.04)	4 - 10
Valid trials	5.11	(1.28)	3 - 7	3.22	(1.39)	2 - 6	4.64	(1.50)	2 - 7
Target baseline	.52	(.15)	.20 - .71	.45	(.18)	.10 - .73	.63	(.10)	.48 - .81
Target test	.57	(.18)	.19 - .91	.55	(.18)	.29 - .89	.51	(.17)	.25 - .78

Note. Nonverbal IQ = Leiter-R Brief IQ; AE = age-equivalent score; PPVT-4 = Peabody Picture Vocabulary Test, Fourth Edition; SS = standard score.

[a] Two typically developing participants were not assessed with the Leiter-R (*n* = 16).[b] Four boys with typical development, one with FXS, and four with ASD were not assessed with the PPVT-4. An additional typically developing boy was younger than the norming sample. [c]ADOS symptom severity scores were only available for seven participants with ASD.

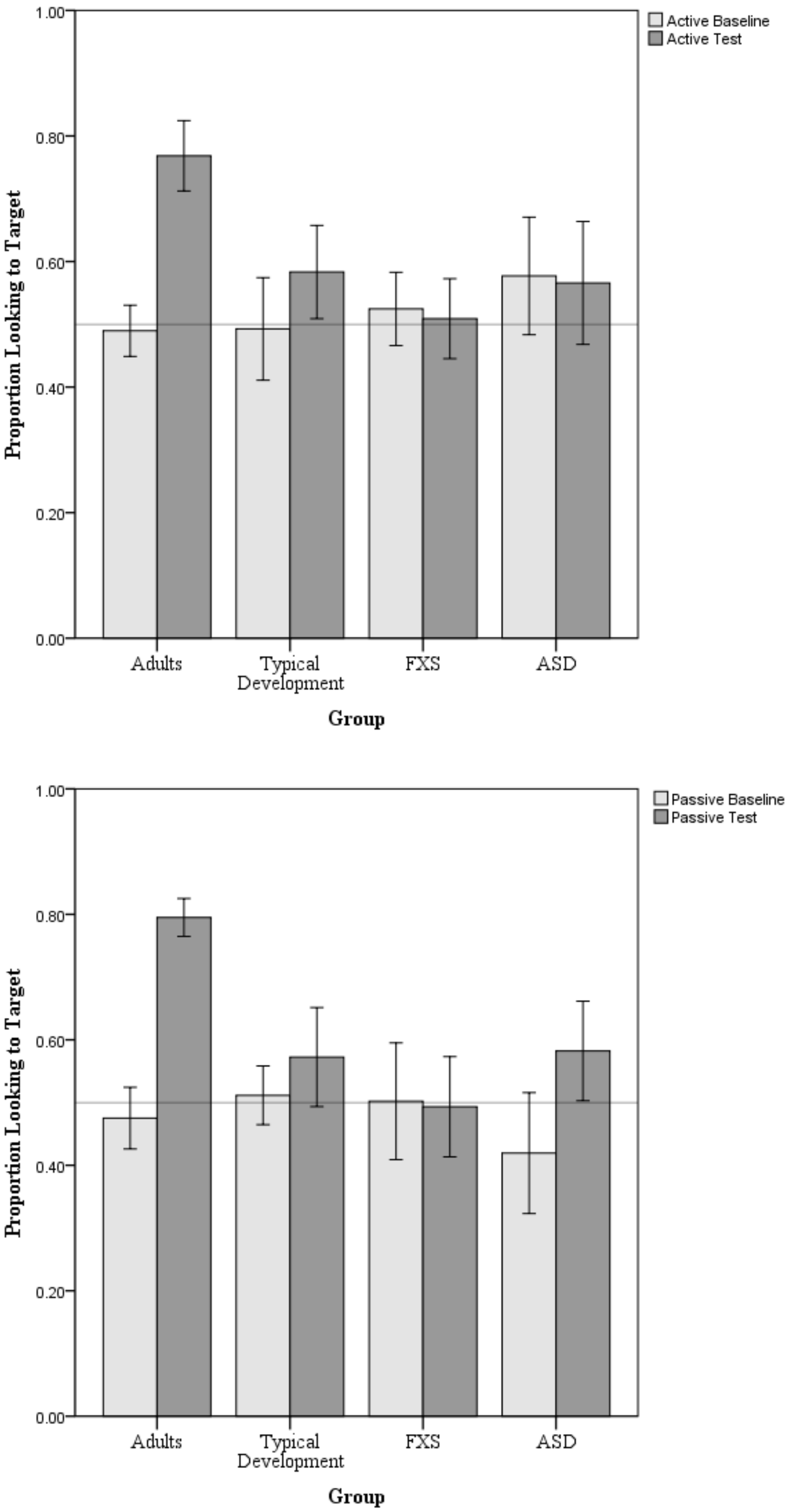

Figure 1. Task performance for word order by group, with baseline and test windows distinguished at the onset of the novel verb (i.e., 3200 ms). Error bars show +/- 2 SE.

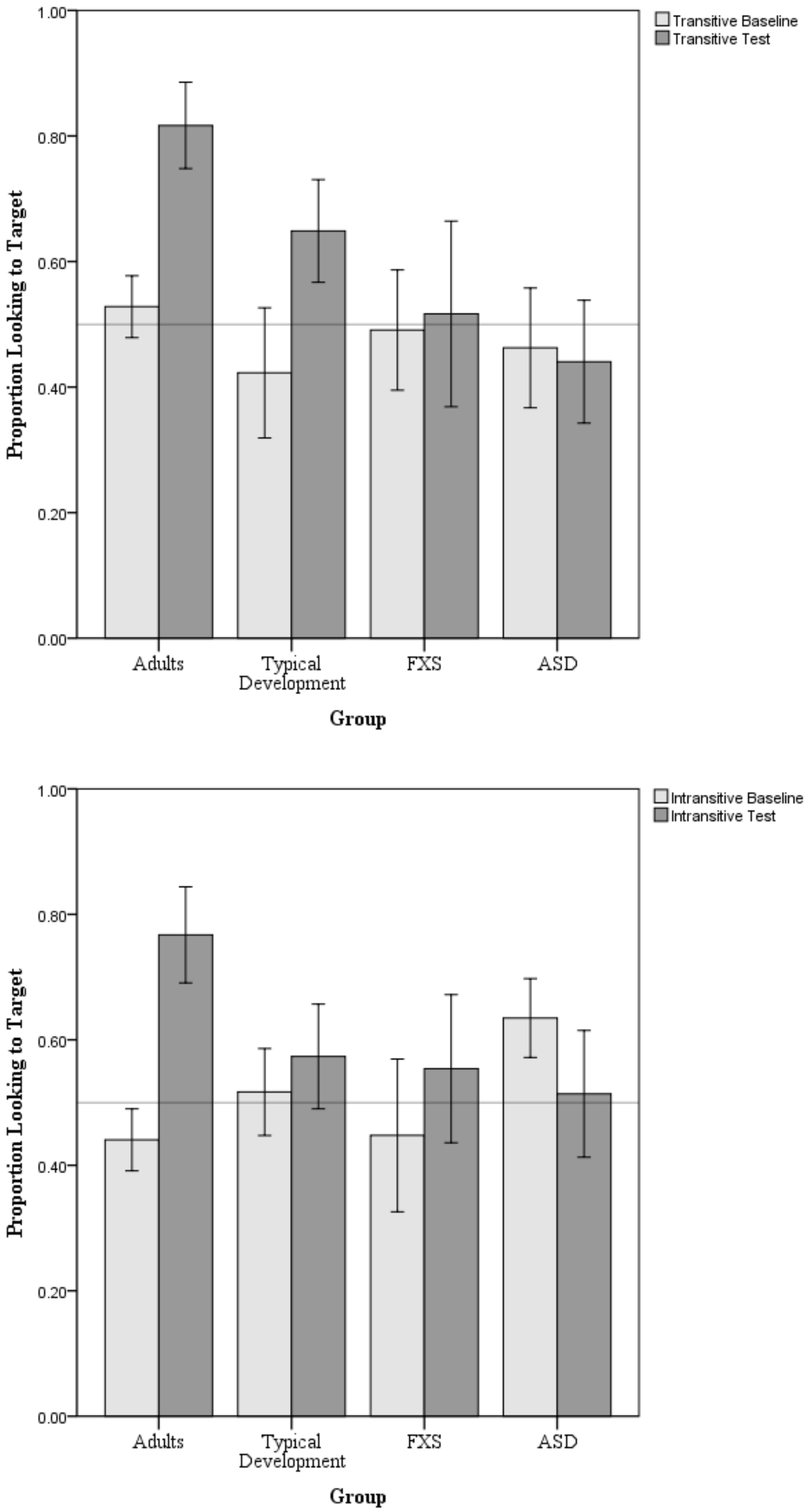

Figure 2. Task performance for transitivity by group, with baseline and test windows distinguished at the onset of the novel verb (i.e., 3200 ms). Error bars show +/- 2 SE.

