NORTHWESTERN UNIVERSITY

# A Longitudinal, Multi-Method Analysis of Pragmatic Language Across Genetically Based Neurodevelopmental Disabilities

A DISSERTATION

SUBMITTED TO THE GRADUATE SCHOOL IN PARTIAL FUFILLMENT OF THE REQUIREMENTS

for the degree

DOCTOR OF PHILOSOPHY

Field of Clinical Psychology

By
Michelle Lee, MS

EVANSTON, IL

June 2018

# ABSTRACT

Pragmatic language, or the use of language in social contexts, is critical to developing meaningful social relationships and is a significant contributor to mental health. Autism spectrum disorder (ASD), fragile X syndrome (FXS) and Down syndrome (DS) are all genetically based neurodevelopmental disabilities characterized by deficits in pragmatic language, although profiles of strengths and weaknesses vary within these populations. Prior work suggests that overlapping features of pragmatic language across ASD and FXS (a monogenic disorder and the most common inherited cause of intellectual disability) may indicate common genetic etiology (i.e., variation in the *FMR1* gene). In contrast, males with DS (the most common cause of intellectual disability that is not inherited) present with many strengths relative to these groups despite comparable language and cognitive abilities. These groups also all demonstrate impairments in linguistic (e.g., vocabulary, syntax), cognitive and social-cognitive abilities related to pragmatics in typical development, providing the opportunity to explore relationships between impairments in these domains and pragmatic skills. Therefore, characterizing profiles of pragmatic language development in these populations holds potential for identifying syndrome specific cognitive and linguistic abilities contributing to pragmatic language, as well as identifying possible common genetic etiologies.

This dissertation incorporates three manuscripts that aim to characterize pragmatic language in these groups. The Introduction provides a brief background and justification for the research questions addressed by this dissertation. Then, three interrelated manuscripts are included. The first, A Systematic Review of Pragmatic Language in Autism Spectrum Disorder and Fragile X Syndrome reviews cross-population comparisons of pragmatic language in ASD

and FXS. The second, A Cross Context, Longitudinal Study of Pragmatic Language Development Across Neurodevelopmental Disabilities, applied standardized measures, detailed hand coding of narrative, and clinical-behavioral ratings of semi-naturalistic conversation in males with ASD-O, FXS-ASD, FXS-O, DS and TD at up to three time points. Finally, the third manuscript, Computational Approaches to Characterizing Language Features in Neurodevelopmental Disabilities, explored the application of computational language tools to narrative and semi-naturalistic conversation samples. Overall, this line of research has critical implications for clarifying developmental and potential genetic mechanisms contributing to pragmatic language impairments across groups, and represents a step in the development of novel language assessment tools.

ACKNOWLEDGEMENTS

First and foremost, I would like to thank the families who devoted time and effort to this research across many years; without their participation, this work would not be possible. Sincerest thanks to Dr. Molly Losh, my primary research mentor, who over the past six years provided invaluable opportunities and support in developing my research skills. Your drive and passion for this work truly inspired me and shaped me into the scientist I am today. I would also like to acknowledge the other members of my committee-Gary E. Martin, for your constant support, careful edits and words of encouragement throughout this process; Klinton Bicknell, for providing excellent training in computational analyses, and Jason Washburn, for your tireless efforts to ensure that the Doctoral program provides an excellent experience for all students. I feel privileged to be mentored by all of you.

This project (nor, frankly, my graduate training at large) could not have been completed without the support of an incredible team of fellow graduate students and staff--I am forever indebted to current and former members of the Northwestern Neurodevelopmental Disabilities Lab and the University of North Carolina-Chapel Hill Neurodevelopmental Disabilities project. I have been lucky to develop such close friendships with such a dedicated, hard-working, and passionate group of individuals. In particular, I want to acknowledge Nell Maltman for her assistance in coding of the narrative data, and Jessica Klusek, Jamie Barstein, Abigail Hogan, and Lauren Bush for contributions to coding semi-naturalistic data. A very special thanks to Adam Goodkind for his work in developing computational models--your enthusiasm and willingness to learn about these populations is inspiring. Thank you to Jan Misenheimer for assistance with data management, and John Sideris for consultation on statistics. On a personal note, much love and thanks to my family, friends, and Colin, who have supported me throughout my graduate career.

Funding for this project was provided by R01MH091131; R01HD038819; R01 HD044935, R01MH091131-01A1, 1R01DC010191-01A1. Finally, I am grateful to the late Dr. Joanne Roberts, whose work laid the foundation for data available for this dissertation.

# TABLE OF CONTENTS

**LIST OF TABLES**

## LIST OF FIGURES

# CHAPTER 1: INTRODUCTION

Pragmatic (i.e., social) language is a complex skill critical to forming and maintaining meaningful social relationships throughout development. Pragmatic language can be broadly defined as the use of language for different social purposes, the methods by which a message is delivered, and the adaptation of language to comply with rules for different social contexts (ASHA, 2015; Grice, 1975; Nelson, 1978; Timler, Olswang, & Coggins, 2005). Within this broad definition, pragmatic language encompasses a range of skills, such as initiating and maintaining reciprocal interactions, selecting appropriate conversation topics, providing an adequate sequence of events (i.e., storytelling), use of paralinguistic cues (e.g., prosody, gestures) to convey meaning, and recognizing and repairing misunderstandings during interactions (Bruner, 1990; Grice, 1975; Nelson, 1978; Timler et al., 2005).

Characterizing pragmatic language in individuals with neurodevelopmental disabilities is especially relevant given that they often present with linguistic, cognitive and behavioral deficits associated with pragmatic language in typical development (Bruner, 1990; Fabbretti, Pizzuto, Vicari, & Volterra, 1997; Gooch, Thompson, Nash, Snowling, & Hulme, 2016; Gopnik, Meltzoff, & Kuhl, 1999; Laws & Bishop, 2004). Indeed, successful communicative interchange requires structural language (e.g., expressive and receptive vocabulary, mastery of grammatical structures) to understand a conversational partner and to express oneself, theory of mind (i.e., the ability to recognize the thoughts and feelings of another as distinct from one’s self) to anticipate the thoughts, interests, and background knowledge of one’s conversational partner and adjust expression accordingly, and executive function to attend, hold information in working memory, and inhibit inappropriate responses. Therefore, examination of pragmatic language development in neurodevelopmental disabilities provides a unique opportunity to examine how deficits within and across these domains contribute to pragmatic skill.

The manuscripts included in this dissertation focus on using multi-method, longitudinal approaches to directly compare three neurodevelopmental disabilities characterized by deficits in pragmatic language as well as impairments in abilities associated with pragmatic langauge in typical development: autism spectrum disorder (ASD), fragile X syndrome (FXS), and Down syndrome (DS). As described below, such a comparison has implications for identifying underlying mechanisms of pragmatic language, potential shared etiologies across groups, and providing information that may ultimately inform clinical assessment and intervention strategies.

Pragmatic language impairments are universally observed in individuals with ASD, a genetically heterogenous disorder characterized by impairments in social interactions and restricted interests and repetitive behaviors that impacts about 1/68 individuals (APA, 2013; CDC, 2014). Pragmatic deficits observed in ASD include difficulties with reciprocity (i.e., building on a conversational partner's statement), overly formal language, off topic remarks, introduction of topics without providing adequate background information, and difficulties with suprasegemental features of speech such as reduced variation of intonation (de Villiers, Fine, Ginsberg, Vaccarella, & Szatmari, 2007; Diehl & Paul, 2012, 2013; Diehl, Watson, Bennetto, Mcdonough, & Gunlogson, 2009; Lam & Yeung, 2012). Individuals with ASD also demonstrate difficulties with narration (i.e., storytelling), and in particular fail to consistently incorporate evaluation, or devices that provide a broader psychological perspective, into their narratives (Colle, Baron-Cohen, Wheelwright, & van der Lely, 2008; Lee, Martin, et al., 2017; Losh &

Capps, 2003; Losh & Gordon, 2014; Loveland, McEvoy, & Tunali, 1990; Loveland & Tunali, 1993; Tager-Flusberg & Sullivan, 1995).

It is well established that ASD is genetic in origin, however, its etiologic picture remains complex, with hundreds of risk genes identifed (see Smith and Scherer, 2018 for review). Examination of ASD phenotypes in monogenic disorders (i.e., disorders of known genetic origin) affords an opportunity to identify pathways from genetic variation to ASD-related symptoms. In particular, a growing body of work has focused on comparisons of ASD of no known genetic origin (ASD-O) and fragile X syndrome (FXS). FXS is caused by a mutation on the *FMR1* gene that limits production of FMRP, a protein critical for brain development (Bagni & Oostra, 2013). FXS is the most common inherited cause of intellectual disability and is also the monogeneic disorder most frequently associated with ASD, as 60-74% of males with FXS meet criteria for ASD in research settings (Hernandez et al., 2009; Klusek, Martin, & Losh, 2014; Zafeiriou, Ververi, Dafoulis, Kalyva, & Vargiami, 2013). *FMR1* also regulates several risk genes in ASD (Bear, Huber, & Warren, 2004; D'Hulst et al., 2006; D'Hulst & Kooy, 2007, 2009; Darnell et al., 2011). Thus, identifying phenotypic overlap between FXS and ASD-O has been proposed as an approach to identify potential downstream effects of *FMR1* variation in the development of ASD-related phenotypes.

Pragmatic language represents a strong candidate overlapping phenotype across these disorders that may be linked to variation in the *FMR1* gene. Individuals with FXS who meet criteria for ASD (FXS-ASD) demonstrate similar pragmatic language profiles to those with ASD-O, including overlap in overall severity of pragmatic impairment and specific types of impairment such as acknowledgment of a conversational partner, topic elaboration, and reciprocity in conversation (Klusek, Losh, & Martin, 2014; Losh, Martin, Klusek, Hogan-Brown, & Sideris, 2012). Further, the presence of ASD symptoms within FXS has been shown to negatively impact several pragmatic skills, including performance on standardized measures of pragmatic language, the ability to signal misunderstanding in conversation, inclusion of narrative elements, and perseverative (or repetitive) speech (Estigarribia et al., 2011; G.E. Martin, Losh, Estigarribia, Sideris, & Roberts, 2013; G. E. Martin, Roberts, Helm-Estabrooks, Sideris, & Assal, 2012; Roberts et al., 2007). Qualitatively similar differences in pragmatic language have also been observed in first degree relatives of individuals with ASD (Landa, Folstein, & Isaacs, 1991; Landa et al., 1992; Losh, Adolphs, & Piven, 2011; Losh, Klusek, et al., 2012; Piven, Palmer, Jacobi, Childress, & Arndt, 1997) and carriers of the *FMR1* premutation (Losh, Klusek, et al., 2012), providing further evidence that overlapping pragmatic language impairments in these groups may index common genetic liability.

DS, which unlike FXS is typically not inherited, is the most common genetic cause of intellectual disability (Presson et al., 2013). Individuals with DS are often included as a control group for research in FXS or ASD given comparable cognitive and language abilities in the perceived absence of significant social disability (Moore, Oates, Hobson, & Goodwin, 2002). Indeed, individuals with DS show several strengths in pragamtic language, including reduced pragmatic violations relative to males ASD-O and FXS-ASD (Abbeduto & Chapman, 2005; Klusek, Losh, et al., 2014; G.E. Martin et al., 2013; Roberts et al., 2007), qualitatively similar parent-reported social relationships relative to younger TD controls (Laws & Bishop, 2004), and a strength in their use of communicative gestures (John & Mervis, 2010; Porto-Cunha & Limongi, 2008; Soares, Pereira, Britto., & Sampaio, 2009). However, individulas with DS also demonstrate difficulties relative to typically developing individuals of similar cognitive abilities, such as reduced topic initiation and less sophisticated topic elaboration (Roberts et al., 2007; Tannock, 1988), reduced signaling of conversational misunderstanding (Abbeduto et al., 2008), and more ambiguous descriptions of a novel stimuli for their conversational partner (e.g., referential communication; Abbeduto et al., 2006). Individuals with DS also show delays in development of pragmatic language relative to younger typically developing controls of comparable mental age (Lee, Bush, et al., 2017; G.E. Martin et al., 2013). Notably, 7-15% of individuals with DS also meet criteria for co-morbid ASD, a substantially greater risk than the general population (Kent, Evans, Paul, & Sharp, 1999; Lowenthal, Paula, Schwartzman, Brunoni, & Mercadante, 2007), suggesting that common patho-physiological pathways (and subsequent underlying impairments) may be shared across a subgroup of individuals with DS and ASD (Ghaziuddin, Tsai, & Ghaziuddin, 1992). Therefore, characterizing the pragmatic profile of individuals with DS provides the opportunity to examine relationships between cognitive and structural language impairment and pragmatic competence, and identification of pragmatic skills that may be indices of common underlying mechanisms of risk to ASD-related impairments across disorders.

ASD-O, FXS and DS are all characterized by deficits in skills contributing to pragmatic language, including structural language, social cognition, and executive function (ASD-O: Baron-Cohen, Boucher, 2012; Leslie, & Frith, 1985; Baron-Cohen, Leslie, & Frith, 1988; Capps, Kehres, & Sigman, 1998; Capps, Losh, & Thurber, 2000; Kjelgaard & Tager-Flusberg, 2001; Losh & Capps, 2003; Loveland & Tunali, 1993; Surian, Baron-Cohen, & van der Lely, 1996; Tager-Flusberg, 2004; Tager-Flusberg & Sullivan, 1995; FXS: Abbeduto & Chapman, 2005;

Garner, Callias, & Turk, 1999; Hooper et al., 2008; Munir, Cornish, & Wilding, 2000; Wilding, Cornish, & Munir, 2002; DS: Abbeduto & Chapman, 2005; Cebula, Moore, & Wishart, 2010; Fabbretti et al., 1997; G.E. Martin, Klusek, Estigarribia & Roberts, 2009; Lanfranchi, Jerman, Dal Pont, Alberti, & Vianello, 2010). However, the relative contributions of these deficits may differ across disabilities and over development. For example, Tager-Flusberg and Anderson (1991) found that gains in mean length of utterance (MLU), a measure of syntactic complexity, over the course of a year resulted in increased conversational contributions in males with DS, but not ASD-O. Therefore, it is possible that observed similarities and differences across groups may vary as a function of changes underlying abilities across development. Longitudinal, cross-population comparisons of pragmatic language development therefore provide an invaluable opportunity to examine developmental mechanisms contributing to features of pragmatic language within and across disorders.

Prior work has utilized a range of assessment contexts and a variety of coding approaches to capture pragmatic language in these groups. For example, an important pragmatic skill is narration (i.e., storytelling), a culturally universal communication style that enables an individual to organize and provide meaning to life experiences (Berman & Slobin, 1994; Bruner, 1987; Ochs & Capps, 2001). Several investigations of pragmatic language have employed narration to assess pragmatic skills in individuals with neurodevelopmental disabilities (Estigarribia et al., 2011; Finestack, Palmer, & Abbeduto, 2012; Hogan-Brown, Losh, Martin, & Mueffelmann, 2013; Keller-Bell & Abbeduto, 2007; Lee, Martin, et al., 2017; Losh & Capps, 2003; Losh & Gordon, 2014). However, prior work suggests more structured assessment contexts such as narrative scaffold the abilities of individuals with ASD-O (Losh & Capps, 2003), and context-dependent patterns of structural language have been observed in DS and FXS (Kover, McDuffie, Abbeduto, & Brown, 2012; Miles & Chapman, 2002). Thus, inclusion of multiple contexts in investigation of pragmatic language is critical to ascertain the extent of pragmatic deficits in these groups and to identify difficulties that may be most relevant to less structured, daily interactions. Discerning whether groups draw on common underlying abilities across contexts can also inform understanding of overlap and divergence across groups.

Research characterizing pragmatic language in these groups primarily relied on detailed coding of specific pragmatic language features, such as tallying instances of new topic initiations or identification of affect during narrative (e.g., Losh and Capps, 2003; Lee et al., 2017; Roberts et al., 2007). Although these strategies provide a rich picture of pragmatic language, they are often time consuming to appy, and can be difficult to establish reliably across sites. Computational linguistic approaches may provide a complementary measure of language features and pragmatic skill that is quantifiable, generalizable, and relatively quick to administer. While such methods show promise in characterizing narration in ASD (Lee, Martin, et al., 2017; Losh & Gordon, 2014), prior work has yet to apply these methods to other neurodevelopmental disabilities, or to extend their application to conversational contexts. Given that individuals with ASD show more impairment in open-ended contexts, extension of quantitative methods to characterize langauge skill in unstructured contexts is critical to characterizing impairments in these groups that are most relevant to daily functioning, and represent a first step in establishing clinical assessment tools.

This dissertation aimed to 1) Compare trajectories of pragmatic development in males with ASD-O, FXS (with and without comorbid ASD), DS and typical development using multiple contexts that varied in structure; 2) Identify skills contributing to pragmatic development in each group and 3) Validate application of computational tools to conversational and narrative samples. Only males were included in empirical analyses due to the low incidence of ASD in females (Fombonne, 2009), and given evidence that females with FXS are less affected than males overall, and specifically show lower incidence of co-morbid ASD (Lee, Martin, Berry-Kravis, & Losh, 2016) because of the protective nature of an additional X chromosome (e.g., Keysor & Mazzocco, 2002).

Manuscript 1, titled A Review of Cross-Population Studies of Pragmatic Language in ASD and FXS addresses aims 1 and 2 by systematically reviewing existing literature on areas of overlap and divergence in the pragmatic language profiles and related abilities in ASD and FXS, summarizing key pragmatic abilities that may index shared genetic liability as well as identifying considerations for future research. Manuscript 2, titled A Cross-Context, Longitudinal Study of Pragmatic Language Development Across Neurodevelopmental Disabilities, similarly addresses aims 1 and 2 by applying standardized measures, detailed hand coding of narrative, and clinical behavioral ratings of semi-naturalistic conversations for males with ASD-O, FXS-ASD, FXS-O, DS and TD at up to three time points. Results show unique profiles of pragmatic language development in these groups, and highlight the role of assessment context in delineating pragmatic abilities in neurodevelopmental disabilities. Manuscript 3, A Computational Analyses of Language in Neurodevelopmental Disabilities, addresses aim 3 of this dissertation by exploring applications of computational language methods to narrative and conversational samples, and validating these methods using the clinical behavioral and hand-coding measures applied in Manuscript 2. Together, these manuscripts provide a comprehensive evaluation of pragmatic language in males with ASD-O, FXS-ASD, FXS-O and DS, with implications for identifying possible shared pragmatic features that may indicated common etiology and further characterization of contributing mechanisms of pragmatic language across groups.

**References**

Abbeduto, L., & Chapman, R. (2005). Language development in Down syndrome and fragile X syndrome: Current research and implications for theory and practice. In P. Fletcher & J. F. Miller (Eds.), *Developmental theory and language disorders* (pp. 53-72). Amsterdam: John Benjamins Publishing Co.

Abbeduto, L., Murphy, M. M., Kover, S. T., Karadottir, S., Amman, A., & Bruno, L. (2008). Signaling noncomprehension of language: A comparison of fragile X syndrome and Down syndrome. *American Journal on Mental Retardation, 113*, 214-230.

Abbeduto, L., Murphy, M. M., Richmond, E. K., Amman, A., Beth, P., Weissman, M. D., . . . Karadottir, S. (2006). Collaboration in referential communication: Comparison of youth with Down syndrome or fragile X syndrome. *American Journal of Mental Retardation, 111*(3), 170-183.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (5th ed.). Arlington, VA: American Psychiatric Association.

Association, A. S.-L.-H. (2015). American Speech-Language-Hearing Association. Retrieved from www.asha.org

Bagni, C., & Oostra, B. A. (2013). Fragile X syndrome: From protein function to therapy. *Am J Med Genet A, 161A*(11), 2809-2821.

Baron-Cohen, S., Leslie, A. M., & Frith, U. (1985). Does the autistic child have 'theory of mind'? *Cognition, 21*, 37-46.

Baron-Cohen, S., Leslie, A. M., & Frith, U. (1988). Soical and pragmatic deficitis in autism: Cognitive or affective? *Journal of Autism and Developmental Disorders, 18*, 379-403.

Bear, M. F., Huber, K. M., & Warren, S. T. (2004). The mGluR theory of fragile X mental retardation. *Trends in Neurosciences, 27*(7), 370-377.

Berman, R., & Slobin, D. (Eds.). (1994). *Relating events in narrative: A cross-linguistic developmental study*. Hillsdale, NJ: Erlbaum.

Boucher, J. (2012). Research review: structural language in autistic spectrum disorder - characteristics and causes. *J Child Psychol Psychiatry, 53*(3), 219-233.

Bruner, J. (1987). Life As Narrative. *Social Research, 54*(1), 11-32.

Bruner, J. (1990). *Acts of meaning*. Cambridge, MA: Harvard University Press.

Budimirovic, D. B., Bukelis, I., Cox, C., Gray, R. M., Tierney, E., & Kaufmann, W. E. (2006). Autism spectrum disorder in fragile X syndrome: Differential contribution of adaptive socialization and social withdrawal. *American Journal of Medical Genetics Part A, 9999*, 1-13.

Capps, L., Kehres, J., & Sigman, M. (1998). Conversational Abilities Among Children with Autism and Children with Developmental Delays. *Autism, 2*(4), 325-344.

Capps, L., Losh, M., & Thurber, C. (2000). The frog ate a bug and made his mouth sad: Narrative competence in children with autism. *Journal of Abnormal Child Psychology, 28*, 193-204.

CDC (2014). Prevalence of autism spectrum disorder among children aged 8 years - autism and developmental disabilities monitoring network, 11 sites, United States, 2010. *MMWR Surveill Summ, 63*(2), 1-21.

Cebula, K. R., Moore, D. G., & Wishart, J. G. (2010). Social cognition in children with Down's syndrome: Challenges to research and theory building. *Journal of Intellectual Disabilities Research*, *54*(2), 113–134.

Colle, L., Baron-Cohen, S., Wheelwright, S., & van der Lely, H. K. (2008). Narrative Discourse in Adults with High Functioning Autism or Asperger Syndrome. *Journal of Autism and Developmental Disorders, 38*, 28-40.

D'Hulst, C., De Geest, N., Reeve, S. P., Van Dam, D., De Deyn, P. P., Hassan, B. A., & Kooy, R. F. (2006). Decreased expression of the GABAA receptor in fragile X syndrome. *Brain Res, 1121*(1), 238-245.

D'Hulst, C., & Kooy, R. F. (2007). The GABAA receptor: a novel target for treatment of fragile X? *Trends Neurosci, 30*(8), 425-431.

D'Hulst, C., & Kooy, R. F. (2009). Fragile X syndrome: from molecular genetics to therapy. *J Med Genet, 46*(9), 577-584.

Darnell, J. C., Van Driesche, S. J., Zhang, C., Hung, K. Y., Mele, A., Fraser, C. E., . . . Darnell, R. B. (2011). FMRP stalls ribosomal translocation on mRNAs linked to synaptic function and autism. *Cell, 146*(2), 247-261.

de Villiers, J., Fine, J., Ginsberg, G., Vaccarella, L., & Szatmari, P. (2007). Brief report: a scale for rating conversational impairment in autism spectrum disorder. *J Autism Dev Disord, 37*(7), 1375-1380.

Diehl, J. J., & Paul, R. (2012). Acoustic Differences In The Imitation Of Prosodic Patterns In Children With Autism Spectrum Disorders. *Res Autism Spectr Disord, 6*(1), 123-134.

Diehl, J. J., & Paul, R. (2013). Acoustic and perceptual measurements of prosody production on the profiling elements of prosodic systems in children by children with autism spectrum disorders. *Applied Psycholinguistics, 34*(1), 135-161.

Diehl, J. J., Watson, D., Bennetto, L., Mcdonough, J., & Gunlogson, C. (2009). An acoustic analysis of prosody in high-functioning autism. *Applied Psycholinguistics, 30*(3), 385-404.

Estigarribia, B., Martin, G. E., Roberts, J. E., Spencer, A., Gucwa, A., & Sideris, J. (2011). Narrative skill in boys with fragile X syndrome with and without autism spectrum disorder. *Applied Psycholinguistics*, 359-388.

Fabbretti, D., Pizzuto, E., Vicari, S., & Volterra, V. (1997). A story description task in children with Down's syndrome: lexical and morphosyntactic abilities. *J Intellect Disabil Res, 41 (Pt 2)*, 165-179.

Finestack, L. H., Palmer, M., & Abbeduto, L. (2012). Macrostructural narrative language of adolescents and young adults with Down syndrome or fragile X syndrome. *American Journal of Speech-Language Pathology, 21*, 29-46.

Fombonne, E. (2009). Epidemiology of pervasive developmental disorders. *Pediatric Research, 65*, 591-598.

Garner, C., Callias, M., & Turk, J. (1999). Executive function and theory of mind performance of boys with fragile-X syndrome. *J Intellect Disabil Res, 43 ( Pt 6)*, 466-474.

Ghaziuddin, M., Tsai, L. Y., & Ghaziuddin, N. (1992). Autism in Down's syndrome: presentation and diagnosis. *J Intellect Disabil Res, 36 ( Pt 5)*, 449-456.

Gooch, D., Thompson, P., Nash, H. M., Snowling, M. J., & Hulme, C. (2016). The development of executive function and language skills in the early school years. *J Child Psychol Psychiatry, 57*(2), 180-187.

Gopnik, A., Meltzoff, A. N., & Kuhl, P. K. (1999). *The scientist in the crib: Minds, brains, and how children learn*. New York: Morrow.

Grice, H. P. (1975). Logic and conversation. In P. C. Morgan & J.L (Eds.), *Syntax and Semantics 3: Speech Acts* (pp. 41-58). New York: Academic Press.

Hernandez, R. N., Feinberg, R. L., Vaurio, R., Passanante, N. M., Thompson, R. E., & Kaufmann, W. E. (2009). Autism spectrum disorder in fragile X syndrome: A longitudinal evaluation. *American Journal of Human Genetics, 149A*(6), 1125-1137.

Hogan-Brown, A. L., Losh, M., Martin, G. E., & Mueffelmann, D. (2013). An investigation of narrative ability in boys with autism and fragile X syndrome. *American Journal on Intellectual and Developmental Disabilities, 118*(2), 77-94.

Hooper, S. R., Hatton, D., Sideris, J., Sullivan, K., Hammer, J., Schaaf, J., . . . Bailey, D. P., Jr. (2008). Executive functions in young males with fragile X syndrome in comparison to mental age-matched controls: baseline findings from a longitudinal study. *Neuropsychology, 22*(1), 36-47.

John, A. E., & Mervis, C. B. (2010). Comprehension of the communicative intent behind pointing and gazing gestures by young children with Williams syndrome or Down syndrome. *J Speech Lang Hear Res, 53*(4), 950-960.

Kau, A. S., Tierney, E., Bukelis, I., Stump, M. H., Kater, W. R., Trescher, W. H., & al., e. (2004). Social behavior profile in young males with fragile X syndrome: Characteristics and specificity. *American Journal of Medical Genetics, 126A*(1), 9-17.

Kaufmann, W. E., Cortell, R., Kau, A. S., Bukelis, I., Tierney, E., Gray, R. M., . . . Stanard, P. (2004). Autism spectrum disorder in fragile X syndrome: Communication, social interaction, and specific behaviors. *American Journal of Medical Genetics, 129*(3), 225-234.

Keller-Bell, Y. D., & Abbeduto, L. (2007). Narrative development in adolescents and young adults with fragile X syndrome. *American Journal on Mental Retardation, 112*, 289-299.

Kent, L., Evans, J., Paul, M., & Sharp, M. (1999). Comorbidity of autistic spectrum disorders in children with Down syndrome. *Dev Med Child Neurol, 41*(3), 153-158.

Keysor, C. S., & Mazzocco, M. M. (2002). A developmental approach to understanding Fragile X syndrome in females. *Microsc Res Tech, 57*(3), 179-186.

Kjelgaard, M., & Tager-Flusberg, H. (2001). An investigation of language impairment in autism: Implications for genetic subgroups. *Language and Cognitive Processes, 16*, 287-308.

Klusek, J., Losh, M., & Martin, G. E. (2014). A comparison of pragmatic language in boys with autism and fragile X syndrome. *Journal of Speech, Language, and Hearing Research, 57*(5), 1692-1707.

Klusek, J., Martin, G. E., & Losh, M. (2014). Consistency between research and clinical diagnoses of autism among boys and girls with fragile X syndrome. *J Intellect Disabil Res, 58*(10), 940-952.

Kover, S. T., McDuffie, A., Abbeduto, L., & Brown, W. T. (2012). Effects of sampling context on spontaneous expressive language in males with fragile X syndrome or Down syndrome. *J Speech Lang Hear Res, 55*(4), 1022-1038.

Lam, Y. G., & Yeung, S. S. S. (2012). Towards a convergent account of pragmatic language deficits in children with high-functioning autism: Depicting the phenotype using the Pragmatic Rating Scale. *Research in Autism Spectrum Disorders, 6*(2), 792-797.

Landa, R., Folstein, S. E., & Isaacs, C. (1991). Spontaneous narrative-discourse performance of parents of autistic individuals. *Journal of Speech and Hearing Research, 34*(6), 1339-1345.

Landa, R., Piven, J., Wzorek, M. M., Gayle, J. O., Chase, G. A., & Folstein, S. E. (1992). Social language use in parents of autistic individuals. *Psychological Medicine, 22*(1), 245-254.

Lanfranchi, S., Jerman, O., Dal Pont, E., Alberti, A., & Vianello, R. (2010). Executive function in adolescents with Down syndrome. *Journal of Intellectual Disabilities Research, 54*(4), 308–319.

Laws, G., & Bishop, D. (2004). Pragmatic language impairment and social deficits in Williams syndrome: a comparison with Down's syndrome and specific language impairment. *Int J Lang Commun Disord, 39*(1), 45-64.

Lee, M., Bush, L., Martin, G. E., Barstein, J., Maltman, N., Klusek, J., & Losh, M. (2017). A multi-method investigation of pragmatic development in individuals with Down syndrome. *Am J Intellect Dev Disabil, 122*(4), 289-309.

Lee, M., Martin, G. E., Berry-Kravis, E., & Losh, M. (2016). A developmental, longitudinal investigation of autism phenotypic profiles in fragile X syndrome. *J Neurodev Disord, 8*, 47.

Lee, M., Martin, G. E., Hogan, A., Hano, D., Gordon, P. C., & Losh, M. (2017). What's the story? A computational analysis of narrative competence in autism. *Autism*, 1362361316677957.

Losh, M., Adolphs, R., & Piven, J. (2011). The Broad Autism Phenotype. In G. Dawson, D. Amaral, & D. Geschwind (Eds.), *Autism Spectrum Disorders* (pp. 457-476). Oxford: Oxford University Press.

Losh, M., & Capps, L. (2003). Narrative ability in high-functioning children with autism or Asperger's syndrome. *Journal of Autism and Developmental Disorders, 33*(3), 239-251.

Losh, M., & Gordon, P. C. (2014). Quantifying narrative ability in autism spectrum disorder: A computational linguistic analysis of narrative coherence. *Journal of Autism and Developmental Disorders, 44*(12), 3016–3025.

Losh, M., Klusek, J., Martin, G. E., Sideris, J., Parlier, M., & Piven, J. (2012). Defining genetically meaningful language and personality traits in relatives of individuals with fragile X syndrome and relatives of individuals with autism. *American journal of medical genetics. Part B, Neuropsychiatric genetics : the official publication of the International Society of Psychiatric Genetics, 159B*(6).

Losh, M., Martin, G. E., Klusek, J., Hogan-Brown, A. L., & Sideris, J. (2012). Social communication and theory of mind in boys with autism and fragile x syndrome. *Front Psychol, 3*, 266.

Loveland, K. A., McEvoy, R. E., & Tunali, B. (1990). Narrative story telling in autism and Down's syndrome. *British Journal of Developmental Psychology, 8*, 9-23.

Loveland, K. A., & Tunali, B. (1993). Narrative Language in autism and the theory of mind hypothesis: A wider perspective. In S. Baron-Cohen, H. Tager-Flusberg, & D. J. Cohen (Eds.), *Understanding other minds: Perspectives from autism*. Oxford, UK: Oxford University Press.

Lowenthal, R., Paula, C. S., Schwartzman, J. S., Brunoni, D., & Mercadante, M. T. (2007). Prevalence of pervasive developmental disorder in Down's syndrome. *J Autism Dev Disord, 37*(7), 1394-1395.

Martin, G. E., Losh, M., Estigarribia, B., Sideris, J., & Roberts, J. (2013). Longitudinal profiles of expressive vocabulary, syntax, and pragmatic language in boys with fragile X syndrome or Down syndrome. *International Journal of Language & Communication Disorders, 48*(4), 432-443.

Martin, G. E., Roberts, J. E., Helm-Estabrooks, N., Sideris, J., & Assal, J. (2012). Perseveration in the connected speech of boys with fragile X syndrome with and without autism spectrum disorder. *American Journal on Intellectual and Developmental Disabilities, 117*(5), 384-399.

Miles, S., & Chapman, R. S. (2002). Narrative content as described by individuals with Down syndrome and typically developing children. *Journal of speech, language, and hearing research : JSLHR, 45*(1), 175-189.

Moore, D. G., Oates, J. M., Hobson, P. R., & Goodwin, J. E. (2002). Cognitive and social factors in the development of infants with Down syndrome. *Down Syndrome Research and Practice, 8*, 172-188.

Munir, F., Cornish, K. M., & Wilding, J. (2000). Nature of the working memory deficit in fragile-X syndrome. *Brain Cogn, 44*(3), 387-401.

Nelson, K. (1978). How children represent knowledge of their world in and out of language: A preliminary report. In R. S. Siegler (Ed.), *Children's Thinking: What Develops?* (pp. 255-273). Mahwah, NJ: Erlbaum.

Ochs, E., & Capps, L. (2001). *Living narrative: Creating lives in everyday storytelling*. Cambridge, MA: Harvard University Press.

Piven, J., Palmer, P., Jacobi, D., Childress, D., & Arndt, S. (1997). Broader autism phenotype: Evidence from a family history study of multiple-incidence autism families. *American Journal of Psychiatry, 154*(2), 185-190.

Porto-Cunha, E., & Limongi, S. C. (2008). Communicative profile used by children with Down syndrome. *Pro Fono, 20*(4), 243-248.

Presson, A. P., Partyka, G., Jensen, K. M., Devine, O. J., Rasmussen, S. A., McCabe, L. L., & McCabe, E. R. (2013). Current estimate of Down Syndrome population prevalence in the United States. *J Pediatr, 163*(4), 1163-1168.

Roberts, J. E., Martin, G. E., Moskowitz, L., Harris, A. A., Foreman, J., & Nelson, L. (2007). Discourse skills of boys with fragile X syndrome in comparison to boys with Down syndrome. *Journal of Speech, Language, and Hearing Research, 50*, 475-492.

Smith, L. E., Barker, E. T., Seltzer, M. M., Abbeduto, L., & Greenberg, J. S. (2012). Behavioral phenotype of fragile x syndrome in adolescence and adulthood. *American Journal on Intellectual and Developmental Disabilities, 117*(1), 1-17.

Soares, E. M. F., Pereira, Britto., M. M. d., & Sampaio, T. M. M. (2009). Pragmatic ability and Down's syndrome. *Revista CEFAC, 11*(4), 579-586.

Surian, L., Baron-Cohen, S., & van der Lely, H. K. J. (1996). Are children with autism deaf to Gricean maxims? *Cognitive Neuropsychiatry, 1*, 55-71.

Tager-Flusberg, H. (2004). Strategies for conducting research on language in autism. *J Autism Dev Disord, 34*(1), 75-80.

Tager-Flusberg, H., & Anderson, M. (1991). The development of contingent discourse ability in autistic children. *Journal of Child Psychology and Psychiatry, 32*, 1123-1134.

Tager-Flusberg, H., & Sullivan, K. (1995). Attributing mental states to story characters: A comparison of narratives produced by autistic and mentally retarded individuals. *Applied Psycholinguistics, 16*(3), 241-256.

Tannock, R. (1988). Mothers' directiveness in their interactions with their children with and without Down syndrome. *American Journal of Mental Retardation, 93*(2), 154-165.

Timler, G. R., Olswang, L. B., & Coggins, T. E. (2005). Social communication interventions for preschoolers: targeting peer interactions during peer group entry and cooperative play. *Semin Speech Lang, 26*(3), 170-180.

Wilding, J., Cornish, K., & Munir, F. (2002). Further delineation of the executive deficit in males with fragile-X syndrome. *Neuropsychologia, 40*(8), 1343-1349.

Woodbury-Smith, M. & Scherer, S.W. (2018). Progress in the genetics of autism spectrum disorder. *Dev Med Child Neurol, 60*(5):445-451.

Zafeiriou, D. I., Ververi, A., Dafoulis, V., Kalyva, E., & Vargiami, E. (2013). Autism spectrum disorders: the quest for genetic syndromes. *Am J Med Genet B Neuropsychiatr Genet, 162B*(4), 327-366.

# CHAPTER 2: A SYTEMATIC REVIEW of PRAGMATIC LANGUAGE in AUTISM SPECTRUM DISORDER and FRAGILE X SYNDROME


## Abstract

A promising approach to disentangling the genetic complexity of Autism Spectrum Disorder (ASD) is to examine the presence of symptoms of ASD in the context of disorders of known genetic origin. Several studies have investigated overlapping features of ASD and fragile X syndrome (FXS), the most common monogenic disorder associated with ASD, in order to discern potential pathways from *FMR1* variation to the development of ASD-related behaviors. Such an approach is in line with a broader shift in psychiatry to focus on clearly defined behavioral, cognitive, and biological markers that cut across categorically defined disorders. Pragmatic language represents an area of phenotypic overlap across individuals with ASD and FXS that is a strong candidate for such an approach. This systematic review aims to summarize cross-population comparisons of pragmatic language (and related abilities) in ASD and FXS, with the goal of informing areas of overlap and divergence across disorders and directions for future research.

Although the study of psychopathology is in some ways rooted in diagnostic classification, it is now well understood that both clinical phenotypes and genetic risk cut across diagnostic categories (Cuthbert & Insel, 2013; Insel, 2014b; S. H. Lee et al., 2013; Ruderfer et al., 2014). Clearly defining behavioral phenotypes and underlying neural and genetic mechanisms across categorically defined disorders has implications for theoretical understanding of human development as well as highly individualized intervention (i.e., "rDOC"; Insel, 2014a). Comparison of clearly defined phenotypes across disorders with known etiologic origin (e.g., monogenic disorders) and more etiologically heterogeneous disorders provides the unique opportunity to identify potential genetic and neurobiological pathways of complex human behaviors (i.e., a "conjunction approach," see Müller, 2005, for review).

A growing body of research examining overlapping phenotypes in fragile X syndrome and autism spectrum disorder (ASD) exemplifies this approach. ASD is characterized by a highly heterogeneous clinical presentation with core impairments in social communication and the presence of atypical restricted and repetitive behaviors, impacting 1/68 school-aged children (CDC, 2014). There is strong evidence for the genetic etiology of ASD; however, this etiology remains highly complex, with hundreds of unique risk genes identified (see Stessman et al., 2017, for review). FXS is caused by a Cytosine-Guanine-Guanine (CGG) repeat expansion of over 200 on the 5' untranslated region of the *FMR1* gene on the X chromosome, inhibiting the production of Fragile X Mental Retardation Protein (FMRP), an essential protein for several aspects of brain development (Bagni & Oostra, 2013; Garber, Visootsak, & Warren, 2008). FXS is characterized by a heterogeneous clinical-behavioral phenotype including intellectual disability, language delay, executive functioning difficulties, anxiety, and behavioral and social deficits (Abbeduto, Brady, & Kover, 2007; Abbeduto & Murphy, 2004; Bagni & Oostra, 2013; Bennetto, Pennington, Hagerman, & Cronister, 2002). Additionally, 60%–74% of males with FXS meet diagnostic criteria for ASD in research settings (Clifford et al., 2007; Hall, Lightbody, & Reiss, 2008; Kaufmann et al., 2004; Philofsky, Hepburn, Hayes, Hagerman, & Rogers, 2004; Rogers, Wehner, & Hagerman, 2001), with more (up to 90%) demonstrating symptoms of ASD (Bailey et al., 1998; Budimirovic et al., 2006; Hagerman, 2002; Hall et al., 2008; Hatton et al., 2006; Hernandez et al., 2009; Kau et al., 2004; Kaufmann et al., 2004; Merenstein et al., 1996). In addition to this phenotypic overlap, the *FMR1* gene regulates multiple implicated risk genes in ASD (Bear, Huber, & Warren, 2004; D'Hulst et al., 2006; D'Hulst & Kooy, 2007, 2009; Darnell et al., 2011). Therefore, it has been hypothesized that FXS may serve as a model for downstream genetic effects in the development of ASD.

Pragmatic, or social, language has emerged as a key shared phenotype across ASD and FXS that may be related to *FMR1* variation. Several studies suggest overlap in social communication in individuals with ASD and those with FXS who also meet criteria for ASD (i.e., FXS-ASD; Klusek, Losh, & Martin, 2014; M. Lee, Martin, Berry-Kravis, & Losh, 2016; Losh, Martin, Klusek, Hogan-Brown, & Sideris, 2012), with one study showing relationships between *FMR1* variation and pragmatic competence in males with FXS (Losh, Martin, et al., 2012). Further, pragmatic language draws on a range of neuro-cognitive abilities, such as structural language, social cognition, and executive function, known to be impaired in both populations and linked to specific neural substrates in typical development (e.g., R. B. Adams et al., 2010; Baron-Cohen, 2000; Castelli et al., 2010; Dove, Pollmann, Schubert, Wiggins, & von Cramon, 2000; Kondo et al., 2004; Mascaro, Rilling, Tenzin Negi, & Raison, 2013; Osaka et al., 2004; Platek, Keenan, Gallup, & Mohamed, 2004; Sato et al., 2016; Schurz, Radua, Aichhorn, Richlan, & Perner, 2014). Therefore, delineating the pragmatic language phenotype of individuals with FXS and idiopathic ASD (ASD-O), along with related abilities, provides an opportunity to examine pathways from *FMR1* variation to pragmatic deficits associated with ASD.

Characterizing pragmatic language in first degree relatives of individuals with ASD (who show greater genetic liability to ASD) and carriers of the *FMR1* premutation (i.e., CGG repeats between 55-200) provide an opportunity to examine overlapping phenotypes in the absence of the significant cognitive or language delays that have been argued to confound comparisons of clinical populations (e.g., Abbeduto, McDuffie, & Thurman, 2014). Such approaches provide further evidence of pragmatic language as a key overlapping phenotype across ASD and FXS that may relate to shared genetic liability. Similar to studies in FXS, carriers of the *FMR1* premutation also demonstrate elevated rates of co-morbid ASD relative to the general population (e.g., Farzin et al., 2006). Several studies suggest that first-degree relatives of individuals with ASD demonstrate qualitatively similar, subclinical differences in pragmatic language, such as over-talkativeness, bluntness, or less coherent narratives as those observed in ASD (Landa, Folstein, & Isaacs, 1991; Landa et al., 1992; Losh, Adolphs, & Piven, 2011; Losh, Klusek, et al., 2012; Piven, Palmer, Jacobi, Childress, & Arndt, 1997), indicating that pragmatic language differences index genetic liability to ASD. Overlapping subclinical differences in pragmatic language (in both severity and specific types of difficulties) have also been observed in carriers of the *FMR1* premutation (i.e., CGG repeats between 55-200), further suggesting that pragmatic language overlap is a strong candidate phenotype that may link to underlying variation in *FMR1* (Losh, Klusek, et al., 2012).

