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2. **Title**

   Mechanism Analysis of Alleviation Effect of Neuropathic Pain Involved in Central Nicotinic Receptors.

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4. **Summary**

Nicotinic acetylcholine receptors (nAChRs) expressed in the ventral posterolateral (VPL) thalamic nucleus involve in antinociceptive effects. In the present study, we aimed to elucidate mechanism of antinociceptive effect involved in nAChRs expressed in the VPL nucleus. Temporal changes in concentration of various neurotransmitters in the VPL nucleus after 5IA, a nAChR agonist, administration were measured by in vivo microdialysis method. In vivo microdialysis examination revealed that the concentration of serotonin (5-HT) and taurine in dialysates significantly increased in a concentration-dependent manner of 5IA. Although 10 nmol of 5IA did not affect the concentration of GABA in dialysates, 50 nmol of 5IA induced significant increase in GABA concentration. Involvement of 5-HT, taurine, and GABA in anti-allodynic effects was examined in a rat model of neuropathic pain. Co-administration of methysergide, a 5-HT receptor antagonist, with 5IA intra-VPL inhibited the anti-allodynic effect of 5IA in a dose-dependent manner. Co-administration of bicuculline, a $GABA_A$ receptor antagonist, with taurine or 5IA intra-VPL also inhibited the anti-allodynic effect of taurine or 5IA in a dose-dependent manner. Based on these findings, the following mechanism could be proposed: (1) Increase in 5-HT, taurine, and GABA release by activation of nAChRs expressed in the VPL, (2) Expression of the anti-allodynic effect by 5-HT bound to 5-HT receptors, and taurine and GABA bound to $GABA_A$ receptors..