EFFECT OF HYDROCORTISONE ON HYPOTHALAMO-HIPPOCAMPAL RELATIONS

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Chronic experiments on rats showed that microinjection of hydrocortisone into the lateral hypothalamic nucleus leads to the appearance of a stable θ-rhythm in the hippocampus and its subsequent transformation into paroxysmal activity. The action of the hormone is stimulated by acetylcholine and is blocked by atropine. It is postulated that hydrocortisone interacts with muscarine-sensitive cholinergic systems of the hypothalamus and hippocampus.

In the active state the EEG of the hippocampus is dominated by a rhythm accompanied by desynchronization of the principal rhythm in the cerebral cortex [3, 15, 16, 18]. Some workers [10, 12, 17, 18, 20, 21] consider that the electrogenesis of the hippocampal rhythm depends on impulses from the hypothalamic centers. Evidence in support of this view is given by strengthening of the θ-rhythm in the hippocampus during electrical stimulation of the middle part of the lateral hypothalamus [10-12, 14, 17, 18, 21]. On the other hand, large doses of steroids are known to induce tonico-clonic convulsions in rats and cats. Paroxysmal

TABLE 1. Changes in Mean Frequency and Amplitude of EEG after Microinjections of Hydrocortisone into Hippocampus (M ± m)

Recordings from	Character of procedure	Time (in min)	n	Mean frequency	Amplitude (in μV)
Lateral hypothalamus	Control	—	76	5,83±0,44	64,6±3,35
	Injection of hydrocortisone	1	73	5,36±0,45	102,19±6,00
		2	98	5,07±0,41	103,5±4,35
		10	79	5,82±0,47	96,71±4,79
		15	46	7,39±0,66	115,22±7,00
		18	42	7,95±0,64	132,62±6,61
Hippocampus	Control	—	80	4,26±0,33	151,14±4,31
	Injection of hydrocortisone	1	98	4,5±0,40	162,96±3,96
		3	85	4,66±0,46	162,35±7,36
		5	109	4,56±0,35	153,23±4,80
		7	88	4,68±0,36	185,0±6,01
		10	102	4,84±0,31	224,41±4,64
		15	57	6,02±0,39	209,29±7,29
		18	56	6,53±0,52	222,86±10,79
Frontal cortex	Control	—	64	4,03±0,29	52,81±3,69
	Injection of hydrocortisone	1	46	7,09±0,57	99,78±7,38
		3	53	4,83±0,37*	63,96±3,40
		5	103	4,03±0,34	164,66±6,64
		15	83	6,2±0,56	99,64±4,21
Amygdala	Control	—	55	6,43±0,76	155,67±4,23
	Injection of hydrocortisone	4	63	5,21±0,28	81,27±5,88
		15	73	7,00±0,58	105,89±5,08

*Here and in Tables 2 and 3, $P > 0.05$.

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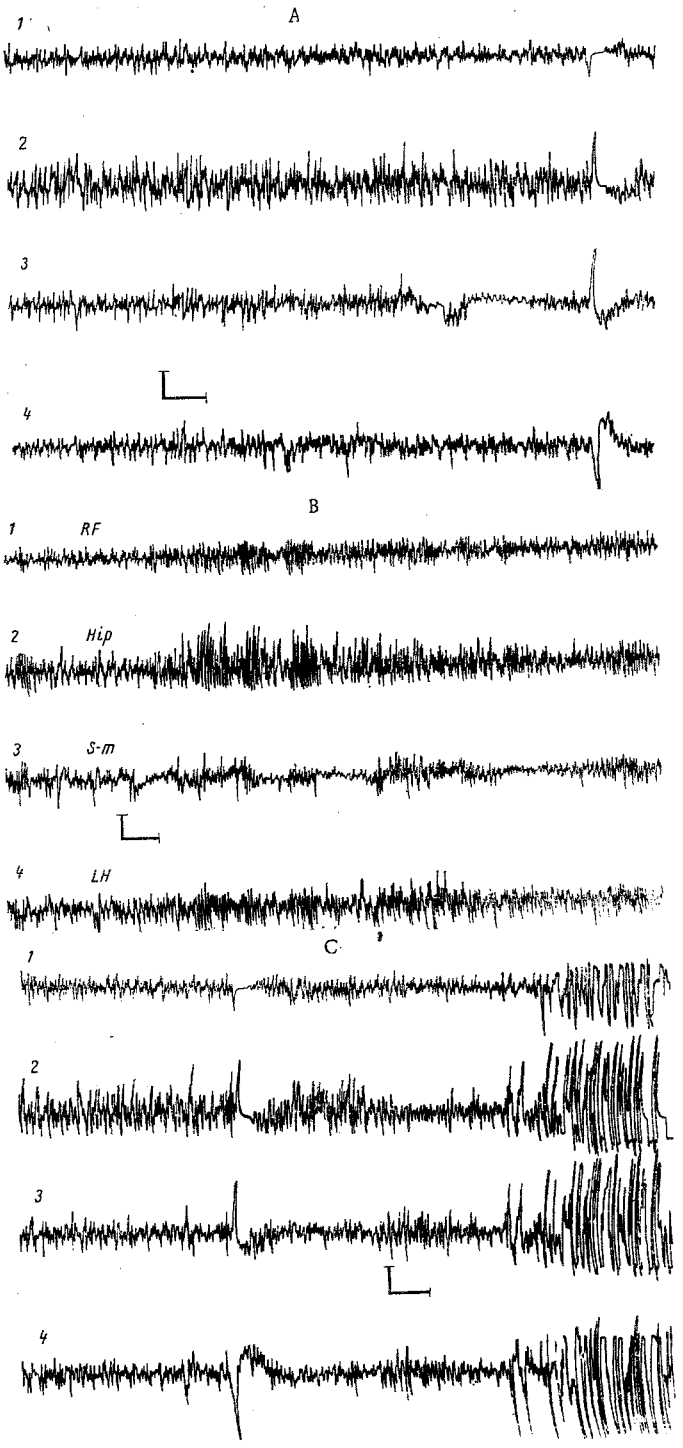