Despite the potential insights to be gained from studies of this overlap, few studies have directly compared pragmatic language in these populations, and have tended to focus on discrete skills (e.g., topic maintenance, repetitive language, repair of communicative breakdowns). This paper aims to comprehensively review and synthesize existing studies characterizing pragmatic language phenotypes, and related abilities, in ASD-O and FXS. We begin by providing a broad overview of pragmatic language and contributing factors in typical development, followed by a brief review of what is known about pragmatic language and related abilities in ASD-O and FXS. We then review in depth direct comparisons of pragmatic language in these populations. This review focuses primarily on males given the paucity of cross-population comparisons of females with FXS and ASD, due to the low incidence of ASD-O in females (Fombonne, 2009), and evidence of reduced impairment in females with FXS due of the protective nature of an additional X chromosome (e.g., Keysor & Mazzocco, 2002). Finally, we conclude with a discussion integrating findings across studies and identifying directions for future research.

## Overview of Pragmatic Language Across Groups

### Pragmatic Language in Typical Development

Pragmatic language encompasses the adjustment of form, content and usage of language in social contexts (ASHA, 2015; Grice, 1975; Nelson, 1978; Timler, Olswang, & Coggins, 2005). This includes skills such as initiating and maintaining conversation, monitoring appropriateness of topics, sequencing events in narrative, use of paralinguistic cues (e.g., prosody, gestures) to convey meaning, and recognizing and repairing conversational breakdown

(Bruner, 1990; Grice, 1975; Nelson, 1978; Timler et al., 2005). Rudimentary pragmatic skills emerge early in development, with social imitation, attempts to obtain adult attention, and brief turn taking. As children age, and concurrent with the development of related abilities such as structural language and social cognition, they acquire more sophisticated and diverse conversational devices, begin to recognize the need to clarify for conversational partners, and increase their use and complexity of narrative. By adolescence, individuals have mastered skills such as adapting speech to their conversational partner, providing adequate background information for conversational topics, modulating response length, and balancing conversational turn-taking (Ciccia & Turkstra, 2002).

In typical development, development of pragmatic language occurs concurrently with the development of cognition and structural language, theory of mind (i.e., the ability to infer thoughts and feelings in others), and executive functioning (e.g., working memory, inhibition, switching of attention; (Bruner, 1987, 1990, 1991; Fiske & Taylor, 1991; Gooch, Thompson, Nash, Snowling, & Hulme, 2016; Gopnik, Meltzoff, & Kuhl, 1999; Laws, 2004). Impairment in any of these domains may lead to pragmatic deficits, with consequences for meaningful social participation. Therefore, understanding pragmatic language impairments and related abilities are particularly relevant to for ASD-O and FXS, described in greater detail below.

## Pragmatic Language Profiles and Related Abilities in Autism Spectrum Disorder and Fragile X Syndrome

### Pragmatic Language in ASD-O

Pragmatic language difficulties are universally observed in ASD-O, even in the absence of structural language impairment, and are included in diagnostic criteria for the disorder

(American Psychiatric Association, 2013). Pragmatic language difficulties observed in ASD-O distinguish them not only from typically developing controls but also those with other disorders characterized by language and social-communication differences, such as Specific Language Impairment and Attention Deficit Hyperactivity Disorder (Geurts & Embrechts, 2008; Geurts et al., 2004). Individuals with ASD-O demonstrate difficulty initiating, elaborating, and sustaining reciprocal conversation (de Villiers, Fine, Ginsberg, Vaccarella, & Szatmari, 2007; Lam & Yeung, 2012), and tend to make more off topic or tangential contributions to conversation (Capps, Kehres, & Sigman, 1998; Paul et al., 1987; Tager-Flusberg & Anderson, 1991). Whereas individuals with ASD recognize the need to remedy a conversational breakdown when explicitly prompted, strategies employed tend to be less effective than typically developing controls, such as making off-topic comments or resisting the task (Geller, 1998; Paul & Cohen, 1984; Volden, 2004).

Numerous studies have also documented differences in narrative, or storytelling, in individuals with ASD across age and ability level (Colle, Baron-Cohen, Wheelwright, & van der Lely, 2008; M. Lee et al., 2017; Losh & Capps, 2003; Losh & Gordon, 2014; Loveland, McEvoy, & Tunali, 1990; Loveland & Tunali, 1993; Tager-Flusberg & Sullivan, 1995). The most robust area of narrative difference is that individuals with ASD are limited in their use of narrative evaluation, or identification and explanation of character thought and emotion (e.g., Capps, Losh, & Thurber, 2000; Lee et al., 2017; Losh & Capps, 2003; Loveland & Tunali, 1993). Narrative evaluation is central to successful storytelling, as it is a tool that engages the listener, provides the narrator's perspective, draws emphasis to the relative importance of various aspects of a narrative, and infuses a story with emotional significance (Bamberg & Damard-Frye, 1991; Bamberg & Reilly, 1996; Berman & Slobin, 1994; Goffman, 1974; Labov and Waletzky, 1967). Together, prior research suggests that pragmatic language represents a central impairment for individuals ASD-O, with particular deficits in social reciprocity and psychological aspects of narrative.

**Abilities Related to Pragmatic Competence in ASD-O**

Impairments in structural language, theory of mind, and executive functioning are all hypothesized to contribute to pragmatic language deficits in ASD-O. Individuals with ASD-O often demonstrate a delay in language acquisition (see Rapin & Dunn, 1997, 2003, for review), and a subset of individuals continue to demonstrate structural language deficits relative to nonverbal cognition (e.g., Boucher, 2012; Kjelgaard & Tager-Flusberg, 2001; Tager-Flusberg, 2004), similar to differences observed in children with Specific Language Impairment (Tager-Flusberg, 2004). Volden et al. (2009) found that greater structural language abilities significantly predicted improved performance on a standardized assessment of pragmatic language in ASD-O (Volden, Coolican, Garon, White, & Bryson, 2009). However, a study by Tager-Flusberg and Anderson (1991) suggested that gains in structural language over the course of a year (in syntactic complexity, as assessed by mean length of utterance or MLU) did not relate to increases in conversational contributions in males with ASD-O. Given that pragmatic language deficits persist in ASD-O in the absence of structural language impairment (Tager-Flusberg, 2005), it is clear that difficulties in structural language cannot entirely account for this deficit.

Theory of mind, or the ability to recognize the thoughts and emotions of others, represents a core impairment in ASD-O and has been associated with pragmatic language deficits across a range of studies (Baron-Cohen, Leslie, & Frith, 1985; Baron-Cohen, Leslie, &

Frith, 1988; Lisa Capps et al., 1998; L. Capps et al., 2000; Losh & Capps, 2003; Loveland & Tunali, 1993; Surian, Baron-Cohen, & van der Lely, 1996; Tager-Flusberg & Sullivan, 1995). Individuals with ASD have been shown to demonstrate impairments in executive function (Garner, Callias, & Turk, 1999a; Hooper et al., 2008; Munir, Cornish, & Wilding, 2000; Wilding, Cornish, & Munir, 2002) that are theorized to contribute to pragmatic difficulties; however, this relationship has not been directly assessed. More recently, theory has shifted from determining a unifying cognitive explanation for deficits associated with ASD-O, and rather examining how difficulties across domains such as executive function and social cognition uniquely contribute to the ASD-O social phenotype (e.g., Baron-Cohen & Swettenham, 1997). Overall, while pragmatic deficits in ASD-O are well characterized, the degree to which possible related abilities contribute to these deficits across social contexts is less clear.

**Pragmatic Language in FXS**

Individuals with FXS also present with pragmatic language impairments, and several studies suggest that the presence of ASD symptoms negatively impacts pragmatic language in this group. The language of males with FXS is characterized by perseverative, or repetitive, language (Levy, Gottesman, Borochowitz, Frydman, & Sagi, 2006; R. Paul et al., 1987; Roberts et al., 2007), and increased non-contingency (Besler & Sudhalter, 2001; Roberts et al., 2007; Sudhalter, Cohen, Silverman, & Wolf-Schein, 1990). Males with FXS, and in particular those with FXS-ASD, have also been shown to signal misunderstandings in interactions less than mental age matched controls, although did not differ from males with Down syndrome (L. Abbeduto et al., 2008; G. E. Martin et al., 2017). In contrast, several studies suggest that males with FXS show relative strengths in narration, including comparable rates of evaluation and use of inferential language relative to typically developing controls with similar nonverbal cognitive abilities (Ashby, Channell, & Abbeduto, 2017; Keller-Bell & Abbeduto, 2007), comparable grammar during a narrative recall task relative to individuals with DS (Channell, McDuffie, Bullard, & Abbeduto, 2015), and similar or even qualitatively better performance on macrostructural measures of narrative relative to controls of similar MLU and mental age (e.g., introduction, cohesion, character mental states; Finestack, Palmer, & Abbeduto, 2012; Hogan-Brown, Losh, Martin, & Mueffelmann, 2013).

Across several pragmatic skills, including non-contingency (Roberts et al., 2007), perseveration (G. E. Martin, Roberts, Helm-Estabrooks, Sideris, & Assal, 2012), narrative (Estigarribia et al., 2011), signaling of non-comprehension (G. E. Martin et al., 2017), semi-structured conversational interactions (Klusek, Losh, et al., 2014; Roberts et al., 2007), and performance on standardized assessments of pragmatic language (Losh, Martin, et al., 2012; G.E. Martin, Losh, Estigarribia, Sideris, & Roberts, 2013), males with FXS-ASD demonstrated significantly greater impairment than males with FXS-O, highlighting the impact of ASD symptomology on pragmatic language in this group. Together, this work suggests that a subset of individuals with FXS demonstrate qualitatively similar pragmatic impairments, such as conversational reciprocity, repetitive language, and narrative, to those with ASD-O. Cross population comparisons can inform whether these observed similarities in difficulties overlap in severity and frequency across these groups.

**Abilities Related to Pragmatic Competence in FXS**

It has been argued that intellectual disability underlies the presence of ASD symptoms, including pragmatic difficulties, in FXS (e.g., Hall, Lightbody, Hirt, Rezvani, & Reiss, 2010).

Prior research indicates that language ability in FXS significantly predicts ability to signal noncomprehension (Abbeduto et al., 2008) and referential communication (Abbeduto et al., 2006). Whereas theory of mind is centrally impaired in individuals with ASD and theorized to contribute to pragmatic deficits in this group, findings on theory of mind in FXS are mixed. Without accounting for ASD status, males with FXS present with theory of mind abilities comparable to other populations with cognitive impairment (e.g., Down syndrome or intellectual disability; Cornish et al., 2005; Garner, Callias, & Turk, 1999) as well as mental-age matched typically developing individuals (Abbeduto et al., 2001). Further, studies assessing relationships between theory of mind and pragmatic competence in FXS (without accounting for ASD status) found that theory of mind was not related to signaling of non-comprehension (Abbeduto et al., 2008) or referential communication (Abbeduto et al., 2006). However, and much like patterns observed in pragmatic language, individuals with FXS-ASD performed significantly or marginally worse on measures of theory of mind than those who did not meet criteria (Grant, Apperly, & Oliver, 2007; Lewis et al., 2006; Losh, Martin, et al., 2012), and it is possible that these deficits may uniquely underlie pragmatic difficulties in the context of ASD co-morbidity. In fact, Losh et al. (2012) found that improved theory of mind predicted pragmatic performance on a standardized measure in males with FXS-ASD. Finally, similar to ASD-O, individuals with FXS present with impairment in executive functioning (Garner et al., 1999; Hooper et al., 2008; Munir et al., 2000; Wilding et al., 2002); however, research on direct relationships between executive functioning and pragmatic competence is lacking.

It is also theorized that high levels of arousal impede the ability to self-regulate in individuals with FXS, resulting in feeling "on edge" during social interactions and subsequent withdrawal from social opportunities (Belser & Sudhalter, 1995; Cornish, Sudhalter, & Turk, 2004; Murphy, Abbecluto, Schroeder, & Serlin, 2007). It is hypothesized that over time, such withdrawal leads to reduced opportunities for social learning and subsequent difficulties in social competence (Rubin and Burgess, 1991). In a case study of two males with FXS greater arousal was related to increased perseveration (Belser & Sudhalter, 1995). In a larger sample of males with FXS, Klusek et al. (2013) found a marginal association between greater arousal change from a passive task to a conversational condition and pragmatic difficulties during a semi-naturalistic conversation task, further suggesting that autonomic dysregulation may impact pragmatic language in this group.

Investigation of related abilities in FXS suggests both potential common pathways (e.g., theory of mind) and differential contributions (e.g., structural language) to pragmatic language impairment relative to males with ASD-O, raising the question of whether common underlying mechanisms lead to comparable observed language features across groups. Cross-population investigations can begin to address these questions by observing areas of overalp in identical assessment contexts across groups.

## Cross-Population Comparisons

### Comparison of Pragmatic Language Skills

Prior work characterizing pragmatic language in ASD-O and FXS suggest several areas of similarity, including impairments in contingency, repetitive language, recognition and repair of conversational breakdowns, and narrative. However, cross-population comparisons are critical to discern more precisely the area of this overlap, and whether similar underlying abilities contribute to these skills. Table 2.1 summarizes cross-population studies of pragmatic language in these groups, reviewed in greater detail below.

Table 2.1 Review of Cross-Population Studies of Pragmatic Language in ASD-O and FXS

| **Study** | **Populations (n)** | **Assessments** | **Key Outcome Measures** | **Chronological Age** | **Mental Age or IQ: ASD-O** | **Mental Age or IQ: FXS-ASD** | **Matching and/or covariates included in group comparisons** |
|---|---|---|---|---|---|---|---|
| Losh et al. (2012) | ASD-O (28), FXS-ASD (40), FXS-O (21), DS (21), TD (20) | CCC-2; CASL | Standardized subscales of CCC-2 and CASL Pragmatic Judgment Age Equivalent | ASD-O (9.21), FXS-ASD (10.55), FXS-0 (9.61), DS (10.86), TD (4.84) | 5.88 | 5.02 | Covariates: MA, EVT, PPVT, MLU |
| Klusek et al. (2014) | ASD-O (29), FXS-ASD (38), FXS-O (16), DS (20), TD (20) | CASL, ADOS | CASL Pragmatic Judgment Age Equivalent and 34 conversational behaviors from Pragmatic Rating Scale-School Age | ASD-O (9.61), FXS-ASD (12.93), FXS-O (11.07), DS (12.90), TD (4.82) | 6.71 | 5.13 | Covariates: MA, EVT, PPVT, MLU |
| Paul et al. (1985) | FXS (15) ASD-O (12) Non-specific ID (12) | Spontaneous speech samples 5-10 minutes long during conversation with examiner | Vocal quality, rate of speech, intonation, echolalia, topic perseveration | FXS (38), ASD (37.5) | 2.70 | 4.13 | Matched: chronological age, IQ, length of institutional stay |
| Sudhalter et al. (1990) | ASD-O (12), FXS (12), DS (9) | Conversational context | Direct responses, initiation of new material, and topic maintenance | ASD-O (11.75), FXS (15.65), DS (13.9) | not assessed | not assessed | Matched: chronological age, Vineland Adaptive Behavior Scale, Vineland Adaptive Behavior Scale-Communication domain |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Ferrier et al. (1991) | ASD-O (18), FXS (18), DS (18) | 4 brief tasks: play, narrative retell, narrative about pictures, spontaneous conversation | Conversational roles, inappropriate utterances, failure to respond, self and other repetition (i.e., perseveration) | ASD (16.88), FXS (21.63) | 54.67 (IQ) | 52.8 (IQ; FXS overall) | Matched: chronological age, Vineland Adaptive Behavior Scale, Vineland Adaptive Behavior Scale-Communication domain |
| Belser and Sudhalter (2001) | ASD-O (10), FXS (10), nonspecific ID (10) | Semi-structured conversation | Utterance type, tangential language (comments, questions, responses) | ASD (19.7), FXS (18.7), ID (14.6) | not assessed | not assessed | Matched: chronological age, Vineland Adaptive Behavior Scale, Vineland Adaptive Behavior Scale-Communication domain |
| Hogan Brown et al. (2013) | ASD-O (20), FXS-ASD (23), FXS-O (18), DS (17), TD (16) | Picture book narrative | Microstructure (MLU, narrative length, complex syntax total and diversity); Macrostructure (evaluation, story structure, thematic maintenance) | ASD-O (9.04), FXS-ASD (10.28), FXS-O (9.73), DS (11.01), TD (4.55) | 5.74 | 5.03 | Matched: EVT and PPVT raw score composite; Covariate: mental age |
| Martin et al. (2017) | ASD-O (33), FXS-ASD (41), FXS-O (11), DS (16), TD (20) | Structured "barrier" task to assess signaling of non-comprehension | Nine signal types | ASD-O (9.8), FXS-ASD (12.4), FXS-O (11.9), DS (12.5), TD (6.1) | 7.6 | 5.1 | Covariates: MA, PPVT |
| Martin et al., in prep | ASD-O (26), FXS-ASD (46), FXS-O (13), DS (20), TD (19) | Autism Diagnostic Observation Schedule | Noncontingency, Perseveration, Initiations, Nonresponsiveness | ASD-O (9.0), FXS-ASD (10.4), FXS-O (9.7), DS (10.9), TD (5.2) | 6.1 | 5 | Covariates: MA, PPVT, EVT, MLU |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Barstein et al., under review | ASD-O (40), FXS-ASD (50), FXS-O (13), DS (22), TD (22) | Structured task to elicit communicative repair type | Verbal and supplementary repair strategies | ASD-O (9.1), FXS-ASD (10.7), FXS-O (9.7), DS (10.9), TD (5.0) | 7.1 | 5 | Covariates: MA, EVT, PPVT, MLU |

Note. *ADOS* = Autism Diagnostic Observation Schedule; *CCC-2*= Children's Communicative Checklist, 2nd Edition; *CASL* = Comprehensive Assessment of Spoken Language-Pragmatic Judgment Subscale; *EVT* = Expressive Vocabulary Test age equivalence; *MA*= mental age; *PPVT* = Peabody Picture Vocabulary Test age equivalence; *IQ* = intellectual quotient

Losh et al. (2012) directly compared performance of males with FXS-O, FXS-ASD, ASD-O, DS, and younger typically developing (TD) controls on the Children's Communicative Checklist Teacher Report-2nd edition, which assesses several domains of pragmatic language, including inappropriate initiation of interactions, stereotyped language, use of context, nonverbal communication, social relationships and interests (Bishop, 2003). After controlling for expressive and receptive vocabulary, nonverbal mental age, and mean length of utterance (MLU), males with FXS-ASD showed greater impairments in initiation of interaction relative to the ASD-O group. All clinical groups did not differ from each other and demonstrated greater impairments relative to TD controls in the domains of context and scripted language, and males with ASD-O, FXS-ASD and FXS-O also demonstrated greater impairment in nonverbal communication.

Direct assessment of pragmatic language more clearly distinguishes males with FXS-ASD and ASD-O from other clinical groups. For example, Losh et al. (2012) and Klusek et al. (2014) directly compared a partially overlapping sample of males with FXS-O, FXS-ASD, ASD-O, DS and TD of comparable mental age in their performance on a standardized measure of pragmatic language. Controlling for mental age, receptive vocabulary, expressive vocabulary, and MLU, males with FXS-ASD and ASD-O did not differ and performed more poorly than males with FXS-O and TD. Klusek et al. (2014) applied the Pragmatic Rating Scale-School Age (PRS-SA) to language samples from the Autism Diagnostic Observation Schedule (ADOS) for males with FXS-ASD, FXS-O, ASD-O, DS and TD. The PRS-SA is a 34-item measure that captures a range of pragmatic behaviors rated on a scale of 0 (absent) -2 (impairment clearly present) (Landa, 2011). After controlling for mental age, expressive and receptive vocabulary age equivalence and MLU, males with ASD-O and FXS-ASD showed the greatest rates of total pragmatic violations, followed by males with FXS-O and DS, who were in turn more impaired than TD controls.

Klusek et al. (2014) further examined the *types* of violations committed by males with ASD-O, FXS-ASD and FXS-O, and results suggested both overlap and divergence of specific pragmatic skills. Males with FXS-ASD and ASD-O demonstrated similar levels of impairment in acknowledgment of their conversational partner, topic elaboration, and reciprocity, which distinguished them from those with FXS-O. Males with FXS, regardless of ASD status, also showed comparable rates of atypical intonation, scripting and inappropriate topic shifts to males with ASD-O. Areas of difference also emerged, in that males with ASD-O demonstrated more atypical signaling of humor and inappropriate modulation of volume.

Prior work focusing on tallying discrete instances of a specific social-communicative behavior offer further insight as to the quantity of specific pragmatic behaviors that may contribute to perceived overlap in impairment. Early research comparing the conversational behaviors of males with ASD-O and FXS (without accounting for ASD status), matched on either chronological age and IQ (Ferrier, Bashir, Meryash, Johnston, & Wolff, 1991) or chronological age and communicative and adaptive functioning (Besler & Sudhalter, 2001) indicated that males with FXS and ASD-O did not differ in their elicitation or continuation of conversational responses. Some studies found that males with FXS demonstrated greater rates of perseveration and tangential language (Besler & Sudhalter, 2001; Ferrier et al., 1991; Sudhalter et al., 1990) than those with ASD-O, and Ferrier et al. (1991) hypothesized that males with FXS may uniquely rely on self-repetition to maintain social interactions. However, Paul et al. (1985) found that adult males with ASD, with FXS and a nonspecific ID group matched on chronological age, IQ and length of institutional stay did not differ in topic level perseveration, although males with ASD-O used more echolalia than other groups. Males with ASD-O have also been found to demonstrate more instances of utterances that violated multiple conversational rules (Besler & Sudhalter, 2001; Ferrier et al., 1991) during conversational tasks.

Recently, Martin et al. (in preparation), compared topic initiation, contingency and responsiveness, and perseveration in school-aged males with FXS-ASD, FXS-O, ASD-O, DS and TD using language samples derived from the Autism Diagnostic Observation Schedule, a semi-naturalistic assessment that is considered a gold-standard ASD diagnostic tool (Lord et al., 2001). Males with FXS-ASD and ASD-O demonstrated similar rates of noncontingency that distinguished them from males with DS, FXS-O and TD, even after accounting for mental age, expressive vocabulary age equivalence, receptive vocabulary age equivalence, and MLU. Similarly, males with FXS-ASD and ASD-O did not differ and were more perseverative than males with DS and FXS-O, although neither group differed from controls. However, males with ASD-O demonstrated significantly reduced initiation, and marginally greater non-responsiveness to their conversational partner, than males with FXS-ASD, demonstrating unique pragmatic deficits in this group

An alternative approach to comparing pragmatic language skills during semi-naturalistic interactions is to examine performance during tasks specifically designed to elicit a skill. Such an approach has been used to examine the recognition and response to communication breakdowns (i.e., misunderstandings), which rely on structured paradigms in which an examiner is purposefully unclear or explicitly prompts for clarification. Martin et al. (2017) and Barstein et al. (under review) compared a largely overlapping sample of males with FXS-O, FXS-ASD, ASD-O, TD and DS in their ability to both signal confusion (Martin et al., 2017) and respond to requests for clarification (Barstein et al., under review) during a communicative breakdown. In both contexts, males with FXS-ASD showed *greater* impairment relative to males with ASD-O (Martin et al., 2017; Barstein et al., under review). Although males with ASD-O did not significantly differ from TD controls in either task, they failed to respond to prompts for clarification at greater rates than males with FXS-ASD and FXS-O, suggesting that groups may show different types of impairment in repair-based contexts (Barstein et al., under review).

Finally, only one study has directly compared narrative ability in males with ASD-O and FXS. Hogan-Brown et al. (2013) compared narrative abilities during a picture book narration task in males with FXS-ASD, FXS-O, ASD-O, DS and TD matched on expressive and receptive vocabulary. They conducted analyses both with and without controlling for mental age; regardless, there were no group differences in macro-structural aspects of narrative (e.g., thematic maintenance, evaluation) or microstructural aspects of narrative (e.g., syntax).

Table 2.2 provides a visual summary of key areas of overlap and divergence across these groups, in which "X's" indicate areas of shared impairment. Overall, cross-population comparisons to date suggest specific areas of overlap in standardized assessment, topic contingency, severity of pragmatic language impairments observed in semi-naturalistic conversational contexts, and perseverative language during a semi-naturalistic conversation context. Males with FXS-ASD demonstrate potentially unique areas of impairment in initiation of interactions and communicative repair, whereas all groups demonstrated comparable abilities in the context of teacher report of several skills and narrative.

Table 2.2. Summary of Overlap in Impairments in Cross-Population Comparisons of Pragmatic Language in ASD and FXS in males with ASD-O, FXS-ASD and FXS-O

| | **ASD-O** | **FXS-ASD** | **FXS-O** |
|---|---|---|---|
| Teacher-Report: Initiation of Interaction | -- | **X** | -- |
| Teacher Report: Context, Scripted Language, Non-verbal Communication | -- | -- | -- |
| Standardized Assessment | **X** | **X** | -- |
| Total Pragmatic Violations | **X** | **X** | -- |
| Contingency | **X** | **X** | -- |
| Initiations | **X** | -- | -- |
| Non-Responsiveness | **X** | -- | -- |
| Perseveration | **X** | **X** | -- |
| Echolalia | **X** | -- | -- |
| Communicative Repair | -- | **X** | -- |
| Narrative | -- | -- | -- |

Note. X's indicate empirical reports of impairment.

## Cross Population Examination of Related Abilities

Cross population comparisons also afford the opportunity to examine whether similar skills contribute to performance during the same task across groups. Studies that included investigation of related abilities in the context of cross-population comparisons of pragmatic language are presented in Table 2.3.

Table 2.3 Related Abilities Assessed in Cross-Population Studies of Pragmatic Language

| Study | Primary Outcome Variables | Related Abilities/Mechanisms Assessed |
|---|---|---|
| Losh et al. (2012) | Standardized subscales of CCC-2 and CASL Pragmatic Judgment Age Equivalent | Theory of mind performance, *FMR1* variation |
| Klusek et al. (2013) | CASL Pragmatic Judgment Age Equivalent and 34 conversational behaviors from Pragmatic Rating Scale-School Age | Cardiac indices of physiological arousal (inter-beat-interval and vagal tone) during two contexts: passive and conversational |
| Klusek et al. (2014) | CASL Pragmatic Judgment Age Equivalent and 34 conversational behaviors from Pragmatic Rating Scale-School Age | Relative contributions of mental age, expressive and receptive vocabulary, and mean length of utterance |
| Hogan Brown et al. (2013) | Narrative microstructure (MLU, narrative length, complex syntax total and diversity); Narrative macrostructure (evaluation, story structure, thematic maintenance) | Contribution of mental age |
| Barstein et al. (under review) | Verbal and supplementary repair strategies | Mental age, EVT and PPVT, performance on measures of theory of mind |
| Bush et al. (in preparation) | Noncontingency, Perseveration, Initiations, Nonresponsiveness | Theory of mind, parent-reported executive functioning impairments |

Note. *CCC-2*= Children's Communicative Checklist, 2nd Edition; *CASL* = Comprehensive Assessment of Spoken Language-Pragmatic Judgment Subscale; *MA*= mental age, *EVT*= Expressive Vocabulary Test age equivalence, *PPVT*= Peabody Picture Vocabulary Test age equivalence

Klusek et al. (2014) examined the relative contributions of mental age, expressive and receptive vocabulary, and mean length of utterance in performance on the CASL-pragmatic judgment subscale and PRS-SA ratings of semi-naturalistic interactions in males with ASD-O and FXS. Mental age, expressive and receptive vocabulary, and mean length of utterance accounted for significant variation in performance on standardized measures in both groups, but contributed to clinical-behavioral ratings for the FXS group only. Similarly, Barstein et al. (under review) found that mental age and structural language correlated with signaling and repair of communicative breakdown in males with FXS-ASD, but that these relationships were more limited in males with ASD-O. In a narrative context, Hogan-Brown et al. (2013) found that mental age predicted macrostructural (e.g., evaluative) aspects of narrative across groups, but that there was a significant interaction between mental age and microstructure in the ASD-O group, in that they showed a significant increase in the use of complex syntax with mental age relative to a more gradual increase in males with FXS. This divergence in relationships with related abilities suggest that groups may differentially draw on underlying cognition and structural language across assessment contexts.

Whereas theory of mind competence related to improved performance on a standardized measure of pragmatic language in males with ASD-O, FXS-ASD, and FXS-O (as well as those with DS and TD; Losh et al., 2012), as well as the ability to repair communicative breakdowns in males with FXS-O (Barstein et al., under review), unpublished results from our group suggests that these relationships were not replicated when assessing discrete pragmatic skills during semi-naturalistic conversations, including initiations, perseveration, contingency, and responsiveness (Bush et al., in prep), or repair of communicative breakdown in males with FXS-ASD (Barstein et al., under review). Bush et al. (in preparation) examined links between parent-reported difficulties in executive functioning and pragmatic language in males with ASD-O, FXS-ASD and FXS-O and found that increased impairment in executive functioning related to non-contingency and perseveration in boys with ASD-O only, suggesting that boys with ASD-O may uniquely draw on executive functioning skills in more open-ended contexts.

One study has compared the contributions of physiological arousal to pragmatic competence in males with ASD-O and FXS. Klusek et al. (2013) examined indices of physiological arousal (heart rate, vagal tone) during a passive task (i.e., watching a movie) and brief conversation with the examiner in males with FXS and ASD-O. They found that both groups demonstrated comparable levels of arousal during both contexts, but differing patterns of relationships across groups. Whereas reduced arousal (i.e., dampened vagal tone) predicted increased pragmatic impairment in the ASD-O group, increased arousal (inter-beat-interval changes from a passive to conversational task) marginally related to increased pragmatic impairment in the FXS group (Klusek, Martin, & Losh, 2013). The fact that both males with ASD and FXS demonstrated comparable levels of arousal during a conversation task suggest a common underlying neurobiology that may be commonly influenced by variation in the *FMR1* gene. However, at the same time, results suggest unique pathways by which autonomic dysregulation may impact pragmatic language specifically in these groups, in that increased arousal improved pragmatic abilities in males with ASD-O but was related to greater impairment in XS.

Although few studies have directly compared relationships between abilities related to pragmatics and subsequent pragmatic competence in males with ASD-O and FXS, to date findings suggest that the abilities drawn on by both groups may vary by context, and that common underlying pathophysiological variation may contribute in unique ways to perceived deficits.

## Discussion

Defining pragmatic language phenotypes that cut across idiopathic ASD (ASD-O) and FXS provides a valuable opportunity to discern shared or divergent etiologic pathways to complex language behaviors. A systematic review of the literature suggests that individuals with ASD-O and FXS, and particularly those with FXS-ASD, demonstrate qualitatively similar impairments across a range of pragmatic features, such as contingency, perseveration, and narrative. Further, several studies indicate that the presence of ASD symptoms negatively impacts pragmatic functioning in FXS, highlighting a potential homogenous subgroup within males with FXS that may guide understanding of the pathway from *FMR1* variation to autism symptomology.

However, there are relatively few direct comparisons of males with FXS and ASD-O (total = 9), and even fewer that have accounted for ASD status within the FXS group (total = 4 published, 2 in prep or under review). These studies suggest a more complex picture of overlap, with areas of shared impairment (e.g., severity as assessed by standardized measures, conversational reciprocity during a semi-naturalistic interaction, repetitive language) but also differences in initiations and responsiveness during a semi-naturalistic conversation, and during more structured tasks assessing non-comprehension and communicative repair. Prior work also suggests that males with ASD-O and FXS-ASD may differentially draw on related skills, such as structural language, theory of mind, and executive function, depending on the assessment context and skill assessed.

Phenotypic differences are equally critical to recognize as shared overlap across disorders. It has been argued elsewhere that divergence in ASD related phenotypes in FXS and ASD-O suggests that the presence of ASD symptoms in FXS may be better accounted for by cognitive and language delays (Abbeduto et al., 2014; Hall et al., 2010). A review of current research confirms that the social-communicative phenotype of ASD symptoms in FXS-ASD is not identical to ASD-O. Indeed, simplifying the overlap (or lack thereof) in pragmatic features between ASD-O and FXS-ASD does not appear to represent the complexity of the social-communicative phenotype of these disabilities. Rather, a more fruitful approach may be to focus on specific shared phenotypes across FXS-ASD and ASD-O that may more directly map to shared genetic and neurobiological pathways.

To this end, the current review suggests that specific features of pragmatic language related to conversational reciprocity (e.g. acknowledgment, elaboration of conversational partner) and perseveration during more open-ended, naturalistic tasks may represent key targets for further investigation of overlap. Integrating findings from prior work also offers insight as to the importance of considering cognitive and language functioning, potential common or distinct contributing mechanisms in these groups, the role of assessment context in patterns of overlap, and directions for future research.

**Role of Cognitive and Language Functioning**

Methods to match populations, and the functioning of populations included, likely impacts inconsistency in findings to date. Because pragmatic language, or the use of language in social context, inherently draws on structural language, accounting for potential differences between groups may be key to identifying the specific nature of pragmatic deficits above and beyond expectations for language ability (see G. E. Martin, Lee, & Losh, 2016, for review).

However, assessment of these abilities (and subsequent accounting for language differences) varied across prior work, ranging from parent-reported impairment (e.g., Vineland interview of adaptive function) to standardized measures. Given the rarity of single gene disorders such as FXS, samples included often represented a wide range chronological ages, nonverbal and verbal functioning, which may confound observed overlap. In the cross-population studies included in the current review, the average chronological age ranged from 9 years to 38 years, mental age ranged from 2 years-7 years, and language ability (when assessed), was primarily in the 5-6 year age equivalence range for expressive and receptive vocabulary. Inconsistencies in patterns observed in perseverative language in prior work exemplifies the possibility that variation in sample characteristics, and methods used to control for related abilities, play a role in divergent findings. Whereas Besler and Sudhalter (2001); Ferrier et al., 1991, and Sudhalter et al., (1990) found that adolescent males and young adults with FXS used more perseverative language than males with ASD, Paul et al. (1985) found no differences in an older, substantially more cognitively impaired group. More recently, Martin et al. (in preparation) accounted for both ASD status but also structural language, and found overlap in perseveration across males with ASD-O and FXS-ASD. Such discrepancies suggest the importance of considering the role of age, functioning and accounting for structural language when considering overlap in these groups.

Given that males with FXS and ASD-O present with heterogeneous levels of cognitive and structural language, it is important to consider whether overlap or divergence may be unique at distinct levels of ability. Lee et al. (2016) examined ASD symptoms longitudinally in males with FXS and found that symptoms related to social-communication increased with chronological age (and in particular increases in structural language), highlighting how comparisons at a single time point may mask impairments observed at a later age. Such findings may extend to specific pragmatic skills. For example, Hogan et al. (2013) hypothesized that the younger mental age of participants included in their study of narrative ability may have obscured potential differences that may be evident in higher functioning samples. In typical development, children as young as three years old begin to use simple evaluative devices in narrative, such as varying the tone of their voice for emphasis or labeling emotions; however, in later adolescence and adulthood (after acquiring more complex grammatical structures), begin to use more sophisticated evaluation, such as including multiple perspectives or drawing connections between a specific narrative event and global theme (Berman & Slobin, 1994). Therefore, it is possible that while individuals with ASD or FXS with lower language levels may demonstrate similar skill in fundamental narrative ability, those with greater language or cognitive ability may show more impairment in their ability to include more sophisticated devices. Together, this review highlights the importance of considering language and cognition when interpreting prior work in ASD and FXS.

**Variation in Abilities Related to Pragmatics**

To date, only four published studies, and two in prep or under review, have examined abilities related to pragmatic competence across groups in the same context, and those that have provide a mixed picture of results. Replicating work examining related abilities within FXS (e.g., Abbeduto et al., 2006; Abbeduto et al., 2008), cross-population comparisons continue to highlight the role of structural language, across both structured and across semi-naturalistic contexts (Barstein et al., under review; Klusek et al., 2014). These relationships were less prominent in males with ASD-O included in the same studies, which is perhaps unsurprising given prior work suggesting more distinction between structural language and pragmatic competence in this group (see Tager-Flusberg, 2005, for review). Further replicating prior work in ASD (e.g., Baron-Cohen et al., 1985; Baron-Cohen et al., 1988; Lisa Capps et al., 1998; Capps et al., 2000; Losh & Capps, 2003; Loveland & Tunali, 1993; Surian et al., 1996; Tager-Flusberg & Sullivan, 1995), theory of mind related to performance on a standardized task of pragmatic competence (Losh et al., 2012). These studies have also identified areas of divergence, such as executive function during semi-naturalistic interactions (Bush et al., in prep), the contribution of mental age in narrative (Hogan-Brown et al., 2013) and relationships between indices of arousal and pragmatic impairment (Klusek et al., 2013). Given the limited research to date, it remains a question as to whether differences in observed related abilities index unique pathways to common observed phenotypes. Research to date, however, suggests that much like patterns of phenotypic overlap, areas of overlap in related abilities may differ based on the specific pragmatic skill assessed, as well as assessment context.

**The Role of Assessment Context**

The current review suggests that assessment context is critical to consider when determining specific overlapping pragmatic skills across groups. In any assessment of pragmatic skill, context is important to consider because expectations for pragmatic competence vary widely based on the social context (e.g., children vs. adult, play based vs. structured). Such a consideration is particularly relevant for individuals with ASD-O, who show greater impairment in less structured contexts (Losh & Capps, 2003; Losh & Gordon, 2014; G. E. Martin et al., 2017; Nadig, Lee, Singh, Bosshart, & Ozonoff, 2010). Current findings suggest that males with FXS-ASD demonstrate greater impairment than males with ASD-O in the context of structured tasks (e.g., Barstein et al., under review; Martin et al., 2017). Research is needed to determine whether the relative strengths of males with ASD-O relative to FXS-ASD in some domains such as communicative repair persist in more naturalistic contexts. It will also be important to examine why males with FXS-ASD do not show the same advantages as males with ASD-O in more structured contexts. Many language interventions for males with ASD-O are highly structured, and it may be that males with FXS-ASD included in research were not exposed to similar strategies given the lower prevalence of clinical diagnoses relative to research classification in this group (Klusek, Martin, & Losh, 2014). Conversely, differences in related abilities may play a role in observed differences in structured contexts. Whereas the theory of mind deficits in ASD hypothesized to related to pragmatic competence may be scaffolded by increased structure (e.g., with pictures of characters to help sequence, clear requests for communicative repair), related abilities such as structural language in FXS may be less influenced by structure.

In contrast, a synthesis of prior work suggests clearer overlap in males with ASD-O and FXS-ASD (as well as FXS without accounting for ASD status) in semi-naturalistic contexts (Besler & Sudhalter, 2001; Ferrier, Bashir, Meryash, Johnston, & Wolff, 1991; Klusek et al., 2014). Semi-naturalistic contexts represent a “gold standard” for pragmatic assessment (Adams, 2002; McTear & Conti-Ramsden, 1992; Prutting & Kittchner, 1987; Roth & Spekman, 1984). Importantly, the current review suggests that less structured contexts elicit areas of similarity (as well as important divergence) across males with FXS-ASD and ASD-O. Future work is needed to continue to explore the role of context on observed similarities, differences, and related abilities across these groups.

**Directions for Future Research**

The current review highlights several directions for future research. First, it should be acknowledged that many of the studies included in the current review drew from partially overlapping samples (e.g., studies authored by Losh, Martin, Lee and Barstein). Although this offers an advantage in consistent methodologies and classification of individuals with FXS and co-morbid ASD, it will also be important for other groups to replicate and extend the current work, particularly related to specific areas of overlap in FXS-ASD and ASD-O. Further, several pragmatic skills have not yet been directly compared across these populations. A particularly useful target of future investigation may be more objective measures of suprasegmental features of speech (e.g., rate, rhythm, intonation), that are impaired in ASD-O (Diehl & Paul, 2012; Diehl & Paul, 2013), and have been shown to be impacted by ASD status in FXS (Zajac, Harris, Roberts, & Martin, 2009).

Given variation in samples included in prior work, longitudinal studies represent a critical next step in characterizing pragmatic language in these groups. Longitudinal studies address the limitations of group comparisons (which often included a range of abilities) by characterizing the sequence of development of skills across disabilities, and may provide insight as to whether disabilities evidence unique "developmental signatures" of pragmatic competence (Cornish, Roberts, & Scerif, 2012; Karmiloff-Smith, 1998). Such an approach may also lend insight as to whether related abilities differ across development, or how development in one domain (e.g., structural language) differentially influences outcomes across groups. Given that the majority of studies to date have focused on school aged-late adulthood, research is also needed examining early pragmatic skills across infants and young children with ASD and FXS.

Whereas Losh et al. (2012) found that *FMR1* related variation predicted increased pragmatic competence on a standardized measure of pragmatic language, few studies have examined links between genetic variation and specific pragmatic phenotypes, or potential moderators of this relationship. Such approaches have proven fruitful for other ASD-related phenotypes across ASD and FXS, such as investigations of gray and white matter volume and a-priori selected brain regions related to restricted and repetitive behaviors in both groups (Hoeft et al., 2011; Wolff et al., 2012; Wolff, Hazlett, Lightbody, Reiss, & Piven, 2013). Klusek et al. (2013)'s examination of autonomic arousal in males with ASD-O and FXS represents a promising direction in this regard. Given that prior cross-population comparisons of FXS-ASD and ASD-O suggest specific overlapping features, such as conversational reciprocity or perseveration, inclusion of assessment of specific pragmatic skills (as opposed to broader measures of symptom severity) in relation to underlying physiology or neurocognitive features may be most fruitful to identifying specific pathways from *FMR1* variation to shared phenotypes.

Future work should also consider sex differences in pragmatic language within and across both disorders. Sex differences in pragmatic and structural language are present in typical development (Berghout, Salehi, & Leffler, 1987; Cook, Fritz, McCornack, & Visperas, 1985; Kothari, Skuse, Wakefield, & Micali, 2013; Leaper, 1991; Sigleman & Holtz, 2013), and there is evidence to suggest sex differences in ASD and FXS. Prior work has shown greater impairment in social abilities in females with ASD relative to males; however, these differences appeared to be driven by lower IQ in females with ASD (see Rivet and Matson, 2011, for review). Other work has suggested that females with ASD engage in strategies to "camouflage" social impairment, such as mimicking the actions of typical peers (e.g., Lai et al., 2011). Females with FXS show less severe cognitive delays than their male counterparts, as the presence of a healthy X chromosome (which includes an FMRP producing copy of FMR1), and show lower rates of co-morbid ASD (Klusek et al., 2014; Lee et al., 2016). Given differences observed in both groups, it is important to examine the nature of overlap in females with both disorders to inform how phenotypes, and potentially related mechanisms, may express differently within sexes.

