CHANGES IN THE EEG OF VARIOUS BRAIN STRUCTURES IN RESPONSE TO INJECTION OF INSULIN INTO THE HYPOTHALAMUS

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After injection of small doses of insulin (0.025 unit/kg) into the various hypothalamic nuclei, their electrical activity is changed, as reflected either by the appearance of synchronized waves on the EEG or the onset of paroxysmal discharges. During the action of insulin on the hypothalamus in some cases this synchronizing effect spreads both to structures of the limbic system and to structures of the neocortex. The peripheral blood sugar level in these cases did not reach hypoglycemic values.

The direct effect of hormones on structures of the CNS still remains inadequately studied.

It was accordingly decided to make a systematic analysis of the neurophysiological mechanisms of action of small doses of insulin, not evoking hypoglycemic reactions, on the CNS.

Investigations demonstrating the active role of such concentrations of insulin in the metabolic processes of the organism [3, 4] and, in particular, their action on the brain [1, 2, 8] have recently been published.

EXPERIMENTAL METHOD

Thirty cats weighing 2.5-3.5 kg were deprived of food for 15-18 h and anesthetized with urethane (1.5-2 g/kg). Crystalline insulin in a dose of 0.025 unit/kg in 0.02 ml physiological saline (pH 7.3) was injected instantaneously through cannula electrodes inserted stereotaxically into the hypothalamic nuclei (anterior hypothalamic, supraoptic, paraventricular, lateral, ventromedial, and posterior hypothalamic nuclei) using coordinates from the atlas of Jasper and Ajmone-Marsan [6].

The electrical activity was recorded simultaneously in several structures of the limbic system (ventral hippocampus, amygdala, septum, anterior zones of the gyrus cinguli) and the principal zones of the cortex (frontal, sensomotor, parietal, temporal, occipital).

The electrodes consisted of nichrome wire insulated with bakelite. The EEG was recorded by a monopolar technique and the reference electrode was inserted into the nasal bone. Potentials were recorded on a type 8 RGE (East Germany) eight-channel electroencephalograph and a 17-channel polygraph (Nixon Kohden, Japan). In some experiments a wide-band frequency analyzer made by the same firm was used. The location of the electrode tips in the subcortical structures was verified by a projection method [7].

Parallel with the recording of the EEG, in some experiments the venous blood sugar level was determined by the toluidine method [5]. Blood was taken from the femoral vein before and 10 and 30 min after injection of the hormone. In control experiments physiological saline was injected into the hypothalamic nuclei in the same volume as in insulin.

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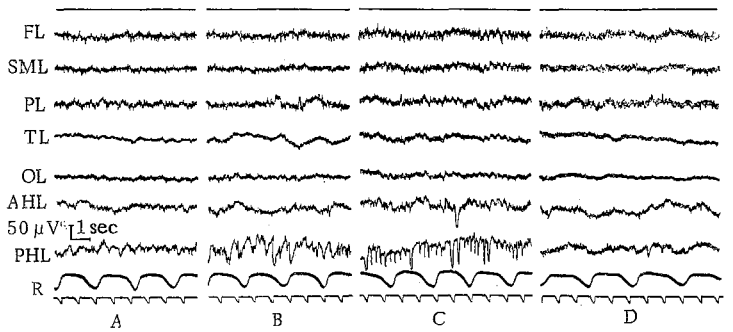

Fig. 1. EEG of various brain structures before (A) and 20 sec (B) and 15 (C) and 30 (D) min after injection of insulin (0.025 unit/kg) into left posterior hypothalamic nucleus. All records monopolar and on the left side. FL) left frontal region of neocortex; SML) left sensomotor area; PL) left parietal region; TL) left temporal region; OL) left occipital region; AHL) left anterior hypothalamic nucleus; PHL) left posterior hypothalamic nucleus; R) respiration. Bottom line: time marker.

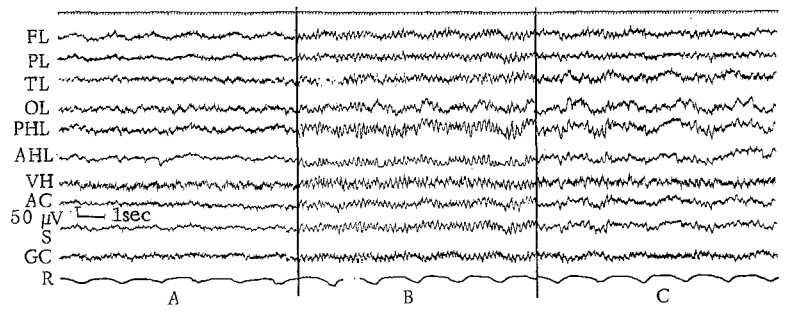

Fig. 2. Synchronizing effect of insulin on brain electrical activity when injected into posterior hypothalamic nucleus. All records monopolar and on the left side. Top line: time marker A) spontaneous activity; B) changes in EEG arising 2 min after injection of 0.025 unit/kg insulin into posterior hypothalamic nucleus; C) changes in EEG 4 min after injection of hormone; VH) ventral zone of hippocampus; AC) cortical nucleus of amygdala; S) septum; GC) anterior zones of gyrus cinguli. Remainder of legend as in Fig. 1.

