A NEURO-HUMORAL MECHANISM OF ACTIVATION OF THE FRONTAL CORTEX DURING PHYSIOLOGICAL STARVATION

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Progress in the study of the functions of the brain as a result of the introduction of new experimental techniques has converted the subject of hunger and satiation into a neurophysiological problem. Important research in this field [4, 5, 6, 9] has shown that the lateral division of the hypothalamic region takes part in the formation of food-acquiring behavior, whereas the medial divisions of the hypothalamus take part in the depression of food activity. The work of Mayer and co-workers [10, 11] is no less important. According to Mayer, satiation develops during the utilization of glucose by special "gluco-receptors" in the medial hypothalamus as soon as the glucose concentration in the blood reaches a certain level.

All these experiments show that the central structures of the nervous system undoubtedly take part in the formation of food behavior. Nevertheless, they shed absolutely no light on the concrete physiological mechanism underlying the different forms of food behavior.

The functional concept of a food center was first proposed in 1911 by I. P. Pavlov [2]. Pavlov considered that the main stimulus for the food center is the chemical composition of the blood of starving animals. He also postulated that purely nervous influences may also take part in the activity of the food center. We do not yet know, however, the nature of the interaction between nervous and humoral factors in the functioning of the food center.

It has been shown that the reaction of desynchronization of the slow activity in the frontal areas of the brain of starving animals under urethane anesthesia is brought about by the "fasting" state of the food center [3]. We must now determine how these nervous and humoral influences play their part in the ascending, selective activation of the frontal cortex in starving animals.

EXPERIMENTAL METHOD AND RESULTS

Experiments were conducted on 42 cats under urethane anesthesia. Urethane was injected intraperitoneally in a dose of 1.5-3.0 g/kg body weight. As a rule the animals fasted for 24 h before the experiment. In some experiments starvation lasted 48 h.

The surface of the skull was exposed in the anesthetized cats and the EEG recorded by means of steel needle electrodes. The potentials were recorded by means of bipolar leads from the frontal and parieto-occipital regions of each hemisphere. The distance between the electrodes was usually 3 mm. A 10-channel electroencephalograph manufactured by the firm "Alvar Electronic" was used.

At the beginning of each experiment the vagus nerves were exposed bilaterally in the neck and ligatures placed around them. A glass cannula filled with physiological saline was introduced into the peripheral end of one carotid artery.

The first stage in the investigations was to study the role of humoral influences on the food center in the mechanism of ascending activation of the frontal divisions of the cortex.

As the humoral agent in these experiments we used a 5% glucose solution for, according to the literature [11], glucose acts on the central structures of the food center. This solution was usually injected into the peripheral end of one carotid artery, i.e., toward the brain. As a rule, 10 ml of this solution was injected after the original background EEG had been recorded (Fig. 1A).

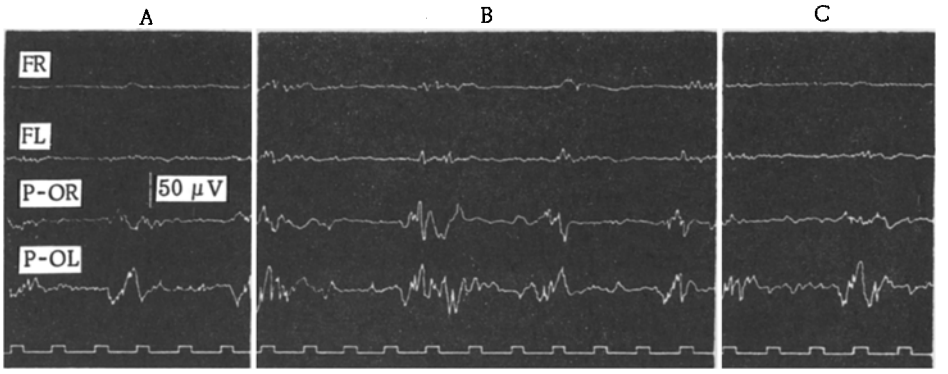

Fig. 1. Changes in the EEG of a fasting cat after injection of glucose solution into the blood stream. A. Initial background cortical activity. B Two min after injection of 10 ml 5% glucose solution into the central end of the left carotid artery. C. Fifteen min after injection of glucose. In Figs. 1-3: FR) right frontal; FL) left frontal; P-OR) right parieto-occipital; P-OL) left parieto-occipital regions. Time marker 1 sec.

