Introduction: The prevalence of the premutation of \textit{FMR1} is of considerable public health significance because carriers are at greatly increased risk of having a child with the full mutation of FXS. In addition, the premutation itself is associated with a range of emotional and physical problems that become increasingly evident in midlife and old age (Hagerman & Hagerman, 2002), including clinically significant emotional problems, primary ovarian insufficiency (FXPOI), and late-onset Parkinson-like neurological problems (Fragile X Tremor Ataxia Syndrome, or FXTAS). The prevalence of the premutation of the \textit{FMR1} gene in the US has not yet been established using epidemiological methods.

Methods: We calculated the prevalence of the premutation of \textit{FMR1} gene and of the "gray zone" using a population-based sample of older adults in Wisconsin (the Wisconsin Longitudinal Study, WLS). Using a high-throughput assay for exact sizing of the number of CGG repeats, we screened DNA from 6747 older adults (48.5% male). We also used WLS data to examine whether identified premutation carriers had elevated rates of symptoms associated with FXTAS or FXPOI, and children with disabilities.

Results: The prevalence of the premutation of the \textit{FMR1} gene was relatively high (1 in 167 females and 1 in 521 males for the premutation and 1 in 12 females and 1 in 21 males for the gray zone). Individuals with the premutation (n = 30, 7 males and 23 females) had a significantly higher rate of divorce than controls, as well as higher rates of symptoms that might be indicative of FXTAS (numbness, dizziness/faintness). Women were more likely to report going through or having gone through menopause than controls. Although not statistically significant (p = .07), premutation carriers were twice as likely as controls to have a child with a disability.

Discussion: To the best of our knowledge, this is the first population-level US study of the prevalence of premutation and gray zone expansions, and the second-largest study in the world literature of the prevalence of \textit{FMR1} expansions to include both males and females.

References:

Language Dysfluencies as a Measure of Executive Function in Premutation Carriers of Fragile X Syndrome

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Introduction: There is a growing body of evidence indicating a continuum of clinical impairment associated with the FMR1 gene, including age-related vulnerabilities in executive function and cognitive decline in premutation carriers (e.g., fragile X tremor/ataxia syndrome; FXTAS). Kogan and Cornish (2011) recently reported cognitive decline in respect to executive function (EF) and working memory in premutation males asymptomatic for FXTAS; however, there has been a lack of research on EF in female carriers. Language dysfluencies are a measure of executive function and have been noted in individuals with Parkinson's in the general population. The purpose of the current paper is to examine the language characteristics indicative of executive function in female premutation carriers of FXS.

Methods: Participants included 192 premutation female carriers of FXS ages 25 to 79 years (M 46 years). They completed a five-minute language sample. Mothers of children with autism (n 50), matched on maternal age and child residential status served as the control group. Interviews were transcribed using standard language transcription procedures, and analyzed for standard language measures including dysfluencies (e.g., repetitive speech, "I went I went to the store"), and the overall structure of language.

Results: After controlling for the amount of talk, we found that maternal age was significantly related to all of the measures of dysfluency (e.g., dysfluencies per utterance, r = .27***). The measures of dysfluencies as well as several other key language variables were related to biological variables associated with FXS (e.g., protein activation ratio and CGG repeat length). Maternal education was not related to any of the language variables. We completed a secondary analysis with the control group and a subset of the permutation carriers. The mothers with the permutation had a significantly more dysfluent pattern of language (F(1, 99) 5.60, p<.05). Maternal age was not significantly related to language dysfluencies in the mothers of children with autism, indicating a unique age effect in FXS.

Discussion: The most striking finding was the relationship between language dysfluencies and maternal age as well as biological variables associated with FXS (i.e., CGG repeat length and protein activation ratio). Given the relationship with maternal age, the language dysfluencies observed in this sample could be an indicator of decline in executive function abilities.

References:
Introduction: Mothers of children with FXS frequently are carriers of the premutation of the FMR1 gene. Premutation carriers were originally considered to be unaffected, but in recent years consensus has been growing that at least some premutation carriers display signs of impairment. FXS is now considered to be part of a multigenerational collection of clinical conditions including the Fragile X Tremor Ataxia Syndrome (FXTAS) and Premature Ovarian Insufficiency (POI). Less is known, however, regarding the extent to which premutation carriers are at risk for other types of health problems. The present study addressed this gap by investigating the frequency of daily health symptoms in premutation-carrier mothers of adolescents and adults with FXS in comparison to a nationally-representative sample of mothers whose children do not have disabilities and also to a group of mothers of individuals with autism spectrum disorders (ASD).

