EFFECT OF DROPERIDOL ON CORTICOFUGAL INFLUENCES IN FOOD MOTIVATION REFLEXES

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The effect of droperidol, a butyrophenone derivative, on the food reflex to electrical stimulation of the hypothalamic food center was studied in experiments on freely moving rabbits. Intravenous injection of droperidol (0.3 mg/kg) lowered the threshold of the evoked food response. Inhibitory influences of the anterior neocortical zones on food responses were absent but facilitatory influences of the caudal regions of the cortex were preserved or even somewhat increased. The effects observed can be explained by the dopamine-negative action of droperidol and by disturbance of the brain inhibitory system.
KEY WORDS: *droperidol; food reflex; inhibitory and facilitatory effects of the neocortex.*

Experiments have shown [1, 3, 6-8, 11, 13, 15, 17] that not only adrenergic but also other brain formations participate in the formation of food responses. The frontal areas of the neocortex have been shown to inhibit the food reflex [4, 8, 9, 16], whereas the caudal areas of the cortex have the opposite effect and facilitate its appearance [4]. Butyrophenone derivatives are known to affect brain structures involved in the functional architecture of food behavior.

In this investigation the action of droperidol was studied on the threshold of the food reflex and on the influence of different cortical areas on the food reflex.

EXPERIMENTAL METHOD

Ten freely moving rabbits weighing 2.5-3 kg were used. The animals taking part in the experiments were those in which a clear food response, expressed as the consumption of ordinary food (cabbage or carrot), was induced by electrical stimulation of the hypothalamic food center. The various brain structures were stimulated and electrical activity recorded by means of thin (0.1 mm) nichrome electrodes, implanted by reference to the atlas of Sawyer et al. into the lateral hypothalamus, the dorsal hippocampus, and also into the frontal and anterior parietal (motor area), posterior parietal (sensory area), and occipital region (visual area) of the cortex. Activity of the subcortical and neocortical formations was recorded on an Alvar 16-channel electroencephalograph. The Soviet ÉSU-1 (with high-frequency attachment) and SIF-4M electrostimulators were used to stimulate the brain. Depending on the accuracy of insertion, threshold intensities of stimulation of the hypothalamic food center were 2-6 V for pulses with a frequency of 50/sec and a duration of 1-3 msec. A current of 5 V, with a frequency of 50 pulses/sec and a pulse duration of 1 msec, was used to stimulate the cortex. Droperidol (Fedeon Richter) was diluted 1:4 with physiological saline and injected in a dose of 0.3 mg/kg body weight into the marginal vein of the ear. The location of the subcortical electrodes was verified histologically.

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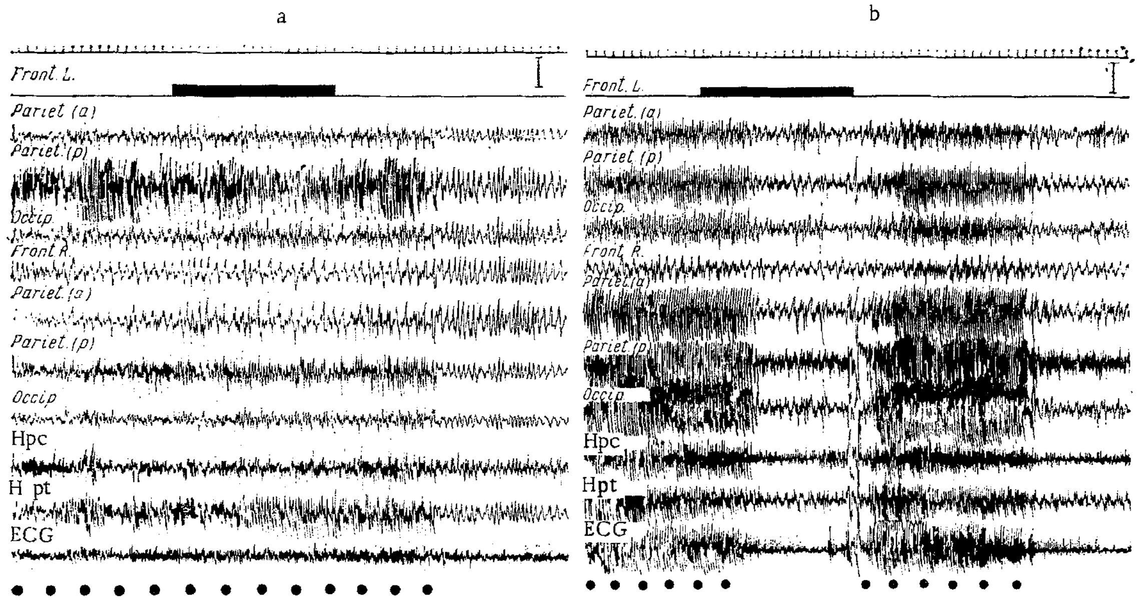

Fig. 1. Effect of stimulation of frontal cortex on food reflex and electrical activity of various brain structures before (b) and after (a) intravenous injection of droperidol. Records from top to bottom: time marker (1 sec); left frontal, left anterior parietal, left posterior parietal, left occipital; right frontal, right anterior parietal, right posterior parietal, right occipital regions; right dorsal hippocampus (Hpc), left lateral hypothalamus (Hpt), and ECG; filled circles show food reflex. Calibration 100 μV. Parameters of stimulation of left frontal region 5 V, 50 pulses/sec, 3 msec.

