PECULIARITIES IN THE COURSE OF THE PYRETIC REACTION ASSOCIATED WITH VARIOUS FUNCTIONAL STATES OF THE ALIMENTARY CENTER

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In studying the development characteristics of the pyretic reaction in the presence of various functional disturbances in higher nervous activity, the course of the fever (temperature reaction) was noted to be dependent upon the state of alimentary excitation of the animal [1].

The purpose of this investigation was to study the effect of the alimentary center's functional state on the course of an experimentally induced pyretic reaction.

EXPERIMENTAL METHOD

The experiments were set up on 4 dogs, two of which were subjected to operations in which gastric fistulas were formed (Seryi and Ryzhii), and two of which were used as controls (Bobik and Nel'ka). In order to increase the excitatory state of the alimentary center, short-term fasting was used (one, two and four days), after which the animals were teased by the sight of meat for $2\frac{1}{2}$ hours.

TABLE 1. Characteristics of the Course of the Experimental Fever (Control Experiments)

Dog	Maximum temperature (numerator) and time of its onset (in hours, denominator)									
Ryzhii	1,4° / 3,5	1,4° / 3,5	1,3° / 3	1,5° / 3,5	1,5° / 3,5	1,3° / 3,5	1,4° / 3,5	1,3° / 3,5	1,4° / 3,5	1,3° / 3,5
Nel'ka	1,4° / 4	1,2° / 4	1,4° / 3,5	1,3° / 3,5	1,3° / 4	1,4° / 4	1,2° / 3,5	1,2° / 3,5	1,2° / 3,5	1,3° / 4
Seryi	1,1° / 3,5	1,1° / 3,5	1,1° / 3,5	1,2° / 3,5	1,1° / 3,5	1,4° / 3,5	1,2° / 3	1,3° / 3	1,1° / 3,5	1,1° / 3,5
Bobik	1,4° / 3,5	1,5° / 4	1,4° / 3,5	1,4° / 3,5	1,4° / 4	1,4° / 3,5	1,3° / 3,5	1,4° / 3,5	1,3° / 3,5	1,4° / 4

To maintain the excited state of the alimentary center, the experiment proceeded without the natural reflex being extinguished: every 5-10 minutes (in the course of $2\frac{1}{2}$ hours) the dog received a small piece of meat. In all the experiments, teasing of the gastrotomized dogs began after preliminary washing of the stomach. The gastric juice was collected for 3 hours with the open fistula, into a measuring glass. Acidity of the gastric juice was determined by titration with 0.1 N KOH.

The pyretic reaction was caused by intravenous injection of a low-toxicity vaccine, prepared from a culture of B. mesentericus, and containing 5 billion killed microbes per ml; each dog was injected with 1.5 ml. Measurement of the rectal temperature was carried out with the usual maximal thermometer every 30 minutes, or with a

thermocouple. Fever was induced no more often than once in 7-10 days; before each experiment (inducing fever against the setting of an altered functional state of the alimentary center), we set up several control experiments (with normal feeding of the dogs).

EXPERIMENTAL RESULTS

Initially, we studied the normal temperature fluctuations in the dogs. Then we investigated the effect of fasting and teasing on temperature changes and gastric secretion (under normal conditions and on the day of fever induction).

Fluctuation in the rectal temperature of the dogs in the course of a day did not exceed 0.2-0.3° under normal conditions. Teasing the animals with meat in the morning (with a feeding regime at 2 P.M.) significantly increased the range of the temperature fluctuations. In Ryzhii, teasing caused marked motor excitation, accompanied by grabbing at meat on the floor (tiny pieces), and elevation of the temperature by 0.8-0.9° within 30 minutes from the

TABLE 2. Characteristics of the Changes in the Gastric Secretion Associated with Teasing by the Sight of Meat, Under Normal Conditions and Following Short Term Fasting (Seryi)

Time after initiation of teasing that gastric juice was taken (in minutes)	Normal conditions			After one day fasting			After two day fasting			After four day fasting
	Experiment No.									
	1	2	3	1	2	3	1	2	3	1
30	50(80) 25	30(80) 26	30(80) 25	60(80) 35	50(90) 33	90(120) 35	60(100) 35	90(100) 33	60(100) 33	80(120) 50
60	60(90) 30	60(90) 25	40(90) 28	90(120) 40	70(120) 35	120(140) 35	100(130) 35	100(110) 40	100(120) 38	100(120) 25
90	60(90) 30	60(90) 28	60(100) 28	110(130) 45	90(130) 40	90(140) 40	80(110) 40	110(130) 40	100(120) 38	0(80) 5
120	70(100) 30	70(100) 28	70(110) 30	110(130) 30	80(130) 28	60(80) 28	60(80) 35	90(100) 40	80(110) 38	0(50) 2
150	60(90) 30	40(80) 30	40(90) 28	100(130) 10	50(130) 9	—	40(80) 33	60(90) 35	60(90) 30	0,5
180	30(60) 5	20(60) 6	20(50) 5	80(100) 7,2	50(120) 6	—	—	—	—	—