Appendix 3A: Auditory Stimuli for Study 2

Word Order

The bear is pugged by the cat.

The bear is pugging the cat.

The cat is pugged by the bear.

The cat is pugging the bear.

The dog is foped by the mouse.

The dog is foping the mouse.

The mouse is foped by the dog.

The mouse is foping the dog.

Transitivity

The bear is kabing the mouse.

The bear is yooking with the mouse.

The cat is kabing the dog.

The cat is yooking with the dog.

The dog is kabing the cat.

The dog is yooking with the cat.

The mouse is kabing the bear.

The mouse is yooking with the dog.

Chapter 4

Study 3: Phonological Memory and Variability in the Fragile X Syndrome Linguistic Phenotype

Despite the common phenotypic features shared by boys with fragile X syndrome (FXS), within-syndrome variability is considerable. As described in Chapter 1, researchers have considered multiple levels of analysis in attempting to characterize the sources of individual variation in the FXS phenotype, including the expression of FMRP, level of nonverbal cognitive ability, and extent of autism symptoms. It is unclear, however, how such variables relate to variability in language ability among boys with FXS. The purpose of this study was to evaluate biological, cognitive, and behavioral predictors of performance on assessments of syntactic comprehension, extensions of syntactic knowledge, and broadly defined language ability in boys with FXS relative to boys with typical development or autism spectrum disorder (ASD).

Variability in the Fragile X Syndrome Phenotype

At the neurobiological level, it has been suggested that reduced FMRP causes processing impairments with cumulative effects across development (Cornish, Turk, et al., 2004). As such, FMRP could be considered a marker for level of impairment at a neurobiological level with important effects on language development. A relationship has been shown between FMRP and both IQ and executive function in FXS (Loesch, Huggins, Bui, Taylor, & Hagerman, 2003; Loesch, Huggins, Bui, Taylor, Pratt, et al., 2003). There is also a relationship between FMRP and symptoms of autism; however, this effect appears to be the result of mutual correlations with IQ (Loesch et al., 2007; McDuffie et al., 2010). Given the pervasive developmental effects of a reduction in FMRP, it was expected that expression of FMRP would be related to language development, perhaps even when taking aspects of nonverbal cognitive ability into account.

Beyond biological variability, there is extensive variation in cognitive and behavioral deficits and this variability could have effects on language and learning processes, such as abstracting syntactic patterns. In most boys with FXS, weaknesses in working memory, attention, and executive function are substantial (Freund & Reiss, 1991; Munir, Cornish, & Wilding, 2000a; Paul et al., 1987). For example, several aspects of memory ability were recently examined in 42 boys with FXS, 7 to 13 years of age, and NVMA-matched boys with typical development, ages 2 to 7 years (Ornstein et al., 2008). Ornstein and colleagues found that auditory and spatial short-term memory were impaired in FXS compared to the comparison group. This finding is line with research on older boys and adolescents with FXS, which has indicated that working memory impairments are especially severe and wide-spread (i.e., including auditory working memory, spatial memory, and executive function; Munir et al., 2000a). There is also recent evidence that impairments are more severe in the phonological loop than the visuo-spatial sketchpad in boys with FXS (Baker et al., 2011).

Attention and executive function are impaired beyond developmental-level expectations in boys with FXS as well. Even infants with FXS have appreciable differences in visual attention relative to typical development at 12 months of age (Roberts et al., 2011). Munir, Cornish, & Wilding (2000b) found that several aspects of attention, including selective and divided attention, were delayed in older children and adolescents with FXS relative to participants with Down syndrome or typical development matched on receptive vocabulary. The authors also found evidence of inhibition deficits relative to the comparison groups. Providing converging evidence for attention and executive function deficits, 8- to 13-year-old boys with FXS were found to show impairment in accuracy, but not speed, in a continuous performance test in both attention and inhibition relative to typically developing boys matched on mental age

(Sullivan et al., 2007). In terms of executive function, Hooper and colleagues (2008) examined inhibition, working memory, shifting, and planning ability in 7- to 13-year-old boys with FXS. They found that, relative to NVMA-matched boys with typical development, those with FXS were significantly impaired in performance on a day-night inhibition task, word span task, and planning tasks. No differences between groups were found for processing speed in rapid naming tasks. In summary, memory, attention, and executive function could be sources of variability in the FXS language phenotype by way of their effects on language processing and learning.

A striking feature of the FXS phenotype is that approximately 30 % meet criteria for autistic disorder (Bailey et al., 1998; Hagerman et al., 1986; Harris et al., 2008; Rogers et al., 2001). A comorbid autism diagnosis in FXS is associated with lower cognitive and language abilities (Bailey et al., 2001; Lewis et al., 2006; Philofsky et al., 2004). Receptive language may be one area of particular impairment for boys with FXS and autism (Philofsky et al., 2004). Increased delays in receptive vocabulary and syntax, but not expressive language, were found in adolescent males with FXS and comorbid autism relative to their cognitive ability-matched peers with FXS without comorbid autism (Lewis et al., 2006). However, some studies have failed to find significant differences in language ability, receptive or expressive, between younger males with FXS or FXS and autism (Price et al., 2007; Roberts, Price, Barnes, et al., 2007), raising the possibility of an age-related change in this aspect of the phenotype.

Clearly, much remains to be determined about how these neurobiological, cognitive, and behavioral phenotypic features relate to the foundational processes on which language development relies. Evaluating variability at different levels of analysis (i.e., biology and behavior) is theoretically relevant to understanding the prerequisites to language learning and clinically relevant to understanding the FXS phenotype. Thus, the current study was designed to assess the relationship of FMRP, specific cognitive processes, and autism symptom severity to syntactic comprehension, the extension of syntactic knowledge, and general language outcomes. Although the deficits in FMRP are specific to FXS, the rationale for investigating the impact of cognitive processes on language development is motivated by evidence from typically developing children and children with language impairment, as described below.

Impact of Cognitive Processing on Typical Language Development

Beginning in infancy, evidence suggests that specific cognitive processes support language development, including working memory (Rose et al., 2009; Rose, Feldman, & Wallace, 1992). As a model of working memory, the current research leans most heavily on the multi-component system posited by Baddeley and Hitch (1974) and refined in subsequent work (Baddeley, 2000; Baddeley, 1986), which is thought to maintain and manipulate mental representations by way of a phonological loop, visuo-spatial sketchpad, and central executive. The phonological loop in particular has been hypothesized to be relevant to language learning, with an emphasis on word learning and much less research regarding syntactic development (Baddeley, Gathercole, & Papagno, 1998; Gathercole, 2006). The impact of attention and executive function abilities on language in typically developing infants and children has not been as well described as those of memory; however, each are described in turn below.

