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Pragmatic Language Features of Mothers with the *FMR1* Premutation are Associated with the Language Outcomes of Adolescents and Young Adults with Fragile X Syndrome

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Abstract

Purpose: Pragmatic language difficulties have been documented as part of the *FMR1* premutation phenotype, yet the interplay between these features in mothers and the language outcomes of their children with fragile X syndrome is unknown. This study aimed to determine whether pragmatic language difficulties in mothers with the *FMR1* premutation are related to the language development of their children. **Method:** Twenty-seven mothers with the *FMR1* premutation and their adolescent/young adult sons with fragile X syndrome participated. Maternal pragmatic language violations were rated from conversational samples using the Pragmatic Rating Scale (Landa et al., 1992). Children completed standardized assessments of vocabulary, syntax, and reading. **Results:** Maternal pragmatic language difficulties were significantly associated with poorer child receptive vocabulary and expressive syntax skills, with medium effect sizes. **Conclusions:** This work contributes to knowledge of the *FMR1* premutation phenotype and its consequences at the family level, with the goal of identifying modifiable aspects of the child's language-learning environment that may promote the selection of treatments targeting the specific needs of families affected by fragile X. Findings contribute to our understanding of the multifaceted environment in which children with fragile X syndrome learn language and highlight the importance of family-centered intervention practices for this group.

Keywords: language development, *FMR1* premutation, pragmatic language, maternal input, fragile X syndrome

Pragmatic Language Features of Mothers with the *FMR1* Premutation Are Associated with the Language Outcomes of Adolescents and Young Adults with Fragile X Syndrome

The *FMR1* Premutation

Fragile X syndrome is the most common inherited form of intellectual disability (Crawford, Acuna, & Sherman, 2001). The disorder is caused by an inherited mutation on the *Fragile X Mental Retardation-1* (*FMR1*) gene on the X chromosome (Brown, 2002). Individuals with fragile X syndrome, or the "full mutation" have an expansion of greater than 200 CGG nucleotide repetitions on *FMR1*, which causes methylation and reduced production of Fragile X Mental Retardation Protein (FMRP), a protein essential for cognitive functioning (Oostra & Willemsen, 2003). While it was once thought that the clinical impact of fragile X was isolated to individuals with the full mutation, it is now clear that fragile X is very much a family condition, with clinical consequences also seen in a subgroup of persons with premutation alleles on *FMR1*.

The *FMR1* premutation is characterized by a moderate expansion of 55-200 CGG repeats and has molecular-genetic consequences that are unique from the full mutation, such as toxically elevated levels of *FMR1* messenger RNA (Tassone et al., 2000). Individuals with the *FMR1* premutation were once considered to be "silent carriers" whose primary clinical concern was the risk of passing the unstable genetic mutation to their offspring. However, it is now known that the *FMR1* premutation is associated with its own phenotypic signature, which includes psychological vulnerability (Bailey, Raspa, Olmsted, & Holiday, 2008; Roberts et al., 2009), executive deficits (Cornish, Manly, James, Mills, & Hillis, 2003), social difficulties (Franke, Leboyer, Gansicke, & Weiffenbacj, 1998; Johnston et al., 2001), risk for autism spectrum disorder (Farzin et al., 2006; Goodlin-Jones, Tassone, Gane, & Hagerman, 2004), and physical health complications such as fragile X-associated premature ovarian insufficiency and fragile X-associated tremor ataxia syndrome (Allingham-Hawkins et al., 1999; Berry-Kravis et al., 2007).

Notably, as many as 1 in 151 women in the United States are affected by the *FMR1* premutation (Seltzer, Baker, et al., 2012). Given its high prevalence and emerging clinical phenotype, it is a public health priority to better define the consequences of the *FMR1* premutation, including the potential impact on family outcomes. Families of children with fragile X syndrome are particularly vulnerable for poor outcomes, due to the combined risks related to the child's genetic status, the genetic status of the parent with the *FMR1* premutation (if they are not affected by the full mutation themselves), and the added environmental stressors associated with the clinical manifestation of both conditions. Better understanding of how parental risk associated with premutation status influences the outcomes of children with fragile X syndrome is essential for the development of intervention protocols that target the specific needs of parent-child dyads. This study aimed to determine how the language outcomes of children with fragile X syndrome may be influenced by pragmatic language difficulties seen in mothers who have the *FMR1* premutation.

Pragmatic Language Phenotype of the *FMR1* Premutation

Although the behavioral phenotype of the *FMR1* premutation is not yet well-defined, a growing body of research supports elevated social difficulties in this group, such as social-cognitive weaknesses (Cornish et al., 2005), shyness and interpersonal difficulties (Franke et al., 1998; Johnston et al., 2001), and elevated rates of autism spectrum disorder and the broad autism phenotype (Farzin et al., 2006; Goodlin-Jones et al., 2004; Losh, Klusek, et al., 2012). Consistent with these features, recent evidence suggests that women with the *FMR1* premutation struggle with social aspects of language use, or pragmatic language. A well-controlled study by Losh et al. (2012) used direct, blind coding of conversational samples to evaluate the pragmatic language skills of 49 women with the *FMR1* premutation relative to age-matched control women with no known genetic or neurodevelopmental diagnosis. Results indicated that more pragmatic violations were observed in the conversation of the women with the *FMR1* premutation than that of the control women, including perseverating on topics, providing too many details, or failing to provide background information. Factor analysis indicated that the pragmatic language violations exhibited by the women could be captured under the subdomains of "dominating" style, associated with conversational dominance, and "withdrawn" style, associated with unengaged, standoff-ish conversational features (Losh, Klusek, et al., 2012). Few other studies have examined pragmatic language skills in the *FMR1* premutation. One report by Simon, Keenan, Pennington, Taylor, & Hagerman (2001) found that women with the *FMR1* premutation (*n* = 25) did not show any impairments in component discourse processing skills, although other reports do support broader language deficits in this group, such as impaired language formulation (Sterling, Mailick, Greenberg, Warren, & Brady, 2013). In contrast to the scarcity of evidence in the *FMR1* premutation, pragmatic language deficits are well-documented in the fragile X full mutation (Abbeduto et al., 2006; Klusek, Martin, & Losh, 2014; Losh, Martin, Klusek, Hogan-Brown, & Sideris, 2012; Martin et al., 2012; Roberts et al., 2007) and are associated with *FMR1*-related variation (i.e., CGG repeat length and percent methylation; Losh, Martin, et al., 2012).

