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Effect of etorphine on brain stem neurones in the rat: a microiontophoretic study

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Morphine and levorphanol, applied microiontophoretically to brain stem neurones produce a stereospecific depression of spontaneous firing and a non-stereospecific excitation (Bradley & Bramwell, 1975, 1977). In this study the effects of the potent narcotic etorphine were compared with those of morphine and D-ala-leucine enkephalin, either on the same neurones or on different neurones.

Male albino rats were prepared under urethane anaesthesia as described previously, and single neurones were recorded from the brain stem reticular formation. Drug solutions used included 25 mM etorphine hydrochloride, pH 5.0; 5 mM 2D-ala,5D-leucine enkephalin (B.W. 180-C), pH 4.9: 25 mM morphine hydrochloride, pH 4.8; 25 mM naloxone hydrochloride, pH 4.6; 25 mM dextrophan tartrate, pH 4.0.

Etorphine, applied with a current of 25–50 nA for 1–4 min, reversibly depressed 76/94 spontaneously firing neurones and excited none. Depression developed slowly (latency 33 ± 3 s, mean $\pm$ s.e. mean, $n = 55$), increasing with time of application, until either a plateau response was achieved or the neurone stopped firing altogether. Spontaneous recovery took 14 ± 1 min ($n = 20$). In the main, however, recovery was induced with naloxone, which invariably reversed and on 20/25 occasions powerfully antagonized etorphine depressions. Naloxone-antagonizable depressions were never produced by dextrorphan (25 nA).

Comparisons of the effects of etorphine and morphine were made on 22 occasions. Of the 18 neurones depressed by atorphine, 5 were excited by morphine, 1 responded biphasically and only 2 neurones were depressed. In addition, morphine excited 3/4 neurones not responding to etorphine.

B.W. 180-C, applied with a current of 0–25 nA for 1/2 to 3 min reversibly depressed 37/44 and excited none. These depressions were antagonized by naloxone on 5/7 occasions. Though dextrorphan was without effect on these neurones, etorphine depressed 8/8 neurones also depressed by B.W. 180-C. In addition, morphine depressed 7 neurones, excited 2 and produced a single biphasic response among 16 neurones also depressed by B.W. 180-C.

Though not observed with etorphine, tachyphylaxis to B.W. 180-C depressions was seen on 5 occasions, making it difficult to conduct antagonism studies.

This tachyphylaxis to B.W. 180-C but not to etorphine depressions raises the possibility that these two classes of opiate might interact with different receptors. Furthermore, the complete lack of excitation with the potent narcotic agonist, etorphine, provides further proof that naloxone-reversible depression represents the pharmacologically significant action of opiates on brain stem neurones.

We are very grateful to Burroughs Wellcome for supplying B.W. 180-C, Endo Laboratories for supplying naloxone and Reckitt and Colman for supplying etorphine.

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