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Language use predicts symptoms of fragile X-associated tremor/ataxia syndrome in men and women with the *FMR1* premutation

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Fragile X-associated tremor/ataxia syndrome (FXTAS) is an age-related neurodegenerative disorder caused by a premutation of the *FMR1* gene on the X chromosome. Despite the pervasive physical and cognitive effects of FXTAS, no studies have examined language in symptomatic males and females, limiting utility as an outcome measure in clinical trials of FXTAS. The goal of this work is to determine (a) the extent to which male and female *FMR1* premutation carriers with FXTAS symptoms differ in their language use and (b) whether language production predicts FXTAS symptoms. Thirty-one individuals with the *FMR1* premutation (21M, 10F), ages 58–85 years with some symptoms of FXTAS, were recruited from a larger cross-sectional study. Participants completed a five-minute monologic language sample. Language transcripts were assessed for rate of dysfluencies, lexical-semantics, syntax, and speech rate. Multivariable linear and ordinal regressions were used to predict FXTAS-associated symptoms, cognitive functioning, and executive functioning. Males and females did not differ in their language use. Language production predicted FXTAS symptom severity, cognitive functioning, and executive functioning. Language production difficulties may co-occur with FXTAS-associated symptoms and may be a viable outcome measure in future clinical trials, with future research needed.

Fragile X-associated tremor/ataxia syndrome (FXTAS) is a late-onset, genetically-based neurodegenerative condition caused by a premutation of the fragile X messenger ribonucleoprotein 1 (*FMR1*) gene. FXTAS is the result of incomplete genetic penetrance, such that ~ 40% of male premutation carriers and ~ 16% of females go on to develop the condition[1]. The clinical signs of FXTAS are intention tremor and cerebellar ataxia[2], and at least one radiological finding including the middle cerebellar peduncle (MCP) sign[3], white matter hyperintensities, or generalized brain atrophy[4]. Characteristics of FXTAS, both clinically and radiologically, differ in severity between males and females[5,6]. Biological males have only one X chromosome, and females have two, which likely influences phenotypic expression associated with FXTAS, as the second X chromosome may be protective[5,7]. Compared to females, males with FXTAS symptoms evidence faster progression of symptoms[8], show more loss in cerebellar volume and white matter disease[9], and greater cognitive impairment[6,10,11]. Nevertheless, it is not yet possible to predict which premutation carriers may go on to develop FXTAS, despite evidence implicating environmental[12], genetic[13–15], and behavioral correlates[16–18].

One behavioral domain that warrants further investigation as it pertains to FXTAS is language production. Using open-ended language samples, prior studies have shown that language fluency, lexical-semantics, syntax, and speech rate are viable markers of cognitive decline prior to a diagnosis (e.g., Parkinson's, Alzheimer's)[19–21]. Language sampling, therefore, may yield promising data to aid in predicting who will go on to display

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FXTAS-associated cognitive decline, and could be a viable outcome measure for FXTAS clinical trials. To the best of our knowledge, no language studies to date have included symptomatic premutation carriers, although a number of studies have investigated language in asymptomatic female premutation carriers[22–28]. There is limited understanding of language characteristics among male premutation carriers, with and without FXTAS symptoms, which could aid in improved phenotypic characterization of the condition, including whether language production changes alongside—or precedes—FXTAS symptoms. The goals of this study are twofold: (1) characterize language production among male and female premutation carriers with symptoms of FXTAS, and (2) discern the extent to which language production is related to cognitive functioning and FXTAS symptom severity.

Language and the *FMR1* premutation

Extant literature on language production and the *FMR1* premutation has almost exclusively focused on asymptomatic females. Such work suggests age-related changes in language production, including pragmatic language, syntactic complexity, and lexical-semantics[25,27,29], and associations between dysfluencies and age, a pattern not seen in a control group of mothers of autistic children[27]. Longitudinal and cross-sectional studies of female premutation carriers indicate increased difficulties with lexical-semantic aspects of language (inconsistent with healthy aging)[29,30], poorer semantic fluency[6], and atypical semantic processing (i.e., Evoked Response Potential [ERP] N400 responses) relative to controls[31]. Finally, recent evidence indicates that female premutation carriers with a family history of FXTAS show sharper declines in syntactic complexity over time relative to female premutation carriers without a family history of FXTAS[25]. Thus, language production in connected language samples is potentially associated with FXTAS as part of the broader phenotype, though no studies to date have investigated this possibility.