Phonological memory. Phonological memory has been perhaps the most studied aspect of cognition in relation to language development. As suggested by Just and Carpenter (1992), the cognitive processes for language comprehension, roughly similar to Baddeley's phonological loop and central executive, are critical for syntactic comprehension and are established predictors of both accuracy and speed of comprehension of syntactic forms across development. Indeed, processing speed and expressive vocabulary at 25 months together predict expressive language at eight years, with the effect mediated by working memory (Marchman & Fernald, 2008). According to Just and Carpenter, increased working memory capacity allows for integrating multiple sources of information, such as from the domains of syntax and semantics. Phonological memory is, therefore, likely to be a critical factor in syntactic development and other aspects of language development because of the support it provides for combining knowledge from multiple linguistic domains and for processing novel input (Baddeley et al., 1998). More generally, phonological memory is a powerful predictor of multiple aspects of language development, from syntactic comprehension to word learning (Gathercole, 2006; Gathercole, Hitch, Service, & Martin, 1997).

Executive function. Research on the relationship between executive function (e.g., inhibition, shifting) and language abilities is limited. Nonetheless, executive function is one aspect of cognitive control that relates explicitly to phonological memory. Although there is much debate regarding the definition, some would suggest that the manipulation of what is held in mind constitutes working memory. In the context of the Baddeley model, the central executive interacts with distinct phonological and visual subsystems (Baddeley, 1986); however, the manipulation of representations in other theoretical frameworks is not distinguished in modality-defined components (Just & Carpenter, 1992). Acknowledging different theoretical frameworks, the terms phonological memory, visual memory, and executive function are used in the current work to denote distinct, yet related, cognitive processes.

Attention. In addition to working memory, attention is also a potential predictor of language learning abilities. It has been proposed that reduced or limited processing abilities, attention, or short-term memory capacity could actually enhance language learning by drawing attention to relevant units (i.e., the Less is More hypothesis; Newport, 1990). Contrary to this viewpoint, it has since been shown that adequate working memory and attention are crucial to the statistical learning involved in word segmentation and syntactic processing, even in adults (Ludden & Gupta, 2000). Although statistical regularities can be extracted from the input without explicit instructions and without feedback, distractions from competing stimuli are likely to affect the extent to which statistical learning mechanisms are effective (Fiser & Aslin, 2001; Toro, Sinnett, & Soto-Faraco, 2005). Moreover, Pacton and Perruchet (2008) have shown in adults that attention to two events in the form of joint processing may be necessary and sufficient to learn the dependency of those events whether the statistics are computed over adjacent or nonadjacent stimuli. Thus, attention deficits could have pervasive effects on language learning processes in children with neurodevelopmental disorders.

Social cues to language. The language impairments of children with ASD provide evidence that social impairments, such as poor joint attention, along with the cognitive phenotype associated with ASD, can impact language development in multiple domains, including vocabulary and syntax (Eigsti et al., 2007; McDuffie, Yoder, & Stone, 2006). For young children with ASD, aspects of social reciprocity, such as engaging in social games and routines, may account for more variability in language ability than other aspects of the phenotype (e.g., limited gesture use; Bopp & Mirenda, 2011). Despite the evidence for the role of cognitive processing per se, sensitivity to social cues and willingness to respond to them might equally constrain language learning for children with certain neurodevelopmental disorders.

In summary, limited memory capacity, abnormal attention regulation, poor executive function, and impaired social reciprocity could be expected to influence language learning for individuals with FXS and other neurodevelopmental disorders.

Impact of Cognitive Processing on Language Impairment

Phonological memory. Research on children with other neurodevelopmental disorders has addressed the role of several key cognitive processes in supporting language development, in general, and syntactic comprehension, in particular. Phonological memory is the cognitive ability most often related to language development, with evidence arising from many populations.

Even in children without intellectual disability, phonological memory may play an important role in language development, especially in the domain of receptive syntax. Leonard et al. (2007) found that several specific aspects of cognitive processing, including auditory working memory, were related to language outcomes in children with SLI. Montgomery and Evans (2009) found that nonword repetition, a marker of phonological memory, and comprehension of simple transitive sentences were correlated after controlling for age in 6- to 12-year-old children with SLI. Thus, syntactic comprehension might be closely related to the ability to meet phonological memory demands for children with language impairments because they have not reached the level of mastery of their typically developing peers.

The relationship between language development and phonological memory has also been tested in children with genetic conditions associated with intellectual disability, such as Williams syndrome. Phonological memory assessed with a nonword repetition task correlates with blocks passed on the TROG-2 in children and adolescents with Williams syndrome between 4 and 16 years of age (Robinson et al., 2003). In adolescents with Down syndrome, Miolo, Chapman, and Sindberg (2005) found comprehension of reversible active and passive transitive sentences to be impaired in a reenactment task compared to younger typically developing children matched on TACL-3 syntactic abilities. Those with Down syndrome were less likely to correctly assign semantic roles (i.e., agent vs. patient). Importantly, the choice of semantic roles was correlated with nonword repetition for participants with Down syndrome, highlighting the role of phonological memory in their syntactic comprehension.

If integrating syntactic, semantic, and contextual information hinges on auditory working memory (Just & Carpenter, 1992), interpreting the meaning of a novel word with syntactic cues may depend on sufficient memory as well. Difficulty using syntax to infer meanings for novel verbs in school-age children with SLI could relate to auditory working memory deficits (O'Hara & Johnston, 1997; Oetting, 1999). Leonard et al. (2007) suggested that auditory working memory limitations might relate to the model proposed by Just and Carpenter (1992) by requiring more exposures to words or forms before being fully acquired or by leading to wrong word form choices when working memory is taxed by the combination of syntactic and non-syntactic information. The current study tested the hypothesis that processing limitations impair the use of syntactic information to make inferences about novel verbs.

For children with intellectual disability, Robinson et al. (2003) suggest that working memory may play an even more important role than for typically developing children in building connections between form and meaning for syntactic development because syntax acquisition involves auditory processing and storage of the language input in addition to shifting attention to, and then combining, other sources of information to get at meaning. In adolescents with Down syndrome, for instance, both syntactic comprehension and auditory working memory are predictors of lexical learning (McDuffie et al., 2007). Pierpont et al. (2011) found that phonological memory and verbal working memory were correlated with syntactic comprehension, even after controlling for nonverbal cognition and autism severity, in adolescents with FXS; however, it is unclear which aspects of language processing are most problematic for boys with FXS and how phonological memory deficits impact those abilities.

The current research tested the hypothesis that variability in both syntactic comprehension and extension of syntactic knowledge can be explained in part by phonological memory.

In summary, phonological memory is a well-established predictor of comprehension in typical development and in those with language impairments, such as SLI and Down syndrome (Just & Carpenter, 1992; Leonard et al., 2007; Miolo et al., 2005). Indeed, memory and even executive functioning may play a larger role for children than adults because language processing is less automatic for those who are still acquiring syntactic abilities (Gathercole & Baddeley, 1993). These cognitive abilities may be an even more important factor for children with syntactic deficits who have more immature linguistic knowledge and are also likely to have memory deficits. For boys with FXS, phonological memory is likely an important cognitive resource for syntactic development and for integrating syntactic and semantic information for further learning. Because phonological memory is impaired in boys with FXS beyond NVMA-expectations (Hooper et al., 2008; Ornstein et al., 2008), its impact could extend beyond comprehension to the interpretation of novel verbs using syntactic cues. To test the specificity of the role of phonological memory, visual memory was also assessed in the present study.

Attention and executive function. A few studies have documented the relationships between attention and executive function and language in children with SLI (e.g., Im-Bolter, Johnson, & Pascual-Leone, 2006). Executive function deficits have also been identified in children with autism (e.g., Ozonoff, Pennington, & Rogers, 1991). As described in Chapter 1, it has been hypothesized that some of the phenotypic language features associated with FXS result from attention and executive function deficits, including tangential and repetitive use of language (Cornish, Sudhalter, et al., 2004; Sudhalter & Belser, 2001). This hypothesis has not been tested with respect to formal aspects of language ability.

