A stereospecific action of morphine on brain stem neuronal activity: a microiontophoretic study

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Work in the unanaesthetized rabbit (Herz, Albus, Metys, Schubert & Teschemacher, 1970) suggests that morphine exerts at least part of its antinociceptive effect through an action in the brain stem. Previous work has confirmed that neurones in the brain stem of urethane-anaesthetized rats are sensitive to microiontophoretically applied morphine (Bradley & Dray, 1973; 1974). Furthermore, morphine excites as well as depresses single neurone activity. Subsequent work (Bramwell & Bradley, 1974) revealed that only morphine-induced depression is sensitive to antagonism by naloxone; morphine-induced excitation being unaffected or potentiated.

The present study was undertaken to show whether morphine-induced depression was produced by another narcotic, namely levorphanol, and to see whether its inactive isomer, dextrorphan, was lacking in activity. An attempt was also made at characterizing morphine excitations in terms of the sensitivity of such cells to acetylcholine (ACh) and acetyl β-methylcholine (MeCh).

Male albino rats were prepared as previously described (Bradley & Dray, 1974) under urethane anaesthesia. Drug solutions were as used previously (Bramwell & Bradley, 1974) except for the following: levorphanol tartrate (0.013-0.026 M, pH 4.5 Roche) dextrorphan tartrate (0.013-0.026 M, pH 4.5 Roche); dextrorphan substance (0.013 M, pH 4.5 Roche) acetyl β-methylcholine chloride (0.25 M, pH 5.0 Koch-Light).

Only spontaneously active brain stem neurones were recorded. 5/52 cells tested with levorphanol were depressed, an effect antagonized by naloxone. 4/52 neurones were excited by levorphanol, an effect not antagonized by naloxone. The response of these cells to morphine tended to parallel their response to levorphanol—i.e. no cell responded to morphine in an opposite way to levorphanol; however, more cells responded to morphine with excitation (12/19).

Although 6/56 cells were depressed by dextrorphan, none of these cells was depressed by morphine, nor were the effects antagonized by naloxone. In addition, 4/56 cells were excited by dextrorphan compared with 15/43 cells excited by morphine. In contrast, 12/56 cells tested with dextrorphan exhibited spike height reduction compared with 20/52 for levorphanol and 0/62 for morphine.

As previously reported for NA and 5-HT (Bradley & Dray, 1974) no correlation existed between the response to morphine and those to ACh and MeCh. Once again, however, (Bramwell & Bradley, 1974) a large proportion (14/14) of cells excited by morphine (15/62) were also excited by ACh, but not by MeCh (8/14). If activation of cholinergic receptors is responsible for morphine excitation in the brain stem these are unlikely to be purely muscarinic in nature.

In conclusion, morphine-induced depression of brain stem neuronal firing, which is sensitive to naloxone reversal at low currents and with dilute solutions, appears to represent a stereospecific narcotic action shared by levorphanol but not by dextrorphan. In contrast, morphine-induced excitation represents an action shared by morphine, levorphanol and dextrorphan which is potentiated by naloxone and nalophine.

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