In contrast to females, there is a limited understanding of language characteristics among male premutation carriers, particularly using open-ended language sampling techniques. Given the more severe phenotypic profile among male premutation carriers[8,12], it is possible that males have more extensive language production changes than females. Virtually all studies of language among male premutation carriers are based on highly structured assessments. Using a battery of neuropsychological measures, Grigsby et al.[32] found that males with FXTAS performed significantly worse than controls on measures of verbal IQ, verbal fluency (a component of executive functioning), and declarative verbal learning and memory. Other studies have identified poorer semantic processing, indicated by ERP N400 responses, among males with FXTAS relative to comparison groups[33,34]. Collectively, there is emerging evidence to indicate that language may be impacted by the presence of FXTAS symptoms in both males and females. However, without the inclusion of data derived from open-ended language sampling techniques, our understanding of the full spectrum of potential language-related changes associated with FXTAS is limited.

Language, cognition, and neurocognitive decline

An important consideration pertaining to FXTAS is how language may be associated with cognitive symptoms of the condition. There is ample evidence to suggest that cognition, and executive functioning in particular, is impacted by the *FMR1* premutation in general, and declines during the course of FXTAS[16,32,35–38]. Executive functioning pertains to the processes involved in planning, working memory, and inhibition[39]. Executive functioning deficits associated with FXTAS include impacted inhibition[40], and lower scores of working memory, processing speed, and temporal sequencing compared to controls[32]. Executive functioning is posited to serve as a prodrome of the condition[16] (i.e., prior to diagnosis), mediates related psychiatric and behavioral symptoms[41], and is associated with corresponding white matter abnormalities[42].

Importantly, executive functioning is hypothesized to play a role in spoken language production[43,44], though how these domains are interrelated in individuals with symptoms of FXTAS has been unexplored. One case study of a male with FXTAS indicated that the subject had monotone voice and slurred speech, impacted pragmatics, mild paraphasias, and low semantic verbal fluency with co-occurring executive functioning deficits[45]. In female *FMR1* premutation carriers without FXTAS, lower working memory was associated with poorer vocal control, suggesting a link with motor speech coordination[46]. On the other hand, prior work did not find links between verbal disinhibition and dysfluencies in females without FXTAS[47]. Together, there is a dearth of evidence investigating links between language and cognition among persons with FXTAS, but evidence from the premutation in general points to the possibility that executive functioning as part of the FXTAS symptom profile may be related to spoken language.

With these considerations in mind, it stands to reason that phenotypically similar conditions to FXTAS may provide insight into possible language markers associated with the disorder. In acquired neurological conditions (e.g., mild cognitive impairment, Alzheimer's, Parkinson's), dysfluencies, lexical-semantics, syntax, and speech rate serve as disease indicators or predict later onset of the condition. Together, these language metrics reflect word retrieval and access[29], linguistic complexity[48], inhibition[43], serve discursive functions[49,50], and are used differently and change earlier relative to healthy aging[20,51], up to 20 years prior to diagnosis[51–53]. Moreover, they may provide indication of motor speech coordination and evidence distinct neural correlates[54,55]. Thus, language production may be a viable marker of FXTAS with implications for both cognitive and motor domains relevant to the condition.

Purpose and research questions

The goals of the present study were to (a) characterize the language features of individuals with FXTAS symptoms and (b) assess relationships with FXTAS symptoms.

The research questions for the study are as follows:

1. To what extent do male and female premutation carriers with FXTAS symptoms differ in their language production?
2. To what extent does language production predict FXTAS-associated symptoms?

We predicted that males with FXTAS would perform more poorly on measures of language production than females, as extant literature suggests more severe FXTAS-associated profiles in part due to biological differences. Further, we anticipated that poorer language production (more dysfluencies, and reduced lexical-semantics, syntax, and speech rate) would be associated with increased FXTAS symptom severity and poorer cognitive functioning.

Methods

Participants

Thirty-one individuals with the *FMR1* premutation (21M, 10F) completed a five-minute monologue[54] as an optional component of a larger study at the University of California-Davis (PI: Hagerman) that included cognitive, neuropsychological, and medical assessments, genetic counseling, and collection of biological samples. Participants ranged in age from 58 to 85 years. All participants self-reported their race as White. Most participants (90.9%) had completed some college. Inclusion criteria for the larger study included the presence of the *FMR1* premutation and neurological symptoms. One participant from the larger study had a stroke in the past without lasting cognitive deficits. Three participants exhibited some dementia symptoms; however, because these symptoms are part of the cognitive profile associated with FXTAS, we did not eliminate these participants from the study. Exclusion criteria consisted of the presence of other life-threatening diseases that affect central nervous system function (e.g., Alzheimer's dementia).

