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CHARACTERISTICS OF FRONTAL-HIPPOCAMPAL INFLUENCES DURING THE FORMATION OF FOOD BEHAVIOR IN RABBITS AFTER BILATERAL DESTRUCTION OF THE LATERAL HYPOTHALAMUS

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KEY WORDS: food behavior; frontal cortex; dorsal hippocampus.

According to the "pacemaker theory of motivation" [2, 4], the decisive role in the transformation of a biological need into a process of central nervous excitation is played by hypothalamic formations whose neurons, by virtue of the unique features of their metabolism and their exceptional informativeness about the state of the various blood constants, perform the functions of special pacemakers. However, starting with the 1960s, investigators have described behavioral reactions aimed at the satisfaction of the most important biological needs in animals with bilateral destruction of the principal motivation-generating hypothalamic formations [5, 6, 8-10]. In this connection it was interesting to analyze the role of certain brain structures and, in particular, of the dorsal hippocampus and frontal neocortex, in the development of the food behavior of rabbits with bilateral destruction in the region of the lateral hypothalamus.

EXPERIMENTAL METHOD

Experiments were carried out on 12 waking rabbits weighing 2.5-3 kg, taken from a total of 24 animals in which the lateral hypothalamus was destroyed bilaterally. The lateral region of the right and left hypothalamus was stimulated and subsequently coagulated through thin (0.1 mm) bipolar nichrome electrodes which, in accordance with Sawyer's atlas, were implanted into the previously scalped rabbit. The animals were fed and then tested for their food behavior in response to electrical stimulation of both the right and left lateral hypothalamus.

The hypothalamic structures were coagulated by a current of 1-2 mA acting for 20-40 sec.

After not less than 3 days the animals with bilateral destruction of the lateral hypothalamus, having successfully survived the recovery period, had electrodes implanted into their dorsal hippocampus and into the frontal region of their neocortex. Conditioning stimulation of these brain structures had the following parameters: 5-7 V, 50 Hz, pulse duration 1 msec.

To analyze the chemical mechanisms determining food behavior in animals with destructive lesions of the lateral hypothalamus and, in particular, the role of cholinergic and dopaminergic structures, atropine (1 mg/kg) and droperidol (0.3 mg/kg) were injected into the marginal vein of the rabbit's ear. The results were subjected to statistical analysis by Student's t-test. The location of the subcortical electrodes was verified histologically in brain sections cut to a thickness of 50-100 μ.

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TABLE 1. Latent Periods (in sec) of Inhibition of Food Reaction in Rabbit with Bilateral Destruction of Lateral Hypothalamus and in Response to Stimulation of Dorsal Hippocampal and Frontal Cortex before and after Intravenous Injection of Atropine and Droperidol (M ± m)

Experimental conditions	Dorsal hippocampus	Frontal cortex
Normal	4,90±0,59	5,42±0,61
Injection of 1 mg/kg atropine	4,66±0,53	4,50±0,67
Injection of 0.3 mg/kg droperidol	6,61±1,16	7,73±1,27

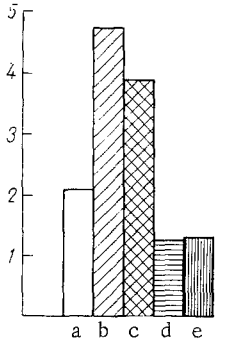

Fig. 1. Latent periods (in sec) of food reaction in rabbits with bilateral destruction of lateral hypothalamus under normal conditions (a), during electrical stimulation of dorsal hippocampus (b) and frontal cortex (c), and after intravenous injections of atropine (d) and droperidol (e).

EXPERIMENTAL RESULTS

Bilateral destruction of the lateral hypothalamus in 24 rabbits was followed by survival of 12 animals without any intervention on the part of the experimenter aimed at improving the state of the animals during the recovery period. The rest of the animals died 2-4 days after electrolytic destruction of the "food center" with signs of aphagia, adipsia, and reduced activity to tactile and nociceptive stimuli.

The animals used in the experiments recovered their food reactions and satisfied their needs of food and water independently; nevertheless, they differed from intact rabbits in the smaller range of their motor activity and, in particular, a sharp reduction in their orienting behavior. With free access to ordinary food the hungry animals did not exhibit search reactions, such as sniffing or alerting, but they began to take food only as a result of direct contact with it.

The active search for food and oriented movement in response to provocation by food were not given by rabbits with bilateral destruction of the hypothalamic "food center."

Electrical stimulation of the dorsal hippocampus and frontal cortex increased the latent period of the food reaction ($P < 0.001$) in 85.7% of cases on the 3rd-5th day after coagulation. It will be clear from Fig. 1 that isolated stimulation of the dorsal hippocampus had a stronger inhibitory effect on the beginning of food consumption than stimulation of the frontal neocortex.

Stimulation of these brain structures, when food consumption was already considerable, also had an inhibitory effect ($P < 0.001$). A few seconds after the beginning of stimulation the animals stopped taking food (Table 1).

In this case also inhibition of the food reaction in response to electrical stimulation of the dorsal hippocampus took place sooner than during electrical stimulation of the frontal cortex.

