

INTEROCEPTOR REFLEXES IN EXPERIMENTAL FEVER IN DOGS

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In previous investigations [6] we obtained data on the significance both of a general and local rise in body temperature in the execution of reflex changes in blood pressure.

The present paper is devoted to study of the changes in the interoceptor reflexes with a general febrile reaction.

EXPERIMENTAL METHODS

The experiments were conducted on 5 dogs (one male and four females) having a fistula of the stomach. Blood pressure and stimulation of the mechanoreceptors of the stomach and rectum were recorded (method described in previous communication [7] after rectal temperature had been established at one level with only slight falls in temperature of some tenths of a degree during the 3-4 hours in which the animal was kept in the laboratory.

Temperature in the rectum was measured with a maximum thermometer. Recording of blood pressure in these experiments was simplified by use of sinantrol.*

As pyrogenic stimuli we used:

- 1) A culture of *B. mesentericus*** (intravenous administration of 0.3 to 1 ml per 1 kg body weight);
- 2) tetra vaccine (intravenously, from 0.3 to 1 ml per 1 kg body weight);
- 3) tetrahydro- β -naphthylamine (subcutaneously in the form of a 5 per cent solution at the rate of 5-10 mg dry substance per 1 kg body weight);
- 4) turpentine (subcutaneously 14 hours before the experiment at a volume of 3-4 ml per animal);
- 5) sulfasin*** (intramuscularly, 1-3 per cent suspension of purified sulphur in peach oil 20-25 hours before the experiment, at a volume of 3 to 19 ml per animal).

The recording of the interoceptor reflexes before introduction of the pyrogenic stimulus, served as the original basis in the first, second, and third experimental series (where a swiftly developing febrile reaction was present); in the fourth and fifth series one or two control experiments were conducted previously over and

*Sinantrol (Kiev Institute of Physiology, Acad. Sci. UkrSSSR) was introduced in the animal in a canula or intravenously. I wish to thank Prof. V. D. Yankovsky for the preparation provided.

**The culture of *B. mesentericus* was made available to us by the Department of General Pathology of the Institute of Experimental Medicine, Acad. Med. Sci. USSR, for which I should like to thank Prof. P. N. Veselkin.

***The preparation is used in the Psychiatric Department of the I. P. Pavlov Institute of Physiology, Acad. Sci. USSR for conducting clinical pyrotherapy.

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above the preliminary investigations to establish the necessary magnitudes of interoceptor stimulations for each animal.

The investigation of the interoceptor reflexes was conducted in various periods of febrile reaction (in the period of rise of body temperature, at its maximum and at the commencement of the period of diminution).

A total of 51 experiments were performed including 32 with fever and 16 controls and 3 methodological experiments.

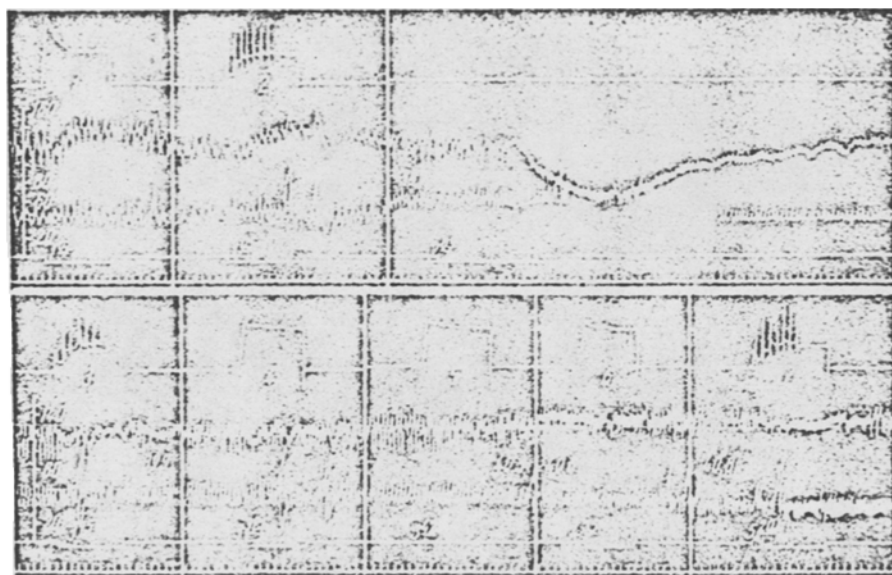
EXPERIMENTAL RESULTS

The use of the above-mentioned pyrogenic stimuli produced a rise in rectal temperature of 0.4-3.5°C. The maximum temperature during the execution of the investigations was 41.7°C and the maximum temperature in the febrile period 41.9°C (after introduction of turpentine).