Although not a primary focus of this review, results may inform future directions for intervention. Increased ASD related symptoms in FXS have been associated with greater impairments in adaptive functioning and increased rates of problem behaviors; thus, it has been proposed that early access to ASD-specific interventions may improve long-term outcomes in FXS (Budimirovic et al., 2006; Kau et al., 2004; McCary & Roberts, 2013). Findings that ASD symptoms in FXS also increase pragmatic language impairments and difficulties in related domains further supports the need to assess for ASD symptoms and to develop tailored language interventions for this group. Results of this review suggest that such interventions should not be identical to those applied in ASD-O, but rather tailored to the specific strengths and challenges of individuals with FXS. Current research also suggests that multi-method assessment of pragmatic language may be best practice for both populations, given the variation in pragmatic impairments observed based on contexts within and across groups.

**Conclusion**

In conclusion, careful delineation of specific shared pragmatic skills in males with ASD and FXS holds significant potential for guiding investigations of the role of *FMR1* in the development of complex clinical-behavioral presentations. Synthesizing prior work highlights the need for specificity in such comparisons, by identifying specific aspects of a complex skill that may best index shared genetic liability. Such comparisons may serve as a model for future investigations of shared phenotypes across disorders more broadly, by highlighting the importance of assessment context, identifying related abilities, and the need for developmental, longitudinal approaches.

**References**

Abbeduto, L., Brady, N., & Kover, S. T. (2007). Language development and fragile X syndrome: profiles, syndrome-specificity, and within-syndrome differences. *Mental Retardation and Developmental Disabilities Research Reviews, 13*(1), 36-46.

Abbeduto, L., McDuffie, A., & Thurman, A. J. (2014). The fragile X syndrome–autism comorbidity: what do we really know? *Frontiers in Genetics, 5*, 355.

Abbeduto, L., & Murphy, M. M. (2004). Language, social cognition, maladaptive behavior, and communication in Down syndrome and fragile X syndrome. In M. L. Rice & S. F. Warren (Eds.), *Developmental Language Disorders: From Phenotypes to Etiologies* (pp. 77-97). New Jersey: Lawrence Erlbaum.

Abbeduto, L., Murphy, M. M., Kover, S. T., Karadottir, S., Amman, A., & Bruno, L. (2008). Signaling noncomprehension of language: A comparison of fragile X syndrome and Down syndrome. *American Journal on Mental Retardation, 113*, 214-230.

Abbeduto, L., Murphy, M. M., Richmond, E. K., Amman, A., Beth, P., Weissman, M. D., . . . Karadottir, S. (2006). Collaboration in referential communication: Comparison of youth with Down syndrome or fragile X syndrome. *American Journal of Mental Retardation, 111*(3), 170-183.

Abbeduto, L., Pavetto, M., Kesin, E., Weissman, M. D., Karadottir, S., O'Brien, A., & Cawthon, S. (2001). The linguistic and cognitive profile of Down syndrome: Evidence from a comparison with fragile X syndrome. In *Down Syndrome: Research & Practice*: Down Syndrome Educational Trust.

Adams, C. (2002). Practitioner review: the assessment of language pragmatics. *Journal of child psychology and psychiatry, and allied disciplines, 43*(8), 973-987.

Adams, R. B., Rule, N. O., Franklin, R. G., Wang, E., Stevenson, M. T., Yoshikawa, S., . . . Ambady, N. (2010). Cross-cultural reading the mind in the eyes: an fMRI investigation. *J Cogn Neurosci, 22*(1), 97-108.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (5th ed.). Arlington, VA: American Psychiatric Association.

Ashby, S. A., Channell, M. M., & Abbeduto, L. (2017). Inferential language use by youth with Down syndrome during narration. *Res Dev Disabil, 71*, 98-108.

American Speech-Language Hearing Association (2015). American Speech-Language-Hearing Association. Retrieved from www.asha.org

Bagni, C., & Oostra, B. A. (2013). Fragile X syndrome: From protein function to therapy. *Am J Med Genet A, 161A*(11), 2809-2821.

Bailey, D. B., Mesibov, G., Hatton, D. D., Clark, R. D., Roberts, J. E., & Mayhew, L. (1998). Autistic behavior in young boys with fragile X syndrome. *Journal of Autism and Developmental Disorders, 28*(6), 499-508.

Baron-Cohen, S. (2000). Theory of mind and autism: A fifteen year review. In S. Baron-Cohen, H. Tager-Flusberg, & D. J. Cohen (Eds.), *Understanding other minds: Perspectives from developmental cognitive neuroscience (2nd ed.)* (pp. 3-20). New York, NY: Oxford University Press.

Baron-Cohen, S., Leslie, A. M., & Frith, U. (1985). Does the autistic child have 'theory of mind'? *Cognition, 21*, 37-46.

Baron-Cohen, S., Leslie, A. M., & Frith, U. (1988). Soical and pragmatic deficitis in autism: Cognitive or affective? *Journal of Autism and Developmental Disorders, 18*, 379-403.

Baron-Cohen, S., & Swettenham, J. (1997). Theory of mind in autism: its relationship to executive function and central coherence. In D. J. Cohen & F. R. Volkmar (Eds.), Handbook for autism and pervasive developmental disorders (pp. 880–893). New York: Wiley.

Barstein, J., Martin, G.E., Lee, M. & Losh, M. (under review). A duck wearing boots?! Pragmatic language strategies for repairing communication breakdowns across genetically-based neurodevelopmental disabilities.

Bear, M. F., Huber, K. M., & Warren, S. T. (2004). The mGluR theory of fragile X mental retardation. *Trends in Neurosciences, 27*(7), 370-377.

Belser, R. C., & Sudhalter, V. (1995). Arousal difficulties in males with fragile X syndrome: A preliminary report. *Developmental Brain Dysfunction, 8*(4-6), 270-279.

Bennetto, L., Pennington, B. F., Hagerman, R. J., & Cronister, A. J. (2002). The neuropsychology of fragile X syndrome. In Anonymous (Ed.), (Vol. 2nd, pp. 210-248). Balitmore, MD: Johns Hopkins University Press.

Berghout Austin, A. M., Salehi, M., & Leffler, A. (1987). Gender and developmental differences in children's conversations. *Sex Roles, 16*(9-10), 497-510.

Berman, R., & Slobin, D. (Eds.). (1994). *Relating events in narrative: A cross-linguistic developmental study*. Hillsdale, NJ: Erlbaum.

Besler, R. C., & Sudhalter, V. (2001). Conversational characteristics of children with fragile X syndrome: Repetitive speech. *American Journal of Mental Retardation, 106*, 28-38.

Bishop, D. (2003). *The Children's Communication Checklist-2*. London: The Psychological Corporation.

Boucher, J. (2012). Research review: structural language in autistic spectrum disorder - characteristics and causes. *J Child Psychol Psychiatry, 53*(3), 219-233.

Bruner, J. (1987). Life as Narrative. *Social Research, 54*(1), 11-32.

Bruner, J. (1990). *Acts of meaning*. Cambridge, MA: Harvard University Press.

Bruner, J. (1991). The Narrative Construction of Reality. *Critical Inquiry, 18*(1), 1-21. doi:10.1086/448619

Budimirovic, D. B., Bukelis, I., Cox, C., Gray, R. M., Tierney, E., & Kaufmann, W. E. (2006). Autism spectrum disorder in fragile X syndrome: Differential contribution of adaptive socialization and social withdrawal. *American Journal of Medical Genetics Part A, 9999*, 1-13.

Capps, L., Kehres, J., & Sigman, M. (1998). Conversational Abilities Among Children with Autism and Children with Developmental Delays. *Autism, 2*(4), 325-344.

Capps, L., Losh, M., & Thurber, C. (2000). The frog ate a bug and made his mouth sad: Narrative competence in children with autism. *Journal of Abnormal Child Psychology, 28*, 193-204.

Castelli, I., Baglio, F., Blasi, V., Alberoni, M., Falini, A., Liverta-Sempio, O., . . . Marchetti, A. (2010). Effects of aging on mindreading ability through the eyes: an fMRI study. *Neuropsychologia, 48*(9), 2586-2594.

Channell, M. M., McDuffie, A. S., Bullard, L. M., & Abbeduto, L. (2015). Narrative language competence in children and adolescents with Down syndrome. *Front Behav Neurosci, 9*, 283.

Ciccia, A. H., & Turkstra, L. S. (2002). Cohesion, communication burden, and response adequacy in adolescent conversations. *Advances in Speech Language Pathology, 4*(1), 1-8.

Clifford, S., Dissanayake, C., Bui, Q. M., Huggins, R., Taylor, A. K., & Loesch, D. Z. (2007). Autism spectrum phenotype in males and females with fragile X full mutation and premutation. *Journal of Autism and Developmental Disorders, 37*(4), 738-747.

Colle, L., Baron-Cohen, S., Wheelwright, S., & van der Lely, H. K. (2008). Narrative Discourse in Adults with High Functioning Autism or Asperger Syndrome. *Journal of Autism and Developmental Disorders, 38*, 28-40.

Cook, A. S., Fritz, J. J., McCornack, B. L. & Visperas, C. (1985). Early gender differences in the functional usage of language. *Sex Roles, 12*(9–10), 909–915.

Cornish, K., Burack, J. A., Rahman, A., Munir, F., Russo, N., & Grant, C. (2005). Theory of mind deficits in children with fragile X syndrome. *J Intellect Disabil Res, 49*(Pt 5), 372-378.

Cornish, K., Roberts, J. E., & Scerif, G. (2012). Editorial: capturing developmental trajectories of change in persons with intellectual and developmental disability. *Am J Intellect Dev Disabil, 117*(2), 83-86.

Cornish, K., Sudhalter, V., & Turk, J. (2004). Attention and Language in Fragile X. In *Fragile X Syndrome: Frontiers of Understanding Gene-Brain-Behavior Relationships*: John Wiley & Sons.

Cuthbert, B. N., & Insel, T. R. (2013). Toward the future of psychiatric diagnosis: the seven pillars of RDoC. *BMC Med, 11*, 126.

D'Hulst, C., De Geest, N., Reeve, S. P., Van Dam, D., De Deyn, P. P., Hassan, B. A., & Kooy, R. F. (2006). Decreased expression of the GABAA receptor in fragile X syndrome. *Brain Res, 1121*(1), 238-245.

D'Hulst, C., & Kooy, R. F. (2007). The GABAA receptor: a novel target for treatment of fragile X? *Trends Neurosci, 30*(8), 425-431.

D'Hulst, C., & Kooy, R. F. (2009). Fragile X syndrome: from molecular genetics to therapy. *J Med Genet, 46*(9), 577-584.

Darnell, J. C., Van Driesche, S. J., Zhang, C., Hung, K. Y., Mele, A., Fraser, C. E., . . . Darnell, R. B. (2011). FMRP stalls ribosomal translocation on mRNAs linked to synaptic function and autism. *Cell, 146*(2), 247-261.

de Villiers, J., Fine, J., Ginsberg, G., Vaccarella, L., & Szatmari, P. (2007). Brief report: a scale for rating conversational impairment in autism spectrum disorder. *J Autism Dev Disord, 37*(7), 1375-1380.

Dove, A., Pollmann, S., Schubert, T., Wiggins, C. J., & von Cramon, D. Y. (2000). Prefrontal cortex activation in task switching: an event-related fMRI study. *Brain Res Cogn Brain Res, 9*(1), 103-109.

Estigarribia, B., Martin, G. E., Roberts, J. E., Spencer, A., Gucwa, A., & Sideris, J. (2011). Narrative skill in boys with fragile X syndrome with and without autism spectrum disorder. *Applied Psycholinguistics*, 359-388.

Farzin, F., Perry, H., Hessl, D., Loesch, D., Cohen, J., Bacalman, S., . . . Hagerman, R. (2006). Autism spectrum disorders and attention-deficit/hyperactivity disorder in boys with the fragile X premutation. *Journal of Developmental and Behavioral Pediatrics, 27*(Supplement 2), S137-144.

Ferrier, L. J., Bashir, A. S., Meryash, D. L., Johnston, J., & Wolff, P. (1991). Conversational skills of individuals with fragile-X syndrome: a comparison with autism and Down syndrome. *Developmental Medicine and Child Neurology, 33*(9), 776-788.

Finestack, L. H., Palmer, M., & Abbeduto, L. (2012). Macrostructural narrative language of adolescents and young adults with Down syndrome or fragile X syndrome. *American Journal of Speech-Language Pathology, 21*, 29-46.

Fiske, S., & Taylor, S. (1991). *Social cognition*. New York: McGraw-Hill.

Fombonne, E. (2009). Epidemiology of pervasive developmental disorders. *Pediatric Research, 65*, 591-598.

Garber, K. B., Visootsak, J., & Warren, S. T. (2008). Fragile X syndrome. *Eur J Hum Genet, 16*(6), 666-672.

Garner, C., Callias, M., & Turk, J. (1999a). Executive function and theory of mind performance of boys with fragile-X syndrome. *J Intellect Disabil Res, 43 ( Pt 6)*, 466-474.

Geller, E. (1998). An investigation of communication breakdowns and repairs in verbal autistic children. *British Journal of Developmental Disabilities, 44*(87), 71-85.

Geurts, H. M., & Embrechts, M. (2008). Language profiles in ASD, SLI, and ADHD. *J Autism Dev Disord, 38*(10), 1931-1943.

Geurts, H. M., Verté, S., Oosterlaan, J., Roeyers, H., Hartman, C. A., Mulder, E. J., . . . Sergeant, J. A. (2004). Can the Children's Communication Checklist differentiate between children with autism, children with ADHD, and normal controls? *J Child Psychol Psychiatry, 45*(8), 1437-1453.

Gooch, D., Thompson, P., Nash, H. M., Snowling, M. J., & Hulme, C. (2016). The development of executive function and language skills in the early school years. *J Child Psychol Psychiatry, 57*(2), 180-187.

Gopnik, A., Meltzoff, A. N., & Kuhl, P. K. (1999). *The scientist in the crib: Minds, brains, and how children learn*. New York: Morrow.

Grant, C. M., Apperly, I., & Oliver, C. (2007). Is theory of mind understanding impaired in males with fragile X syndrome? *Journal of Abnormal Child Psychology, 35*(1), 17-28.

Grice, H. P. (1975). Logic and conversation. In P. C. Morgan & J.L (Eds.), *Syntax and Semantics 3: Speech Acts* (pp. 41-58). New York: Academic Press.

Hagerman, R., & Hagerman, P. (2002). *Fragile X Syndrome: Diagnosis, Treatment, and Research Third Edition*. Baltimore: Johns Hopkins University Press.

Hall, S. S., Lightbody, A. A., Hirt, M., Rezvani, A., & Reiss, A. L. (2010). Autism in fragile X syndrome: a category mistake? *Journal of the American Academy of Child and Adolescent Psychiatry, 49*(9), 921-933.

Hall, S. S., Lightbody, A. A., & Reiss, A. L. (2008). Compulsive, self-injurious, and autistic behavior in children and adolescents with fragile X syndrome. *American Journal of Mental Retardation, 113*(1), 44-53.

Hatton, D. D., Skinner, M., Sideris, J., Mankowski, J. B., Bailey, D. B., Roberts, J. E., & Mirrett, P. (2006). Autistic behavior in children with fragile X syndrome: Prevalence, stability, and the impact of FMRP. *American Journal of Medical Genetics, 140*(17), 1804-1813.

Hernandez, R. N., Feinberg, R. L., Vaurio, R., Passanante, N. M., Thompson, R. E., & Kaufmann, W. E. (2009). Autism spectrum disorder in fragile X syndrome: A longitudinal evaluation. *American Journal of Human Genetics, 149A*(6), 1125-1137.

Hoeft, F., Walter, E., Lightbody, A. A., Hazlett, H. C., Chang, C., Piven, J., & Reiss, A. L. (2011). Neuroanatomical differences in toddler boys with fragile x syndrome and idiopathic autism. *Arch Gen Psychiatry, 68*(3), 295-305.

Hogan-Brown, A. L., Losh, M., Martin, G. E., & Mueffelmann, D. (2013). An investigation of narrative ability in boys with autism and fragile X syndrome. A*merican Journal on Intellectual and Developmental Disabilities, 118(*2), 77-94.

Hooper, S. R., Hatton, D., Sideris, J., Sullivan, K., Hammer, J., Schaaf, J., . . . Bailey, D. P., Jr. (2008). Executive functions in young males with fragile X syndrome in comparison to mental age-matched controls: baseline findings from a longitudinal study. N*europsychology, 22(*1), 36-47.

Insel, T. R. (2014). The NIMH Research Domain Criteria (RDoC) Project: precision medicine for psychiatry. A*merican Journal of Psychiatry, 171(*4), 395-397.

CDC (2014). Prevalence of autism spectrum disorder among children aged 8 years - autism and developmental disabilities monitoring network, 11 sites, United States, 2010. M*MWR Surveill Summ, 63(*2), 1-21.

Karmiloff-Smith, A. (1998). Development itself is the key to understanding developmental disorders. T*rends Cogn Sci, 2(*10), 389-398.

Kau, A. S., Tierney, E., Bukelis, I., Stump, M. H., Kater, W. R., Trescher, W. H., & al., e. (2004). Social behavior profile in young males with fragile X syndrome: Characteristics and specificity. A*merican Journal of Medical Genetics, 126A(*1), 9-17.

Kaufmann, W. E., Cortell, R., Kau, A. S., Bukelis, I., Tierney, E., Gray, R. M., . . . Stanard, P. (2004). Autism spectrum disorder in fragile X syndrome: Communication, social interaction, and specific behaviors. A*merican Journal of Medical Genetics, 129(*3), 225-234.

Keller-Bell, Y. D., & Abbeduto, L. (2007). Narrative development in adolescents and young adults with fragile X syndrome. A*merican Journal on Mental Retardation, 112,* 289-299.

Keysor, C. S., & Mazzocco, M. M. (2002). A developmental approach to understanding Fragile X syndrome in females. M*icrosc Res Tech, 57(*3), 179-186. doi:10.1002/jemt.10070

Kjelgaard, M., & Tager-Flusberg, H. (2001). An investigation of language impairment in autism: Implications for genetic subgroups. L*anguage and Cognitive Processes, 16,* 287-308.

Klusek, J., Losh, M., & Martin, G. E. (2014). A comparison of pragmatic language in boys with autism and fragile X syndrome. J*ournal of Speech, Language, and Hearing Research, 57(*5), 1692-1707.

Klusek, J., Martin, G. E., & Losh, M. (2013). Physiological arousal in autism and fragile X syndrome: group comparisons and links with pragmatic language. A*m J Intellect Dev Disabil, 118(*6), 475-495.

Klusek, J., Martin, G. E., & Losh, M. (2014). Consistency between research and clinical diagnoses of autism among boys and girls with fragile X syndrome. J *Intellect Disabil Res, 58(*10), 940-952.

Kondo, H., Morishita, M., Osaka, N., Osaka, M., Fukuyama, H., & Shibasaki, H. (2004). Functional roles of the cingulo-frontal network in performance on working memory. N*euroimage, 21(*1), 2-14.

Kothari, R., Skuse, D., Wakefield, J., & Micali, N. (2013). Gender differences in the relationship between social communication and emotion recognition. *Journal of the American Academy of Child & Adolescent Psychiatry, 52*(11), 1148–1157.

Lam, Y. G., & Yeung, S. S. S. (2012). Towards a convergent account of pragmatic language deficits in children with high-functioning autism: Depicting the phenotype using the Pragmatic Rating Scale. *Research in Autism Spectrum Disorders, 6*(2), 792-797.

Landa, R. (2011). *The Pragmatic Rating Scale for School-Age Children (PRS-SA).* Unpublished manual.

Landa, R., Folstein, S. E., & Isaacs, C. (1991). Spontaneous narrative-discourse performance of parents of autistic individuals. *Journal of Speech and Hearing Research, 34*(6), 1339-1345.

Landa, R., Piven, J., Wzorek, M. M., Gayle, J. O., Chase, G. A., & Folstein, S. E. (1992). Social language use in parents of autistic individuals. *Psychological Medicine, 22*(1), 245-254.

Laws, G. (2004). Contributions of phonological memory, language comprehension and hearing to the expressive language of adolescents and young adults with Down syndrome. *Journal of Child Psychology and Psychiatry, 45*(6), 1085-1095.

Leaper, C. (1991). Influence and involvement in children's discourse: Age, gender, and partner effects. *Child Development, 62*(4), 797–781.

Lee, M., Martin, G. E., Berry-Kravis, E., & Losh, M. (2016). A developmental, longitudinal investigation of autism phenotypic profiles in fragile X syndrome. J *Neurodev Disord, 8,*

Lee, M., Martin, G. E., Hogan, A., Hano, D., Gordon, P. C., & Losh, M. (2017). What's the story? A computational analysis of narrative competence in autism. *Autism,* 1-10.

Lee, S. H., Ripke, S., Neale, B. M., Faraone, S. V., Purcell, S. M., Perlis, R. H., . . . (IIBDGC), (2013). Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. *Nat Genet, 45*(9), 984-994.

Levy, Y., Gottesman, R., Borochowitz, Z., Frydman, M., & Sagi, M. (Writers). (2006). Language in boys with fragile X syndrome. In J*ournal of Child Language.* US: Cambridge Univ Press.

Lewis, P., Abbeduto, L., Murphy, M., Richmond, E., Giles, N., Bruno, L., & Schroeder, S. (2006). Cognitive, language and social-cognitive skills of individuals with Fragile X Syndrome with and without autism. J*ournal of Intellectual Disability Research, 50,* 532-545.

Lord, C., Rutter, M., DeLavore, P. C., & Risi, S. (2001). *Autism Diagnostic Observation Schedule*. Los Angeles, CA: Western Psychological Services.

Losh, M., Adolphs, R., & Piven, J. (2011). The Broad Autism Phenotype. In G. Dawson, D. Amaral, & D. Geschwind (Eds.), A*utism Spectrum Disorders* (pp. 457-476). Oxford: Oxford University Press.

Losh, M., & Capps, L. (2003). Narrative ability in high-functioning children with autism or Asperger's syndrome. J*ournal of Autism and Developmental Disorders, 33(*3), 239-251.

Losh, M., & Gordon, P. C. (2014). Quantifying Narrative Ability in Autism Spectrum Disorder: A Computational Linguistic Analysis of Narrative Coherence. J*ournal of Autism and Developmental Disorders, 44(*12), 3016–3025.

Losh, M., Klusek, J., Martin, G. E., Sideris, J., Parlier, M., & Piven, J. (2012). Defining genetically meaningful language and personality traits in relatives of individuals with fragile X syndrome and relatives of individuals with autism. A*merican journal of medical genetics. Part B, Neuropsychiatric genetics : the official publication of the International Society of Psychiatric Genetics, 159B(*6).

Losh, M., Martin, G. E., Klusek, J., Hogan-Brown, A. L., & Sideris, J. (2012). Social communication and theory of mind in boys with autism and fragile x syndrome. F*ront Psychol, 3,* 266.

Loveland, K. A., McEvoy, R. E., & Tunali, B. (1990). Narrative story telling in autism and Down's syndrome. B*ritish Journal of Developmental Psychology, 8,* 9-23.

Loveland, K. A., & Tunali, B. (1993). Narrative Language in autism and the theory of mind hypothesis: A wider perspective. In S. Baron-Cohen, H. Tager-Flusberg, & D. J. Cohen (Eds.), U*nderstanding other minds: Perspectives from autism.* Oxford, UK: Oxford University Press.

Martin, G. E., Barstein, J., Hornickel, J., Matherly, S., Durante, G., & Losh, M. (2017). Signaling of noncomprehension in communication breakdowns in fragile X syndrome, Down syndrome, and autism spectrum disorder. J *Commun Disord, 65,* 22-34.

Martin, G. E., Lee, M., & Losh, M. (2016). Intellectual Disability. In I. L. Cummings (Ed.), R*esearch in Clinical Pragmatics* (Vol. 11, pp. 109-129). Cham, Switzerland: Springer-Verlag.

Martin, G. E., Losh, M., Estigarribia, B., Sideris, J., & Roberts, J. (2013). Longitudinal profiles of expressive vocabulary, syntax, and pragmatic language in boys with fragile X syndrome or Down syndrome. I*nternational Journal of Language & Communication Disorders, 48(*4), 432-443.

Martin, G. E., Roberts, J. E., Helm-Estabrooks, N., Sideris, J., & Assal, J. (2012). Perseveration in the connected speech of boys with fragile X syndrome with and without autism spectrum disorder. A*merican Journal on Intellectual and Developmental Disabilities, 117(*5), 384-399.

Martin, G.E. (in preparation). A Multi-Method Language Sample Analysis of Pragmatic Skills in Children and Adolescents with Neurodevelopmental Disabilities

Mascaro, J. S., Rilling, J. K., Tenzin Negi, L., & Raison, C. L. (2013). Compassion meditation enhances empathic accuracy and related neural activity. S*oc Cogn Affect Neurosci, 8(*1), 48-55.

McCary, L. M., & Roberts, J. E. (2013). Early identification of autism in fragile X syndrome: a review. J *Intellect Disabil Res, 57(*9), 803-814.

McTear, M., & Conti-Ramsden, G. (1992). P*ragmatic disability in children.* London: Whurr.

Merenstein, S. A., Sobesky, W. E., Taylor, A. K., Riddle, J. E., Tran, H. X., & Hagerman, R. J. (1996). Molecular-clinical correlations in males with an expanded FMR1 mutation. A*m J Med Genet, 64(*2), 388-394.

Munir, F., Cornish, K. M., & Wilding, J. (2000). Nature of the working memory deficit in f ragile-X syndrome. B*rain Cogn, 44(*3), 387-401.

Murphy, M. M., Abbecluto, L., Schroeder, S., & Serlin, R. (2007). Contribution of social and information-processing factors to eye-gaze avoidance in fragile X syndrome. A*merican Journal on Mental Retardation, 112(*5), 349-360.

Müller, R.-A. (2005). Neurocognitive studies of language impairments: The bottom-up approach. *Applied Psycholinguistics, 26(1).*

Nadig, A., Lee, I., Singh, L., Bosshart, K., & Ozonoff, S. (2010). How does the topic of conversation affect verbal exchange and eye gaze? A comparison between typical development and high-functioning autism. N*europsychologia, 48(*9), 2730-2739.

Nelson, K. (1978). How children represent knowledge of their world in and out of language:

A preliminary report. In R. S. Siegler (Ed.), C*hildren's Thinking: What Develops?* (pp. 255-273). Mahwah, NJ: Erlbaum.

Osaka, N., Osaka, M., Kondo, H., Morishita, M., Fukuyama, H., & Shibasaki, H. (2004). The neural basis of executive function in working memory: an fMRI study based on individual differences. N*euroimage, 21(*2), 623-631.

Paul, R., & Cohen, D. J. (1984). Responses to contingent queries in adults with mental retardation and pervasive developmental disorders. A*pplied Psycholinguistics, 5(*4), 349-357.

Paul, R., Dykens, E., Leckman, J. F., Watson, M., Breg, W. R., & Cohen, D. J. (1987). A comparison of language characteristics of mentally retarded adults with fragile X syndrome and those with nonspecific mental retardation and autism. J *Autism Dev Disord, 17(*4), 457-468.

Philofsky, A., Hepburn, S. L., Hayes, A., Hagerman, R., & Rogers, S. J. (2004). Linguistic and cognitive functioning and autism symptoms in young children with fragile X syndrome. A*m J Ment Retard, 109(*3), 208-218.

Piven, J., Palmer, P., Jacobi, D., Childress, D., & Arndt, S. (1997). Broader autism phenotype: Evidence from a family history study of multiple-incidence autism families. A*merican Journal of Psychiatry, 154(*2), 185-190.

Platek, S. M., Keenan, J. P., Gallup, G. G., & Mohamed, F. B. (2004). Where am I? The neurological correlates of self and other. B*rain Res Cogn Brain Res, 19(*2), 114-122.

Prutting, C. A., & Kittchner, D. M. (1987). A clinical appraisal of the pragmatic aspects of l anguage. J*ournal of Speech and Hearing Disorders, 52(*2), 105-119.

Rapin, I., & Dunn, M. (1997). Language disorders in children with autism. S*emin Pediatr Neurol, 4(*2), 86-92.

Rapin, I., & Dunn, M. (2003). Update on the language disorders of individuals on the autistc spectrum. B*rain & Development, 25(*3), 166-172.

Roberts, J. E., Martin, G. E., Moskowitz, L., Harris, A. A., Foreman, J., & Nelson, L. (2007). Discourse skills of boys with fragile X syndrome in comparison to boys with Down syndrome. J*ournal of Speech, Language, and Hearing Research, 50,* 475-492.

Rogers, S. J., Wehner, D. E., & Hagerman, R. (2001). The behavioral phenotype in fragile X: Symptoms of autism in very young children with fragile X syndrome, idiopathic autism, and other developmental disorders. J*ournal of Developmental Behavioral Pediatrics, 22(*6), 409-417.

Roth, F. P., & Spekman, N. J. (1984). Assessing the pragmatic abilities of children: Part 2. Guidelines, considerations, and specific evaluation procedures. J*ournal of Speech and Hearing Disorders, 49,* 12-17.

Ruderfer, D. M., Fanous, A. H., Ripke, S., McQuillin, A., Amdur, R. L., Gejman, P. V., . . . Consortium, C.-D. W. G. o. P. G. (2014). Polygenic dissection of diagnosis and clinical dimensions of bipolar disorder and schizophrenia. M*ol Psychiatry, 19(*9), 1017-1024.

Sato, W., Kochiyama, T., Uono, S., Sawada, R., Kubota, Y., Yoshimura, S., & Toichi, M. (2016). Structural Neural Substrates of Reading the Mind in the Eyes. F*ront Hum Neurosci, 10,* 151.

Schurz, M., Radua, J., Aichhorn, M., Richlan, F., & Perner, J. (2014). Fractionating theory of mind: a meta-analysis of functional brain imaging studies. N*eurosci Biobehav Rev, 42,* 9-34.

Sigelman, C. K., & Holtz, K. D. (2013). Gender differences in preschool children's commentary on self and other. *Journal of Genetic Psychology, 174*(2), 192–206.

Stessman, H. A. F., Xiong, B., Coe, B. P., Wang, T., Hoekzema, K., Fenckova, M., . . . Eichler, E. E. (2017). Targeted sequencing identifies 91 neurodevelopmental-disorder risk genes with autism and developmental-disability biases. N*ature Genetics, 49,* 515.

Sudhalter, V., Cohen, I. L., Silverman, W., & Wolf-Schein, E. G. (1990). Conversational analyses of males with fragile X, Down syndrome, and autism: Comparison of the emergence of deviant language. A*merican Journal on Mental Retardation, 94(*4), 431-441.

Surian, L., Baron-Cohen, S., & van der Lely, H. K. J. (1996). Are children with autism deaf to Gricean maxims? C*ognitive Neuropsychiatry, 1,* 55-71.

Tager-Flusberg, H. (2004). Strategies for conducting research on language in autism. J *Autism Dev Disord, 34(*1), 75-80.

Tager-Flusberg, H., & Anderson, M. (1991). The development of contingent discourse ability in autistic children. J*ournal of Child Psychology and Psychiatry, 32,* 1123-1134.

Tager-Flusberg, H., & Sullivan, K. (1995). Attributing mental states to story characters: A comparison of narratives produced by autistic and mentally retarded individuals. A*pplied Psycholinguistics, 16(*3), 241-256.

Timler, G. R., Olswang, L. B., & Coggins, T. E. (2005). Social communication interventions for preschoolers: targeting peer interactions during peer group entry and cooperative play. S*emin Speech Lang, 26(*3), 170-180.

Volden, J. (2004). Conversational repair in speakers with autism spectrum disorder. I*nternational Journal of Language & Communication Disorders, 39(*2), 171-189.

Volden, J., Coolican, J., Garon, N., White, J., & Bryson, S. (2009). Brief report: pragmatic language in autism spectrum disorder: relationships to measures of ability and disability. J *Autism Dev Disord, 39(*2), 388-393.

Wilding, J., Cornish, K., & Munir, F. (2002). Further delineation of the executive deficit in males with fragile-X syndrome. N*europsychologia, 40(*8), 1343-1349.

Wolff, J. J., Bodfish, J. W., Hazlett, H. C., Lightbody, A. A., Reiss, A. L., & Piven, J. (2012). Evidence of a distinct behavioral phenotype in young boys with fragile X syndrome and autism. J *Am Acad Child Adolesc Psychiatry, 51(*12), 1324-1332.

Wolff, J. J., Hazlett, H. C., Lightbody, A. A., Reiss, A. L., & Piven, J. (2013). Repetitive and self-injurious behaviors: associations with caudate volume in autism and fragile X syndrome. J *Neurodev Disord, 5(*1), 12.

# Chapter 3: A CROSS CONTEXT, LONGITUDINAL STUDY OF PRAGMATIC LANGUAGE DEVELOPMENT ACROSS NEURODEVELOPMENTAL DISABILITIES

## Abstract

Pragmatic (i.e., social) language impairments are observed across males with Autism Spectrum Disorder (ASD), fragile X syndrome (FXS), the most common inherited cause of intellectual disability and the monogenic disorder most frequently associated with ASD, and Down syndrome (DS). Careful characterization of pragmatic language across groups has important implications for identifying syndrome specific profiles of pragmatic language that may indicate index genetic liability. An important question concerns how pragmatic skills, and underlying abilities, in each group present across different contexts and over development. Using standardized measures, detailed hand-coding of narrative and clinical-behavioral ratings of semi-naturalistic conversation, this longitudinal study aimed to comprehensively characterize pragmatic language development in 43 males with ASD-O, 57 males with FXS-ASD, 13 males with FXS-O, 22 males with DS and 24 males with TD. Males with ASD-O showed deficits in pragmatic language across all contexts that were stable across time points. Within the conversational context, males with FXS-ASD also demonstrated a similar quality of pragmatic language difficulties to males with ASD-O. Notably, both ASD groups showed significantly greater impairment in the conversational context relative to the structured narrative. Assessment context drew on different skills across groups, with standardized measures and narratives more strongly related to mental age and structural language. Observed overlap both in severity and quality of pragmatic violations in males with ASD-O and FXS-ASD across development

suggests specific shared pragmatic skills that may relate to variation in the *FMR1* gene. Results also have important methodological implications for comparisons of pragmatic skills across groups.

Pragmatic (i.e., social) language is a complex language domain critical to developing meaningful social relationships and mental health (Cohen, Farnia, & Im-Bolter, 2013; Gilmour, Hill, Place, & Skuse, 2004; Helland & Heimann, 2007; Helland, Lundervold, Heimann, & Posserud, 2014). Understanding profiles of pragmatic skill development is especially relevant for individuals with neurodevelopmental disabilities, who present with deficits in abilities known to be associated with pragmatic language in typical development, such as nonverbal cognition, structural language, social cognition and executive function (Bruner, 1990; Fabbretti, Pizzuto, Vicari, & Volterra, 1997; Gooch, Thompson, Nash, Snowling, & Hulme, 2016; Gopnik, Meltzoff, & Kuhl, 1999; Laws & Bishop, 2004). In typical development, pragmatic competency increases with age, concurrent with cognitive, language and social cognitive development (e.g., Berman and Slobin, 1994); however less is known about the course of pragmatic development in individuals with neurodevelopmental disabilities.

Autism spectrum disorder (ASD), fragile X syndrome (FXS), and Down syndrome (DS) are all genetically based neurodevelopmental disabilities characterized by deficits in pragmatic langauge as well as impairments in associated abilities. Pragmatic language impairments are universally observed in individuals with ASD, a genetically heterogenous disorder characterized by impairments in social interactions and restricted interests and repetitive behaviors (American Psychiatric Association, 2013; CDC, 2014). FXS, the most common inherited cause of intellectual disability as well as the most common monogenic disorder associated with ASD, is caused by a mutation in the *FMR1* gene that results in the reduction of FMRP, a protein which plays a critical role in activity dependent synaptic function, maturation and plasticity during development (Bakker & Oostra, 2003; Kooy et al., 1996; Weiler & Greenough, 1999). As a result, FXS is characterized by a heterogenous clinical behavioral profile including intellectual disabilitity, executive functioning and behavioral challenges, anxiety, and social communicative deficits (Bagni & Oostra, 2013). In particular, individuals with FXS who meet diagnostic criteria for ASD (FXS-ASD) demonstrate similar social-communicative profiles to those with idiopathic ASD (i.e., no known genetic origin; ASD-O), suggesting that overlapping pragmatic langauge impairments in these disorders may indicate common genetic etiology (Budimirovic et al., 2006; Kau et al., 2004; Kaufmann et al., 2004; Klusek, Losh, & Martin, 2014; M. Lee, Martin, Berry-Kravis, & Losh, 2016; Smith, Barker, Seltzer, Abbeduto, & Greenberg, 2012). DS is the most common non-inherited cause of Intellectual Disability, occurring in approximately 1/700 live births (Parker et al., 2010). DS is typically a result of an extra copy of chromosome 21, although translocation and mosaicism of chromosome 21 have also been observed (CDC, 2014; Parker et al., 2010; Presson et al., 2013; Shin et al., 2009). DS is associated with a unique pragmatic profile characterized by several pragmatic strengths relative to individuals with ASD and FXS with comparable cognitive and language abilities, but areas of difficulty relative to typically developing individuals (Abbeduto et al., 2006; Klusek et al., 2014; M. Lee, Bush, et al., 2017; G. E. Martin, Klusek, Estigarribia, & Roberts, 2009; Moore, Oates, Hobson, & Goodwin, 2002; Roberts et al., 2007; Wishart & Johnston, 1990). Therefore, cross-population comparisons of individulas with ASD, FXS and DS provide a unique opportunity to clarify whether certain aspects of pragmatic langauge are etiology specific.

Despite the promising implications of characterizing pragmatic language features and development across these groups, few cross-population studies have been conducted. Further, prior assessment of pragmatic langauge skills has varied widely in methodology and specific skill assessed. As a result, it is unclear whether patterns of strengths and weaknesses, and subsequent observed overlap in pragmatic langauge features in these groups, are context specific, or whether different social contexts draw on the same underlying abilities across disabilities. Equally important to determining overlap at a single time point is to determine whether disabilities evidence common "developmental signatures" of pragmatic competence (Cornish, Roberts, & Scerif, 2012; Karmiloff-Smith, 1998).

This study applies a longitudinal, multi-method approach to analyze pragmatic language and related abilities in school-aged males with ASD-O, FXS (with and without co-morbid ASD), DS and younger TD controls at up to three time points. Results have key implications for understanding patterns of overlap or divergence in these populations, with implications for identifying potential shared or unique genetic, cognitive and behavioral abilities contributing to pragmatic skills in these groups. Below, we review in more detail what is known about pragmatic skills and development, the role of pragmatic context, and related abilities in these groups.

**Pragmatic Language in Autism Spectrum Disorder (ASD-O)**

Pragmatic language deficits are universally observed in ASD-O, even in the absence of structural langauge impairment, and are included in the diagnostic critera for ASD-O (APA, 2013). Individuals with ASD-O demonstrate difficulties acknowledging and elaborating on statements of their conversaitonal partner (Klusek et al., 2014; Lam & Yeung, 2012), initiating and maintaining appropriate topics, and engaging in appropriate turn-taking (Capps, Kehres, & Sigman, 1998; Lam & Yeung, 2012; R. Paul et al., 1987; Tager-Flusberg & Anderson, 1991). When they do contribute to conversation, the language of individuals with ASD-O is characterized by pedantic, idiosyncratic or perseverative (i.e., repetitive) word choice, as well as unclear references (Fine, Bartolucci, Szatmari, & Ginsberg, 1994; Ghaziuddin & Gerstein, 1996; Ross, 2002). Although individuals with ASD-O recognize and attempt to remedy conversational breakdowns, they rely on less effective strategies than their typically developing peers and show greater rates of non-responsiveness to direct requests for clarification (Barstein, Martin, Lee, & Losh, under review; Geller, 1998; Rhea Paul & Cohen, 1984; Volden, 2004). When asked to narrate, individuals with ASD produce stories of comparable length, grammatical complexity, and with similar rates of key story elements relative to controls (Beaumont & Newcombe, 2006; Capps, Losh, & Thurber, 2000; Colle, Baron-Cohen, Wheelwright, & van der Lely, 2008; Diehl, Bennetto, & Young, 2006; Hogan-Brown, Losh, Martin, & Mueffelmann, 2013; Loveland, McEvoy, & Tunali, 1990; Rumpf, Kamp-Becker, Becker, & Kauschke, 2012; Siller, Swanson, Serlin, & George, 2014; Tager-Flusberg & Sullivan, 1995). However, prior work suggests that individuals with ASD-O produce less coherent narratives characterized by reduced evaluation, or strategies that provide a psychological perspective, and are less likely to use narratives in their day to day interactions (Beaumont & Newcombe, 2006; Capps et al., 1998; Capps et al., 2000; M. Lee, Martin, et al., 2017; Losh & Capps, 2003; Siller et al., 2014). Therefore, while core narrative skills may appear intact in highly structured contexts, individuals with ASD have difficulty integrating these skills in their social interactions.

Prior work examining the developmental trajectories of symptoms in ASD are largely equivocal, with some suggesting minimal change over time (Billstedt & Gillberg, 2005; Billstedt, Gillberg, & Gillberg, 2011; Cederlund, Hagberg, Billstedt, Gillberg, & Gillberg, 2008; Farley et al., 2009; Howlin, Moss, Savage, & Rutter, 2013; Larsen & Mouridsen, 1997; Moss & Howlin, 2009; Piven, Harper, Palmer, & Arndt, 1996; Sigman & McGovern, 2005), and others showing improvement in social communication impairments with age (Gillespie-Lynch et al., 2012; Piven et al., 1996). Tager-Flusberg and Anderson (1991) found that males with ASD did not increase in their level of contingency over the course of one year, despite gains in mean length of utterance (MLU). However, research has yet to study pragmatic skills longitudinally across contexts, or to compare rates of development with males with FXS.

**Pragmatic Language in Fragile X Syndrome (FXS)**

Males with FXS present with qualitatively similar pragmatic impairments to those observed in ASD-O, including increased perseveration (Levy, Gottesman, Borochowitz, Frydman, & Sagi, 2006; Roberts et al., 2007; Sudhalter, Cohen, Silverman, & Wolf-Schein, 1990; Wolf-Schein et al., 1987), non-contingency (Besler & Sudhalter, 2001; Wolf-Schein et al., 1987), lack of referential communication (Abbeduto et al., 2006), and less frequent signaling of conversational breakdown (Abbeduto et al., 2008). Findings on narrative ability in FXS are more mixed, with some studies showing no group differences in story telling elements such as thematic mainteance, evaluation, or inferential statements (Ashby, Channell, & Abbeduto, 2017; Hogan-Brown et al., 2013; Keller-Bell & Abbeduto, 2007), or even better quality of story introduction relative to MLU matched typically developing controls (Finestack, Palmer, & Abbeduto, 2012). Notably, several studies suggest that the presence of ASD symptoms negatively impacts pragmatic language in males with FXS. For example, males with FXS-ASD have been shown to perform more poorly on standardized measures of pragmatic langauge (Losh, Martin, Klusek, Hogan-Brown, & Sideris, 2012; G.E. Martin, Losh, Estigarribia, Sideris, & Roberts, 2013), evidence greater rates of non-contingency (Roberts et al., 2007), signal communicative breakdowns less (G. E. Martin et al., 2017) and perseverate more (G. E. Martin, Roberts, Helm-Estabrooks, Sideris, & Assal, 2012) than boys with FXS-O. Some work suggests that ASD status in FXS may also impact narrative ability, as boys with FXS-ASD used less story grammar (e.g., features of plot, characters) than boys with FXS-O in one study (Estigarribia et al., 2011) although Hogan-Brown et al., 2013 found no differences between FXS-ASD and FXS-O groups during a picture book task.

