Abstract

Sleep deprivation alters the functions of hippocampus and amygdala at several molecular and cellular levels that may affect memory formation. Recent studies have indicated that leptin could cross the blood-brain barrier to regulate synaptic plasticity in the hippocampus by inhibiting PTEN signaling and facilitating spatial memory. Indeed, sleep deprivation reduced the level of leptin and resulted in fear contextual memory impairment. Therefore, whether sleep deprivation induced fear memory impairment is due to reduction of leptin and dis-inhibition of PTEN signaling needs to be clarified. In this study, we investigated the effect of leptin on the sleep deprivation-induced cognitive deficit. Mice were subjected to 24 hr sleep deprivation after fear conditioning in small platform water tank. We found that sleep deprivation resulted in both cue and contextual fear memory impairment. In parallel, surfaced GluR1 and GluR2 were reduced in amygdala after sleep deprivation. Furthermore, intraperitoneal injection of leptin to sleep-deprived mice rescued fear memory impairment and reversed surface AMPA receptor reduction. Using whole cell recording to evaluate the synaptic function of the central amygdala (CeA), we found decreased frequency spontaneous and miniature EPSC in sleep-deprived mice. Besides, the AMPA/NMDA ratio and paired-pulse ratio were also decreased. These results indicate that both pre- and post-synaptic functions were changed in
sleep-deprived mice and leptin could rescued fear memory impairment and reversed surface AMPA receptor reduction.