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Original Article

Regulation of GABAA receptors by fragile X mental retardation protein

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Abstract: Fragile X syndrome (FXS) is caused by the loss of fragile X mental retardation protein (FMRP). The deficiency of GABAA receptors (GABAARs) is implicated in FXS. However, the underlying mechanisms remain unclear. To investigate the effect of FMRP on GABAARs, we transfected FMRP cDNAs in rat cortical neurons. We measured the protein expression of GABAARs and phosphatase PTEN, and recorded GABAAR-mediated whole-cell currents in the transfected neurons. We show that the transfection of FMRP cDNAs causes increased protein expression of GABAARs in cortical neurons, but GABAAR-mediated whole-cell currents are not potentiated by FMRP transfection. These results suggest the possibility that intracellular signaling antagonizing GABAAR activity may play a role in inhibiting GABAAR function in FMRP-transfected neurons. We further show that FMRP transfection results in an enhanced protein expression of PTEN, which contributes to the inhibition of GABAAR function in FMRP-transfected neurons. These results indicate that GABAARs are regulated by FMRP through both an up-regulation of GABAAR expression and a PTEN enhancement-induced inhibition of GABAAR function, suggesting that an abnormal regulation of GABAAR and PTEN by the loss of FMRP underlies the pathogenesis of FXS. (IJPPP1307006).

Keywords: Fragile X syndrome, fragile X mental retardation protein, GABAA receptor, PTEN

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