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Reduced Eye Contact and Anxiety in Women with the FMR1 Premutation

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Thesis Summary

Appropriate eye contact is an integral part of effective social communication; however, some clinical populations have difficulty making eye contact. In particular, reduced eye contact is a hallmark of fragile X syndrome, a neurodevelopmental disorder associated with intellectual disabilities, autistic behaviors, and ADHD (Tassone et al., 2000; Hatton et al., 2006; Sullivan et al., 2006). Fragile X syndrome is a highly genetic disorder resulting from an expansion mutation on the *Fragile X Mental Retardation-1* (*FMR1*) gene located on the X chromosome. Mothers of children with fragile X syndrome have a shorter version of this expansion known as the *FMR1* premutation and exhibit their own unique phenotype characterized by social difficulties, including problems with social language use (Franke, Leboyer, Gansicke, & Weiffenbacj, 1998; Losh, Klusek et al., 2012) and psychological vulnerability (Roberts et al., 2009). Women with the *FMR1* premutation have elevated rates of social anxiety (Franke et al., 1998; Bourgeois et al., 2011), which have been linked to eye contact avoidance in other populations (Schneier, Rodebaugh, Blanco, Lewin, & Liebowitz, 2011), suggesting women with the *FMR1* premutation may exhibit reduced eye contact during social interactions. While several studies have suggested women with *FMR1* premutation have reduced eye contact (Tassone et al., 2000; Losh, Klusek et al., 2012; Riddle et al., 1998), no study has empirically examined reduced eye contact in this population. Women with the *FMR1* premutation may share additional social difficulties with their children who have fragile X syndrome, and thus, may be slow to warm-up to social interactions (Roberts, Weisenfeld, Hatton, Heath, & Kaufmann, 2007). Because of this, their eye contact may improve toward the end of social interactions.

This study examined reduced eye contact in relation to social and general anxiety in women with the *FMR1* premutation compared to control women without the *FMR1* premutation.

Participants had a semi-structured conversation with an interviewer; this conversational sample was recorded and rated at a later date. Eye contact during the first and last minutes of the conversational sample was rated independently by two blind raters and consensus scores were produced. Both social anxiety and general anxiety were measured through self-reported questionnaires.

The analysis utilized a series of mixed effects linear models. A mixed model testing group, condition, and their interaction indicated significant effects of group ($p = .012$) and condition ($p < .0001$); their interaction was not significant. Both women with the *FMR1* premutation and control women had higher eye contact scores (indicating more reduced eye contact) during the first minutes of the interaction than during the final minutes, indicating both groups could warm-up; however, women with the *FMR1* premutation had reduced eye contact during both conditions compared to controls. Secondary mixed models adding social anxiety or general anxiety as predictors indicated no significant effect of social anxiety or general anxiety. Thus, there was no association between social anxiety or general anxiety and eye contact in women with the *FMR1* premutation, suggesting reduced eye contact is a feature of the premutation phenotype independent of social anxiety and general anxiety.

These findings support previous reports of reduced eye contact in the *FMR1* premutation (e.g., Tassone et al., 2000; Riddle et al., 1998); however, because this is the first study to empirically examine eye contact in women with the *FMR1* premutation, there is insufficient supporting evidence confirming our results, and replication studies are needed. Establishing reduced eye contact as a feature of the *FMR1* premutation will shed light on the social phenotype of the premutation and may have further clinical implications, as reduced eye contact can make effective social communication more difficult. Because the *FMR1* premutation is highly

prevalent, efforts to further define characteristics of the *FMR1* premutation and their mechanistic underpinnings have large implications for public health.