Longitudinal studies in FXS have focused primarily on ASD-related symptoms, with some studies showing relative stability or slight increase with age (Cornish, Cole, Longhi, Karmiloff-Smith, & Scerif, 2012; Hatton et al., 2006; Hernandez et al., 2009; M. Lee, Martin, Berry-Kravis, & Losh, 2016; Sabaratnam, Murthy, Wijeratne, Buckingham, & Payne, 2003). To date, only one study has longitudinally examined pragmatic language in males with FXS. Martin et al. (2013) examined trajectories of pragmatic language development in males with FXS-ASD, FXS-O and DS using the CASL-pragmatic judgment subscale and found that both FXS groups evidenced slower rates of development relative to males with TD, but did not differ from one another in rates of development. It is unknown whether divergent patterns may be observed in more specific pragmatic skills.

**Pragmatic Language in Down syndrome (DS)**

Despite comparable cognitive and language deficits as those with FXS, individuals with DS are known for their sociability (Moore et al., 2002; Wishart & Johnston, 1990), and present with several conversational and narrative abilities comparable to typically developing children of similar mental age (Beeghly, Weiss-Perry, & Cicchetti, 1990; Boudreau & Chapman, 2000; Miles & Chapman, 2002; Tannock, 1988). Further, individuals with DS demonstrate fewer pragmatic violations overall as well as reduced specific violations, such as perseverative language, relative to individuals with FXS and ASD-O of comparable mental age (Abbeduto, Brady, & Kover, 2007; Abbeduto & Chapman, 2005; Klusek et al., 2014; G.E. Martin et al., 2013; G. E. Martin et al., 2012; Roberts et al., 2007). However, individuals with DS also demosntrate vulnerabilities in pragmatic language, including reduced topic introduction and elaboration, less sophisticated topic maintenance in conversation, greater difficulty signaling communicative intent, and reduced identification of character action in narratives (Abbeduto et al., 2008; Ashby et al., 2017; M. Lee, Bush, et al., 2017; Roberts et al., 2007; Tannock, 1988).

Longitudinal assessment of social phenotypes in DS are limited, but there are mixed findings overall related to development of other abilities across age ranges, with some studies suggesting “plateaus” in development and other suggesting no differences in rates of development between preschool and adult years (Cuskelly, Povey, & Jobling; de Graaf & de Graaf, 2016; Dykens, Hodapp, & Evans, 2006). Lee et al. (2017) conducted clinical behavioral ratings of pragmatic skills in males with DS during conversation across a period of approximately two years and found that overall pragmatic impairment did not change with age. Rather, a “trade-off” was observed, in that as individuals with DS developed language, they improved in more fundamental pragmatic skills (e.g., reciprocal conversation, acknowledgment of conversational partner), whereas impairments in higher-level pragmatic skill (e.g., failure to signal humor, length of conversational turn) became more pronounced.

**Cross Population Comparisons**

Although prior work has compared pragmatic language of males with FXS and DS (Abbeduto et al., 2008; Ashby et al., 2017; Channell, McDuffie, Bullard, & Abbeduto, 2015; Finestack & Abbeduto, 2010; Finestack et al., 2012; Keller-Bell & Abbeduto, 2007; G. E. Martin et al., 2012; Roberts et al., 2007) and ASD-O and DS (Tager-Flusberg & Anderson, 1991), respectively, few studies have directly compared the pragmatic language abilities of males with ASD-O, FXS (with and without accounting for ASD status), DS, and TD in the same study. Given variation in context and assessment methodology in prior work, direct comparisons are critical to accurately determine whether patterns of overlapping impairment persist when using identical methodologies.

Ferrier et al. (1991) compared males with FXS (without accounting for ASD status), DS and ASD-O, and found that the males with FXS evidenced the greatest rates of self-repetition, whereas males with ASD-O used qualitatively greater echolalia (Ferrier, Bashir, Meryash, Johnston, & Wolff, 1991). Losh et al. (2012) examined performance across these groups on a standardized measure of social communication (the CASL-PJ) and teacher-report (CCC-2). On the CASL-PJ, males with ASD-O and FXS-ASD performed comparably and evidenced greater impairment than males with FXS-O and TD; the ASD-O also showed greater impairment than the DS group. In contrast, the CCC-2, a teacher-report measure, was not as sensitive to variation within the clinical groups, with the exception that males with FXS-ASD evidenced the fewest initiations. Klusek et al. (2014) rated 34 aspects of pragmatic language (PRS-SA rating scale) and found that males with ASD-O and FXS-ASD evidenced the greatest impairment, followed by males with DS and FXS-O, who showed greater impairments than males with TD. Further, individuals with FXS-ASD and ASD-O showed overlap across several specific types of violations (e.g., topic elaboration, conversational reciprocity) that distinguished them from other clinical groups. Conversely, males with ASD-O, FXS-ASD, FXS-O, DS and TD did not differ on macrostructural elements of narrative (e.g., evaluation; Hogan Brown et al., 2013), and only males with FXS-ASD and DS showed differences from controls in their ability to signal non-comprehension (G. E. Martin et al., 2017). Together, such studies suggest potential areas of overlap in males with ASD-O and FXS-ASD, such as topic elaboration during semi-naturalistic interactions, but also key differences, such as response to communicative breakdowns. More work is needed to define specific areas of overlap and divergence to identify the most fruitful targets of both intervention and etiologic research.

**The Role of Context**

Cognitive, linguistic, and social demands vary widely based on context, and thus different pragmatic tasks are likely to influence observed patterns of similarity and differences. For example, prior work suggests that standardized assessment of pragmatic language, which occurs outside of the context of a true social exchange, may not generalize to day-to-day interactions (Adams, 2002; Prutting & Kittchner, 1987). Such considerations are especially relevant for individuals with ASD-O, where interpretation of social context is a known deficit (Clark & Rutter, 1981; Loukusa, Leinonen, Jussila, et al., 2007; Loukusa, Leinonen, Kuusikko, et al., 2007; D. L. Williams, Goldstein, & Minshew, 2006). Prior work suggests that greater social communicative impairments are observed during semi-structured conversation relative to more structured narrative (Losh & Capps, 2003), and it has been argued that the visual supports provided by storybook narrative tasks, commonly used in clinical assessments, may scaffold the abilities of individuals with ASD-O (e.g., Diehl et al., 2006).

Less is known about the role of assessment context in males with FXS and DS with regards to observed pragmatic impairment, although studies of structural language suggest that males with DS demonstrate more complex syntax during narrative, whereas males with FXS show minimal differences in the complexity of their language across narrative and semi-structured interactions (Kover, McDuffie, Abbeduto, & Brown, 2012; Miles & Chapman, 2002). However, Kover et al. (2012) found that ASD symptoms impacted expressive language in FXS in a conversational context only, highlighting how specific social contexts may better elicit ASD-related impairments in pragmatic language. Martin et al. (2012) examined perseveration in males with FXS-O, FXS-ASD, DS, and mental age matched TD controls in both narrative and conversational contexts, and found that males with FXS-O and FXS-ASD produced significantly more topic-level perseveration during conversation, whereas the TD group produced more utterance-level perseveration during narration. However, less is known whether context effects are similar or different across groups, or whether they draw on similar related abilities, which is important for identifying shared features across disorders, as well as identifying the best methodologies to capture pragmatic competence in these groups.

**Cognitive-Behavioral Underpinnings of Pragmatic Language**

Beyond characterizing pragmatic language phenotypes, it is important to understand how similar or different abilities contribute to pragmatic development, and whether different contexts uniquely tap these abilities. In typical development, successful communicative interchange draws on nonverbal cognition, structural language, theory of mind and executive functioning (Blain-Brière, Bouchard, & Bigras, 2014; Bruner, 1990; Fiske & Taylor, 1991; Gooch et al., 2016; Gopnik et al., 1999), and pragmatic skills develop concurrent with development in related domains. For example, the ability to recognize a breakdown in communication (i.e., that the conversational partner does not understand their partner), emerges around age 5 in typical development (Brinton, Fujiki, & Sonnenberg, 1988), concurrent with theory of mind (Dunn, 1988). Further, the gradual development of more complex syntax throughout adolescence can enhance clarity and richness of communication, in turn impacting conversational competency (Nippold, Hesketh, Duthie, & Mansfield, 2005).

Not surprisingly, cognitive and structural language difficulties have been shown to contribute to pragmatic language in ASD-O, FXS and DS (Abbeduto et al., 2006; Finestack, Richmond, & Abbeduto, 2009; Klusek et al., 2014; Volden, Coolican, Garon, White, & Bryson, 2009). However, variance in structural language does not entirely account for deficits, particularly in ASD-O, where impairments are evident in the absence of structural language deficits (e.g., Tager-Flusberg, 2000). Individuals with ASD-O, FXS and DS have all been found to demonstrate delays in theory of mind, although findings in FXS are more mixed (Grant, Apperly, & Oliver, 2007; P. Lewis et al., 2006; Losh et al., 2012). Extensive research suggests that theory of mind deficits contribute to pragmatic functioning in ASD-O (e.g., Baron-Cohen, Leslie, & Frith, 1985; Baron-Cohen, Leslie, & Frith, 1988; Lisa Capps et al., 1998; L. Capps et al., 2000; Losh & Capps, 2003; Loveland & Tunali, 1993; Surian, Baron-Cohen, & van der Lely, 1996; Tager-Flusberg & Sullivan, 1995) and some studies have also found relationships between theory of mind and pragmatic competence in males with DS and FXS on standardized assessments (M. Lee, Bush, et al., 2017; Losh et al., 2012). Finally, males with ASD-O, FXS and DS also demonstrate deficits in executive functioning (Garner, Callias, & Turk, 1999; Hooper et al., 2008; Munir, Cornish, & Wilding, 2000; Wilding, Cornish, & Munir, 2002); however, no studies have directly assessed relationships between executive functioning and pragmatic competence in these groups in the same assessment contexts.

**Current Study Aims**

The current study aimed to compare trajectories of pragmatic language development and related abilities during the school-age years for males with ASD-O, FXS (with and without co-morbid ASD), DS and a younger group of TD males of similar mental age. Specifically, this study aimed to 1) compare pragmatic language features at the initial visit and rates of development of these features across a parent questionnaire, standardized, narrative, and semi-naturalistic conversational context, 2) examine the role of context on observed pragmatic profiles, and 3) identify related abilities within each context and across development.

## Methods

### Participants

Participants included 43 males with ASD-O, 71 males with FXS (57 males with FXS-ASD; 14 males with FXS-O), 22 males with DS and 24 males with TD. Participants were part of a longitudinal study of pragmatic language development in which assessments were completed approximately once a year for up to three time points. Based on the structure of the study, not all assessments were completed at all time points and due to subject attrition not all participants completed three visits. The number of participants receiving each assessment is summarized in Table 3.1.

Table 3.1. Number of Participants with Each Assessment and at Each Visit

| Visit | Groups | MA | EVT | PPVT | MLU | CCC-2 | CASL | PRS-SA | Narrative |
|---|---|---|---|---|---|---|---|---|---|
| 1 | ASD-O | 43 | 43 | 42 | 41 | 28 | 37 | 35 | 22 |
| | FXS-ASD | 57 | 57 | 56 | 54 | 37 | 52 | 42 | 30 |
| | FXS-O | 14 | 14 | 14 | 13 | 10 | 15 | 14 | 10 |
| | DS | 22 | 22 | 21 | 21 | 14 | 21 | 21 | 18 |
| | TD | 24 | 24 | 24 | 23 | 15 | 23 | 22 | 15 |
| 2 | ASD-O | 21 | 10 | 21 | 20 | 18 | 20 | 4 | --- |
| | FXS-ASD | 45 | 32 | 43 | 44 | 32 | 43 | 4 | --- |
| | FXS-O | 11 | 6 | 11 | 10 | 6 | 11 | 1 | --- |
| | DS | 20 | 5 | 19 | 19 | 13 | 20 | --- | --- |
| | TD | 18 | 15 | 18 | 15 | 8 | 18 | 1 | --- |
| 3 | ASD-O | 16 | 16 | 16 | 14 | 14 | 15 | 15 | 9 |
| | FXS-ASD | 32 | 32 | 32 | 32 | 21 | 32 | 27 | 19 |
| | FXS-O | 5 | 5 | 5 | 5 | 2 | 5 | 5 | 4 |
| | DS | 14 | 14 | 14 | 14 | 8 | 14 | 14 | 11 |
| | TD | 11 | 10 | 9 | 8 | 6 | 11 | 11 | 7 |

Note. Narrative data was not collected at the second visit. Due to changes in study protocol, only a limited number of participants completed EVT assessments at Visit 2. MA = mental age assessed by Leiter, EVT=Expressive Vocabulary Test, PPVT = Peabody Picture Vocabulary Test, MLU = Mean Length of Utterance, CCC-2= Children's Communicative Checklist-2$^{nd}$ Edition, CASL = Comprehensive Assessment of Spoken Language, PRS-SA = Pragmatic Rating Scale-School Age

Participants were recruited through advertisements at genetic clinics, physicians' offices, advocacy groups, schools, and the University of North Carolina Research Registry Core. All participants spoke English as a first and primary language and were using three word phrases at the time of enrollment according to parent report. Males with ASD-O were excluded if they had a known genetic disorder associated with ASD (e.g., FXS or Tuberous Sclerosis). Males with FXS were included based on prior genetic testing confirming FXS status. One set of siblings with ASD-O, seven sets of siblings with FXS, and one set of siblings with TD were included. Males with DS and TD did not meet ASD criteria at any point over the course of the longitudinal study. Because of the longitudinal nature of the study and special nature of the populations included, participants were given the option to complete testing in their home or child's school if the family was unable to travel to the lab. Every effort was made to standardize administration and to minimize distractions across these contexts.

Table 3.2 summarizes participant characteristics at baseline and across time points. This study was approved by University Institutional Review Boards.

Table 3.2. Group Characteristics

| | **Groups** | **Chronological Age M(SD) Range** | **Leiter Mental Age** | **EVT M(SD) Range** | **PPVT M(SD) Range** | **MLU M(SD) Range** |
|---|---|---|---|---|---|---|
| **Visit 1** | ASD-O | 8.27 (2.90)[a]<br>3.24-13.27 | 6.11 (1.8)[a]<br>2.33-10.50 | 5.57(1.89)<br>2.58-10.08 | 6.02 (2.7)[a,b]<br>2.58-17.00 | 4.13(1.12)[a]<br>1.88-6.44 |
| | FXS-ASD | 10.56 (2.47)[b]<br>6.58-15.07 | 5.00 (.56)[b]<br>3.50-6.25 | 5.08 (1.25)<br>2.67-9.92 | 5.71 (1.43)[a,b]<br>2.42-9.33 | 3.52 (.79)[c]<br>1.80-6.05 |
| | FXS-O | 9.34 (3.24)[a,b]<br>5.59-14.98 | 5.64 (1.42)[a,b]<br>3.67-9.17 | 5.77 (2.33)<br>3.42-12.33 | 6.63 (2.95)[b]<br>2.75-13.83 | 3.99 (.73)[a,c]<br>2.27-4.74 |
| | DS | 10.94 (2.07)[b]<br>6.81-14.86 | 5.33 (.81)[b]<br>4.33-8.25 | 5.33 (1.33)<br>3.58-8.58 | 5.15 (1.41)[a]<br>2.42-7.50 | 3.11 (.75)[b,c]<br>1.76-4.76 |
| | TD | 4.74 (1.10)[c]<br>3.15-7.07 | 5.23 (1.21)[b]<br>3.58-7.67 | 5.64 (1.53)<br>2.92-8.83 | 6.05 (1.56)[a,b]<br>2.17-8.67 | 4.75 (.70)[d]<br>3.14-6.06 |
| | **Groups** | **Chronological Age M(SD) Range** | **Leiter Mental Age** | **EVT M(SD) Range** | **PPVT M(SD) Range** | **MLU M(SD) Range** |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Visit 2** | ASD-O | 10.31 (2.20)[a]<br>6.41-13.92 | 6.34 (1.57)[a]<br>4.42-10.25 | N/A | 6.53 (2.41)[a]<br>3.25-11.58 | 4.51 (1.06)[a]<br>1.81-5.93 |
| | FXS-ASD | 12.02 (2.53)[b]<br>7.95-16.75 | 5.07 (.58)[b]<br>3.25-6.58 | N/A | 7.13 (2.91)[a]<br>3.75-8.50 | 3.61 (.70)[b]<br>2.14-5.25 |
| | FXS-O | 11.47 (3.56)[a,b]<br>7.50-16.40 | 5.72 (1.29)[a,b]<br>4.50-9.17 | N/A | 7.13 (2.92)[a,b]<br>3.92-15.00 | 3.61 (.66)[b]<br>2.27-4.43 |
| | DS | 12.39 (2.03)[b]<br>7.93-16.09 | 5.66 (1.09)[a,b]<br>3.08-8.25 | N/A | 5.96 (1.34)[a]<br>3.50-8.25 | 3.28 (.82)[b]<br>1.9-4.6 |
| | TD | 6.41 (1.54)[c]<br>4.60-10.33 | 6.80 (1.65)[a,c]<br>5.58-11.67 | N/A | 8.70 (3.21)[b]<br>5.25-17.75 | 4.68 (.78)[a]<br>3.56-6.21 |
| **Visit 3** | ASD-O | 11.69 (2.34)[a]<br>7.54-15.77 | 6.94 (1.71)[a]<br>4.42-10.25 | 6.89 (2.30)[a]<br>3.42-12.50 | 7.82 (1.93)[a,c]<br>4.75-11.17 | 4.78 (1.56)[a]<br>2.72-9.33 |
| | FXS-ASD | 13.10 (2.55)[a,b]<br>9.10-17.90 | 5.15 (.55)[b]<br>4.42-6.67 | 5.48 (1.32)[b]<br>3.42-8.25 | 6.45 (1.50)[b]<br>3.33-9.00 | 3.59 (.70)[b,c]<br>2.13-5.56 |
| | FXS-O | 11.64 (2.87)[a,b]<br>8.73-16.38 | 5.11 (.75)[b]<br>4.00-6.00 | 6.60 (1.41)[a,b,c]<br>4.33-8.00 | 7.43 (.81)[a,c]<br>6.08-8.17 | 4.58 (1.64)[a,c]<br>2.89-7.30 |
| | DS | 14.14 (2.51)[b]<br>9.63-17.93 | 5.99 (1.33)[a,b]<br>4.58-9.58 | 6.24 (1.28)[a,b]<br>3.33-8.33 | 7.82 (1.93)[a,b]<br>3.83-10.92 | 3.41 (.83)[b]<br>1.91-5.08 |
| | TD | 7.73 (1.70)[c]<br>6.15-11.55 | 8.49 (3.11)[c]<br>6.00-17.08 | 8.25 (2.00)[c]<br>6.33-13.08 | 8.48 (1.44)[a,c]<br>6.67-10.42 | 5.32 (1.16)[a]<br>4.17-7.22 |

Note. Differing superscripts indicate significant differences at the level of $p < .05$. EVT=Expressive Vocabulary Test, PPVT = Peabody Picture Vocabulary Test, MLU = Mean Length of Utterance

## Pragmatic Language Assessment Contexts

**Parent questionnaire: The Children's Communication Checklist, Second Edition (CCC-2).** The Children's Communication Checklist, Second Edition (CCC-2, Bishop, 2003), is a 70-item scale that comprehensively assesses elements of both structural language and social communicative abilities. The measure provides standard scores (ranging from 1-19) for 10 subscales, assessing both structural language (Speech, Syntax, Semantics, Coherence) and social aspects of language (Initiation, Scripted Language, Context, Nonverbal Communication, Social Relations, and Interests). The measure also provides an overall General Communication

Composite (GCC) standard score (ranging from 40 to 160). The CCC-2 demonstrates strong internal consistency (ranging from .94-.96 across age groups; Bishop, 2003, as well as test-retest reliability greater than .85; Bishop, 2013).

**Standardized measure: Comprehensive Assessment of Spoken Language Pragmatic Judgment Subtest (CASL-PJ).** The Pragmatic Judgment subtest of the Comprehensive Assessment of Spoken Language (CASL-PJ; Carrow-Woolfolk, 1999) measured how participants would respond to certain social situations (e.g., "how would you greet an unfamiliar adult?"). The CASL-PJ has been used extensively in populations with both typical and delayed development and has strong internal consistency (reliability ranging from .77-.92, depending on participant age) and test-retest reliability (ranging from .66 for children ages 14-16 to .85 for children ages 5 years to 6 years, 11 months; Carrow-Woolfolk, 1999). Age equivalents were used in the current analyses because they represented a meaningful metric (as opposed to raw scores), and have been used extensively in prior work in these populations (Losh et al., 2012; Martin et al., 2013; Klusek et al. 2014; Lee et al., 2017).

**Narrative.** Participants completed a structured narrative task to assess aspects of storytelling ability. Participants viewed a short, silent cartoon (Pingu's Parents Go to a Concert, Mazola, 1991), which features two young penguins that make a mess while their parents are away, and subsequently must clean the mess prior to their parents' return. Narrative elicitation procedures were as follows. First, participants were instructed to view the video on a laptop in its entirety without speaking. During this viewing, the examiner made a standardized set of guiding comments related to key plot points to facilitate basic understanding (e.g., "look, the parents are leaving"). Participants were then prompted to tell the examiner the story again while viewing the video a second time. The video was paused at six key points to allow the participant to narrate, although participants could speak throughout the playing of the video. Examiners were instructed to use prompts as needed to manage behaviors (e.g., “sit down”) or neutral prompts to facilitate narration (e.g., “tell me more”).

Research assistants trained to 80% word and utterance segmentation reliability transcribed narratives from video using the Systematic Analysis of Language Transcripts (SALT; Miller & Chapman, 2008) software. A second, senior transcriber listened to high quality audio and added any additional intelligible words to transcripts with greater than 80% unintelligible utterances. Transcribers were blind to participant diagnosis. Ten percent of files from each diagnostic group were re-transcribed to assess transcription reliability, with mean 87.5% word reliability (range: 75-100%) and mean 83.3% utterances segmentation reliability (range: 62-100%). Those files with less than 80% reliability were discussed and all discrepancies resolved prior to analyses. Participants were excluded from subsequent narrative analyses if 1) less than 80% of participant utterances were codable due to unintelligibility (1 participant excluded), 2) refusal to verbalize during the task (4 participants excluded) or 3) technical difficulties, such as video malfunction or examiner error (4 participants excluded).

The narrative coding scheme was adapted from prior work analyzing narratives in these populations (Capps et al., 2000; Estigarribia et al., 2011; Hogan-Brown et al., 2013; Losh & Capps, 2003; Reilly, 1992; Reilly, Klima, & Bellugi, 1990; Reilly, Losh, Bellugi, & Wulfeck, 2004). Reliability coding was completed for 10% of files at the conclusion of the coding process, and all disagreements were resolved. As a result of regular consensus meetings as well as final reliability coding, 26 (17%) of files were consensus coded. ICCs conducted for primary narrative outcome variables indicated ICC (3,2) greater than .9, signifying “excellent agreement” apart from off-topic, which was .62, representing "good" agreement (Cicchetti, 1994). The coding scheme assessed the following aspects of narrative.

***Length.*** The total propositions (defined as a verb and its arguments), were totaled to assess narrative length.

***Story grammar.*** Story grammar included the presence of an introduction, or establishment of setting or characters, initiating event (parents leaving), the inclusion of 4 main episodes (penguins playing, penguins making a mess, penguins recognize their parents will come home soon, parents clean up), and a resolution (parents returning and children in bed). In addition, any references to the overall theme (that the children would be in trouble if they did not clean up before parents came home or that parents were unaware what the children were doing) were totaled. Each of the four main episodes was scored based on the inclusion of episode-specific details, so that it was possible to receive a total of 14 points for all episodes together.

***Character relationships.*** Each mention of a relationship between the characters (e.g., brother, sister, mother, father, baby) was totaled.

***Total evaluation.*** The total use of evaluative devices (i.e., devices that infuse psychological meaning into a narrative) was calculated by summing instances of affect, cognition and causality and audience engagement devices, as described below.

*Affect, cognition and causality.* Instances of mention of affective states and affective behaviors (e.g., sad, happy, crying, laughing), cognitive states or behaviors (e.g., thinks, sees, knows, sleeps), and causal explanations of affect, cognition or behavior were totaled.

*Audience engagement.* Audience engagement devices included the use of story-telling devices, such as "once upon a time" or "the end," intensifiers, which were defined as any instance when the participant used an adverb or adjective to strengthen a descriptor or repeated for emphasis (e.g., he cleaned the *whole entire* house; *faster* Pingu *faster*), sound effects (e.g., "splish splash"), and audience hooks, or instances when the child attempted to gain the examiner's attention or engage them in the narrative (e.g., "look at that?", "why would he do that?"). Character speech was also coded, either as signaled character speech (e.g., "the penguin said bye") or enacted character speech, when the participant gave voice to the characters without clearly signaling that the character was speaking (e.g., "pass me the ball!").

***Off- topic utterances.*** In addition to story elements, any utterances that were not directly relevant to the narrative were totaled. Off topic utterances included resistance to the task, such as requesting to skip scenes in the video, asides (e.g., "I once saw a penguin at the zoo"), responses to events in the immediate environment (e.g., a bell rings and the child says, "time to go back to class"), and unrelated utterances (e.g., "can I have some goldfish?").

**Semi-naturalistic conversational interactions.** The Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DeLavore, & Risi, 2001) was used as the context to assess pragmatic language during semi-naturalistic conversational interactions. The ADOS was chosen because administration includes a range of activities designed to prompt social interactions (e.g., conversational bids, completing imaginary play, taking turns narrating a story) that is standardized across participants. However, in contrast to highly standardized measures, during the ADOS examiners have the opportunity to follow the child's lead, resulting in more naturalistic interactions (Tager-Flusberg et al., 2009).

Videos of the ADOS were rated using the Pragmatic Rating Scale-School Age (PRS-SA; Landa et al., 2012), a clinical-behavioral rating system of 34 operationally defined features of pragmatic language assessing a range of impairments in the following theoretically defined subscales: theory of mind (e.g., failure to provide background information, providing too much detail), discourse management (e.g., limited topic initiation and elaboration, reduced acknowledgment of conversational partner), speech and language behaviors impacting pragmatics (e.g., overly formal speech, repetitive speech), suprasegmentals (e.g., atypical prosodic features of speech such as rate, volume and fluency) and nonverbal communication (e.g., eye contact, facial expressions). Each item is rated on a three-point scale (0, absent; 1, mild impairment; or 2, impairment present); items are then totaled to provide an overall sum of pragmatic violations.

PRS-SA ratings were completed by individuals who were either considered research reliable following completion of training with Dr. Landa, the developer of the PRS-SA, or who maintained 80% reliability with a research reliable individual. Due to the longitudinal nature of the study, there was a shift in raters actively coding files over time. The composition of files assessed for reliability accounted for these changes by including both files assigned to individuals coding concurrently and between raters coding at different times (i.e., coding of earlier videos by later raters). Overall, this resulted in 52 total files (approximately 20% of each group) assessed for reliability. Reliability files were consensus coded to resolve discrepancies if both coders were present at the time of coding (as consensus could not be achieved with coders no longer a part of the project). ICCs indicated overall reliability as .86 (.71 for ASD, .80 for FXS, .84 for DS and .84 for TD), signifying "good-excellent agreement."

**ASD Classification**

In addition to serving as a conversational context, the ADOS (Lord et al., 2001) confirmed diagnosis in males with ASD-O and determined ASD status in males with FXS. Males with FXS were classified as FXS-ASD if their average severity score (across longitudinal assessments) was consistent with an ASD classification as defined by updated ADOS algorithms

(Gotham, Pickles, & Lord, 2009; Hus, Gotham, & Lord, 2012). Average severity scores were used to ensure consistency in classification over time and to reflect a best estimate classification based on the most information available.

**Assessment of Related Abilities**

**Mental age.** Nonverbal mental age was assessed using the Leiter International Performance Scale-Revised (Roid & Miller, 1997).

**Expressive and receptive vocabulary.** The Expressive Vocabulary Test (EVT; (K. T. Williams, 1997) and Peabody Picture Vocabulary Test -3rd or 4th editions (PPVT; (Dunn & Dunn, 1997, 2007), assessed expressive and receptive age equivalents, respectively.

**Mean length of utterance.** Mean Length of Utterance (MLU) was used to provide a measure of syntactic complexity of spoken language. MLU was calculated by mean length of utterance in morphemes derived from complete, intelligible utterances from transcriptions of the ADOS (using SALT; Miller & Chapman, 2008). Interrater reliability for calculation of MLU for the broader project was .97.

**Theory of mind.** Participants completed one of two possible batteries to assess theory of mind, based on time of study enrollment. Both batteries included assessments of perspective taking, diverse desires and beliefs, false belief and explicit false belief and knowledge access (Slaughter, Peterson, & Mackintosh, 2007; Wellman & Liu, 2004). The earlier version of the task included primarily verbal presentation; however, the verbal demands of the task were too challenging for some participants. Therefore, the battery was modified to include nonverbal presentations of tasks as well as more basic tasks of desire, intention, and appearance vs. reality (Flavell, Flavell, & Green, 1983; C. Lewis & Mitchell, 1994; Matthews, Dissanayake, & Pratt, 2003; Repacholi & Gopnik, 1997; Slaughter, Peterson, & Mackintosh, 2007). Factor analysis scores (mean of 10, standard deviation of 1) across batteries were derived to produce a composite comparable across batteries (see Losh et al., 2012, for further detail).

**Executive function.** Primary caregivers completed the Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P; Gioia, Espy, & Isquith, 2003), an 86-item parent questionnaire that assesses multiple domains of a child's executive functioning, such as behavioral inhibition, shifting attention, emotional control, and working memory. The preschool version was administered because items were more appropriate for the nonverbal mental ages of participants, consistent with prior literature (Hall et al., 2016; N. R. Lee et al., 2011).

## Analysis Plan

**Aim 1: Compare pragmatic language features and rates of development of these features across groups.** For the CCC-2 (total score, pragmatic subscales), CASL, and PRS-SA (total and theoretically derived subscales), hierarchical linear models (HLM) were conducted, with age as a marker of time nested within participant, to assess the main effect of group, the main effect of age, and interaction between age and group (i.e., whether rates of development differed across groups). Random intercepts and random slopes of age were included when they could be validly fit to the model. Each HLM was run covarying for mental age. Covariates were grand mean centered to reduce collinearity. In addition, for the PRS-SA, which included item-level analyses that were not appropriate for HLM, Multivariate Analysis of Covariance (MANCOVAs) were completed for the total and all 34 individual items at the initial time point, covarying for mental age. These were then followed by within group Wilcoxin-Ranked non-parametric repeated measures to assess patterns of change in specific skills across visits.

Given the relatively small narrative samples and nature of the data collected (i.e., count variables), narrative analyses focused primarily on the initial visit. Poisson analyses were conducted, to compare narrative outcome variables. These analyses were conducted including mental age as a predictor and offset by the log of propositions (an index of length). Residual plots were examined in order to determine the fit of the poisson models and assess for non-normality of residuals. In cases where this examination indicated skew (i.e., poor model fit to the distribution of the data), caution is noted in interpretation and these analyses were followed up by a more conservative approach of binary logistic regressions with group as a predictor and mental age as a covariate to determine whether group status predicted an amount of a narrative element below or above the overall mean. Given the low use of causal language across groups, analyses were conducted using logistic regression to predict whether group membership predicted the presence or absence of causality. In addition, Pearson bi-variate correlations were used to assess whether relationships between features of narrative were similar or different across groups. Narrative outcome variables for the correlations were calculated as a proportion of total propositions to account for length, except for story elements, which represented a total score. Within group non-parametric repeated measures, Wilcoxon Ranked Sum Tests assessed changes in proportions of narrative features over time within groups.

**Aim 2: Examine the effect of context on pragmatic skills.** Z-scores at the first visit point were calculated comparing the means of each individual to the mean of the TD groups for the CASL-PJ age equivalent, narrative summary score (summed proportion of story elements, character relationships, affect, cognition, causality, and audience engagement), and total PRS-SA violations. Repeated measures then compared changes in Z scores across the contexts at visit one, controlling for mental age. Additionally, Pearson bi-variate correlations assessed relationships between measures of pragmatic language within individuals.

**Aim 3: Identify related abilities within each context and across development.** To assess the role of language, the HLM analyses for CCC-2 Composite, CASL-Age Equivalence, and PRS-SA totals, as well as comparisons of total story elements and evaluation during narrative at visit one, were replicated including PPVT age equivalence and MLU. EVT was also included for the PRS-SA models, but included only in an exploratory way for CASL and CCC-2 because the EVT was not consistently administered at the second visit. Bivariate correlations between, cognition, language, and theory of mind and executive function at each time point and within each context were also conducted.

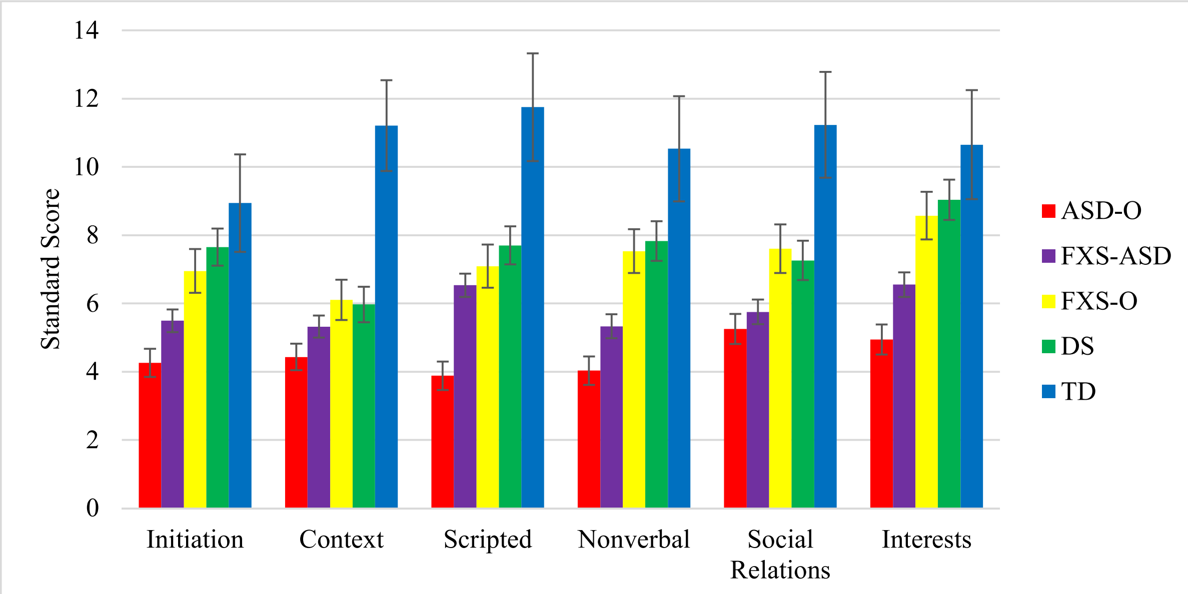
## Results

### Parent Questionnaire: CCC-2

Fixed effects of the hierarchical linear models for the CCC-2 composite and pragmatically related subscales are summarized in Table 3.3. There was a main effect of group for all outcome variables. Standardized scores decreased with age in the domains of Interests (slope ASD-O = -.36; FXS-ASD = -.18; FXS-O = -.50; DS = -.14; TD = -.12) and Initiations (slope ASD-O = -.26; FXS-ASD = -.28; FXS-O = -.52; DS = -.25; TD = -.36), but there was no other significant main effect of age and no age by group (i.e., no differences in rates of change across groups) interactions.

Figure 3.1 summarizes the patterns of mean group differences estimated by the HLM. On the CCC-2 composite and scripted language subscales, the ASD-O group showed greater impairment than the FXS-ASD, FXS-O, and DS groups; all clinical groups were more impaired than those with TD. On the Context subscale, males with ASD-O showed greater impairment than males with FXS-O, DS and TD; all groups were more impaired than the TD group. On the Initiations, Nonverbal, and Interests subscales, a stepwise pattern was observed in that males with ASD-O showed the greatest impairment, followed by males with FXS-ASD, who were more impaired than males with FXS-O, DS and TD. Males with FXS-ASD and ASD-O did not differ and showed greater impairment than males with FXS-O and DS on the Social Relations subscale; all clinical groups showed more impairment than TD.

Figure 3.1 Estimated Marginal Means from HLM for CCC-2 Subscales




Note. Significant differences are reported in text.

Table 3.3. Fixed Effects of HLM for CCC-2 Composite and Subscales

| **CCC-2 Composite** | | |
|---|---|---|
| **Effect** | **F-Value** | **p-value** |
| Group | 11.71 | .000 |
| Chronological Age | 3.11 | .08 |
| Group*Chronological Age | .44 | .78 |
| Mental Age | 9.95 | .002 |
| **CCC-2: Context** | | |
| Group | 8.48 | .000 |
| Chronological Age | .03 | .86 |
| Group*Chronological Age | .29 | .88 |
| Mental Age | .79 | .38 |
| **CCC-2: Initiation** | | |
| Group | 9.76 | .00 |
| Chronological Age | 13.00 | .00 |
| Group*Chronological Age | .38 | .83 |
| Mental Age | 7.77 | .01 |
| **CCC-2: Scripted Language** | | |
| Group | 15.51 | .00 |
| Chronological Age | 2.57 | .11 |
| Group*Chronological Age | .71 | .59 |
| Mental Age | 3.65 | .06 |

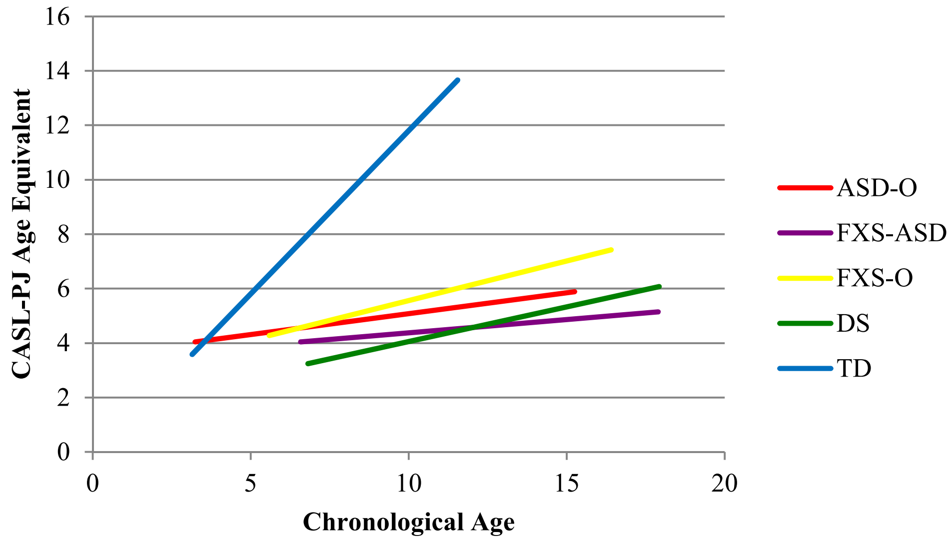
| | | |
|---|---|---|
| **CCC-2: Nonverbal** | | |
| Group | 13.52 | .00 |
| Chronological Age | .09 | .77 |
| Group*Chronological Age | 1.02 | .40 |
| Mental Age | .00 | .99 |
| **CCC-2: Social Relations** | | |
| Group | 6.91 | .00 |
| Chronological Age | .07 | .78 |
| Group*Chronological Age | .58 | .68 |
| Mental Age | .10 | .76 |
| **CCC-2: Interests** | | |
| Group | 12.58 | .00 |
| Chronological Age | 7.28 | .01 |
| Group*Chronological Age | .85 | .50 |
| Mental Age | 1.70 | .19 |

Note. * indicates an interaction.

**Standardized Measure: CASL-PJ**

Figure 3.2 demonstrates rates of change in CASL-PJ with age. Results of the HLM revealed a significant main effect of group ($F = 27.77$, $p < .001$), age ($F = 70.47$, $p < .001$), and group by age interaction for the CASL-PJ ($F = 9.02$, $p < .001$). Mental age was also a significant predictor ($F = 39.76$, $p = .00$). Males with ASD-O, FXS-ASD and DS performed significantly worse than FXS-O, and all groups performed lower than the TD group. Whereas the TD group showed growth in age equivalence with chronological age (slope = .77), and the FXS-O group showed moderate change (FXS-O = .30), other clinical groups were relatively stable (ASD-O = .14; FXS-ASD = .12; DS = .15). Figure 3.2 demonstrates the different rates of development across age for the CASL age equivalence.

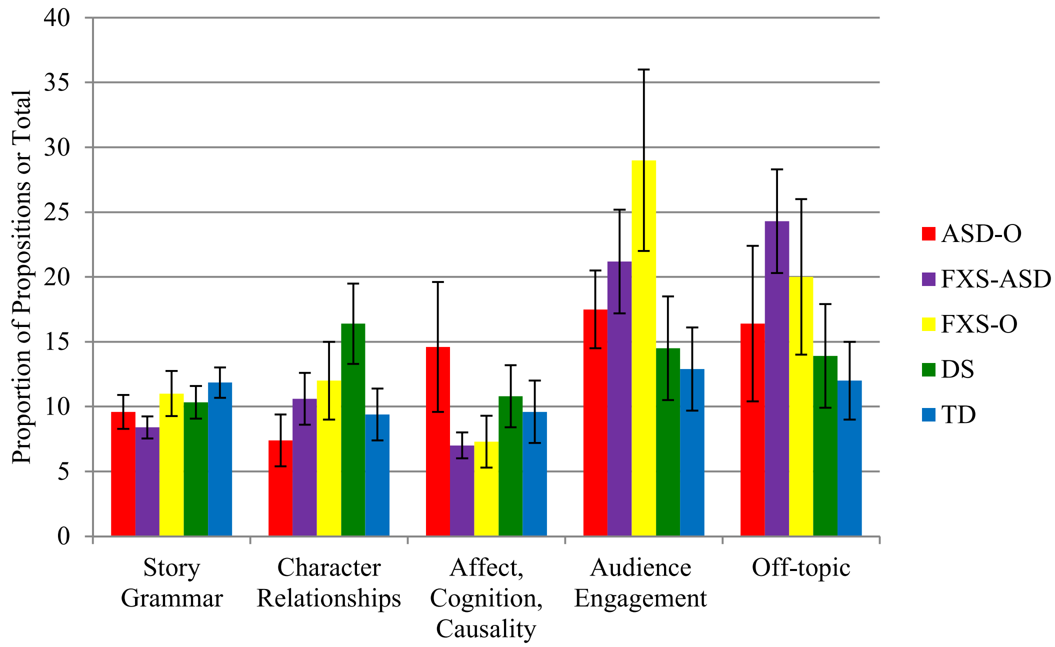
Figure 3.2 Changes in CASL Age Equivalence with Age




## Narrative

**Group differences at visit one.** Figure 3.3 summarizes patterns of group performance on narrative variables at the initial visit.