Only participants who had symptoms of FXTAS were included in the study. Symptoms of FXTAS were evaluated by the UC-Davis team of neurologists and clinicians, who rated FXTAS symptoms (based on clinical description) on a scale of 0 (no symptoms) to 5 (definite and severe FXTAS symptoms); participants who met at least stage 2 were included[57,58]. Participants' FXTAS status was characterized as possible (22.6%), probable (32.3%), and definite (45.2%). Criteria are defined elsewhere[57,58] and include clinical description of movement and gait problems, and the extent to which symptoms interfered with daily life. For additional description of these criteria, see Bacalman et al., 2006 and Jacquemont et al., 2003.

All participants provided DNA samples to determine *FMR1* CGG repeats and confirm premutation status, as previously described[59,60]. For females, the long CGG allele (i.e., the premutation allele) was selected for genetic analyses to examine potential differences from males (who have only one X chromosome). Increasing CGG length may be associated with earlier onset and more severe FXTAS motor symptoms[61,62] and was examined as a potential covariate. However, no associations between CGG and language variables was observed (r-values < 0.44, p-values > 0.470). See Table 1 for sample characteristics. Participants were recruited from fragile X clinics, the National Fragile X Foundation, and word of mouth. Study procedures were IRB-approved, and all participants completed informed consent (IRB 254134-27). All experimental procedures were performed in accordance with relevant guidelines and regulations.

Language sample elicitation

Participants completed a monologic language sample, as has been described previously[27,56]. All monologues were video and/or audio recorded for offline transcription. Video files were transcribed using the Systematic Analysis of Language Transcripts (SALT) at UW-Madison[63,64]; if unavailable, audio files were used. All transcripts were completed by trained student transcribers who achieved 80% or greater on a minimum of three transcripts in a row with an expert in SALT. Two primary transcribers completed the original transcripts, and two additional transcribers verified each file. Utterances were segmented into C-Units, which reflects an independent clause and its modifiers. Reliability was completed at the utterance and word level for 20% of transcripts. Utterance reliability was 86% and word-level reliability was 88%. Participant speaking time ranged from 180 to 300 s ($M = 275$ s).

Variable	Males $n = 21$ $M(SD)$	Females $n = 10$ $M(SD)$
Chronological age	65.69 (5.35)	67.09 (10.83)
Education[a]	3.13 (.99)	3.00 (1.15)
FMR1 CGG repeat length (long allele)	89.81 (12.62)	78.83 (19.18)
FXTAS Stage[b]	2.86 (.73)	2.65 (.67)
No. FXTAS Diagnosis (%)[c]	14 (66)	8 (80)
MMSE Total	28.50 (1.82)	29.33 (1.00)
BDS-2 Total	21.43 (3.49)	23.20 (4.10)

Table 1. Sample characteristics. Mini mental state exam (MMSE); behavioral dyscontrol scale—2nd edition (BDS-2). [a]Education ranged from 1(high school degree) to 4(Masters/Doctorate). [b]FXTAS stage ranged from 0 (no FXTAS symptoms present) to 5 (FXTAS definitely present). [c]FXTAS diagnosis was classified as possible, probable, and definite. Only those classified as probable or definite are reflected here.

All transcripts were assessed for the following linguistic categories using SALT's report function, derived from the analysis set (i.e., total complete and intelligible utterances): lexical diversity, semantic productivity, dysfluencies, and syntactic complexity. Speech rate was calculated in words per minute by dividing the total number of words by the time spent speaking (in seconds), multiplied by 60. Lexical diversity indicates the number of different words. Semantic productivity reflects the noun and verb rate per utterance. Dysfluencies refer to the rate per utterance of fillers (e.g., *"uh," "um"*), revisions ("[*the dog] the cat*"), and repetitions ("[*the] the cat*"). Syntactic complexity reflects the mean length of utterance (MLU) in morphemes. These linguistic categories have been shown to be sensitive markers of age-related cognitive decline among neurodegenerative conditions such as Alzheimer's disease and Parkinson's[19–21,55].