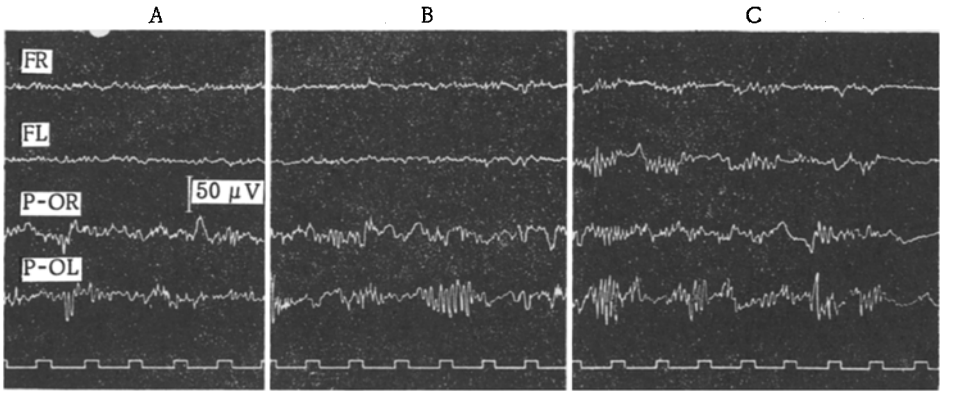

Fig. 2. Changes in the EEG of the fasting cat after division of both vagus nerves in the neck and of the spinal cord at the level of the 5th thoracic vertebra. A. Initial cortical activity. B. Fifteen min after division of the vagus nerve. C. After division of the spinal cord.

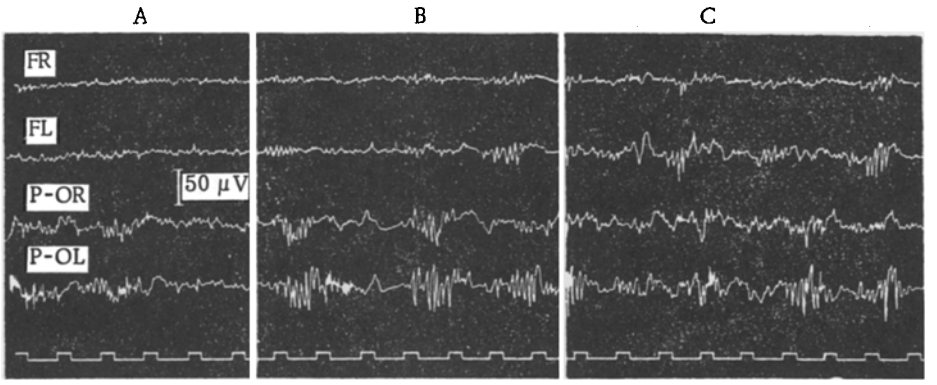

Fig. 3. Changes in the EEG of a fasting cat after injection of glucose solution, preceded by division of both vagus nerves and the spinal cord. A. Initial EEG. B. After division of both vagus nerves in the neck and spinal cord at the level of the 5th thoracic vertebra. C. After injection of 10 ml 5% glucose.

When we injected glucose solution into the animals' blood stream, we were acting on the assumption that if "fasting" blood does, in fact, play an essential role in the activation of the frontal divisions of the brain, the removal of this factor must weaken to some extent this activation.

In 10 of 18 experiments, injection of glucose solution into fasting animals caused a slight increase in the amplitude of the potentials in the frontal cortex (Fig. 1B); this reaction was of brief duration and was observed for not more than 10-15 min, after which a low-amplitude, high-frequency activity was again seen in the frontal cortex (Fig. 1C). In the remaining experiments the injection of glucose into animals with an empty stomach had absolutely no effect.

It might therefore be thought that not only humoral influences were concerned in this case. Subsequent experiments were carried out to study the role of afferent nervous impulses coming from the empty stomach in the mechanism of ascending activation of the frontal divisions of the cortex in fasting animals.

In order to exclude influences from the empty stomach and the other digestive organs on the food center, in a series of experiments the afferent nerve supply of the abdominal viscera was interrupted. Both vagus nerves were divided at the level of the third cervical vertebra, and the spinal cord at the level of the 3rd-5th thoracic vertebrae. The principal afferent supply from the digestive organs to the central nervous system is known to enter through these two routes [7,8].

These experiments showed that rapid and careful division of the vagus nerves or the spinal cord separately caused no appreciable change in the initial background EEG of the fasting animals (Fig. 2A, B). In only a few experiments was a transient reaction of desynchronization of the EEG observed in all parts of the brain immediately after section. Special experiments showed that this reaction was associated with traction on the vagus nerves or with the grosser manipulations involved in opening the spinal canal. This reaction usually disappeared after 5-10 min, and the initial activity of the EEG was restored.

When, however, both vagus nerves and the spinal cord were divided in the animals, after 10-15 min a considerable increase in the amplitude of the potentials in the frontal cortex was observed. The reaction of desynchronization of the EEG in these divisions was replaced by high-amplitude, slow activity, like that observed in other parts of the brain; this reaction continued for more than 1 h (Fig. 2C).

For control purposes, in a series of experiments, after the vagus nerves had been divided,the spinal cord was divided initially in the lumbo-sacral division. In these experiments the slow activity did not develop in the frontal cortex. It appeared only when the spinal cord was also divided in the thoracic division. These experiments showed that the development of high-amplitude slow activity in the frontal divisions of the cortex after division of both vagus nerves and of the spinal cord at the thoracic level was connected with the removal of the afferent influences coming from the empty stomach.

