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VERBAL INTELLIGENCE QUOTIENT (VIQ) IS ASSOCIATED WITH FMR1 REPEAT SIZE AND REPRODUCTIVE CYCLING CHARACTERISTICS IN WOMEN

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A CGG repeat sequence in the 5' UTR of the FMR1 gene leads to fragile X-associated disorders. Premutation alleles (55-200 unmethylated repeats) have been associated with ovarian insufficiency (FXPOI) and a late-onset tremor/ataxia syndrome (FXTAS). Several groups have reported neuropsychological deficits among carriers of the premutation, particularly among males with FXTAS. We have previously shown an effect of FMR1 repeat size on verbal intelligence quotient (VIQ) as measured by the Wechsler Adult Intelligence Scale – III (WAIS-III) among women between the ages of 18 and 50 years. We have confirmed this association, and expanded the model by including a variable for reproductive cycling characteristics in women. Subjects completed a neuropsychological test battery, a reproductive questionnaire, and provided a blood sample for hormone measurement. We have tested 232 women, and they have been categorized as having normal cycles (non-carriers n=48; premutation carriers n=52), irregular cycles (non-carriers n=43; premutation carriers n=44), and being menopausal (non-carriers n=4; premutation carriers n=41). In a linear regression model, repeat size, as a continuous variable, explained 4% of the variation in VIQ ($p = 0.002$), and reproductive status explained 3% of the variation in VIQ ($p=0.018$) after adjusting for age, race, and education. Upon examination of WAIS-III verbal index scores, Verbal Comprehension Index (VCI) and Working Memory Index (WMI), an association with repeat size and reproductive status ($p=0.001$ and $p=0.003$, respectively) was identified for the VCI, but not the WMI. Finally, we stratified the dataset by reproductive status and re-examined the model. A significant association with repeat size and VIQ was observed only among women with normal cycles, with 10% of the variance in VIQ being explained (p-value for repeat size=0.002). Hormone replacement did not affect these results. We will finalize hormone results to further define reproductive stage in the next series of tests. These findings will be presented.