Cognitive functioning

Cognitive functioning was evaluated using the mini mental state examination (MMSE). The MMSE[65] assesses cognitive function in individuals 18–85. Participants respond to questions concerning orientation, registration, attention, calculation, and language[66,67]. It yields a total possible score of 30, with higher scores indicative of better cognitive functioning.

Executive functioning was assessed with the Behavioral Dyscontrol Scale-2nd Edition (BDS-2). The BDS-2[68] is a nine-item measure that evaluates motor behaviors requiring executive functioning. It includes tasks of working memory, motor learning, and behavioral inhibition, with strong reliability and validity[69,70]. It yields a total possible score of 27, with higher scores indicative of better executive functioning.

Statistical analysis

Data analyses were conducted using IBM SPSS Statistics version 28[71]. All language variables met assumptions for normality (p-values > 0.089) except for MLU ($p = 0.008$). MLU was log transformed to normalize the variable[72] (see Table 2).

Independent t-tests were completed to examine potential differences in sample characteristics between males and females. Males and females were matched on chronological age and education (p-values > 0.705; variance ratios < 0.238[73]). Age was associated with language variables ($rs < |.384|$, $ps < 0.044$) and was controlled in analyses. Education was not associated with language variables ($rs < |.307|$, $ps > 0.165$). Males and females did not significantly differ in *FMR1* CGG repeat length (long allele; $p = 0.130$), FXTAS symptom severity ($p = 0.453$), MMSE total score ($p = 0.211$), or BDS-2 total score ($p = 0.221$). Pearson Chi-square tests were used to examine rates of definite or probable FXTAS diagnoses between males and females, and indicated no significant differences $\chi^2 = 0.59$, $p = 0.445$; 66.7% M vs 80% F.

Relationships were observed between language variables in males and females (see Table 3), and subsequent analyses of group differences (research question 1) were completed using univariate analyses of covariance, controlling for chronological age. For research question 2, we conducted multivariable ordinal logistic regressions to assess whether language variables were predictive of FXTAS symptom severity. We conducted multivariable ordinary least squares regressions to assess the extent to which language variables predicted cognitive- (MMSE scores) and executive functioning (BDS-2 scores). In each regression model, we included sex and age as covariates. Regression diagnostics were completed using Cook's D based on the criteria $D > 4 = (1\text{-}k\text{-}n)$ and no outliers were observed (D-values < 0.14).

Results

Research question 1: To what extent do male and female premutation carriers differ in their language production?

No differences were observed between males and females in lexical diversity $F(1,30) = 0.22$, $p = 0.645$), semantic productivity $F(1,30) = 0.86$, $p = 0.363$, dysfluencies $F(1,30) = 0.23$, $p = 0.634$, syntactic complexity $F(1,30) = 0.46$, $p = 0.505$, or speech rate $F(1,30) = 0.59$, $p = 0.447$.

Language variable	Definition	Males $M(SD)$, Range	Females $M(SD)$, Range
Lexical diversity	Number of different words	212.10 (51.76), 117–298	216.90 (46.83), 106–287
Semantic productivity	Noun + verb rate per utterance	3.70 (.84), 2.25–5.33	3.35 (.97), 2.24–5.75
Dysfluency	Total dysfluencies[a]	41.90 (18.33) 15–86	39.20 (16.62) 20–76
Syntactic complexity	Mean length of utterance in morphemes[b]	11.57 (2.29), 7.08–17.87	10.96 (3.01), 7.24–18.53
Speech rate	Number of words/Time(s)*60	112.72 (31.52) 49.74–161.17	119.61 (26.15) 80.67–160.99

Table 2. Language characteristics among males and females with FXTAS symptoms. [a]Total dysfluencies are listed here for descriptive purposes. However, we used rate of dysfluencies per utterance in analyses to minimize differences due to language sample length. [b]Mean length of utterance was log transformed for analyses. The uncorrected data are reflected here.

Group	Language variable	Lexical diversity	Semantic productivity	Dysfluencies	Syntactic complexity
Males	Semantic productivity	.133			
$n = 21$	Dysfluencies	− .343	.634**		
	syntactic Complexity	.115	.880	.625**	
	Words per min	.906**	.052	− .226	.168
Females	Semantic Productivity	.379			
$n = 10$	Dysfluencies	− .217	.461		
	Syntactic complexity	.416	.960	.528	
	Words per min	.854**	.167	− .330	.158

Table 3. Correlations between language variables. **$p < .010$.

