Title: Paradoxical sleep deprivation in rats causes a selective reduction in the expression of type-2 metabotropic glutamate receptors in the hippocampus

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<AT>Paradoxical sleep deprivation in rats causes a selective reduction in the expression of type-2 metabotropic glutamate receptors in the hippocampus

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<ABS-Head><ABS-HEAD>Graphical abstract

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<ABS-HEAD>Abstract

<ABS-P>Paradoxical sleep deprivation in rats is considered as an experimental animal model of mania endowed with face, construct, and pharmacological validity. We induced paradoxical sleep deprivation by placing rats onto a small platform surrounded by water. This procedure caused the animal to fall in the water at the onset of REM phase of sleep. Control rats were either placed onto a larger platform (which allowed them to sleep) or maintained in their home cage. Sleep deprived rats showed a substantial reduction in type-2 metabotropic glutamate (mGlu2) receptors mRNA and protein levels in the hippocampus, but not in the prefrontal cortex or corpus striatum, as compared to both groups of control rats. No changes in the expression of mGlu3 receptor mRNA levels or mGlu1α and mGlu5 receptor protein levels were found with exception of an increase in mGlu1α receptor levels in the striatum of SD rats. Moving from these findings we treated SD and control rats with the selective mGlu2 receptor enhancer, BINA (30 mg/kg, i.p.). SD rats were also treated with sodium valproate (300 mg/kg, i.p.) as an active comparator. Both BINA and sodium valproate were effective in reversing the manic-like phenotype evaluated in an open field arena in SD rats. BINA treatment had no effect on motor activity in control rats, suggesting that our findings were not biased by a non-specific motor-lowering activity of BINA. These findings suggest that changes in the expression of mGlu2 receptors may be associated with the enhanced motor activity observed with mania.

<KWD>Keywords: paradoxical sleep deprivation; mGlu2 receptor; motor activity; BINA.

<H1>1. Introduction