Maternal Communication Style and the Language Development of Children

There is considerable evidence showing that maternal communication style and content is a salient predictor of child language outcomes. For example, children whose mothers display highly responsive behaviors during communicative interactions, such as responding contingently to child initiations or asking questions to maintain the child's focus, have a language advantage compared to their peers with less responsive mothers (Baumwell, Tamis-LeMonda, & Bornstein, 1997; Landry, Smith, & Swank, 2006; Tamis-LeMonda, Bornstein, & Baumwell, 2001). This effect generalizes to families of children with developmental disorders (McDuffie & Yoder, 2010; Siller & Sigman, 2002, 2008; Yoder, Burack, Benedetto, & Frye, 1998). Warren et al. (2010) examined the impact of maternal responsivity on the later communication outcomes of young children with fragile X syndrome. Maternal responsivity was measured from mother-child interactions embedded in daily routines in the home, and defined by the mother's use of specific communicative behaviors, such as requests for verbal complies, comments and interpretations of the child's communication act. Early maternal responsivity was predictive of children's rate of total communication, number of different words used in a conversational sample, and performance on standardized receptive and expressive language measures at a 3-year follow-up, even after controlling for the severity of the child's symptoms of autism spectrum disorder (Warren, Brady, Sterling, Fleming, & Marquis, 2010). Similar findings were reported by Wheeler et al. (2007), who found that higher rates of maternal maintaining and scaffolding behaviors related to increased receptive language skills in young children with fragile X syndrome. Thus, maternal communication patterns have a significant influence on the language development of children with typical and atypical development, including fragile X syndrome.

Mechanistically, maternal responsivity has been reported to be negatively affected by elevated maternal stress and anxiety (Essex, Klein, Cho, & Kalin, 2002) which may potentially be rooted in atypical responsivity or modulation of stress and anxiety. In fragile X, mothers of children with the full mutation display abnormal regulation of the hypothalamic-pituitary-adrenal (HPA) axis with atypical cortisol regulation associated with maternal responsivity (Robinson, McQuillin, Brady, Warren, & Roberts, in press) and elevated child problem behavior (Hartley et al., 2012). Mothers with the *FMR1* premutation also show heightened rates of mood and anxiety disorders (Bourgeois et al., 2011; Roberts et al., 2009), which have been shown to negatively impact mother-child engagement (Wheeler et al., 2007). Importantly, maternal communicative behaviors are an aspect of the child's environment that is modifiable; intervention strategies aimed at shaping the communication patterns of mothers are successful in promoting long-term language gains in children with developmental disabilities (Mahoney & Perales, 2005; Yoder & Warren, 2001a, 2001b).

Although the importance of maternal communicative behaviors for the language development of children has been established, existing literature has focused on maternal communicative features occurring exclusively during mother-child interactions. The present study addresses the impact of broader communication patterns, such as those exhibited during adult-adult interactions, including the pragmatic language weaknesses that are exhibited by a subset of women as part of the *FMR1* premutation phenotype. Studies aimed at understanding the impact of the *FMR1* premutation phenotype on child outcomes can shed light on environmental factors that can account for phenotypic variability in fragile X and inform treatment. Often the primary caregivers, mothers are a main determinant of the type of language that young children are exposed to during daily routines. The influence of mothers may be amplified in fragile X syndrome, where social and intellectual impairments often limit the child's participation in the community and mothers may continue to serve as the child's primary communication model well into adulthood. Pragmatic language difficulties associated with the *FMR1* premutation may increase risk for poor child language outcomes, as mothers who struggle with adhering to the conventions of social-conversation may provide a communication environment that fails to support the heightened language-learning needs of children with fragile X syndrome. Thus, pragmatic language impairments in the *FMR1* premutation may place children with fragile X syndrome at a “double vulnerability” associated with their own genetic predisposition coupled with a suboptimal learning environment, highlighting the complexity and importance of the consideration of multiple factors affecting child language.

The Present Study

Our main objective was to determine the relationship between pragmatic language impairments in mothers with the *FMR1* premutation and the language skills of their children with fragile X syndrome. Given emerging evidence from family studies of autism spectrum disorder showing differential relationships between maternal performance on specific pragmatic subdomains and child communication impairments (Klusek, Losh, & Martin, 2014), we sought to determine whether child language acquisition would be differentially related to maternal pragmatic difficulties of the “dominating” and “withdrawn” subtypes. We focused on the child outcomes of vocabulary, syntax, and reading as core language-related domains that are impaired in individuals with fragile X syndrome (i.e., Abbeduto, Brady, & Kover, 2007). Given the lack of prior research in this area, it was unclear whether maternal pragmatics would differentially relate to certain domains of child language and, therefore, we chose to explore potential relationships across several different domains of language; no hypotheses were made regarding specific relationships with select language domains. The focus of prior work has been on relationships in early childhood, with emerging evidence that maternal responsivity has cumulative effects on the language development of children with fragile X into middle childhood (Brady, Warren, Fleming, Keller, & Sterling, 2014). Given that knowledge of the fragile X phenotype and its correlates in adolescence and early adulthood is limited, we were particularly interested in maternal influences on the language outcomes of adolescent and young adult-aged “children.” Determining the interplay between the pragmatic language phenotype of the *FMR1* premutation and child outcomes has implications for a) contributing to knowledge of the *FMR1* premutation phenotype and its potential functional consequences at the family level and b) identifying modifiable aspects of the child's language-learning environment that may promote targeted treatments that meet the specific needs of families affected by fragile X. Our research questions were:

1. Do pragmatic language difficulties in mothers with the *FMR1* premutation predict concurrent language skills of their adolescent/young adult-aged children with fragile X syndrome?