Autism. As previously described, the presence of autism symptoms, either alone or in conjunction with an identified genetic cause, can have implications for language development.

Research Questions and Hypotheses

The purpose of this study was to examine the effects of biological, cognitive, and behavioral predictors of language ability in boys with FXS. Although not comprehensive, this framework addressed several important components of language learning and may distinguish between language delays caused by cognitive processing limitations and other sources of difficulty. Three analyses were conducted to determine the role of cognitive processing in syntactic comprehension, extensions of syntactic knowledge, and standardized test performance.

Hypothesis 1. Based on evidence for the role of phonological memory in syntactic processing, it was hypothesized that phonological memory would be significantly related to extending syntactic knowledge to sentences with novel verbs (Study 2), but that this relationship would be mediated by syntactic comprehension (Study 1). See Figure 1 for a schematic.

Hypothesis 2. The second hypothesis was based on evidence of impairment in memory, attention, and executive function in boys with FXS and the effects these abilities can have on standardized language assessment performance. It was expected that these cognitive abilities, along with the "pure" language abilities assessed in Studies 1 and 2, would account for unique variance in standardized language test performance. See Figure 2.

Exploratory analysis. For boys with FXS, I also explored biological, cognitive, and behavioral predictors of performance in Study 1, Study 2, and standardized language assessments. It was generally expected that expression of FMRP, nonverbal cognitive ability, selected measures of cognitive processing, and autism symptom severity would explain variation among boys with FXS in language ability. See Figure 3.

Method

Participants

Participants with FXS (*n* = 29), ASD (*n* = 17), or typical development (*n* = 34) were drawn from the longitudinal project on early word learning previously described and completed Study 1 and/or Study 2. The participant groups were generally similar on nonverbal cognitive ability, based on the Leiter-R Brief IQ subtests (Roid & Miller, 1997), as seen in Table 1.

Measures

Autism symptom severity. Boys with FXS or ASD were assessed in the context of the larger project by a research-reliable examiner using the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999). An autism severity score was assigned based on the revised algorithm and calibrated metric (Gotham et al., 2009; Gotham et al., 2007). Although some symptoms of ASD may abate with age in children with FXS (McDuffie et al., 2010), this issue has not been examined with prospective longitudinal studies. As such, the appropriate span of time within which autism symptoms remain stable has not been standardized in the field and thus, an autism evaluation at the initial visit (usually 18 months prior to the experimental tasks) was considered valid for the present study.

Language processing. Separate within-group z-scores were created based on (1) accuracy of noun comprehension in Study 1, (2) accuracy of reversible active sentence comprehension in Study 1, (3) accuracy of reversible passive sentence comprehension in Study 1 and (4) extension of word order cues in active sentences in Study 2 and (5) extension of cues in passive sentences in Study 2. These scores were not combined because correlations were weaker for boys with FXS and ASD than for boys with typical development.

Standardized assessments. Four standardized measures were used to assess receptive and expressive vocabulary and syntax. Receptive and expressive vocabulary were assessed with the Peabody Picture Vocabulary Test, 4th edition (PPVT-4; Dunn & Dunn, 2007) and the Expressive Vocabulary Test, 2nd edition (EVT-2; Williams, 2007), respectively. Receptive and expressive syntax were assessed with the Test for the Reception of Grammar, 2nd edition (TROG-2; Bishop, 2003) and the Syntax Construction subtest of the Comprehensive Assessment of Spoken Language (CASL; Carrow-Woolfolk, 1999a), respectively. Within-group z-scores were created from growth scores for the vocabulary measures, items passed on the TROG-2, and CASL raw scores. Each participant's four z-scores were then averaged to create a single language composite variable as an index of language outcome. Due to the inappropriateness of the measures for the participants' developmental level, this composite omitted the TROG-2 and CASL for two participants with ASD and the CASL for one participant with FXS.

Cognitive processing. Separate composite scores for phonological memory and visual working memory were created to assess their impact on syntactic processing and language outcomes, as described below. Attention and executive function were also assessed.

Memory and attention. The Working Memory Test Battery for Children (WMTB; Pickering & Gathercole, 2001) Digit Recall and Word List Recall subtests were administered to assess auditory memory (i.e., phonological loop), and Block Recall was used to assess visual memory (i.e., visuo-spatial sketchpad). In Digit Recall, the child recalls sequences of numbers of increasing length, beginning with a single digit. Word List Recall follows the same procedure with sequences of English words. Digit Recall and Word List Recall were selected instead of Nonword List Recall because they had the highest bivariate correlation in the norming sample ($r = .52$; Pickering & Gathercole, 2001, p. 21). Block Recall involves copying a sequence of block tapping by the examiner. Number of trials correct provided the variable of interest for each subtest. Normative data are available for 5- to 15-year-olds. Subtest test-retest reliability ranges from .43 to .82. Total administration was 15 minutes.

The Leiter-R Attention and Memory Battery (Roid & Miller, 1997) is comprised of standardized subtests for ages 2 through 20 requiring minimal verbal instructions and exclusively nonverbal responses. The Associated Pairs and Forward Memory subtests were administered to measure visual working memory. The child is asked to recall picture matches and to point to pictures in a sequence in these subtests, respectively. Subtest growth scores were the variables of interest. The Sustained Attention subtest was the measure of attention, and raw scores were used as the basis of z-scores. The child marks target objects in an array in a timed subtest. For these subtests, internal consistency (alpha) ranges from .61 to .92 and test-retest reliability ranges from .60 to .85. Total administration was 20 minutes.

Executive function. The Dimensional Change Card Sort (DCCS) is a measure of executive function that is sensitive to developmental improvement in flexible rule use in typically developing children from three to five years of age (Zelazo, 2006). The child first sorts colored shape cards by one dimension (i.e., color pre-switch) and then by the other dimension (i.e., shape post-switch). Those who passed the post-switch phase (at least 5 correct out of 6) went on to the complex phase, in which the dimensional switches are contingent on the presence or absence of a black border. Performance is scored dichotomously (either passing or failing at least 5 of 6 trials for pre- and post-switch; 9 out of 12 for complex); thus, a score of 0 was assigned for failing the pre-switch phase, 1 for passing the pre-switch but failing post-switch, 2 for passing pre- and post-switch, and 3 for passing the complex phase (Zelazo, 2006). Administration was less than 10 minutes.

The Behavior Rating Inventory of Executive Function (BRIEF; ages 5 - 18; Gioia, Isquith, Guy, & Kentworthy, 2000) and the Behavior Rating Inventory of Executive Function – Preschool (BRIEF-P; ages 2;0-5;11; Gioia, Espy, & Isquith, 2003) were administered. These are parent questionnaires that assess child executive functioning over a period of 6 months. Item scales relate to inhibition (e.g., "is impulsive"), shifting (e.g., "has trouble changing activities), working memory (e.g., "has a short attention span"), etc. The summary score, Global Executive Composite, was the dependent variable of interest. Alphas for internal consistency range .80 to .97 (BRIEF) and .80 to .97 (BRIEF-P). Test-retest correlations average .79 in clinical (BRIEF) and .86 in normative samples (BRIEF-P). Parents of boys 4;11 or younger received the BRIEF-P. The 86 BRIEF and 63 BRIEF-P items were completed in 15 minutes.

Composite scores. Four scores were created, each reflecting one cognitive processing domain of interest (i.e., phonological memory, visual working memory, attention, and executive function). Correlations among measures were verified before combining. Composites were formed by averaging participant's z-scores: (1) Digit Recall and Word List Recall for phonological memory (for 1 participant who was missing the Word List Recall subtest, only Digit Recall was included), (2) Associated Pairs, Forward Memory, and Block Recall for visual memory (based only on Block Recall for 5 boys with typical development, 6 boys with ASD, and 5 boys with FXS; based only on Associated Pairs for 1 boy with FXS; based only on Block span and Associated Pairs for 2 boys with typical development and 1 boy with ASD), (3) Sustained Attention for attention, and (4) DCCS for executive function. The original intention was to combine DCCS and BRIEF or BRIEF-P Global Executive Composite, reverse scored, for executive function; however, the scores were only significantly correlated for boys with ASD.

