

**Title:** Fragile X related protein 1 localizes to large dendritic spines in the hippocampus

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**Abstract:** In response to synaptic activity, several new proteins are synthesized in dendrites. These proteins are required for long-lasting changes in synaptic strength and spine size and likely allow for synaptic modifications that are important for learning and memory. Fragile X Related Protein 1 (FXR1P) controls mRNA translation in the cytoplasm of non-neuronal cells. We previously showed that FXR1P is expressed in the developing hippocampus and localizes to a subset of spines in pyramidal neurons. However, it is not yet known whether FXR1P regulates mRNA translation in neurons and whether this regulation can occur locally in dendrites and at dendritic spines. We hypothesized that if FXR1P controls protein synthesis at spines, then overexpressing FXR1P might lead to a change in spine size. To test this hypothesis, we used biolistic transfection to introduce FXR1P tagged with green fluorescent protein and membrane targeted red fluorescent protein (RFPf) into CA1 pyramidal cells in mouse hippocampal slices. We imaged RFPf signals from dendrites expressing FXR1P and control dendrites to compare spine density, shape and size. We found that neurons expressing FXR1P were similar in overall spine density, shape and size to control dendrites. Further analysis on spines from FXR1P overexpressing dendrites showed that FXR1P localized to spines that were on average larger than spines lacking FXR1P. These spines may be those that require ongoing protein synthesis to maintain their size and synaptic strength. Taken together our findings suggest that FXR1P controls mRNA translation at these large spines.

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