## Abstract

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## Vitamin B12 affects non-photic entrainment of circadian locomotor activity rhythms in mice.

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**BACKGROUND**: Administration of vitamin B12 (VB12) has been reported to normalize human sleep-wake rhythm disorders such as non-24-h sleep-wake syndrome (HNS), delayed sleep phase syndrome (DSPS) or insomnia. However, the mechanisms of the action of VB12 on the rhythm disorders are unknown.

**OBJECTIVE**: In the present study, therefore, effects of VB12 on circadian rhythms of locomotor activity were examined in mice.

**METHODS**: In the first experiment, CBA/J mice were maintained under continuous light condition (LL) or blinded, and after free-running rhythms became stable, the mice were intraperitoneally injected with either VB12 or saline at a fixed time every day.

**RESULTS**: In all the mice with tau > 24 h, saline injections resulted in entrainment of circadian rhythms, whereas not all the mice with tau < 24 h entrained to the injection. In contrast to saline injections, VB12 injections did not always induce entrainment and about half of the mice with tau > 24 h free-ran during the injection. In the second experiment, the amount of phase advances of circadian rhythms induced by a single injection of saline at circadian time (CT) 11 under LL was compared between the mice with and without VB12 silastic tubes.

**CONCLUSIONS**: The results showed that the amplitude of phase advances was smaller in the mice with VB12 than those without VB12. In the third experiment, daily injections of saline were given to the mice with VB12 silastic tubes maintained under LL. In this chronic treatment of VB12 as well, attenuating effects of VB12 on saline-induced entrainment were observed. These results suggest that VB12 affects the mechanisms implicated in non-photic entrainment of circadian rhythms in mice.

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