ANGIOTENSINERGIC MECHANISMS OF AURICULAR ACUPUNCTURE DENTAL ANALGESIA

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Two basic neurochemical mechanisms of acupuncture analgesia are now known: opioid and serotoninergic [1], and which mechanism is activated depends on the frequency of acupuncture stimulation [4]. It has been shown, for instance, that the analgesic effects of acupuncture stimulation (APS) with a frequency of 1-30 Hz are blocked by naloxone [1, 2, 10] and are reduced by a serotonin blocker [8], whereas the effects of APS with a frequency of 100 Hz or more are not blocked by naloxone, as has been shown by the action of thermal and electrodental (EDS) nociceptive stimuli [2, 10].

At the same time, injection of angiotensin II (AII) is known to have an analgesic effect also against nociceptive stimulation of the dental pulp in rabbits [3, 9] and thermal stimulation of the skin in rats [5].

The aim of this investigation was to study the role of AII in the analgesic effects of auricular acupuncture electrostimulation (AAS) with a frequency of 15 and 100 Hz, relative to changes in the amplitude of EP of the somatosensory cortex in response to nociceptive electrical stimulation of the dental pulp in rabbits, an objective indicator of a change in the pain sensitivity of man [6] and animals [1, 7].

EXPERIMENTAL METHOD

Experiments were carried out on 35 conscious male Chinchilla rabbits, lightly secured to a frame, weighing 2.5-3 kg, and scalped beforehand under procaine anesthesia. The experimental method involving electrical stimulation of the dental pulp, recording, and statistical analysis of the components of EP, was described by the writers previously [3, 9].

As the source of AAS we used electrical stimulation through an "Analgident" apparatus (sinusoidal current, 100-200 μA, 15 and 100 Hz, 25 min, of acupuncture points on the rabbit's ear in the projection region of the trigeminal nerve, and with the reference electrode located in the region of the upper gum. EP was recorded every 10 min, with 10 presentations each time in the course of 30-40 min before application of AAS, and also during the 2-3 h after its discontinuation.

By means of a microsyringe 10 μl of aqueous solutions of saralasin ("Sigma," 100 ng/kg), AII ("Serva," 50 ng/kg), methysergide ("Sandoz," 500 μg) and distilled water in the same volume, as the control, were injected into the third ventricle through a cannula previously secured to the skull. Naloxone ("Endo") was injected intravenously in a dose of 0.15 mg/kg. L-parachlorophenylalanine ("Sigma") was injected intraperitoneally in a dose of 500 mg/kg 3 days before the experiment. All the animals were first subjected to the action of AAS alone, and only in the subsequent experiments were the drugs injected and AAS used, so that the effect of the substances on that of AAS could be compared in the same animal.

EXPERIMENTAL RESULTS

In response to EDS, EP was recorded with a latent period (LP) of the primary response of 8-12 msec and with an amplitude of 50-70 μV, followed by a negative-positive component (NPC) with LP of 20-40 msec, whose peak amplitude varied in the course of 30-40 min between 80 and 100 μV, and was taken to be 100% (Figs. 1 and 2).

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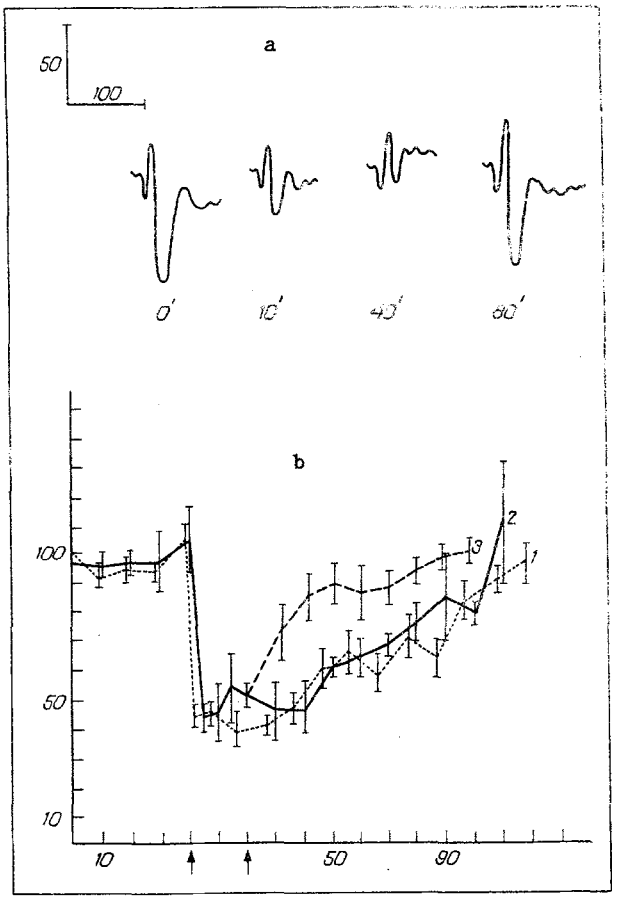

