Signaling through cGMP-dependent protein kinase I in the amygdala is critical for auditory-cued fear memory and long-term potentiation.

Abstract:
Long-term potentiation (LTP) of inputs relaying sensory information from cortical and thalamic neurons to principal neurons in the lateral amygdala (LA) is thought to serve as a cellular mechanism for associative fear learning. Nitric oxide (NO), a messenger molecule widely implicated in synaptic plasticity and behavior, has been shown to enhance LTP in the LA as well as consolidation of associative fear memory. Additional evidence suggests that NO-induced enhancement of LTP and amygdala-dependent learning requires signaling through soluble guanylyl cyclase (sGC) and cGMP-dependent protein kinase (cGK). Mammals possess two genes for cGK: the prkg1 gene gives rise to the cGK type I isoforms, cGK\textalpha{} and cGK\textbeta{}, and the prkg2 gene encodes the cGK type II. Reportedly, both cGKI and cGKII are expressed in the amygdala, and cGKII is involved in controlling anxiety-like behavior. Because selective pharmacological tools for individual cGK isoforms are lacking, we used different knock-out mouse models to examine the function of cGKI and cGKII for LTP in the LA and pavlovian fear conditioning. We found robust expression of the cGKI specifically in the LA with cGK\textbeta{} as the prevailing isoform. We further show a marked reduction of LTP at both thalamic and cortical inputs to the LA and a selective impairment of auditory-cued fear memory in
cGKI-deficient mutants. In contrast, cGKI null mutants lack these phenotypes. Our data suggest a
function of cGKI, likely the beta isoform, in the LA, supporting synaptic plasticity and consolidation of
fear memory.