Abstract

Background. Mothers of children with fragile X syndrome (FXS) have the *FMR1* premutation, which affects approximately 1 in 151 women (Seltzer et al., 2012). Women with the *FMR1* premutation display elevated social anxiety (Bourgeois et al., 2011), which has been linked with higher levels of gaze anxiety and avoidance in other clinical groups (Schneider et al., 2011). While several studies have suggested women with *FMR1* premutation have reduced eye contact (Tassone et al., 2000; Losh, Klusek et al., 2012; Riddle et al., 1998), no study has empirically examined reduced eye contact in the female *FMR1* premutation. Like their children with FXS, women with the *FMR1* premutation may be slow to warm-up socially (Roberts et al., 2007), resulting in better eye contact toward the end of social interactions. **Objective.** This study examined reduced eye contact in relation to social and general anxiety in 43 women with the *FMR1* premutation compared to 28 control women without the *FMR1* premutation. **Methods.** Eye contact during the first and last minutes of a semi-structured conversational sample was rated independently by two blind raters on a 5-point scale and consensus scores were produced. Social anxiety was measured with the Liebowitz Social Anxiety Scale (LSAS; Liebowitz et al., 1987) and general anxiety was measured with the Beck Anxiety Inventory (BAI; Beck, 1990). **Results.** A mixed model testing group, condition, and their interaction indicated significant effects of group (F [1, 65] = 6.68, p = .012) and condition (F [1, 65] = 18.65, p < .0001); their interaction was not significant (p=.556). Secondary mixed models adding social anxiety or general anxiety as predictors indicated no significant effect of social anxiety (p=.415) or general anxiety (p = .214).

Conclusions. Both groups exhibited a warm-up effect; however, women with the *FMR1* premutation had overall reduced eye contact during both initial and final conditions compared to control women. Neither social anxiety nor general anxiety was related to reduced eye contact in the *FMR1* premutation, suggesting reduced eye contact is a feature of the premutation phenotype independent of social anxiety and general anxiety.

Introduction

Fragile X Syndrome and the *FMR1* Premutation

Fragile X syndrome (FXS) is the most common known cause of inherited developmental disability, affecting approximately 1 in 2,500 individuals (Hagerman, 2008). FXS results from a trinucleotide expansion of a CGG repeat on the *fragile X mental retardation 1* (*FMR1)* gene. Individuals with the full mutation (> 200 CGG repeats) typically have hypermethylation of the *FMR1* gene promoter (Oberle et al., 1991) resulting in gene silencing and a reduction of the gene's product, fragile X mental retardation protein (FMRP), which plays an important role in neuronal synaptic development (Sidorov, Auerbach, & Bear, 2013). This reduction or absence of FMRP results in limited synaptic plasticity (Sidorov et al., 2013) and has been implicated with clinical symptoms of FXS including intellectual disability, autistic behavior, and ADHD (Tassone et al., 2000; Hatton et al., 2006; Sullivan et al., 2006). Levels of FMRP are also associated with cognitive, communicative, and personal-social development (Bailey et al., 2001). Additionally, FXS is the leading known genetic cause of autism and thus has some phenotypic overlap with autism, including social anxiety and reduced eye contact (Cohen et al., 2005).

Mothers of children with FXS are genetic carriers of the disorder and have premutation alleles on *FMR1* known as the *FMR1* premutation or the fragile X premutation. These alleles consist of a shortened version of the trinucleotide expansion (55-200 CGG repeats) compared to

the full mutation found in individuals with FXS. The premutation alleles expand to greater repeat sizes when transmitted through mothers (Tassone et al., 2000), and approximately 1 in every 151 women has the *FMR1* premutation (Seltzer et al., 2012). While it was once thought that individuals with the *FMR1* premutation were "silent carriers" with no clinical manifestations of FXS, there is evidence that the *FMR1* premutation is associated with its own novel phenotype characterized by social difficulties (Franke et al., 1998; Losh, Klusek et al., 2012), risk for autism spectrum disorder (ASD; Farzin et al., 2006), and psychological vulnerability (Roberts et al., 2009).

The FMR1 Premutation Social Phenotype

Mothers of children with FXS have been found to have elevated rates of social anxiety (Franke et al., 1998; Bourgeois et al., 2011) and general anxiety symptoms (Hall et al., 2016). Specifically individuals with the *FMR1* premutation have a significantly higher lifetime prevalence of social anxiety disorder (34.2%) than individuals without the premutation (12.6%). This heightened prevalence of lifetime anxiety is expanded to any anxiety disorder, including general anxiety, in individuals with the *FMR1* premutation who have fragile X-associated tremor-ataxia syndrome, a late onset neurodegenerative disorder; however, when males with the *FMR1* premutation were examined independently of females, there were no significant differences in lifetime prevalence of social anxiety compared to prevalence in the general population (Bourgeois et al., 2011). This suggests that elevated social anxiety may be a unique characteristic of the female *FMR1* premutation phenotype.

