CHANGES IN SENSITIVITY TO PAIN DURING ELECTRICAL STIMULATION OF EMOTIOGENIC ZONES OF THE RABBIT HYPOTHALAMUS

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Emotions alter the pain threshold and tolerance to pain in man [4, 7]. However, during electrical stimulation (ES) of emotiogenic zones in animals, changes in pair sensitivity may be of different kinds, depending on differences in the localization of the emotiogenic zones concerned and in the parameters of stimulation [1, 8].

The object of the present investigation was accordingly to study the effect of ES of the emotiogenic zones of the hypothalamus on changes in sensitivity of rabbits to pain.

EXPERIMENTAL METHOD

Experiments were carried out on 58 male rabbits. To assess sensitivity to pain, in a shuttle box, the latent period (LP) averaged from six realizations of the avoidance reaction to a thermal nociceptive stimulus (TNS) was investigated. The stimulus was applied to a grid in the floor of the box, the temperature of which could be raised from room temperature to 80°C at the mean rate of 3°C/sec (hot plate test). The index of changes in sensitivity to pain was the change in LP for avoidance of TNS, calculated by the equation [5]:

$$\text{change (in \%) in LP of TNS avoidance} = \frac{\text{LP during intracerebral ES} - \text{background LP}}{\text{MT} - \text{background LP}} \cdot 100,$$

where MT is the maximal allowable time of exposure to the given stimulus without causing damage to the tissues. In the present experiments it was 115 sec, after which TNS caused burns of the skin. Intracerebral ES was applied as square pulses of current (100 μsec, 100 Hz, groups of 30 pulses with a frequency of 0.5 Hz, 50-250 μA). During self-stimulation (SS), each time the animal pressed the lever, one group of pulses was applied. SS of aversive zones occupied 1 min. TNS was presented either during SS or immediately after the end of ES of the aversive zones. In a separate series of experiments on unanesthetized, semi-immobilized rabbits the evoked potential (EP) of the parafascicular complex (PFC) of the thalamic nuclei in response to single electrodermal stimulation (EDS) or to flashes, applied either alone or 0.5 sec after the end of intracerebral ES, was recorded. EDS (square pulses, 0.5 sec, 30-50 V) was applied through needle electrodes inserted subcutaneously into the region of the left leg. This EDS, applied to the animal under free behavioral conditions, evoked a flight response characteristic of nociception [2]. The EPs, derived by a bipolar technique, were recorded on a Disa oscilloscope by superposition of five presentations, and also on the display of an Orion NTA-1024 analyzer (Hungary) with fivefold averaging. The statistical significance of changes in the indices was determined by Student's two-sample t-test. After the experiments the location of the tips of the stimulating and recording electrodes was verified histologically.

EXPERIMENTAL RESULTS

Changes in sensitivity to pain during ES of the hypothalamic emotiogenic zones, as reflected in LP of avoidance of TNS and the amplitude of EP of thalamic PSP in response to painful EDS are shown in Table 1. It was shown that ES of positive points of the hypothalamus, inducing an SS phenomenon, differs in its effect on sensitivity to pain, depending on the locations of these points (Fig. 1). It will be clear from the data in Table 1 that the

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TABLE 1. LP of TNS Avoidance Reaction (in sec) and Amplitude of Second Positive Wave of EP of PEC (in μV) in Response to Nociceptive EDS before and during ES of Emotiogenic Points of Various Hypothalamic Structure

