The Effect of Morphine on the Activity Evoked in Ventrolateral Tract Axons of the Cat Spinal Cord*

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Summary. The effect of morphine on the activity in ventrolateral tract axons was studied in intercollicularly decerebrate cats with and without spinal section. Activity was elicited by electrical stimulation of Aδ- and C-fibres in the sural nerves. In spinal animals, morphine injected intravenously in a dose as low as 0.5 mg/kg reduced the post-stimulus discharge of impulses recorded in ventrolateral tract axons below the site of transection. The depression was not only abolished but reversed by levallorphan and naloxone. Pretreatment with reserpine did not diminish the effect of morphine. The effect of morphine was considerably weaker in deccrebrate cats. Reversible block of the spinal cord produced by cold revealed that morphine reduced inhibition from the brain stem controlling the impulse transmission to ventrolateral tract axons.

It is concluded that a spinal effect contributes to the analgesic action of morphine.

Key words: Ventrolateral tract axons — Morphine — Morphine antagonists — Analgesia.

Introduction

Noxious stimuli applied to the skin give rise to activity in Aδ (Zotterman, 1939; Burgess and Perl, 1967; Perl, 1968) as well as in C afferents (Iggo, 1959, 1960; Hensel et al., 1960; Iriuchijima and Zotterman, 1960; Witt, 1962; Bessou and Perl, 1969; Van IIees and Gybels, 1972), activity which is associated with pain reception. Recently, Pomeranz (1973) demonstrated that electrical stimulation of small diameter afferents (Aδ or C) in skin nerves evokes activity in axons of the ventrolateral tract of the cat spinal cord, as does applying noxious stimuli to the skin, and it was suggested that these axons are specifically nociceptive and involved in the process of pain perception.

In a previous investigation (Grossmann and Jurna, 1974) the activity evoked in ventrolateral tract axons in spinal cats by electrical stimulation of Aδ fibres

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in the sural nerve was depressed by an intravenous injection of morphine in a dose as low as 0.5 mg/kg. This pointed to a spinal site of action involved in the analgesic effect of morphine. In the present study the number of axons activated by stimulation of Aδ afferents and tested under the influence of morphine was extended, and the effect of the drug was also assessed on ventrolateral tract axons activated by C fibre stimulation. In this connection, two problems deserved particular interest. One is that of a participation of monoamines in the effect of morphine at the spinal level, and this has been studied by pretreating the preparations with reserpine. The other concerns the question as to whether morphine depresses sensory impulse transmission in the spinal cord by activating inhibitory pathways descending from the lower medulla oblongata (Satoh and Takagi, 1971). As will be shown, the spinal depressant effect of morphine on the activity in ventrolateral tract axons is not directly dependent on changes of the monoamine content in the spinal cord but may be modulated by an action of the drug on supraspinal centres.

Methods

The experiments were performed on 19 cats (2.0—3.3 kg body weight) operated under halothane anesthesia and decerebrated at the intercollicular level. The spinal cord was exposed from Th₁₁ to L₅ for the recording of activity from axons in the ventrolateral tract; 9 animals were spinalized at the level of Th₁₀, and in 5 the spinal cord was additionally exposed from Th₁ to Th₁₄ for reversible spinalization by cooling the spinal cord. In the latter experiments, two separate pools of paraffin oil were formed covering the spinal cord. The sural nerves were isolated over a length of 8—10 cm, mounted on pairs of recording and stimulation electrodes and cut distal to the site of stimulation. After completion of the surgical procedures anesthesia ceased, and the preparations were immobilized with gallamine triethiodide and artificially respired. The temperature in the rectum and of the paraffin oil covering the lumbar and (when not cooled) the thoracic spinal cord, and the sural nerves was maintained between 37° and 38°. In order to produce spinal block, water at 4° was perfused through a thin polyethylene tube coiled around the thoracic spinal cord and, in addition, the warm oil was exchanged for oil of a temperature of 10—12°. Blood-pressure was recorded in one of the carotid arteries; the mean pressure ranged from 120 to 180 mm Hg. Drugs were injected by a cannula inserted into one of the jugular veins.

The sural nerves were stimulated electrically with a pair of platinum wire electrodes. Stimulation was performed either with single rectangular pulses or with trains of 300 pulses/sec and 10—20 msec duration. The duration of the rectangular pulses was 0.05 msec and the repetition rate of the single pulses or pulse trains 0.25 Hz. Compound action potentials were recorded with bipolar platinum wire electrodes placed at a distance of 6—8 cm proximal from the stimulating electrodes. Potentials of axons in the ventrolateral tract were recorded from the left side at the level of L₁—L₅ with steel electrodes (tip diameter 1 μm; resistance 5—10 MΩ) connected to an electrometer (W-P Instruments Model M-4ARM), and were amplified, displayed on a cathode ray oscilloscope and evaluated with an averaging computer (Fabri-Tek 1062; the number of computer addresses used was 512 or 1024) after having been stored on tape (Philips Ana-Log 7).

The experiments were not started until 1 hr had passed after discontinuing the anesthesia. When the effect of morphine on the activity of an axon had been tested, current (500—600 nA for 15—30 sec) was passed through the electrode and the tip position determined histologically by Prussian blue staining. The localization of the points recorded from when testing the effect of morphine is presented in Fig. 2C.

The drugs used were halothane (Fluoathane®, Rhein-Pharma, Heidelberg), gallamine triethiodide (Flaxedil®, Boehringer, Ingelheim/Rhein, morphine hydrochloride (Merck,