Figure 3.3. Profiles of Narrative Features at Visit One




Note. All variables graphed are proportions of propositions, except for story grammar, which represented a total score. Group differences are reported in text.

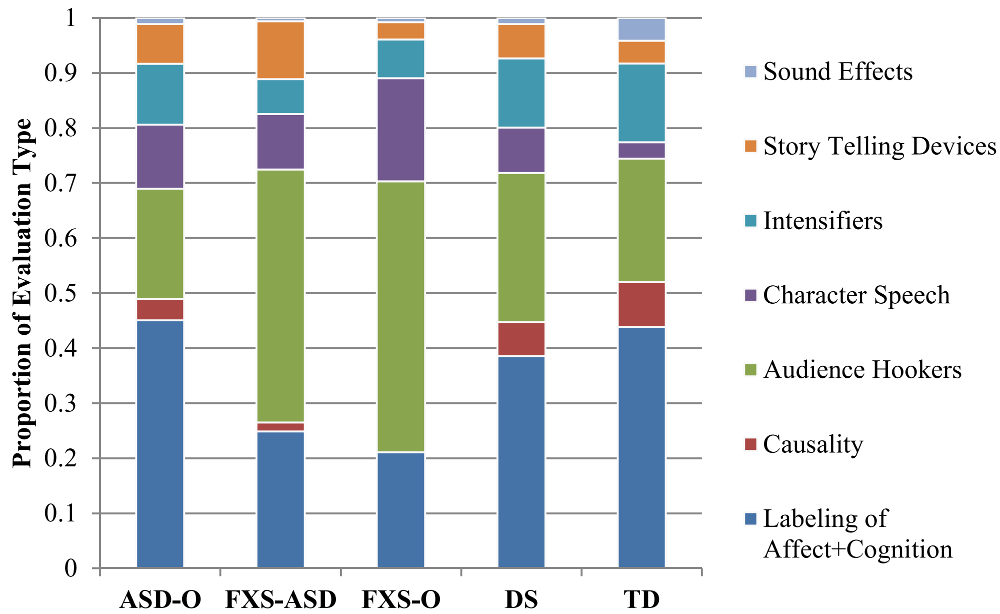
***Length.*** Significant group differences were present for narrative length, as measured by total propositions (Wald = 57.38, $p < .001$). Males with FXS-O used the greatest propositions relative to all other groups; males with TD also included more propositions than males with FXS-ASD and DS.

***Story grammar and character relationships.*** Males with ASD-O and FXS-ASD demonstrated significantly reduced story grammar relative to the other groups (Wald=11.12, p = .025). Males with DS included significantly more character relationships than all other groups, and males with ASD included significantly fewer character relationships than males with FXS-ASD and FXS-O (Wald=21.32, p= .001).

***Evaluation.*** Groups also differed significantly in their use of evaluative devices. Overall, males with FXS-O used significantly greater evaluation than all other groups (Wald = 25.22, $p < .001$); males with ASD-O and FXS-ASD also used more total evaluation than males with DS.

Models of evaluation showed evidence of skew of residuals, and therefore should be interpreted with some caution. Figure 3.4 demonstrates the distribution of types of evaluation used by diverse groups.

Figure 3.4. Distribution of Types of Evaluative Devices Employed by Each Group




This overall group difference in total evaluation appeared driven by the fact that males with FXS-O used the greatest amount of audience engagement devices overall, followed by males with FXS-ASD, who used significantly more than all other groups (Wald = 54.01, $p < .001$; binomial logistic regression: overall Wald for group = 9.12, $p = .06$; parwise comparisons $ps < .05$ for FXS-O group only). Within audience engagement devices, males with FXS-O used a greater proportion of audience hooks than all other clinical groups, and males with FXS-ASD used more of this device than males with DS (Wald = 65.28, $p < .001$; binomial logistic regression overall Wald for group = 8.95, $p = .06$; pairwise comparisons FXS-O show greater likelihood of being above mean than ASD, DS and TD groups, $ps < .05$). Group differences were also observed in evaluative devices related to affect, cognition and causality. Males with ASD-O included significantly more affective states and behaviors relative to males with DS and FXS-ASD (Wald = 13.33, $p = .01$), although this was not replicated with a binomial logistic regression. Males with FXS-ASD were also significantly less likely to mention causality than males with TD (B = -1.915, $p = .04$).

***Off topic.*** There was a main effect of group for off-topic statements (Wald = 71.5, $p < .001$), in that males with FXS-O and FXS-ASD made more off topic statements than all other groups.

***Relationships among narrative variables.*** Overall, greater narrative length was consistently associated with inclusion of story grammar across groups (rs > .5 for all groups with the exception of FXS-O, $r = .39$). However, patterns of relationships within groups varied. Narrative length and story grammar were associated with fewer off topic comments in the ASD-O groups (|r|s > .35). For both the FXS-ASD and DS groups, those that incorporated more character relationships used fewer audience engagement devices ($r = -.46$, $r = -.49$). Finally, incorporation of affect, cognition and causality was positiviely correlated with story elements in the FXS-ASD group, and total propositions in the TD group ($r = .64$).

***Changes in narrative elements over time.*** Non-parametric repeated measures within groups assessed changes in use of narrative elements over time. Overall, patterns of narrative device use were largely stable within groups. Males with ASD-O demonstrated a decline in their inclusion of cognitive states and behaviors over time ($Z = -2.4$, $p = .02$). Both males with FXS-ASD and TD increased in their inclusion of character relationships ($Z = -2.0$, $p = .047$; $Z = -2.4$, $p = .02$) and decreased their inclusion of audience hooks ($Z = 2.33$, $p = .02$; $Z = 2.2$, $p = .03$) across time points. Males with TD also increased their inclusion of story grammar ($Z=2.1$, $p = .03$), and males with DS increased their inclusion of enacted character speech ($Z=-2.0$, $p = .04$).

**Semi-Naturalistic Conversation Context: PRS-SA**

**Comparisons at visit one.** Males with ASD-O and FXS-ASD did not differ in total pragmatic violations and demonstrated the greater total pragmatic impairment relative to males with DS and FXS-O, who in turn demonstrated greater impairment than males with TD ($F(4, 121) = 26.00$, $p < .001$).

Item-level analyses were conducted to examine the specific types of pragmatic language violations that distinguished groups (summarized in Table 3.4). Males with FXS-ASD and ASD-O showed overlapping impairment in initiation of appropriate topics, interrupting, response elaboration, reciprocal conversation, atypical intonation, facial expressions, and eye contact. Males with ASD-O and FXS-ASD also used more scripted language than males with DS (although did not differ from FXS-O), and all groups used more scripted language than males with TD. However, males with ASD-O showed distinct difficulties in signaling humor. The TD group showed the fewest motor mannerisms and difficulties with management of personal space.

Table 3.4 Patterns of Differences on Item Level PRS-SA at Visit One

| | ASD-O | | FXS-ASD | | FXS-O | | DS | | TD | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Coding Item** | **Mean** | **S.E.** | **Mean** | **S.E.** | **Mean** | **S.E.** | **Mean** | **S.E.** | **Mean** | **S.E.** |
| **Personal candidness** | 0.85 | 0.16 | 1.00 | 0.15 | 1.23 | 0.26 | 0.85 | 0.18 | 0.59 | 0.18 |
| **Swearing** | 0.00 | 0.00 | 0.15 | 0.09 | 0.15 | 0.15 | 0.00 | 0.00 | 0.18 | 0.13 |
| **Overly talkative** | 0.70 | 0.13 | 0.54 | 0.13 | 0.62 | 0.21 | 0.25 | 0.12 | 0.32 | 0.10 |
| **Overly detailed** | 0.48 | 0.14 | 0.23 | 0.09 | 0.23 | 0.17 | 0.00 | 0.00 | 0.27 | 0.12 |
| **Failure to provide background** | 1.30 | 0.15 | 1.00 | 0.12 | 1.08 | 0.21 | 0.90 | 0.18 | 0.73 | 0.15 |
| **Redundancy** | 0.24 | 0.10 | 0.21 | 0.09 | 0.15 | 0.10 | 0.05 | 0.05 | 0.14 | 0.07 |
| **Failure to signal humor** | **0.85[a]** | **0.16** | **0.28[b]** | **0.10** | **0.31[b]** | **0.17** | **0.00[b]** | **0.00** | **0.05[b]** | **0.05** |
| **Failure to clarify** | 0.48 | 0.13 | 0.33 | 0.10 | 0.23 | 0.12 | 0.15 | 0.08 | 0.45 | 0.14 |
| **Reduced topic initiation** | **1.21[a]** | **0.17** | **1.13[a]** | **0.16** | **0.15[b]** | **0.15** | **0.50[b]** | **0.20** | **0.27[b]** | **0.15** |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Inappropriate topic shift** | **1.03[a]** | **0.18** | **1.33[a]** | **0.15** | **0.77[a,b]** | **0.28** | **0.60[b]** | **0.21** | **0.45[b]** | **0.18** |
| **Interrupting** | **1.12[a]** | **0.15** | **1.05[a]** | **0.15** | **0.46[b]** | **0.22** | **0.40[b]** | **0.15** | **0.77[a]** | **0.17** |
| **Failure to acknowledge** | **1.18[a]** | **0.15** | **0.79[b]** | **0.15** | **0.23[b,c]** | **0.12** | **0.55[b,c]** | **0.18** | **0.27[c]** | **0.13** |
| **Lack of response elaboration** | **1.30[a]** | **0.13** | **1.46[a]** | **0.10** | **0.85[b]** | **0.10** | **0.85[b]** | **0.17** | **0.32[c]** | **0.12** |
| **Topic perseveration** | 0.97 | 0.18 | 1.03 | 0.16 | 0.77 | 0.28 | 0.40 | 0.18 | 0.45 | 0.18 |
| **Inappropriate vocal noises** | **1.09[a]** | **0.16** | **0.44[b]** | **0.13** | **0.62[a,b]** | **0.24** | **0.60[a]** | **0.21** | **0.18[b]** | **0.13** |
| **Reduced reciprocal conversation** | **1.52[a]** | **0.12** | **1.56[a]** | **0.10** | **0.92[b,c]** | **0.21** | **1.10[b]** | **0.19** | **0.41[c]** | **0.13** |
| **Overly formal** | 0.33 | 0.11 | 0.13 | 0.08 | 0.38 | 0.21 | 0.25 | 0.12 | 0.23 | 0.11 |
| **Scripted** | **1.36[a]** | **0.15** | **1.41[a]** | **0.14** | **1.23[a,b]** | **0.26** | **0.75[b]** | **0.20** | **0.14[c]** | **0.07** |
| **Errors in grammar and vocabulary** | 1.58 | 0.13 | 1.59 | 0.12 | 1.69 | 0.17 | 1.55 | 0.18 | 1.68 | 0.15 |
| **Difficulty with intelligibility** | **0.42[a,c]** | **0.10** | **1.18[b]** | **0.10** | **0.62[a]** | **0.14** | **1.60[b]** | **0.11** | **0.23[c]** | **0.09** |
| **Rate of speech** | **1.27[a,b]** | **0.17** | **1.38[b]** | **0.15** | **0.77[a,c]** | **0.28** | **1.10[a,b]** | **0.23** | **0.27[c]** | **0.15** |
| **Atypical intonation** | **1.58[a]** | **0.13** | **1.38[a,b]** | **0.13** | **0.92[b]** | **0.26** | **0.50[c]** | **0.15** | **0.09[c]** | **0.09** |
| **Atypical volume** | 1.21 | 0.15 | 1.10 | 0.14 | 0.85 | 0.25 | 0.65 | 0.20 | 0.77 | 0.17 |
| **Use of character speech** | 0.55 | 0.16 | 0.26 | 0.11 | 0.46 | 0.24 | 0.20 | 0.14 | 0.09 | 0.09 |
| **Difficulties with formulation** | 0.79 | 0.17 | 0.26 | 0.11 | 0.62 | 0.27 | 0.50 | 0.20 | 0.82 | 0.21 |
| **Stuttering** | **0.06[a]** | **0.06** | **1.08[b]** | **0.16** | **0.31[a]** | **0.21** | **1.20[b]** | **0.22** | **0.09[a]** | **0.09** |
| **Mismanagement of personal space** | **1.73[a]** | **0.10** | **1.69[a]** | **0.10** | **1.62[a]** | **0.21** | **1.65[a]** | **0.17** | **1.14[b]** | **0.17** |
| **Reduced gestures** | **1.48[a]** | **0.13** | **1.18[b]** | **0.12** | **0.77[b,c]** | **0.23** | **0.20[c]** | **0.12** | **0.59[c]** | **0.17** |
| **Atypical motor mannerisms** | **1.03[a]** | **0.15** | **0.95[a,b]** | **0.15** | **0.85[a,b,c]** | **0.25** | **0.50[b,c]** | **0.20** | **0.36[c]** | **0.14** |
| **Atypical facial expressions** | **1.27[a]** | **0.17** | **1.03[a]** | **0.16** | **0.31[b]** | **0.21** | **0.10[b]** | **0.10** | **0.18[b]** | **0.13** |
| **Atypical eye contact** | **1.70[a]** | **0.10** | **1.54[a]** | **0.10** | **1.08[b]** | **0.21** | **0.50[c]** | **0.14** | **0.50[c]** | **0.13** |
| **Inappropriate hygiene** | 0.79 | 0.17 | 0.56 | 0.15 | 0.31 | 0.21 | 0.80 | 0.22 | 0.27 | 0.15 |

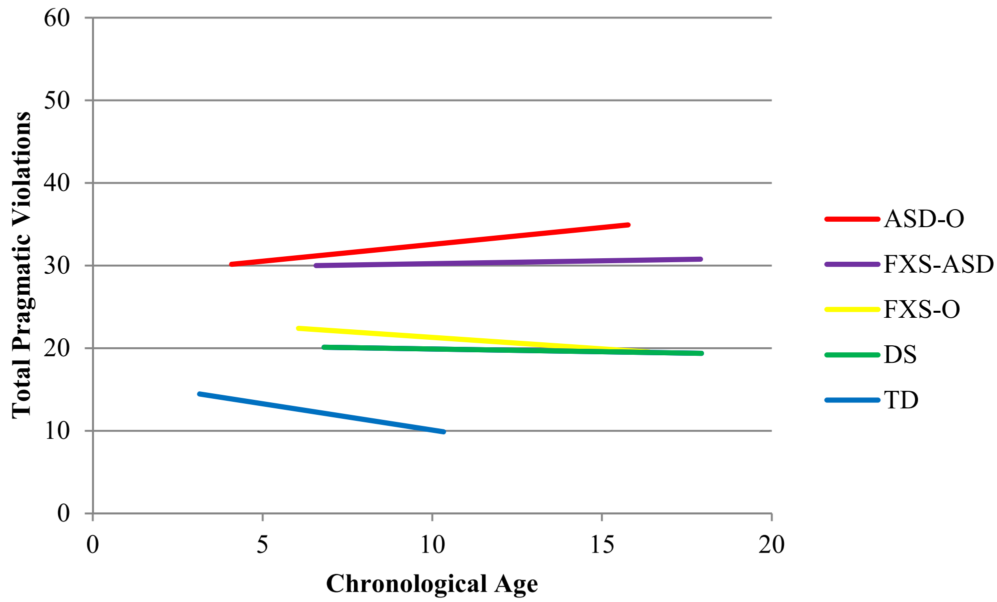
Note. Bolded findings indicate significant overall models (Fs > 2.5, ps < .05). SE = standard error. Differing superscripts indicate group differences at the level of p < .05.

**Change over time in total violations and subscales.** Hierarchical linear models assessed changes in PRS-SA total with age, as well as the theoretically driven subscales of the PRS-SA.

There was a main effect of group for all outcome variables, but no main effects of age or group * age interactions ($Fs < 1$, $ps > .30$). Trajectories of total pragmatic violations are summarized in Figure 3.5.

For total pragmatic language violations, males with ASD-O showed the most significant pragmatic impairment, followed by males with FXS-ASD, who showed significantly greater impairment than males with DS, FXS-O and TD ($F(4,194) = 24.21$, $p < .001$). Patterns of group differences on subscales revealed areas of overlap and divergence in males with FXS-ASD and ASD-O. Males with ASD-O and FXS-ASD group overlapped on the discourse management subscale ($p = .096$), and both groups showed greater impairment than males with DS and FXS-O, and ASD-O showed greater impairment than males with TD; F(4,140.81 = 14.03, $p < .001$). Males with ASD-O and FXS-ASD similarly overlapped ($p = .71$) and showed significantly greater impairment in suprasegmental features of speech than all other groups, and males with FXS-O showed greater impairment than males with TD; F(4, 135.31 = 6.61, $p < .001$). Males with ASD-O and FXS-ASD also overlapped ($p = .07$) and showed greater impairment than all other groups in nonverbal aspects of pragmatics ($F(4,194) = 25.99$, $p < .05$). Males with ASD-O showed significantly greater impairment on the theory of mind subscale than males with DS, FXS-ASD and FXS-O ($F(4,194) = 4.73$, $p = .001$). Finally, all clinical groups showed greater impairment than males with TD in speech and language behaviors contributing to pragmatic language ($F(4,194) = 3.67$, $p < .001$).

Figure 3.5. Overall Changes in Pragmatic Violations with Age




Note. Greater PRS-SA total score indicates greater impairment.

**Changes in specific pragmatic skills.** Changes over time in individual skills assessed by the PRS-SA are presented in Table 3.5. Males with ASD-O demonstrated a significantly increased difficulty in repetitiveness (i.e., redundancy) and perseveration on a preferred topic, and a marginal increased impairment ($p < .1$) in including too much detail, atypical intonation and volume, and reduced facial expressions. Males with FXS-ASD demonstrated a significant increase in impairments in signaling of humor, inappropriate vocal noises, unintelligibility, and gesture use; they also demonstrated a marginal increase in redundancy and marginal improvement in management of personal space. Males with FXS-O showed significant improvement in using overly-candid language, but greater impairments in rate. Males with FXS-O also showed marginal improvement in their ability to engage in reciprocal conversation and manage personal space appropriately, and an increase in difficulty initiating appropriate topics. Males with DS demonstrated a significant increase in impairments related to rate, and several marginal changes. Specifically, males with DS demonstrated improvement in engagement in reciprocal conversation and management of personal space, but increased impairment in topic initiation, inappropriate signaling of humor, excessive talkativeness, and reduced gestures and facial expressions.

Table 3.5. Repeated Measures-Item Level PRS-SA

| | **ASD-O** | | **FXS-ASD** | | **FXS-O** | | **DS** | | **TD** | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Coding Item** | 1st | 2nd | 1st | 2nd | 1st | 2nd | 1st | 2nd | 1st | 2nd |
| **Personal candidness** | 1.14 | 0.86 | 1.09 | 0.83 | **1.33** | **0** | 0.93 | 1 | 0.91 | 0.45 |
| **Swearing** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.36 | 0 |
| **Overly talkative** | 0.79 | 0.79 | 0.48 | 0.3 | 0.67 | 0.50 | ***0.21*** | ***0.43*** | 0.27 | 0.73 |
| **Overly detailed** | **0.36** | **1.07** | 0.3 | 0.26 | 0.33 | 0 | 0 | 0.14 | 0.27 | 0.45 |
| **Failure to provide background** | 1.36 | 1.5 | 1 | 1.26 | 1.17 | 1.00 | ***0.57*** | ***1.07*** | ***0.36*** | ***0.91*** |
| **Redundancy** | ***0*** | ***0.57*** | ***0*** | ***0.26*** | 0.17 | 0.50 | 0.07 | 0.5 | 0.09 | 0.09 |
| **Failure to signal humor** | 0.64 | 1.21 | **0.13** | **0.65** | 0.67 | 0.50 | ***0*** | ***0.21*** | 0.09 | 0.27 |
| **Failure to clarify** | 0.36 | 0.64 | 0.3 | 0.35 | 0 | 0.33 | 0.07 | 0.29 | 0.18 | 0.09 |
| **Reduced topic initiation** | 1.14 | 0.86 | 1.13 | 1.04 | ***0*** | ***1.00*** | 0.43 | 0.86 | 0 | 0.36 |
| **Inappropriate topic shift** | 1.14 | 1.14 | 1.13 | 1.48 | 0.67 | 1.33 | 0.57 | 0.71 | 0.55 | 0.73 |
| **Interrupting** | 1.00 | 1.5 | 0.96 | 0.83 | 0.33 | 0.83 | 0.21 | 0.64 | 1.00 | 1.09 |
| **Failure to acknowledge** | 1.21 | 1 | 0.61 | 0.78 | 0.17 | 0.17 | 0.57 | 0.21 | 0.18 | 0.09 |
| **Lack of response elaboration** | 1.14 | 1.07 | 1.39 | 1.43 | 0.83 | 0.67 | 0.86 | 0.57 | 0.18 | 0.36 |
| **Perseveration** | **1.14** | **1.71** | 0.96 | 1.48 | 1.00 | 0.67 | 0.57 | 0.71 | 0.36 | 0 |
| **Inappropriate vocal noises** | 0.64 | 0.86 | **0.17** | **0.91** | 0.83 | 0.67 | 0.43 | 0.36 | 0.36 | 0.18 |
| **Reduced reciprocal conversation** | 1.57 | 1.36 | 1.52 | 1.57 | ***1.17*** | ***0.67*** | ***1.21*** | ***0.57*** | 0.27 | 0.55 |
| **Overly formal** | 0.43 | 0.93 | 0.22 | 0.26 | 0.67 | 0 | 0.29 | 0.14 | 0.27 | 0.45 |
| **Scripted** | 1.5 | 1.5 | 1.57 | 1.30 | 1.50 | 1.33 | 0.93 | 0.29 | 0 | 0.18 |
| **Errors in grammar and vocabulary** | 1.43 | 1.43 | 1.43 | 1.65 | 1.67 | 1.83 | 1.5 | 1.86 | **1.82** | **0.91** |
| **Difficulty with intelligibility** | 0.14 | 0.36 | **1.00** | **1.52** | 0.67 | 0.50 | 1.50 | 1.36 | 0.18 | 0.09 |
| **Rate of Speech** | 0.86 | 1.43 | 1.22 | 1.57 | **0.33** | **1.33** | ***0.86*** | ***1.86*** | 0.18 | 0.18 |
| **Atypical intonation** | ***1.5*** | ***1.86*** | 1.30 | 1.70 | 0.67 | 1.00 | 0.64 | 0.5 | 0 | 0 |

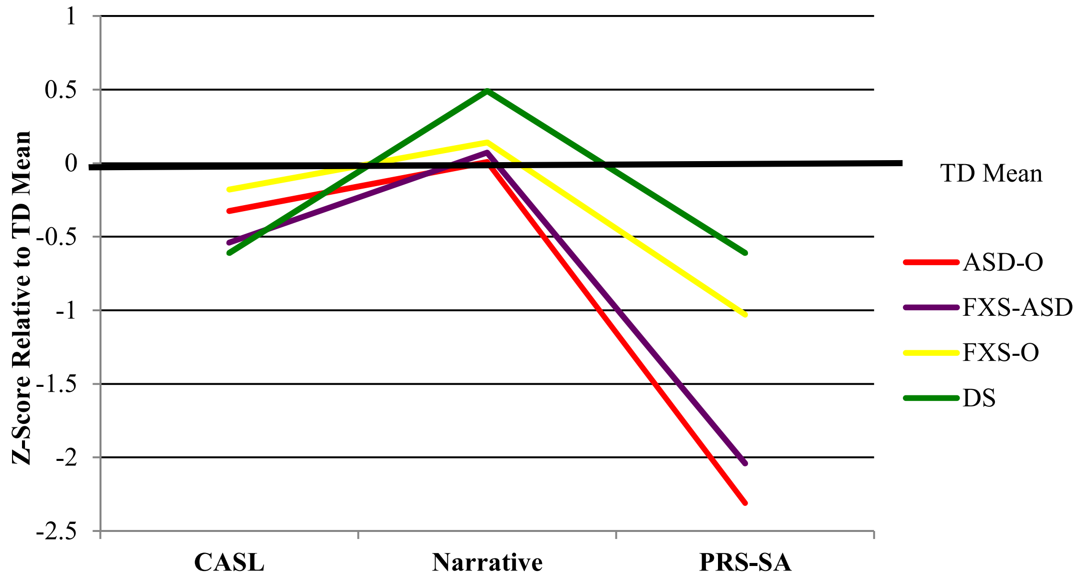
| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Atypical volume** | ***1.14*** | ***1.64*** | 1.04 | 1.17 | 1.00 | 0.83 | 0.5 | 0.43 | 0.91 | 0.55 |
| **Use of character speech** | 0.71 | 0.86 | 0.17 | 0.87 | 0.67 | 0.67 | 0 | 0.14 | 0.18 | 0.18 |
| **Difficulties with formulation** | 0.29 | 0.57 | 0.17 | 0.26 | 0.33 | 0.33 | 0.29 | 0.57 | **0.91** | **0.18** |
| **Stuttering** | 0 | 0.14 | 0.96 | 0.87 | 0 | 0.67 | 0.86 | 1.29 | 0.18 | 0 |
| **Mismanagement of personal space** | ***1.79*** | ***1.21*** | 1.83 | 1.57 | ***1.67*** | ***0.50*** | ***1.71*** | ***0.79*** | 1.18 | 0.91 |
| **Gestures** | 1.36 | 1.36 | **1.13** | **1.61** | 0.83 | 0.83 | ***0.14*** | ***0.5*** | 0.82 | 0.36 |
| **Atypical motor mannerisms** | 0.57 | 1.00 | 0.87 | 0.74 | 1.00 | 0.67 | 0.43 | 0.36 | 0.45 | 0 |
| **Atypical facial expressions** | ***1.00*** | ***1.71*** | 1.04 | 1.39 | 0.33 | 0.67 | ***0.14*** | ***0.57*** | 0 | 0.18 |
| **Atypical eye contact** | 1.71 | 1.79 | 1.52 | 1.57 | 1.00 | 0.67 | 0.5 | 0.29 | 0.64 | 0.45 |
| **Inappropriate hygiene** | 0.86 | 1.00 | 0.61 | 0.87 | 0.33 | 0 | 0.71 | 0.43 | 0.18 | 0.55 |

Note. 1st and 2nd indicate first and second time points included in repeated measures. **Bolded** findings indicate a change significant at the level of $p < .05$. ***Italic*** findings indicate marginally significant change at the level of $p < .1$.

## Cross-Context Comparisons at Visit One

**Patterns of performance at visit one.** There was a significant group * context interaction ($F(6, 122) = 4.69$, $p < .001$) and main effect of group ($F(3, 61) = 4.25$, $p = .01$) in patterns of performance across contexts. As demonstrated in Figure 3.6, males with ASD-O and FXS-ASD demonstrated a steeper decline between more structured tasks (i.e., CASL and narrative) and the semi-naturalistic task, and showed reduced overall Z scores relative to males with DS.

Figure 3.6. Z Scores Across Contexts




**Correlations between contexts.** Cross-context correlations revealed relatively few significant relationships between measures. On the CCC-2 parent report, greater parent-reported competence was associated with better performance on the CASL-PJ for males with ASD-O (r = .45), and fewer pragmatic impairments in males with DS (r = -.72). Better performance on the CASL-PJ was associated with reduced PRS-SA totals for the DS, FXS-ASD and FXS-O groups (rs < -.3). Greater CASL-PJ performance was also associated with increased story grammar during narrative in the ASD-O, FXS-ASD, DS and TD groups, and with moderate effect size in the FXS-O group (rs > .4). Finally, greater PRS-SA total pragmatic violations were associated with increased use of audience engagement devices during narrative in the DS group (r = .59) and off topic remarks in the FXS-O group (r = .66), but reduced off topic comments in the TD group (r = -.55).

**Exploration of Related Abilities**

**Replication of models with language covariates.** Table 3.6 summarizes the significance of receptive vocabulary age equivalence, mean length of utterance, and expressive vocabulary age equivalence as predictors in the HLM for CCC-2 Composite, CASL-PJ Age Equivalent and PRS-SA total. Overall, language covariates contributed most strongly to CASL-PJ change. Overall findings related to the main effect of group, age, and age * group interactions were largely consistent with models run without language covariates, with a few notable exceptions. When language was included in the model for CCC-2, a significant main effect of chronological age emerged, in that all groups decreased in standard score slightly with age. For the CASL-PJ subscale, the pattern of males with ASD-O developing more slowly than males with FXS-O became significant.

Table 3.6. Contributions of Structural Language to HLM.

| | | CCC-2 Composite | CASL-AE | PRS-SA Total |
|---|---|---|---|---|
| **PPVT-AE** | *Fixed Effect* | F = 3.57, p = .06 | **F=111.82, p < .001** | **F = 9.14, p = .003** |
| | *Slope Estimate* | 1 point increase in standard score/year | .44 years AE/ 1 year AE in PPVT | -1.5 decrease violations/1 year AE |
| **MLU** | *Fixed Effect* | F = .53, p = .47 | **F = 13.53, p < .001** | F = .71, p = .40 |
| | *Slope Estimate* | .73 increase in standard score/year | .23 years AE/ 1 unit MLU | -.5 decrease in violations/1 unit increase in MLU |
| **EVT-AE** | *Fixed Effect* | F = .029, p = .86 | **F=22.87, p < .001** | F = .54, p = .46 |
| | *Slope Estimate* | .13 increase in standard score/year | .28 years AE/ 1 year AE | .43 increase in violations/ 1 year AE |

Notes. Significant effects are bolded. AE = age equivalent. Slopes represent estimates derived from HLM. EVT=Expressive Vocabulary Test, PPVT = Peabody Picture Vocabulary Test, MLU = Mean Length of Utterance

For the narrative comparisons at visit one, there were no longer group differences in total story elements after including language covariates in the model (Wald=4.7 p = .32). Males with DS continued to use more character relationships than males with ASD, FXS-ASD and TD, and males with ASD used fewer than males with FXS-O (Wald = 15.92, p = .003). Males with FXS-O continued to use greater total evaluation than all other groups, and males with FXS-ASD and

ASD-O more than DS (Wald = 23.31, p < .001). Consistent with findings controlling for mental age, this overall difference continued to be driven by greater use of audience engagement in males with FXS-O relative to all other groups, and greater use in FXS-ASD relative to the DS and TD groups (Wald =39. 33, p < .001; binomial logistic regression Wald = 9.18, p = .06, FXS-O greater than all other groups p < .05). Males with FXS-O and FXS-ASD used greater audience hooks than all other groups (Wald = 54.26, p < .001; binomial logistic regression Wald = 8.12, p = .09; pairwise FXS-O greater than TD, DS, ASD-O at p < .05). Males with FXS-O and FXS-ASD also made greater off topic comments (Wald = 80.46, p < .001), than males with ASD-O, DS, and TD.

**Bivariate correlations.** Bivariate correlations of mental age and structural language and measures of pragmatic language in each context are presented in Table 3.8. There were no significant relationships with character relationships or instances of affect, cognition or causality in narratives. Across groups, few variables were related to parent-report on the CCC-2, with the notable exception of strong positive relationships within the typically developing group. In contrast, across groups, CASL-PJ age equivalence and the inclusion of story grammar during narrative were strongly positively associated with measures of mental age and structural language. These patterns were largely consistent across visits.

Table 3.7. Bi-Variate Correlations Between Primary Pragmatic Variables and Mental Age and Structural Language

| **Outcome Measure** | | **Group** | | | | |
|---|---|---|---|---|---|---|
| | | **ASD-O** | **FXS-ASD** | **FXS-O** | **DS** | **TD** |
| **CCC-2** | Leiter | .24 | .19 | .56 | -.004 | .82* |
| | PPVT | .21 | .16 | .53 | .24 | .81* |
| | EVT | .24 | .23 | .61 | .46 | .85* |
| | MLU | .09 | .21 | .66 | .20 | -.15 |
| **CASL** | Leiter | .68* | .19 | .95* | .64* | .82* |
| | PPVT | .81* | .64* | .90* | .79* | .81* |
| | EVT | .84* | .60* | .97* | .78* | .85* |
| | MLU | .57* | .37* | .22 | .50* | -.15 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Narrative: Story Grammar** | Leiter | .45* | .28 | .53 | .49* | .83* |
| | PPVT | .55* | .56 | .59 | .62* | .73* |
| | EVT | .49* | .70* | .75* | .79* | .75* |
| | MLU | .44* | -.003 | .31 | .76* | -.25 |
| **Narrative: Audience Engagement** | Leiter | -.14 | .20 | .73* | .-.17 | .02 |
| | PPVT | -.21 | -.15 | .62 | -.32 | .01 |
| | EVT | -.23 | .05 | .61 | -.40 | -.04 |
| | MLU | -.40 | -.25 | .36 | -.06 | .17 |
| **Narrative: Off Topic** | Leiter | -.30 | -.39* | -.36 | -.42 | -.29 |
| | PPVT | -.37 | -.10 | -.54 | -.53* | -.42 |
| | EVT | -.34 | -.17 | -.51 | -.43 | -.31 |
| | MLU | -.60* | .41* | .17 | -.34 | .36 |
| **PRS-SA-Total Violations** | Leiter | .09 | .08 | -.51 | -.31 | -.04 |
| | PPVT | -.19 | -.17 | -.54* | -.35 | -.02 |
| | EVT | -.10 | .26 | -.58* | -.41 | -.10 |
| | MLU | -.23 | -.03 | -.28 | -.25 | -.04 |

Notes. EVT=Expressive Vocabulary Test, PPVT = Peabody Picture Vocabulary Test, MLU = Mean Length of Utterance. PRS-SA = Pragmatic Rating Scale-School Age. * p < .05

Table 3.9 summarizes correlations between theory of mind, executive function and pragmatic outcome variables. Greater theory of mind was associated with higher CASL-PJ age equivalence in males with ASD-O, FXS-ASD, DS and TD, as well as the use of affect, cognition and causality during narrative in the TD group. Greater executive function impairment was related to increased PRS-SA totals in males with FXS-ASD and DS. These patterns were largely consistent at the later time point.

Table 3.9 Relationships Between Pragmatic Outcome Measures, Executive Function and Theory of Mind

| **Outcome Measure** | | **Group** | | | | |
|---|---|---|---|---|---|---|
| | | **ASD-O** | **FXS-ASD** | **FXS-O** | **DS** | **TD** |
| **CCC-2** | ToM | .28 | .27 | -.07 | -.19 | .55 |
| | Brief | -.23 | -.52* | -.22 | -.48 | -.74* |
| **CASL-PJ** | ToM | .46* | .17 | .68* | .52* | .55* |
| | Brief | -.72* | -.36* | -.27 | -.54 | .22 |
| **Narrative: Story Grammar** | ToM | .12 | .10 | .72* | .32 | .78* |
| | Brief | -.32 | .08 | -.56 | -.67* | -.12 |
| **Narrative:** | ToM | -.24 | -.27 | .80 | .27 | -.26 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Proportion Character Relationships** | Brief | .33 | -.15 | -.34 | .16 | .07 |
| **Narrative: Affect, Cognition, Causality** | ToM | -.01 | -.10 | .13 | .12 | .57* |
| | Brief | -.10 | -.23 | -.06 | -.15 | -.02 |
| **Narrative: Audience Engagement** | ToM | .39 | -.07 | .14 | -.29 | -.09 |
| | Brief | -.15 | .29 | .03 | .47 | .14 |
| **Narrative: Off Topic** | ToM | -.04 | .14 | -.78* | -.34 | -.27 |
| | Brief | .07 | -.12 | .71 | -.08 | .47 |
| **PRS-SA Total Violations** | ToM | -.35 | -.03 | -.48 | -.11 | -.19 |
| | Brief | -.001 | .45* | .37 | .75* | .11 |

Notes. BRIEF= BRIEF parent report of executive function, CCC-2 = Children's Communicative Checklist-2nd Edition, CASL-PJ = CASL pragmatic judgment subscale, ToM = Theory of Mind Factor Score, PRS-SA = Pragmatic Rating Scale-School Age. * $p < .05$

## Discussion

This study is the first longitudinal analysis of pragmatic language ability, across multiple contexts, directly comparing males with ASD-O, FXS-ASD, FXS-O, DS and TD. Results suggest that males with ASD-O showed the greatest pragmatic impairment across contexts, with several specific areas of overlap with FXS-ASD observed. Clinical groups demonstrated minimal changes in overall pragmatic impairments with age, and thus patterns of group differences persisted over time. Across groups, structured tasks drew more on structural language skills than the semi-naturalistic contexts, and relationships with theory of mind and executive function varied across groups and context.

### Group Profiles Over Time

**Standardized measures.** Consistent with prior work relying on partially overlapping samples (M. Lee, Bush, et al., 2017; Losh et al., 2012), the CCC-2 composite distinguished the clinical groups from controls. In contrast to Losh et al. (2012), which did not examine performance longitudinally and included teacher report, the parent report CCC-2 showed sensitivity to differences within clinical groups, with males with ASD-O showing worse performance than all other clinical groups over time on the composite and on several subscales.

This difference in findings may reflect variation in reporters, as parent-report was included in the current study as opposed to teacher report to reduce the confound of changes in raters (and potential interpretation of items) across visits. Given that this measure was designed specifically to tap communicative behaviors related to ASD-O, parents of children with clinically diagnosed ASD may have naturally been more attuned to these behaviors at home, resulting in greater reported severity. Of note, males with ASD-O and FXS-ASD demonstrated a similar degree of impairment in parent-reported social relations, which reflects interactions with peers and friendships, that distinguished them from other groups, which may reflect common “real-world” social difficulties within these groups.

Building on Martin et al. (2013)’s longitudinal analysis of CASL pragmatic judgment performance, the FXS-O group continued to show improved performance relative to males with FXS-ASD and DS, and this study demonstrates that this group also outperformed males with ASD-O. Further, all clinical groups showed a delay in development of skill as assessed by this measure. Together, these results highlight that the presence of pragmatic language deficits across clinical groups as assessed by parent-report and standardized measures, provide further evidence for pragmatic deficits as a core feature of ASD-O, and highlight areas of relative strength in males with FXS-O as compared to males with FXS-ASD.

**Narrative.** Analysis of narrative language revealed more specific similarities and differences within clinical groups. Similar to prior work, males with ASD-O in the current study produced narratives of comparable length to males with TD and, once accounting for structural language, a comparable number of story elements (Beaumont & Newcombe, 2006; L. Capps et al., 2000; Colle et al., 2008; Diehl et al., 2006; Hogan-Brown et al., 2013; Loveland et al., 1990; Rumpf et al., 2012; Tager-Flusberg & Sullivan, 1995). In contrast to prior work demonstrating differences in evaluation in ASD-O, findings in the current study were more mixed (Beaumont & Newcombe, 2006; L. Capps et al., 2000; M. Lee, Martin, et al., 2017; Losh & Capps, 2003). Of note, the occurrence of causal language related to affect or cognition, an area of difficulty in ASD (e.g., Losh et al., 2003; Lee et al., 2016), was limited across groups, and it may be that the highly structured nature of the narrative task did not elicit this type of language. The greater rates of affect observed in ASD-O may also relate to a tendency to label, rather than integrate emotions, which has been observed in prior work (Tager-Flusberg et al., 1995).

ASD symptoms impacted narrative quality in FXS-ASD to some extent, in that, consistent with Estigarribia et al. (2012), males with FXS-ASD used fewer story elements than males with FXS-O. However, a notable feature of narratives of both FXS groups, and in particular the FXS-O group, was their increased use of audience engagement devices. Although attempts to engage the audience in a story can contribute to successful narration (Bamberg & Damred-Frye, 1991; Bamberg & Reilly, 1996; Reilly, 1992) excessive attempts to do so may detract from narrative quality, and such findings have been reported in Williams syndrome (Losh, Bellugi, & Anderson, 2001). In the current study, qualitative analysis revealed males with FXS in both groups tended to use audience engagement in a repetitive way. For example, one male with FXS-ASD (mental age = 5.2 years) repeatedly began statements by saying “look” as in, “look the penguins, look he broke it, look at his ball.” Ferrier et al. (1991) hypothesized that males with FXS may uniquely rely on perseverative language to maintain social interactions; although findings in the current study should be interpreted with some caution given distribution of data, it is possible that such repetitive use of audience engagement may serve a similar function in a narrative context. Both FXS groups also used more off-topic or inappropriate statements, replicating findings for males with FXS-ASD in other more structured tasks (Barstein et al., under review).

Consistent with prior work suggesting that narrative may represent an area of relative strength for males with DS (e.g., Bordeau and Chapman, 2000; Miles and Chapman, 2002), males with DS included the greatest number of character relationships in their narratives. Qualitative analysis revealed that males with DS tended to refer to characters in relational terms early and throughout the narrative, whereas males with ASD-O referred to characters primarily by name (e.g., "Pingu"). For example, whereas a male with ASD-O began his story "once upon a time *they were penguins* are little"; a male with DS began his story, "*mother and the father* are saying goodnight to the *kids."* In contrast to Asbhy et al. (2017) males with DS did not show differences in *types* of evaluation relative to males FXS; however, as noted previously, this may have reflected the highly structured nature of the task.

**Semi-Naturalistic Conversations.** Assessment of pragmatic deficits during semi-naturalistic conversations revealed that, across development, males with ASD-O demonstrated the greatest difficulty, followed by males with FXS-ASD, who showed greater impairments than males with FXS-O, DS, and TD. It is important to note that *all* clinical groups showed deficits relative to younger typically developing peers at the initial visit, including males with DS, a population which is often characterized by a social and engaging nature (Moore et al. 2002; Wishart and Johnston 1990). However, difficulties emerged both at the initial visit and across development that were specific to males with ASD-O, in particular impairments in pragmatic langauge deficits theoretically associated with theory of mind (e.g., offering the appropriate amount of information in conversation, recognizing breakdowns). These difficulties observed in the ASD-O group are consistent with an extensive body of literature documenting pragmatic language impairment as a core feature of ASD (e.g., Capps, Kehres, & Sigman, 1998; Lam & Yeung, 2011; Paul et al., 1987; Adams et al. 2002; Tager-Flusberg & Anderson 1991).