Indices tested		Brain structures according to atlas of Sawyer (1954)						
		points of self-stimulation				average points		
		LHA LPO	DHA	AHA	PHA	VMH	DMH	LHA, DHA, AHA, SOD MPO, STH P_F/F_X
Changes in sensitivity to pain not significant								
LP	Before ES	**20±2,2**	20±0,7	—	19±3,0	17±1,2	18±1,5	19±3,4
	During ES	**27±4,0**	22±1,4	—	21±1,2	20±1,4	22±3,1	22±5,3
Increase in LP, %*		**7**	27	—	2	3	4	3
Amplitude EP	Before ES	**49±2,8**	45±5,8	—	59±8,2	60±4,1	54±6,8	69±12,4
	During ES	**54±2,2**	42±1,4	—	48±4,3	45±13,3	49±1,6	65±6,2
Number of points		**1**	3	0	2	2	2	2
Slight decrease in sensitivity to pain								
LP	Before ES	**16±0,3** †	18±0,5	18±1,4	17±1,5	18±0,2	16±0,4	19±1,7
	During ES	**59±0,9** †	58±5,9*	69±3,5*	55±12,7*	36±2,8*	37±3,9*	33±1,9*
Increase in LP, %		**43**	41	53	39	18	21	15
Amplitude EP	Before ES	**59±2,5**	44±1,0	51±2,8	67±4,2	58±3,2	59±0,8	63±2,1
	During ES	**28±2,7***	15±1,5*	8±4,2*	15±2,8*	17±3,8*	8±2,6*	19±1,7*
Number of points		**11**	5	3	3	9	7	8
Marked decrease in sensitivity to pain								
LP	Before ES	**21±1,3**	17±2,1	14±3,2	—	—	—	—
	During ES	**119±4,2***	121±2,8*	138±17,1*	—	—	—	—
Increase in LP, %		**104**	112	123	—	—	—	—
Amplitude EP	Before ES	**73±3,1**	43±4,9	52±2,7	—	—	—	—
	During ES	**12±8,4***	0	7±1,8*	—	—	—	—
Number of points		**2**	3	1	0	0	0	0
Total	. . .		34				30	

*P < 0.01.

†Calculated by the formula given in the section "Experimental Method."

greatest decrease in sensitivity to pain was observed during ES of three points of the dorsal (DHA), two points of the lateral (LHA), and one point of the anterior (AHA) hypothalamus, causing an increase in LP of avoidance (by 104-123%) and the virtually total suppression of EP in response to EDS (Fig. 1). Meanwhile, ES of 11 points of LHA and the lateral preoptic region (LPO), three points of AHA, five points of DHA, and three points of the posterior hypothalamus (PHA) evoked only a small decrease in sensitivity to pain, manifested by much smaller changes in amplitude of EP of PFC in response to EDS and of LP of avoidance of TNS (Table 1). Finally, ES of one point of LHA, three points of DHA, and two points of PHA caused no significant changes in sensitivity to pain or in EP of PFC (Table 1), just as in the case of ES of all the 16 "neutral" points that were tested, electrical and stimulation of which with a strength of between 50 and 250 μA caused neither avoidance reaction nor SS. ES of only 17.6% of the positive points of the hypothalamus tested thus evoked a marked decrease in sensitivity to pain, ES of 64.8% of points led to a slight decrease, and ES of 17.6% of points caused no change in sensitivity to pain.

Stimulation of three positive points located in PHA and LHA of below threshold strength for evoking the phenomenon, but inducing a behavioral response of alertness, caused no significant change in LP of TNS avoidance (18 ± 1 and 19 ± 4 sec) or in the amplitude of EP of PFC (55 ± 4 and 50 ± 6 μV), evidence of absence of changes in sensitivity to pain. ES of eight negative points of the ventromedial (VMH) and dorsomedial (DMH) hypothalamus, and also of AHA, in a subthreshold strength for evoking an aversion reaction, but causing a behavioral response of alertness, significant reduced LP of TNS avoidance on average from 18 ± 1 to 15 ± 1 sec and increased the amplitude of EP of PFC on average from 55 ± 4 to 75 ± 12 μV (Fig. 1), suggesting an increase in sensitivity to pain.

Conversely, ES of threshold strength of 24 negative points in VMH, DMH, AHA, DHA, LHA, the supraoptic (SOD), subthalamic (STH), medial preoptic (MPO), and perifornical (PF/Fx) re-