Note. Numerator) free HCl (in units per 100 ml of gastric juice); in parenthesis) total acidity (in units per 100 ml of gastric juice); denominator) gastric secretion (in ml).

beginning of the teasing. In Seryi, the reaction was less pronounced, and was accompanied by an elevation in the temperature by 0.3-0.4°. When the teasing was stopped, the temperature rapidly fell to its original level. As a rule, output of gastric juice began 5-6 minutes after the initiation of teasing, and attained its maximum after 2 hours; in this case, the acidity of the gastric juice was equal to a mean of 0.256% (free HCl) and 0.365% (total acidity). After one and two day fastings, the temperature of the animals remained practically unchanged. After a four day fasting, the temperature showed an average lowering of 0.2°.

In the control experiments, the introduction of the standard dose of vaccine caused a regular and constant development of fever (Table 1). After one and two day fasting (without teasing), the fever reaction was practically unchanged; after four days of fasting, it did not change in Ryzhii, and was lowered slightly in Seryi (in the control, by 1.1°; in the experiment, by 0.9°).

The character of the gastric secretion changed in the following manner. After one and two day fastings, the latent period of secretion was shortened from 5-6 to 3-4 minutes; the maximum increase in secretion and acidity of the gastric juice was observed after $1\frac{1}{2}$ hours (from the beginning of teasing), and was equal to a mean of 0.365% (free HCl) and 0.474% (total acidity). After a four day fasting, elevation of the acidity was observed only in the first hour; after an hour, secretion and acidity of the gastric juice fell sharply (Table 2).

Convinced that short term fasting by itself does not cause lowering of fever, or causes only a minimal depression of it (Seryi), we undertook teasing of the hungry animals with meat, and obtained the following data. After one and two day fasting, teasing (before administration of the pyrogen and after its injection for a period of $2\frac{1}{2}$ hours) resulted in a more rapid and marked elevation in the temperature in all cases (8 trials). Teasing of the animals after administration of the pyrogen left the course of the fever almost unaffected. After four days fasting, teasing (before administration of the pyrogen and after its injection) caused a mild elevation of the fever in Ryzhii, and lowered it somewhat in Seryi. The typical fever curves are presented in Fig. 1.

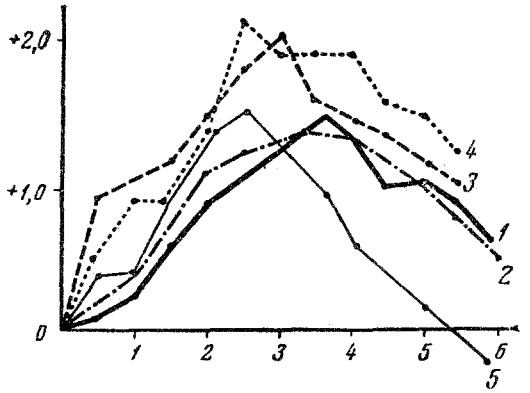

Fig. 1. Fever course following short term fasting with teasing (Ryzhii). 1,2) Control pyretic reactions; 3-5) pyretic reactions following fasting with teasing by the sight of meat for 15-20 minutes before administration of the pyrogen and over a course of $2\frac{1}{2}$ hours after its injection; 3) after one day fasting; 4) after two day fasting; 5) after four day fasting.

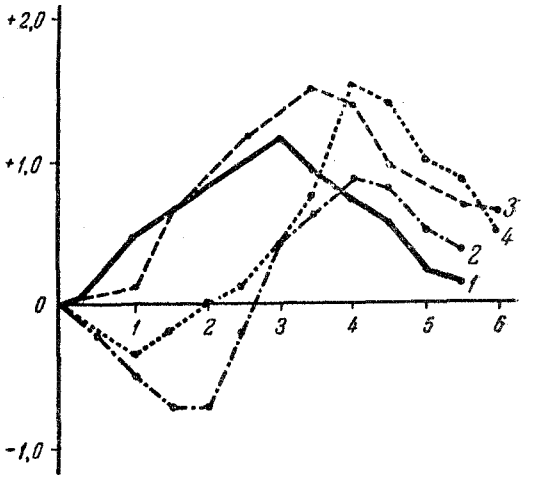

Fig. 2. Fever course after feeding of the animals. 1) Control pyretic reaction (Seryi); 2) pyretic reaction against the setting of "satiation" (Seryi); 3) control pyretic reaction (Ryzhii); 4) pyretic reaction against the setting of satiation (Tyzhii).

