Reversal of sleep deprivation-induced cognitive deficit by leptin supplementation

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Introduction

REM 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 REM sleep deprivation reduced the level of leptin and resulted in spatial memory impairment. Leptin is a peptide hormone secreted by adipocytes. It has been reported that leptin could cross the blood-brain barrier to regulate synaptic plasticity in the hippocampus by inhibiting PTEN signaling and facilitating spatial memory. Therefore, whether REM sleep deprivation induced fear memory impairment is due to reduction of leptin and dis-inhibition of PTEN signaling in amygdala needs to be clarified.

Methods

• Animal: Male C57BL/6 mice (8–10 weeks)
• Behavior:
  • Fear training
  • Western Blot
• Electrophysiology: Whole cell recording

Results

1. REM sleep deprivation impaired consolidation of fear memory.

2. Leptin restored REMD-induced impairment of fear memory.

3. No difference in body weight and locomotion after leptin supplement.

4. The alteration of surfaced GluR1 in REMD group could be rescued by leptin.

5. Decreased both frequency and amplitude of miniature excitatory postsynaptic currents (mEPSCs) in the lateral amygdala (LA) neurons in the REM sleep deprivation mice and was reversed by leptin supplement.

6. REM sleep deprivation decreased AMPA/NMDA ratio in the LA neurons and could be rescued by leptin supplement.

7. Leptin rescued EPSC amplitude are associated with increased rectification of AMPA receptors in REM sleep deprivation mice.

8. Leptin did not reverse the paired-pulse ratio (PPR) which was increased after REM sleep deprivation in LA neurons.

9. Leptin restored fear memory via affection of PTEN-Akt-GSK 3β signaling.

Conclusion

REM sleep deprivation resulted in both cue and contextual fear memory impairment by decrease surface GluR1 expression. Furthermore, we used whole cell recording and found that both pre- and post-synaptic functions were changed in REM sleep-deprived mice. Intraperitoneal injection of leptin could only rescued the observed post-synaptic changes via affection of PTEN-Akt-GSK 3β signaling. We suggested that leptin reversed REMD-induced fear memory impairment via enhancing AMPA receptor insertion. Our results indicated that leptin may contribute to sleep disorder-induced cognitive dysfunction.