

The role of hypocretin in footshock stress-induced REM sleep suppression

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Objective: To elucidate the involvement of hypocretin (hcr) projections from the lateral hypothalamic area (LHA) to locus coeruleus (LC), and dorsal raphe nucleus (DRN), and the sleep alterations when rats received an inescapable footshock stimulation (IFS).

Methods: Male Sprague-Dawley rats (250 - 300 g; BioLASCO, Taiwan) were used in present study. The IFS consisted of twelve times of electrical stimuli (5.0 mA, 133 V, and 50 ms of duration for each stimulation), which were randomly given within 10-min period. The sleep-wake activity was recorded for 24 hours. To clarify the involvement of hcr in stress-induced sleep alterations, a high dose (2.5 µg) and a low dose (1.25 µg) of hypocretin receptor (hcrR) antagonist, TCS-1102, were directly microinjected into the DRN and LC. In the other groups of rats, the brain tissues were collected at three different zeitgeber times (ZT), ZT0, ZT1, and ZT2 after rats received the IFS, and the expression of prepro hypocretin (prepro-hcr), hypocretin 1 (hcr-1), and c-fos at LHA were determined after the IFS.

Results: The IFS suppressed rapid eye movement (REM) sleep during the first 6 hours of the light period; however, a compensatory REM sleep enhancement appeared during the subsequent dark period. Administration of hcrR antagonist TCS-1102 into the LC and DRN blocked the IFS-induced REM sleep alterations. Immunoreactive cells of prepro-hcr and hcr-1 were increased in the LHA after the IFS. Cells expressing both prepro-hcr and hcr-1 were increased from 12,003 to 13,640 at ZT0; from 11,049 to 11,932 at ZT1; and from 12,929 to 16,323 at ZT2. We also found that the IFS increased c-fos expression in the LHA; however, there are more c-fos expressing neurons beyond the hcr-1 expressing neurons.

Conclusion: Our results indicate that the IFS activated the neurons in the LHA, increased the expression of prepro-hcr, and increased the cleavage of prepro-hcr to hcr-1. The IFS suppressed REM sleep and this REM sleep suppression was blocked when hcrR antagonist was administered into the LC or DRN, suggesting the involvement of hcr projections from LHA to LC and DRN in the stress-induced REM suppression.

中文題目：食慾肽對足刺激所引起快速動眼期睡眠減少之影響

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