EXPERIMENTAL RESULTS

From 15 to 20 sec after injection of insulin into the posterior hypothalamic nucleus (Fig. 1) characteristic changes were observed in the spontaneous electrical activity of this structure. The background activity consisting chiefly of high-frequency waves changed principally into slow (2-3 Hz) high-amplitude (80-100 μV) waves on which low-voltage potentials were superposed. After 10-15 min, as the response developed, the hypersynchronization was terminated by the appearance of a paroxysmal rhythm. Other brain structures were activated at the same time, namely the anterior hypothalamus and various zones of the neocortex, the EEG of which at this time was dominated by slow potentials differing in phase (Fig. 1c). As a rule the EEG of these structures was closely similar to their original spontaneous activity after 25-30 min. The state of electroencephalographic activation described above was accompanied by deepening of respiration, indicating the onset of a state of stress in the CNS.

Changes in basic activity obtained in response to injection of insulin into the anterior hypothalamic, supraoptic, paranventricular, lateral, and ventromedial hypothalamic nuclei were on the whole similar to

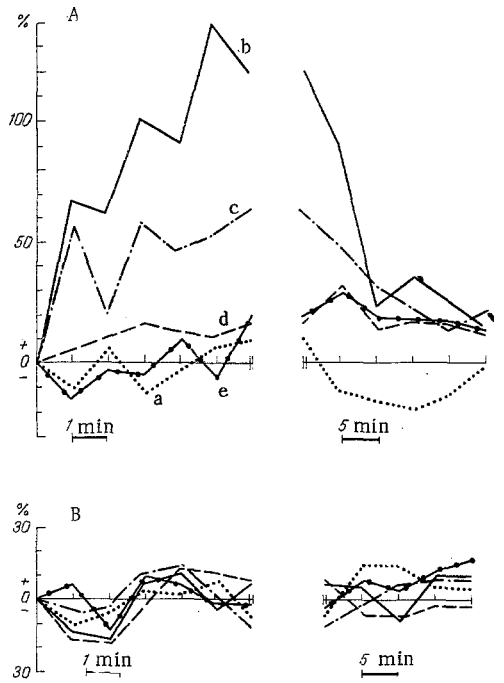

Fig. 3. Dynamics of EEG rhythms of posterior hypothalamic nucleus in response to injection of 0.025 unit/kg insulin (A) and 0.02 ml physiological saline (B) into it: a) σ-rhythm (2-5 Hz); b) θ-rhythm (4-7 Hz); α-rhythm (8-13 Hz); d) β_1-rhythm (13-20 Hz); e) β_2-rhythm (20-30 Hz). Ordinate, changes in each EEG rhythm compared with original background (in percent); abscissa, time before and after injection of insulin (in min).

electrical responses of the posterior hypothalamic nucleus. However, the duration of these EEG changes was shorter, only 10-15 min, and they occurred chiefly in the anterior hypothalamic region.

In some cases in response to injection of insulin into the hypothalamus, especially into its posterior and lateral zones, a synchronization response was observed. It will be clear from Fig. 2, for instance, that 1-2 min after microinjection of insulin into the posterior hypothalamic nucleus the synchronization response spread to the anterior hypothalamic nucleus, the ventral zones of the hippocampus, the amygdala, septum, anterior zones of the gyrus cinguli, and various parts of the cortex. This synchronizing effect lasted not more than 2 min, after which it was converted into an irregular rhythm which was gradually replaced by the spontaneous activity. In this case also respiration was deepened.

Analysis of the frequency spectrum of the EEG before and after injection of insulin showed that synchronization of the electrical waves affected mainly the θ-rhythm and to a lesser degree the α-waves. These changes were particularly clear during the first minutes of action of insulin on the hypothalamus. Groups of fast rhythms of the β-wave type were not so clearly defined and essentially they showed no significant changes (Fig. 3).

Under the influence of physiological saline the EEG pattern did not exceed the variation in spontaneous activity of these brain structures which were examined. The peripheral blood sugar level in no case reached hypoglycemic values.

These investigations thus showed that insulin directly affects the electrical activity of hypothalamic structures, mainly by strengthening the slow waves. A special feature of the action of insulin is its synchronizing effect, which was observed not only at the site of injection of the hormone, but also in other hypothalamic nuclei. The EEG changes in the limbic system and neocortex are regarded as the activating influence of the hypothalamus on higher brain structures, which appears from the results of these investigations to be of the cholinergic type.

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