Fig. 1. Changes in EEG of rat after microinjection of hydrocortisone into lateral hypothalamic nucleus: A) control EEG; B) EEG 1 min after microinjection; C) 30 min after microinjection; 1) mesencephalic reticular formation; 2) hippocampus; 3) sensomotor cortex; 4) lateral hypothalamic nucleus.

TABLE 2. Changes in Mean Frequency and Amplitude of EEG after Microinjections of Hydrocortisone into Hippocampus (M ± m)

Recordings from	Character of procedure	Time (in min)	n	Mean frequency	Amplitude (in μV)
Hippocampus	Control	—	91	6,23±0,67	69,45±2,02
	Injection of acetylcholine into hippocampus	1	93	5,24±0,65	64,09±2,39
		2	77	6,13±0,81	62,47±2,77
		3	87	5,68±0,65	63,69±2,71
		15	90	5,25±0,73	58,67±2,15
Reticular formation	Control	—	91	5,97±0,66	58,46±2,51
	Injection of acetylcholine into hippocampus	1	79	5,02±0,74	41,52±1,68
		2	82	5,58±0,71	44,39±1,31
		3	85	4,52±0,67	59,76±2,33
		15	85	4,82±0,81	46,23±1,63
Amygdala	Control	—	92	5,06±0,52	48,59±1,35
	Injection of acetylcholine into hippocampus	1	80	4,64±0,06	151,25±8,59
		2	75	5,05±0,7	30,93±1,47
		3	81	5,91±0,76*	39,88±0,48
		15	81	4,67±0,89*	36,67±0,34
Hippocampus	Control	—	80	4,26±0,33	156,45±0,97
	Injection of atropine into hippocampus after preliminary injection of hydrocortisone	1	64	4,03±0,29*	56,81±3,65
		3	67	3,96±0,65	45,87±1,23
		5	56	3,09±0,56	34,65±2,34
		15	87	4,89±0,98*	56,77±1,65*
		20	81	4,65±0,75*	65,76±2,34
Lateral hypothalamus	Control	—	42	6,98±0,65	132,62±6,61
	Injection of atropine into hippocampus after preliminary injection of hydrocortisone	1	65	5,07±0,41*	98,67±5,78
		3	73	5,67±0,76	67,89±4,65
		5	76	5,97±0,44*	98,76±3,65*
		15	71	6,09±0,67*	110,67±2,56
		20	56	5,98±0,78	98,56±1,45*

TABLE 3. Changes in Mean Frequency and Amplitude of EEG after Microinjections of Atropine into Lateral Hypothalamic Nucleus after Preliminary Injection of Hydrocortisone (M ± m)