In all these series of experiments, apart from the period of the febrile reaction, suppression of the interoceptor pressor reflexes was observed and sometimes a manifestation of mildly expressed depressor reflex reactions.

Increase in blood pressure greater than before introduction of the pyrogenic substance was noted only before vomiting or during vomiting which easily occurred during fever under the influence of inflation of the stomach. This rise in blood pressure should be considered not as an interoceptor reflex but as the result of antiperistalsis movements of the intestines and contractions of the muscles of the animal accompanying the pre-emetic state and the act of vomiting.

An example of the results of the experiment with use of tetravaccine (1 ml per 1 kg body weight) is given in the figure, in which suppression of the pressor shifts in blood pressure both with stimulation of the mechanoreceptors of the rectum and with stimulation of the stomach is visible.



Interoceptor reflexes in fever, induced by introduction of tetravaccine (dog Roza, Experiment of May 10, 1954). Significance of tracings, top to bottom: pressure in organ, blood pressure, respiration, zero line of blood pressure and (same) indication of stimulation, indication of time (5 seconds). 1, 4, 5, 6, — reflex from rectum upon introduction of 150 ml of air; 2, 3, 7, — reflex from stomach upon introduction of 1000 ml of air.

TABLE 1

Interoceptor Reflexes in Fever, Induced by Tetrahydro- β -Naphthylamine (5 mg per 1 kg body weight)*

Point of experiment	Temperature in rectum (in degrees)	Maximum increase in body temperature	Time after introduction of preparation	Change in blood pressure in mm Hg			
				stimulation of stomach (800 ml air)	stimulation of rectum		
					100 ml	150 ml	200 ml
Original value	37.6-37.5	—	1 hr 08	10	19	34	40
With fever	39.1-39.9	2.4	1 hr 39	4	7	6	8

* Experiment of November 17, 1954 on dog Malka, weight 13.1 kg.

In principle the same result was obtained in the entire period of development of fever, induced by intravenous introduction of the culture of *B. mesentericus*. Here sometimes we also observed slight depressor reactions.

Suppression of the pressor interoceptor reflexes was confirmed in the experiments with use of tetrahydro- β -naphthylamine (Table 1).

In view of the uniform result in the change in the interoceptor reflexes in various periods of fever we are not able to characterize them according to the phases of development of the febrile reaction.

The remaining experiments (series 4 and 5) were conducted after the fever had persisted in the animal for a few hours, at the moment of maximum rise in temperature and at the commencement of the period of its fall.

In these experiments the result obtained was analogous to the results of the previous investigations.

As is clear from Table 2 the interoceptor reflexes in fever, induced by introduction of sulfasin were not only considerably diminished or completely suppressed but occasionally showed inversion from pressor shifts to depressor ones.

The same was observed with a febrile state induced by introduction of turpentine; in these experiments the highest rise in temperature was observed. While in the control experiments a distinct pressor reaction was observed (Table 3) to all the repeatedly applied interoceptor stimulations, with turpentine-induced fever only slight pressor reflexes were maintained solely on inflation of the stomach; with stimulation of the rectum they were completely suppressed (Table 3).

With this there appeared distinctly marked depressor reactions especially to strong interoceptor stimulations with inflation of the rectum with 300 ml of air and with inflation of the stomach with 2000 ml of air.

Thus, the interoceptor pressor reflexes were considerably suppressed and were fully removed or partially distorted in the febrile state of the animal.

DISCUSSION OF RESULTS

The findings shed light on the difference between change in the interoceptor reflexes in fever and in heating of the animal. In the earlier investigations [6] in conditions both of general and local increase in body temperature a considerable growth in pressor shifts of blood pressure was observed; in fever the pressor interoceptor reflexes in the majority of experiments were clearly suppressed.

This difference indicates that fever and overheating cannot be regarded as synonymous states, with a uniform change in excitability of the peripheral and central nervous apparatus.

