

Abstract 30

PENETRANCE OF *FMR1* PREMUTATION ASSOCIATED PATHOLOGIES IN FRAGILE-X SYNDROME FAMILIES

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Within the past few years, there has been a significant change in identifying and characterizing the *FMR1* premutation associated phenotypes. The premutation has been associated with elevated *FMR1* mRNA levels and slight to moderate reductions in FMRP levels. Furthermore, it has been established that ~ 20% of female premutation carriers present primary ovarian insufficiency and that FXTAS occurs in one-third of all male premutation carriers older than 50 years. Besides primary ovarian insufficiency and FXTAS, new disorders have recently been described among individuals (especially females) with the *FMR1* premutation. Those pathologies include thyroid disease, hypertension, seizures, peripheral neuropathy, and fibromyalgia. However there are few reports related to FXTAS penetrance among female premutation carriers or regarding these disorders recently associated to the *FMR1* premutation. Therefore we have evaluated 398 fragile X syndrome families in an attempt to provide an estimation of the premutation associated phenotypes penetrance. Our results show that signs of FXTAS are detected in 16.5% of female premutation carriers and in 45.5% of premutated males older than 50 years. Furthermore, among females with the *FMR1* premutation, penetrance of primary ovarian insufficiency, thyroid disease and chronic muscle pain is 18.6%, 15.9% and 24.4%, respectively. The knowledge of this data might be useful for accurate genetic counselling as well as for a better characterization of the clinical phenotypes of *FMR1* premutation carriers.

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