Fig. 1. Changes in somatosensory cortical EP of a rabbit in response to EDS. a) Changes in somatosensory cortical EP of rabbit in response to EDS before (0), and 10 min, 40 min, and 80 min after AAS with a frequency of 15 Hz. Calibration: 50 μV, 100 msec; b) dynamics of changes in amplitude of NPC of somatosensory cortical EP of rabbits in response to EDS (in %) relative to mean background values before and after (first arrow) AAS with a frequency of 15 Hz (1) and with subsequent injection (second arrow) of saralasin (2) and naloxone (3). Abscissa, time (in min); ordinate, amplitude of NPC of EP (in %).

After AAS for 25 min with a frequency of 15 Hz (n = 13) the amplitude of NPC of EP in response to the same EDS was significantly reduced to 40-50 μV, i.e., on average to 40-50% of its initial level, which was observed on average for 45-60 min, followed by a gradual increase to the original values 80-120 min after discontinuation of AAS with a frequency of 15 Hz (Fig. 1). Injection nf saralasin (n = 5) 15-20 min after AAS with a frequency of 15 Hz did not significantly affect the dynamics of the changes in amplitude of NPC of EP in response to EDS compared with the isolated action of AAS (Fig. 1). Injection of naloxone (n = 6) 15-20 min after AAS led to an increase in the amplitude of NPC 10 min after the injection, to 70% of the initial level, and after a further 10 min to values not significantly different from the original ones (Fig. 1). Thus injection of saralasin did not change, whereas injection of naloxone abolished the effect of a decrease in the amplitude of NPC of EP in the somatosensory cortex in response to EDS induced by AAS with a frequency of 15 Hz.

After AAS with a frequency of 100 Hz (n = 17) the amplitude of NPC of the somatosensory cortical EP in response to EDS also was reduced to 50-60% of the original values (Fig. 2), and this was observed for 50-60 min, followed by gradual recovery to the background values by 90-100 min after AAS (Fig. 2). Injection of saralasin (n = 5) 15-20 min after AAS led after a further 15-20 %in to a sharp increase in amplitude of NPC of EP up to the background values, and this was observed during the subsequent 60 min also. Conversely, injection of AII (n = 5) 20 min after AAS led to an even greater decrease in the amp-

