Hypnotic effects of a novel adenosine transporter inhibitor on caffeine-induced insomnia in mice

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Abstract

Objective: Insomnia is a global health issue bothering many people. Current hypnotics are mainly targetting on the benzodiazepine binding site of the γ-aminobutyric acid type A ($GABA_A$) receptors. However, the potential adverse effects of these benzodiazepine-based hypnotics cannot be ignored. Meanwhile, adenosine, an intrinsic sleep promoter within the brain, can be a potential mechanism for developing the novel hypnotics. Our study aims to evaluate the effect of a novel adenosine transporter inhibitor on sleep disruption. We hypothesized that this inhibitor can block the effects of caffeine-induced insomnia.

Methods: In our study, we used an in vivo electrocorticogram (ECoG) to record 24-hour brain wave activities. The low-dose caffeine (10 mg/kg) and the high-dose caffeine (20 mg/kg) intraperitoneal injection was performed 10-15 minutes before the light onset to induce insomnia. Three different dosages (1, 6, and 12 mg/kg) of the adenosine transporter inhibitor were administrated 3 hours before the light onset.

Results: In our experiments, we evaluated three different dosages (1, 6, and 12 mg/kg) of the adenosine transporter inhibitor under the low-dose caffeine and the high-dose caffeine injection. In the low-dose caffeine injection, our results revealed that all three inhibitor dosages could reverse immediate insomnia; in the high-dose caffeine injection, although unable to reverse immediate insomnia, three dosages increased the sleep amount during the sleep rebound after immediate insomnia. These results showed the hypnotic effect of the novel adenosine transporter inhibitor.

Conclusion: Our current results suggest that the novel adenosine transporter inhibitor can be a potential hypnotic.