Finally, an overall cognitive processing composite was created by averaging phonological memory, visual memory, sustained attention, and DCCS z-scores.

Expression of FMRP. FMRP expression in peripheral blood lymphocytes was estimated with a state-of-the-art method for quantifying the amount of FMRP expressed in blood using a sandwich enzyme-linked immunosorbent assay (ELISA; Iwahashi et al., 2009).

Procedures

The PPVT-4 was administered before the EVT-2, followed by the TROG-2 and CASL. The WMTB was administered prior to the DCCS and the Attention and Memory subtests of the Leiter-R. The BRIEF or BRIEF-P was completed by the parent during or prior to the visit.

Analysis Strategy

Participants who completed the Leiter-R Brief IQ tests are described in Table 1. Further analyses included only the participants with each of the independent and dependent measures of interest, as seen in Tables 2 - 5. The focus of the current study was on boys with FXS, although analyses were repeated for boys with ASD or typical development when appropriate.

Results

First, bivariate correlations between phonological memory, cognitive processing, and language processing and language outcomes were estimated for each participant group. For the 14 boys with FXS, phonological memory just failed to reach significance as a predictor of noun comprehension, $r = .45$, $p = .055$, one-tailed. For boys with ASD, phonological memory was correlated with noun comprehension, active sentence comprehension, and passive sentence comprehension from Study 1, *p*s < .025. For typically developing boys, phonological memory was correlated with active and passive sentence comprehension, *p*s < .005.

Table 2 shows the partial correlations (controlling for Leiter-R Growth scores) between phonological memory and comprehension of nouns, active sentences, and passive sentences in Study 1. For each group, phonological memory accounted for variability in language outcome z-scores based on standardized language tests. For typically developing boys, phonological memory was also significantly related to passive sentence comprehension accuracy. Patterns of partial correlations with visual memory were less consistent; visual memory correlated with active comprehension for boys with ASD, $r = .83$, $p = .003$, one-tailed, and with language outcome composite scores for boys with typical development, $r = .38$, $p = .047$.

The Role of Phonological Memory in Language Processing

Hypothesis 1 was that syntactic comprehension would mediate the relationship between phonological memory and the extension of syntactic knowledge for boys with FXS. In this mediation analysis, the independent variable of interest was the phonological memory z-score composite. The contribution of phonological memory to active and passive syntactic comprehension in Study 1 (i.e., the putative mediators) was evaluated in a regression model (the alpha path). The contribution of syntactic comprehension to extending syntactic knowledge in Study 2 was tested, partialing phonological memory (the beta path). A significant beta path coefficient indicates that syntactic comprehension mediates the relationship between phonological memory and extending syntactic knowledge (Cohen & Cohen, 1983; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002). It was not expected that visual memory would be related to syntactic processing to the same degree.

After controlling for nonverbal cognition, phonological memory did not predict active or passive sentence comprehension for boys with FXS; active and passive sentence comprehension did not predict extension of syntactic knowledge. Results are shown in Table 3.

Analyses were repeated for the remaining two groups, shown in Tables 4 and 5. For typically developing boys, phonological memory significantly predicted active sentence comprehension and active sentence comprehension predicted active syntactic extension, partialing phonological memory. For boys with ASD, phonological memory predicted active and passive sentence comprehension. Controlling for nonverbal cognitive ability, passive sentence comprehension predicted extending syntactic knowledge about passives, suggesting that comprehension of passive sentences mediates the relationship between phonological memory and use of syntactic knowledge about complex sentences for boys with ASD.

Standardized Tests Assess Language and General Cognitive Processing

Hypothesis 2 was that cognitive processing abilities, along with language processing, would account for variability in performance on standardized language measures. This was tested within each group using separate regressions. Language processing z-scores based on accuracy from active and sentence passive comprehension or extension from Study 1 and Study 2, respectively, and the cognitive processing z-score composite, were entered as predictors of the language outcome z-score, controlling for nonverbal cognition. In general, language outcome composite scores were significantly predicted by the combination of language processing, the cognitive processing composite, and Leiter-R growth scores, with cognitive processing ability being the most robust independent predictor. Table 6 shows results for boys with FXS. Results were similar for boys with typical development; results for boys with ASD were similar for active and passive extension, but not comprehension, for which results were not significant. Results were also similar when utilizing noun comprehension from Study 1 as a predictor.

Biological, Behavioral, and Cognitive Sources of Variability in FXS

For boys with FXS, nonverbal cognitive ability, cognitive processing, autism symptom severity, and FMRP were considered as predictors of language processing and outcomes. Sixteen boys with FXS were included in the regression predicting language outcomes (i.e., the z-score language composite based on standardized tests). See Table 7. All predictors were significant and positive with the exception of FMRP, which was negatively related to language outcomes. Removing an outlier eliminated the unexpected FMRP finding and the other results were unchanged.

Repeating this analysis for accuracy of language processing from Study 1 yielded non-significant results for active and passive accuracy. Only for noun accuracy was the regression significant for the nine participants with FXS, $F(4, 8) = 24.16, p = .005$, with Leiter-R growth scores positively predicting performance, $b = .023, p = .015$, and autism severity symptoms unexpectedly positively predicting performance, $b = .089, p = .012$. The analysis for Study 2 was omitted due to a sample size of five participants.

Discussion

The goal of this study was to examine predictors from multiple levels of analysis with respect to syntactic comprehension, extension of syntactic knowledge, and language outcomes in boys with FXS. Evaluating individual differences in cognition is theoretically relevant to understanding the prerequisite processes that support language learning and clinically relevant to understanding variability in FXS, thereby allowing predictions about outcomes to be made. In particular, it was hypothesized the well-documented link between phonological memory and word learning would extend to other aspects of language processing, including comprehension of active and passive sentences and the extension of that syntactic knowledge for boys with FXS.

Phonological memory, assessed with digit and word recall, was correlated with performance on standardized language tests for boys with FXS, even after controlling for nonverbal cognition. It was also expected that phonological memory would account for variance among individuals with FXS in performance in syntactic comprehension. Furthermore, syntactic comprehension was expected to mediate the relationship between phonological memory and syntactic bootstrapping. Although several aspects of language processing ability were related to phonological memory across groups, many of these effects no longer held after accounting for nonverbal cognitive ability. An exception was accuracy in comprehension of passive sentences for typically developing children, for whom a correlation of medium strength with phonological memory remained after partialing nonverbal cognition. This finding underscores the role of memory capacity for emerging complex language (Just & Carpenter, 1992).

For typically developing boys, the mediation relationship among phonological memory, syntactic comprehension, and extension of syntactic knowledge was found. These effects held for active, but not passive, sentences. Given that passive sentences are understood and produced later in development, it is not unexpected that the most robust effects would be found for active sentences. The typically developing boys ranged in age from two to seven years, meaning that all should have been acquiring or have mastered competence with active SVO sentence structure, whereas passive sentences were perhaps outside the developmental abilities of some boys.

In contrast, for boys with ASD, the significant mediation relationship was for passive sentences, and only when controlling for nonverbal cognitive ability. Despite language delays, boys with ASD had nonverbal cognitive abilities on par with the typically developing children and advanced age, perhaps leading one to suspect that the comprehension of passive sentences and the ability to interpret novel verbs using those complex sentences might be emerging in boys with ASD with stronger cognitive and phonological memory abilities. That syntactic comprehension of particular grammatical constructions would relate to the extension of that syntactic knowledge to novel words is in line with a recent study on younger boys with ASD. Naigles and colleagues (2011) found that SVO word order processing of familiar verbs predicted syntactic bootstrapping for transitive verbs eight months later in 3-year-olds with autism.

