

## EFFECT OF ETHANOL ON CENTRAL MECHANISMS OF THE FOOD RESPONSE TO ELECTRICAL STIMULATION OF THE LATERAL HYPOTHALAMUS

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The study of the central mechanisms of biological motivations forming goal-directed behavioral reactions aimed at satisfying vitally important demands has shown that every biological motivation is the result of specific integration of cortical and subcortical brain formations [5], in which an important role is played by limbico-mesencephalic structures [9]. More recently interest in the study of the central mechanisms of various motivational reactions and their disturbances under the influence of ethanol have aroused increased interest. Disturbances of drinking behavior [7], the self-stimulation response [4], and so on, have been described under the influence of ethanol.

The aim of the present investigation was to study the action of ethanol on the formation of food motivation in rabbits and also on the character of the influence of the dorsal hippocampus and mesencephalic reticular formation on excitability of the "food center" of the lateral hypothalamus.

### EXPERIMENTAL METHOD

Experiments were carried out on 14 unrestrained rabbits weighing 2.5-3 kg. The animals were fed before taking part in the experiments. To obtain goal-directed behavior, fine (0.1 mm) nichrome bipolar electrodes were implanted, taking coordinates from the atlas of Sawyer et al. (1957), into the lateral hypothalamus of the previously scalped rabbit. Electrodes also were implanted in the dorsal region of the hippocampus and mesencephalic reticular formation. Threshold stimulation of the hypothalamic "food center" varied from 2 to 6 V depending on the accuracy of placing of the electrode, and the frequency of stimulation was 50 Hz and the pulse duration 1 msec. Conditioning stimulation of the dorsal hippocampus and mesencephalic reticular formation in experiments to study changes both in the threshold of stimulation of the lateral hypothalamus and in the latent period of the evoked food response was given with an intensity of 5-7 V, a frequency of 50 Hz, and a pulse duration of 1 msec. The total duration of conditioning stimulation of the limbico-mesencephalic structures was 10 sec.

A 40% solution of ethanol in ampul-packed physiological saline was injected in a dose of 0.5 g/kg body weight into the marginal vein of the rabbit's ear. The time course of the threshold of lateral hypothalamic stimulation and changes in latent periods of the food response after conditioning stimulation of the dorsal hippocampus and mesencephalic reticular formation began to be determined 15 min after the injection. The results of the investigations were subjected to statistical analysis. The location of the subcortical electrode was determined histologically by examination of brain sections cut to a thickness of 50-100  $\mu$ .

### EXPERIMENTAL RESULTS

Threshold stimulation of the hypothalamic "food center" evoked food consumption by the fed animals, usually preceded by a brief orienting-investigative response. The writers showed previously [6] that the excitability of the various motivation centers of the hypothalamus is under the influence of several limbico-mesencephalic formations. In particular, conditioning

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Region of stimulation	Latent period of food behavior					
	Before administration of ethanol			After injection of ethanol		
	Reduced	Increased	No effect	Reduced	Increased	No effect
Dorsal hippocampus	—	13 92,86%	1 7,14%	—	3 21,43%	11 78,57%
Mesencephalic reticular formation	8 80,0%	1 10,0%	1 10,0%	2 20,0%	1 10,0%	7 70,0%

Fig. 1

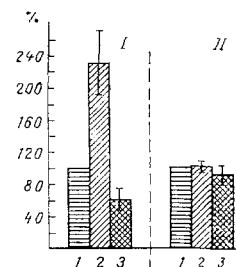


Fig. 2

Fig. 1. Effects of stimulation of dorsal hippocampus and mesencephalic reticular formation on development of food behavior in rabbits before and after i.v. injections of ethanol (0.5 g/kg).

Fig. 2. Changes (in percent) in latent periods of food response to stimulation of subcortical structures before (I) and after (II) intravenous injections of ethanol in a dose of 0.5 g/kg ( $P < 0.05$ ). 1) Isolated threshold stimulation of lateral hypothalamus; 2) threshold stimulation of lateral hypothalamus after 10 sec of conditioning stimulation of dorsal hippocampus; 3) threshold stimulation of lateral hypothalamus after 10 sec of conditioning stimulation of mesencephalic reticular formation. Parameters of conditioning stimulation: 5-7 V, 50 Hz, 1 msec.

stimulation of the dorsal hippocampus significantly raised the threshold of stimulation of the lateral hypothalamus, whereas conditioning stimulation of the mesencephalic reticular formation, on the contrary, had a facilitating effect on the development of goal-directed food behavior in the animals.

Analysis of changes in the threshold of stimulation of the lateral hypothalamus after intravenous injections of 40% ethanol into the animals showed that after a brief fall (to 30 min) excitability of the hypothalamic "food center" was restored.

Under the influence of ethanol the animals showed changes in the character of hippocampal-reticular influences on food behavior formation. Data on the effect of conditioning stimulation of the dorsal hippocampus and mesencephalic reticular formation on the latent period of the animals' food response to electrical stimulation of the lateral hypothalamus before and after intravenous injections of ethanol are given in the scheme in Fig. 1. In the above-mentioned concentration, ethanol abolished not only inhibitory hippocampal influences on excitability of the hypothalamic "food center" but also facilitatory influences on formation of food behavior from the mesencephalic reticular formation.

The results of a concrete analysis of changes in latent periods of the food response under the influence of conditioning stimulation of the dorsal hippocampus and mesencephalic reticular formation are given in Fig. 2. Under normal conditions conditioning hippocampal stimulation increased the latent period of the food response to 229.4% ( $P < 0.05$ ), whereas conditioning stimulation of the mesencephalic reticular formation reduced the latent period to 60.2% ( $P < 0.05$ ).

Intravenous injections of ethanol (0.5 g/kg) were accompanied by structural changes in the central mechanisms of food behavior, as a result of which the latent periods of the food response to isolated stimulation of the hypothalamic "food center" taken as 100%, did not differ significantly ( $P < 0.05$ ) from the latent periods of the food response after preliminary stimulation of the dorsal hippocampus and mesencephalic reticular formation (100.5 and 90.92%, respectively).

The authors showed previously [6] that inhibitory influences of different brain formations on the mechanisms of formation of the food response in rabbits were abolished by muscarinic cholinolytics and dopamine blockers, whereas facilitatory influences of, for example, the mesencephalic reticular formation were abolished by an  $\alpha$ -adrenoblocker.

Analysis of the results of these experiments, in which ethanol disturbed both inhibitory and facilitatory influences of limbico-mesencephalic structures on the development of the food response leads to the conclusion that ethanol affects monoaminergic and cholinergic brain

mechanisms. This conclusion is in agreement with the opinions of investigators on disturbance of the metabolism of various neurotransmitters, especially dopamine, noradrenalin, serotonin, and GABA, by ethanol [1-3].

However, interpretation of disturbances of the chemical mechanisms of brain activity by ethanol is complicated by the fact that ethanol itself powerfully stimulates the production of certain biologically active substances in the gastrointestinal tract, such as gastrin and secretin [12], substances of a peptide nature which, in turn, have complex effects on neuromediator processes in the central and autonomic nervous systems [8, 10, 11, 13].

Disturbances of the central mechanisms of the food response and, in particular, of inhibitory hippocampal and facilitatory reticular influences on excitability of the hypothalamic "food center" are thus the result of complex disintegration of the chemical mechanisms of the brain, affecting widely different neuromediator systems.

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