DISAPPEARANCE OF ELECTROACUPUNCTURE EFFECT IN RABBITS AFTER DESTRUCTION OF THE DORSOMEDIAL HYPOTHALAMUS

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UDC 617-089.584-092:612.826.4

KEY WORDS: dorsomedial hypothalamus; electroacupuncture; evoked potentials.

Despite the use of acupuncture throughout the ages, the neurophysiological mechanisms of its analgesic effect are still largely unknown. After the discovery of analgesic effects of stimulation of the periaqueductual region of the midbrain [10] it was suggested that acupuncture anesthesia is effected through opiate mechanisms of the "central gray matter–nuclei raphe" system [6, 8]. Meanwhile, another analgesic mechanism connected with the functions of the dorsomedial hypothalamus has been discovered [1]. Electrical stimulation of this region in animals induces a state of analgesia, detectable by behavioral tests [1, 11]. This state is accompanied in rabbits by disappearance of evoked potentials in response to electrodermal stimulation in the centrum medianum of the thalamus [1], which is considered to be the main intermediate structure for nonspecific nociceptive sensation [4]. Similar changes in behavior [8] and evoked potentials in the centrum medianum of the thalamus are also observed during electrical stimulation of the nucleus magnus raphe [1].

Electroacupuncture stimulation in rabbits also induces a state of analgesia detectable by behavioral tests [3, 5] and by corresponding changes in EEG parameters [2, 3] and evoked potentials [2].

The investigation described below was accordingly undertaken to study the effect of destruction of the nucleus magnus raphe – the key structure in the analgesic system of the brain stem [7] – and of the dorsomedial hypothalamus on the analgesic effect of electroacupuncture in rabbits.

EXPERIMENTAL METHOD

Ten experiments were carried out on ten waking rabbits in which changes in evoked potentials arising in the centrum medianum of the thalamus to electrodermal stimuli were investigated during electroacupuncture stimulation of Tsu-san-li points [3] before and after electrolytic destruction of the dorsomedial hypothalamic nuclei and the nucleus magnus raphe.

Electrodermal stimuli, consisting of single square pulses 1 msec in duration and with a strength of 3-9 mA, were applied to the lateral surface of the lower third of the leg from an ÉST-14 electrostimulator, either alone or in the interval between volleys of pulses of electroacupuncture stimulation. Electroacupuncture stimulation was carried out with bipolar square pulses, applied in series of 6 pulses with a duration of 500 μsec, frequency of 3 Hz, and a strength of 400 μA. Evoked potentials in the centrum medianum of the thalamus in response to electrodermal stimulation were derived by a monopolar technique, led through a type UFU-BK amplifier (Experimental Instrumental Workshop, All-Union Institute of Experimental Medicine), and recorded with tenfold averaging on an NTA-1024 amplitude-phase analyzer (Orion). The dorsomedial hypothalamic nuclei and nucleus magnus raphe were destroyed by passage of an anodal direct current of 400 μA for 30-40 sec, followed by histological verification [12].

EXPERIMENTAL RESULTS AND DISCUSSION

As a first step, the threshold strength of electrodermal stimulation to induce a behavioral response of flight was determined in all rabbits under unrestrained conditions, and the value obtained varied in different

Laboratory of the Physiology of Pain, P. K. Anokhin Institute of Normal Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Fedorov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 89, No. 6, pp. 643-645, June, 1980. Original article submitted October 10, 1979.

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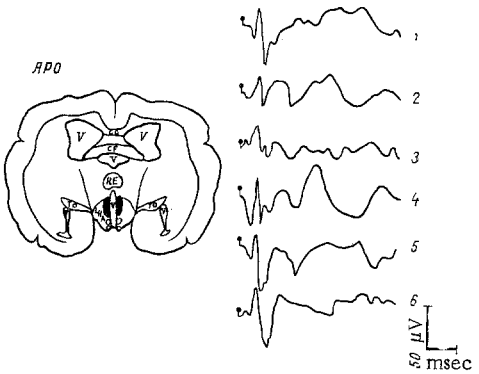

Fig. 1. Effect of suppression of evoked potential of centrum medianum of thalamus during electroacupuncture and disappearance of this effect after destruction of dorsomedial hypothalamic nuclei. 1) Evoked potential of centrum medianum of thalamus in response to electrodermal stimulation; 2) the same 10 min after beginning of electroacupuncture stimulation; 3) 20 min after its beginning; 4) recovery of evoked potential of centrum medianum of thalamus during continued electroacupuncture stimulation, 5 min after bilateral destruction of dorsomedial hypothalamic nuclei; 5) the same, 10 min after, and 6) 15 min after destruction (region of destruction is shaded).

