HHS Public Access

Author manuscript

Dev Neurorehabil. Author manuscript; available in PMC 2019 February 01.

Published in final edited form as:

Dev Neurorehabil. 2018 February ; 21(2): 137–140. doi:10.1080/17518423.2018.1424264.

Gaze avoidance and perseverative language in fragile X syndrome and autism spectrum disorder: Brief Report

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Abstract

Gaze avoidance and perseverative language impact pragmatics in autism spectrum disorder (ASD) and fragile X syndrome (FXS). We examined these features during conversation samples in boys with ASD (n=10) and boys with FXS and ASD (FXS+ASD; n=10). Both groups had similar high rates of gaze avoidance and topic and conversation device perseverations, yet these features were not correlated with one another. Boys with FXS+ASD produced a higher proportion of single utterance perseverations. Results from this study highlight the need for future research to identify potential mechanisms influencing the presence of language perseverations and gaze avoidance.

Keywords

fragile X syndrome; autism spectrum disorder; eye gaze avoidance; perseverative language; pragmatics

Introduction

Fragile X syndrome (FXS) is the most common inherited cause of intellectual disability. Males with FXS have language impairments and a high co-morbidity with autism spectrum disorder (ASD) with recent rates at 27–75%, depending on the diagnostic measures [1,2]. The behavioural phenotype is similar in FXS and idiopathic ASD, and includes deficits in pragmatics. Both groups have frequent gaze avoidance and language perseverations, either of which can negatively impact pragmatic skills, and taken together, cause difficulty in an

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Declaration / Statement of Interest

This study was funded NIDCD grants R03 DC011616 (Sterling) and T32 DC05359 (Ellis Weismer), NICHD grants T32 HD007489 (Mailick) and P30 HD03352 (Messing), and start-up funds from the University of Wisconsin-Madison awarded to Audra Sterling.

individual's ability to engage with a communication partner [3,4,5]. These behaviours negatively impact social development and hinder academic progress, as social skills and school success are related [6]. An early study on FXS found a link between these two behaviours [3], but this has not been examined in boys with FXS and co-occurring ASD (FXS+ASD). Studying boys with FXS+ASD and boys with idiopathic ASD together can provide insight on the underlying differences between these groups beyond the impact of ASD.

Perseverative language is a hallmark feature of the language phenotype in FXS, and is defined as the excessive repetition of utterances or topics during conversation [3,4]. Individuals with FXS produce increased perseverative language in comparison to age-matched groups with neurodevelopmental disorders [3,4,7,8]. There is variation in the literature regarding the difference in perseverations between boys with FXS-only and FXS +ASD, such that some research reports that boys with FXS+ASD produce more topic-based perseverations [4], while other research reports no difference between FXS+ASD and FXS-only groups [7].

Gaze avoidance during conversation is a consistent impairment in FXS and ASD. Boys with FXS produce more gaze avoidance than their typically developing siblings (80% and 10%, respectively) [9], and also have more gaze avoidance than cognitively-matched individuals with Down syndrome [10]. Studies have included children with FXS-only, thus it is unknown if individuals with FXS+ASD share a similar profile. The influence of an ASD co-diagnosis on pragmatic features such as gaze avoidance and perseverative language is a critical gap in the literature. Examining similarities and differences of these pragmatic features in boys with FXS+ASD and idiopathic ASD may clarify the unique behaviour profile of FXS in these areas.

Gaze avoidance and perseverative language are key features of FXS and idiopathic ASD, and highlight that pragmatic deficits are characterized by verbal and nonverbal behaviours [3,4,9]. These behaviours may be linked, and connected to arousal and/or anxiety, which underlie pragmatic deficits in FXS [3,11]. A link between gaze avoidance and perseverative language in FXS+ASD may indicate that an underlying mechanism is responsible for their co-occurrence.

