

# ROLE OF THE RETICULAR FORMATION OF THE BRAIN STEM IN THE MECHANISM OF DEVELOPMENT OF FEVER

L. I. Gorbatsевич

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It has been shown by methods of local electrical stimulation and recording that the anterior and posterior parts of the hypothalamus play an intimate part in heat regulation [2, 5-7, 11-14, 16]. It has been postulated that the reticular formation of the brain stem also participates in heat regulation, for it is very closely connected with the hypothalamus [1]. However, judging from the literature, this problem has not been studied experimentally. The only reference to the matter is the statement by Euler [9] that the thermosensitive structures of the anterior portion of the hypothalamus are projected on the reticular zone of the brain stem.

In the present investigation the effect of changes in the functional tone of the reticular formation of the brain stem on the course of the febrile reaction was studied.

## EXPERIMENTAL METHOD

Experiments were carried out on 25 rabbits weighing from 2700 to 3000 g with electrodes permanently implanted in the reticular formation of the brain stem and the cerebral cortex. The potentials were detected from the sensorimotor cortex and from the mesencephalic reticular formation by means of bipolar needle electrodes 1 mm apart. The electrodes were implanted by means of a stereotaxic apparatus using the coordinates given in the atlas of Sawyer, Everett, and Green [15]. The potentials were recorded on a 4-channel electroencephalograph made in the workshops of the Institute. The reticular formation was stimulated by rectangular electric pulses, 1 msec in duration, with a frequency of 200 pulses/sec and voltage 2 V. The rectangular pulses were generated by a type IEM-T-10 stimulator. The position of the electrodes was verified by electrolytic destruction of the zone of stimulation by feeding a direct current of 2 mA strength into the circuit of the stimulating electrode for 1-2 min.

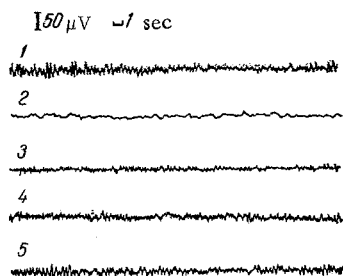


Fig. 1. Desynchronization reaction after stimulation of the reticular formation (rabbit No. 118). 1) Initial ECOG of sensorimotor region; 2) bio-potentials recorded from reticular formation of brain stem; 3) ECOG immediately after stimulation of reticular formation; 4) ECOG 15 min after stimulation; 5) ECOG 30 min after stimulation.

The febrile reaction was evoked by intravenous injection of pyrogenal in a dose of 2  $\mu\text{g}$ /kg body weight. The experiments were started 6-7 days after implantation of the electrodes. The rectal temperature was recorded by means of a thermocouple, and the recording was made continuously on the potentiometer tape throughout the period of the febrile reaction.

## EXPERIMENTAL RESULTS

In control experiments intravenous injection of pyrogenal into rabbits produced a bimodal febrile reaction with a duration of 5-6 h and a mean maximal rise of temperature of 1.2° three hours after injection of the preparation. Electrical stimulation was carried out for 15 min with intervals of 15 sec every minute.

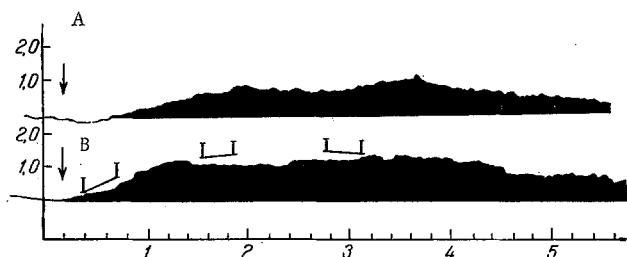


Fig. 2. Elevation of temperature against background of electrical stimulation of reticular formation of the brain stem (rabbit No. 118). A) Control experiment; B) fever against background of electrical stimulation. The arrow denotes injection of pyrogenal. The period of stimulation is indicated above the temperature curve. Ordinate - temperature; abscissa - time in hours.

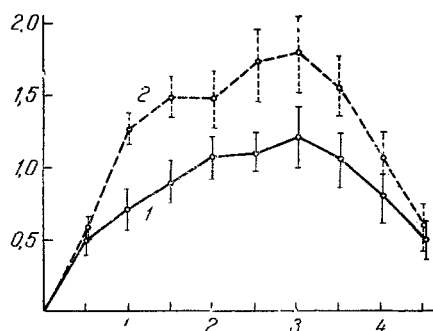


Fig. 3. Course of the febrile reaction in normal conditions (1) and against the background of electrical stimulation of reticular formation of the brain stem (2) (mean results of experiments on 25 rabbits). Ordinate - temperature; abscissa - time in hours.

This result suggests that chlorpromazine, which blocks the action of the adrenergic substance of the mesencephalic reticular formation [3, 8, 10] nevertheless does not completely block the reaction of the heat-regulating centers of the hypothalamus to a pyrogenic stimulus.

It is not possible to conclude from these results whether the effects observed from electrical stimulation are associated with ascending influences of the reticular formation on the anterior hypothalamic structures of the brain or with descending reticular influences on the heat regulating apparatus.

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Electrical stimulation of the reticular formation itself produced no appreciable changes in body temperature, but gave rise to some slight generalized motor excitation of the animals and an increased respiration rate.

Tracings made of the potentials from the sensorimotor cortex immediately after stimulation of the reticular formation showed a typical desynchronization reaction (Fig. 1).

In the course of the fever usually the structures of the reticular formation were stimulated three times: in the period of the first rise of temperature, at the height of the fever, and in the period of its decline.

A typical curve of the rectal temperature as recorded in the control experiment and during fever, against the background of stimulation of the reticular formation in the same rabbit receiving the same dose of pyrogenal, is shown in Fig. 2.

The mean results of the experiments are illustrated in Fig. 3.

It may be concluded from the analysis of these results that direct electrical stimulation of the nervous structures of the reticular formation of the brain stem in rabbits causes a more marked rise of temperature than that observed in control experiments on the same animals. This conclusion is in agreement with the results of the author's previous investigation [4] showing that blocking the reticular formation with chlorpromazine (5 mg/kg) is accompanied in rabbits by marked depression of the febrile reaction when the external temperature was normal (18°), although it did not prevent the animals from giving a febrile reaction if the external temperature was higher (23-24°).

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