This conclusion is confirmed by comparison of a number of published findings on the changes in the excitability of the nerves and muscles in overheating of the organism [6, 9, 11, 14] and the reflex reactions in fever [3, 7].

TABLE 2

Interoceptor Reflexes in Fever Induced by Introduction of Sulfasin

Date	Dog and its weight	Character of experiment	Dose of sulfasin	Time after introduction of sulfasin (in hours)	Rectal temperature (in degrees)	Maximum rise in temperature	Stimulation	Change in blood pressure in mm Hg upon repeated stimulations			
								1	2	3	4
July 5, 1954	Zhuchka, 13.7 kg	Control	-	-	38.5	-	Inflation of rectum (150 ml air)	30	18	28	
July 17, 1954	Ditto	After introduction of sulfasin	12 ml 3%	25-27	39.8-40.5	2.0	Ditto	10	-4+12*	12	
July 15, 1954	Zhuka, 19.7 kg	Control	-	-	38.2	-	Inflation of rectum (300 ml air)	28	27	25	
July 17, 1954	Ditto	After introduction of sulfasin	19 ml 2%	22-24	39.5-39.8	1.6	Ditto	0	-14	-7+6	-6+4

* A minus sign before figures indicates depressor shift in blood pressure, a plus sign indicates pressor shift.

TABLE 3

Interoceptor Reflexes in Control Experiments and During Fever Induced by Introduction of Turpentine (average findings for 5 tests) Experiment on dog Zhuchka weighing 19.8 kg

Experiment	Date	Temperature in rectum (in degrees)	Change in blood pressure in mm Hg	
			upon stimulation of stomach (1500 ml)	upon stimulation of rectum (200 ml)
Control	9/27/54	38.3-38.6	17	24
Control	9/29/54	38.4-38.5	18	13
With experimental fever	10/2/54	41.7-41.2 (before experiment 41.9)	5	- 33

The very fact of disturbance of thermoregulation in fever, namely retardation of the processes of heat emission in the presence of a high temperature level in the organism, points to the unusual insensitivity of the internal thermoreceptors and centers to its specific heat stimulus.

The results of our experiments do not coincide with the conclusion of P. S. Khomulo [12] concerning an increase in the pressor interoceptor reflexes in fever in rabbits. However on the basis of the findings of the author (a small number of experiments, increase in pressor reflexes in 60 per cent of the control investigations, reduction in reflexes or absence of changes in some of the experiments with fever, disparity in results with stimulation of the mechanoreceptors of the urinal bladder) his conclusion cannot be regarded as sufficiently substantiated.

In addition the author himself noted a fall in the pressor reflexes in conditions of fever at such temperature levels (40.4-41.4°C) while in the experiments with overheating the reflexes remained elevated.

The results of our experiments (suppression, and occasionally distortion of the pressor interoceptor reflexes in fever) are in line with the conclusions of N. Mitropolsky [5] who reported on the change in activity of the vasomotor center in fever, which, in the view of the author, is the cause of the distortion (or absence) observed by him of the reflex vasomotor reactions in febrile states.

The possibility of depressor reactions in fever is confirmed by the findings of Heidenhain [13] who observed in these conditions enlargement (instead of contraction as in normal) of the internal vessels upon reflex stimulation of the vasomotor center.

There is no doubt that the changed state of the vasomotor center in fever is associated with the change in the function of the thermoregulatory centers. This question requires still further special study particularly since at present there is no agreed appraisal of the functional state of the heat centers in a febrile reaction.

Support for the hypothesis on change in excitability of the interoceptors themselves is provided by the investigations of V. V. Astakhova who found morphological changes in the vascular receptor apparatuses in experimental fever in rabbits. In addition, there are the statements of clinicians that such a disease as bronchial asthma, in the genesis of which a definite role is assigned to the receptors of the superior respiratory passages, does not appear or is considerably ceased in a febrile state [1].

There are grounds for assuming that suppression of the interoceptor reflexes in fever may be one of the causes of the favorable effect of pyrotherapy in certain diseases. This hypothesis is reinforced, on the one hand, by a number of statements on the significance of the changes in reception from the internal organs in the development of certain psychic disturbances (K. M. Bikov, V. A. Gilyarovsky, V. N. Chernigovsky, etc), and on the other is confirmed by declarations to the effect that removal of pathological interoceptor signalization leads to recovery in certain forms of psychomotor delirium [4].

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* In Russian.