Recordings from	Character of procedure	Time (in min)	n	Mean frequency	Amplitude (in μV)
Lateral hypothalamus	Control		85	5,88±0,45	68,9±4,32
	Injection of hydrocortisone	1	73	6,41±0,83	87,4±2,86
		5	51	7,22±0,55	87,0±4,86
		10	51	6,41±0,26	100,9±6,06
		15	63	7,38±0,76	125,2±6,93
		30	32	9,2±1,08*	226,3±8,73
	Injection of atropine	1	52	5,71±0,46	66,7±2,49
		5	59	4,82±0,25	41,9±1,4*
		10	63	4,95±0,46*	81,02±3,09*
		15	77	2,53±0,14	78,7±2,17*
Hippocampus	Control		80	4,26±0,33	151,14±4,31
	Injection of hydrocortisone	1	88	4,57±0,42	168,97±3,76
		5	98	5,76±0,35	157,26±4,82
		10	96	5,27±0,52	92,6±3,15
		15	93	4,49±0,51	144,83±3,86
		30	80	4,72±0,41*	294,41±3,23*
	Injection of atropine	1	91	4,9±0,43*	112,3±2,2*
		5	99	3,9±0,23	123,7±0,89
		10	67	4,4±0,21*	98,8±3,34*
		15	94	3,9±0,26	114,2±4,65

discharges in such cases always arise first in the hippocampus [19]. Injection of hydrocortisone directly into the hippocampus of rabbits is also accompanied by the development of paroxysmal activity [7].

Changes in the global electrical activity of the hippocampus after direct stimulation of the lateral hypothalamus with hydrocortisone were investigated and the results are described below.

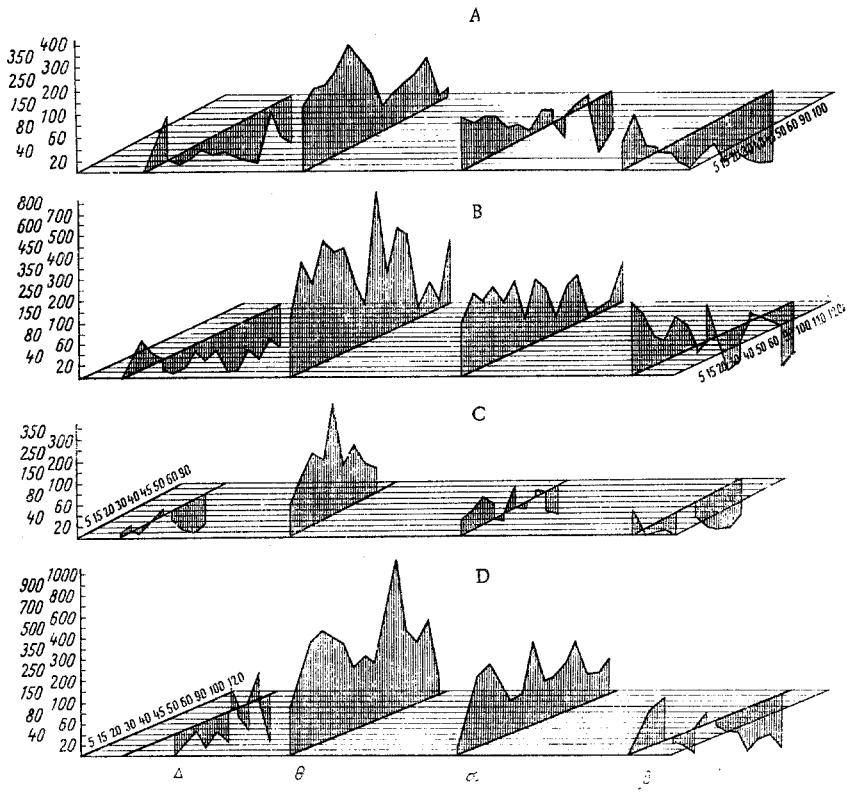

Fig. 2. Results of graphic analysis of EEG of lateral hypothalamic nucleus (A), hippocampus (B), sensomotor cortex (C), and mesencephalic reticular formation (D) of rat after microinjection of hydrocortisone into lateral hypothalamic nucleus. Abscissa, frequency of waves, grouped into 4 classes (Δ-, θ-, α-, and β-); ordinate, "power" of waves in conventional units. Time intervals (minutes) shown along horizontal plane.

