EFFECT OF MOTROPINE AND NALOXONE ON ELECTROACUPUNCTURE ANALGESIA

V. V. Zakusov, V. V. Yasnetsov,
L. V. Kalyuzhnyi, and E. V. Golanov

UDC 615.844.4.015.2:615.211.015.23/.076.9

KEY WORDS: electroacupuncture; analgesia; evoked potentials; motropine.

This paper describes a study of a compound belonging to the tropane class, motropine, on electroacupuncture analgesia, the development of which is associated with the secretion of endogenous opioid peptides [2]. Motropine was synthesized and studied on a number of experimental models in the Institute of Pharmacology, Academy of Medical Sciences of the USSR [1]. As reference substance of antagonists of the narcotic analgesics, naloxone was chosen: This abolishes electroacupuncture analgesia both in man [3] and in animals [4].

EXPERIMENTAL METHOD

Experiments were carried out on 12 rabbits of both sexes weighing 2.2-3.2 kg. The animals were loosely fixed by their paws to the operating table. Electroacupuncture (EA) was carried out by applying square pulses of current to acupuncture needles made from stainless steel 0.3-0.5 mm in diameter and located at Tsu Sang-li points. The parameters of EA were: 0.7-1.0 mA, 1-5 Hz, 0.5 msec. Evoked potentials (EP) were recorded in the somatosensory cortex in response to nociceptive electrodermal stimulation (EDR) of the animal's contralateral hind limb. EPs were averaged on an NTA-1024 amplitude-phase analyzer (Orion) for 10 realizations. Simultaneously with recording of EP, sensitivity to pain was determined from the latent period (LP) of withdrawal of a rabbit's tail from a noxious thermal stimulus (the tail-flick test) every 5 min. Naloxone and motropine were injected intravenously.

EXPERIMENTAL RESULTS

EA in the course of 20-40 min caused an increase in LP to the noxious thermal stimulus on average by 43 ± 3% from the initial background and inhibition of the second positive component of EP on average by 99 ± 4% (from 13.6 ± 0.6 to 27.0 ± 1.1 sec). Complete correlation was thus observed between analgesia, as revealed by the behavioral test, and its electrophysiological component — inhibition of EP. These effects of EA were completely abolished by injection of naloxone in a dose of 0.05 mg/kg in six animals against the background of EA (Fig. 1B and Fig. 2A). In one rabbit naloxone was ineffective in this does, but doubling the dose of the drug, i.e., to 0.1 mg/kg, led to cessation of the electroacupuncture analgesia. Naloxone also was injected into the remaining five animals in a dose of 0.1 mg/kg against the background of EA, and complete blocking of the effect of the latter was observed (Figs. 1C and 2B). In doses of under 0.05 mg/kg naloxone caused only very slight weakening of the electroacupuncture analgesia. The minimal doses of naloxone completely suppressing the effects of EA described above were thus 0.05-0.1 mg/kg.

The rabbits tested for EA and abolition of its effects by naloxone were used for repetition of EA, against the background of which motropine was injected in increasing doses. Motropine in a dose of 1 mg/kg did not change the effects of EA, i.e., LP was unchanged in response to the noxious thermal stimulus (Fig. 2C) and recovery of EP did not take place (Fig. 1D). Motropine in a dose of 5 mg/kg partially abolished EA as shown both by the tail-flick test (Fig. 2D) and by the change in EP (Fig. 1E), but in a dose of 10 mg/kg it completely abolished the effects of EA (Figs. 1F and 2E). In a dose of 20 mg/kg motropine also abolished EA (Figs. 1G and 2F), but the effect did not exceed that of a dose of 10 mg/kg. Conversely, with this dose of motropine the effects of EA were restored faster than with a dose of 10 mg/kg (compare Figs. 1F, G and 2E, F). Motropine in doses of 10-20 mg/kg thus

P. K. Anokhin Institute of Normal and Pathological Physiology, and Institute of Pharmacology, Academy of Medical Seiences of the USSR, Moscow. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 92, No. 10, pp. 440-442, October, 1981. Original article submitted April 10, 1981.

0007-4888/81/9210-1369$07.50

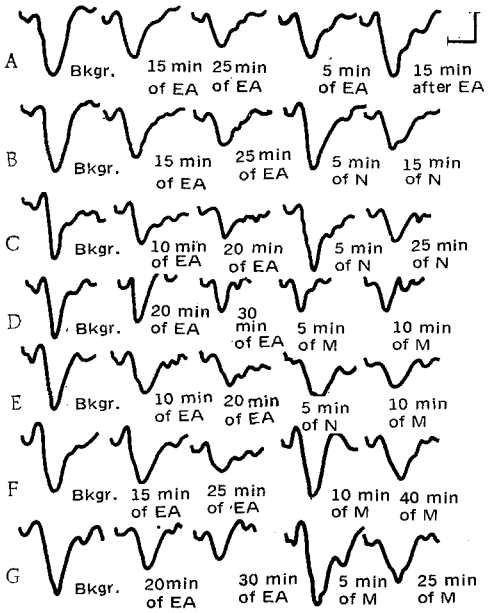

Fig. 1. Effect of motropine and naloxone on EP in somatosensory cortex of rabbits against the background of electroacupuncture analgesia. A) Suppression by EA of second positive component of EP; B, C) action of naloxone (N) against the background of EA in doses of 0.05 and 0.1 mg/kg respectively; D-G) action of motropine (M) against the background of EA in doses of 1, 5, 10, and 20 mg/kg, respectively. Calibration: 50 msec, 50 μV.

