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


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.


Kalzium ist nicht alles.

Bush AI.

Source

Mental Health Research Institute, 155 Oak Street, Parkville, Victoria 3052, Australia.
abush@mhri.edu.au

Abstract

Elevation of cerebral Mg2+ with a novel orally delivered ionophore, magnesium threonate, enhances cognition in young and old rats over a 12-24 day treatment interval, as outlined in a paper by Slutsky et al. in this issue of Neuron. Despite both Mg2+ and Zn2+ blocking the NMDA receptor channel, sustained extracellular Mg2+ elevation mimics sustained synaptic Zn2+ concentrations by increasing hippocampal NR2B expression and bouton density.


Enhancement of learning and memory by elevating brain magnesium.


Source

Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA 02139, USA.
Abstract
Learning and memory are fundamental brain functions affected by dietary and environmental factors. Here, we show that increasing brain magnesium using a newly developed magnesium compound (magnesium-L-threonate, MgT) leads to the enhancement of learning abilities, working memory, and short- and long-term memory in rats. The pattern completion ability was also improved in aged rats. MgT-treated rats had higher density of synaptophysin-/synaptobrevin-positive puncta in DG and CA1 subregions of hippocampus that were correlated with memory improvement. Functionally, magnesium increased the number of functional presynaptic release sites, while it reduced their release probability. The resultant synaptic reconfiguration enabled selective enhancement of synaptic transmission for burst inputs. Coupled with concurrent upregulation of NR2B-containing NMDA receptors and its downstream signaling, synaptic plasticity induced by correlated inputs was enhanced. Our findings suggest that an increase in brain magnesium enhances both short-term synaptic facilitation and long-term potentiation and improves learning and memory functions.


The role of the medial prefrontal cortex-amygdala circuit in stress effects on the extinction of fear.
Akirav I, Maroun M.

Source
Department of Psychology, The Brain and Behavior Research Center, University of Haifa, Haifa 31905, Israel.
Abstract
Stress exposure, depending on its intensity and duration, affects cognition and learning in an adaptive or maladaptive manner. Studies addressing the effects of stress on cognitive processes have mainly focused on conditioned fear, since it is suggested that fear-motivated learning lies at the root of affective and anxiety disorders. Inhibition of fear-motivated response can be accomplished by experimental extinction of the fearful response to the fear-inducing stimulus. Converging evidence indicates that extinction of fear memory requires plasticity in both the medial prefrontal cortex and the amygdala. **These brain areas are also deeply involved in mediating the effects of exposure to stress on memory.** Moreover, extensive evidence indicates that gamma-aminobutyric acid (GABA) transmission plays a primary role in the modulation of behavioral sequelae resulting from a stressful experience, and may also partially mediate inhibitory learning during extinction. In this review, we present evidence that exposure to a stressful experience may impair fear extinction and the possible involvement of the GABA system. Impairment of fear extinction learning is particularly important as it may predispose some individuals to the development of posttraumatic stress disorder. We further discuss a possible dysfunction in the medial prefrontal cortex-amygdala circuit following a stressful experience that may explain the impaired extinction caused by exposure to a stressor.