Effects of intrathecal and intracerebroventricular injections of substance P on nociception in the rat and mouse

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Recently, it has been reported that substance P, given either parenterally or intracerebrally, increases reaction latencies in the mouse hot-plate test (Frederickson, Burgis, Harrell & Edwards, 1978; Starr, James & Gaytten, 1978; Stewart, Getto, Neldner, Reeve, Krivoy & Zimmermann, 1976) and in the rat tail-flick test (Malick & Goldstein, 1978). The present experiments extend the above studies by examining the effects of substance P, given intrathecally in rats or intracerebroventricularly in mice, on nociception using a wider range of analgesic tests.

Dose groups of 10 male mice of three different strains (AHM/I/ICI: CR/CDI/SWISS; B & K/T.O.) were used in hot-plate (55°C) and acetylcholine writhing tests. Mice were injected with either substance P, dissolved in acetic acid (0.01 M), morphine or placebo. The latency to front-paw lick was noted in the hot-plate at 30, 60 and 90 min after i.c.v. injection, and the number of writhes occurring in the first 5 min interval after acetylcholine (3 mg/kg i.p.), was noted 30 min after injection. All testing was carried out blind. Morphine (300–3000 ng) produced significant ($P < 0.05$) dose-dependent antinociception in both tests in all strains examined. However, substance P (2–2000 ng) had no significant effect on pain threshold in either test, despite causing marked reductions in locomotor activity and body tremors at the highest dose.

In the rat, the techniques for chronic catheterization of the spinal subarachnoid space and for the intrathecal microinjections were essentially the same as those of Yaksh & Rudy (1976). Each rat received intrathecal injections of morphine or substance P and placebo. Different groups, containing at least 6 rats, were assigned for testing at 30 min after morphine or at 3, 10 or 30 min after substance P. Pain threshold were measured using paw-pressure, tail-immersion (50°C) and hot-plate (52°C) tests. Morphine (3–100 μg intrathecally) produced significant ($P < 0.05$) dose-related antinociception of the hindquarters in all three tests. However, substance P (10–10,000 ng intrathecally) produced a significant ($P < 0.01$) decrease in reaction time to the hind-paw lick response in the hot-plate test at 3 min post-injection (placebo-induced change in reaction time was $+2.0 \pm 3.26$ sec; 1000 ng substance P-induced change was -10.17 ± 1.72 s). There was no significant effect of substance P (1–10,000 ng) in the other two tests or in the hot-plate test at 10 and 30 min post-injection.

Thus, in the present study, substance P failed to produce antinociception, a result which agrees with the recent findings of Growcott & Shaw (1979).

Indeed, given intrathecally, substance P produces a transient hyperalgesia in the hot-plate test. Reports that substance P produces analgesia are based mainly on results from the hot-plate test, where it is likely that the increases in reaction time may be due partly to the known sedative effects of substance P.

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