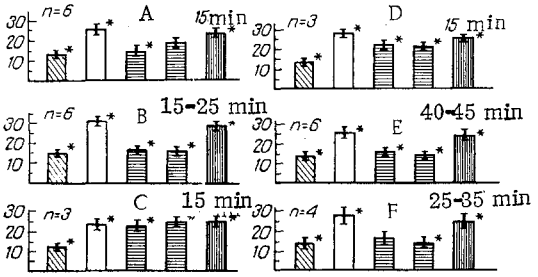

Fig. 2. Effect of motropine and naloxone on LP of tail flixck by rabbits under the influence of a noxious thermal stimulus and against the background of electroacupuncture analgesia. A, B) Action of naloxone against the background of EA in doses of 0.05 and 0.1 mg/kg, respectively; C-F) action of motropine in doses of 1, 5, 10, and 20 mg/kg, respectively. Oblique shading — initial LP; no shading — LP against the background of EA; horizontal shading — changes in LP after injection of drugs at 5th and 10th minutes, respectively, against the background of EA; vertical shading — recovery of EA analgesia. Ordinate, time (in sec). Asterisk indicates statistical significance of changes ($P < 0.05$).

completely abolishes the effects of EA, i.e., it acts similarly to naloxone in doses of 0.05-0.1 mg/kg. Consequently, motropine, as an antagonist of the narcotic analgesics, when tested on electroacupuncture analgesia, is about 100-200 times weaker than naloxone, the classical opiate antagonist. It must be remembered, however, that the toxicity of naloxone is much greater that of motropine, and this is undoubtedly a favorable property of the new drug.

The experimental data given in this paper are evidence that motropine can antagonize endogenous opioid peptides which are secreted during electroacupuncture analgesia. Considering this fact, and also previous data on antagonism of motropine and exogenous opiates, as shown by analgesia tests [1], it can be tentatively suggested that motropine is the first preparation of the tropane class which possesses marked affinity for opiate receptors, interaction of endogenous and exogenous opiates with which is accompanied by the development of an analgesic effect.

LITERATURE CITED

1. V. V. Zakusov and V. M. Bulaev, Vestn. Akad. Med. Nauk SSSR, No. 9, 48 (1980).
2. G. S. Chen, Am. J. Chin. Med., 5, 25 (1977).
3. D. J. Mayer, D. D. Price, and A. Rafii, Brain Res., 121, 368 (1977).
4. B. Pomeranz and D. Chin, Life Sci., 19, 1757 (1976).

COMPARATIVE CHARACTERISTICS OF SELF-STIMULATION REACTION IN RABBITS RECEIVING ANGIOTENSIN II BY THE INTRAVENTRICULAR ROUTE AND BY APPLICATION TO THE CONJUNCTIVA

V. I. Badikov, E. A. Lomakina, and K. V. Sudakov

UDC 612.821.014.46:577.175.852

KEY WORDS: self-stimulation; angiotensin II; intraventricular injection; application to the conjuctiva.

Recent experimental studies have shown conclusively that endogenous neuropeptides play an active part in the formation of learning and memory processes, motivations, and sleep [1, 3, 12]. However, the role of oligopeptides in the mechanisms of formation of emotional behavior has so far received little study.

The object of the investigation described below was accordingly to study the effect of angiotensin II on the self-stimulation reaction in rabbits, regarded by some workers as an adequate model of a positive emotional behavioral reaction. In view of indications in the literature that certain substances, when applied to peripheral receptors, can penetrate directly into the CNS, by-passing the blood stream [2, 5, 10], it was decided to compare the action of angiotensin II on self-stimulation when injected into the cerebral ventricles and when applied to the conjunctiva.

EXPERIMENTAL METHOD

Experiments were carried out on 28 adult male waking rabbits weighing 2.5-3 kg. Bipolar electrodes were implanted into the lateral region of the hypothalamus of each animal. Freely behaving rabbits were tested for the self-stimulation reaction. The parameters of the stimulating current were: frequency 100 Hz, pulse duration 1.4 msec, duration of series of pulses 0.3 sec, voltage 2-5 V. The self-stimulation reaction was evaluated on the basis of changes in the frequency with which the animal closed the electric circuit in each 32-sec interval.

P. K. Anokhin Research Institute of Normal Physiology, Academy of Medical Sciences of the USSR. I. M. Sechenov First Moscow Medical Institute.

Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 92, No. 10, pp. 442-443, October, 1981. Original article submitted February 19, 1981.

0007-4888/81/9210-1371$07.50