

THE ELECTROENCEPHALOGRAM AND NEUROHUMORAL MECHANISMS OF SATIETY

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Until recently the great majority of investigators have estimated satiety chiefly in terms of feeding behavior [3, 4, 6-11]. As a rule the criterion is the refusal of food offered. Nevertheless refusal to take food does not always indicate that appetite has been satisfied, because sometimes it may result from the action on the feeding center of other stronger non-feeding central excitation. Therefore it is natural in studying the true mechanism of satiety that other more precise objective indications of the functional condition of the feeding center should be sought. As our previous experiments have shown the electroencephalogram may serve as an index [5].

From published reports [1, 2] it is known that satisfaction of appetite is a complex neurohumoral process.

However the problem of how the inter-relation between the nervous and humoral mechanisms is established during the process of satiation of the appetite remains unsolved. To take the initial steps in an approach to this problem in the present investigation we have studied the changes in the EEG in animals in response to stimulation of receptors in the intestinal tract sensitive to food, and also in response to the entry of nutritive substances into the blood stream.

EXPERIMENTAL METHOD

The experiments were carried out on male and female cats weighing from 2 to 3.5 kg which had been kept without food for 24 hours. We carried out 30 acute experiments under 1.5-2.5 g/kg intraperitoneal urethane. The electroencephalogram was recorded from the surface of the skull by means of steel needle electrodes. Recording was unipolar. The indifferent electrode was placed in the midline above the frontal sinus. The EEG was recorded by a "Al'var Elektronnik" ink-writing 10-channel electroencephalograph.

In the first set of experiments we investigated changes in the EEG of hungry animals in response to artificial stimulation of the receptors of the oral cavity and stomach. As food stimulus we used 80-100 ml of warm milk.

In the second set of experiments we studied the changes in the EEG occurring in hungry and satiated animals after injection into the blood stream of glucose solutions.

EXPERIMENTAL RESULTS

It has already been shown [5] that urethane anaesthesia selectively leaves unblocked the central mechanisms related to the digestive system, and under urethane anaesthesia the condition of hunger is indicated by a high-frequency, low-amplitude electrical activity in the anterior portions of the cerebral cortex, which occur during slow high-amplitude oscillations in the parieto-occipital regions (Fig. 1, A).

During stimulation of the receptors of the oral cavity only in animals in which the esophagus was divided in the neck, in 17 experiments there was some increase in the amplitude of cerebral potentials, including the anterior regions (Fig. 1, B). This result indicated a decrease of cortical activation. This reaction usually developed 15-30 seconds after the onset of stimulation and continued for not more than 5 minutes.

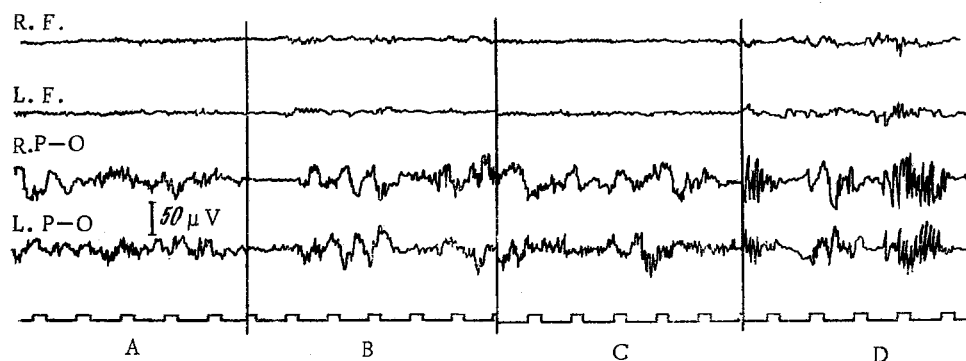


Fig. 1. Reflex changes in the EEG of a hungry animal during artificial feeding under urethane anaesthesia. A) initial EEG of hungry animal; B) EEG after irrigation of the oral cavity with milk and subsequent introduction of milk into the stomach; C) EEG 15 minutes after introduction of milk into the stomach; D) EEG 60 min after introduction of milk into the stomach. R. F.) left frontal region; R. P-O) right parieto-occipital region; L.P-O) left parieto-occipital region. Time marker 1 second.

Subsequent introduction of milk into the stomach increased this reaction, and also increased its duration to 15-20 minutes.

Subsequently the original EEG pattern was restored (Fig. 1, C). In only 2 of the experiments in which we stimulated the gastric receptors and receptors of the oral cavity with milk were we unable to record any EEG changes. Stimulation of the gastric receptors alone (without any previous stimulation of the receptors of the oral cavity, as was effected by the introduction of 60-80 ml of milk through a tube directly into the stomach) as a rule caused no changes in the EEG. Then, although the stomach was filled with milk, desynchronization of the EEG was maintained in the anterior cortical regions. Only in 3 of the 13 experiments did we then observe a brief increase in the amplitude of the potentials, and in these experiments the stomach contained more than 80 ml of milk. All these results indicate that initial stimulation of the receptors of the oral cavity appears to create conditions which facilitate subsequent reflex influences on the feeding center exerted by the lower parts of the digestive tract.

From these experiments we came to the conclusion that stimulation of receptors of the oral cavity and stomach may reflexly eliminate activation of the anterior portion of the cortex (activation which is observed in hungry animals). However this reaction is of short duration.