It is surprising that mediation effects were detected for typically developing boys and boys with ASD, and have been found for much younger children with ASD, and yet not boys with FXS in the current sample. It is possible that the wide variation in engagement with the language processing tasks contributed to the null results for the participants with FXS.

Cognitive Demands of Standardized Tests

Above and beyond nonverbal cognition, memory, attention, and executive function were hypothesized, along with performance on Study 1 and Study 2 tasks, to independently account for variability in standardized language test outcome scores. In general, the language processing variables were not significant predictors of language outcome scores, with or without controlling for cognitive processing abilities. For boys with FXS, the relationship between cognitive processing and language outcomes was significant, even when controlling for general nonverbal cognition. Passive sentence comprehension from Study 1 was the only aspect of language processing to predict standardized language test scores. These results suggest that cognitive processing factors unduly influence standardized language test performance relative to language. The utility of these standardized assessments for measuring language ability in children with FXS should be called into question. The role of phonological memory, visual memory, attention, and executive function for language development in boys with FXS is worth further examination.

Variability in the FXS Linguistic Phenotypes

For the exploratory regression analyses, it was hypothesized that cognitive processing composite scores (i.e., phonological memory, visual memory, attention, executive function) would account for variance among individuals with FXS, as would expression of FMRP and autism severity. All predictors were significant.

As expected, nonverbal cognitive ability was significantly related to language outcome performance. Also hypothesized was the positive relationship between cognitive processing and standardized language test performance. It is not surprising that language abilities are related to general nonverbal cognition, in line with interactionist, emergentist, and neuroconstructivist perspectives. Furthermore, standardized language test performance is related to the cognitive processing abilities that might be drawn into use by the task demands of the assessments. Alternate methods for measuring language competence in children with FXS should also be considered. For example, interactive tasks that allow an examiner to actively engage a child and maintain his or her attention throughout a given trial might highlight language learning strengths of children with FXS (McDuffie et al., under review).

The unexpected negative relationship between language outcomes and FMRP was reduced by removing an outlier with particularly high FMRP expression; however, even without this outlier, the positive relationship between autism severity and language outcomes remained. Unexpectedly, higher autism severity was associated with higher language outcomes, although the relationship was only significant when FMRP was included in the model. It is possible that more verbal boys with FXS were more likely to reveal qualitative impairments in interaction.

Strengths and Limitations

Historically, eye gaze studies on language comprehension or language learning have not been examined the relationship between language processing performance and other directly measured aspects of behavior. In the current study, boys with FXS, ASD, and typical development were assessed in terms of several aspects of cognitive processing.

A major limitation of this work was the failure to test auditory working memory, which have been posited as an important constraint on language given the need to not only hold in mind linguistic information, but also manipulate it, for successful comprehension or learning (Just & Carpenter, 1992). Many working memory tasks would have been outside of the ability levels of participants in the current study, although performance on such tasks has been shown to be important predictors of change in verbally fluent adolescents with FXS (Pierpont et al., 2011). Future research might more successfully identify independent effects of cognitive processing by examining phonological memory in relation to noun comprehension in younger boys with FXS and auditory working memory in relation to syntactic comprehension in older boys with FXS.

One goal of the current study was to demonstrate the specificity of the relationship between phonological memory and language processing. However, the eye gaze tasks themselves demanded visual processing and, perhaps, the ability to keep two images in mind while shifting between them. Although not the focus of the primary hypotheses, future work would benefit from more sensitive measures of visual memory and visual attention.

Conclusions

Relationships among phonological memory and other aspects of cognitive processing were identified for boys with typical development, FXS, and ASD with respect to language outcomes and some aspects of language processing. In many cases, effects of phonological memory could be accounted for by general nonverbal cognitive ability; however, exceptions to this suggest that phonological memory might be an important mechanism for language learning for children with neurodevelopmental disorders.

Table 1

Participant Characteristics and Cognitive Processing Performance

	Typical Development				Fragile X Syndrome				ASD			
Measure	*n*	*M*	(*SD*)	Range	*n*	*M*	(*SD*)	Range	*n*	*M*	(*SD*)	Range
Age	34	4.51	(1.56)	2 - 7	29	9.24	(2.03)	5 - 12	17	8.46	(2.22)	4 - 12
Nonverbal IQ	34	116.35	(14.08)	87 - 143	29	50.69	(10.68)	36 - 71	17	70.12	(29.72)	36 - 141
Nonverbal AE	34	5.45	(1.82)	3 - 10	29	4.39	(.89)	3 - 6	17	5.81	(2.89)	2 - 12
Phonological mem.												
Digit recall*	27	21.48	(5.98)	6 - 30	25	11.68	(4.90)	4 - 22	13	17.62	(11.03)	0 - 35
Word recall*	26	15.88	(3.55)	11 - 24	25	9.20	(4.00)	1 - 21	13	11.69	(7.39)	0 - 21
Visual memory												
Block recall*	24	17.71	(4.56)	7 - 26	19	9.26	(5.35)	1 - 19	11	18.27	(8.77)	6 - 30
Associated pairs	19	17.42	(8.48)	5 - 38	15	13.13	(8.31)	2 - 27	5	16.40	(8.76)	5 - 27
Forward mem.*	17	12.65	(4.30)	4 - 18	14	6.21	(3.33)	2 - 12	4	15.00	(8.52)	3 - 22
Attention sustained	18	47.44	(9.62)	26 - 61	12	44.83	(19.12)	3 - 69	3	61.67	(10.12)	50 - 68
Executive function												
DCCS*	21	2.24	(.44)	2 - 3	24	1.04	(.69)	0 - 3	9	1.33	(1.23)	0 - 3
BRIEF/-P GEC*	24	44.92	(8.06)	33 - 68	24	66.75	(8.87)	48 - 80	13	63.62	(8.56)	49 - 76
Autism severity[a]	-	-	-	-	27	6.26	(1.66)	3 - 10	10	7.40	(1.78)	4 - 10
FMRP expression	-	-	-	-	17	3.66	(6.51)	0 - 25	-	-	-	-

Note. Raw scores presented unless otherwise noted.

[a] ADOS symptom severity from initial assessment. * $p < .05$ for one-way ANOVA testing group differences.

Table 2

Partial Correlations of Phonological Memory Composite with Study 1 Language Comprehension and Language Outcome Composite

Language Variable	Typical Development			Fragile X Syndrome			ASD		
	df	*r*	*p*	*df*	*r*	*p*	*df*	*r*	*p*
Study 1 accuracy									
Noun	19	-.06	.403	11	-.05	.434	8	.534	.056
Active	19	.11	.313	12	.07	.411	8	.457	.092
Passive	19	.54	.005*	8	.18	.311	7	.537	.068
Outcome composite	19	.47	.016*	18	.50	.012*	5	.76	.024*

Note. Partial correlations control for nonverbal cognitive ability using Leiter-R growth scores.

**p* < .05, one-tailed.

Table 3

Hierarchical Regression Analyses for Syntactic Comprehension Mediating Memory and Extension of Syntactic Knowledge for Boys with FXS

	Active				Passive			
Predictor	*n*	R^2	*b*	*p*	*n*	R^2	*b*	*p*
Step 1 (alpha)								
Phonological memory	15	.04	.21	.471	11	.01	.06	.873
Visual memory	12	.16	.50	.200	8	.16	-.39	.334
Step 2 (beta)								
Phonological memory	8	.32	.36	.277	5	.91	1.63	.048*
Comprehension			.37	.304			.17	.625
Visual memory	7	.51	.40	.420	4	.98	-.68	.094*
Comprehension			.39	.389			.26	.263
Step 3 (controlling Leiter-R)								
Phonological memory	8	.39	.25	.524	5	.92	1.60	.220
Comprehension			.33	.388			.202	.754
Nonverbal cognition			.025	.540			.01	.925
Visual memory	7	.54	.08	.930	4	1.00	-.58	-
Comprehension			.35	.503			.24	-
Nonverbal cognition			.05	.665			-.02	-

* $p < .05$. † $p < .05$, one-tailed.