2. Is child language level specifically related to select pragmatic language subdomains ("dominating" or "withdrawn" pragmatic language profiles)?

Methods

Participants

Participants were 27 mothers with the *FMR1* premutation and their adolescent/young adult sons with fragile X syndrome (mean age = 17.98 years, range = 15.00-23.83). The sons were participating in a large, cross-site longitudinal study of language development in young adult males with fragile X syndrome (PI: Abbeduto). Mothers were participating in a related study on communication profiles in the *FMR1* premutation (PI: Klusek) and were recruited through their sons. Descriptive and demographic information for the mothers is presented in Table 1 and Table 2 presents descriptive information on the children. All participants were native speakers of English and the inclusionary criteria for the broader study required that all the children with fragile X syndrome were able to speak in a minimum of 2-3 word phrases (according to parent report). *FMR1* premutation status of the mothers (55-200 CGG repeats) was confirmed via blood tests and medical records were obtained to confirm the full mutation in the son with fragile X syndrome. Families were recruited from Eastern and Midwestern regions of the United States through the South Carolina Department of Disabilities, Greenwood Genetics, the Research Participant Registry Core of the Carolina Institute for Developmental Disabilities, and social media. The majority of families (82%) were Caucasian.

Procedure

Participant assessments took place in a University laboratory setting within the context of a broader research protocol that spanned two days. Maternal and child data were collected concurrently. Participant consent was obtained as approved by the Institutional Review Board of the University of South Carolina.

Measures

Maternal Pragmatic Language Skills. Maternal pragmatic language skills were directly assessed from a 20-minute conversational sample in which participants conversed with an interviewer about their "life history." Interviewers followed a series of standard probe questions designed to elicit conversation on neutral, easily-discussed topics, such as "What activities did you enjoy most as a child?" and "Did you participate in any extra-curricular activities in high school?". To ensure ample opportunities for conversational exchange, interviewers were trained to comment, offer information, and ask follow-up questions along with administering the probe questions. Pragmatic language violations were rated from videotape using a modified version of the Pragmatic Rating Scale (Landa et al., 1992), which has been described previously (see Klusek, Losh, et al., 2014; Losh, Klusek, et al., 2012). The Pragmatic Rating Scale was originally developed as a tool for capturing subclinical pragmatic language difficulties in unaffected relatives of children with autism spectrum disorder, and has proven sensitive to variation in pragmatic language abilities among women with the *FMR1* premutation (Losh, Klusek, et al., 2012). The scale consists of 26 items representing potential pragmatic language violations, which are scored on a 3-point scale denoting whether each violation was mild ("1"), striking and present ("2"), or absent ("0"), based on operationally defined definitions. Example items capture the form and content of the message, such as "fails to provide background information," "pedantic," as well as suprasegmental features such as "too loud," "interrupts," and "unusual intonation." A total pragmatic language score, consisting of the tally of all items, was computed, as well as two factor-based subdomain scores: (a) Dominating style, which is composed of items associated with conversational dominance, such as "overly frank," "topic perseveration," "tangential," and "overly detailed" and (b) Withdrawn style, which captures the failure to actively engage in a way that meets the expectations of the conversational turn and consists of items such as “fails to reciprocate,” “vague,” and “overly terse.” These factor-based subscales have been used in prior investigations of pragmatic language in adults with the *FMR1* premutation and the broad autism phenotype, and mothers’ performance on these subscales has been shown to differentially relate to child outcomes in family studies of autism spectrum disorder (Klusek, Losh, et al., 2014). Two trained independent judges coded each sample and final consensus scores were produced via discussion. Prior to consensus, intra-class correlations were computed to determine average inter-rater reliability (ICC [3, 2]): Total Score: 0.69; Dominating subscale: 0.92; Withdrawn subscale: 0.63.

Child Vocabulary Skills. Receptive and expressive vocabulary scores were measured with the Peabody Picture Vocabulary Test-4 (PPVT-4; Dunn & Dunn, 2007) and the Expressive Vocabulary Test-2 (EVT-2; Williams, 2007). Growth scale value (GSV) scores were used, as they provide an estimate of absolute performance on an equal-interval scale (unlike raw or age-equivalent scores, which are not equal-interval) and are less susceptible to floor effects than are standard scores.

Child Syntactic Skills. Receptive syntax was measured with the Test for Reception of Grammar-2 (TROG-2; Bishop, 2003), which requires participants to select a picture that best corresponds to a spoken prompt representing a series of grammatical contrast. Expressive syntax was assessed with the Syntax Construction subtest of the Comprehensive Assessment of Spoken Language (CASL; Carrow-Woolfolk, 1999), which uses a series of pictures and verbal prompts to elicit specific syntactic forms from the participant. Due to floor effects observed in the standard and age-equivalent scores, raw scores were used for these assessments, which is consistent with prior studies using these measures in fragile X samples (McDuffie, Kover, Abbeduto, Lewis, & Brown, 2012).

Child Word Reading Ability. The Word Identification subtest of the Woodcock Johnson Reading Mastery Tests-III (Woodcock, 2011) was used as an index of word reading ability. This subtest assesses oral reading skills of individual words of increasing difficulty. GSV scores were the unit of analysis.