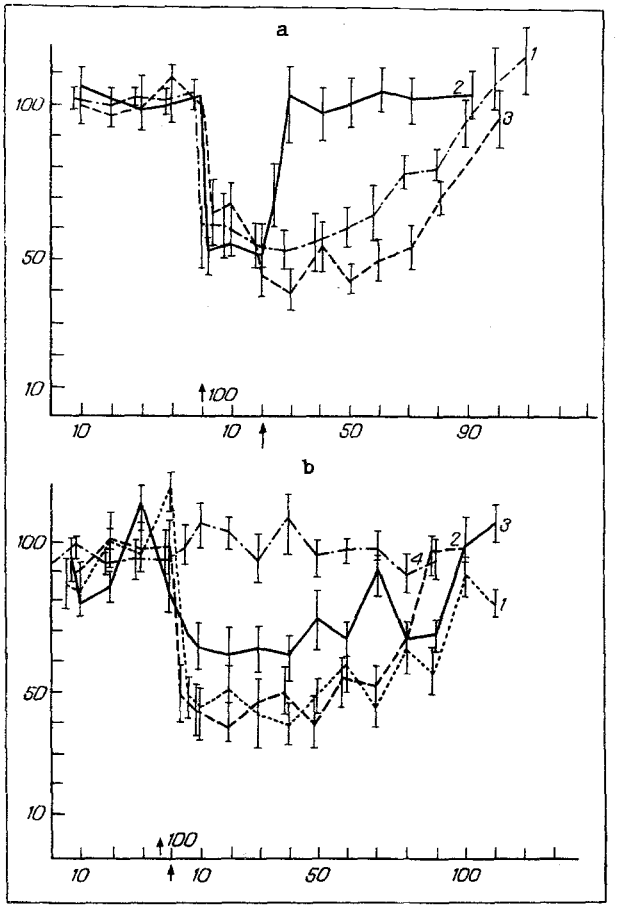

Fig. 2. Time course of changes in amplitude of NPC of somatosensory cortical EP of rabbits in response to EDS (in %) relative to average background values before and after (first arrow) AAS with a frequency of 100 Hz (1). a) With subsequent injection (second arrow) of saralasin (2) and AII (3); b) after preliminary injection (first arrow) of distilled water (1), naloxone (2), methysergide (3), and saralasin (4). Legend as to Fig. 1b.

litude of NPC of EP in response to the same EDS, which was reduced to 40-50% of the initial level, and these differences compared with the isolated action of AAS were observed for 40-50 min after injection of AII (Fig. 2).

Injection of saralasin (n = 6) 5 min after application of AAS with a frequency of 100 Hz led to disappearance of the decrease in amplitude of NPC of EP in response to EDS after the action of AAS for 25 min (Fig. 2). Injection of distilled water at this time (n = 4), and also injection of naloxone (n = 5), however, preserved the decrease in amplitude of NPC of EP in response to EDS after application of AAS for 25 min (Fig. 2). Injection of methysergide at the same time (n = 2) or preliminary injection of parachlorophenylalanine (n = 3) led to reduction of the effect of AAS with a frequency of 100 Hz: the amplitude of NPC of EP was reduced only to 70% of its initial level, with gradual restoration of the background values toward 90-100 min after AAS (Fig. 2).

The experiments described above thus showed that AAS with a frequency of 15 and 100 Hz lowered about equally the amplitude of NPC of the somatosensory cortical EP of a rabbit in response to EDS, evidence of a decrease in dental nociceptive sensitivity, i.e., of the analgesic effect of AAS, for changes in the amplitude of the somatosensory cortical EP correlate with sensations of pain in man [6] and can be used as objective indicators of nociception in animals [1, 7]. However, this effect of AAS with a frequency of 15 Hz was blocked by naloxone but was not blocked by the AII antagonist, saralasin, evidence of the opioid mechanism of this acupuncture analgesia, and in agreement with data obtained by other workers [2, 10]. Meanwhile the effect of AAS with a frequency of 100 Hz was not blocked by naloxone, in agreement with observations of other workers [2, 10], and was only reduced under the influence of the serotonin blockers, methysergide and parachlorophenylalanine, as also was observed in the case of acupuncture stimulation with a frequency of 3 Hz [8], but it completely disappeared when saralasin was

injected either before or after application of AAS. Conversely, injection of AII potentiated the analgesic effect of AAS with a frequency of 100 Hz. This indicates that the latter is mediated, not through the opioid, but evidently through the angiotensinergic antinociceptive mechanism of dental nociceptive sensitivity, which the writers demonstrated previously [3, 9].

Incidentally, in experiments conducted by other workers [10] some rabbits were sensitive to AAS at 15 Hz and tolerant to AAS at 100 Hz, and vice versa. In our experiments, 24 of the 35 rabbits were sensitive to AAS at 15 and 100 Hz, four were resistant to AAS at 15 Hz but sensitive to AAS at 100 Hz, three were resistant to AAS at 100 Hz but sensitive to AAS at 15 Hz, and finally, four animals were resistant to AAS at both 15 Hz and 100 Hz. This is evidence that the mechanisms of acupuncture analgesia induced by AAS with frequencies of 15 and 100 Hz are independent.

Thus besides the basic opioid and serotoninergic mechanisms of acupuncture analgesia, there also exists an angiotensinergic mechanism, activated by AAS with a frequency of 100 Hz, and which is evidently connected with regulation of dental nociceptive sensitivity or, at least, with regions innervated by the trigeminal nerve, for injection of AII caused an analgesic effect against an electrodental, but not an electrodermal corporeal nociceptive stimulus [3, 9].

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