

ABSTRACT:

Molecular and cognitive predictors of the continuum of autistic behaviours in fragile X

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The distributions of scores for autistic behaviours obtained from the Autism Diagnostic Observation Scale—Generic (ADOS-G) were investigated in 147 males and females affected with the full mutation in the fragile X mental retardation 1 (FMR1) gene, in 59 individuals with the premutation, and in 42 non-fragile X relatives, aged 4–70 years. The scores representing communication and social interaction were continuously distributed across the two fragile X groups, and they were significantly elevated compared with the non-fragile X controls. Strong relationships were found between both these scores and FMRP deficits, but they became insignificant for social interaction, and the sum of social interaction and communication scores, when FSIQ was included as another predictor of autism scores. Other significant predictors of these scores in both sexes were those executive skills which related to verbal fluency, and to the regulation and control of motor behaviour. Overall, our data have shown that cognitive impairment, especially of verbal skills, best explains the comorbidity of autism and fragile X. This implies some more fundamental perturbations of specific neural connections which are essential for both specific behaviours and cognition. We also emphasize that FXS offers a unique molecular model for autism since FMRP regulates the translation of many other genes involved in synaptic formation and plasticity which should be natural targets for further exploration.

Keywords: Fragile X; Autism spectrum; ADOS-G; Cognitive impairments; FMRP; Predictors of autism behaviours

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