animals from 2 to 9 mA. In the restrained animals, when above-threshold electrodermal stimuli were applied, evoked potentials were recorded in the centrum medianum of the thalamus with a latent period of the primary positive wave of 19-21 msec and with an amplitude of 15-20 μV, followed by a negative wave with a latent period of 42-46 msec and an amplitude of 20-30 μV, followed in turn by a second positive wave with a latent period of 70-75 msec and an amplitude of about 70 μV (Fig. 1).

Electroacupuncture stimulation led in the course of 15-20 min to a gradual decrease in amplitude of the components of the evoked potential (EP) of the centrum medianum of the thalamus (CMT) in response to electrodermal stimulation, amounting in some cases to their virtually complete disappearance (Fig. 1). This indirectly indicates the development of a state of analgesia in the animal, for the corresponding disappearance of EP of CMT observed in animals during electrical stimulation of the dorsomedial hypothalamus was accompanied by inhibition of the defensive behavioral response to noxious temperature stimulation [1]. Furthermore, as experiments [2] showed, it is toward the 20th minute of electoacupuncture stimulation in rabbits that disappearance of the second positive wave of EP, of the EEG desynchronization reaction in the sensomotor cortex, and the autonomic response of quickening of the heart rate to electrodermal stimulation is observed; this may also be evidence of the development of a state of analgesia toward this period of the action of electroacupuncture [2, 3].

On discontinuation of the electroacupuncture, gradual recovery of the initial values of the components of EP of CMT in response to electrodermal stimulation also was observed within 15-20 min.

In five experiments, after it had first been established that EP of CMT in response to electrodermal stimulation disappeared as a result of the action of electroacupuncture stimulation, the dorsomedial hypothalamic nuclei (DHN) were destroyed. EP of CMT in response to electrodermal stimulation were restored after 3-5 min, despite continuing electroacupuncture stimulation (Fig. 1d). The amplitude of the second positive wave of EP was increased, moreover, on average by 1.5 times (Fig. 1). In two experiments of this series, the mere insertion of the electrode into DHN was sufficient to cause recovery of EP in CMT in response to electrodermal stimulation during continuing electroacupuncture stimulation, although electrical stimulation of DHN through these electrodes caused their rapid suppression in CMT.

In five experiments, against the background of depression of EP of CMT in response to electrodermal stimulation by electroacupuncture stimulation, the nucleus magnus raphe (NMR) was destroyed beforehand

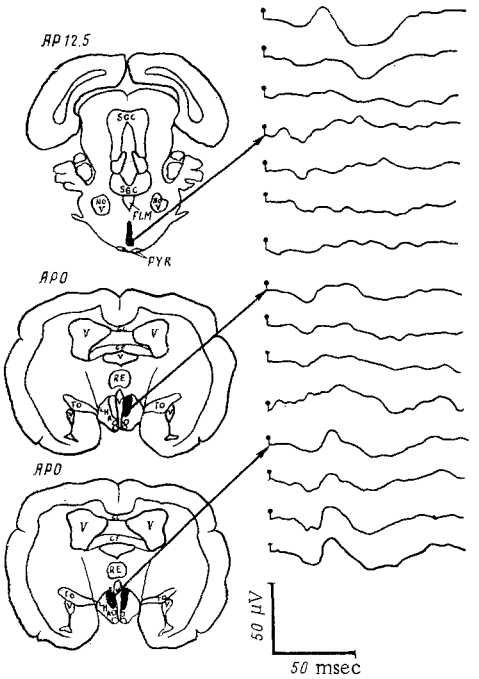

Fig. 2. Effect of successive destruction of nucleus magnus raphe and unilateral and bilateral destruction of DHN on suppression of EP of CMT during electroacupuncture stimulation. First three EP: potential before electroacupuncture stimulation and 10 and 20 min after its beginning, respectively. Arrows indicate EP immediately after destruction of the particular structure and 5, 10, and 15 min respectively thereafter, during continued electroacupuncture stimulation (region of destruction is shaded).