Research question 2: To what extent does language production predict FXTAS-associated symptoms?

FXTAS symptom stage

FXTAS symptom severity was predicted by lexical diversity (Estimate = − 0.023, Wald $\chi^2 = 6.43$, $p = 0.011$; pseudo $R^2 = 0.33$) and speech rate (Estimate = − 0.045, Wald $\chi^2 = 8.20$, $p = 0.004$; pseudo $R^2 = 0.38$; see Fig. 1), but not semantic productivity ($p = 0.951$), dysfluencies ($p = 0.266$), or syntactic complexity ($p = 0.952$).

Age was a significant predictor of FXTAS symptom severity in the model including dysfluencies ($p = 0.037$), but not in the models including lexical diversity, semantic productivity, syntactic complexity, or speech rate ($ps > 0.056$). Sex was not a significant predictor of FXTAS symptom severity in these models (p-values > 0.484).

Cognitive functioning

Overall cognitive functioning (i.e., MMSE scores) was predicted by lexical diversity ($b = 0.022$, $p < 0.001$; $R^2 = 0.50$), but not semantic productivity ($p = 0.166$), dysfluencies ($p = 0.467$), syntactic complexity ($p = 0.226$), or speech rate ($p = 0.642$).

Executive functioning (i.e., BDS-2 score) was predicted by lexical diversity ($b = 0.039$, $p = 0.008$; $R^2 = 0.28$; see Fig 2), dysfluencies ($b = -8.07$, $p = 0.036$, $R^2 = 0.20$), and speech rate ($b = 0.064$, $p = 0.006$; $R^2 = 0.29$), but not semantic productivity ($p = 0.604$), or syntactic complexity ($p = 0.561$). In models including language variables, sex and age were not significant predictors of cognitive- (p-values > 0.092) or executive functioning (p-values > 0.256).
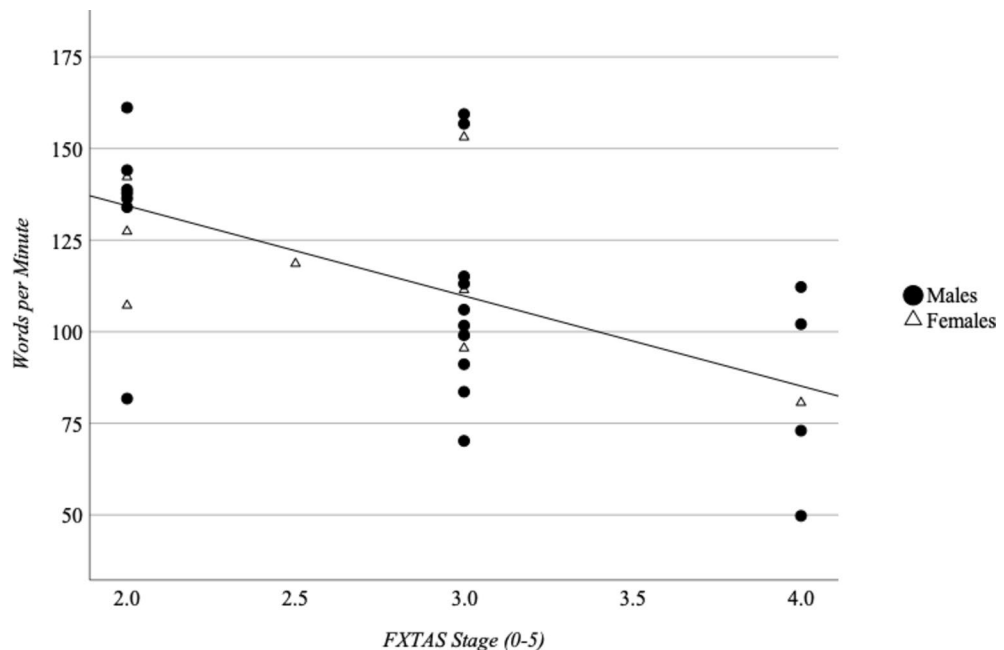