Intravenous injections of atropine (1 mg/kg) and, in particular, of droperidol (0.3 mg/kg) were accompanied by marked changes in the animals' behavior. Orienting reactions were intensified and food-getting activity increased. The rabbits began to grasp food more rapidly than before the injections, as shown by the shorter latent periods of onset of the food reaction (Fig. 1). The character of the food reaction changed: The duration of food consumption and the number of chewing movements increased. However, despite intensification of food behavior of the rabbits with bilateral destruction of the hypothalamic "food center" by atropine and droperidol, the inhibitory influences of the dorsal hippocampus and frontal cortex on this behavioral reaction still remained ($P < 0.01$).

These observations appear to be extremely important, for in intact animals inhibitory influences of the dorsal hippocampus and frontal region of the neocortex on food reactions were abolished through the action both of the dopamine blocker droperidol and of the muscarinic cholinergic blocker atropine [3].

The investigations showed that bilateral destruction of the lateral hypothalamus was accompanied by considerable disorders of the mechanisms responsible for homeostasis, in what has been called the "lateral hypothalamus syndrome" [10]. Like many workers [5, 6, 8-10], we found recovery of food behavior in animals with bilateral destruction of the hypothalamic "food center." However, the restored food behavior of animals with destroyed food motivation centers differed from the food behavior of intact animals, mainly in its passive character, the absence of searching for food, and depression of orienting and investigative activity.

Some workers [5, 6, 9] have paid particular attention to the different types of sensomotor dysfunctions arising in bilateral destructive lesions of the lateral hypothalamus, for in their opinion these dysfunctions are the leading factors in the disturbances of feeding and drinking behavior. These disturbances are linked with a decrease in the dopamine concentration in the brain of animals after these operations [7].

The results of the present experiments showed that destruction of the lateral hypothalamus was accompanied by considerable and many sided disturbances of the mechanisms of maintenance of homeostasis. However, the motivational aspect of the animals' behavior was directly affected in this case.

Some differences in food behavior in animals with bilateral coagulation of the lateral hypothalamus from the behavior of intact animals were observed in the present experiments with atropine and droperidol, just as in other investigations using 2-deoxyglucose [11]. It can be postulated that in the recovery period after coagulation of the lateral hypothalamus some adjustment to cortico-subcortical interrelations takes place, when other brain formations, for example the brain-stem reticular formation [1], can perform the role of pacemakers. This readjustment is also characterized by a new integration, in particular, of the cholinergic and dopaminergic structures of the brain, which are ultimately responsible for behavior directed toward the satisfaction of vitally important needs.

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EFFECT OF ANTITHYROID ANTIBODIES ON THYROID HORMONE SECRETION

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KEY WORDS: secretion; hormones; autoimmune thyroiditis; antibodies.

Extensive factual material has now accumulated on the discovery of circulating antithyroid autoantibodies in patients with various thyroid gland diseases, but their pathogenetic role has not been finally established. Several investigations suggest that circulating autoantibodies have a different point of application in the pathogenesis of autoimmune thyroiditis from direct injury to the thyroid gland tissues, namely their effect on secretion and peripheral utilization of thyroid gland hormones [3, 4].

The object of the present investigation was accordingly to study secretion of thyroid hormones both in animals with experimental autoimmune thyroiditis and in rats with passive immunization with immune sera and with antithyroid antibodies.

EXPERIMENTAL METHOD

Experiments were carried out on Chinchilla rabbits weighing 3 kg and on noninbred rats weighing 180 g. The rabbits were divided into four groups: 1) healthy rabbits not receiving thyroid-stimulating hormone (–TSH), 2) immunized rabbits (–TSH), 3) healthy rabbits (+TSH), 4) immunized rabbits (+TSH).

The experimental rats were kept for 11 days on an iodine-free diet and the animals were divided into five groups: 1) healthy rats (+TSH) – control, 2) immunized (+TSH), 3) receiving serum of healthy rats (+TSH) – control, 4) receiving serum of immunized rats (+TSH), 5) receiving antibodies (+TSH).

Autoimmune thyroiditis was reproduced in the rabbits and rats by the method of Witebsky and Rose [5]. The rabbits received a single injection of 3 units TSH, and measurements were made 24 h after its injection. Rats were passively immunized with sera and antibodies twice, with an interval of 3 days between injections, each in a volume of 1 ml intraperitoneally. Each animal received 50 microunits TSH intraperitoneally 30 min before sacrifice. To assess thyroid secretion, the method of counting colloid droplets in 100 cells, measurement of acid protease activity, pH 3.8, and radioimmune determination of the concentrations of serum triiodothyronine (T_3) and total thyroxine (T_4) by means of kits from the Radiochemical Centre, Amersham (England), was used.

EXPERIMENTAL RESULTS

Proteolytic enzyme activity in the thyroid gland of healthy rabbits was 19.6 ± 1.7 mg tyrosine/g weight of gland, whereas in the animals with autoimmune thyroiditis it was reduced to 6.1 ± 0.6 mg tyrosine/g weight of gland (Table 1). Injection of 3 units TSH into healthy rabbits increased activity of the enzyme to 26.1 ± 0.01 mg tyrosine/g weight of gland, and this was used as the control for activity of this hormone because a manifestation of the early action of TSH is known to be proteolysis of colloid. A single injection of TSH into rabbits with autoimmune thyroiditis led to an increase in acid protease activity.

Colloid endocytosis and secretion of hormones into the blood were studied in rats kept on an iodine-free diet. Without stimulation of healthy rats with TSH the colloid endocytosis

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