(Fig. 2). As these experiments showed, this destruction, if electroacupuncture stimulation was continued, did not lead to recovery of EP of CMT in response to electrodermal stimulation (Fig. 2). Consequently, the analgesic effect of electroacupuncture was preserved after destruction of NMR. Subsequent unilateral destruction of DHN led to brief (for 3-5 min) appearance of EP of CMT in response to electrodermal stimulation, but the EP disappeared again later (Fig. 2). Subsequent destruction of DHN on the other side led to the stable appearance of EP of CMT in response to electrodermal stimulation, despite continuing electroacupuncture stimulation. The duration of the second positive wave of EP also increased somewhat in this case (Fig. 2).

The experimental results thus showed that destruction of the dorsomedial hypothalamus, unlike destruction of NMR, causes disappearance of the effect of suppression of EP in CMT in response to electrodermal stimulation, observed during electroacupuncture stimulation, i.e., it causes disappearance of the analgesic action of electroacupuncture. This, in turn, suggests that electroacupuncture analgesia is evidently mediated through mechanisms connected with the functions of the dorsomedial hypothalamus.

It has been claimed that the analgesic action of acupuncture may be connected with activation of the pituitary gland [9], which produces endorphins, and, consequently, on the basis of the results of the present experiments, a role of hypothalamic-hypophyseal connections can be postulated in the mechanism of acupuncture analgesia. However, excitation of the dorsomedial hypothalamus, which evidently arises during electroacupuncture stimulation, may be considered to have an independent inhibitory effect also on the conduction of nociceptive sensation through the intralaminar nuclei of the thalamus, for electrical stimulation of this formation leads after only 4 min to inhibition of the behavioral defensive response to noxious temperature stimulation, and after 30-40 sec, to disappearance of EP of CMT in response to electrodermal stimulation [1]. As the present experiments show, destruction of DHN causes recovery of EP of CMT in response to an electrodermal stimulus almost immediately after destruction. If the effect of electroacupuncture was connected entirely with liberation of pituitary endorphin, the termination of the effect could not be so rapid.

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EFFECT OF THYROTROPHIC HORMONE ON THE MEMBRANE POTENTIAL OF THYROID GLAND CELLS AND ON THYROID HORMONE SECRETION DURING AGING

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UDC 612.67:612.441.014.423.018.2:612.433.441:591.147.1

KEY WORDS: aging; endocrine system; thyroid gland; membrane potential; secretion of thyroid hormones.

Much factual evidence has now been obtained on age changes in thyroid function and their role in the mechanism of aging [2, 3, 5]. However, the biophysical properties of the membranes of secretory cells of the thyroid gland, which play an important role in the maintenance of cell metabolism, transmembrane transport of materials, and regulation of protein biosynthesis and the cell energy balance, have been inadequately studied [1, 4, 6-8].

The object of this investigation was to study correlation between changes in the membrane potential (MP) of the follicular epithelial cells of the thyroid gland and secretion of thyroid hormones under the influence of thyrotrophic hormone (TTH) during aging.

EXPERIMENTAL METHOD

Experiments were carried out on isolated thyroid glands of male Wistar rats of two age groups: adult (7-12 months) and old (27-32 months). The value of MP of the follicular epithelial cells, the total thyroxine (T_4) level in the blood, and the concentration of cyclic AMP in the thyroid gland tissue were determined. Isolated thyroid glands were perfused with Krebs–Henseleit solution (t = 37°C; pH 7.3-7.4), aerated with a mixture of 95% O_2 and 5% CO_2. MP was recorded by a standard microelectrode technique. Glass microelectrodes filled with 2.5 M KCl solution, with a resistance of 15-30 MΩ and a characteristic tip potential of not more than −5 mV were used. Total T_4 in the blood was determined by means of "Thyropac-4" radioisotope kits (Radiochemical Centre, Amersham, England). Cyclic AMP in the thyroid gland tissue was determined by means of radioimmunologic kits supplied by the same firm. Thyroid gland function was activated by intravenous injection of TTH in doses of 5 or 0.5 units/100 g body weight. MP of the follicular cells of the thyroid gland and the total T_4 concentration in the blood were investigated 1, 2, and 3 h, and the cyclic AMP concentration in the thyroid gland tissue 10 min, after injection of TTH.

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(Presented by Academician of the Academy of Medical Sciences of the USSR D. F. Chebotarev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 89, No. 6, pp. 645-648, June, 1980. Original article submitted March 13, 1979.