THE EFFECT OF STIMULATION OF THE HYPOTHALAMUS ON THE SECRETORY FUNCTION OF THE STOMACH IN LONG-TERM EXPERIMENT

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The number of references to the effect of hypothalamic stimulation on the secretory function of the stomach is very small. Such investigations have been carried out by J. Beattie [2] who found in short-term experiments on cats under barbiturate anesthesia that faradic stimulation of the lateral wall of the hypophysial infundibulum elicited secretion of gastric juice. T. Heslop [3] has shown that stimulation of the anterior hypothalamus in cats and dogs increases the secretion of gastric juice with a rise in acidity and higher content of free HCl. Similar changes in gastric secretion have been observed on stimulation of the vagus. Stimulation of the posterior part of the hypothalamus increased the amount of mucus secreted, and, in the presence of acid gastric juice, diminished its acidity. Similar reactions were observed on stimulation of the splanchnic nerve.

D. Sheehan [5] also found that stimulation of the posterior and especially of the lateral part of the hypothalamus led to considerable increase in the secretion of gastric mucus, accompanied by a series of sympathetic effects; this suggests the possibility of the existence of a sympathetic center in the hypothalamus.

There is much less data available on the increase of gastric juice acidity on stimulation of the anterior part of the hypothalamus. R. Porter, H. Movius and J. French [4] studied the effect of the hypothalamus on HCl secretion in short-term experiments on monkeys under cyclopropane anesthesia. Stimulation of the anterior part of the hypothalamus gave an HCl secretion curve similar to that obtained on stimulation of the vagus. Bilateral vagotomy abolished completely the effect of anterior hypothalamic stimulation and diminished the reactions of stimulation of the posterior hypothalamus. Preliminary extirpation of the adrenals abolished entirely the effect of stimulation of the posterior hypothalamus without altering the results of stimulation of the anterior hypothalamus. When vagotomy and adrenal extirpation were combined, stimulation of both parts of the hypothalamus proved ineffective. On the basis of these results the authors have postulated a theory of the existence of two different pathways mediating the action of the hypothalamus on HCl secretion by the stomach: the first originates in the anterior hypothalamus and reaches the stomach by way of the vagus, the second pathway begins in the posterior hypothalamus and is mediated by the pituitary-adrenal system.

Literature data show that the hypothalamus plays an important role in the regulation of the secretory function of the stomach. However, this subject has been relatively little studied and the data obtained are contradictory. The majority of investigations have been carried out in short-term experiments.

The present work is concerned with the study of the effect of hypothalamic stimulation on the secretory function of the fasting stomach under new experimental conditions.

EXPERIMENTAL METHOD

Our experiments were performed under long-term conditions on dogs with fistulas of the fundal part of the stomach (Basov's method), The animals were subjected to experiments on the 6th-7th postoperative day.

The dogs were kept fasting for 18-20 hours prior to experiment, and were allowed to rest for a day after the experiment. Gastric juice was collected in a measuring cylinder with subsequent determination of total acidity and of digestive power according to Mett over a period of 24 hours. Gastric juice was collected every 5, 10, 15 and 30 minutes depending on the aim of the experiment. Free HCl and total acid content were determined by titration with 0.1 N solution of NaOH, using dimethylamidoazobenzene (0.5% alcoholic solution) and phenolphthalein (1% alcoholic solution) as indicators. Determinations were made on 1 to 10 ml gastric juice. Acidity of the latter was expressed in the number of milliliters of alkali calculated on 100 ml gastric juice.

Following careful investigation of the secretory function of the stomach and accumulation of sufficient data, the animals were subjected to the operation necessary for application of 4-polar electrodes to the hypothalamus. The technique of application of multipolar electrodes to the hypothalamus for long-term experiments on dogs involving approach to the hypothalamus from the base of the brain has been developed in collaboration with P. G. Bogach and described in previous reports [1, 2]. Hypothalamic stimulation was achieved by means of electric current from a sound generator of "GZ-1" type.

EXPERIMENTAL RESULTS

Secretory function of the stomach was investigated in 5 dogs, of which one served as control. Following formation of the gastric fistula the gastric content was regularly examined. It was possible to collect from 2 to 10 ml gastric contents, usually opalescent mucus, from each dog over a period of 4-5 hours. Free HCl was absent, total acidity was within the range 15-25, digestive power 0. No change in gastric secretion was observed following the procedure of application of 4-polar electrodes to the hypothalamus.