Building on a growing body of work suggesting that pragmatic language in FXS is impacted by ASD symptoms (Losh et al., 2012; Klusek et al., 2014; Martin et al., 2012; Martin et al., 2013; Roberts et al., 2007), males with FXS-ASD showed significantly greater impairment than males with FXS-O in pragmatic violations across chronological age. Further, whereas pragmatic langauge violations were not *identical* in males with FXS-ASD and ASD-O, results suggested more specific areas of overlap consistent across age, primarily related to discourse management, or fundamental skills critical to reciprocal interaction such as elaboration on a partner's response or engagement in back and forth conversation. Overlap was also observed in suprasegmental features of speech, consistent with prior work suggesting prosodic differences in males with FXS-ASD relative to males with FXS-O (Zajac, Harris, Roberts, & Martin, 2009), as well as nonverbal communication. Together, this overlap suggests specific aspects of pragmatic skill that may serve as fruitful targets of investigation of pathways from *FMR1* to ASD-related phenotypes in ASD-O and FXS-ASD.

**Change Over Time**

This study was also novel in its inclusion of multiple time points during the school age years for individuals with developmental disabilities, a time when pragmatic language becomes increasingly complex (and relevant to social relationships) in typical development (Ciccia and Turkstra, 2002). Across contexts and groups, profiles of abilities remained relatively constant with variation in age. Prior work in these populations have suggested relative stability in social-behavioral phenotypes with age (e.g., Cuskelly, Povey & Jobling, 2016; Dykens et al., 2006; de Graaf & de Graaf, 2016; Lee et al., 2017; Billstedt, Gillberg, & Gillberg, 2011; Cederlund, Hagberg, Billstedt, Gillberg, & Gillberg, 2008; Farley et al., 2009; Howlin, Moss et al., 2013; Larsen & Mouridsen, 1997; Piven, Harper, Palmer, & Arndt, 1996; Sigman & McGovern, 2005; Tager-Flusberg et al., 1991), and it may be that pragmatic language impairments are stable in these groups during this time period. However, it is important to note that groups demonstrated both improvement and worsening in specific skills contributing to narration and semi-naturalistic conversation, suggesting that while overall composite measures of pragmatic language do not change, specific skills may fluctuate with development. It is notable that because there was little change with age, patterns of group differences were largely stable with development, suggesting that areas of overlap observed may be central features of these disorders, as opposed to a product of variation in structural language or mental age, which has been argued in the case of overlap between ASD-O and FXS-ASD (e.g., Hall et al., 2010).

**The Role of Context**

By including multiple pragmatic contexts, this study allowed for the identification of another key area of overlap between males with FXS-ASD and ASD-O: the marked increase in difficulties during a less structured context relative to other groups. Prior work has suggested that males with ASD-O benefit from increased structure (Clark & Rutter, 1981; Loukusa et al., 2007; Losh and Capps, 2003; Williams, Goldstein, & Minshew, 2006). Current results confirm these findings and extend them to males with FXS who also meet criteria for ASD, suggesting that impairments in both groups are likely to be most prominent in less structured contexts. In contrast, males with DS and FXS-O showed reduced variation across contexts, suggesting that while all clinical groups show differences in pragmatic language, the degree to which structure supports pragmatic competence may be unique to the ASD phenotype. Males with DS also showed the most similarity to TD across contexts, again highlighting areas of pragmatic strength within this group. Further, within groups, minimal relationships were observed between pragmatic language abilities as assessed by different contexts, highlighting the importance of multiple assessment approaches across clinical groups, and the unique contribution of each measure to an overall picture of an individual's pragmatic language competence.

**Related Abilities**

The inclusion of multiple contexts also allowed for assessment of whether groups draw on the same abilities across contexts. Whereas structural language and mental age were highly and consistently correlated with pragmatic competence in both the CASL-PJ and aspects of narrative, they were less related in both parent report and language features during semi-structured conversation. In fact, observed group differences in story grammar were attenuated after including structural language as a control, whereas group differences remained consistent in the semi-structured interaction context. Structural language and mental age are building blocks of pragmatic competence in typical development, and thus relationships between structural language and pragmatic competence are not surprising. Rather, these findings suggest that the degree to which groups draw on related abilities may vary by context, and that structured contexts may draw to a greater degree on structural language and cognition.

Somewhat surprisingly, theory of mind was not consistently related to pragmatic language skills across groups, except for relationships with the CASL-Pragmatic Judgment scale, replicating results of Losh et al., 2012. This finding stands in contrast to several studies suggesting relationships between pragmatic language and theory of mind in ASD-O (Baron-Cohen, 1988; Baron-Cohen et al., 1985; Loveland and Tunali, 1993; Tager-Flusberg and Sullivan, 1995; Surian et al., 1996; Capps et al., 1998, 2000; Tager-Flusberg, 2000; Losh and Capps, 2003). It may be that the theory of mind composite utilized in the current study was not sensitive enough to variation in social cognitive skills in the semi-naturalistic context. Future studies should continue to assess these relationships across contexts, and with more specific measures of theory of mind. In both the FXS-ASD and DS group, greater impairments in executive function were associated with greater impairments during the semi-naturalistic context specifically. Given that difficulties in executive function have been observed in both groups (Garner et al., 1999; Hooper et al., 2008; Munir et al., 2000; Wilding et al., 2002), it is likely that a less structured contexts draw on this skill, in that it requires individuals not only to recognize appropriate pragmatic responses but also to attend to the examiner, remember content shared, and inhibit inappropriate behaviors.

**Clinical Implications**

Results of this study may inform clinical work. First and foremost, results highlight the importance of multi-methods assessments, particularly for those with ASD-O and FXS-ASD. Current results suggest that deficits may be masked by structured clinical assessments in these groups. Results also highlight unique pragmatic profiles within each group, and offer potential specific targets for intervention. For example, males with FXS may require specific support in the regulation of pragmatic behaviors that detract from narrative, such as repetitive language or excessive seeking of attention. Further, interventions specifically targeting executive function skills in males with DS and FXS-ASD may improve social-communication. Indeed, it is critical that ASD status be assessed in FXS, as males with FXS-ASD demonstrated greater deficits in social-communication during semi-naturalistic contexts as well as several specific pragmatic behaviors related to reciprocity. Finally, current results suggest that assessments of change over time during the school age years should move beyond global measures, which may not be as sensitive to change, to specific features of pragmatic language.

**Limitations and Future Directions**

The limitations of the current study should be recognized and built upon in future work. Future work should attempt to replicate these findings with larger samples, particularly across time points. Other developmental windows should also be assessed, and the inclusion of a chronologically age matched group may help better assess the magnitude of difficulty, as well as differences in rates of development that individuals with neurodevelopmental disabilities may experience relative to same-aged peers. Further, it is important to consider that social experiences, and thus opportunities to practice and develop pragmatic skills, will be greater in chronological age matched controls, which may influence patterns of difference. Future work should also include females given sex differences observed across clinical groups in previous studies (Berglund, Eriksson, & Johansson, 2001; Hagerman, 2002; M. Lee, Bush, et al., 2017). Finally, additional contexts should continue to be analyzed, such as parent-child or peer interactions, which may provide less structure than an interaction with a trained examiner.

**Conclusions**

Results of the current study provide a comprehensive picture of pragmatic language development across ASD-O, FXS-ASD, FXS-O, DS and TD, and highlight the importance of multi-method assessments to identifying impairments in these groups and related abilities. Semi-naturalistic interactions most clearly distinguished phenotypes related to ASD, and specific areas of overlap in reciprocity that may index common genetic etiologies. The stability of performance across development highlights the unique trajectories of these groups. Longitudinal, multi-method approaches will continue to inform clinical intervention and understanding of the complex pathways by which genetic variation and linguistic and neurocognitive factors impact critical language skills.

**References**

Abbeduto, L., Brady, N., & Kover, S. T. (2007). Language development and fragile X syndrome: profiles, syndrome-specificity, and within-syndrome differences. *Mental Retardation and Developmental Disabilities Research Reviews, 13*(1), 36-46.

Abbeduto, L., & Chapman, R. (2005). Language development in Down syndrome and fragile X syndrome: Current research and implications for theory and practice. In P. Fletcher & J. F. Miller (Eds.), *Developmental theory and language disorders* (pp. 53-72). Amsterdam: John Benjamins Publishing Co.

Abbeduto, L., Murphy, M. M., Kover, S. T., Karadottir, S., Amman, A., & Bruno, L. (2008). Signaling noncomprehension of language: A comparison of fragile X syndrome and Down syndrome. *American Journal on Mental Retardation, 113*, 214-230.

Abbeduto, L., Murphy, M. M., Richmond, E. K., Amman, A., Beth, P., Weissman, M. D., . . . Karadottir, S. (2006). Collaboration in referential communication: Comparison of youth with Down syndrome or fragile X syndrome. *American Journal of Mental Retardation, 111*(3), 170-183.

Adams, C. (2002). Practitioner review: the assessment of language pragmatics. *Journal of child psychology and psychiatry, and allied disciplines, 43*(8), 973-987.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (5th ed.). Arlington, VA: American Psychiatric Association.

Ashby, S. A., Channell, M. M., & Abbeduto, L. (2017). Inferential language use by youth with Down syndrome during narration. *Res Dev Disabil, 71*, 98-108.

Bagni, C., & Oostra, B. A. (2013). Fragile X syndrome: From protein function to therapy. *Am J Med Genet A, 161A*(11), 2809-2821.

Bakker, C. E., & Oostra, B. A. (2003). Understanding fragile X syndrome: insights from animal models. *Cytogenet Genome Res, 100*(1-4), 111-123.

Bamberg, M., & Damred-Frye, R. (1991). On the ability to provide evaluative comments: Further exploration of children's narrative competencies. *Journal of Child Language, 18*, 689-710.

Bamberg, M., & Reilly, J. (1996). Emotion, narrative, and affect: How children discover the relationship between what to say and how to say it. In D. I. Slobin, J. Gerhardt, A. Kyratzis, & J. Guo (Eds.), *Social interaction, social context and language: Essays in honor of Susan Ervin-Tripp.* Norwood, NJ: Lawrence Erlbaum Associates.

Barstein, J., Martin, G. E., Lee, M., & Losh, M. (under review). A duck wearing boots?! A study of communicative repair strategies across genetically-based neurodevelopmental disabilities.

Beaumont, R., & Newcombe, P. (2006). Theory of mind and central coherence in adults with high-functioning autism or Asperger syndrome. *Autism, 10*(4), 365-382.

Beeghly, M., Weiss-Perry, B., & Cicchetti, D. (1990). Beyond sensorimotor functioning: Early communicative and play development of children with Down syndrome. In D. Cicchetti & M. Beeghly (Eds.), *Children with Down syndrome: A developmental perspective* (pp. 329-368). New York: Cambridge University Press.

Berglund, E., Eriksson, M., & Johansson, I. (2001). Parental Reports of Spoken Language Skills in Children With Down Syndrome. *Journal of Speech, Language, and Hearing Research, 44*(1), 179-191.

Besler, R. C., & Sudhalter, V. (2001). Conversational characteristics of children with fragile X syndrome: Repetitive speech. *American Journal of Mental Retardation, 106*, 28-38.

Billstedt, E., & Gillberg, C. (2005). Autism after adolescence: population-based 13- to 22-year follow-up study of 120 individuals with autism diagnosed in childhood. *Journal of Autism & Developmental Disorders, 35*(3), 351-360 310p.

Billstedt, E., Gillberg, I. C., & Gillberg, C. (2011). Aspects of quality of life in adults diagnosed with autism in childhood: a population-based study. *Autism, 15*(1), 7-20.

Bishop, D. (2003). *The Children's Communication Checklist-2*. London: The Psychological Corporation.

Blain-Brière, B., Bouchard, C., & Bigras, N. (2014). The role of executive functions in the pragmatic skills of children age 4-5. *Front Psychol, 5*, 240.

Boudreau, D. M., & Chapman, R. S. (2000). The relationship between event representation and linguistic skill in narratives of children and adolescents with Down syndrome. *Journal of speech, language, and hearing research : JSLHR, 43*(5), 1146-1159.

Bruner, J. (1990). *Acts of meaning*. Cambridge, MA: Harvard University Press.

Budimirovic, D. B., Bukelis, I., Cox, C., Gray, R. M., Tierney, E., & Kaufmann, W. E. (2006). Autism spectrum disorder in fragile X syndrome: Differential contribution of adaptive socialization and social withdrawal. *American Journal of Medical Genetics Part A, 9999*, 1-13.

Capps, L., Kehres, J., & Sigman, M. (1998). Conversational Abilities Among Children with Autism and Children with Developmental Delays. *Autism, 2*(4), 325-344.

Capps, L., Losh, M., & Thurber, C. (2000). The frog ate a bug and made his mouth sad: Narrative competence in children with autism. *Journal of Abnormal Child Psychology, 28*, 193-204.

Carrow-Woolfolk, E. (1999). *CASL: Comprehensive assessment of spoken language*. Circle Pines, MN: American Guidance Services.

Cederlund, M., Hagberg, B., Billstedt, E., Gillberg, I. C., & Gillberg, C. (2008). Asperger syndrome and autism: a comparative longitudinal follow-up study more than 5 years after original diagnosis. *J Autism Dev Disord, 38*(1), 72-85.

Channell, M. M., McDuffie, A. S., Bullard, L. M., & Abbeduto, L. (2015). Narrative language competence in children and adolescents with Down syndrome. *Front Behav Neurosci, 9*, 283.

Cicchetti, D. V. (1994). Multiple comparison methods: establishing guidelines for their valid application in neuropsychological research. *J Clin Exp Neuropsychol, 16*(1), 155-161.

Clark, P., & Rutter, M. (1981). Autistic children's responses to structure and to interpersonal demands. *J Autism Dev Disord, 11*(2), 201-217.

Cohen, N. J., Farnia, F., & Im-Bolter, N. (2013). Higher order language competence and adolescent mental health. *J Child Psychol Psychiatry, 54*(7), 733-744.

Colle, L., Baron-Cohen, S., Wheelwright, S., & van der Lely, H. K. (2008). Narrative Discourse in Adults with High Functioning Autism or Asperger Syndrome. *Journal of Autism and Developmental Disorders, 38*, 28-40.

Cornish, K., Cole, V., Longhi, E., Karmiloff-Smith, A., & Scerif, G. (2012). Does attention constrain developmental trajectories in fragile x syndrome? A 3-year prospective longitudinal study. *Am J Intellect Dev Disabil, 117*(2), 103-120.

Cuskelly, M., Povey, J., & Jobling, A. Trajectories of Development of Receptive Vocabulary in Individuals with Down Syndrome.

de Graaf, G., & de Graaf, E. (2016). *Development of Self-Help, Language, and Academic Skills in Persons With Down Syndrome: Skill Development in Down Syndrome* (Vol. 13).

Diehl, J. J., Bennetto, L., & Young, E. C. (2006). Story recall and narrative coherence of high-functioning children with autism spectrum disorders. *Journal of Abnormal Child Psychology, 34*(1), 83-98.

Dunn, L. M., & Dunn, D. M. (1997). *Peabody Picture Vocabulary Test*. Circle Pines, MN: American Guidance Service.

Dunn J.  (1988) The beginnings of social understanding. Cambridge, MA: Harvard University Press.

Dykens, E. M., Hodapp, R. M., & Evans, D. W. (2006). Profiles and development of adaptive behavior in children with Down syndrome. *Downs Syndr Res Pract, 9*(3), 45-50.

Estigarribia, B., Martin, G. E., Roberts, J. E., Spencer, A., Gucwa, A., & Sideris, J. (2011). Narrative skill in boys with fragile X syndrome with and without autism spectrum disorder. *Applied Psycholinguistics*, 359-388.

Fabbretti, D., Pizzuto, E., Vicari, S., & Volterra, V. (1997). A story description task in children with Down's syndrome: lexical and morphosyntactic abilities. *J Intellect Disabil Res, 41 ( Pt 2)*, 165-179.

Farley, M. A., McMahon, W. M., Fombonne, E., Jenson, W. R., Miller, J., Gardner, M., . . . Coon, H. (2009). Twenty-year outcome for individuals with autism and average or near-average cognitive abilities. *Autism Res, 2*(2), 109-118.

Ferrier, L. J., Bashir, A. S., Meryash, D. L., Johnston, J., & Wolff, P. (1991). Conversational skills of individuals with fragile-X syndrome: a comparison with autism and Down syndrome. *Developmental Medicine and Child Neurology, 33*(9), 776-788.

Fine, J., Bartolucci, G., Szatmari, P., & Ginsberg, G. (1994). Cohesive discourse in pervasive developmental disorders. *J Autism Dev Disord, 24*(3), 315-329.

Finestack, L. H., & Abbeduto, L. (2010). Expressive language profiles of verbally expressive adolescents and young adults with Down syndrome or fragile X syndrome. *J Speech Lang Hear Res, 53*(5), 1334-1348.

Finestack, L. H., Palmer, M., & Abbeduto, L. (2012). Macrostructural narrative language of adolescents and young adults with Down syndrome or fragile X syndrome. *American Journal of Speech-Language Pathology, 21*, 29-46.

Finestack, L. H., Richmond, E. K., & Abbeduto, L. (2009). Language Development in Individuals with Fragile X Syndrome. *Topics in Language Disorders, 29*(2), 133-148.

Fiske, S., & Taylor, S. (1991). *Social cognition*. New York: McGraw-Hill.

Flavell, J. H., Flavell, E. R., & Green, F. L. (1983). Development of the appearance--reality distinction. *Cogn Psychol, 15*(1), 95-120.

Garner, C., Callias, M., & Turk, J. (1999). Executive function and theory of mind performance of boys with fragile-X syndrome. *J Intellect Disabil Res, 43 ( Pt 6)*, 466-474.

Geller, E. (1998). An investigation of communication breakdowns and repairs in verbal autistic children. *British Journal of Developmental Disabilities, 44*(87), 71-85.

Ghaziuddin, M., & Gerstein, L. (1996). Pedantic speaking style differentiates Asperger syndrome from high-functioning autism. *J Autism Dev Disord, 26*(6), 585-595.

Gillespie-Lynch, K., Sepeta, L., Wang, Y., Marshall, S., Gomez, L., Sigman, M., & Hutman, T. (2012). Early childhood predictors of the social competence of adults with autism. *J Autism Dev Disord, 42*(2), 161-174.

Gilmour, J., Hill, B., Place, M., & Skuse, D. H. (2004). Social communication deficits in conduct disorder: a clinical and community survey. *J Child Psychol Psychiatry, 45*(5), 967-978.

Gioia, G. A., Espy, K. A., & Isquith, P. K. (2003). Behavior rating inventory of executive function-Preschool version (BRIEF-P). In. Lutz, FL: PAR.

Gooch, D., Thompson, P., Nash, H. M., Snowling, M. J., & Hulme, C. (2016). The development of executive function and language skills in the early school years. *J Child Psychol Psychiatry, 57*(2), 180-187.

Gopnik, A., Meltzoff, A. N., & Kuhl, P. K. (1999). *The scientist in the crib: Minds, brains, and how children learn*. New York: Morrow.

Gotham, K., Pickles, A., & Lord, C. (2009). Standardizing ADOS scores for a measure of severity in autism spectrum disorders. *J Autism Dev Disord, 39*(5), 693-705.

Grant, C. M., Apperly, I., & Oliver, C. (2007). Is theory of mind understanding impaired in males with fragile X syndrome? *Journal of Abnormal Child Psychology, 35*(1), 17-28.

Hagerman, R., & Hagerman, P. (2002). *Fragile X Syndrome: Diagnosis, Treatment, and Research Third Edition*. Baltimore: Johns Hopkins University Press.

Hall, D., Todorova-Koteva, K., Pandya, S., Bernard, B., Ouyang, B., Walsh, M., . . . Berry-Kravis, E. (2016). Neurological and endocrine phenotypes of fragile X carrier women. *Clin Genet, 89*(1), 60-67.

Hatton, D. D., Skinner, M., Sideris, J., Mankowski, J. B., Bailey, D. B., Roberts, J. E., & Mirrett, P. (2006). Autistic behavior in children with fragile X syndrome: Prevalence, stability, and the impact of FMRP. *American Journal of Medical Genetics, 140*(17), 1804-1813.

Helland, W. A., & Heimann, M. (2007). Assessment of pragmatic language impairment in children referred to psychiatric services: a pilot study of the Children's Communication Checklist in a Norwegian sample. *Logoped Phoniatr Vocol, 32*(1), 23-30.

Helland, W. A., Lundervold, A. J., Heimann, M., & Posserud, M. B. (2014). Stable associations between behavioral problems and language impairments across childhood - the importance of pragmatic language problems. *Res Dev Disabil, 35*(5), 943-951.

Hernandez, R. N., Feinberg, R. L., Vaurio, R., Passanante, N. M., Thompson, R. E., & Kaufmann, W. E. (2009). Autism spectrum disorder in fragile X syndrome: A longitudinal evaluation. *American Journal of Human Genetics, 149A*(6), 1125-1137.

Hogan-Brown, A. L., Losh, M., Martin, G. E., & Mueffelmann, D. (2013). An investigation of narrative ability in boys with autism and fragile X syndrome. *American Journal on Intellectual and Developmental Disabilities, 118*(2), 77-94.

Hooper, S. R., Hatton, D., Sideris, J., Sullivan, K., Hammer, J., Schaaf, J., . . . Bailey, D. P., Jr. (2008). Executive functions in young males with fragile X syndrome in comparison to mental age-matched controls: baseline findings from a longitudinal study. *Neuropsychology, 22*(1), 36-47.

Howlin, P., Moss, P., Savage, S., & Rutter, M. (2013). Social outcomes in mid- to later adulthood among individuals diagnosed with autism and average nonverbal IQ as children. *J Am Acad Child Adolesc Psychiatry, 52*(6), 572-581.e571.

Hus, V., Gotham, K., & Lord, C. (2012). Standardizing ADOS Domain Scores: Separating Severity of Social Affect and Restricted and Repetitive Behaviors. *J Autism Dev Disord*.

CDC (2014). Prevalence of autism spectrum disorder among children aged 8 years - autism and developmental disabilities monitoring network, 11 sites, United States, 2010. *MMWR Surveill Summ, 63*(2), 1-21.

Kau, A. S., Tierney, E., Bukelis, I., Stump, M. H., Kater, W. R., Trescher, W. H., & al., e. (2004). Social behavior profile in young males with fragile X syndrome: Characteristics and specificity. *American Journal of Medical Genetics, 126A*(1), 9-17.

Kaufmann, W. E., Cortell, R., Kau, A. S., Bukelis, I., Tierney, E., Gray, R. M., . . . Stanard, P. (2004). Autism spectrum disorder in fragile X syndrome: Communication, social interaction, and specific behaviors. *American Journal of Medical Genetics, 129*(3), 225-234.

Keller-Bell, Y. D., & Abbeduto, L. (2007). Narrative development in adolescents and young adults with fragile X syndrome. *American Journal on Mental Retardation, 112*, 289-299.

Klusek, J., Losh, M., & Martin, G. E. (2014). A comparison of pragmatic language in boys with autism and fragile X syndrome. *Journal of Speech, Language, and Hearing Research, 57*(5), 1692-1707.

Kooy, R. F., D'Hooge, R., Reyniers, E., Bakker, C. E., Nagels, G., De Boulle, K., . . . Willems, P. J. (1996). Transgenic mouse model for the fragile X syndrome. *Am J Med Genet, 64*(2), 241-245.

Kover, S. T., McDuffie, A., Abbeduto, L., & Brown, W. T. (2012). Effects of sampling context on spontaneous expressive language in males with fragile X syndrome or Down syndrome. *J Speech Lang Hear Res, 55*(4), 1022-1038.

Lam, Y. G., & Yeung, S. S. S. (2012). Towards a convergent account of pragmatic language deficits in children with high-functioning autism: Depicting the phenotype using the Pragmatic Rating Scale. *Research in Autism Spectrum Disorders, 6*(2), 792-797.

Larsen, F. W., & Mouridsen, S. E. (1997). The outcome in children with childhood autism and Asperger syndrome originally diagnosed as psychotic. A 30-year follow-up study of subjects hospitalized as children. *Eur Child Adolesc Psychiatry, 6*(4), 181-190.

Laws, G., & Bishop, D. (2004). Pragmatic language impairment and social deficits in Williams syndrome: a comparison with Down's syndrome and specific language impairment. *International Journal of Language & Communication Disorders, 39*(1), 45-64.

Lee, M., Bush, L., Martin, G. E., Barstein, J., Maltman, N., Klusek, J., & Losh, M. (2017). A multi-method investigation of pragmatic development in individuals with Down syndrome. *Am J Intellect Dev Disabil, 122*(4), 289-309.

Lee, M., Martin, G. E., Berry-Kravis, E., & Losh, M. (2016). A developmental, longitudinal investigation of autism phenotypic profiles in fragile X syndrome. *J Neurodev Disord, 8*, 47.

Lee, M., Martin, G. E., Hogan, A., Hano, D., Gordon, P. C., & Losh, M. (2017). What's the story? A computational analysis of narrative competence in autism. *Autism*, 1-10.

Lee, N. R., Fidler, D. J., Blakeley-Smith, A., Daunhauer, L., Robinson, C., & Hepburn, S. L. (2011). Caregiver report of executive functioning in a population-based sample of young children with Down syndrome. *Am J Intellect Dev Disabil, 116*(4), 290-304.

Levy, Y., Gottesman, R., Borochowitz, Z., Frydman, M., & Sagi, M. (Writers). (2006). Language in boys with fragile X syndrome. In *Journal of Child Language*. US: Cambridge Univ Press.

Lewis, C., & Mitchell, P. (Eds.). (1994). *Children's early understanding of mind*. East Sussex, UK: Lawrence Erlbaum Associates Publishers.

Lewis, P., Abbeduto, L., Murphy, M., Richmond, E., Giles, N., Bruno, L., & Schroeder, S. (2006). Cognitive, language and social-cognitive skills of individuals with Fragile X Syndrome with and without autism. *Journal of Intellectual Disability Research, 50*, 532-545.

Lord, C., Rutter, M., DeLavore, P. C., & Risi, S. (2001). *Autism Diagnostic Observation Schedule*. Los Angeles, CA: Western Psychological Services.

Losh, M., Bellugi, U., & Anderson, J. D. (2001). Narrative as a social engagement tool: The excessive use of evaluation in narratives from children with Williams syndrome. *Narrative Inquiry, 10*(2), 265-290.

Losh, M., & Capps, L. (2003). Narrative ability in high-functioning children with autism or Asperger's syndrome. *Journal of Autism and Developmental Disorders, 33*(3), 239-251.

Losh, M., Martin, G. E., Klusek, J., Hogan-Brown, A. L., & Sideris, J. (2012). Social communication and theory of mind in boys with autism and fragile x syndrome. *Front Psychol, 3*, 266.

Losh, M., Klusek, J., Martin, G. E., Sideris, J., Parlier, M., & Piven, J. (2012). Defining genetically meaningful language and personality traits in relatives of individuals with fragile X syndrome and relatives of individuals with autism. *American journal of medical genetics. Part B, Neuropsychiatric genetics : the official publication of the International Society of Psychiatric Genetics, 159B*(6).

Loukusa, S., Leinonen, E., Jussila, K., Mattila, M. L., Ryder, N., Ebeling, H., & Moilanen, I. (2007). Answering contextually demanding questions: pragmatic errors produced by children with Asperger syndrome or high-functioning autism. *J Commun Disord, 40*(5), 357-381.

Loukusa, S., Leinonen, E., Kuusikko, S., Jussila, K., Mattila, M. L., Ryder, N., . . . Moilanen, I. (2007). Use of context in pragmatic language comprehension by children with Asperger syndrome or high-functioning autism. *J Autism Dev Disord, 37*(6), 1049-1059.

Loveland, K. A., McEvoy, R. E., & Tunali, B. (1990). Narrative story telling in autism and Down's syndrome. *British Journal of Developmental Psychology, 8*, 9-23.

Martin, G. E., Barstein, J., Hornickel, J., Matherly, S., Durante, G., & Losh, M. (2017). Signaling of noncomprehension in communication breakdowns in fragile X syndrome, Down syndrome, and autism spectrum disorder. *J Commun Disord, 65*, 22-34.

Martin, G. E., Klusek, J., Estigarribia, B., & Roberts, J. E. (2009). Language Characteristics of Individuals With Down Syndrome. *Topics in Language Disorders, 29*(2), 112-132.

Martin, G. E., Losh, M., Estigarribia, B., Sideris, J., & Roberts, J. (2013). Longitudinal profiles of expressive vocabulary, syntax, and pragmatic language in boys with fragile X syndrome or Down syndrome. *International Journal of Language & Communication Disorders, 48*(4), 432-443.

Martin, G. E., Roberts, J. E., Helm-Estabrooks, N., Sideris, J., & Assal, J. (2012). Perseveration in the connected speech of boys with fragile X syndrome with and without autism spectrum disorder. *American Journal on Intellectual and Developmental Disabilities, 117*(5), 384-399.

Matthews, R., Dissanayake, C., & Pratt, C. (2003). The relationship between the theory of mind and conversation abilities in children using active/inactive paradigm. *Australian Journal of Psychology, 55*, 35-42.

Miles, S., & Chapman, R. S. (2002). Narrative content as described by individuals with Down syndrome and typically developing children. *Journal of speech, language, and hearing research : JSLHR, 45*(1), 175-189.

Miller, J. F., & Chapman, R. S. (2008). Systematic Analysis of Language Transcripts (SALT).

Moore, D. G., Oates, J. M., Hobson, P. R., & Goodwin, J. E. (2002). Cognitive and social factors in the development of infants with Down syndrome. *Down Syndrome Research and Practice, 8*, 172-188.

Moss, J., & Howlin, P. (2009). Autism spectrum disorders in genetic syndromes: Implications for diagnosis, intervention and understanding the wider autism spectrum disorder. *Journal of Intellectual Disability Reasearch, 53*(10), 852-873.

Munir, F., Cornish, K. M., & Wilding, J. (2000). Nature of the working memory deficit in fragile-X syndrome. *Brain Cogn, 44*(3), 387-401.

Nippold, M. A., Hesketh, L. J., Duthie, J. K., & Mansfield, T. C. (2005). Conversational versus expository discourse: a study of syntactic development in children, adolescents, and adults. *J Speech Lang Hear Res, 48*(5), 1048-1064.

Parker, S. E., Mai, C. T., Canfield, M. A., Rickard, R., Wang, Y., Meyer, R. E., . . . Network, N. B. D. P. (2010). Updated National Birth Prevalence estimates for selected birth defects in the United States, 2004-2006. *Birth Defects Res A Clin Mol Teratol, 88*(12), 1008-1016.

Paul, R., & Cohen, D. J. (1984). Responses to contingent queries in adults with mental retardation and pervasive developmental disorders. *Applied Psycholinguistics, 5*(4), 349-357.

Paul, R., Dykens, E., Leckman, J. F., Watson, M., Breg, W. R., & Cohen, D. J. (1987). A comparison of language characteristics of mentally retarded adults with fragile X syndrome and those with nonspecific mental retardation and autism. *J Autism Dev Disord, 17*(4), 457-468.

Piven, J., Harper, J., Palmer, P., & Arndt, S. (1996). Course of behavioral change in autism: a retrospective study of high-IQ adolescents and adults. *J Am Acad Child Adolesc Psychiatry, 35*(4), 523-529.

Presson, A. P., Partyka, G., Jensen, K. M., Devine, O. J., Rasmussen, S. A., McCabe, L. L., & McCabe, E. R. (2013). Current estimate of Down Syndrome population prevalence in the United States. *J Pediatr, 163*(4), 1163-1168.

Prutting, C. A., & Kittchner, D. M. (1987). A clinical appraisal of the pragmatic aspects of language. *Journal of Speech and Hearing Disorders, 52*(2), 105-119.

Reilly, J. (1992). How to tell a good story: The intersection of language and affect in children's narratives. *Journal of Narrative and Life History, 2*, 355-377.

Reilly, J., Klima, E. S., & Bellugi, U. (1990). Once more with feeling: Affect and language in atypical populations. *Development and Psychopathology, 2*(4), 367-391.

Reilly, J., Losh, M., Bellugi, U., & Wulfeck, B. (2004). "Frog, where are you?" Narratives in children with specific language impairment, early focal brain injury, and Williams syndrome. *Brain and Language, 88*(2), 229-247.

Repacholi, B. M., & Gopnik, A. (1997). Early reasoning about desires: evidence from 14- and 18-month-olds. *Developmental Psychology, 33*(1), 12-21.

Roberts, J. E., Martin, G. E., Moskowitz, L., Harris, A. A., Foreman, J., & Nelson, L. (2007). Discourse skills of boys with fragile X syndrome in comparison to boys with Down syndrome. *Journal of Speech, Language, and Hearing Research, 50*, 475-492.

Roid, G. H., & Miller, L. J. (1997). *Leiter International Performance Scale-Revised*. Wood Dale, IL: Stoelting.

Ross, D. E. (2002). Replacing faulty conversational exchanges for children with autism by establishing a functionally equivalent alternative response. *Education and Training in Mental Retardation and Developmental Disabilites, 37*, 343-363.

Rumpf, A. L., Kamp-Becker, I., Becker, K., & Kauschke, C. (2012). Narrative competence and internal state language of children with Asperger Syndrome and ADHD. *Res Dev Disabil, 33*(5), 1395-1407.

Sabaratnam, M., Murthy, N. V., Wijeratne, A., Buckingham, A., & Payne, S. (2003). Autistic-like behaviour profile and psychiatric morbidity in fragile X sydnrome: A prospective ten-year follow-up study. *European Child and Adolescent Psychiatry, 12*, 172-177.

Shin, M., Besser, L. M., Kucik, J. E., Lu, C., Siffel, C., Correa, A., & Collaborative, C. A. M. P. a. S. (2009). Prevalence of Down syndrome among children and adolescents in 10 regions of the United States. *Pediatrics, 124*(6), 1565-1571.

Sigman, M., & McGovern, C. W. (2005). Improvement in cognitive and language skills from preschool to adolescence in autism. *J Autism Dev Disord, 35*(1), 15-23.

Siller, M., Swanson, M. R., Serlin, G., & George, A. (2014). Internal State Language in the Storybook Narratives of Children with and without Autism Spectrum Disorder: Investigating Relations to Theory of Mind Abilities. *Res Autism Spectr Disord, 8*(5), 589-596.

Slaughter, V., Peterson, C. C., & Mackintosh, E. (2007). Mind what mother says: narrative input and theory of mind in typical children and those on the autism spectrum. *Child Development, 78*(3), 839-858.

Smith, L. E., Barker, E. T., Seltzer, M. M., Abbeduto, L., & Greenberg, J. S. (2012). Behavioral phenotype of fragile x syndrome in adolescence and adulthood. *American Journal on Intellectual and Developmental Disabilities, 117*(1), 1-17.

Sudhalter, V., Cohen, I. L., Silverman, W., & Wolf-Schein, E. G. (1990). Conversational analyses of males with fragile X, Down syndrome, and autism: Comparison of the emergence of deviant language. *American Journal on Mental Retardation, 94*(4), 431-441.

Tager-Flusberg, H. (2000). Understanding the language and communicative impairments in autism. *International Review of Research in Mental Retardation, 23*, 185-205.

Tager-Flusberg, H., & Anderson, M. (1991). The development of contingent discourse ability in autistic children. *Journal of Child Psychology and Psychiatry, 32*, 1123-1134.

Tager-Flusberg, H., Rogers, S., Cooper, J., Landa, R., Lord, C., Paul, R., . . . Yoder, P. (2009). Defining spoken language benchmarks and selecting measures of expressive language development for young children with autism spectrum disorders. *Journal of Speech, Language, and Hearing Research, 52*, 643-652.

Tager-Flusberg, H., & Sullivan, K. (1995). Attributing mental states to story characters: A comparison of narratives produced by autistic and mentally retarded individuals. *Applied Psycholinguistics, 16*(3), 241-256.

Tannock, R. (1988). Mothers' directiveness in their interactions with their children with and without Down syndrome. *American Journal of Mental Retardation, 93*(2), 154-165.

Volden, J. (2004). Conversational repair in speakers with autism spectrum disorder. *International Journal of Language & Communication Disorders, 39*(2), 171-189.

Volden, J., Coolican, J., Garon, N., White, J., & Bryson, S. (2009). Brief report: pragmatic language in autism spectrum disorder: relationships to measures of ability and disability. *J Autism Dev Disord, 39*(2), 388-393.

Weiler, I. J., & Greenough, W. T. (1999). Synaptic synthesis of the Fragile X protein: possible involvement in synapse maturation and elimination. *Am J Med Genet, 83*(4), 248-252.

Wilding, J., Cornish, K., & Munir, F. (2002). Further delineation of the executive deficit in males with fragile-X syndrome. *Neuropsychologia, 40*(8), 1343-1349.

Williams, D. L., Goldstein, G., & Minshew, N. J. (2006). Neuropsychologic functioning in children with autism: further evidence for disordered complex information-processing. *Child Neuropsychol, 12*(4-5), 279-298.

Williams, K. T. (1997). *Expressive Vocabulary Test*. Circle Pines, MN: American Guidance Service.

Wishart, J. G., & Johnston, F. H. (1990). The effects of experience on attribution of a stereotyped personality to children with Down syndrome. *Journal on Mental Defiency Research, 34*, 409-420.

Wolf-Schein, E. G., Sudhalter, V., Cohen, I. L., Fisch, G. S., Hanson, D., Pfadt, A. G., . . . Brown, W. T. (1987). Speech-language and the fragile X syndrome: initial findings. *ASHA, 29*(7), 35-38.

Zajac, D. J., Harris, A. A., Roberts, J. E., & Martin, G. E. (2009). Direct magnitude estimation of articulation rate in boys with fragile X syndrome. *Journal of Speech, Language, and Hearing Research, 52*(5), 1370-1379.

# Chapter 4: COMPUTATIONAL APPROACHES to CHARACTERIZING LANGUAGE FEATURES in NEURODEVELOPMENTAL DISABILITIES

## Abstract

Computational, or automated, methods to characterize language and social-communication offer a promising alternative to traditional methods of characterizing language samples, which often involve time-intensive hand coding. Such approaches are particularly relevant for neurodevelopmental disabilities such as autism spectrum disorder (ASD), which are characterized by core impairments in pragmatic (i.e., social) communication that are hypothesized to be related to genetic liability to this disorder. This study applied two computational methods: Linguistic Inquiry Word Count (LIWC), a measure of types of word use, and Vector Semantic Analysis, a quantitative measure of semantic similarity between bodies of text, to narratives and semi-structured conversations in three neurodevelopmental disabilities characterized by impairments in pragmatic language: ASD, fragile X syndrome, and Down syndrome (DS), as well as younger typically developing controls. Although both metrics distinguished groups, these differences varied by context. Computational measures related to key hand-coded elements of narrative and semi-naturalistic conversation, but these relationships were attenuated when accounting for structural language in the semi-naturalistic context. Results have implications for continued refinement of computational indices of language.

The need for quantitative, objective, and sensitive tools in psychological research has become increasingly relevant with advances in large-scale genetic studies, an emphasis on tailored interventions, and an increasing focus on identifying areas of behavioral, cognitive, and biological overlap across complex psychiatric disorders. Computational and machine learning methods have shown promise in several aspects of psychology, such as automating methods to identify structural changes in the brain that predicted risk to ASD in infants (Hampton, 2017; Hazlett et al., 2017), automated assessments of behaviors identifying markers of suicide risk in individuals who served in the armed forces (Baucom et al., 2017), or synchronizing multiple indices of behavior to predict the quality of romantic relationships (Timmons et al., 2017). Assessment of language, and especially pragmatic (i.e., social) language exemplifies the need for such approaches. Pragmatic language competence is crucial for mental health, and pragmatic impairments are observed across a range of psychiatric disorders, such as schizophrenia, Attention Deficit Hyperactivity Disorder (ADHD), conduct and oppositional defiant disorders, and anxiety (N. J. Cohen, Farnia, & Im-Bolter, 2013; Elvevag, Foltz, Weinberger, & Goldberg, 2007; Gilmour, Hill, Place, & Skuse, 2004; Helland & Heimann, 2007; Helland, Lundervold, Heimann, & Posserud, 2014; Rosenstein, Diaz-Asper, Foltz, & Elvevåg, 2014), suggesting that quantification of language features may be integral to studies investigating shared risk as well as clinical assessment for a range of populations.

Characterizing language use in individuals with autism spectrum disorder (ASD) is particularly relevant both for intervention planning and informing the genetic etiology of this disorder. ASD is a neurodevelopmental disability characterized by social communication deficits and the presence of restricted and repetitive behaviors and in the majority of cases is caused by the interaction of multiple genes (although about 6% of cases are associated with known, single genetic variants; see Yoo, 2015 for review). Pragmatic language is universally impaired in ASD, including difficulties in reciprocal interaction, overly formal word choice, tangential contributions to interactions, and difficulties with narration (i.e., storytelling; American Psychiatric Association, 2013; Tager-Flusberg, Paul, & Lord, 2005). Several studies have identified qualitatively similar pragmatic language differences in first-degree relatives of individuals with ASD (Landa, Folstein, & Isaacs, 1991; Landa et al., 1992; Losh, Childress, Lam, & Piven, 2008), suggesting that pragmatic language differences may index genetic liability to ASD. Further, overlap in pragmatic language phenotypes has been observed between ASD and fragile X syndrome (FXS), a disorder caused by a mutation in the *FMR1* gene and the most common inherited cause of intellectual disability (Hagerman, 2002; Klusek, Losh, & Martin, 2014; Losh, Martin, Klusek, Hogan-Brown, & Sideris, 2012). Pragmatic language overlap has also been observed in parents of individuals with ASD and carriers of the *FMR1* premutation (Losh, Klusek, et al., 2012), suggesting that the *FMR1* gene plays a role in development of pragmatic skills, particularly those that represent areas of deficit in ASD. Therefore, careful characterization of ASD phenotypes related to pragmatic language holds significant promise for clarifying the genetic etiology of features of ASD.

However, pragmatic language assessment can pose considerable challenges. Naturalistic interactions are considered the "gold standard" assessment of pragmatic language. As opposed to standardized measures, which often assess pragmatic knowledge or present de-contextualized questions, more naturalistic interactions better approximate day to day experiences, and as a result are likely to yield the richest picture of strengths and deficits (Adams, 2002; McTear & Conti-Ramsden, 1992; Prutting & Kittchner, 1987; Roth & Spekman, 1984). Assessment of pragmatic language in more naturalistic contexts, such as semi-structured conversation, has relied primarily on either clinical-behavioral ratings or hand coding of discrete frequencies of language and other social behaviors. Such studies have provided much information about impairments evident across different neurodevelopmental disabilities, especially individuals with ASD and FXS (e.g., Klusek et al., 2014). However, such methods also present challenges in implementation in that they are time consuming, require rigorous training of coders and regular assessment of coding reliability, and are difficult to generalize across sites. Therefore, such measures are not feasible for genetic or neurobiological research, which typically require large samples across multiple sites, as well as a quantitative measure that will show variance across affected and non-affected individuals (Gottesman & Gould, 2003; Greenwood et al., 2013). Thus, there exists a clear need for computational approaches to characterizing linguistic and pragmatic features of ASD.