Table 4

Hierarchical Regression Analyses for Syntactic Comprehension Mediating Memory and Extension of Syntactic Knowledge for Typically Developing Boys

	Active				Passive			
Predictor	*n*	R^2	*b*	*p*	*n*	R^2	*b*	*p*
Step 1 (alpha)								
Phonological memory	22	.20	.42	.035*	22	.48	.54	< .001*
Visual memory	19	.07	.27	.282	19	.22	.41	.043*
Step 2 (beta)								
Phonological memory	15	.42	.01	.968	13	.33	.20	.563
Comprehension			.64	.054†			.58	.252
Visual memory	13	.44	-.31	.330	12	.21	-.08	.783
Comprehension			.65	.020*			.51	.164
Step 3 (controlling Leiter-R)								
Phonological memory	15	.42	.02	.954	13	.49	-.22	.594
Comprehension			.64	.072†			.56	.235
Nonverbal cognition			-.01	.960			.04	.124
Visual memory	13	.49	.01	.983	12	.52	-.74	.080†
Comprehension			.71	.018*			.39	.199
Nonverbal cognition			-.03	.379			.06	.052†

* $p < .05$. † $p < .05$, one-tailed.

Table 5

Hierarchical Regression Analyses for Syntactic Comprehension Mediating Memory and Extension of Syntactic Knowledge for Boys with ASD

	Active				Passive			
Predictor	*n*	R^2	*b*	*p*	*n*	R^2	*b*	*p*
Step 1 (alpha)								
Phonological memory	11	.38	.77	.042*	10	.62	1.06	.007*
Visual memory	10	.54	.87	.016*	10	.44	.61	.037*
Step 2 (beta)								
Phonological memory	8	.15	-.33	.602	5	.86	-.08	.919
Comprehension			.48	.397			1.22	.188
Visual memory	7	.33	-.81	.298	5	.89	.24	.501
Comprehension			.78	.244			1.01	.097
Step 3 (controlling Leiter-R)								
Phonological memory	8	.15	-.43	.654	5	.99	-.62	.082†
Comprehension			.48	.454			1.27	.030*
Nonverbal cognition			.01	.875			.03	.044*
Visual memory	7	.61	-2.42	.145	5	.99	-.54	.083†
Comprehension			1.08	.140			.95	.026*
Nonverbal cognition			.08	.234			.05	.051†

* $p < .05$. † $p < .05$, one-tailed.

Table 6

Hierarchical Regression Analyses for Testing the Contributions of Language and Cognitive Processing to Language Outcomes in Boys with Fragile X Syndrome

	Language Processing Predictor of Language Outcomes											
	Active Comprehension			Passive Comprehension			Active Extension			Passive Extension		
Predictor	ΔR^2	*b*	*p*	ΔR^2	*b*	*p*	ΔR^2	*b*	*p*	ΔR^2	*b*	*p*
Step 1	.16			.01			.20			.07		
Language processing		.35	.162		-.03	.936		.50	.268		.19	.582
Step 2	.68			.95			.71			.81		
Language processing		-.01	.969		.25	.039		-.34	.163		.08	.572
Cognitive processing		1.10^{*}	$< .001$		1.33^{*}	$< .001$		1.36^{*}	.002		$.91^{*}$	.008
Step 3	.02			.03			.03			.05		
Language processing		.01	.950		$.33^{*}$	.004		-.37	.127		.08	.576
Cognitive processing		$.88^{*}$	.006		$.99^{*}$	$< .001$		1.17^{*}	.009		$.66^{\dagger}$	.078
Leiter-R growth score		.02	.284		.03	.022		.027	.232		.02	.279
Total R^2	.86			.98			.94			.92		
n	14			10			8			7		

Note. Comprehension language processing scores (active and passive comprehension) are accuracy z-scores from Study 1. Extension language processing scores (active and passive comprehension) are accuracy z-scores from Study 2.

* $p < .05$. † $p < .05$, one-tailed.

Table 7

Hierarchical Regression Predicting Language Outcome Composite for Boys with Fragile X Syndrome (n = 16)

	Language composite z-score			
Predictor	*F*	R^2	*b*	*t*
Step 1	25.06*	.64		
Leiter-R growth score			.07	5.01*
Step 2	25.19*	.80		
Leiter-R growth score			.04	2.91*
Cognitive composite			.53	3.12*
Step 3	15.95*	.80		
Leiter-R growth score			.04	2.87*
Cognitive composite			.52	2.95*
Autism severity			.03	.52
Step 4	27.71*	.91		
Leiter-R growth score			.04	4.04*
Cognitive composite			.58	4.61*
Autism severity			.17	2.93*
FMRP[a]			-.05	-3.67*

[a] Removing an outlier with an FMRP value more than twice the size of the next highest score yielded, $p = .283$ for FMRP and substantively similar results for the other predictors.

* $p < .05$.

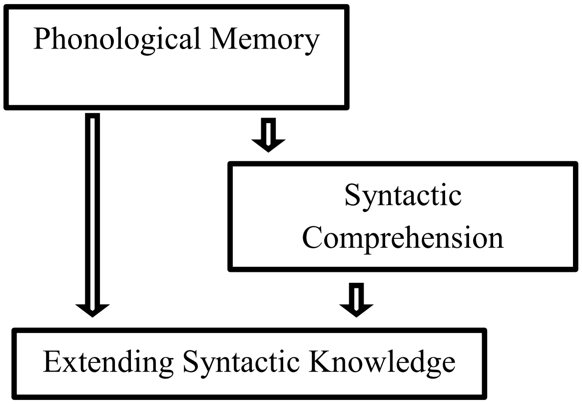

Figure 1. Hypothesis 1: The impact of phonological memory on syntactic bootstrapping is mediated by syntactic comprehension.

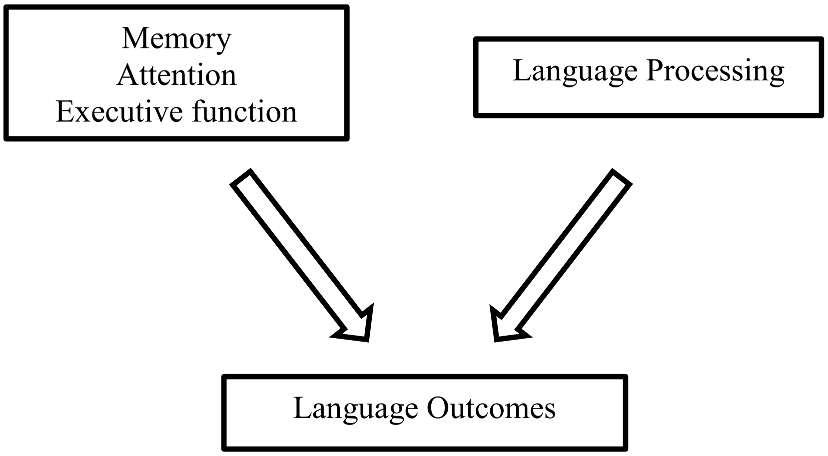

Figure 2. Hypothesis 2: Cognitive processing and language processing make independent contributions to performance on standardized language assessments.