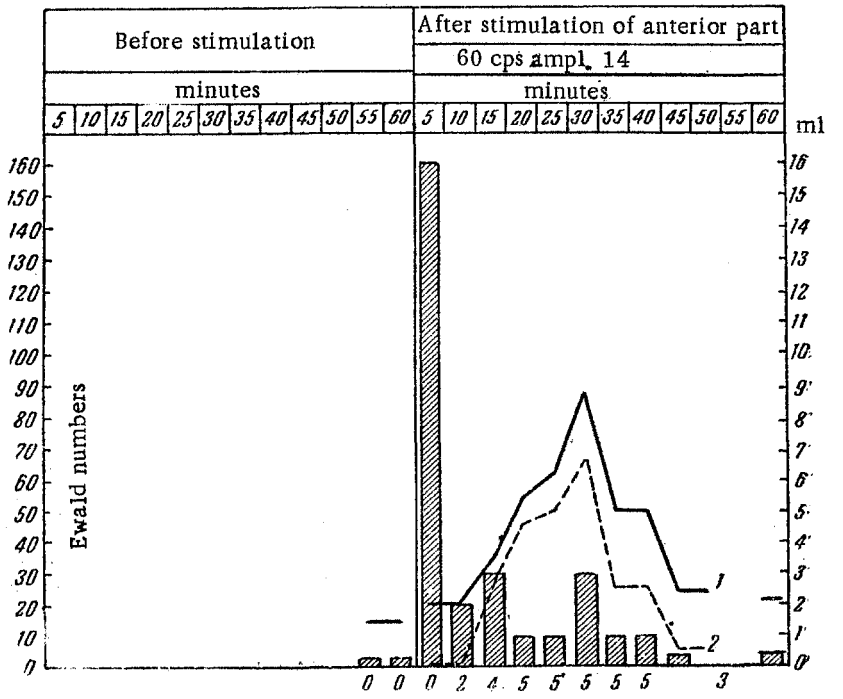

Fig. 1. Change in the gastric secretion following single stimulation of the anterior hypothalamus with electric current (frequency 60 cps, amplitude 14, duration of stimulation 1 minute). 1) Total acidity in Ewald numbers, 2) free HCl; columns show amount of gastric juice in milliliters for every 5 minutes, figures below – digestive power in millimeters of protein bar for 24 hours (Mett). Experiment No. 18, December 12, 1955, on dog Dzhek.

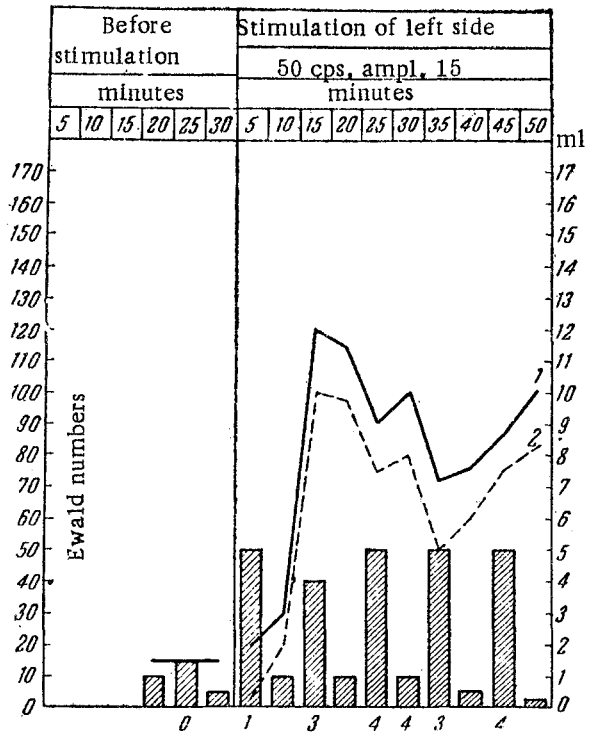

Fig. 2. Change in gastric secretion on stimulation of the left side of hypothalamus repeated every 10 minutes (electric current, 50 cps, amplitude 15, duration of stimulation 1 minute). Records the same as in Fig. 1. Experiment No. 20, December 16, 1955, on dog Dzhek.

Having satisfied ourselves that the operation of electrode application to the hypothalamus exerted no influence on the secretory function of the empty stomach, we began the experiments by investigating the gastric contents without the use of stimulation over a period of 1-2 hours and then started stimulating various areas of the hypothalamic region. Investigations showed that on stimulation of hypothalamic areas lying at the level of the anterior and lateral borders of the hypophysial infundibulum large amounts of gastric juice were secreted (from 20 to 150 ml), with high free HCl values (from 80 to 120), total acidity of 100-140 and digestive power of 3-7 mm.

Single stimulation was immediately followed by secretion of a large amount of gastric juice (up to 16 ml); the rate of secretion then gradually declined and secretion ceased after 50-60 minutes. Throughout the experiment (2-4 hours) single stimulation was associated with secretion of 20 to 30 ml gastric juice. The acidity of gastric juice following single stimulation reached a maximum at the 20-35th minute. The acidity decreased by the end of the experiment. The activity of gastric juice underwent changes parallel to the acidity.

Experiment No. 18, December 12, 1955, on the dog Dzhek can serve as illustration of the above (Fig. 1).