Social anxiety disorder is characterized by excessive fear of social scrutiny by others and attentional bias for cues of negative social evaluation. Eye contact is thought to play a major role in the disorder as it may cause feelings of being scrutinized. Additionally, avoidance of eye

contact may have a functional role in sustaining anxiety, as important nonverbal social information is lost that could counteract the biases concerning social criticalness and rejection. Individuals with social anxiety disorder reported higher levels of gaze anxiety and gaze avoidance due to that anxiety than individuals without social anxiety (Schneier et al., 2011). Social anxiety disorder can also be comorbid with generalized anxiety disorder, and individuals meeting criteria for both diagnoses had elevated social anxiety and social avoidance (Mennin, Heimberg, & MacAndrew, 2000). These findings may also apply to females with the *FMR1* premutation given the high prevalence of social anxiety in this population.

In addition to elevated anxiety, women with the *FMR1* premutation exhibit shyness, social avoidance, and interpersonal sensitivity (Bourgeois et al., 2011; Johnston et al., 2001). These features may make navigating social interactions challenging, leading to discomfort in or avoidance of social situations. Even generalized anxiety symptoms, such as worry, nervousness, or the inability to relax, affect a person on a day-to-day basis, including within social contexts and may contribute to social difficulties exhibited by mothers of children with FXS.

Several studies have suggested eye contact may be reduced in the *FMR1* premutation. A case study of six individuals with the *FMR1* premutation reported both female participants (a young girl and an adult woman) had poor eye contact. The 9-year-old girl with the premutation was observed to have reduced eye contact after three years of age and the 33-year-old woman with the premutation reported "having difficulty making eye contact after 10th grade;" however, Tassone and coworkers did not discuss whether there are reports of the 33-year-old woman having reduced eye contact prior to 10th grade nor did they include their own observations of the woman's eye contact. While Riddle et al. (1998) found no significant difference in self-reported eye contact problems between women with the *FMR1* premutation and control women without

the premutation, the participants were more likely to be categorized into the correct groups when a clinician's evaluation of their eye contact was taken into account. This suggests many women with the *FMR1* premutation may be socially unaware of their reduced eye contact. Women with the *FMR1* premutation have also been found to have elevated pragmatic language (social language) errors during live social interviews. In particular, they scored higher on the "atypical suprasegmental" subcategory of a social language error scale, which included measures of atypical eye contact; however, eye contact measures were not examined independently of other items in the subcategory (Losh, Klusek et al., 2012). Little other supporting evidence has been published confirming reduced eye contact in women with the *FMR1* premutation. This gap in literature may be, in part, due to both the novelty and subtlety of the *FMR1* premutation phenotype in comparison with the FXS phenotype. Women with the *FMR1* premutation seem to exhibit much subtler reduced eye contact than their children with the full FXS mutation; this has been found with other shared features, including cognitive and social language delays, in boys with FXS and boys with the *FMR1* premutation. Boys with the *FMR1* premutation were also found to have a varying severity of these features (Aziz et al., 2003), suggesting some women with the *FMR1* premutation may be more clinically affected than others with more reduced eye contact.

Social avoidance is another key feature of FXS, and individuals with the disorder are slow to warm-up to social interactions. It is possible women with the *FMR1* premutation display similar social behavior patterns as their children with FXS. Young boys with FXS were found to exhibit a "warm-up" effect, having significantly increased social approach behaviors with more time spent with their assessor; however, eye contact was less improved by time spent with the assessor than other behaviors like physical movement and facial expression (Roberts et al.,

2007). This suggests that eye contact may have a stronger underlying physiological connection farther removed from the control of the individual. Thus, mothers of children with FXS may also have difficulty improving their eye contact during social interactions.