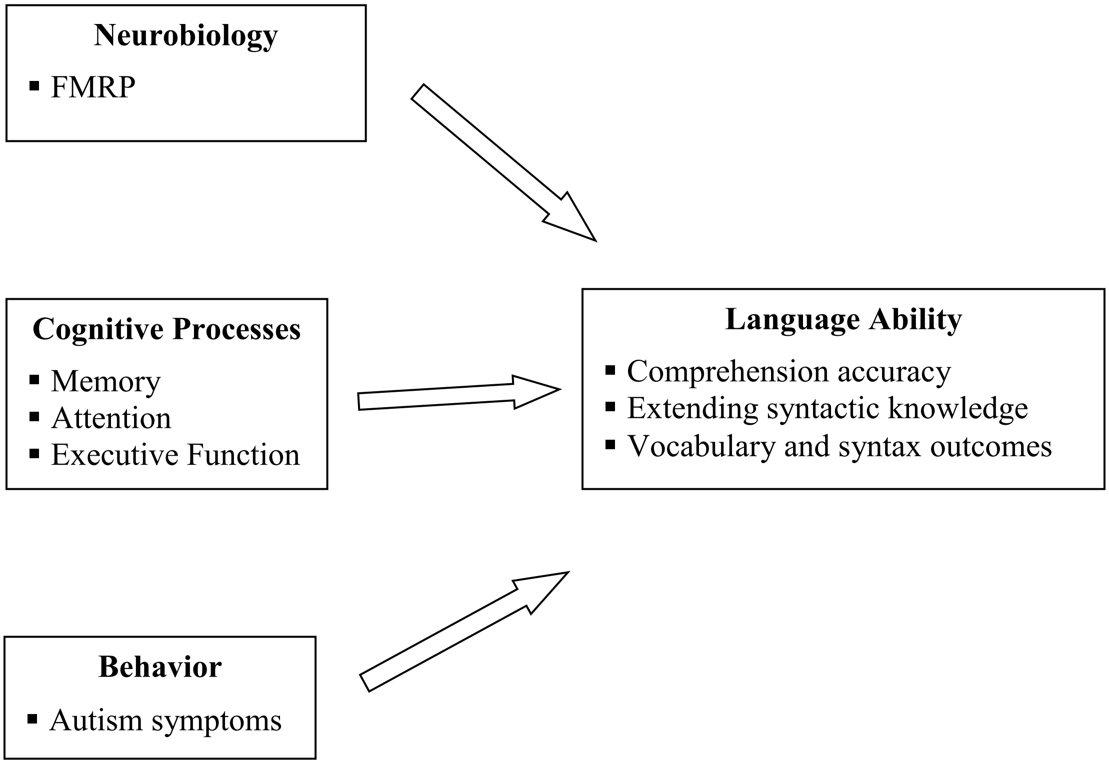

Figure 3. Predictors of comprehension, extending syntactic knowledge, and outcomes.

Chapter 5

General Discussion: Advancing the Study of Linguistic Phenotypes

This research contributes to the understanding of the connection between cognitive processes and the linguistic phenotype of FXS. Results suggest that individuals with FXS demonstrate less robust comprehension of familiar nouns and transitive sentences, and little understanding of sentences in the passive voice. Despite a different behavioral phenotype, boys with ASD also failed to show comprehension of passive sentences. In extending syntactic knowledge to novel words, boys with FXS and ASD appear to approach the interpretation of novel actions in different ways, with somewhat different patterns of performance for various syntactic cues. Lastly, evidence for the role of phonological memory and other cognitive abilities for language ability is beginning to mount and will prove fruitful for the development of specific hypotheses about learning mechanisms for children with neurodevelopmental disorders.

Extracting Distributional Cues from Language

The current research sought to address only a few aspects of the extent to which children with neurodevelopmental disorders extract distributional cues from language input. Statistical learning occurs across multiple domains and over many types of cues in typical development (Gomez & Gerken, 1999; Graf Estes et al., 2007; Saffran & Thiessen, 2003). No research has examined statistical learning in individuals with FXS and there is mixed evidence regarding statistical learning in individuals with ASD (Brown et al., 2010; Scott-Van Zeeland et al., 2010). Delineating the use of learning mechanisms by children with neurodevelopmental disorders will continue to be desirable for understanding the ways in which language learning is affected by genetic, neural, behavioral, and cognitive variability.

From a perspective that emphasizes the informative nature of the language input to which a language learner is exposed, the child's ability to extract probabilistic information from sounds, words, and phrases is of primary importance. Although language acquisition likely starts with the identification of structural patterns in the sequential input, language ultimately has meaning. The notion of studying pure syntactic competence (e.g., SVO word order) is to an extent artificial because grammar operates in concert with phonology, morphosyntax, and pragmatics. The power of SVO word order cues arises from the fact that the subject signals an agent and the object signals a patient. Thus, extension of word order to novel verbs provides cues for interpretation of semantic roles (e.g., Dittmar et al., 2011), although such 'semantic' cues might operate at a different level than those for transitivity and causation. In the present study, word order stimuli provided syntactic information from which the participant imposed a semantic interpretation to the visual stimuli (i.e., subject as agent). Segregating semantic impairments from syntactic impairments in children with neurodevelopmental disorders should be done with care. A balance between identifying weaknesses in specific domains of language ability and understanding language impairments as they functionally relate to social, academic, and work settings should be sought.

The Role of Phonological Memory in Language Development

Results from the current studies suggest that phonological memory is likely to play an important role in language development for children with neurodevelopmental disorders. However, phonological memory is one of several factors to constrain language learning. Other cognitive domains, including attention and executive function, are worthy of greater attention in research on language development in children with neurodevelopmental disorders, which are often associated with deficits in attention and effortful control.

Although an improvement over many other assessment techniques, including some standardized tests, the present results suggest that eye gaze measures are not a panacea for assessing children with neurodevelopmental disorders. In both eye gaze studies, the number of valid trials contributed by participants was often correlated with accuracy. This was true for boys with FXS and ASD for familiar noun comprehension and for typically developing boys for passive sentence comprehension. For extending syntactic knowledge to novel verbs, number of valid trials was not correlated with accuracy for boys with FXS, but was in some conditions for typically developing boys and boys with ASD. For individuals with intellectual disability, who are likely to have impaired memory, attention, and executive function, limitations of eye gaze measures may be especially evident. The extent to which aspects of cognitive processing affect the performance of typically developing children in eye gaze paradigms should also be examined, as accounting for the role of domain-general cognitive abilities in language learning tasks would be valuable to understanding typical acquisition, as well.

For children with neurodevelopmental disorders, who vary widely in task engagement, there is an immediate need to parse apart the impact of various dimensions of behavioral phenotypes on assessment performance from their impact on language learning. Does a count of valid trials serve as a proxy for attention and engagement? Do group differences in task engagement reflect an artifact of assessment or demonstrate meaningful differences in the ways in which children approach learning opportunities? Answers to these questions have serious methodological and theoretical implications for research on typical and atypical development.

Implications for Intervention

Examining cognitive processes that support language development has led to the identification of putative predictors of language outcomes and is relevant to the bodies of research on typical language acquisition, children with language impairments with normative cognitive functioning, and children with intellectual disabilities. Understanding strengths and weaknesses among specific grammatical constructions will eventually lay the groundwork for targeted interventions, which may require interdisciplinary techniques and integration of multiple perspectives. For boys with FXS, interventions for language development might need to focus on syntactic competence, but also call attention to syntax-semantics relations or otherwise reduce cognitive load during learning opportunities with existing knowledge. Specific training for phonological memory, attention, or executive function might maximize the child's ability to process the linguistic input to which he or she is exposed.

Future Directions

A recently proposed theoretical account for delayed vocabulary in late-talking toddlers draws from a framework in line with that presented here. Termed "extended statistical learning", this theory posits that late-talkers are delayed in grasping the statistical (phonological) regularities of their language that support word learning, and that once they do, they are delayed in reducing constraints based on that learning, leading to lexicons qualitatively distinguished by denser word neighborhoods and lower frequency words than expected in typical development (Stokes, Kern, & Dos Santos, 2012). Although this theory was not developed with neurodevelopmental disorders in mind, it puts forth testable hypotheses about the profiles of language ability expected from children who under- or over-utilize particular learning mechanisms and how those patterns might interact with cognitive processes, such as phonological memory. Testing this account in children with FXS and ASD, and then extending it from lexical to syntactic development, will be the natural extensions of this dissertation.

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