The current study examined perseverative language and gaze avoidance in boys with FXS +ASD and idiopathic ASD to determine if these pragmatic features occur similarly, and thus a potential link exists between these behaviours. We addressed the following questions: (a) Are there differences in gaze avoidance and perseverative language between boys with FXS +ASD and boys with ASD during a conversation sample?; and (b) Is perseverative language related to gaze avoidance in boys with FXS+ASD and boys with ASD?

Methods

Recorded videos of 10 boys with FXS+ASD and 10 boys with idiopathic ASD from a larger, prior study were used for this sample [12]. Boys with idiopathic ASD had a mean age of 13.45 years (SD = 1.81) and boys with FXS+ASD had a mean age of 12.31 years (SD =

2.26). Participants for the present study were selected based on availability of videos of conversation samples with a clear view of the boys' faces, which was critical for successful eye gaze coding. Boys with FXS+ASD had the full mutation, confirmed via previous genetic testing. Boys with idiopathic ASD had prior genetic testing to rule out FXS, as well as a community diagnosis of ASD, which was provided previously by a physician, neurologist, psychiatrist, or psychologist. Participants were Standard American English Speakers. The visits took place at the Waisman Center at the University of Wisconsin-Madison. The university's Institutional Review Board approved the study. Legal guardians provided informed consent, and the boys provided written or oral assent.

The groups were similar on chronological age, $t(18) = -1.25$, $p = 0.229$, 95% CI [−3.07, 0.78] and ADOS severity scores $t(18) = -1.81$, $p = 0.087$, 95% CI [−2.59, 0.19] [13]. Boys with idiopathic ASD had a mean ADOS severity score of 8.20 ($SD = 1.87$) and boys with FXS+ASD had a mean score of 7.00 ($SD = 0.94$). Because a t-test is fairly robust to deviations from normality and sample sizes were equal between groups, it was appropriate to use. Nonverbal IQ was significantly different between the groups (ASD: $M = 78.30$, $SD = 1.81$; FXS+ASD: $M = 45.60$; $SD = 7.59$, $t(18) = -3.94$, $p = 0.002$, 95% CI [−51.03, −14.37]).

Procedures

Nonverbal IQ was measured using the Leiter International Performance Scale – Revised (Leiter-R) [14]. The ADOS, first and second edition [15,16] measured ASD severity. Parents completed the Autism Diagnostic Interview – Revised (ADI-R) [17], an interview on past and present child behaviours, and all children met criteria on both measures.

Participants completed a 10-minute semi-structured audio and video-taped conversation sample with a trained examiner. The examiner followed a list of conversation prompts, including open-ended questions on personal interests, pets, and school. The participant and the examiner were seated adjacent to one another at a table. The examiner did not prompt the participant for eye contact. Samples were transcribed and coded following the *Systematic Analysis of Language Transcript* (SALT) procedures [18]. A second transcriber completed reliability for 25% of the transcripts. Transcripts were compared line-by-line. Average agreement on standard language measures were as follows: utterance segmentation: 85.34%; unintelligible utterances: 93.18%; number of morphemes: 83.60%; number of words: 85.16%; and word identification: 86.80%. Two trained coders then coded the transcripts for perseverative language using a published system [4,7]. Codes included single utterance perseverations, utterance perseverations repeated two or more times, topic perseverations, and conversation devices. Table 1 includes definitions and examples. To control for variation in the total number of utterances, each perseverative language code was calculated as a proportion (e.g. number of topic perseverations out of the total number of utterances). Reliability for perseverative language codes was completed for 20% of the transcripts. Kappa values were .87 for utterance perseverations, .90 for topic perseverations, and conversation device perseverations were .30, all indicating at least fair agreement [19]. The video recordings were also coded for gaze avoidance using Procoder video encoding software [20]. Coders followed guidelines from a published coding system [9]. Eye gaze was

coded when the child looked toward the examiner's face; gaze avoidance was coded when the child looked away from the examiner's face. Each video was coded by two coders. Interrater reliability was assessed using a two-way random, absolute agreement intraclass correlation (ICC) [21]. The ICCs for each code were in the excellent range (0.98 for eye gaze; 0.92 for gaze avoidance). Disagreements were resolved via consensus coding.

