**Title:** Working Memory and Processing Speed Do Not Account for Reduced Sentence Processing Speed in Women with the *FMR1* Premutation

**Authors:** Thomas R. Christensen[[1]](#footnote-1), William Matchin1, Laura Friedman1, Jessica Klusek1

**Introduction:** The *FMR1* premutation is an X-linked genetic abnormality characterized by an expansion of 55-200 CGG repeats on the *FMR1* gene. The cognitive-linguistic profile in women with the *FMR1* premutation is characterized by deficits in executive function, working memory, and processing speed (Grigsby et al., 2014; Shelton et al., 2016; Yang et al., 2013) in addition to language deficits (Klusek et al., 2018, 2022). It is unclear if linguistic deficits in this population are secondary to deficits in other cognitive domains or if they reflect language-specific differences. This study aims to explore the role that working memory and processing speed play in sentence processing in women with the *FMR1* premutation using a self-paced reading paradigm. Understanding the clinical phenotype of language processing in women with the *FMR1* premutation can help us better understand the full range of cognitive processes that are impacted by the *FMR1* premutation and downstream influences on brain and behavior.

**Methods:** Participants included 76 women with an average age of 62 years (range 45-80; SD = 10), 48 of whom had the *FMR1* premutation and 28 were controls. The groups did not differ in age (*p* = .061), education (*p* = .669), or IQ (*p* = .064). To be included in the present study, participants needed to be a proficient English speaker, have normal or corrected to normal eyesight, and have an IQ of at least 80.

The self-paced reading task presented 48 sentences of high or low levels of syntactic complexity, followed by a comprehension question about the sentence. The participants progressed through the sentences at their own pace, phrase-by-phrase on a computer, with the reading time of each sentence region being recorded. Reading time at the relative clause region of the sentence and comprehension question accuracy were used as measures of sentence processing efficiency (Gordon & Lowder, 2012; Waters & Caplan, 2001), with reduced speed or accuracy suggesting deficits in sentence processing. Working memory was measured using the working memory index score of the Wide Range Assessment of Memory and Learning—Third Edition (Adams & Sheslow, 2021) and processing speed was measured using the NIH Toolbox pattern comparison test (Weintraub et al., 2013).

**Results:** In a linear mixed model controlling for age and education, the *FMR1* premutation group showed longer reading times than controls (*p* = .007, 95% CI [0.09,0.58]), indicating that women with the *FMR1* premutation show less efficient sentence processing. Additionally, sentences with high syntactic complexity showed longer reading times (*p* < .001, 95% CI [ 0.20, 0.75]) with no group-by-syntactic complexity interaction (*p* = .387). Group differences persisted after accounting for working memory and processing speed (*p* = .009, 95% CI [0.07, 0.48]), suggesting that differences in working memory and processing speed did not fully account for reduced sentence processing efficiency in women with the *FMR1* premutation. While working memory was a significant predictor of reading time (*p* < .001), processing speed was not (*p* = .183). Women with the *FMR1* premutation did not differ from controls in comprehension question accuracy (*p* = .843) Syntactic complexity showed lower comprehension accuracy (*p* < .001), but there was no group-by-syntactic complexity interaction (*p* = .797).

**Discussion**: Results show deficits in sentence processing in women with the *FMR1* premutation, which is consistent with other emerging evidence of language weaknesses in adult women who carry this genotype (Klusek et al., 2022; Sterling et al., 2013). Because working memory and cognitive processing speed did not fully explain deficits in sentence processing efficiency in this population, women with the *FMR1* premutation may have language-specific processing deficits. There is a need to examine risk for language-based disorders such as developmental language disorder and dyslexia in carriers of the *FMR1* premutation.

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1. Department of Communication Sciences and Disorders, Arnold School of Public Health, University of South Carolina [↑](#footnote-ref-1)