Methods: Participants were mothers of adolescents and adults with fragile X syndrome (FXS; n=112), mothers of similarly-aged children without disabilities (n=230), and mothers of adolescents and adults with ASD (n=96). Mothers were interviewed by telephone each evening for 8 consecutive days and reported health symptoms in the previous 24 hours, using an adapted version of the Larsen and Kasimatis (1991) symptom checklist.

Results: We used analysis of covariance (ANCOVA) to describe the daily health symptoms of premutation-carrier mothers of adolescents and adults with FXS in comparison to (a) mothers of individuals with ASD and (b) mothers of individuals without disabilities. Bonferroni post hoc multiple comparisons were used to determine the specific differences between the groups. Both mothers of a son or daughter with FXS and mothers of a son or daughter with ASD had a higher proportion of days with headaches, backaches, muscle soreness, fatigue, and hot flashes than mothers of children without disabilities. Both groups of caregiving mothers reported at least one health symptom on approximately three-fourths of days in the 8-day diary study, compared with about 50% of days for the mothers of children without disabilities (F(1, 433) = 31.25, p < .001).

Discussion: The present study documented elevated levels of daily health symptoms in premutation-carrier mothers of adolescents and adults with FXS and mothers of similarly-aged children with ASD, indicating a need for services that support the health and well-being of parents of children with disabilities across the life course.

References:

Introduction: Adults with developmental disabilities experience a wide range of difficulties in performing daily activities; some might encounter severe limitations in self-care and basic tasks necessary for independent living, while others have few limitations in these areas. Activities of Daily Living (ADLs) are considered durable indicators of activity limitations—consistent with the World Health Organization's dimensional framework for disability (WHO). ADL instruments have been used extensively in clinical applications and research. However, there is a paucity of freely-available and high quality tools for measuring activity limitations among adults with developmental disabilities. The purpose of this analysis is to describe the development of the Waisman Activities of Daily Living (W-ADL) Scale, and to thoroughly evaluate its measurement properties for adults with developmental disabilities.

Methods: This analysis utilized four well-characterized and longitudinally-studied groups of adults with developmental disabilities: 406 adults with autism; 147 adolescents and adults with fragile-X syndrome; 169 adults with Down syndrome, and 292 adults with intellectual disability. The 17 W-ADL items pertain to the target adult's current performance in daily activities such as grooming, bathing, running errands, and preparing meals. The performance of each activity is rated on a 3-point scale (0="does not do at all", 1="with help", 2="independent"), and summed to produce an overall score. W-ADL items were administered at the beginning of each study, and re-administered at several additional time points for adults with autism, Down syndrome, or intellectual disability. We evaluated the W-ADL according to an established set of quality criteria for the measurement properties of health status questionnaires (Terwee et al).

Results: Cronbach alphas for the W-ADL ranged from 0.88 to 0.94 in the four disability groups, and a single-factor structure was most parsimonious. We observed high reliability between consecutive time points with weighted kappas ranging from 0.92 to 0.93. Construct validity was supported through substantial associations between the W-ADL and the level of employment or degree-seeking education, maternally-reported need for respite services, maternal caregiving burden, and target adult IQ. Criterion validity was demonstrated with a correlation of 0.78 between the W-ADL and Vineland Screener among adults with autism. The W-ADL demonstrated no floor or ceiling effects in any of the four groups. Among adults with Down syndrome and intellectual disability, there were significant group differences in W-ADL scores by subjective maternal ratings of "mild", "moderate", "severe", and "profound" intellectual disability. We estimate that a 1-point change in W-ADL scores is detectable in samples of at least 35 people.

Discussion: The W-ADL exceeded the recommended threshold for each quality criterion we evaluated, and appears to have desirable measurement properties as a research instrument. Additional work is needed to evaluate its utility and applicability in different cultures and contexts. This freely-available tool has practical applications as an efficient measure of activities of daily living for research concerning adults with developmental disabilities.

References:
