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ANTINOCICEPTIVE EFFECT FOLLOWING PERIPHERAL ADMINISTRATION
OF ADENOSINE ANALOGS IN THE FORMALIN TEST IN MICE.

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Abstract. The aim of the present study was to investigate the effects of peripheral administration of R-PIA and NECA on a persistent pain stimulus using the formalin test. Both compounds significantly reduced licking activity.

Adenosine administered intravenously to humans have been reported to induce pain e.g. angina pectoris-like pain (1), epigastric pain (2) and headache, backache and pain in arms and legs (3). Adenosine analogs on the other hand have been shown to possess antinociceptive effects after peripheral and intrathecal administration in rats and mice (4,5,6). The methods used to test nociceptive response have mainly consisted of the tail flick, tail immersion or the hot plate test (4,5,6). These tests use heat to provoke an escape reaction which is expressed as the latency of the nociceptive reflex response. The aim of the present study was to investigate the effects of peripheral administration of two adenosine receptor agonists, R-PIA and NECA, on a persistent pain stimulus.

Male NMRI-mice weighing 18-21 gram were used. The formalin test was used basically as described by Hunskaar and Hole (7,8), with the only difference being that we injected the test substance mixed with the formalin solution. 20 µl of 1% formalin in 0.9% saline with or without was injected subcutaneously into the dorsal hind paw. The time the mouse spent licking the injected paw or leg during the first 5 minutes was recorded. The Wilcoxon rank sum test was used to evaluate statistical differences.

Following injection of 1% formalin the licking activity lasted 114 sec. NECA induced a significant dose dependent reduction of licking activity to 65 sec in the

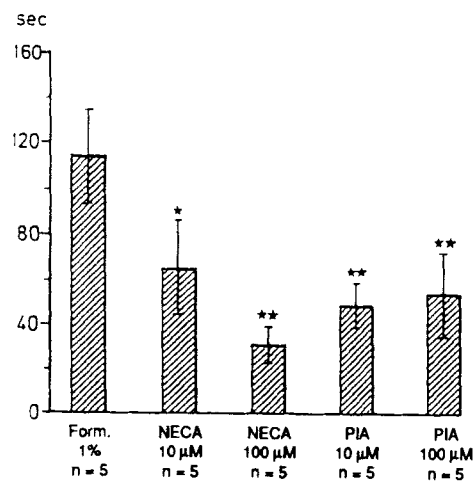


FIG.1 Formalin test after administration of NECA and R-PIA. Values are presented as means \pm SD. * $p < .05$ ** $p < .01$

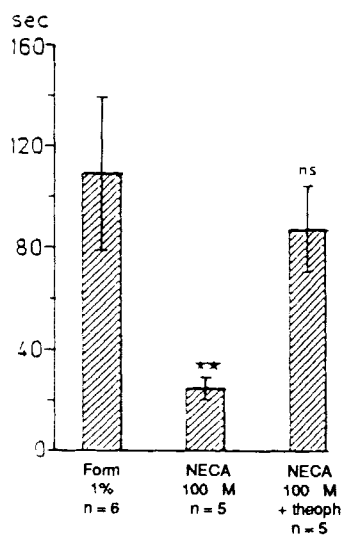


FIG.2 Formalin test. Pretreatment with theophylline. Values are presented as means \pm SD. ** $p < .01$

group receiving 10 μ M NECA and 31 sec in the 100 μ M group. R-PIA also significantly reduced licking activity, but no difference could be seen between the 10 and 100 μ M groups. (FIG.1).

After pretreatment with theophylline 50 mg/kg subcutaneously 15 minutes prior to the formalin test with 100 μ M NECA, no reduction of licking activity could be seen. (FIG.2).

In the present study, using the formalin test, the adenosine receptor agonists R-PIA and NECA induced an antinociceptive effect as compared to a control group. This is in accordance with earlier studies using other nociceptive tests (4,5,6). No difference could be seen between the two compounds R-PIA and NECA. The algesic effect of adenosine infusions seen in humans (1,2,3) could not be reproduced in this model.

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