The Present Study

This study's aims are as follows:

1. To determine whether eye contact during a semi-structured conversational exchange differs between women with the *FMR1* premutation and control women without the *FMR1* premutation, and whether a warm-up effect is observed in either group. *Hypothesis: A warm-up effect will occur in both groups; however, women with the FMR1 premutation will have reduced eye contact overall compared to control women during both the first three minutes and last three minutes of the social interaction.*
2. To examine social and general anxiety as correlates of reduced eye contact. *Hypothesis: Only social anxiety will be associated with reduced eye contact in both groups.*

Methods

Participants

Participants included 43 mothers with the *FMR1* premutation and 28 mothers of typically developing children who were participating in a study on communication profiles in the *FMR1* premutation (F32DC013934; PI: Klusek). The mothers with the *FMR1* premutation were recruited through their sons who were participating in a larger longitudinal study of language development in FXS (5R01HD024356; PI: Abbeduto). Genetic testing confirmed *FMR1* premutation status in the *FMR1* premutation group. The mothers of typically developing children confirmed their children had never been diagnosed or treated for any developmental delay or disorder. They also filled out the Social Communication Questionnaire (SCQ; Rutter et al., 2003)

to screen their children for ASD. All participants were native speakers of American English. Groups did not differ significantly in IQ or education level; however groups did differ significantly in age and race; see Table 1.

Procedure

Participant assessments were administered as part of a larger research protocol, which lasted roughly three hours. Approximately, the first hour of testing consisted of standardized cognitive tests and eye tracking tasks. These were followed by a life history interview, which served as the first opened-ended social task. Assessments were completed in the university laboratory setting or in a quiet room in the participant's home. Participant consent was obtained as approved by the institutional review board of the University of South Carolina.

Measures

Eye contact. Eye contact was observed in the context of a "life history interview" task, which consisted of a 20-minute conversational sample between the participant and an interviewer concerning the participant's "life history." The interview was semi-structured, as interviewers followed a standard template of easily discussed topics such as "Tell me about your family when you were younger" And "What did you do after high school?" Interviewers were trained to facilitate conversational exchange by commenting on participants' responses, asking follow-up questions, and offering information for reciprocation. Each conversation sample was videotaped so it could be rated at a later date.

Eye contact was measured during the first three minutes, when the social interaction is new and anxiety is theoretically highest, and the final three minutes, when participants have habituated to the interaction, of the videotaped conversational sample using an eye contact code developed for this study. This eye contact code consisted of a 5-point scale, with 0 indicating

"eye contact is contextually appropriate and well integrated with speech", 1 indicating "eye contact is reduced", and 2 indicating "eye contact is significantly reduced, rare, or atypical." A score of 0.5 indicated eye contact was between scores of 0 and 1, and a score or 1.5 indicated eye contact was between scores of 1 and 2. Two blinded coders were trained to rate eye contact utilizing this code. The training process consisted of an explanation of the code and instruction in applying the code to a practice sample not part of the current dataset. Then, the coders each rated practice samples independently until achieving 100% reliability on codes for three consecutive samples from each participant group. The coders then began independently rating the conversational samples for the present study, and later, consensus was performed between the two coders, resulting in a final consensus score for the eye contact during the first three minutes and a separate final consensus score for eye contact during the last three minutes. Intraclass correlations were computed to determine average interrater-reliability prior to consensus. The interrater-reliability of initial eye contact scores was ICC (3, 2) = .928 and the interrater-reliability of final eye contact scores was ICC (3, 2) = .921.

Social anxiety. Self-reported social anxiety experienced in the past week was measured using the Leibowitz Social Anxiety Scale (LSAS-SR; Liebowitz et al., 1987). The LSAS-SR form has high agreement with the clinician-administered version of the LSAS (LSAS-CA), which has strong psychometric characteristics. Both the LSAS-SR and LSAS-CA have internal consistency of 0.95 and no pairwise comparisons were significantly different between individuals' scores on each version (Fresco et al., 2001). The LSAS-SR consists of 24 items rated on two different 4-point subscales: the fear/anxiety subscale and the avoidance subscale. Ratings on the fear/anxiety subscale are 0 (none), 1 (mild), 2 (moderate), and 3 (severe). Ratings on the avoidance subscale are 0 (never), 1 (occasionally), 2 (often), and 3 (severe). Items

represent actions in social situations including, "talking with people you don't know very well" and "looking at people you don't know very well in the eyes." Total LSAS scores were examined.