Fig. 1. Relationship between speech rate and FXTAS-associated symptoms. This figure represents the association between Words per Minute (i.e., speech rate) and predicted FXTAS Stage. FXTAS stage was rated from 0 (no symptoms) to 5 (definite and severe FXTAS symptoms). Fewer words per minute predicted greater FXTAS severity (Estimate = -.045, Wald $\chi^2 = 8.20$, $p = .004$; pseudo $R^2 = .38$), above and beyond the effects of age and sex.
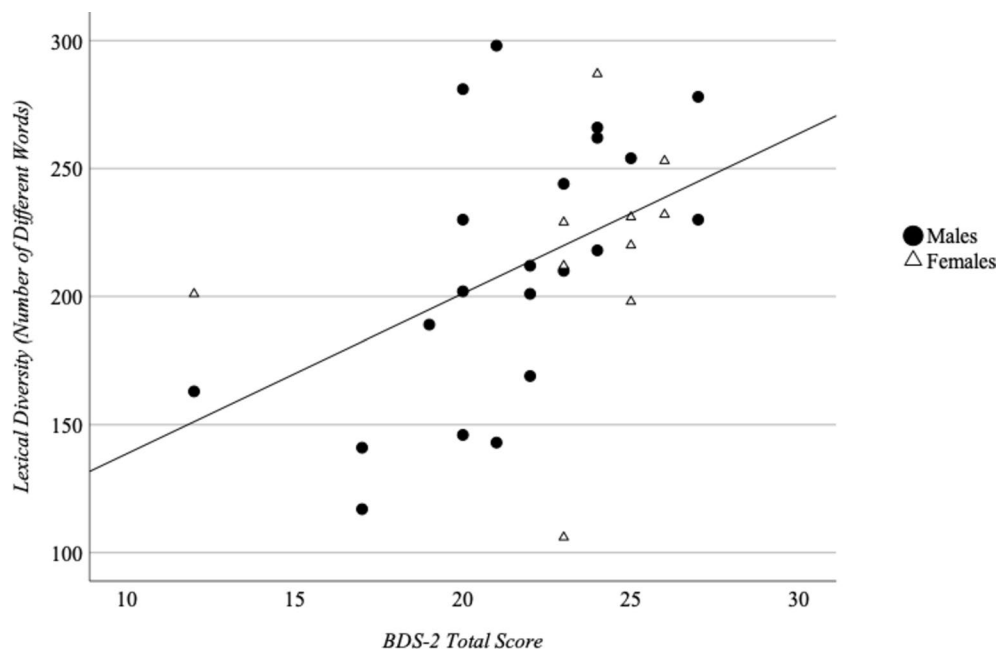
Fig. 2. Associations between executive functioning and lexical diversity. BDS-2: Behavioral Dyscontrol Scale -2nd edition. This figure represents the association between lexical diversity and executive functioning. Specifically, poorer executive functioning was predicted by lower rates of lexical diversity, above and beyond the effect of age and sex (b = .039, p=.008; R^2 = .28).

Discussion

This study explored language production among males and females with FXTAS symptoms using an open-ended language sampling procedure. Findings from this study demonstrated that males and females with FXTAS symptoms were similar in their lexical-semantics, syntax, dysfluencies, and speech rate. We identified associations between lexical diversity and speech rate with FXTAS severity and cognitive functioning. Poorer executive functioning was associated with increased rates of dysfluencies. These findings provide preliminary evidence that language production difficulties may co-occur with FXTAS-associated symptoms.

Males and females with FXTAS symptoms did not differ from one another in their language production patterns. Prior work suggested that males have more severe FXTAS-associated phenotypes than females[74]; however, language production does not appear to be differentially affected according to sex. Interestingly, males and females diverged in how their language features were interrelated, such that dysfluencies were associated with both semantic productivity and syntactic complexity; for females, no associations were observed between dysfluencies and other language domains. Dysfluencies are posited to reflect difficulties with word finding, sentence planning, discourse management, or inhibition[43,44,75]. Therefore, for male premutation carriers with FXTAS but not females, it is possible that dysfluencies may reflect semantic access or word retrieval processes in connected speech. Given that males and females had similar rates of dysfluencies, these findings potentially indicate divergent underlying influences on similar language expression.

Lower lexical diversity predicted increased FXTAS symptom severity and poorer cognitive and executive functioning, above and beyond the impact of age and sex. Prior work in female *FMR1* premutation carriers[29] found declines in word retrieval over time, measured in part by lexical diversity, and poorer word retrieval on the five-minute monologic task (used here), relative to a conversational language sample. These findings suggest that lexical diversity may provide insight into motor and cognitive declines associated with FXTAS, as has been observed in studies of Alzheimer's and Parkinson's[20]. Given these parallels, further studies including healthy aging controls and clinically-affected comparison groups (e.g., mild cognitive impairment, Alzheimer's, Parkinson's) are necessary to disambiguate these findings.