Data analysis

Gaze avoidance was analysed as a percentage of the total video time. Independent samples *t*-tests were done to examine differences in gaze avoidance between the two groups. Data met the assumptions for a *t*-test. There were no outliers. Data were normally distributed when assessed by Shapiro-Wilk's test ($p > 0.05$), and there was homogeneity of variances as assessed by Levene's test for equality of variances ($p > 0.05$). Due to large variability in perseverative language between groups however, a series of nonparametric Mann-Whitney U tests were done to examine differences in perseverative language. Effect sizes (*d)* were calculated for these comparisons and we interpreted effect sizes to be small ($d = .20$), medium ($d = .50$), or large ($d = .80$) [22]. Spearman correlations were completed to examine relationships between gaze avoidance and perseverative language. To determine if IQ should be considered in our analyses, Spearman correlations between IQ, perseverative language, and gaze avoidance codes were calculated within each group. In boys with ASD, there was a significant negative correlation between IQ and single utterance perseverations such that boys with higher IQs had fewer single utterance perseverations ($r_s = -.764$, $p = 0.010$), however this correlation was not significant in boys with FXS+ASD ($r_s = -.088$, $p = 0.808$). IQ was not correlated with any other gaze avoidance or perseverative language codes.

Results and Discussion

Means, standard deviations, and Mann-Whitney U values for all proportions of perseverative language codes are presented in Table 2. The groups did not significantly differ on proportions of conversation devices, topic perseverations, or utterance perseverations repeated two or more times. Effect sizes for the latter two codes suggest that with increased power, we may find a significant difference between groups. The small effect size for conversation devices suggests that, even with increased statistical power, there would be similarities between these groups on the use of phrases that added no new information. The boys with FXS+ASD produced significantly more single utterance perseverations than the boys with ASD; previous findings indicate males with FXS produce more perseverations including dysfluencies and reformulations than males with ASD [23], which is similar to our finding of utterance perseveration differences. This code was correlated with IQ in the boys with ASD, but not boys with FXS+ASD. The group differences, along with this correlation, may suggest that IQ is related to single utterance perseverations. However, there were no group differences on other codes, and IQ was not correlated with topic perseverations or conversation device perseverations, suggesting that something other than IQ accounts for the presence of these features in these participants. Studies with greater power may allow for the exploration of additional variables such as anxiety that may reveal an influence on topic and utterance perseverations in boys with FXS+ASD.

The conversation sample allowed us to simultaneously measure gaze avoidance and perseverative language. Boys with FXS+ASD directed eye gaze to the examiner on average 17.92% (*SD* = 11.88%) of the time and avoided gaze 82.09% (*SD* = 11.88%). Boys with ASD directed gaze to the examiner on average 22.18% (*SD* = 13.80%) of the time and avoided gaze 77.80% (*SD* = 13.81%). This high amount of gaze avoidance is not seen in typically developing children, as noted in a previous study, where siblings of children with FXS avoided eye gaze only 10% of the time [9]. No significant differences were found in amount of gaze avoidance during conversation between the two groups, $t(18) = 0.74$, $p = 0.466$, $d = 0.33$, 95% CI [0.04, 0.06], which was similar to previous reports [24], and suggest that both groups have frequent gaze avoidance. Other studies found differences in eye gaze between these two groups, with individuals with FXS with or without a co-diagnosis of ASD either demonstrating eye gaze more than peers with ASD [25] or less [26,27]. These studies included younger children. The present study includes older children, along with a task that was not experimental nor object-centred.