Multiple stimulation every 5, 10, 15 and 30 minutes of the same hypothalamic areas was associated with gastric secretion which was maintained at a high level throughout. During 3-4 hours of experiment from 40 to 150 ml gastric juice was secreted. Gastric juice acidity, as in experiments with single stimulation, reached a maximum after 20-30 minutes from the beginning of stimulation, but then remained high, with small fluctuations, until the end of the experiment. Similar changes were seen in the digestive power of the gastric juice.

Figure 2 shows the data obtained in experiment No. 20, December 16, 1955, in which the dog Dzhek was subjected to stimulation of the left side of the hypothalamus repeated every 10 minutes. The digestive power of gastric juice under these experimental conditions remained high throughout the experiment, whereas on single stimulation it decreased toward the end of the experiment.

Stimulation of the hypothalamic region lying at the level of the posterior border of the hypophysial infundibulum, both single and repeated, did not produce secretion of acid, active gastric juice; there was only slight increase in secretion of mucus without a rise in acidity and digestive power. This is well illustrated in Fig. 3 which shows the data for experiment No. 7, January 25, 1956, performed on the dog Grem.

We have used in our experiments a new method of isolated stimulation of the hypothalamus which permits precise localization of the area stimulated, whereas other authors carried out experiments under short-term conditions, using buried electrodes which have a number of disadvantages.

The findings of these authors are very incomplete, since they only noted an increase in acidity (Porter, Movius and French) or a rise in acidity accompanied by changes in the rate of gastric juice secretion (Heslop).

Our investigations were carried out under long-term conditions which permitted detailed study over a period of many months of all aspects of change in the secretory function of the empty stomach following stimulation of the hypothalamus. In addition to quantitative and qualitative examination of gastric juice we also

studied the character of changes in gastric secretion associated with single and repeated stimulation of the hypothalamus.

Moreover a careful study was made of the character of change undergone by the digestive power of gastric juice.

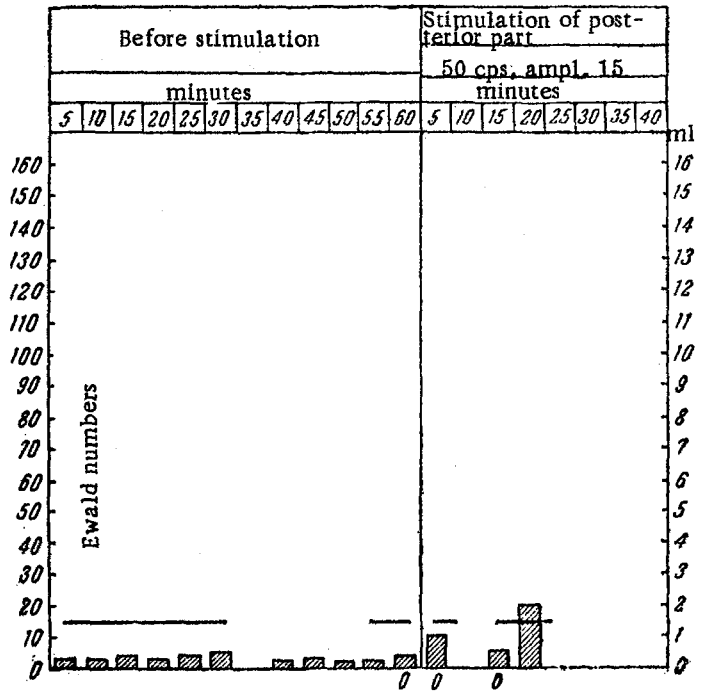

Fig. 3. Change in gastric secretion after single stimulation of posterior part of hypothalamus by electric current (frequency 50 cps, amplitude 15, duration of stimulation 1 minute). Records the same as in Fig. 1. Experiment No. 7, January 25, 1956, on dog Grem.

The results of our investigations suggest that stimulation of the anterior part of the hypothalamus produces a predominantly parasympathetic effect while stimulation of that part of the hypothalamus which is situated at the level of the posterior border of the hypophysial infundibulum gives a sympathetic effect. Stimulation of the anterior part of the hypothalamus leads to secretion of large amounts of active gastric juice with high acidity (predominantly parasympathetic effect), whereas stimulation of the hypothalamus at the level of the posterior border of the hypophysial infundibulum produces secretion of small amounts of gastric mucus (sympathetic effect).

SUMMARY

The effect of electrical stimulation of the hypothalamus on the secretory function of the stomach was studied in long-term experiments on dogs. It was revealed that stimulation of the anterior part of the hypothalamus during the period when there is no digestion causes secretion of large quantities of gastric juice with high acidity and digestive power. Stimulation of the hypothalamus with the level of the posterior edge of the infundibulum of the hypophysis gives a negligible increase of mucus secretion without the rise of acidity or of the digestive power.

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