Findings from this study also demonstrate that higher rates of dysfluencies predicted poorer executive functioning. Prior work using the same language elicitation context identified associations between age and dysfluencies among asymptomatic female premutation carriers, but not in a comparison group, which was posited by the authors to reflect preclinical executive declines[27]. In that study, the mean dysfluency total for premutation carriers was 21.60; whereas in this study, mean dysfluencies in the full sample were 41.03 (using the same assessment), suggesting a potentially higher rate of dysfluencies associated with observable FXTAS symptoms in premutation carriers. It should be noted, however, that the present study did not include a control group of premutation carriers without FXTAS, limiting interpretability. Interestingly, prior work does suggest that in other related neurodegenerative conditions and in healthy aging, dysfluencies increase with age[19,75], a pattern not observed in this study. Taken together, these findings suggest that dysfluencies could precede or coincide with FXTAS-associated executive decline.

Lower speech rate (i.e., fewer words per minute) predicted greater FXTAS severity and poorer executive functioning. Speech rate may reflect two dimensions of language production: lexical-semantic access and motor speech coordination[55,76–80]. Extant literature suggests that speech rate among individuals with neurocognitive conditions may be lower than that of healthy controls, with average speech rate at ~1.7 words per second for frontotemporal lobar degeneration, 1.8 words per second for Alzheimer's, and 2.4 words per second among healthy controls[77]. A separate study found that individuals with Parkinson's spoke an average of ~1.6 words per second on a monologue task[55]. The present study found that individuals with FXTAS symptoms produced about 1.9 words per second (though analyses reflect words per minute), suggesting that FXTAS-associated speech rate may be similar to that observed in other neurodegenerative conditions. Given that FXTAS affects both cognitive and motor functioning, it is likely that speech rate reflects both lexical-semantic access and motor speech coordination. Further exploration into associations with neurological signals of FXTAS is warranted.

Without clear predictors of FXTAS, language may provide a window into the neural mechanisms associated with the condition. FXTAS is indicated in part by radiologic findings of white matter hyperintensities and/or the middle cerebellar peduncle sign[3,81,82]. The cerebellum has long been known to play a role in motor speech[83–85], including speech rate, and language production[86–91]. Notably, the middle cerebellar peduncle receives projections from multiple regions known to be involved in language production. Therefore, it will be crucial in future work to determine the extent to which cerebellar involvement in individuals with FXTAS impacts language production and associated cognitive changes.

Limitations and future directions

This study had a number of strengths, such as the inclusion of both males and females with symptoms of FXTAS, and a language analysis system commonly used in clinical settings. However, in addition to the small sample size, most participants had completed at least some college and self-identified as White. Education may predict FXTAS-associated outcomes[92], thus the inclusion of more participants from diverse educational and racial/ethnic backgrounds is necessary. This study did not include healthy aging controls, nor asymptomatic premutation carriers. Thus, we are not able to conclude definitively that the patterns observed are specific to FXTAS-associated symptoms. However, given that this study evaluated language comparably to other studies on the premutation, healthy controls, and related conditions, it is likely these findings reflect a pattern of language associated with FXTAS, rather than typical age-related processes. Finally, this study only included one language sampling context and did not include standard assessments of language, potentially limiting the ability to examine deviations from the norm. Future work should include a comprehensive battery of language assessments to better characterize the FXTAS-associated language phenotype.

Conclusions

This study evaluated language production in both males and females with symptoms of FXTAS in an open-ended language sampling context. Findings suggest no differences in language production between males and females but do point to co-occurring language patterns and FXTAS-associated symptoms. This work will set the stage for evaluation alongside related conditions, whereby patterns over time may distinguish FXTAS patients from those with similar neurodegenerative conditions (e.g., Alzheimer's, frontotemporal dementia, Parkinson's). Language production may also be a viable outcome measure in clinical trials of FXTAS.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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NM: Conceptualization, writing (first draft), analysis, interpretation; AS: Conceptualization, oversight of language transcription; ES: Data acquisition; RH: Conceptualization; oversight of data acquisition, interpretation, funding acquisition. All authors read and approved the final manuscript.

Competing interests

The authors declare no competing interests.

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