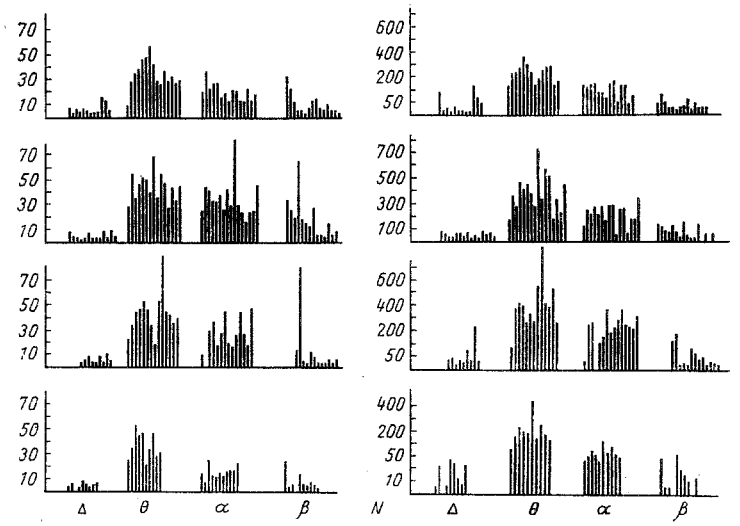

Fig. 3. Results of quantitative analysis of changes in EEG of a rat after injection of hydrocortisone into lateral hypothalamic nucleus. Distribution of total activity of Δ-, θ-, α-, and β-waves of EEG from lateral hypothalamus, hippocampus, reticular formation, and sensomotor cortex (from top to bottom) – on the left; "power" of the same classes of waves and records – on right.

EXPERIMENTAL METHOD

Experiments were carried out on 160 adult albino rats and on 2 rabbits with electrodes implanted into the sensomotor cortex, hippocampus, lateral hypothalamic nucleus, medio-dorsal thalamus, and mesencephalic reticular formation. Polyethylene cannulas were inserted into the lateral ventricles. Microinjections of hydrocortisone (from 5 to 10 μg), acetylcholine, atropine, noradrenalin, and serotonin (in a dilution of 10^{-4}) in a volume of 0.005-0.01 ml were given into the lateral hypothalamic nucleus under the recording electrode by a modified technique of Allikmets et al. [1, 2, 4]. Deep recording electrodes and chemical electrodes were inserted in accordance with the atlas [13]. Potentials were recorded by a monopolar method on a four-channel electroencephalograph (4ÉÉ-I) and eight-channel ink-writing recorder (ÉÉChS-I). Preliminary tests showed that mechanical pressure during microinjection of distilled water in a volume of 0.005-0.01 ml, at pH 4.6, has no significant effect on the spontaneous electrical activity and excitability of the brain structures of the rabbits and rats. The animals were used not more than 3 times in the experiments. After the completion of the experiments contrast radiography and ventriculopneumography were carried out and the localization of the chemical and recording electrodes and cannulas was verified histologically [5]. The results of analysis of the EEG are given as curves of the "power" of the EEG [6]. Frequencies of the waves grouped in 4 classes (Δ-, θ-, α-, and β-) were plotted along the abscissa. The "power" of the waves, i.e., the product of the number of waves of each class of frequencies and the conventional value of their amplitudes, was plotted along the ordinate.

EXPERIMENTAL RESULTS

Microinjections of hydrocortisone into the lateral hypothalamic nucleus induced marked changes in the EEG not only at the site of injection, but also in the hippocampus, in the sensomotor cortex, and in the mesencephalic reticular formation (Fig. 1). The character of the EEG changes differed in the various brain structures and at different times after microinjection of the hormone (Fig. 2). Immediately after injection of hydrocortisone (but especially after 1-3 min) a stable θ-rhythm appeared in the hippocampus, and after 15-50 min it was transformed into paroxysmal activity. Phenomena of desynchronization (Fig. 3) were observed in the mesencephalic reticular formation and the sensomotor cortex at the moment of injection of the hydrocortisone, and against this background bursts of an α-like rhythm, described by the writer previously [8,9], appeared.

To explain the mechanism of the effect of hydrocortisone, when injected into the lateral hypothalamus, on hippocampal activity a series of experiments was carried out in which acetylcholine and atropine were injected. These showed that microinjection of acetylcholine into the lateral hypothalamic nucleus leads to the development of paroxysmal activity both at the site of application immediately after injection and in the hippocampus after 1-3 min. Injection of acetylcholine (like hydrocortisone) into the hippocampus is also accompanied by the appearance of paroxysmal discharges (Tables 1 and 2).

Injection of atropine into the lateral hypothalamic nucleus blocked paroxysmal activity induced both by acetylcholine and by hydrocortisone (Table 3). Since the atropine is a central muscarine-like cholinolytic, hydrocortisone can be considered to have an excitatory effect on muscarine-sensitive cholinergic systems of the hypothalamus and hippocampus.

The possibility cannot be ruled out that changes in the emotional state associated with endocrine disturbances are connected with the direct action of corticosteroids on hypothalamo-hippocampal relations.

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