Data Analysis

A series of multiple linear regressions were conducted to test maternal pragmatic language skills as a predictor of each of the child outcomes. Each model was conducted in two levels where maternal education was first entered as a covariate, given the well-documented relationship between maternal education level and children's language development (Campbell et al., 2003; Dollaghan et al., 1999). The maternal pragmatic predictor(s) were entered in the second level to examine variance explained above and beyond maternal education level. Two sets of models were completed for each child outcome, the first examining overall maternal pragmatic language skills as a predictor and the second examining the relative contributions of dominating and withdrawn pragmatic subdomains on the child outcome. Cohen's f^2 local effect sizes were computed, which allow the effect size of a single variable within a multivariate model to be estimated. Cohen (1988, 1992) suggests that an f^2 value of "0.02" denotes a small effect, "0.15" a medium effect, and "0.35" or greater a large effect. Because *p*-values are not a reliable indicator of the magnitude of an effect (e.g., Cohen, 1994), effect sizes are presented as an index of the "practical" significance of an effect, even in the absence of statistical significance (Nakagawa & Foster, 2004). We felt that reporting of effect sizes was particularly appropriate given that power calculations for inferential statistics of the larger study were motivated by a different set of questions and assumptions than of interest in this study.

Results

Relationship between Maternal Pragmatic Language Difficulties and Child Vocabulary Skills

Receptive Vocabulary. The combined effect of maternal education level and pragmatic language ability did not significantly predict the expressive vocabulary skills of the children with fragile X syndrome, although a trend was observed in the data (F [2, 25] = 2.98, p = .069), with 19% of the variance explained by these variables. There was a trend for maternal pragmatic language skills to predict unique variance beyond maternal education level (ΔR^2= 0.12, p = .068), with each unit increase in the pragmatic language difficulties corresponding to a .36-unit decrease in receptive vocabulary scores. Cohen's f^2 effect size was estimated at 0.15 for receptive vocabulary, which is consistent with a medium effect (Cohen, 1992). A second regression model tested the relative contributions of the dominating and withdrawn pragmatic subdomains on child receptive vocabulary, controlling for maternal education level. The overall model was significant (F [3, 24] = 3.17, p = .043) and maternal dominating and withdrawn pragmatic features accounted for significant unique variance in child receptive vocabulary, beyond maternal education (ΔR^2 = 0.21, p = .046), with 28% of the variance explained by these variables. Examination of the regression coefficients showed that dominating pragmatic features significantly predicted decreased vocabulary scores (Beta = -0.41, p = .034). There was also a trend for withdrawn pragmatic features to predict lower receptive vocabulary skills (Beta = -0.36, p = .059). Cohen's f^2 effect sizes were estimated at 0.21 for dominating and at 0.23 for withdrawn pragmatic style, which are consistent with an effect of medium magnitude (Cohen, 1992). Regression coefficients are presented in Tables 3 and 4.

Expressive Vocabulary. The combined influence of maternal education level and pragmatic language skill on child expressive vocabulary level was not statistically significant, F (2, 25) = 2.01, p = .154, with 14% of the variance explained. Cohen's f^2 effect size was estimated at 0.15 for maternal pragmatic language which is consistent with a medium effect size (Cohen, 1992). The second model testing the relative influences of dominating and withdrawn pragmatic subdomains was also non-significant, F (5, 24) = 2.07, p = .131, with 21% of the variance explained. Cohen's f^2 effect sizes were estimated at 0.15 for dominating and at 0.017 for withdrawn pragmatic style, which are consistent with medium effects (Cohen, 1992). Regression coefficients for the expressive vocabulary models are presented in Tables 3 and 4.

Relationship between Maternal Pragmatic Language Difficulties and Child Syntax Skills

Receptive Syntax. Overall maternal pragmatic language skill was not a significant predictor of child receptive syntax after accounting for maternal education level, F (2, 24) = 1.96, p = .103. Cohen's f^2 effect size was estimated at 0.04 indicating little effect of this variable; the overall model accounted for 14% of the variance. The regression testing the relative contributions of the dominating and withdrawn pragmatic subdomains, after accounting for maternal education level, showed a trend, F (3, 23) = 2.37, p = .097, with 24% of the variance accounted for. Examination of the regression coefficients suggested that this trend was driven by withdrawn pragmatic style (Beta = -0.38, p = .058); Cohen's f^2 effect size was estimated at 0.17 for withdrawn pragmatic style, which is consistent with a medium effect (Cohen, 1992).

Expressive Syntax. The maternal pragmatic language total score was not a significant predictor of child expressive syntax after accounting for maternal education level, F (2, 24) = 1.75, p = .196, with these variables accounting for 13% of the variance. Cohen's f^2 effect size was estimated at 0.08 indicating a small effect of maternal pragmatics on expressive language. However, the model testing the relative contributions of the dominating and withdrawn pragmatic was significant (F [3, 23] = 3.11, p = .046), with the pragmatic subdomains accounting for significant unique variance in child expressive syntax beyond maternal education (ΔR^2 = 0.23, p = .041) and the overall model accounting for 29% of the variance. The effect was driven by the impact of withdrawn pragmatic style, which was significantly associated with decreased expressive syntax scores (Beta = -0.51, p = .012), with a medium Cohen's f^2 effect size estimated at 0.32. Regression coefficients are presented in Tables 5 and 6.

Relationship between Maternal Pragmatic Language Difficulties and Child Word Reading Skills

A trend was detected for the combined effects of maternal education level and pragmatic language ability to predict the word identification skills of the children with fragile X syndrome (F [2, 24] = 3.26, p = .056, R^2 = 0.21), with pragmatic language skills accounting for significant unique variance beyond the effect of education level (ΔR^2 = 0.21, p = .018), with each unit increase in pragmatic language difficulties corresponding to a 0.48-unit decrease in child word identification scores. Cohen's f^2 effect size was estimated at 0.27 for the impact of pragmatic language in the model, which is consistent with a medium effect (Cohen, 1992). The second model testing the relative contributions of the pragmatic subdomains was not significant (F [3, 23] = 2.19, p = .117), although examination of the regression coefficients showed a moderate effect of dominating pragmatic language violations on child word identification skills (f^2 = .24), with a small effect of withdrawn pragmatic difficulties. Regression coefficients are presented in Tables 7 and 8.