In order to elucidate the effect of feeding on the development of fever, experiments were carried out involving the injection of the pyrogen immediately after giving the animal the normal portion of food. In contradistinction to the control experiments, in these cases the fever reaction developed more slowly, and was accompanied by the appearance of an initial hypothermic phase; in addition, in Seryi it was lowered (Fig. 2).

I. P. Pavlov regarded the alimentary center as a functional union of all the cellular elements from the various levels of the central nervous system that receive stimuli related to the act of eating.

Anderson [5, 6], Brobeck [7, 8] and other investigators showed that the central nucleus of the alimentary center is located in the middle of the hypothalamus; its medial portions are responsible for "satiation", and its lateral, for "appetite".

On the other hand, there are enumerable experimental data indicating that the central link in heat regulation is also located in the hypothalamus. Evidence of interrelationships between these centers under normal and pathological conditions is extremely fragmental. Thus, for example, Brobeck [7, 8] rather categorically maintains that "regulation of food uptake is part of the control of temperature regulation". V. S. Matkovskii [3] points out the changes in the secretory acitivity of the stomach associated with dysenteric intoxication and infection, dependent, according to his data, on the varying functional state of the central nervous system at different periods in the course of the infection. It is known that the very act of eating (simulated eating and/or drinking) causes significant changes in gas exchange, as well as in the vascular reaction and the state of the muscular system [4].

Teasing the animals with meat (with occasional reinforcement by the use of small pieces of meat) in our experiments caused motor and general excitation of the animals, and some elevation in the temperature. Change in the functional state of the alimentary center was also reflected by the course of the fever reaction.

Intensification of the fever with an increase in the alimentary excitation in combination with general motor excitation of the animals is apparently explained by irradiation of the excitation from the alimentary center, disseminating into the thermoregulatory center.

Reduction of the reaction to the pyrogen with extreme elevation of alimentary excitation is possibly related to the development of threshold inhibition in the cortex and subcortical structures. Reduction of the pyretic reaction with injection of the pyrogen against the setting of "satiation" (Seryi) is apparently also connected with the development of inhibition, not only in the cortical portion of the alimentary center, but also in the subcortical structures.

The foregoing explanation of the facts obtained is supported by the characteristics of the changes in gastric secretion, and in the conditioned reflex activity of the animals associated with fasting and artificial "satiation". It is known that the magnitude of conditioned reflexes is markedly lowered on a day of "satiation", and the force relationships in performance of the conditioned reflexes are also disrupted [2].

The obtained data confirm the importance of the functional state of the cerebral cortex in determining the character of reaction in the subcortical centers of thermoregulation, not only under normal conditions, but also in pathological states.

SUMMARY

Chronic experiments were performed on 2 gastrectomized dogs. A study was made of the development and the course of experimental pyretic reaction and of the changes in the gastric secretion in various functional conditions of the alimentary center. After a 24- and 48-hour starvation and an additional stimulation by teasing dogs with a piece of meat a marked rise of the alimentary excitation of animals was noted, manifested in the rise of the motor and secretory reaction (a rise of the gastric juice secretion and of its acidity); the administration of a pyrogenic stimulus against this background causes a more rapid and marked temperature rise in comparison with control experiments. With an excessive rise of alimentary excitability (after 4 days of starvation) there is either not a very pronounced increase or even some reduction of pyrexia.

The data obtained show the significance of the functional state of alimentary center for the development and the course of pyrexia.

LITERATURE CITED

1. L. I. Gorbatsevich, Zh., VND im. Pavlova, Vol. XI, No. 2, p. 254-260 (1961).
2. A. M. Lukaneva, Changes in the Conditioned Reflexes of Dogs Associated with Artificial Alterations of the Normal Alimentary Reaction. Avtor. diss. Kiev (1958).
3. V. S. Maykovskii, On Changes in the Secretory Function of the Stomach and Disturbances in the Mechanisms of Its Regulation. These from the Reports of the Scientific Session of the VMA [in Russian]. Leningrad (1953).
4. A. D. Slonim, Some Results of Ecolo-physiological Investigations. Works of the Pavlov Institute of Physiology [in Russian], Vol. 8, p. 194-205 (1959).
5. B. Andersson, Acta physiol. Scandinav, Vol. 33, fasc. 4, p. 333 (1955).
6. B. Andersson and S. Larsson, Acta physiol. Scandinav, Vol. 38, fasc. 1, p. 22 (1955).
7. I. R. Brobeck, Vale J. Biol. Med., 20, 545 (1948).
8. I. R. Brobeck, S. Larsson, and E. Reyes, J. Physiol. 132, 358 (1956).