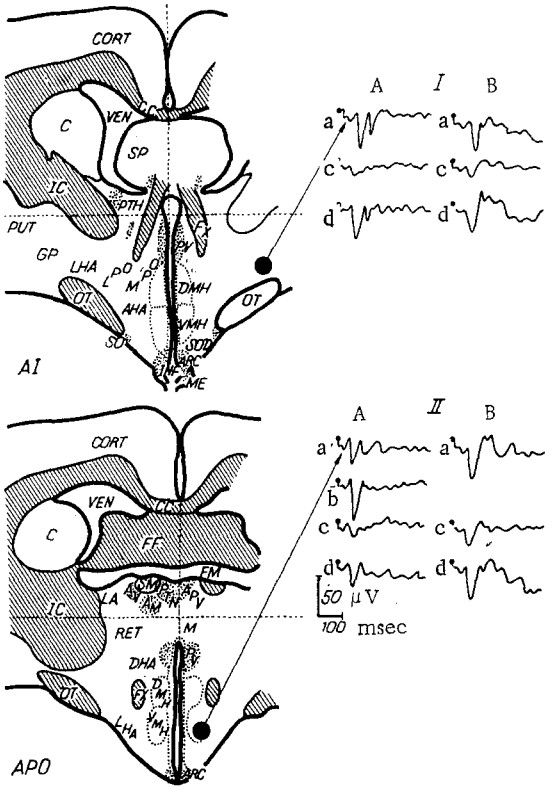

Fig. 1. Changes in EP of PFC in response to nociceptive EDS (A) and EP of sensomotor cortex in response to flashes (B) during stimulation of a positive point of LHA (I) and a negative point of VMH (II). a) Before, b) during below-threshold electrical stimulation, c) during threshold electrical stimulation, d) 3 min after electrical stimulation of emotiogenic points. Calibration: 100 msec and 50 μV. From atlas [10].

gions, evoked a significant increase in LP of TNS avoidance (Table 1) and a decrease in amplitude of EP of PFC (Table 1, Fig. 1). Meanwhile ES of six negative points located in these same zones caused no significant change either in LP of TNS avoidance or in EP of PFC (Table 1), evidence of no change in sensitivity to pain.

Characteristically ES of the emotiogenic points also reduced the amplitude of the second positive wave of EP of the sensomotor cortex in response to flashes on average by 26 ± 4%. However, this decrease was 2.5 times less than the decrease in amplitude of EP of PFC in response to nociceptive EDS (Fig. 1).

The results of these experiments thus showed that ES of not all positive points of the hypothalamus reduces sensitivity to pain. However, ES of 82% of them reduced sensitivity to pain estimated by behavioral tests. In addition, a decrease in amplitude of EP of PFC was observed in response to nociceptive EDS, in agreement with data of other workers [9] who showed that ES of positive points in the hypothalamus reduces responses of thalamic relay neurons to nociceptive EDS. This points to inhibition of conduction of nociceptive impulses.

A reduction of sensitivity to pain also was observed during ES of threshold strength of 80% of negative points in the hypothalamus. Under these circumstances EP of PFC in response to EDS also was depressed. Characteristically, ES of VMH reduced by 41% the number of thalamic neurons which responded to acetylcholine during nociceptive stimulation [3], evidence of inhibition of conduction of nociceptive impulses. Meanwhile, the less marked depression of EP in response to flashes during ES of the emotiogenic cones is evidence of definite specificity of the effect of such ES on conduction of nociceptive impulses.

It is a noteworthy fact that practically complete inhibition of EP of PFC was observed during ES of the negative points, whereas the increase in LP of TNS avoidance did not amount to more than 20%. This is in agreement with the conclusion [6] that stress analgesia may have a powerful, but only a short action. Finally, it must be noted that below-threshold ES only of negative points, but not of positive points in the hypothalamus reduced LP of TNS aboidance and increased the amplitude of EP of PFC in response to nociceptive EDS. This is evidence that only emotional stress of negative sign increases sensitivity to pain. This is of definite biological importance, for it acts together with the defensive reactions of the animal during avoidance of harmful factors. Strong emotional excitation, on the other hand, depresses sensitivity to pain, and this also supports the animal's defensive reactions aimed either at achieving a useful adaptive result in the case of positive emotions, or defensive reactions aimed at combating factors directly threatening the animal's life in the case of negative emotions.

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EFFECT OF STIMULATION OF THE PALEOCEREBELLAR CORTEX ON A MULTIFOCAL CORTICAL EPILEPTIC COMPLEX

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To depress epileptic activity (EA) many workers have used stimulation of the cerebellar cortex [4, 9, 11, 12, 14, 16]. However, the results of these investigations are inconsistent or even contradictory: Besides an inhibitory effect, potentiation of EA also has been found [15, 16]. Yet the solution to this problem is of great practical as well as theoretical importance, for it is a matter of identifying brain structures whose stimulation can cause inhibition of EA through activation of physiological "antisystems" [2].

The aim of this investigation was to study the effect of electrical stimulation of the paleocerebellar cortex on a multifocal cortical epileptic complex (EC), separately and in combination with administration of benzodiazepines (BD) which, as we know, also inhibit EA [1-3, 5, 10, 14].

EXPERIMENTAL METHOD

Acute experiments were carried out on 40 cats. A multifocal EC was created by application of penicillin to different zones (a piece of filter paper 2 mm^2 in area was soaked with

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