Discussion

Fragile X is an inherited disorder associated with clinical consequences not only for family members affected by full mutation fragile X syndrome, but also for those with the *FMR1* premutation. Given the familial nature of the disorder, children with fragile X syndrome are particularly vulnerable for poor outcomes in that the child's own biological risk for developmental delay is compounded by environmental risk factors related to the genetic susceptibility of carrier parents, who likely have the *FMR1* premutation themselves or potentially the full mutation. This study examined composite and subdomain levels of pragmatic language difficulties in mothers with the *FMR1* premutation as factors that might hinder language development in children with fragile X syndrome. Findings showed a significant association between maternal pragmatic language difficulties and the language abilities of their children, with child receptive language level negatively influenced by both dominating and withdrawn maternal pragmatic language styles, whereas child expressive syntax ability was specifically linked with withdrawn maternal pragmatic language features. A number of trends with medium effect size estimates were also detected; namely, relationships between maternal pragmatic language features and child skills in the domains of receptive syntax and word identification. These findings help delineate the multifaceted environment in which children with fragile X syndrome learn language and suggest that family-centered intervention practices may be particularly important for this group.

Although accumulating evidence shows that the *FMR1* premutation is associated with its own phenotypic signature, little is known about the impact of this phenotype on family outcomes. Recently, elevated pragmatic language violations have been documented among women with the *FMR1* premutation, which are thought to be linked to variation on the *FMR1* gene (Losh et al., 2012). The results of the present study show that maternal pragmatic language impairments can have a broad impact on the language proficiency of children with fragile X syndrome, accounting for significant variance in receptive vocabulary and expressive syntax, and with trends in the data suggesting impacts on word reading and receptive syntax ability as well. Detected effects were medium in size and persisted after controlling for maternal education level. These findings highlight the many layers of vulnerability faced by children with fragile X syndrome. A diathesis-stress model has been proposed to explain risk in genetic conditions, where a diathesis, or genetic vulnerability, is coupled with environmental risk to increase the likelihood of disordered behavior (Rende & Plomin, 1992). This model is particularly relevant to understanding risk in fragile X syndrome, where the child's own genetic status predisposes for language involvement. Likewise, the language learning environments of children with developmental delays, such as fragile X, can be less than optimal, as the child's own phenotype can disrupt the normal learning environment. For instance, reduced responsiveness exhibited by children with developmental delays can restrict the dynamic interaction between communication partners that is crucial for language development (Hauser-Cram et al., 2001; Slonims & McConachie, 2006; Van IJzendoorn et al., 2007). This study suggests that risk for suboptimal language outcomes in fragile X syndrome is further compounded by differences in the communication environment related to the genetic vulnerability of family members.

Although the most likely direction of influence is from parent to child, the cross-sectional design of the study makes it difficult to identify causal relationships with certainty. Evidence from longitudinal studies suggests that maternal interaction styles do have causal impacts the language outcomes of children with fragile X syndrome (Brady et al., 2014; Warren et al., 2010), and we would assume the same direction of relationships holds here. However, in the study of mother-child interactions, it is also understood that maternal behaviors do not function independently of child behaviors; communication is bi-directional, with both partners capable of enhancing or disrupting the interaction (Kelly & Barnard, 2000). According to the transactional model of development, these reciprocal, bi-directional effects accumulate over time and have a long-term impact on the development of the child, including language outcomes (Sameroff & Fiese, 2000). Yet, the present study examined maternal communication patterns during conversation with another adult when the child was not present. It seems unlikely that the maternal pragmatic difficulties observed in this context would have been caused by the communicative behaviors of their child. Longitudinal research or intervention studies aimed at shaping maternal pragmatic behaviors could provide more definitive answers about these cause and effect relationships.

Prior research aimed at determining the impact of mothers' speech on the language acquisition of children has focused almost exclusively on the language used by mothers during interaction with their children. This study extends this work by demonstrating that maternal conversational patterns in general, as indexed during conversation with another adult, are related to child language outcomes. Moreover, this study examined maternal influences on the development of adolescent or young-adult aged “children,” which is a developmental period that has been largely ignored in developmental disabilities research. The importance of maternal communicative styles during early childhood has been well documented (e.g., Warren et al., 2010) and recent evidence shows that the quality and consistency of maternal responsivity predicts language development in fragile X syndrome at least until 9 years of age (Brady et al., 2014). In the present study, we have demonstrated that the maternal communication behaviors continue to influence the language acquisition of children into early adulthood. The continued influence of mothers past early developmental periods is somewhat unexpected, although maternal influences may be particularly salient for individuals with fragile X syndrome. Individuals with fragile X show reduced reciprocal interactions with peers during childhood and adolescence (McDuffie et al., 2010) and in adulthood are unlikely to develop substantial friendships, hold a full time job, or live independent of their parents (Hartley et al., 2011). Thus, the influence of mothers may be amplified in fragile X syndrome, as mothers may serve as the child’s primary communication model throughout childhood and well into adulthood. This finding has implications for continued speech and language services into adolescence and early adulthood, a transition period commonly marked by the termination of speech-and-language and other services for individuals with developmental disabilities (Shattuck, Wagner, Narendorf, Sterzing, & Hensley, 2011). In addition, these findings suggest that family-centered approaches that address the familial nature of fragile X and its potential influences on the child’s learning environmental may maximize treatment gains for this population. For instance, interventions that maximize family involvement through strategies such as embedding interaction in the family’s natural environment, supporting parents emotionally, and shaping the communication patterns of parents are evidence-based approaches that may be particularly relevant for families of children with fragile X syndrome.

A remaining question is the relative contribution of biological and environmental factors to explain the detected mother-child relationships. On the one hand, language and reading show modest heritability, with genetic factors accounting for one-third to one-half of the variability in language ability in non-disordered populations (Stromswold, 2001). Thus, it is possible that the mother-child associations detected here reflect genetically-based within-family aptitude for language. Along these lines, pragmatic language difficulties in individuals with the *FMR1* premutation are thought to be linked to variation on the *FMR1* locus (Losh, Klusek, et al., 2012) and impairments in this domain are directly linked with CGG repeat length and percent methylation in the fragile X full mutation (Losh, Martin, et al., 2012). It is reasonable to believe that other aspects of the fragile X language phenotype may be associated with *FMR1*-related variation, although few studies have explored these relationships.

