

DSIP の抗侵害作用の作用機序
1. 内因性オピオイド系の関与について

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ENDOGENOUS SLEEP FACTORS

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**THE MECHANISM OF ANTINOCICEPTIVE EFFECTS OF DSIP
I : INVOLVEMENT OF ENDOGENOUS OPIOID SYSTEMS**

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ABSTRACT DSIP produced antinociceptive effects in both the mouse and the rat. I.c.v. and i.cist. injections of DSIP were, but i.t. injection was not, effective in the tail-pinch and hotplate tests. This shows the site(s) of antinociceptive action of DSIP to locate in the supra-spinal regions. These DSIP-induced antinociceptive effects were antagonized with naloxone pretreatment and showed cross-tolerance with morphine, suggesting that the endogenous opioid system(s) plays an important role in modulating the antinociceptive action of DSIP. We further investigated on the action of DSIP on opioid receptor(s). DSIP did not have a binding ability to any subtypes of the opioid receptor. In superfusion experiments, DSIP at doses of 1 pM - 100 pM significantly increased the release of Met-enk from superfused slices of the rat lower brainstem. These results demonstrate that Met-enk releasing effect of DSIP in the lower brainstem is one of possible mechanisms of the antinociceptive effect of DSIP. In addition, the lower brainstem is related to sleep induction. Coupled with the naloxone-reversible sleep-inducing effect of DSIP, Met-enk, released in the lower brainstem by DSIP, may therefore, play an important role in the induction of sleep.

抄録 DSIP は, 内因性睡眠物質候補として, 1977年に発見された。この物質には, 睡眠誘発作用の他にも多くの生理作用があることが報告されてきた。我々も, DSIP に抗侵害作用があることを発見し, その作用機序を追究してきた。本研究において, DSIP の抗侵害作用は, オピオイド拮抗薬である Naloxone で拮抗されることから, DSIP のこの作用には内因

性オピオイド系が関与していること、DSIPは直接オピオイドレセプターに対し Agonist として働くのではなく、中枢 Met-Enkephalin (Met-Enk) 含有神経に作用し、Met-Enk 含有神経から Met-Enk を遊離することにより遊離 Met-Enk を介して抗侵害作用を示すことを明らかにした。