General symptoms of anxiety. Self-reported symptoms of general anxiety were measured using the Beck Anxiety Inventory (BAI; Beck, 1990). Meta-analysis findings confirm the BAI has internal consistency of .91 and test-retest reliability of .65 (Bardhoshi, Duncan, & Erford, 2015). The questionnaire asks participants to rate their experience of each item "today or in recent weeks" on a 4-point scale. Ratings include 0 (not at all), 1 (mildly- did not bother me much), 2 (moderately- very unpleasant but tolerable), and 3 (severely- I could barely stand it). The BAI contains 21 items regarding symptoms of general anxiety including "unable to relax," "heart pounding or racing," and "nervous." Total BAI scores were examined.

Data Analysis

Analyses were carried out using SAS 9.4 (SAS Institute; 2013). First, a Pearson correlation was run to examine if age had an impact on eye contact during each condition in either group since age differed significantly between groups. It revealed no significant relationship between eye contact and age in women with the *FMR1* premutation during both initial (p = .962) and final (p = 0.981) conditions. There was also no significant relationship between eye contact and age in control women for both initial (p =.928) and final conditions (p = .484). Next, to determine group differences in eye contact across initial and final conditions (Research Question 1), a mixed effects linear model was fit to test for group differences in eye contact scores across both conditions. Group, condition, and their interaction were included as predictors. Participants' race was included as a covariate because race also differed significantly between groups and had to be controlled for. An unstructured covariance matrix was specified.

Additional analyses were run to determine if general anxiety or social anxiety were associated with reduced eye contact in either group (Research Question 2). The same mixed model was expanded to include total BAI scores and the interaction between total BAI scores and condition as predictors to examine any relationship between eye contact and general anxiety. Next, the original mixed model was again expanded to include total LSAS scores and the interaction between total LSAS scores and condition as predictors to examine a possible relationship between eye contact and social anxiety.

Results

Differences in Eye Contact

A mixed model analysis revealed significant effects of group (F [1, 65] = 6.68, p = .012), condition (F [1, 65] = 18.65, p < .0001), and race (F [1, 65] = 3.28, p = 0.044). The group-condition interaction was not significant (p = .556). Both groups had lower mean eye contact scores during the final condition than during the initial condition, indicating a warm-up effect occurred in both groups; however, women with the *FMR1* premutation had higher mean eye contact scores (indicating more reduced eye contact) compared to controls across conditions; see Figure 1.

Association between Eye Contact and Anxiety

Another mixed model analysis revealed there was no significant effect of total LSAS score (p = .415) and no significant interaction between total LSAS score and condition (p = .921). A final mixed model analysis revealed there was also no significant effect of total BAI score (p = 0.214) and no significant interaction between total BAI score and condition (p = .113).

Discussion

The *FMR1* premutation has been associated with social deficits including social avoidance, interpersonal sensitivity, and greater numbers of pragmatic language violations (Bourgeois et al., 2011; Johnston et al., 2001; Losh, Klusek et al., 2012). While several studies have suggested women with the *FMR1* premutation exhibit reduced eye contact, this is the first study to attempt to quantify eye contact in the female *FMR1* premutation during a semi-structured social interaction. As expected, findings showed both women with the *FMR1* premutation and control women "warmed-up" during the social interaction, resulting in better eye contact during the final minutes of the social interaction; however, women with the *FMR1* premutation had reduced eye contact compared to controls during both the initial and final minutes of the social interaction. Contrary to hypotheses, neither social anxiety nor general anxiety was associated with reduced eye contact in either group. This study informs the emerging *FMR1* social phenotype, particularly in regard to nonverbal social communication patterns, and suggests further exploration of eye contact in possible *FMR1* subgroups and its mechanistic underpinnings as aims of future research.

Reduced Eye Contact in Women with the FMR1 Premutation

Despite warming up to the social interaction, women with the *FMR1* premutation had higher mean eye contact scores compared to controls during both initial and final conditions, indicating they had consistently reduced eye contact. These findings corroborate previous reports of reduced eye contact in the *FMR1* premutation (e.g., Tassone et al., 2000; Riddle et al., 1998). Insufficient supporting evidence has been published confirming reduced eye contact in women with the *FMR1* premutation and replication studies are needed. Establishing reduced eye contact as a feature of the *FMR1* premutation will shed light on the clinical phenotype of the premutation

and may have further clinical implications, as reduced eye contact can impact social interactions and make effective social communication more difficult.

