# Mechanism may explain aspects of brain impairment seen in Fragile X Syndrome

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Scientists report that a protein associated with a common form of mental retardation plays an important role in intracellular trafficking within neurons. The research, published by Cell Press in the June issue of the journal *Developmental Cell*, reveals new information about how neuronal communication and plasticity are affected in Fragile X Syndrome (FXS).

FXS is a highly prevalent form of inherited mental impairment that also contributes to autism spectrum disorders. Most people with fragile X have a mutation that interferes with production of fragile X mental retardation protein (FMRP). FMRP binds to certain messenger RNAs (mRNAs), molecules that serve as chemical blueprints for production of proteins. Although FMRP targets mRNAs known to be critical for neuronal development and plasticity, exactly how FMRP influences these mRNAs was not well understood.

Neurons extend tendrils called "dendrites" outward from the main body of the cell so that they can communicate with other neuronal cells. These sites of communication, called "synapses", are important for learning and memory. Many neurons normally respond to stimuli, including synaptic signals from other neurons, by shunting certain key mRNAs to their dendrites. Study author Dr. Jason Dictenberg from City University of New York and colleagues, including Dr. Gary J. Bassell from Emory University, used high resolution fluorescence imaging methods in cultured neurons from embryonic mouse brain to explore how FMRP affects the intracellular localization of several target mRNAs in response to neuronal stimulation.

The researchers found that neurons lacking FMRP could not properly traffic mRNAs in response to stimuli. FMRP appeared to act as an adaptor for motor molecules involved in mRNA transport. Importantly, acute suppression of FMRP transport in normal neurons resulted in both diminished mRNA transport and a significant increase in the length and number of dendritic outgrowths called spine protrusions. This phenotype is similar to what is seen in the mouse model and in humans with FXS.

These results suggest that defects in stimulus-induced synaptic localization of FMRP target mRNAs may make a significant contribution to the synaptic and cognitive defects observed in FXS. "The present study has identified several key FMRP targets that are dysregulated in dendrites and may provide insight into new therapeutics for the treatment of FXS that target the mRNA localization pathway and its signaling components," concludes Dr. Bassell.

Source: Cell Press