

ABSTRACT OF DISSERTATION

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| Title | Dual orexin receptor antagonist drug suvorexant can help in amelioration of predictable chronic mild stress-induced hyperalgesia (デュアルオレキシン受容体拮抗薬であるスボレキサントは軽度な慢性ストレスが誘発する痛覚過敏を改善する) |
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| <p>Aims:</p> <p>This study aimed to evaluate the involvement of the orexin system in predictable chronic mild stress (PCMS) and the effects of suvorexant, a dual orexin receptor antagonist, on nociceptive behavior in PCMS.</p> <p>Materials and methods:</p> <p>Male C57BL/6 J mice were separated into various PCMS groups: a control group with sawdust on the floor of the rearing cage (C), a group with mesh wire on the floor (M), and a group with water just below the mesh wire (W). Activation of lateral hypothalamic orexin neurons was assessed using immunofluorescence. In another experiment, half of the mice in each group were administered an intraperitoneal injection of suvorexant (10 mg/kg), and the remaining mice were injected with the same amount of vehicle (normal saline). Thermal hyperalgesia was examined using tail immersion and hot plate tests, while mechanical hyperalgesia was investigated using the tail pinch test after 21 days of PCMS.</p> <p>Key findings:</p> <p>Animals subjected to PCMS showed an increased percentage of activated orexin neurons in the lateral hypothalamic region after 21 days. Mice raised in the PCMS environment showed increased pain sensitivity in several pain tests; however, the symptoms were significantly reduced by suvorexant</p> | |

administration.

Significance:

The findings revealed that PCMS activates hypothalamic orexin neuronal activity, and the use of suvorexant can help attenuate PCMS-induced thermal and mechanical hyperalgesia.