Lack of Association between Anxiety and Reduced Eye Contact

Contrary to hypotheses, social anxiety was not related to reduced eye contact in women with the *FMR1* premutation. While women with the *FMR1* premutation have been found to have elevated social anxiety (Bourgeois et al., 2011), and individuals with social anxiety disorder reported higher levels of gaze anxiety and gaze avoidance than individuals without social anxiety (Schneier et al., 2011), our results did not suggest a similar occurrence in females with the *FMR1* premutation. We conclude reduced eye contact is a feature of the *FMR1* premutation phenotype independent of social anxiety. General anxiety was previously found to be associated with greater social anxiety in another clinical group (Mennin et al., 2000) but no evidence suggested a relationship between general anxiety, which is characterized by expansive and excessive worry about everyday life events rather than fear of social evaluation, and reduced eye contact. As predicted, general anxiety was also not related to eye contact. Because anxiety was not found to be related to reduced eye contact in women with the *FMR1* premutation, other possible correlates should be explored in future work.

Other Possible Correlates of Reduced Eye Contact

Fragile X syndrome (FXS) is the leading known genetic cause of autism and thus has some phenotypic overlap with autism, including social anxiety and reduced eye contact (Cohen et al., 2005). As indicated by the results of this study and previous research, mothers of children with FXS who have the *FMR1* premutation often exhibit some mild symptoms of autism, including social avoidance, elevated social anxiety, and reduced eye contact. Some women with the *FMR1* premutation may also have a more difficult time warming-up to social interactions

than others, resulting in less improved eye contact throughout a social interaction. Roberts et al. (2007) found that eye contact change scores of boys with FXS were inversely correlated with CARS scores (Schopler, Reichler, & Renner, 1988), a measure of autistic behavior, suggesting phenotypic differences in eye contact patterns between boys with FXS and autism spectrum disorder (ASD), and boys with FXS alone. This implies reduced eye contact in FXS is related to other autistic features of the broad autism phenotype (BAP), comprising a deficit in social awareness or social interest, and a similar association may be present in the *FMR1* premutation. In one screening study, 14% of males and 5% of females with the premutation also met criteria for an ASD diagnosis (Clifford et al., 2007). Even among carriers who do not meet criteria for an ASD diagnosis, traits associated with ASD are more common than among controls. In particular, women with the *FMR1* premutation display elevated rates of social language and personality features, including rigid personality, of the BAP (Losh, Klusek et al., 2012), and reduced eye contact may be related to these autistic features. Thus, it is possible a subgroup exhibiting greater autistic features and more reduced eye contact exists in the *FMR1* premutation.

It is also possible that reduced eye contact is related to deficits in executive function and social cognition. Executive function is important for emotional control, attentional control, and cognitive flexibility, and is believed to have some overlap with social cognition. Direct gaze (eye contact) is a prerequisite of social interactions and basic aspects of social cognition are associated with gaze processing (Itier & Batty, 2009). Reduced eye contact during a Skype conversation negatively correlated with executive functioning in children with ASD (Hutchins & Brien, 2016), and there may be a similar relationship in the *FMR1* premutation. Women with the *FMR1* premutation have been found to have deficits in executive function compared to control women (Shelton et al., 2016; Sterling, Mailick, Greenberg, Warren, & Brady, 2013), but little

research exists concerning social cognition in the female *FMR1* premutation phenotype. Men with the *FMR1* premutation did display deficits in social cognition compared to men without the *FMR1* premutation (Cornish et al., 2016), however, and it is possible these deficits extend to the female *FMR1* premutation phenotype as well.

Limitations and Future Directions

This study has a few limitations. Self-reported symptoms rather than clinical measures of general and social anxiety were used; future work may incorporate diagnostic measures to confirm findings. We also did not include a second comparison group (such as mothers of children with other types of developmental disorders) to take into account the stresses of parenting a child with a developmental disorder; however, our group is unaware of research suggesting that parenting stress would have impact on eye contact. Future research aims to examine measures of BAP features, executive function, and social cognition in relation to reduced eye contact in women with the *FMR1* premutation.