In order to examine the relationship between gaze avoidance and perseverative language, Spearman correlations were calculated within each group. No significant relationships were found between perseverative language and gaze avoidance in either group (FXS+ASD gaze avoidance with: single utterance perseverations: $r_s = 0.55$, $p = 0.103$; two or more perseverations: $r_s = 0.30$, $p = 0.403$; conversation devices: $r_s = 0.01$, $p = 0.986$; topic perseverations: $r_s = 0.32$, $p = 0.365$; ASD gaze avoidance with: single utterance perseverations: $r_s = 0.14$, $p = 0.710$; conversation devices: $r_s = 0.20$, $p = 0.590$; topic perseverations: $r_s = 0.12$, $p = 0.738$). This indicates that an increase in gaze avoidance is not related to an increase in perseverative language. Perhaps we do not see a relationship between these features because they are not explained by the same underlying mechanism (e.g. arousal), as was initially proposed [3]. It is important to consider the impact of small sample sizes. Although Spearman correlations partially account for the underpowered nature of the study, these results should be interpreted with caution, as a larger sample size may reveal significant correlations between these features. As it stands, the present finding indicates that these two pragmatic features are not necessarily linked.

The current study presents with several limitations. First, the sample sizes were small, and may not capture the heterogeneity of these populations. Although we used nonparametric statistics when appropriate, low statistical power remains a concern. Despite this, when considering the effect sizes, our findings can inform future research. We also did not compare boys with FXS-only to FXS+ASD, which would inform the impact of ASD on FXS. Additionally, the reliability value for conversation devices was in the “fair agreement” range; higher reliability would provide more certain conclusions for conversation device findings. This study also excluded girls with FXS or ASD, which are important and understudied groups.

Anxiety has been proposed to have an impact on ASD symptoms in FXS [11]. Exploring correlations between anxiety, perseverative language, and gaze avoidance would help clarify the factors that drive one or both of these pragmatic deficits. Perhaps an increase in anxiety in FXS+ ASD can explain the significant group difference in single utterance perseverations.

This study contributes to research on the phenotype of FXS+ASD and the overlap with ASD. Despite differences in nonverbal IQ, gaze avoidance and perseverative language patterns did not differ between groups, except for single utterance perseverations. Gaze avoidance and perseverative language were not related, which provides preliminary evidence suggesting a difference in underlying mechanisms for these behaviours in FXS+ASD and idiopathic ASD.

Acknowledgements

Thank you to the children and families who participated in this research. We also thank Susan Ellis Weismer and Lyn Turkstra for their comments on this project. We would like to thank Susen Schroeder, Kellie Willis, Emily Lorang, Holly Huth, Sara Kover, Courtney Venker, Rachel Brewer, Michelle Cramer, Erin Schwartz, Courtney Ramczyk, and Kirsten Larson for their help with recruitment, data collection, transcription, data coding, and data entry.

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Table 1:

Perseverative language codes and definitions

Code name	Code definition	Code examples
Conversation device	Phrases that do not add meaning to, or advance the conversation produced by the child and were repeated three times.	“That’s about it;” “Neat”
Topic perseveration	Topics brought up by the child, at least three times.	Any topic of interest, (e.g. Batman, a friend at school, a favorite movie)
Single utterance perseverations	Utterance level perseverations produced by the child, repeated one time	“I like hockey. I like hockey.”
Utterance perseverations repeated two or more times	Utterance level perseverations produced by the child, repeated two or more times	“I want the ball. I want the ball. I want the ball.”

Note. Coding system based on Martin et al. (2012).

Table 2:

Means, standard deviations, and Mann-Whitney U results for amount of perseverative language used between groups

	ASD						FXS+ASD	
	Mean (SD)	**Mean Rank**	***U***	***z***	***p***	***d***	**Mean(SD)**	**Mean Rank**
Single utterance perseverations	.004(.007)	7.15	16.5	−2.67	.008	1.47	.025(.019)	13.85
Utterance perseverations repeated two or more times	0.0(0.0)	8.50	30.0	−2.17	.143	1.01	.005(.007)	12.50
Conversation device	.051(.048)	11.85	36.5	−1.04	.315	0.28	.036(.058)	9.15
Topic	.082(.063)	8.15	26.5	−1.78	.075	0.82	.180(.157)	12.85

Note. Means and standard deviations represent proportions; *U* = Mann-Whitney U score, *z* = *z* score, *p* = exact *p* value