

# Gastric Secretion Mediated by Extravagal Neural Influences\*

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Clinical and experimental evidence amassed in the last 25 years attests to the importance of cortical and sub-cortical structures in the control and regulation of gastrointestinal function (Eliasson, 1960). Electrical stimulation of diencephalic and limbic areas in experimental animals has been shown to alter the secretory activity of the stomach and to produce acute gastrointestinal lesions (Feldman, Birnbaum, and Behar, 1961a and 1961b; French *et al.*, 1952; Heslop, 1937; Sen and Anand, 1957a and 1957b). Studies by French and his colleagues (French *et al.*, 1953; Porter, Movius, and French, 1953) have drawn attention to extravagal influences evoked by stress stimuli. These investigators showed that the stomach can be induced to secrete gastric juice by two distinct routes. When stimuli were delivered to the anterior hypothalamus, an early fall in pH was produced with the stimulus mediating a response via the vagus nerve, whereas in vagotomized animals, activation of the posterior hypothalamus exerted its influence through the pituitary-adrenal system, resulting in a delayed secretion of gastric juice.

In the pilot experiments reported here, evidence is presented which supports the existence of an extravagal influence upon the elaboration of gastric secretion.

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## Methods

Eighteen adult cats, weighing between 2.6 and 4.1 kg, were used in these experiments. Since an earlier observation had shown these animals to retain food in their stomachs for lengthy periods of time, 24 to 48 hours before an experiment glucose and water were substituted for the regular diet of the animal.

Under ether anesthesia, a tracheotomy was performed, a catheter inserted into the femoral vein, and the animal was immobilized with gallamine triethiodide (Flaxedil). Artificial respiration was maintained with a Harvard pump. Prior to all surgery the operative sites were profusely infiltrated with procaine hydrochloride. In all animals the pylorus was ligated to prevent regurgitation from the duodenum, and a shortened Levine tube was introduced into the stomach through the pyloric sphincter. Following the abdominal surgery, a 5% glucose solution was infused at the rate of 8 drops per minute.

In eight animals both blood pressure and heart rate were recorded on a Sanborn Polygraph. Formvar-coated stainless steel bipolar electrodes (0.010 inch) were stereotaxically placed in the anterior hypothalamus, posterior hypothalamus, and central gray substance of the midbrain. The insulating enamel was scraped approximately 0.5 mm from the electrode tips, which were separated by 1 mm. Two Grass stimulators delivered symmetrical biphasic pulses (50 cps; 1 millisecond). Prior to each stimulation the electrode impedance was measured with a bridge

circuit. The stimulating current was kept constant at 0.5 ma and was monitored on a Tektronix oscilloscope, and the stimulus lasted for a 4-minute period.

Gastric juice was collected at hourly intervals by gentle manipulation of a hypodermic syringe which was attached to the Levine tube. Volume was measured and free acid was determined by titration with NaOH.

In six animals with electrodes previously implanted in the central gray substance of the midbrain, the spinal cord was severed at the level of the second cervical vertebra. Following the section, a second stimulating electrode was lowered into the lateral funiculus of the distal cut end of the cord.

Each experiment usually lasted from 6 to 8 hours. In order to achieve a baseline for purposes of comparison, three 1-hour samples were collected before and after electrical stimulation of a cerebral locus.

At the end of each study, the stomach was removed and opened along the line of the lesser curvature, care being taken not to disturb the position of the Levine tube. All electrode placements were verified histologically.

## Results

The quantity of gastric juice secreted per hour bore no relation to the animal's body weight. Prior to electrical stimulation of cerebral loci, the mean secretion was 1.7 ml per hour with a range between 0.4 and 4.6 ml.

Electrical stimulation of loci in the hypothalamus and central gray sub-

stance produced both an increase in the volume of gastric juice secreted and in its free acid content. The increase in volume within the first hour following electrical stimulation varied from 21 to 200%, the largest increase in volume resulting from stimulation of the posterior hypothalamus. An increase in free acid occurred from 1 to 3 hours following electrical stimulation at all loci, the increase being from 50 to 250%.

In two animals with electrode placements in the posterior hypothalamus, and one with a placement in the central gray, there were no changes either in volume of juice secreted or acid content following electrical stimulation.

Sectioning of the spinal cord at C-2 usually elicited an immediate and copious secretion of gastric juice. Following cordotomy, electrical stimulation of the central gray substance had no effect whatsoever upon gastric secretion which was usually inhibited by the section; however, subsequent stimulation of the distal end of the severed cord, in the lateral funiculus, elicited a profuse secretion of gastric juice during the first hour following the onset of stimulation.

Control animals that did not receive stimulation typically showed a gradual reduction in hourly volume of gastric secretion with a concomitant decrease of acid content in the sample. In animals in which blood pressure and heart rate were recorded, electrical stimulation of the stated loci also elicited marked arterial blood pressure elevations, arrhythmic electrocardiographic complexes, pupillary dilatation, piloerection, and urination.

A visual examination of the stomach of all experimental animals revealed irregular hemorrhagic erosions from one to several millimeters in length. Although in some animals these lesions appeared to be superficial, in most they were both mucosal and submucosal and were filled with extravasated blood. The severity of the lesions did not appear to bear any relation to the area stimulated.

It appeared that, in some animals, mechanical withdrawal of hourly samples might account for an irritation of the stomach mucosa, especially where the rugae came into contact with the openings in the Levine tube. A careful examination of the position

of the tube confirmed our suspicion in some animals.

#### Discussion

These pilot studies support the results of other investigators by showing that gastric secretion can be altered by electrical stimulation of cerebral loci, and present further evidence for extravagal control of gastric secretion.

In animals from which blood pressure was recorded, a significant pressor response was always observed during electrical stimulation of the stated cerebral loci. This was usually accompanied by other sympathetic phenomena, including pupillary dilatation, piloerection, and urination. It is noteworthy that this massive sympathetic activation accompanied the experimental production of the acute gastrointestinal lesions which were observed. Although some superficial erosions were undoubtedly the result of the mechanical procedure of sample withdrawal, we can confidently state that this was not the case for all lesions which were observed. We draw attention to this point since a similar method has been used by other investigators.

French *et al.* (1953) and Porter *et al.* (1953) have suggested that the extravagal route for gastric secretion might be humorally mediated. Although this possibility is not disputed by the present study, the fact that stimulation of the central gray substance did not elicit secretion following cordotomy, and that subsequent stimulation of the distal cut end of the cord caused an immediate secretion, would seem to argue for a more direct neural influence. Additional experimental work in this area is required in order to permit an assessment of the role played by the sympathetic division of the autonomic nervous system in the control of gastrointestinal function. However, these results suggest that the sympathetic division does indeed play a role in the elaboration of gastric secretion. This raises important and interesting questions with respect to stress-provoking stimuli and their relation to psychosomatic disturbances of the gastrointestinal tract.

#### Summary

In adult cats anesthetized with ether and immobilized with Flaxedil, the effects of electrical stimulation of cerebral loci on gastric secretion were studied. Stimulation of mesencephalic

and diencephalic areas increased both the volume and acidity of samples collected hourly. Section of the spinal cord at the level of the second cervical vertebra abolished this secretion; however, subsequent stimulation in the lateral funiculus of the distal end of the severed cord elicited the response. These pilot studies present further evidence for extravagal mediation of gastric secretion.

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