EXPERIMENTAL RESULTS AND DISCUSSION

The appearance of a goal-directed food reflex in the animals to stimulation of the hypothalamic food center was accompanied by the appearance of a theta-rhythm in the hippocampus and mesencephalic reticular formation and of desynchronization in the neocortical areas. Stimulation of the frontal and anterior parietal cortex raised, whereas stimulation of the posterior parietal and occipital areas lowered the threshold of the food response. Electrical stimulation of the frontal zones of the cortex abolished an existing well-developed food reflex (Fig. 1a).

Intravenous injection of droperidol into the animals did not change the spontaneous activity of the subcortical structures or cortical areas studied. However, droperidol had a facilitatory effect on the food reflex of rabbits when evoked by stimulation of the hypothalamic food center: The threshold of the reflex was lowered and no inhibitory effects were exerted by the frontal neocortical areas.

The degree of lowering of the threshold of the food reflex in different animals depended on its initial level. The maximal decrease in the level of threshold stimulation was 85%.

After injection of droperidol stimulation of the frontal neocortical areas, if applied at the time of taking food, did not interrupt the animal's food reflex, as was usually the case (Fig. 1b).

Electrical stimulation of the caudal areas of the cortex before injection of droperidol led to a decrease in the threshold of the evoked food reflex or even to the appearance of satiated animals (Fig. 2a). Injection of droperidol not only preserved but actually potentiated cortical facilitatory influences: The duration of the food reflex was increased (Fig. 2b).

The food response of animals after injection of droperidol acquired the character of "food automatism," i.e., a food reflex aimed at inedible objects: pieces of wood, bandages, and so on. The "food automatism" was particularly marked when the animals had finished eating their natural food and it was characterized by regular masticatory movements (Fig. 2b).

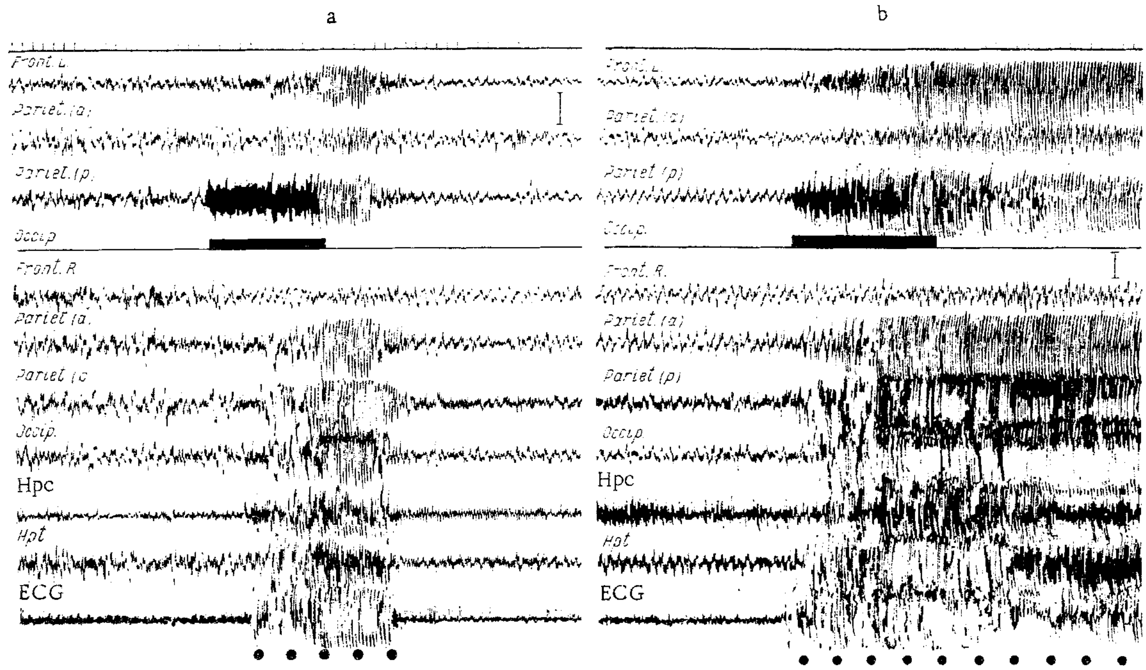

Fig. 2. Food reflex evoked by electrical stimulation of occipital cortex before (a) and after (b) intravenous injection of droperidol. Legend as in Fig. 1.

Certain areas of the cortex and subcortical structures are known to have both inhibitory and facilitatory influences on behavioral (including food) responses. Besides the limbic structures, the caudate nuclei and substantia nigra are known to occupy a special place in the production of these inhibitory influences [6, 12, 14]. High concentrations of dopamine have been found in these structures [10]. According to Valzelli [18], drugs of the butyrophenone group, which includes droperidol, are more dopamine-negative than α-adrenolytic in their central action. Despite the contradictory nature of data on the mechanism of action of butyrophenones [2, 3, 5, 18], the writers consider that droperidol selectively blocks brain structures containing dopamine, with the result that the threshold of the evoked food reflex must be lowered and the inhibitory influences of anterior cortical zones on this reflex are abolished.

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