Prior work has explored the application of computational and automated analyses to characterize a range of features of language. Linguistic Inquiry Word Count (LIWC) is an automated language tool that calculates proportions of word types in a written language sample, such as proportion of verbs or proportion of words related to emotions. Originally developed to characterize the narratives of trauma survivors to predict long-term outcomes (Pennebaker, Mayne & Francis, 1997); LIWC has been applied to a range of language contexts, including identifying linguistic markers of depression (Rude, Gortner & Pennebaker, 2004), correlates of physical health (Pennebaker & King, 1999), indicators of psychological adjustment to life events (Robins et al., 2013), and relationships between pronoun use during a problem-solving discussion and marital health (Gordon and Chambliss, 2005). Turk et al. (2010) applied LIWC to analyze the linguistic content of narratives produced by individuals with agenesis of the corpus callosum, and found that several indices of word use, including words related to emotional, cognitive and social processes, as well as present tense verbs, distinguished this group from controls. Together, this work suggests that word level analyses may hold utility in characterizing a range of communicative samples, including tasks that specifically tap pragmatic skills such as narrative.

Previous work has applied word level analyses to distinguish individuals with ASD from controls, by modeling idiosyncratic speech by detecting words that were unlikely to co-occur (Prud'hommeaux & Rouhizadeh, 2012), or examining types of words used during a narrative recall task (Rouhizadeh, Prud'hommeaux, Roark, & van Santen, 2013). Notably, across studies, the ASD group showed greater within group variability as opposed to controls, highlighting the heterogeneity of word use, and, more broadly, language features of ASD. However, little is known about whether patterns of word use vary across neurodevelopmental disabilities associated with ASD, or how the language sampling context impacts observed differences.

Another promising method for characterizing language in ASD is the use of vector semantic space models, such as latent semantic analysis (LSA). LSA produces a quantitative measure, ranging from -1 to 1, of how similar words, phrases or bodies of text are at a semantic level. LSA has been applied to model text coherence, word learning, automate essay scoring (Landauer et al., 2007), and to characterize the synchrony of dyadic interactions (Babcok, Ta and Ickes, 2013). Suggesting its potential as a tool for characterizing language use in clinical populations, several studies have applied LSA to quantify features of language in individuals with schizophrenia, including reduced coherence in narrative and narrative recall (Elvevag et al., 2007; Rosenstein et al., 2014) and lack of coherence during category fluency task (i.e., quantifying the degree to which words produced diverge from the category presented) in patients with schizophrenia (Elvevag, Foltz, Rosenstein, & Delisi, 2010; Elvevag et al., 2007;

Holshausen, Harvey, Elvevåg, Foltz, & Bowie, 2014), as well as both narrative and category fluency in first degree relatives (Elvevag et al., 2010; Rosenstein et al., 2014). Nicodemus et al. (2014) extended this approach by examining whether LSA metrics during a category fluency task were associated with 39 previously identified risk genes in schizophrenia that have been associated with verbal fluency, cognitive processing, and recall. They found significant relationships between LSA outcome measures and several risk genes. Although exploratory, such findings demonstrate the potential utility of applying computational methods of characterizing language to larger-scale genomic research (Nicodemus et al., 2014).

Prior work has applied LSA to distinguish narratives of ASD from controls across two different samples and narrative tasks (Lee et al., 2017; Losh & Gordon, 2014). Importantly, both studies found that greater LSA scores (i.e., closer to 1) related to meaningful aspects of narrative, including complex syntax and narrative evaluation, even after accounting for verbal IQ. Together, this work provides preliminary evidence that such an approach holds utility for characterizing deficits in language and social communication related to ASD. However, studies have yet to apply vector semantic methods to narrative from other neurodevelopmental disabilities, or to extend this method to less structured contexts.

The inclusion of more open-ended contexts is particularly relevant given evidence that individuals with ASD show reduced pragmatic impairments in more structured tasks (e.g., Losh et al., 2003), and thus assessment of these contexts are highly relevant to accurately characterizing strengths and weaknesses in this disability. However, it is less clear whether computational measures may generalize to these contexts, as in contrast to studies of narrative, there is not necessarily a “gold standard” to compare language samples. Further, it is important to consider the degree to which computational measures may be sensitive to structural language and cognition, which are often impaired in ASD and related neurodevelopmental disabilities. Finally, there exists a need for objective outcome measures in neurodevelopmental disabilities that are more sensitive to change over time (see Berry-Kravis, 2013, for review), and thus it is relevant to assess whether such computational measures may be sensitive to variation with age.

This study evaluated the application of computational linguistic tools to child and adolescent males with ASD-O, FXS with and without co-morbid diagnosis of ASD (FXS-ASD, FXS-O), Down syndrome (DS), and younger typically developing controls assessed at two time points. Analyses were completed on language samples derived from both narrative and conversational contexts, and included assessment of both word level markers of grammar and content as well as more global measures of semantic content. Males with ASD-O and FXS were included given prior work demonstrating overlap in observed pragmatic language features (e.g., Klusek et al., 2014; Losh et al., 2012); males with Down syndrome, the most common cause of intellectual disability, and a disorder of known genetic origin that is not typically inherited, were included as a control, given their unique profile of strengths in pragmatic language despite comparable deficits in structural language to the other groups.

Specifically, this study aimed to 1) identify whether methods distinguished groups and were sensitive to change over time 2) validate computational measures with prior clinical-behavioral ratings and hand coding of language samples, and 3) to explore relationships with non-verbal cognition and structural language (i.e., expressive and receptive vocabulary, mean length of utterance) across groups. Across aims 1-3, the impact of assessment context was also explored. Results have important implications for understanding how computational metrics may be applied to characterizing language use in neurodevelopmental disabilities, as well as providing future directions for refining tools for these populations.

# Methods

## Participants

Participants included 42 school age males with ASD-O, 69 males with FXS (56 meeting criteria for ASD, 13 not meeting criteria), 22 males with DS and 24 younger TD male controls at the first visit. One set of siblings with ASD-O, six sets of siblings with FXS, and one set of siblings with TD were included. At the initial visit, males with ASD-O had a significantly greater mental age than males with FXS-ASD, DS and TD. Groups did not differ in expressive vocabulary age equivalence, but males with DS had significantly lower receptive vocabulary age equivalence relative to males with FXS-O. Males with TD had a significantly greater MLU than all other groups; males with ASD-O had a significantly greater MLU than males with FXS-ASD and DS, and males with FXS-O also had a significantly greater MLU than males with DS. Table 4.1 summarizes participant characteristics at both visits.

Participants were drawn from a previously completed longitudinal study of pragmatic language development. At both visits (mean 2.86 years apart), cognition, structural language, pragmatic language and related abilities were assessed. Because of some subject attrition, not all participants were able to complete both visits. Participants were recruited through advertisements at genetic clinics, physicians' offices, advocacy groups, the UNC research registry, and schools and local community advertisements. Eligibility criteria included parent reported use of three word utterances and English as a first and primary language. Additionally, participants with ASD-O were excluded if they had a known genetic disorder associated with ASD (e.g., FXS or Tuberous Sclerosis). Males with FXS had previous genetic testing to confirm ASD status.

The ADOS (Lord, Rutter, DeLavore, & Risi, 2001) was used to confirm diagnosis in males with ASD and to determine ASD status in males with FXS. Males with FXS were classified as meeting criteria for ASD if their average severity score (across longitudinal assessments in the larger study) was consistent with an ASD classification as defined by updated ADOS algorithms (Gotham, Pickles, & Lord, 2009; Hus, Gotham, & Lord, 2012). Individuals with DS or TD who met ASD criteria on the ADOS at any time point were also excluded from the study.

Table 4.1 Participant Characteristics

| | **Groups (ns for narrative, conversation)** | **Age M(SD) Range** | **Leiter Mental Age M(SD) Range** | **EVT AE M(SD) Range** | **PPVT AE M(SD) Range** | **MLU M(SD) Range** |
|---|---|---|---|---|---|---|
| **Visit 1** | ASD-O<br>(22, 42) | 8.27 (2.9)[a]<br>3.24-13.37 | 6.12 (1.86)[a]<br>2.33-10.50 | 5.61 (1.90)<br>(2.58-10.08) | 6.08 (2.70)[a,b]<br>(2.58-17.00) | 4.13 (1.12)[a]<br>(1.88-6.44) |
| | FXS-ASD<br>(30, 53) | 10.50 (2.46)[b]<br>6.58-15.07 | 5.01 (.56)[b]<br>3.50-6.25 | 5.10 (1.25)<br>2.67-9.92 | 5.71 (1.45)[a,b]<br>2.42-9.33 | 3.52 (.79)[b,c]<br>1.80-6.05 |
| | FXS-O<br>(10, 13) | 9.67 (3.30)[a,b]<br>6.06-14.98 | 5.51 (.99)[a,b]<br>4.42-8.25 | 5.44 (1.48)<br>3.83-9.25 | 6.54 (2.61)[b]<br>3.42-13.83 | 3.99 (.73)[a,b]<br>2.27-4.74 |
| | DS<br>(18, 22) | 10.93 (2.07)[b]<br>6.81-14.86 | 5.33 (.81)[b]<br>4.33-8.25 | 5.33 (.81)<br>4.33-8.25) | 5.15 (1.41)[a]<br>2.42-7.50 | 3.11 (.75)[c]<br>1.76-4.76 |
| | TD<br>(15, 21) | 4.91 (1.35)[c]<br>3.15-8.78 | 5.40 (1.43)[b]<br>3.58-9.17 | 5.93 (2.02)<br>2.92-12.33 | 6.28 (1.90)[a,b]<br>2.17-11.58 | 4.75 (.70)[d]<br>3.14-6.06 |
| **Visit 2** | ASD-O<br>(9,14) | 11.69 (2.35)[a]<br>4.42-10.25 | 6.94 (1.71)[a]<br>4.42-10.25 | 6.89 (2.35)[a,c]<br>3.42-12.50 | 7.82 (1.93)[a,c]<br>4.75-11.17 | 4.78 (1.56)[a]<br>2.72-9.33 |
| | FXS-ASD<br>(22,32) | 13.10 (2.54)[a,b]<br>9.10-17.90 | 5.15 (.55)[b]<br>4.42-6.67 | 5.48 (1.32)[b]<br>3.42-8.25 | 6.45 (1.5)[b]<br>3.33-9.00 | 3.59 (.70)[b,c]<br>2.13-5.56 |
| | FXS-O<br>(4,5) | 11.64 (2.87)[a,b]<br>8.73-16.38 | 5.12 (.75)[b,c]<br>(4.0-6.0) | 6.60 (1.41)[a,b,c]<br>4.33-8.0 | 7.43 (8.81)[a,b,c]<br>6.08-8.17 | 4.58<br>(1.64)[a,c]<br>2.89-7.30 |
| | DS<br>(12,14) | 14.14 (2.51)[b]<br>9.63-17.93 | 5.99 (1.33)[c]<br>4.58-9.58 | 6.23 (1.28)[a,b]<br>3.33-8.33 | 6.70 (1.67)[a,b]<br>3.83-10.92 | 3.41 (.83)[b]<br>1.91-5.08 |
| | TD<br>(5,10) | 7.73 (1.70)[c]<br>6.15-11.55 | 8.49 (3.11)[a]<br>6.00-17.08 | 8.25 (1.99)[c]<br>6.33-13.08 | 8.48 (1.44)[c]<br>6.67-10.42 | 5.32 (1.16)[a]<br>4.17-7.22 |

Note. Differing superscripts indicate group differences at the level of $p < .05$. AE= Age Equivalent, EVT=Expressive Vocabulary Test, PPVT = Peabody Picture Vocabulary Test, MLU = Mean Length of Utterance. At baseline, one male with ASD, two males with FXS-ASD and one male with TD were missing MLU; one male with ASD, one male with DS, one male with FXS-ASD was missing PPVT AE. At the second visit, two males with ASD and 3 males with TD were missing MLU, two males with TD were missing PPVT AE, and one male with TD was missing EVT.

**Language Sampling Contexts**

**Narrative.** Narratives were elicited using a short cartoon video without sound (Pingu's Parents Go to a Concert, Mazola, 1991). The video features two penguins whose parents leave for an evening. While their parents are gone, the penguins engage in a series of activities that result in a mess, which they must clean up before their parents return home. Participants were first instructed to simply view the video, which was played on a laptop. Then, the participants were prompted to tell the examiner the story while viewing the video a second time. The video was paused at six key points to allow the participant to narrate, although participants could speak throughout the playing of the video. Neutral prompts (e.g., "tell me more") as well as prompts to manage behaviors (e.g., "stay seated," "please don't touch that,") were used at the examiner's discretion to facilitate narration.

Narratives were transcribed by research assistants trained to 80% word and utterance segmentation reliability, using Systematic Analysis of Language Transcripts (SALT; Miller & Chapman, 2008) software. Transcribers were blind to participant diagnosis. A second transcriber listened to high quality audio and added any additional intelligible words to transcripts with greater than 80% unintelligible utterances. A second, independent transcriber also transcribed 10% of files from each diagnostic group to assess transcription reliability (word agreement mean 87.5%, range: 75%-100%; utterance segmentation agreement mean 83.3%, range: 62%-100%). Those files with less than 80% reliability were discussed and all discrepancies resolved prior to analyses.

**Semi-naturalistic conversational interaction.** The Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2001) was used as the context to assess pragmatic language during semi-naturalistic conversations. The ADOS was chosen as a language sample because administration includes a range of activities designed to elicit social interactions (e.g., conversational prompts, completing imaginary play, taking turns narrating a story) that is standardized across participants. However, in contrast to highly standardized measures, during the ADOS the examiner has the opportunity to follow the child's lead in conversation, resulting in more naturalistic interactions (Tager-Flusberg et al., 2009).

Similar to procedures for narrative transcription, conversational transcription was completed by research assistants trained to 80% word and utterance segmentation reliability, using Systematic Analysis of Language Transcripts (SALT; Miller & Chapman, 2008) software. For the purposes of computational analyses, the first 55 intelligible turns from play-based tasks (e.g., activities involving toys) and the first 55 intelligible turns from non-play-based tasks (e.g., describing a picture, telling a story) were transcribed. Consistent with Roberts et al. (2007) a "turn" was defined as the number of utterances that continued until a speaker concluded their turn or was interrupted. Transcription was completed this way so that 1) only activities that provided the best opportunity for conversation were coded, and 2) to attempt to maintain consistency in contexts assessed across participants (i.e., providing a range of samples and accounting for unintelligibility or lack of talkativeness). As part of the larger project, a subsample of transcripts (approximately 10% of each diagnostic group) was re-transcribed by a second reliable transcriber to assess reliability, and mean morpheme-morpheme agreement was 75%. ICC's from the larger project for MLU calculation was .97 across groups.

### Computational Analyses of Language Samples

**Linguistic Inquiry Word Count (LIWC).** Transcripts of the narratives and semi-naturalistic contexts were processed using Linguistic Inquiry Word Count (LIWC; Pennebaker, Francis, & Booth, 2001). Transcripts processed through LIWC were first cleaned to exclude examiner utterances, transcription markings, and mazes (i.e., repetition of phrases when formulating an utterance) to avoid inflation of proportions due to language dysfluencies. LIWC generates proportions of word use across a range of categories. For the current analyses, the following categories were included as indices of structural language that may also have contributed to pragmatic features of language: pronoun usage (e.g., "I", "he/she," "they"), articles (e.g., "a," "an," "the"), verbs, adverbs, prepositions as well as potential markers of difficulty during the tasks: non-fluencies (e.g., "uh," "um") and fillers (e.g., "you know," "I mean").

**Vector semantics: Comparison to gold standard.** Word2Vec, a vector semantic model, was applied to quantify semantic similarity of narratives and conversation to "gold standards" derived from the TD group. Vector semantic models are first "trained" on large corpuses of text (in this case Google news embeddings; Mikolov, Corrado, Chen & Dean, 2013) to "learn" the frequency of co-occurrence of words in semantic space. Subsequently, each participant's transcript is processed through the model to create a 400-dimension vector space representation of all the words included, which is then reduced by summing and normalizing the vector. The semantic "distance" of the sum of all the word vectors from a given transcript to the gold standard vector is then calculated (i.e., the cosine between vectors), resulting in a single, quantitative measure of semantic similarity ranging from -1 to 1, with 1 being the most similar. The scripts used to process these transcripts were developed by two of the authors (Goodkind and Bicknell) and are available on an open source repository.

For narratives and semi-naturalistic conversations, two gold standards were selected from the typically developing control group based on representativeness of pragmatic competence for that context (e.g., evaluation and story elements in narrative, lack of pragmatic violations in conversation). Gold standards were excluded from all other analyses. For all Word2Vec analyses, partially or unintelligible utterances, as well as mazes (i.e., repetitions and reformulations within an utterance) were excluded from analyses to minimize intelligibility and inflation of semantic content from reformulation as possible confounds.

**Vector semantics: Similarity within participant-examiner exchanges.** In addition to comparisons to gold standards, in the semi-structured conversational context vector semantics were applied to compute semantic similarity between the child and examiner utterances across conversational "exchanges". An "exchange" was defined as the following: examiner's statement, child's response, examiner's response, child's response. The inclusion of two examiner-child turns was selected based on the definition of conversation used in the ADOS, a gold standard diagnostic measure for ASD (Lord et al., 2001). The mean and standard deviations across all exchanges in a transcript were computed for each participant. Participants with less than 42 exchanges (nearly 2 standard deviations below the mean across groups) were excluded from analyses (2 males with ASD-O, 1 male with FXS-ASD, 2 males with DS, 1 male with TD).

**Previous Characterization of Language Samples**

**Hand coding of narratives.** The narrative coding scheme was adapted from prior work analyzing narratives in these populations (Capps, Losh, & Thurber, 2000; Estigarribia et al., 2011; Hogan-Brown, Losh, Martin, & Mueffelmann, 2013; Losh & Capps, 2003; Reilly, 1992; Reilly, Klima, & Bellugi, 1990; Reilly, Losh, Bellugi, & Wulfeck, 2004). Details of this coding scheme are provided in Chapter 3. Briefly, this coding scheme assessed *total story grammar* (e.g., introduction, key plot points), *identification of character relationships* (calculated as a proportion of total propositions), *affect, cognition and causality* (e.g., both labeling and causal explanations of different affective, cognitive, or behavioral states; calculated as a proportion of total propositions), *audience engagement* (e.g., story-telling devices, attempts to maintain the examiner's attention), and *off-topic statements* (e.g., irrelevant statements, protests). Hand coding was completed for all narrative samples.

**Characterization of semi-naturalistic conversations.** Two methods characterized semi-naturalistic conversation: clinical-behavioral ratings and hand coding of transcripts.

***Clinical-behavioral ratings.*** The Pragmatic Rating Scale-School Age (PRS-SA; Landa, 2011) is a clinical-behavioral rating system of 34 operationally defined features of pragmatic language assessing a range of skills including linkage of ideas to conversation, appropriate topic initiation and elaboration, as well as prosodic features of speech and nonverbal communication. Each item is rated on a three-point scale (0, absent; 1, mild impairment; or 2, impairment present); items are then totaled to provide an overall sum of pragmatic violations. Chapter 3 and Klusek et al. (2014) provide greater detail. For the current study, PRS-SA ratings were completed from video of the entire ADOS. PRS-SA outcome variables included total pragmatic violations, and total violations specifically related to elements targeted by computational measures of conversation (e.g., total of acknowledgment, response elaboration, conversational reciprocity, topic initiation and inappropriate topic shifts). PRS-SA ratings were completed for 35 participants with ASD-O, 39 participants with FXS-ASD, 13 participants with FXS-O, 21 participants with DS and 22 participants with TD at the first visit, and 13 participants with ASD-O, 14 participants with FXS-ASD, 5 participants with FXS-O and 14 participants with DS at the second visit.

***Hand coding.*** Previously applied by Roberts et al. (2007) and Martin et al. (in prep), coding was based on 100 turns of the ADOS transcript and included assessment of non-contingency (i.e., a child's turn changed the topic abruptly or did not meet the expectations of the previous conversational turn), perseveration (repetitive language at the word, phrase or turn level), initiations (child initiated a turn), and non-responsiveness (failure to provide a verbal response to a direct question or examiner utterance which required a response). All variables were calculated by dividing the total instance of a behavior by the total codable utterances, except for nonresponse, which was calculated as a proportion of all obligatory (i.e., required) responses + non-responses. Martin et al. (in prep) provides a more detailed explanation of the coding system. Hand-coding ratings were completed for 42 participants with ASD, 47 participants with FXS-ASD, 13 participants with FXS-O, 21 participants with DS and 19 participants with TD at the first visit, and 10 participants with ASD, 26 participants with FXS-ASD, 5 participants with FXS-O and 14 participants with DS at the second visit.

**Assessment of Relationships with Cognition and Structural Language**

The Leiter International Performance Scale-Revised provided an estimate of participant nonverbal mental age (Roid & Miller, 1997). Expressive language was measured by the Expressive Vocabulary Test (EVT; Williams, 1997) and receptive vocabulary was measured by the Peabody Picture Vocabulary Test -3rd or 4th editions (PPVT; Dunn & Dunn, 1997, 2007). Finally, syntactic complexity was measured by mean length of utterance in morphemes derived from complete, intelligible utterances from transcriptions of the ADOS (using the Systematic Analysis of Language Transcripts (SALT; Miller & Chapman, 2008).

**Analysis Plan**

The first aim of this study was to determine whether computational measures distinguished groups and were sensitive to change over time. Within the narrative and semi-structured conversational contexts, group comparisons for each computational outcome variable were conducted using non-parametric Kruskal-Wallis one-way analysis of covariance for each computational outcome variable. Group comparisons were followed by planned comparisons between all groups. Due to the exploratory nature of the study and to reduce the possibility of Type 2 error, significance was interpreted if $p < .05$. Additionally, Wilcoxon Test repeated measures were conducted from the first to second visit to determine whether computational measures were sensitive to change over time.

The second aim of the study was to validate computational measures with previous characterization of the narrative and semi-structured conversational samples. To address this aim, Pearson bi-variate correlations assessed relationships between primary computational outcome measures and specific characterization of each context. Correlations were interpreted using both statistical significance ($p < .05$), and, given variable sample sizes, by effect size ($r < .3$ as a small effect, $.3 < r < .5$ as a medium effect, $r > .5$ as a large effect; J. Cohen, 1992). Correlations were completed at both visits, but interpretation focused on the initial visit due to larger sample sizes at that time point.

The third aim of the study was to explore relationships with non-verbal cognition and structural language (i.e., expressive and receptive vocabulary, mean length of utterance) across groups in each context. Bi-variate correlations at visit one were conducted to assess relationships between computational outcomes and mental age, expressive and receptive vocabulary, and MLU. Correlations between vector semantic similarity and characterizations of narrative and semi-naturalistic conversational samples were also replicated controlling for MLU to determine whether these effects persisted after accounting for syntactic complexity. Finally, exploratory analyses were conducted replicating group comparisons and correlations within groups below or above the mean mental age and mean sum of expressive and receptive vocabulary raw scores to explore whether results varied at different levels of ability.

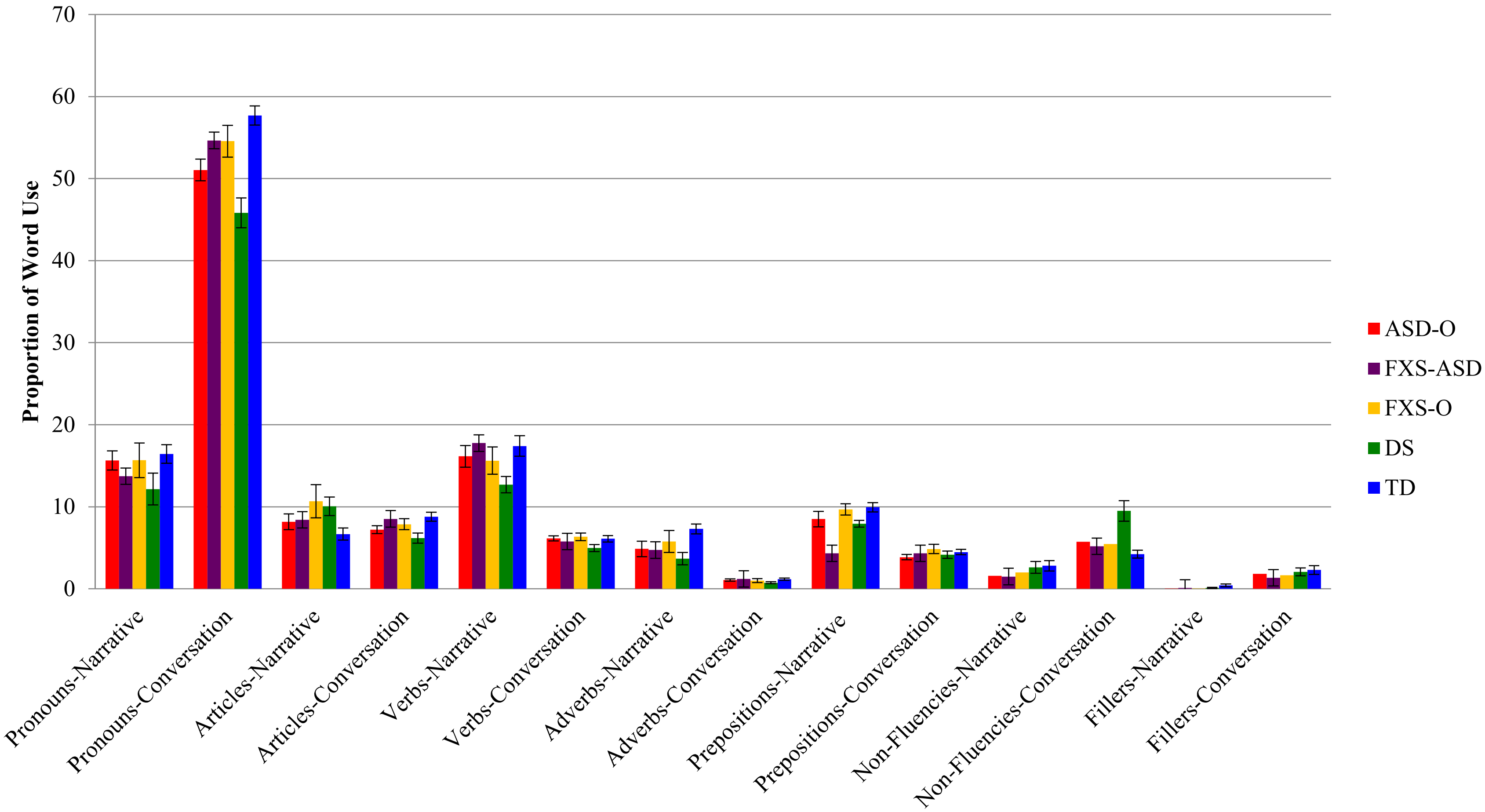
## Results

### Group Comparisons of Word Use at Visit One and Change Over Time

**Narrative.** Figure 4.1 demonstrates patterns of word use across groups at the initial visit across both contexts. Several group differences emerged in patterns of word use in the narrative context. Specifically, there were group differences in the use of verbs ($H = 6.70$, $p = .04$), adverbs ($H = 15.39$, $p = .004$), prepositions ($H = 9.90$, $p = .04$), nonfluencies ($H = 10.55$, $p = .032$) and fillers ($H= 12.50$, $p = .048$). Males with DS used proportionally fewer verbs than males with ASD-O, FXS-ASD and TD. Males with ASD-O, DS and FXS-ASD used significantly fewer adverbs than males with TD (ps < .01). Finally, the TD group demonstrated significantly greater non-fluencies and fillers than males with FXS-ASD and ASD-O (ps < .05).

**Semi-naturalistic conversation.** Comparisons of patterns of word use in the conversational context revealed overall group differences in use of pronouns ($H = 28.25$, $p < .001$), articles ($H = 16.55$, $p = .002$) and non-fluencies ($H = 20.33$, $p < .001$; see Figure 4.1). Males with DS used significantly fewer pronouns than all other groups, and males with ASD-O also used significantly fewer pronouns than males with TD (ps < .03). Analysis of patterns of pronoun use indicated that males with DS and ASD-O both used fewer types of several pronouns overall (e.g., I, we, she/he, they). Males with ASD-O and DS used fewer articles than males with TD and FXS-ASD. Males with DS had greater non-fluencies than all other groups (ps < .04).

**Figure 4.1 Patterns of Word Use Across Contexts**



**Changes in word use across visits**. In the narrative context, TD males decreased in their use of adverbs ($Z = -2.20$, $p = .028$) and their narratives included fewer nonfluencies ($Z = -2.2$, $p = .028$). Males with DS increased their use of prepositions ($Z = -2.31$, $p = .021$). In the conversation context, across time points, TD males decreased in their use of adverbs ($Z = -2.24$, $p = .025$), males with ASD-O decreased in their use of nonfluencies ($Z = -2.10$, $p = .035$), and males with FXS-O decreased their use of fillers ($Z=-2.02$, $p = .043$).

**Group Comparisons of Vector Semantic Measures at Visit One and Change Over Time**

**Narrative: Similarity to gold standard.** No group differences were observed in overall semantic similarity to a gold standard at the visit one ($H = 6.30$, $p = .18$), although greater variability was observed in the ASD groups (see Figure 4.2).

**Semi-structured conversation-similarity to a gold standard.** In contrast to narrative findings, vector semantic analyses comparing transcripts from semi-naturalistic contexts to a TD gold standard distinguished all clinical groups from TD controls at the initial visit (overall model: $H = 20.61$, $p < .001$, pairwise comparisons $p < .05$; see Figure 4.3).

Figure 4.2 Semantic Similarity to the Gold Standard in Narrative at Visit One

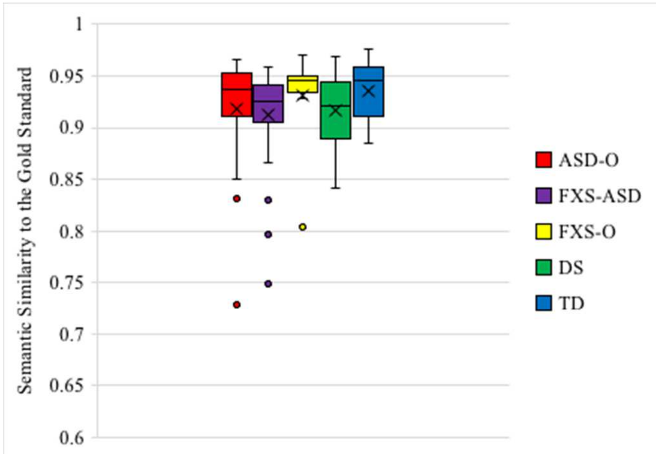
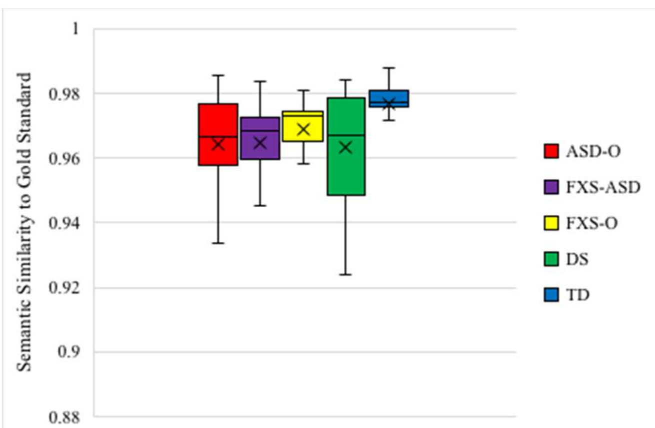



Figure 4.3 Semantic Similarity to the Gold Standard in Semi-Structured Conversation at Visit One




Note. In both Figure 4.2 and 4.3, X's indicate the mean.

**Semi-structured conversation: Conversational exchange similarity.** Males with ASD-O, FXS-ASD and DS demonstrated a lower mean interchange similarity relative to TD controls

(H = 20.31, p < .001). Groups did not differ in the standard deviation of interchange (i.e., an index of variance across interchanges; H = 1.45; p = .84).

**Change over time in vector semantic variables.** Within group repeated measures revealed no significant changes in semantic similarity to a gold standard in the narrative or conversational contexts (Zs < 1.42, ps > .16; Ws < 1.6, ps > .20). Similarly, there were no significant within group changes for average interchange similarity (Ws < 1.61, ps > .1), or standard deviation of interchanges (Ws < 1.7, ps > .1).

**Validation of Computational Measures: LIWC**

**Narrative.** Several significant relationships emerged between patterns of word use and hand-coded aspects of narrative. In males with DS and FXS-ASD, greater pronoun use was associated with fewer mentions of character relationships (r = -.72; r = -.39). Increased frequency of articles was associated with more story grammar in males with TD (r = .68). Greater verb use was associated with reduced proportion character relationships and affect, cognition and causality in the FXS-ASD group (r=-.53, r = -.45), as well as story elements in the TD group (r = -.55). Greater adverb use was associated with fewer story elements in FXS-O group (r = -.76). In the ASD-O group, greater use of prepositions was associated with increased story grammar. In both the ASD-O and FXS-ASD groups, greater non-fluencies were associated with increased audience engagement (r = .63, r = .59).

**Semi-Structured Conversation.**

***Word use and clinical-behavioral ratings.*** Increased pronoun use was significantly related to greater pragmatic competence (i.e., lower PRS-SA Total) in the ASD-O groups (r = -.40) and with a moderate effect size in the DS group (r = -.40), whereas increased article usage was related greater pragmatic competence in the DS group (r = -.44), and increased prepositions were related to greater pragmatic competence in the FXS-O group (r = -.62).

***Word use and hand coding of conversations.*** Increased pronoun and adverb use related to decreased non-responsiveness in the ASD-O group (rs < -.38), increased adverbs related to decreased non-responsiveness in the TD group, and greater verb use and reduced non-fluencies related greater responsiveness in the FXS-ASD group. Greater non-fluencies were related to reduced turn initiation across the DS, FXS-ASD and TD groups (|r| >.4), and increased pronoun use (|r| > .4), and increased articles were related to topic initiation in the DS and FXS-ASD groups, respectively. Finally, greater verb use was associated with lower perseveration in the ASD-O group (r = -.44) and pronoun and article use in the DS group was associated with reduced perseveration (rs < -.4).

## Validation of Vector Semantic Similarity Measures

**Narrative.** Correlations between semantic similarity to the gold standard and hand-coded elements of narrative are summarized in Table 4.2. Across groups, higher semantic similarity to the gold standard was associated with increased total story elements. Additionally, greater semantic similarity was significantly related to reduced use of audience engagement in the FXS-ASD group and with a medium effect size in males with FXS-O. Table 4.3 provides an example narrative from the gold standard, high and lower vector semantic similarity transcripts to demonstrate qualitative differences captured by semantic similarity.

Table 4.2. Correlations Between Vector Semantic Similarity to Gold Standard A and Hand-Coded Elements of Narrative

| **Narrative Element** | | **Group** | | | | |
|---|---|---|---|---|---|---|
| | **Visit** | **ASD-O** | **FXS-ASD** | **FXS-O** | **DS** | **TD** |
| **Total Story Grammar** | 1 | **.74*** | **.60*** | **.39** | **.70*** | **.74*** |
| | 2 | **.74*** | **.65*** | -- | **.61*** | **--** |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Character Relationships** | 1 | .34 | .17 | -.28 | -.33 | .03 |
| | 2 | **.51** | **.48*** | -- | -.32 | -- |
| **Affect, Cognition, Causality** | 1 | .08 | .27 | .28 | -.07 | .39 |
| | 2 | -.28 | **-.53*** | -- | -.27 | -- |
| **Audience Engagement** | 1 | -.04 | **-.51*** | **.39** | -.02 | -.11 |
| | 2 | **.75*** | -.14 | -- | -.51 | -- |
| **Off Topic** | 1 | **-.87*** | -.08 | .05 | **-.37*** | **-.43** |
| | 2 | **-.60** | .21 | -- | -.22 | **--** |

* $p < .05$. Note. Correlation values that represent a medium-large effect size are bolded. Correlations are not reported for visit two for sample sizes of five or less.

Table 4.3. Example High and Low Similarity Narratives

| **Gold Standard:<br>TD, Mental Age= 5.17, Word Count=200** | **Similarity Value=.94,<br>FXS-O, Mental Age =6.0, Word Count=153** | **Similarity Value = .87, FXS-ASD, Mental Age = 5.25, Word Count = 155** |
|---|---|---|
| okay well their mom and dad are going away okay? and so they had to sleep when their mom and dad are going. they're not scared because the light's on and they could play. so now they're jumping on the beds.<br>and now they move off and he is playing basketball.<br>they're playing basketball.<br>and now they destroyed that thing.<br>and now they destroyed the shelf.<br>so now he's opening and why he wants to take all those clothes out. so he could go to bed fast. I think so. and he is getting on dad's new hat. and he has got this hat. and he wants to play and he wants to make soapy bath. so then he turns on the soap and that guy jumps in and then it's a soap bath. so now they fall out ah oh soap's out.<br>and they're stuck inside. well the mom and dad are coming home. so they have to clean up. and now he fixed the shelf. and now he cleaned up the bathtub. so now they put it back on. now he goes oh and then dad was already home. and mom. now they're already at bed time. | the mom and the baby father and mother. mom and dad are leaving. going somewhere. mom says goodbye. the kids say goodbye too. mom dad leaving. they bounce on the bed. I used to do that. they're playing basketball. they're playing. the picture falls down. the bookshelf fell over. the pairs fell down. and the mess. the kids turn the closet. playing dress up. they find a hat. the closet mess. the kids in the tub.<br>in the tub. they're in there with cream. it's soap. the tub fell over. mom and dad are coming home soon. got to clean up.<br>baby's cleaning the mess up. they see a picture it's happy. the penguins clean up the floor.<br>they clean up the bookshelf. the baby clean up the floor.<br>the closet fell over.<br>wow it's messy. mom and dad are home. the son keeps sleeping. very quietly. sleeping.<br>I'm good. they were sleeping. | Pingu. Pingu. mom and dad are like him. the sister's still working. might come home. wave goodbye. sad. all done. all done. Pingu went back bounce bounce the ball. play back. fall down. it's done? it's done? done. all done. Pingu mess mess. mess. mess. and. closet. went to sleep. falls asleep. went to sleep. went to sleep. and went to sleep. and dressup dressup. take a bath. take a bath. lay down washing. wash. wash.<br>wash together. splashing. splash. falling. woah falling. falling. falling. mom and dad home soon. hey please stop. that's good. cleaning. rubbing rubbing rubbing. cleaning. rubbing. fix the picture. fix the picture. fix the picture. fix the picture. wash in the water. back. closet. clean the closet. clean the closet.<br>clean the closet. clean closet. clean the closet. mom and dad home. and Pingu and sister went to sleep. and went to sleep. and went to sleep. I did it. |

**Semi-naturalistic conversation.** Table 4.4 summarizes correlations between vector semantic measures (similarity to gold standard and conversational exchange measures) and characterizations of conversations (i.e., hand-coding and PRS-SA total ratings). In both ASD groups (i.e., ASD-O, FXS-ASD), lower semantic similarity to the gold standard was associated with greater hand-coded non-responsiveness and non-contingency at visit one. Similarly, exchange similarity was associated with reduced non-responsiveness, non-contingency, and perseveration in the ASD-O group, and associated with reduced pragmatic violations related specifically to reciprocity on the PRS-SA in both the ASD-O and FXS-ASD groups. Reduced semantic similarity to the gold standard was correlated with greater total pragmatic violations (PRS-SA) in the DS group.

Table 4.4. Relationships Between Hand-Coded Measures of Conversation Quality and Computational Semantic Similarity Measures Across Visits

| | ASD-O | | | FXS-ASD | | | FXS-O | | | DS | | | TD | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Visit 1** | GS | M | SD | GS | M | SD | GS | M | SD | GS | M | SD | GS | M | SD |
| HC-Initiations | .08 | -.03 | .17 | .05 | .13 | .01 | -.30 | -.05 | .06 | **.56*** | -.17 | **.50*** | **-.31** | .04 | -.17 |
| HC-Non Responses | **-.45*** | **-.39*** | .22 | **-.40*** | -.22 | .04 | .27 | -.07 | -.19 | **-.36** | -.15 | -.27 | **-.31** | .38 | **-.51*** |
| HC-Non-Contingency | **-.40*** | **-.60*** | .31 | **-.41*** | -.13 | .06 | -.23 | .06 | -.12 | **-.30** | **-.36** | .43 | -.05 | .22 | -.17 |
| HC-Perseveration | -.20 | -.44* | .43* | -.24 | .07 | -.10 | -.23 | -.10 | -.15 | **-.45*** | **-.58*** | **.63*** | .04 | -.25 | -.21 |
| PRS-SA Total | -.24 | **-.30** | -.05 | -.19 | -.28 | .15 | **-.56*** | **-.75** | **.79*** | **-.45*** | **-.40** | .20 | -.21 | -.14 | -.19 |
| PRS-SA Items Related to Reciprocity | **-.48*** | **-.47*** | .15 | -.24 | **-.33*** | .07 | **-.40** | **-.46** | **.35** | **-.52*** | **-.49*** | .24 | **-.46*** | .07 | **-.33** |
| **Visit 2** | GS | M | SD | GS | M | SD | GS | M | SD | GS | M | SD | GS | M | SD |
| HC-Initiations | **-.59** | -.24 | .53 | .07 | -.31 | .24 | | | | -.27 | **-.36** | **.50** | | | |
| HC-Non-Responses | **-.47** | .25 | -.15 | -.18 | -.26 | -.03 | | | | .12 | .03 | -.11 | | | |
| HC-Non-Contingency | -.20 | **.49** | -.16 | -.31 | -.23 | **.38** | | | | -.79* | **-.45** | **.49** | | | |
| HC-Perseveration | .09 | .31 | -.35 | -.18 | **-.33** | **.48*** | | | | -.80* | **-.56*** | **.66*** | | | |
| PRS-SA Total | **-.32** | .02 | -.27 | .09 | -.06 | .20 | | | | .12 | -.06 | .09 | **-.43** | -.26 | **.49** |
| PRS-SA Items Related to Reciprocity | -.24 | .21 | -.27 | -.10 | -.20 | .16 | | | | -.03 | -.28 | .22 | **-.69** | **-.42** | .23 |

Note. Data not reported when $n < 5$. HC=Hand-Coded; GS=Semantic Similarity to Conversational Gold Standard, M=Mean Interchange Similarity, SD=Standard Deviation of Interchange Similarity. * $p < .05$. Bolding indicates medium-large effect size. Correlations are reported at $p < .05$.

**Associations with Nonverbal Cognition and Structural Language-Word Use**

**Narrative.** Table 4.5 summarizes correlations between LIWC outcome variables and measures of cognition and structural language. Patterns of word use were not consistently related to measures of cognition and structural language across groups, except that greater mental age, expressive, and receptive vocabulary age equivalents was associated with greater article use in the TD group.

