Fragile X syndrome (FXS) is the most commonly inherited form of mental impairment and autism. Current understanding of the molecular and cellular mechanisms underlying FXS symptoms is derived mainly from studies on the hippocampus and cortex. However, FXS is also associated with strong emotional symptoms, which are likely to involve changes in the amygdala. Unfortunately, the synaptic basis of amygdalar dysfunction in FXS remains largely unexplored. Here we describe recent findings from mouse models of FXS that have identified synaptic defects in the basolateral amygdala that are in many respects distinct from those reported earlier in the hippocampus. Long-term potentiation and surface expression of AMPA-receptors are impaired. Further, presynaptic defects are seen at both excitatory and inhibitory synapses. Remarkably, some of these synaptic defects in the amygdala are also amenable to pharmacological rescue even after the disease has had months to leave its mark in the adult brain. These results also underscore the need to modify the current hippocampus-centric framework to better explain FXS- synaptic dysfunction in the amygdala.

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