Subsequent experiments showed that 45-60 min after the introduction of food into the stomach through a tube the amplitude of cortical potentials once more increased, and after a certain time slow high-amplitude activity was recorded from all parts of the brain (Fig. 1, D). Subsequently the slow high-amplitude waves were maintained in the EEG for a long time. This maintained high-amplitude electrical activity was recorded under urethane anaesthesia also in animals which had been fed before the experiment. We therefore suppose that the maintained elimination of "hunger" activation of the cerebral cortex is due to the direct action on the feeding center of nutritive substances which have entered the blood stream from the digestive tract.

To study the role of humoral factors in the mechanism of we have studied EEG changes in hungry animals after introduction of glucose into the blood. These experiments showed that the injection of glucose into the blood of a hungry animal caused only a brief increase in amplitude of the potentials in the anterior parts of the cortex (Fig. 2, A). This reaction did not continue for more than 10-15 min, after which the low-amplitude high-frequency activity was resumed in the anterior regions. However the introduction of the same glucose solution after irrigation of the oral cavity with milk and subsequent introduction of milk into the stomach caused a considerable increase in the amplitude of the potentials in all parts of the cortex including the anterior regions (Fig. 2, B). This slow high-amplitude cortical activity was maintained for along time.

All these experiments indicated that the state of satiety of the feeding center develops only as a result of a close mutual interaction of nervous and humoral mechanisms; the most prolonged effect on the controlling action of the feeding center occurred only after contact of the receptors of the oral cavity and stomach with the food. The nervous mechanism of satiety appears to play only a preparatory part, and the maintained changes in the feeding

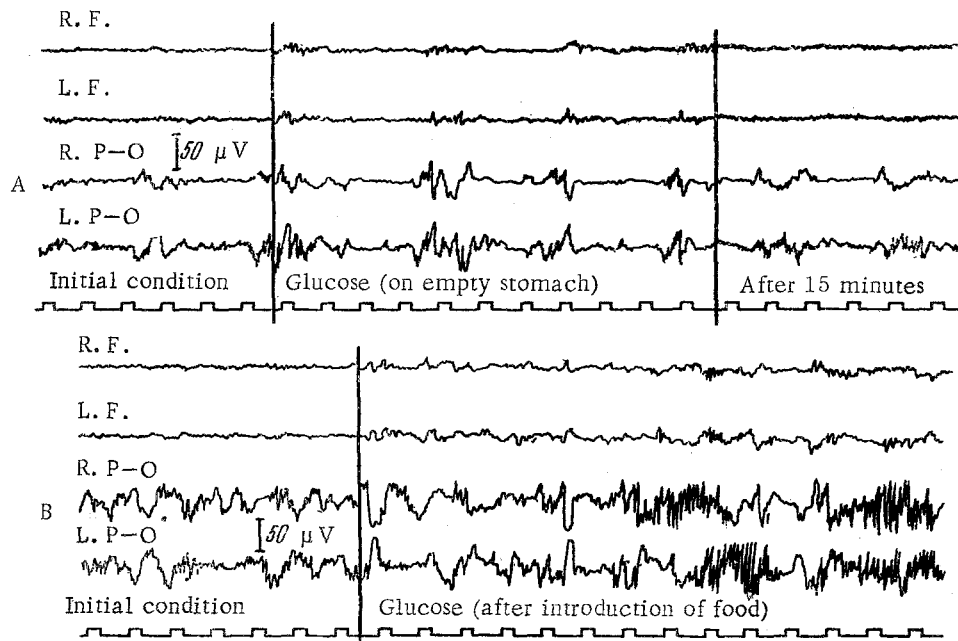


Fig. 2. Changes in the EEG after injection of glucose solution into the blood and after the artificial introduction of food into the empty stomach. A) 10 ml of 5% glucose injected intra-arterially with the stomach empty; B) injection of glucose solution 20 min after irrigation of the oral cavity with milk, and after the stomach had been filled with milk. Leads as in Fig. 1.

center are superimposed upon it and are mediated by the action of "sated" blood. The fact that after food has been taken the selective activation of the anterior cortical regions disappears, an activation which is clearly shown in the hungry state, indicates that during satiety there is a considerable reduction in the ascending activating influence arising from subcortical structures related to the feeding center.

Reduction in the functional activity which develops in the feeding center when food enters the oral cavity is reinforced by subsequent afferent impulses from the stomach. However these changes are brief. Only after the food has been absorbed into the blood stream do such impulses evoke a maintained reduction in the excitability of the feeding center. Thus to bring about satiety the chief requirement is the natural succession of events associated with feeding. Our experiments indicate that any natural disturbance in the sequence of this process, as for example by the introduction of food directly into the stomach or of glucose into the blood stream while the stomach is empty causes only a brief change in the EEG characteristic of the sated condition.

From these results we may conclude that satiety is a cyclic neurohumoral process.

SUMMARY

An electroencephalographic analysis was made of neurohumoral mechanisms associated with satiety. The experiments were performed on cats under urethane anaesthesia. Specific ascending activation of the anterior parts of the cortex of hungry animals disappeared after the introduction of food into the mouth or stomach. The effect was only temporary, and within one to two hours after introduction of food into the stomach "hunger" activation of the cortex regularly disappeared. A similar effect was obtained when food was introduced into the stomach at the same time that a glucose injection was given into the blood stream. These experiments showed that the mechanism of satiety was neurohumoral in origin. The nervous mechanism of satiety operated as a trigger, while the main effect in diminishing "hunger" activation was due to absorption of food from the intestine. The most remote effect was observed when food was introduced into the body by natural means, i.e. when it first came in contact with the oral and gastric receptors and was subsequently absorbed into the blood stream.

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