On the other hand, there is abundant evidence supporting maternal input as a feature of the child's environment that can support or hinder the language acquisition (see Hoff, 2006, for a review). Pragmatic language difficulties in mothers may affect child development in two ways: first by impacting the language model to which children are exposed, and second by directly impacting the quality of mother-child communicative interactions. Theories of language acquisition suggest that both of these aspects are essential for language development (Hoff, 2006). Children whose mothers struggle with pragmatic aspects of language are likely exposed to ineffective communication models when observing their mothers engage in daily communicative interactions with other adults. Moreover, it is probable that the pragmatic language features mothers' exhibit during conversation with other adults "spill over" into their interactions with children as well, potentially having a direct impact on the quality of the communicative interactions between the mother and child. Whether of biological or environmental origins, this study demonstrates that the presence of pragmatic language impairments in mothers places children with fragile X syndrome at heightened risk for language involvement. Gene-by-environment studies have been useful in understanding the presentation of other fragile X-related phenotypes, such as evidence showing that the interaction between genetic factors (activation ratio) and stress related to child behaviors impairs the physiological stress responses in mothers with the *FMR1* premutation (Seltzer, Barker, et al., 2012), which, in turn, can negatively impact the quality of maternal behaviors during mother-child interactions (Robinson et al., in press). Future studies investigating gene-by-environment interactions in the presentation of maternal pragmatic language difficulties and associated consequences for child language will be useful in understanding the influences on language acquisition in fragile X syndrome that may be amenable to intervention.

Both dominating and withdrawn maternal pragmatic language subdomains were significantly associated with decreased receptive vocabulary skills in children with fragile X syndrome, and the model testing overall pragmatic language features showed a trend in the same direction. This suggests that low-quality maternal conversational styles, either marked by dominating or withdrawn pragmatic language violations, negatively impact the receptive vocabulary development of their children. This finding is consistent with a large body of research showing that children learn to talk through linguistic interaction with adults and the quality of incoming speech influences children's language learning (Conti-Ramsden, 1990; Hoff, 2006; Hoff & Naigles, 2002; Huttenlocher, Haight, Bryk, Seltzer, & Lyons, 1991). Associations with child expressive vocabulary were similar in their direction, magnitude, and pattern of relationships, but did not reach statistical significance. The medium effect sizes detected in the expressive vocabulary models support the presence of a moderate association between maternal pragmatic features and child expressive vocabulary. Future research including larger samples can clarify whether this null finding regarding expressive vocabulary was related to lack of statistical power, or alternatively, dyadic relationships may be specific to the receptive domain of vocabulary.

Child expressive syntactic ability was uniquely associated with withdrawn maternal pragmatic language difficulties, and was not significantly associated with dominating or overall maternal pragmatic language features. A trend-level association was also detected between withdrawn maternal pragmatic language violations and the child's receptive syntax ability, suggesting that a similar relationship may exist across receptive and expressive domains that we may have been underpowered to detect. Withdrawn pragmatic language violations are characterized by reduced active participation in the conversational back-and-forth, such as by giving short, terse responses or by failing to follow-up on the conversational partner's leads. Studies of typical development have shown that children achieve higher syntactic proficiency when mothers model syntactically rich structures and engage the child in linguistic interaction

(Hoff-Ginsberg, 1990). The non-elaborative, disengaged conversational style of mothers who exhibited withdrawn pragmatic language features may spill over into interactions with their child, hindering syntactic development. For instance, mothers with withdrawn pragmatic language features failed to follow-up on the conversational bids of their communicative partner when conversing with another adult; these mothers may also be less likely to expand and extend on their child's utterances, which is a feature linked with increased child language production (Barnes, Gutfreund, Satterly, & Wells, 1983; McDuffie & Yoder, 2010; Nelson, 1973). Likewise, mothers who exhibited terse, non-elaborative conversational turns during conversation with another adult might also tend to use short utterances with their children, thereby failing to model complex, multi-clause sentences that have been show to facilitate syntactic growth in children (Huttenlocher, Vasilyeva, Cymerman, & Levine, 2002).

Clinically, the results of this study underscore the importance of family-centered practices for this group. Interventions focused exclusively on modifying the child's behavior, without addressing the familial nature of fragile X and its potential influences on the child's learning environmental, may not be optimally effective for this population. Fortunately, a number of scientifically-based treatments have proven successful at promoting language acquisition in children with developmental disabilities through family-centered tactics such as shaping the communication patterns of parents, embedding interaction in the family's natural environment, supporting parents emotionally, and promoting engagement of the entire family (i.e., Brady, Warren, & Sterling, 2009; Carter et al., 2011; Mahoney & Perales, 2005; Rogers et al., 2012; Yoder & Warren, 2001b). In general, a family-centered approach should always be considered when working with families affected by fragile X syndrome, as the multi-generational, transactional nature of the condition can have a broad impact on family functioning. For instance, mothers with the *FMR1* premutation are also at elevated risk for mood and anxiety disorders (Bourgeois et al., 2011; Roberts et al., 2009) that have been shown to negatively impact mother-child engagement (Wheeler et al., 2007) and can aggravate problem behaviors exhibited by the child (Hessl et al., 2001). Likewise, aspects of the child's phenotype, such as the severity of problem behaviors, can aggravate maternal symptoms of depression and anxiety (Bailey, Sideris, Roberts, & Hatton, 2008; Seltzer, Barker, et al., 2012). Family-centered services are critical for fragile X because the family experience is heavily influenced by complex transactions between biological predisposition and environmental influence within and between family members and across multiple domains. Service providers should be aware of the wide range of developmental, psychiatric, neurological, and reproductive concerns posed by fragile X and be prepared to refer families for services as appropriate.