It could be concluded from these experiments that activation of the frontal divisions of the cerebral cortex in fasting animals is largely determined by the afferent impulses entering the central nervous system from the empty stomach. Removal of the "fasting" impulses leads to a considerable lowering of the level of the activating influences on the cerebral cortex. This is evidently associated with depression of the activity of the food center. It is important to emphasize that the activating influence of the stomach is evidently mediated equally through the two afferent channels, viz., the vagus nerves and the sensory fibers coming from the stomach through the spinal cord. The removal of only one of these channels does not appreciably diminish the activating influence of the food center on the cerebral cortex.

It remained to be explained how far the purely nervous influences coming from the empty stomach were responsible for the mechanism of activation of the frontal divisions of the cerebral cortex during starvation, and what was the role of the humoral factors in this process.

In order to solve this problem, glucose solution was injected into animals with an empty stomach after division of the vagus nerves and spinal cord. In all the experiments, without exception, the administration of glucose after combined division of the vagus nerves and spinal cord led to a still further increase in the slow activity of the frontal cortex (Figs. 3A, B, C). Admittedly this effect in its original form was observed for not longer than 10-15 min. If the glucose solution were injected after division of either the vagus nerves or the spinal cord alone, slow activity appeared irregularly in the frontal cortex.

These experiments show that activation of the frontal divisions of the brain in fasting animals under urethane anesthesia is brought about by both nervous and humoral factors influencing the food center. These factors include the "fasting" composition of the blood and the afferent impulses reaching the food center from the empty stomach along the vagus nerves and along the afferent fibers passing through the posterior roots. The high level of functional activity of the cerebral cortex is maintained if only one of these mechanisms of activation – nervous or humoral – is removed.

Hence, the cortical cells of the frontal divisions of the brain in fasting animals are seemingly under the simultaneous control of the three subcortical apparatuses of the food center. One of these apparatuses is excited by "fasting" blood, another by afferent impulses coming along the vagus nerves from the empty stomach and, finally, the third apparatus of activation of the frontal cortex is excited by afferent impulses passing from the empty stomach along the spinal cord.

All these apparatuses ultimately have the same effect on the cortical neurons of the frontal divisions of the brain, producing a state of selective activation in the cortex which is not blocked by general anesthesia.

These physiological mechanisms evidently determine the complex sensation of hunger, the food behavior, and the moment of satiation; the last of these is known to appear before the digested food has been absorbed into the blood stream.

On the basis of the experiments we have described, we can explain the absence of a sensation of satiation after an intravenous injection of glucose solution when the stomach is empty. In the same way, we can explain the continuing sensation of hunger in one of conjoined twins, with a common circulation, when the other is satiated [1].

It is possible that the afferent influences reaching the central nervous system from the empty stomach are formed before the fasting blood begins to act. The relative importance of these two factors at different stages of food activity may of course differ.

These experiments do not reveal where the primary integration of the nervous and humoral influences takes place – whether in the subcortical structures of the food center or at the cortical level. There is reason to suppose that this integration takes place in the hypothalamic region. Further research is required to confirm this hypothesis.

SUMMARY

Experiments were staged on cats under urethane anesthesia, fasting for 24 h. An inquiry was made into the role played by the nervous and humoral effects in the mechanism of ascending activation of the frontal areas of cerebral cortex.

As shown, selective activation of the frontal areas of the cerebral cortex was conditioned in fasting animals by a simultaneous action of the nervous and humoral factors. The nervous mechanism of activation was determined by the nervous impulses from the empty stomach along the vagus nerves and the afferent fibers, passing to the spinal cord. The humoral activation is connected to some extent with the reduction of glucose content in blood.

LITERATURE CITED

1. T. T. Alekseeva, Fiziol. zh., SSSR, No. 4, 295 (1958).
2. I. P. Pavlov, Trudy Obshch. Russkikh. Vrachei v. S.-Peterburge, 78, 21 (1911).
3. K. V. Sudakov, Fiziol. zh. SSSR, 48, 2, 150 (1962).
4. B. K. Anand and J. R. Brobeck, Yale J. Biol. Med., 24, 123 (1951).
5. J. R. Brobeck, Yale J. Biol. Med., 29, 565 (1957).
6. J. M. R. Delgado and B. K. Anand, Am. J. Physiol., 172 162 (1953).
7. J. O. Foley and F. S. Dubois, J. compt. Neurol., 67, 49 (1937).
8. J. T. Irving et al., J. Physiol. (Lond.)., 89, 407 (1937).
9. S. Larsson, Acta physiol. scand., 32, Suppl. 115 (1954).
10. J. Mayer, J. J. Vitale, and M. W. Bates, Nature, 167, 562 (1951).
11. J. Mayer, Ann. N. Y. Acad. Sci., 63, 15 (1955).