**Semi-naturalistic conversation.** Table 4.5 summarizes correlations between computational measures and measures of cognition and structural language during the semi-naturalistic context. Pronoun use of was consistently correlated with greater MLU across groups, and within the FXS-ASD group nearly all LIWC variables were related to MLU (with fillers and non-fluencies negatively related). Otherwise, patterns of word use were minimally influenced by mental age or structural language

Table 4.5. Correlations Between Computational Measures Word Use and Measures of Cognition and Structural Language at Visit One

| Groups | Measure | Mental Age | EVT AE | PPVT AE | MLU |
|---|---|---|---|---|---|
| **ASD-O** | Pronoun-Narrative | -.07 | -.15 | -.17 | .07 |
| | Pronoun-Conversation | .12 | .29 | .29 | **.71*** |
| | Article-Narrative | .12 | .10 | .13 | **-.32** |
| | Article-Conversation | -.02 | -.04 | -.06 | .15 |
| | Verb-Narrative | -.03 | -.02 | -.04 | **.54*** |
| | Verb-Conversation | -.002 | -.02 | -.05 | **.33*** |
| | Adverb-Narrative | **.37** | **.30** | **.42** | **.52*** |
| | Adverb-Conversation | -.22 | -.03 | -.18 | .21 |
| | Prepositions-Narrative | **.35** | .29 | **.38** | **.60** |
| | Prepositions-Conversation | .11 | .21 | .25 | .11 |
| | Nonfluencies-Narrative | -.12 | -.13 | -.13 | -.13 |
| | Nonfluencies-Conversation | .03 | .05 | .07 | -.26 |
| | Fillers-Narrative | **31** | .28 | **.44*** | **.39** |
| | Fillers-Conversation | .26 | **.37*** | **.36*** | .14 |
| **FXS-ASD** | Pronoun-Narrative | -.28 | .03 | .04 | **.61*** |
| | Pronoun-Conversation | -.03 | **.30*** | **.30*** | **.60*** |
| | Article-Narrative | .09 | .25 | .24 | -.12 |
| | Article-Conversation | .22 | .20 | .29* | .06 |

| | | | | | |
|---|---|---|---|---|---|
| | Verb-Narrative | **-.30** | -.15 | -.17 | **.62*** |
| | Verb-Conversation | -.20 | -.10 | .05 | **.31*** |
| | Adverb-Narrative | .26 | **.35** | **.38** | -.04 |
| | Adverb-Conversation | -.27 | -.18 | -.29 | **.38*** |
| | Prepositions-Narrative | -.21 | -.21 | -.13 | .08 |
| | Prepositions-Conversation | .19 | .10 | .11 | .07 |
| | Nonfluencies-Narrative | .15 | -.24 | **-.37** | -.26 |
| | Nonfluencies-Conversation | .06 | -.13 | -.10 | **-.62*** |
| | Fillers-Narrative | .07 | .27 | .05 | .04 |
| | Fillers-Conversation | .13 | .16 | .14 | **-.37*** |
| **FXS-O** | Pronoun-Narrative | -.21 | -.12 | -.23 | .03 |
| | Pronoun-Conversation | .12 | .29 | .29 | **.71*** |
| | Article-Narrative | -.14 | -.18 | -.09 | **-.40** |
| | Article-Conversation | -.02 | -.04 | -.06 | .15 |
| | Verb-Narrative | **-.66*** | **-.58** | **-.66*** | -.03 |
| | Verb-Conversation | -.09 | -.16 | -.23 | **.54** |
| | Adverb-Narrative | -.21 | **-.43** | -.22 | -.07 |
| | Adverb-Conversation | -.22 | -.14 | -.23 | .18 |
| | Prepositions-Narrative | **.45** | **.64** | **.56** | **.46** |
| | Prepositions-Conversation | **.47** | **.40** | **.42** | **.46** |
| | Nonfluencies-Narrative | -.13 | -.05 | -.07 | **-.55** |
| | Nonfluencies-Conversation | -.06 | -.04 | .05 | **-.65*** |
| | Fillers-Narrative | .10 | -.11 | -.20 | -.20 |
| | Fillers-Conversation | **.35** | **.37** | **.43** | **-.39** |
| **DS** | Pronoun-Narrative | -.17 | -.33 | -.23 | .16 |
| | Pronoun-Conversation | .27 | **.50*** | **.34** | **.68*** |
| | Article-Narrative | **.38** | .22 | **.30** | **.44** |
| | Article-Conversation | .11 | .15 | .01 | .23 |
| | Verb-Narrative | -.19 | -.25 | -.12 | .15 |
| | Verb-Conversation | .07 | .07 | -.08 | **.41** |
| | Adverb-Narrative | -.17 | .02 | **.37** | -.03 |
| | Adverb-Conversation | .29 | .01 | -.02 | .19 |
| | Prepositions-Narrative | -.06 | .24 | -.10 | -.27 |
| | Prepositions-Conversation | -.12 | .12 | -.18 | -.10 |
| | Nonfluencies-Narrative | -.15 | .01 | -.05 | -.01 |
| | Nonfluencies-Conversation | -.14 | -.14 | -.13 | **-.57*** |
| | Fillers-Narrative | .24 | .28 | **.46** | **.45** |
| | Fillers-Conversation | -.13 | .01 | -.16 | .15 |
| **TD** | Pronoun-Narrative | -.17 | -.10 | -.28 | **.30** |
| | Pronoun-Conversation | -.10 | -.25 | **-.33** | **.71*** |
| | Article-Narrative | **.85*** | **.79*** | **.79*** | .22 |
| | Article-Conversation | -.04 | -.04 | -.17 | **.37** |
| | Verb-Narrative | **-.48** | **-.58** | **-.61** | .07 |
| | Verb-Conversation | -.10 | -.20 | -.13 | -.11 |
| | Adverb-Narrative | -.23 | -.10 | **-.45** | **-.48** |
| | Adverb-Conversation | -.30 | -.25 | -.26 | .13 |
| | Prepositions-Narrative | -.13 | -.11 | -.06 | **-.46** |
| | Prepositions-Conversation | .05 | .12 | -.03 | .22 |

| | | | | | |
|---|---|---|---|---|---|
| | Nonfluencies-Narrative | -.12 | -.13 | -.13 | -.13 |
| | Nonfluencies-Conversation | .07 | .20 | .08 | -.05 |
| | Fillers-Narrative | **-.37** | -.23 | -.18 | **-.40** |
| | Fillers-Conversation | .08 | .10 | .08 | -.24 |

Note. EVT=Expressive Vocabulary Test, PPVT = Peabody Picture Vocabulary Test, MLU = Mean Length of Utterance. Medium effect sizes are bolded. * $p < .05$.

**Associations with Nonverbal Cognition and Structural Language-Vector Semantic Analyses**

**Narrative.** Greater structural language across groups was associated with better similarity to a gold standard, with moderate-large effect size across groups except for males with FXS-O. Whereas greater mental age was associated with higher semantic similarity to a gold standard similarity in the TD and ASD-O groups, this was minimally related in the FXS-ASD or DS groups. Correlations are reported in Table 4.6

**Semi-structured conversation.** Vector semantic metrics were also correlated most strongly with MLU, in that greater MLU was related to increased similarity (with the exception that MLU was minimally correlated with similarity to the conversational gold standard for males with FXS-O). Higher turn unit semantic similarity was related to greater cognition and structural language for the DS group, and related with small-medium effect size in the FXS-O group. Correlations are reported in Table 4.6

Table 4.6. Correlations Between Vector Semantic Measures and Structural Language and Cognition at Visit One

| Groups | Measure | Mental Age | EVT AE | PPVT AE | MLU |
|---|---|---|---|---|---|
| ASD-O | Similarity to Gold Standard Narrative | **.44*** | **.57*** | **.48*** | **.58*** |
| | Similarity to Gold Standard Conversation | .24 | **.39*** | .28 | **.55*** |
| | Mean Exchange Similarity | .14 | .24 | .17 | **.66*** |
| FXS-ASD | Similarity to Gold Standard Narrative | .001 | **.57*** | **.59*** | .17 |
| | Similarity to Gold Standard Conversation | .003 | .12 | .06 | **.46*** |
| | Mean Exchange Similarity | .05 | .26 | **.36*** | **.72*** |
| FXS-O | Similarity to Gold Standard Narrative | .25 | .22 | .33 | .15 |

| | | | | | |
|---|---|---|---|---|---|
| | Similarity to Gold Standard Conversation | .26 | **.31** | **.30** | .06 |
| | Mean Exchange Similarity | **.34** | **.45** | **.39** | **.68*** |
| **DS** | Similarity to Gold Standard Narrative | .14 | **.52** | **.44** | **.81*** |
| | Similarity to Gold Standard Conversation | .24 | .29 | .27 | **.58*** |
| | Mean Exchange Similarity | **.59*** | **.47** | **.41** | .24 |
| **TD** | Similarity to Gold Standard Narrative | -.10 | -.25 | **-.33** | **.71*** |
| | Similarity to Gold Standard Conversation | .03 | .08 | -.10 | **.43** |
| | Mean Exchange Similarity | -.18 | **-.35** | **-.45*** | **.51*** |

Note. EVT=Expressive Vocabulary Test, PPVT = Peabody Picture Vocabulary Test, MLU = Mean Length of Utterance

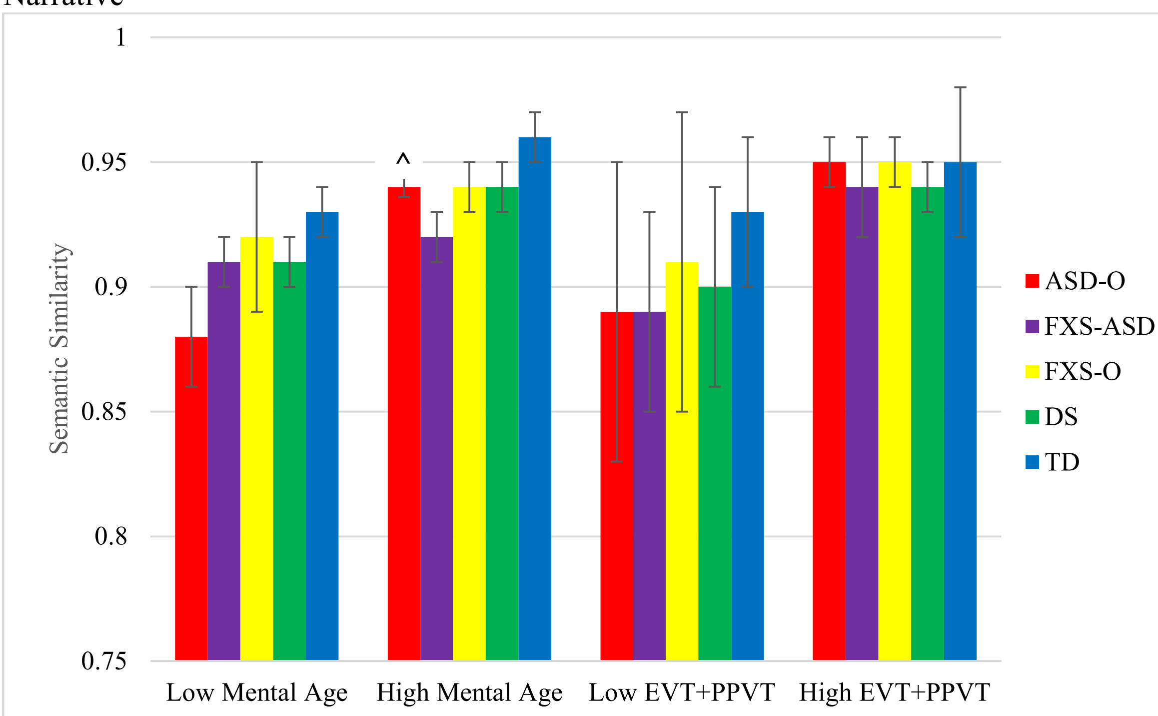
**Replication of associations with hand coding accounting for mean length of utterance.**

***Narrative.*** When controlling for MLU, correlations between semantic similarity and total story elements persisted for males with ASD-O, FXS-ASD and TD (rs > .6), as did relationships between greater similarity and reduced audience engagement in the FXS-ASD group (r = -.48).

***Semi-structured conversation.*** When controlling for MLU, there remained a marginal relationship between similarity to the gold standard and PRS-SA impairments related to reciprocity for males with ASD-O, DS, and TD (rs < -.3, .05 < ps < .07), and a marginal relationship between similarity to the gold standard and total pragmatic violations in males with FXS-O (r = -.57, p = .053). There was also a significant relationship between exchange similarity and reduced pragmatic violations related to reciprocity in the DS group (r = -.47), and reduced total violations in the FXS-O group (r = -.80), and a relationship of moderate effect size between interchange similarity and violations related to reciprocity (r = -.32). Other significant relationships no longer held after controlling for MLU.

**Exploratory analyses of impact of cognition and structural language.** When dividing groups into "low" and "high" groups for mental age and structural language, a consistent pattern, was observed in that all groups showed higher scores with greater mental age and structural language; however, patterns of difference remained consistent. In the narrative context, there was a marginal overall effect of group in the high mental age group, with FXS-ASD showing lower scores than TD (see Figure 4.4). However, differences were no longer significant in "high" language or mental age group in the semi-naturalistic conversational context. Patterns of relationships between vector semantics and hand-coded variables were not consistently different across the subgroups.

Figure 4.4 Patterns of Semantic Similarity Across Different Levels of Cognition and Language in Narrative




Note. Low=below mean, High = above mean. EVT=Expressive Vocabulary Test, PPVT = Peabody Picture Vocabulary Test, EVT+PPVT= sum of raw scores

# Discussion

This study evaluated the application of two computational linguistic methods to characterize language use during narrative and semi-naturalistic conversations in a longitudinal sample of males with ASD-O, FXS-ASD, FXS-O, DS and TD. Both measures distinguished clinical groups from controls, and in some cases from one another, although vector semantic analyses were more sensitive in the semi-structured context. Computational measures changed minimally across time points. Computational measures related to prior characterization of pragmatic features of both contexts, although these relationships were somewhat attenuated in the semi-naturalistic context after accounting for syntactic complexity. Together, these results represent a first step in the application of computational linguistic tools to characterize features of structural and pragmatic language in neurodevelopmental disabilities, and offer several areas of future direction.

## Group Comparisons and Validation with Hand Coding: LIWC

Characterization of patterns of word use during narrative revealed differences consistent with prior work characterizing narrative in these groups. For example, males with DS showed the greatest differences in markers of structural language (i.e., verbs, adverbs, prepositions). This is perhaps not surprising given the structural language difficulties present in DS more broadly. Prior work suggests that males with DS show difficulties with verb use above and beyond MLU (Channell, McDuffie, Bullard, & Abbeduto, 2015; Hesketh & Chapman, 1998), and Ashby, Channell and Abbeduto (2017) hypothesized that these difficulties may contribute to reduced inferential language during narration, although relationships between verb use and evaluation were not observed in the DS group in the current study. The fact that males with TD showed greater non-fluencies and fillers during narration is also consistent with Martin et al. (2012)'s finding that TD males showed greater within utterance repetition than clinical groups during narrative only. Martin et al. (2012) hypothesized that this difference may have reflected controls' greater effort to formulate more complex syntax (resulting in repetition) during narrative, a hypothesis further supported by these results.

Correlations between patterns of word use and narrative were largely intuitive. For example, increased pronoun use was related to reduced character relationships in males with DS and FXS-ASD, which likely reflected greater continued references to relationships (e.g., sister, brother) rather than pronoun substitutions (e.g., she, he). It is notable, however, that patterns of word use related to grammatical markers such as verbs and propositions were not consistently related to narrative elements across groups, perhaps highlighting that increased use of grammatical markers does not necessarily translate to higher quality narratives. In fact, in both ASD groups (ASD-O and FXS-ASD) greater verb use was related to fewer instances of affect, cognition and causality, perhaps reflecting a greater focus on actions of characters rather than emotional or causal descriptors. It is also notable that greater non-fluencies were also associated increased audience engagement in both ASD groups, given findings in Chapter 3 that the FXS-ASD group tended to use such devices repetitively. Audience engagement is an evaluation device that emerges earlier in development and typically reduces in school age years in typical development (Reilly, 1992); the relationship with non-fluencies may reflect more global delays in narrative competence, or suggest that such devices may serve as a compensatory strategy for difficulties in narration. The overlap in FXS-ASD and ASD-O groups in these relationships also suggests ASD specific phenotypes, quantifiable at a word level, that may reflect shared genetic liability across groups.

In contrast to the narrative context, fewer differences were observed in word use during the semi-naturalistic conversation context, although both males with ASD-O and DS used fewer pronouns. Several studies have documented difficulties with pronoun use in males with ASD-O, and in particular greater ambiguity of pronouns (Colle, Baron-Cohen, Wheelwright, & van der Lely, 2008; Novogrodsky, 2013) and pronoun reversal (see (Wilkinson et al., 1998, for review); however, these differences have not been noted in DS. Of note, in both groups increased pronoun use was related to greater pragmatic competence during conversation, including increased topic initiation. A limitation of LIWC is that it provides only word count frequency, and does not assess word order; therefore, although males with ASD-O and DS showed similar differences in *pronoun frequency*, they may have differed in their appropriate usage. Context differences in patterns of word use also further highlight the importance of multi-method assessments to characterizing language in these groups. It may be that the more scaffolded nature of narrative provides greater opportunities for more complex speech, and in turn opportunities to observe subtler differences in patterns of word use than during conversation (Kover, McDuffie, Abbeduto, & Brown, 2012; Miles & Chapman, 2002).

**Group Comparisons and Validation with Hand Coding: Vector Semantic Analyses**

Although two prior studies have demonstrated that vector semantics distinguished individuals with ASD-O from controls in a narrative context (Lee et al., 2017; Losh & Gordon, 2014), in the current study this method did not distinguish groups. Several factors may account for this discrepancy. The population included in the current study had a lower language ability and mental age than those included in prior work, and the narrative elicitation task was far more structured and shorter than the recall (Losh and Gordon, 2014) or open-ended tasks (Lee et al., 2017) previously used, in that participants viewed the short video while narrating. Given the younger age of the TD participants included, it may be that group difference in narrative are less robust, and as a result not best captured by a global semantic measure, than at later chronological and mental ages, a hypothesis supported by hand-coded studies of narratives that show a similar lack of differences between lower functioning groups (i.e., Hogan-Brown et al., 2013). More consistent with prior work (Losh and Gordon, 2014; Lee et al., 2017; Prud'hommeaux et al., 2011) were findings that both ASD groups (ASD-O and FXS-ASD) showed greater heterogeneity in semantic similarity than other groups, suggesting that this measure is sensitive to within-group variation in narrative quality. Further, semantic similarity was strongly related to indices of narrative quality that distinguished groups (see Chapter 3), such as story grammar and audience engagement, suggesting that this metric may be sensitive to meaningful aspects of narration.

This study also extended the application of vector semantic similarity methods to semi-structured conversations. Results revealed that two measures of semantic similarity (similarity to semantic content of TD group and average similarity of examiner-child exchanges) distinguished males with ASD-O, FXS-ASD and DS from TD controls. However, these measures did not show differences within clinical groups, despite a robust body of literature suggesting differences in social communication between groups (e.g., Klusek et al., 2014; Losh, Martin, et al., 2012; Martin, Losh, Estigarribia, Sideris, & Roberts, 2013), including findings from Chapter 3 of this dissertation, which included an almost identical sample of participants. More encouraging was that variation in semantic similarity was associated with hand-coded and clinical-behavioral ratings of pragmatic language difficulties associated with ASD in both the ASD-O and FXS-ASD groups, and specifically reciprocity. Similar to findings at the word level, such overlap reflects specific pragmatic skills, and in particular those related to reciprocity, shared across disorders, and that may serve as targets for the refinement of computational measures that may map to common genetic variation. Further, reduced interchange similarity was correlated with increased non-contingency across all groups at least a moderate effect size, suggesting the potential of this measure to automatically model contingency within an interaction. These results suggest that vector semantic analyses may hold greater utility as an index of variability of specific features of pragmatic language, rather than a method to classify clinical groups.

**Sensitivity to Change Over Time**

Computational measures of both word choice and semantic similarity were largely stable across visits in both contexts. However, analyses of hand coding of narrative and clinical-behavioral ratings of conversation also indicated minimal changes with age (see Chapter 3). This is not to argue that pragmatic language does not change with age in clinical groups; rather, the more global quantitative measure of semantic similarity may better represent core impairments that remain relatively stable over time relative to typically developing groups. Future work should continue to refine measures that may be more sensitive to specific aspects of pragmatic language over time, and in larger samples.

**Relationships with Measures of Cognition and Structural Language**

Important to note are the relationships between vector semantic similarity and indices of nonverbal mental age, expressive and receptive vocabulary, and grammatical complexity (i.e., MLU) across groups, which varied by context. Exploratory analyses indicated that a subgroup of participants with higher mental age and structural language showed greater semantic values across contexts, and that the narrative appeared more sensitive to possible group differences in the higher mental age group, consistent with prior work that has applied vector semantic analysis to narrative samples (e.g., Lee et al., 2017; Losh and Gordon, 2014). Further, relationships between vector semantic analysis and hand-coded quality remained after accounting for mean length of utterance. This suggests that a more structured task, where there is a clear “gold standard” may diminish the relative impact of structural language and cognition on vector semantic measures, particularly in higher-functioning groups.

However, in the conversational context vector semantic similarity measures better distinguished the lower-functioning groups. Further, co-varying for MLU negated several significant relationships between semantic similarity and clinical-behavioral and hand-coding measures. It is somewhat intuitive that greater syntactic complexity is related to richer semantic content, and it may be that co-varying for MLU may have obscured meaningful relationships. Notably, trending findings remained in relationships between semantic similarity measures and clinical-behavioral ratings after controlling for MLU, suggesting that this measure may be sensitive to variation above and beyond structural language. Nevertheless, findings that such measures are associated with a range of indices of structural language highlight the importance of assessment of structural language in future studies of computational methods to characterizing language in ASD and related neurodevelopmental disabilities, where structural language and social communication are often closely related.

**Limitations and Future Directions**

Taken together, computational measures of both word use and semantic similarity show utility in characterizing linguistic and pragmatic aspects of language in two social contexts. Specifically, and across contexts, these measures were related to comprehensive ratings of pragmatic language features. Limitations of these measures were also observed, in that, consistent with prior work (i.e., Prud’hommeaux et al., 2011), they were less sensitive to differences between clinical groups or to change over time. Differences also appeared to be attenuated in the conversational context when accounting for structural language.

It is important to recognize the limitation of the computational measures applied in this study. Both LIWC and semantic analyses do not account for word order, which limits the ability to assess qualities of language beyond semantic content. Assessment of semantic similarity within examiner-participant exchanges also did not discriminate between repetition of an examiner's utterance (which would have near perfect semantic similarity) and meaningful contributions to the interaction. Finally, while these measures were more automated than traditional hand coding, they continued to require transcription by highly trained student transcribers (taking anywhere from 30-60 minutes to transcribe on average), and thus further developments in automated language transcription may be required to increase the utility of such measures.

The current results offer several directions for future research in computational methods for characterizing language in neurodevelopmental disabilities. Results indicating variation in findings across computational methods and contexts highlighted the importance of comprehensive assessment, and suggested that certain methods, such as vector semantic similarity to a gold standard, may be less influenced by language and cognition in a more structured context.  However, future studies should replicate these findings across different narrative samples varying in structure, where prior differences have been observed, and in larger samples. Given that prior work has documented greater impairment in pragmatic language in less structured contexts for individuals with ASD-O (see Chapter 3, (Losh & Capps, 2003), there remains a need to develop more sensitive measures in open-ended contexts. Whereas the current results suggest that preliminary, vector semantic analysis distinguished clinical groups and related to hand-coding measures and clinical-behavioral ratings, structural language emerged as a potential confound, and it did not distinguish between clinical groups. Therefore, future work should replicate these methods on language samples more closely matched in mean length of utterance, or perhaps in conversational samples of individuals without significant cognitive and language delay.

It is also important to consider the different application of computational tools within these groups. For example, the current study suggests that vector semantics may better reflect within group variability as opposed to a method to *classify* groups; therefore, future refinement of these tools may focus on increasing their sensitivity to varying language features, such as conversational reciprocity or narrative evaluation, across groups rather than the ability to clearly distinguish groups. Further, the current study took a more hypothesis driven approach, by attempting to model specific features known to distinguish groups, and then comparing clinical groups. An alternative approach would be to apply machine learning to language samples to identify specific linguistic features (or a combination thereof) that best distinguish groups, or to apply methods to a larger sample to explore whether specific subgroups emerge independent of diagnosis. Finally, alternative analyses of word choice and vector semantics previously applied, such as reduced coherence *within* a participant's utterance (as has been applied in schizophrenia, see Elvevag et al., 2010), or frequency of atypical words for a narrative context (i.e., Prud'hommeaux et al., 2011) may hold utility in these groups.

Finally, these metrics showed insignificant variation across visits; however, the current study focused on a school age period, where minimal changes were observed in hand-coded elements as well (see Chapter 3). Therefore, application of these tools should be explored across other age ranges, or in well-characterized samples where change has been previously established, to further refine their use in longitudinal samples.

**Conclusion**

This study represents a first step in the development of automated tools to characterize language in neurodevelopmental disabilities. Results demonstrate the potential benefits of such measures, while also highlighting the importance of considering assessment context and related abilities when adapting such computational linguistic methods for individuals with neurodevelopmental disabilities. Future work should continue to refine these measures, with the goal of developing tools that may be sensitive to variation in aspects of pragmatic skill and adaptable to both large-scale research and clinical contexts.

**References**

Adams, C. (2002). Practitioner review: the assessment of language pragmatics. *Journal of child psychology and psychiatry, and allied disciplines, 43*(8), 973-987.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (5th ed.). Arlington, VA: American Psychiatric Association.

Baucom, B. R., Georgiou, P., Bryan, C. J., Garland, E. L., Leifker, F., May, A., . . . Narayanan, S. S. (2017). The Promise and the Challenge of Technology-Facilitated Methods for Assessing Behavioral and Cognitive Markers of Risk for Suicide among U.S. Army National Guard Personnel. *Int J Environ Res Public Health, 14*(4).

Capps, L., Losh, M., & Thurber, C. (2000). The frog ate a bug and made his mouth sad: Narrative competence in children with autism. *Journal of Abnormal Child Psychology, 28*, 193-204.

Channell, M. M., McDuffie, A. S., Bullard, L. M., & Abbeduto, L. (2015). Narrative language competence in children and adolescents with Down syndrome. *Front Behav Neurosci, 9*, 283.

Cohen, J. (1992). A power primer. *Psychol Bull, 112*(1), 155-159.

Cohen, N. J., Farnia, F., & Im-Bolter, N. (2013). Higher order language competence and adolescent mental health. *J Child Psychol Psychiatry, 54*(7), 733-744.

Colle, L., Baron-Cohen, S., Wheelwright, S., & van der Lely, H. K. (2008). Narrative Discourse in Adults with High Functioning Autism or Asperger Syndrome. *Journal of Autism and Developmental Disorders, 38*, 28-40.

Dunn, L. M., & Dunn, D. M. (1997). *Peabody Picture Vocabulary Test*. Circle Pines, MN: American Guidance Service.

Dunn, L. M., & Dunn, D. M. (2007). *Peabody Picture Vocabulary Test, Fourth Edition*. San Antonio: Pearson Assessments.

Elvevag, B., Foltz, P. W., Rosenstein, M., & Delisi, L. E. (2010). An automated method to analyze language use in patients with schizophrenia and their first-degree relatives. *J Neurolinguistics, 23*(3), 270-284.

Elvevag, B., Foltz, P. W., Weinberger, D. R., & Goldberg, T. E. (2007). Quantifying incoherence in speech: an automated methodology and novel application to schizophrenia. *Schizophr Res, 93*(1-3), 304-316.

Estigarribia, B., Martin, G. E., Roberts, J. E., Spencer, A., Gucwa, A., & Sideris, J. (2011). Narrative skill in boys with fragile X syndrome with and without autism spectrum disorder. *Applied Psycholinguistics*, 359-388.

Gilmour, J., Hill, B., Place, M., & Skuse, D. H. (2004). Social communication deficits in conduct disorder: a clinical and community survey. *J Child Psychol Psychiatry, 45*(5), 967-978.

Gotham, K., Pickles, A., & Lord, C. (2009). Standardizing ADOS scores for a measure of severity in autism spectrum disorders. *J Autism Dev Disord, 39*(5), 693-705.

Gottesman, I. I., & Gould, T. D. (2003). The endophenotype concept in psychiatry: Etymology and strategic intentions. *Am J Psychiatry, 160*(4), 636-645.

Greenwood, T. A., Swerdlow, N. R., Gur, R. E., Cadenhead, K. S., Calkins, M. E., Dobie, D. J., . . . Braff, D. L. (2013). Genome-wide linkage analyses of 12 endophenotypes for schizophrenia from the Consortium on the Genetics of Schizophrenia. *Am J Psychiatry, 170*(5), 521-532.

Hagerman, R., & Hagerman, P. (2002). *Fragile X Syndrome: Diagnosis, Treatment, and Research Third Edition*. Baltimore: Johns Hopkins University Press.

Hampton, T. (2017). Early Brain Imaging in Infants May Help Predict Autism. *JAMA, 318*(13), 1211-1212.

Hazlett, H. C., Gu, H., Munsell, B. C., Kim, S. H., Styner, M., Wolff, J. J., . . . Analysis, S. (2017). Early brain development in infants at high risk for autism spectrum disorder. *Nature, 542*(7641), 348-351.

Helland, W. A., & Heimann, M. (2007). Assessment of pragmatic language impairment in children referred to psychiatric services: a pilot study of the Children's Communication Checklist in a Norwegian sample. *Logoped Phoniatr Vocol, 32*(1), 23-30.

Helland, W. A., Lundervold, A. J., Heimann, M., & Posserud, M. B. (2014). Stable associations between behavioral problems and language impairments across childhood - the importance of pragmatic language problems. *Res Dev Disabil, 35*(5), 943-951.

Hesketh, L. J., & Chapman, R. S. (1998). Verb use by individuals with Down syndrome. *Am J Ment Retard, 103*(3), 288-304.

Hogan-Brown, A. L., Losh, M., Martin, G. E., & Mueffelmann, D. (2013). An investigation of narrative ability in boys with autism and fragile X syndrome. *American Journal on Intellectual and Developmental Disabilities, 118*(2), 77-94.

Holshausen, K., Harvey, P. D., Elvevåg, B., Foltz, P. W., & Bowie, C. R. (2014). Latent semantic variables are associated with formal thought disorder and adaptive behavior in older inpatients with schizophrenia. *Cortex, 55*, 88-96.

Hus, V., Gotham, K., & Lord, C. (2012). Standardizing ADOS Domain Scores: Separating Severity of Social Affect and Restricted and Repetitive Behaviors. *J Autism Dev Disord*.

Klusek, J., Losh, M., & Martin, G. E. (2014). A comparison of pragmatic language in boys with autism and fragile X syndrome. *Journal of Speech, Language, and Hearing Research, 57*(5), 1692-1707.

Kover, S. T., McDuffie, A., Abbeduto, L., & Brown, W. T. (2012). Effects of sampling context on spontaneous expressive language in males with fragile X syndrome or Down syndrome. *J Speech Lang Hear Res, 55*(4), 1022-1038.

Landa, R. (2011). *The Pragmatic Rating Scale for School-Age Children (PRS-SA)*. Unpublished manual.

Landa, R., Folstein, S. E., & Isaacs, C. (1991). Spontaneous narrative-discourse performance of parents of autistic individuals. *Journal of Speech and Hearing Research, 34*(6), 1339-1345.

Landa, R., Piven, J., Wzorek, M. M., Gayle, J. O., Chase, G. A., & Folstein, S. E. (1992). Social language use in parents of autistic individuals. *Psychological Medicine, 22*(1), 245-254.

Lee, M., Martin, G. E., Hogan, A., Hano, D., Gordon, P. C., & Losh, M. (2017). What's the story? A computational analysis of narrative competence in autism. *Autism*, 1-10.

Lord, C., Rutter, M., DeLavore, P. C., & Risi, S. (2001). *Autism Diagnostic Observation Schedule*. Los Angeles, CA: Western Psychological Services.

Losh, M., & Capps, L. (2003). Narrative ability in high-functioning children with autism or Asperger's syndrome. *Journal of Autism and Developmental Disorders, 33*(3), 239-251.

Losh, M., Childress, D., Lam, K., & Piven, J. (2008). Defining key features of the broad autism phenotype: A comparison across parents of multiple- and single-incidence autism families. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 147B*(4).

Losh, M., & Gordon, P. C. (2014). Quantifying Narrative Ability in Autism Spectrum Disorder: A Computational Linguistic Analysis of Narrative Coherence. *Journal of Autism and Developmental Disorders, 44*(12), 3016–3025.

Losh, M., Klusek, J., Martin, G. E., Sideris, J., Parlier, M., & Piven, J. (2012). Defining genetically meaningful language and personality traits in relatives of individuals with fragile X syndrome and relatives of individuals with autism. *American journal of medical genetics. Part B, Neuropsychiatric genetics : the official publication of the International Society of Psychiatric Genetics, 159B*(6).

Losh, M., Martin, G. E., Klusek, J., Hogan-Brown, A. L., & Sideris, J. (2012). Social communication and theory of mind in boys with autism and fragile x syndrome. *Front Psychol, 3*, 266.

Martin, G. E., Losh, M., Estigarribia, B., Sideris, J., & Roberts, J. (2013). Longitudinal profiles of expressive vocabulary, syntax, and pragmatic language in boys with fragile X syndrome or Down syndrome. *International Journal of Language & Communication Disorders, 48*(4), 432-443.

McTear, M., & Conti-Ramsden, G. (1992). *Pragmatic disability in children*. London: Whurr.

Miles, S., & Chapman, R. S. (2002). Narrative content as described by individuals with Down syndrome and typically developing children. *Journal of speech, language, and hearing research : JSLHR, 45*(1), 175-189.

Miller, J. F., & Chapman, R. S. (2008). Systematic Analysis of Language Transcripts (SALT).

Nicodemus, K. K., Elvevåg, B., Foltz, P. W., Rosenstein, M., Diaz-Asper, C., & Weinberger, D. R. (2014). Category fluency, latent semantic analysis and schizophrenia: a candidate gene approach. *Cortex, 55*, 182-191.

Novogrodsky, R. (2013). Subject pronoun use by children with autism spectrum disorders (ASD). *Clin Linguist Phon, 27*(2), 85-93.

Pennebaker, J. W., Francis, M. E., & Booth, R. J. (2001). *Linguistic inquiry and word count (LIWC)*. Mahwah, NJ: Erlbaum.

Pennebaker, J.W., Mayne, T.J., & Francis, M.E. (1997). Linguistic predictors of adaptive bereavement. Journal of Personality and Social Psychology, 72, 863–871.

Pennebaker, J.W., & King, L.A. (1999). Linguistic styles: Language use as an individual difference. Journal of Personality and Social Psychology, 77, 1296–1312

Prud'hommeaux, E., & Rouhizadeh, M. (2012). Automatic detection of pragmatic deficits in children with autism. *Workshop Child Comput Interact, 2012*, 1-6.

Prutting, C. A., & Kittchner, D. M. (1987). A clinical appraisal of the pragmatic aspects of language. *Journal of Speech and Hearing Disorders, 52*(2), 105-119.

Reilly, J. (1992). How to tell a good story: The intersection of language and affect in children's narratives. *Journal of Narrative and Life History, 2*, 355-377.

Reilly, J., Klima, E. S., & Bellugi, U. (1990). Once more with feeling: Affect and language in atypical populations. *Development and Psychopathology, 2*(4), 367-391.

Reilly, J., Losh, M., Bellugi, U., & Wulfeck, B. (2004). "Frog, where are you?" Narratives in children with specific language impairment, early focal brain injury, and Williams syndrome. *Brain and Language, 88*(2), 229-247.

Roid, G. H., & Miller, L. J. (1997). *Leiter International Performance Scale-Revised*. Wood Dale, IL: Stoelting.

Rosenstein, M., Diaz-Asper, C., Foltz, P. W., & Elvevåg, B. (2014). A computational language approach to modeling prose recall in schizophrenia. *Cortex, 55*, 148-166.

Roth, F. P., & Spekman, N. J. (1984). Assessing the pragmatic abilities of children: Part 2. Guidelines, considerations, and specific evaluation procedures. *Journal of Speech and Hearing Disorders, 49*, 12-17.

Rouhizadeh, M., Prud'hommeaux, E., Roark, B., & van Santen, J. (2013). Distributional semantic models for the evaluation of disordered language. *Proc Conf, 2013*, 709-714.

Rude, S., Gortner, E.M., & Pennebaker, J. (2004). Language use of depressed and depression-vulnerable college students. *Cognition & Emotion,* 18, 1121–1133.

Simmons, R. A., Gordon, P. C., & Chambless, D. (2005). Pronoun use in marital interaction: What do "you" and "I" say about marital health? *Psychological Science, 16*(12), 932-936.

Tager-Flusberg, H., Paul, R., & Lord, C. (2005). Language and communication in autism. In F. Volkmar, R. Paul, & A. Klin (Eds.), *Handbook on autism and pervasive developmental disorders* (3rd ed., pp. 335-364). New York: Wiley.

Tager-Flusberg, H., Rogers, S., Cooper, J., Landa, R., Lord, C., Paul, R., . . . Yoder, P. (2009). Defining spoken language benchmarks and selecting measures of expressive language development for young children with autism spectrum disorders. *Journal of Speech, Language, and Hearing Research, 52*, 643-652.

Timmons, A. C., Baucom, B. R., Han, S. C., Perrone, L., Chaspari, T., Narayanan, S. S., & Margolin, G. (2017). New Frontiers in Ambulatory Assessment: Big Data Methods for Capturing Couples' Emotions, Vocalizations, and Physiology in Daily Life. *Social Psychological and Personality Science, 8*(5), 552-563.

Turk, A. A., Brown, W. S., Symington, M., & Paul, L. K. (2010). Social narratives in agenesis of the corpus callosum: Linguistic analysis of the Thematic Apperception Test. *Neuropsychologia, 48*, 43-50.

Wilkinson, K. M. (1998). Profiles of language and communication skills in autism. *Mental Retardation and Developmental Disabilities Research Reviews*(2).

Williams, K. T. (1997). *Expressive Vocabulary Test*. Circle Pines, MN: American Guidance Service.

Yoo, H. (2015). Genetics of Autism Spectrum Disorder: Current Status and Possible Clinical Applications. *Exp Neurobiol, 24*(4), 257-272.

## Chapter 5: SUMMARY

The three manuscripts included in this dissertation provide a comprehensive evaluation of pragmatic language in males with ASD-O, FXS-ASD, FXS-O and DS, with implications for identifying possible shared pragmatic features that may indicated common etiology and further characterization of contributing mechanisms of pragmatic language across groups. Across these manuscripts, three common themes emerged: specific aspects of pragmatic skill may best capture shared genetic liability across ASD-O and FXS-ASD, multi-method and longitudinal approaches are critical to assessing pragmatic language in neurodevelopmental disabilities, and consideration of related abilities can inform both methodology and understanding of mechanisms driving pragmatic competence.

### Specific Pragmatic Skills May Reflect Shared Genetic Liability across ASD-O and FXS-ASD

Chapter 2 highlighted the variation in patterns of strengths and weaknesses observed in pragmatic skills across ASD-O and FXS-ASD, with specific areas of overlap in difficulties related to conversational reciprocity and perseveration. Chapter 3 extended these findings, by demonstrating areas of overlap, particularly in the semi-naturalistic context, that persisted over time. It is equally important; however, to recognize the differences observed across ASD-O and FXS-ASD, in domains such as narrative, aspects of conversation related to theory of mind, and parent-reported difficulties. There has been previous debate about the “validity” of an ASD diagnosis in FXS, and this dissertation supports that ASD in the context of FXS is not identical to ASD-O. Rather, assessment of specific pragmatic skills, across development, can inform specific pragmatic domains that may be related to common underlying *FMR1* variation.

**Multi-method and Longitudinal Approaches are Critical to Assessing Pragmatic Language in Neurodevelopmental Disabilities**

A review of previous cross-population comparisons of ASD-O and FXS (Chapter 2) highlighted how variation in methodologies and developmental level of participants included significantly impacted observed patterns of overlap. Empirical investigation of pragmatic language skill across four assessment contexts (Chapter 3) confirmed the role of context in pragmatic skill in two ways-first, in that impairments were more prominent in both ASD groups in less structured contexts, and second, that different contexts drew on different related abilities. The role of assessment context was equally critical in the validation of computational methods assessed in Chapter 4, in that computational tools better distinguished groups in the less structured contexts, but were less influenced by structural language and cognition in the more structured narrative context. Although in the current study pragmatic profiles were largely stable over time, changes in specific skills across ages suggest the importance of considering the influence of development on the manifestation of pragmatic skills.

**Consideration of Related Abilities Can Inform Both Methodology and Understanding of Mechanisms Driving Pragmatic Competence**

Chapter 2 raised the importance of considering structural language in cross-population comparisons of pragmatic language, given that patterns of results changed across studies based on covariates included. Further, this review prompted questions as to whether common underlying abilities influenced pragmatic competence in ASD-O and FXS-ASD. Chapter 3 provided an empirical evaluation of the role of structural language, cognition, executive function and theory of mind in pragmatic competence across groups. Interestingly, structural language influenced patterns of group difference (and contributed to change over time) more significantly in structured contexts such as the CASL- pragmatic judgment subscale, and narrative, suggesting that such tasks may draw more heavily on structural language in these groups. The fact that group differences persisted after including structural language as covariates also refutes the argument that deficits in FXS-ASD may be attributed primarily to lower language and cognition. Of note, the contributions of executive function and theory of mind also differed across groups; for example, parent-reported executive functioning difficulties were related to pragmatic violations in the FXS-ASD and DS groups, but not the ASD-O groups. Although future studies should account for the methodological limitations of the current work (e.g., incorporating direct assessment, more focused assessment of theory of mind), these discrepancies suggest that even in the context of shared genetic liability, disruptions in different mechanisms may contribute to common outcomes.

Consideration of structural language and cognition also impacted interpretation of computational linguistic measures, and raised an important question as to whether such metrics can tap unique aspects of pragmatic ability beyond structural language difficulties. Results of the Chapter 4 suggested that such measures continue to relate to indices of pragmatic competence to some extent-but that further refinement of these tools is needed for populations characterized by language impairment.

**Future Directions**

Results of the current work offer several areas of future direction. Future work should further assess specific aspects of pragmatic language that overlap in ASD-O and FXS-ASD, narrowing in on topic initiation, elaboration and reciprocity across less-structured contexts. Future work should also continue to refine more objective, quantitative measures that may capture the variation in pragmatic language observed across groups. As the pragmatic phenotypes and course of development are further defined within these groups (as well as novel metrics), findings may inform the development of tailored outcome measures and interventions across disabilities. Research should also extend the current work to females, and across the lifespan.

**Conclusion**

Pragmatic language is a critical to mental health in typical development. Results of this dissertation highlight features of pragmatic skill that may relate to *FMR1* variation, and the unique roles of structural language, cognition, executive function and theory of mind in aspects of pragmatic competence. A movement towards more open-ended assessments will be critical to understanding pragmatic competence both in typical and atypical development-as will the need for more objective measures. This dissertation represents a step towards these goals for individuals with ASD-O, FXS-ASD, FXS-O, DS, investigations within these populations may ultimately form the complex genetic, neurobiological and behavioral components contributing to pragmatic language that cut across disorders.