This study has certain strengths and limitations. Strengths include the detailed, direct-assessment method used to characterize maternal pragmatic language impairments and a focus on adolescent/young adult-aged individuals with fragile X. Another strength is the use of statistical models that allowed maternal education, a maternal factor broadly linked with child language and literacy development, to be accounted for, which builds on prior correlational evidence suggesting a relationship between maternal pragmatics and child communication outcomes in other clinical groups (i.e., Klusek, Losh, et al., 2014). This study was limited by a relatively small sample that may have reduced statistical power, although the medium effect sizes detected allow for confidence in the strength of the detected identified relationships in the face of trend-level *p*-values. Another limitation of the study is the possible unrepresentative sample, which consisted of families who were primarily Caucasian and had a high annual income. It is unclear to what extent findings may generalize to more diverse groups. As discussed above, we also recognize that while the direction of influence is most likely to be from parent to child, it is difficult to make conclusions regarding causal direction given the concurrent correlational design of the study.

There are a number of future directions of this work, including the examination of these relationships longitudinally in earlier childhood, which would answer questions regarding direction of causation, possible bidirectional mother-child transactional relationships, and how effects may accumulate across time, as well as help identify critical developmental periods that may be most prime for intervention. Determining the impact of maternal pragmatic language profiles on mother-child interaction patterns, such as maternal responsivity, may also be informative in understanding how phenotypes related to the *FMR1* premutation may directly influence family interactions. It may also be fruitful to explore potential impacts on other child language domains not addressed here, such as pragmatic language.

Looking beyond impact at the family level, it will also be important for future research to address the potential consequences of pragmatic language difficulties at the level of the individual, as these features may affect the quality of life and level of social support, for example. Although pragmatic language difficulties associated with the *FMR1* premutation are generally assumed to represent mild, subclinical features, the clinical impact of these features has not been studied empirically. The results of this study demonstrate that these features, although subtle in nature, do have a clinical impact at the family level. Whether these features also have consequences at the individual level is unknown. Finally, research focused on determining the biological and cognitive underpinnings of pragmatic language impairments in the *FMR1* premutation will be useful in tailoring prevention or treatment efforts for the family as a whole. In particular, future investigations of psychological vulnerability as a potential cause of pragmatic language difficulties in the *FMR1* premutation may be informative, given that mood and anxiety disorders occur at elevated rates among women with the *FMR1* premutation and have been shown to impact the quality of mother-child interactions (Wheeler et al., 2007). Future work aimed at determining the impact of maternal pragmatic language behaviors and their mechanisms will be important for identifying family-centered prevention and intervention practices that meet the specific needs of families affected by fragile X-associated conditions.

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Table 1

Maternal Demographics and Descriptives

Variable	Group Values
Age in years	
M (SD)	46.50 (6.86)
Range	29.90-59.80
Full Scale IQ	
M (SD)	107.61 (11.37)
Range	85.00-130.00
Household Income	
<20k	3.6%
21-40k	14.3%
41-60k	3.6%
61-80k	17.9%
81-10k	7.1%
>101k	53.6%
Maternal Education	
High School/GED	42.9%
Associates degree	10.7%
Bachelor's degree	21.4%
Master's degree	21.4%
Professional degree	3.6%

Note. Maternal IQ measured with the Kaufman Brief Intelligence Test-2 (Kaufman & Kaufman, 1990).

Table 2

Child Characteristics

	Characteristic							
	Age in years	Full Scale IQ[1]	Autism Symptom Severity[2]	Receptive Vocabulary Age[3]	Expressive Vocabulary Age[4]	Receptive Syntax Age[5]	Expressive Syntax Age[6]	Word Identification Age[7]
M (SD)	17.98 (2.45)	39.26 (5.62)	6.00 (2.26)	6.89 (3.14)	6.26 (2.80)	4.19 (0.46)	4.07 (1.90)	6.70 (1.02)
Range	15.00-23.83	36.00-56.00	2.00-10.00	2.00-14.67	2.00-13.92	4.00-5.92	2.08-8.42	6.17-11.33

Note. Measured with the Brief IQ Scale of the Leiter International Performance Scale-Revised (Roid & Miller, 1997). [2]Indexed with the Comparison Score of the ADOS-2 (Lord et al., 2012). Scores ≥3 are consistent with a diagnosis of ASD (scores within the range of 3-4 indicate low level of ASD-related symptoms, 5-7 a moderate level, and 8-10 a high level). [3]Indexed with the Peabody Picture Vocabulary Test-4 (Dunn & Dunn, 2007). [4]Indexed with the Expressive Vocabulary Test-2 (Williams, 2007). [5]Indexed with the Test for Reception of Grammar-2 (Bishop, 2003). [6]Indexed with the Syntax Construction subtest of the Comprehensive Assessment of Spoken Language (Carrow-Woolfolk, 1999). [7]Indexed with the Word Identification subtest of the Woodcock Johnson Reading Mastery Tests-III (Woodcocks, 2011).

Table 3

Regression Coefficients Depicting Maternal Pragmatic Language as a Predictor of Child Vocabulary Skill

	Child Receptive Vocabulary					*Child Expressive Vocabulary*				
Effect	*B (SE)*	*t*	*p*	f^2	R^2	*B (SE)*	*t*	*p*	f^2	R^2
Step 1										
Intercept	204.77 (44.54)	4.60	.001*		.08	156.64 (32.52)	4.82	.001*		.01
Maternal Edu.	-4.25 (2.93)	-1.45	.159			-1.05 (2.14)	-0.49	.630		
Step 2										
Intercept	227.38 (44.05)	2.27	.001*			173.36 (39.09)	5.40	.001*		
Maternal Edu.	-2.07 (2.96)	-1.44	.423	.03	.19	0.32 (2.15)	0.15	.883	.01	.14
Pragmatic Skill	-5.14 (2.69)	-2.35	.068†	.15		-3.80 (1.96)	-1.94	.064†	.15	

Note. f^2 = Cohen's f^2 local effect size; values of "0.02" generally represent a small effect, "0.15" a medium effect, and "0.35" or greater a large effect (Cohen, 1988; 1992).