In conclusion, this study provided novel insight into the female *FMR1* premutation phenotype because it was the first study to empirically examine and document reduced eye contact in women with the *FMR1* premutation compared to control women without the premutation. We found that women with the *FMR1* premutation had consistent reduced eye contact compared to controls during both the final and initial minutes of a social conversational task despite both groups warming-up to the social interaction, resulting in better eye contact toward the end of the interaction. Reduced eye contact was not related to general or social anxiety in either group. Our results confirm reduced eye contact as a phenotypic feature of the *FMR1* premutation and suggest this feature is independent of anxiety. Reduced eye contact may contribute to other social difficulties exhibited by women with premutation, including pragmatic

language errors, as vital non-verbal cues, such as appropriate conversational turn taking and emotional information, are lost when eye contact is reduced. These findings add to a growing knowledge base concerning the social phenotype of the *FMR1* premutation. Because the *FMR1* premutation is highly prevalent, efforts to further define characteristics of the *FMR1* premutation and their mechanistic underpinnings have large implications for public health.

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Table 1

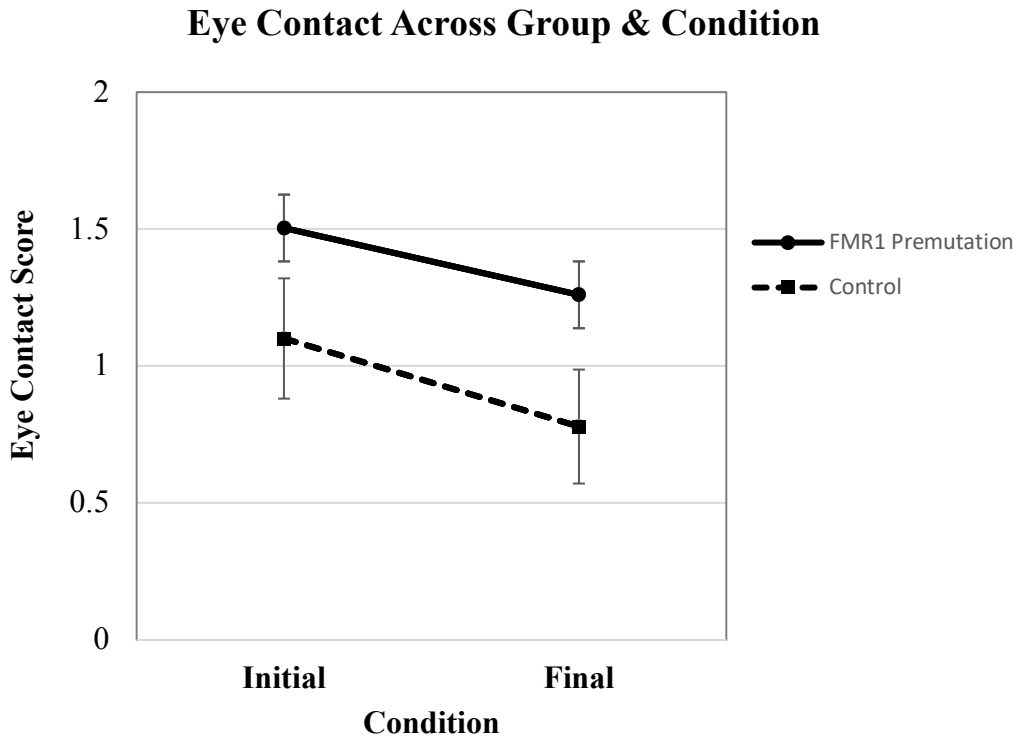
Group Characteristics

Variable	Group		
	Women with the *FMR1* Premutation (N = 43)	Control Women (N = 28)	Test of Group Differences
IQ[1]			
M (*SD)*	105.71 (13.03)	104.18 (11.39)	.655
Range	81.00-130.00	83.00-135.00	
Highest Education Level (%)			
High school or lower	51.01	31.97	
Bachelor's degree	27.88	32.07	.232
Master's degree	18.60	21.40	
Professional degree	2.33	14.2	
Age in years			
M (*SD)*	45.73 (9.11)	40.35 (8.55)	.015*
Range	25.53-64.30	26.68-64.02	
Race (%)			
African American	2.44	17.86	.047*
Caucasian	92.68	82.14	
Other	4.88	0.00	

Note. [1]IQ measured with the Kaufman Brief Intelligence Test, second edition (KBIT-2; Kaufman & Kaufman, 2013).

*$p < .05$

Figure 1



Note. Bars show standard error.