J Neurosci. 2011 Oct 19;31(42):14871-81. doi: 10.1523/JNEUROSCI.3782-11.2011.

Effects of elevation of brain magnesium on fear conditioning, fear extinction, and synaptic plasticity in the infralimbic prefrontal cortex and lateral amygdala

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PMID: 22016520 PMCID: PMC6623582 DOI: 10.1523/JNEUROSCI.3782-11.2011

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Abstract

Anxiety disorders, such as phobias and posttraumatic stress disorder, are among the most common mental disorders. Cognitive therapy helps in treating these disorders; however, many cases relapse or resist the therapy, which justifies the search for cognitive enhancers that might augment the efficacy of cognitive therapy. Studies suggest that enhancement of plasticity in certain brain regions such as the prefrontal cortex (PFC) and/or hippocampus might enhance the efficacy of cognitive therapy. We found that elevation of brain magnesium, by a novel magnesium compound [magnesium-l-threonate (MgT)], enhances synaptic plasticity in the hippocampus and learning and memory in rats. Here, we show that MgT treatment enhances retention of the extinction of fear memory, without enhancing, impairing, or erasing the original fear memory. We then explored the molecular basis of the effects of MgT treatment on fear memory and extinction. In intact animals, elevation of brain magnesium increased NMDA receptors (NMDARs) signaling, BDNF expression, density of presynaptic puncta, and synaptic plasticity in the PFC but, interestingly, not in the basolateral amygdala. In vitro, elevation of extracellular magnesium concentration increased synaptic NMDAR current and plasticity in the infralimbic PFC, but not in the lateral amygdala, suggesting a difference in their sensitivity to elevation of brain magnesium. The current study suggests that elevation of brain magnesium might be a novel approach for enhancing synaptic plasticity in a regional-specific manner leading to enhancing the efficacy of extinction without enhancing or impairing fear memory formation.

Figures