**p* <.05, †*p* < .09

Table 4

Regression Coefficients Depicting Maternal Dominating and Withdrawn Pragmatic Subdomains as Predictors of Child Vocabulary Skill

	Child Receptive Vocabulary					*Child Expressive Vocabulary*				
Effect	*B (SE)*	*t*	*p*	f^2	R^2	*B (SE)*	*t*	*p*	f^2	R^2
Step 1										
Intercept	204.79 (44.54)	4.60	.001*		.08	156.64 (32.52)	4.82	.001*		.01
Maternal Edu.	-4.25 (2.93)	-1.45	.159			-1.05 (2.14)	-0.49	.630		
Step 2										
Intercept	228.89 (41.97)	5.45	.001*		.28	173.91 (31.18)	5.58	.001*		.21
Maternal Edu.	-3.43 (2.71)	-1.26	.218	.03		-0.52 (2.01)	-0.26-	.797	.01	
Dominating Style	-8.35 (3.70)	-2.26	.034*	.21		-5.17 (2.75)	1.88	.072†	.15	
Withdrawn Style	-11.80 (5.94)	-1.99	.059†	.23		-8.98 (4.11)	-2.03	.053†	.17	

Note. f^2 = Cohen's f^2 local effect size; values of "0.02" generally represent a small effect, "0.15" a medium effect, and "0.35" or greater a large effect (Cohen, 1988; 1992).

**p* <.05, †*p* < .09

Table 5

Regression Coefficients Depicting Maternal Pragmatic Language as a Predictor of Child Syntactic Skill

	Child Receptive Syntax					*Child Expressive Syntax*				
Effect	*B (SE)*	*t*	*p*	f^2	R^2	*B (SE)*	*t*	*p*	f^2	R^2
Step 1										
Intercept	53.32 (17.95)	2.98	.006		.10	24.98	2.28	.032*		.06
Maternal Edu.	-2.01 (1.19(	-1.69	.103			-0.91	-1.26	.218		
Step 2										
Intercept	59.52 (18.85)	3.16	.004			29.00 (11.19)	2.58	.016*		
Maternal Edu.	-1.63 (1.24)	-1.32	.201	.07	.14	-0.55 (0.76)	-0.73	.476	.02	.13
Pragmatic Skill	-1.21 (1.17)	-1.03	.314	.04		-0.96 (0.71)	-1.36	.118	.08	

Note. f^2 = Cohen's f^2 local effect size; values of "0.02" generally represent a small effect, "0.15" a medium effect, and "0.35" or greater a large effect (Cohen, 1988; 1992).

**p* <.05, †*p* < .09

Table 6

Regression Coefficients Depicting Maternal Dominating and Withdrawn Pragmatic Subdomains as Predictors of Child Syntactic Skill

	Child Receptive Syntax					*Child Expressive Syntax*				
Effect	*B (SE)*	*t*	*p*	f^2	R^2	*B (SE)*	*t*	*p*	f^2	R^2
Step 1										
Intercept	53.52 (17.95)	2.98	.006*		.10	24.98 (10.97)	2.28	.032*		.06
Maternal Edu.	-2.01 (1.19)	-1.69	.103			-0.91 (0.72)	-1.26	.218		
Step 2										
Intercept	61.45 (17.99)	3.42	.002*		.24	31.27 (10.23)	3.06	.006*		.29
Maternal Edu.	-1.92 (1.14)	-1.68	.107	.12		-0.74 (0.67)	-1.12	.276	.05	
Dominating Style	-0.81 (1.89)	-0.46	.654	.01		-1.06 (0.93)	-1.15	.264	.06	
Withdrawn Style	-4.99 (2.50)	-2.00	.058†	.17		-4.14 (1.53)	-2.71	.012*	.32	

Note. f^2 = Cohen's f^2 local effect size; values of "0.02" generally represent a small effect, "0.15" a medium effect, and "0.35" or greater a large effect (Cohen, 1988; 1992).

**p* <.05, †*p* < .09

Table 7

Regression Coefficients Depicting Maternal Pragmatic Language Features as a Predictor of Child Reading Skill

	Child Word Identification				
Effect	*B (SE)*	*t*	*p*	f^2	R^2
Step 1					
Intercept	380.54 (966.86)	5.69	.001*		.00
Maternal Edu.	0.71 (4.42)	0.16	.875		
Step 2					
Intercept	430.76 (63.69)	6.76	.001*		
Maternal Edu.	3.84 (4.19)	0.92	.369	.03	.21
Pragmatic Skill	-10.08 (3.96)	-2.55	.018*	.27	

Note. f^2 = Cohen's f^2 local effect size; values of "0.02" generally represent a small effect, "0.15" a medium effect, and "0.35" or greater a large effect (Cohen, 1988; 1992).

**p* <.05, †*p* < .09

Table 8

Regression Coefficients Depicting Maternal Dominating and Withdrawn Pragmatic Subdomains as Predictors of Child Syntactic Skill

	Child Word Identification				
Effect	*B (SE)*	*t*	*p*	f^2	R^2
Step 1					
Intercept	380.54 (66.86)	5.69	.001*		.00
Maternal Edu.	0.72 (4.42)	0.16	.875		
Step 2					
Intercept	424.79 (64.09)	6.63	.001*		.22
Maternal Edu.	1.31 (4.08)	0.32	.751	.01	
Dominating Style	-14.95 (6.34)	-2.35	.028*	.24	
Withdrawn Style	-14.87 (8.90)	-1.65	.113	.12	

Note. f^2 = Cohen's f^2 local effect size; values of "0.02" generally represent a small effect, "0.15" a medium effect, and "0.35" or greater a large effect (Cohen, 1988; 1992).

$^*p < .05$, $^{\dagger}p < .09$