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VAGO-VAGAL REFLEX EFFECTS ON GASTRIC AND PANCREATIC SECRETION AND GASTRO-INTESTINAL MOTILITY

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Pavlov (1902) in his account of the nervous regulation of digestion, stressed the importance of the discharge down the efferent vagal fibres to the abdominal viscera. This discharge he conceived as the reflex result of a 'secretory centre' in the brain stem being bombarded in the earlier stages of digestion by impulses from cephalic nerve endings, followed in the later stages by an inflow of impulses along visceral afferent fibres in the abdominal vagus and sympathetic nerves. The importance, or even the existence, of this second type of reflex arc seemed doubtful when it was discovered that gastro-intestinal secretion and motility could, except for the cephalic reflexes, continue and be adjusted to the requirements of digestion in the absence of the extrinsic nerve supply to the abdomen (McSwiney, 1931; Alvarez, 1948). With the discovery of secretin, increasing stress was laid on the importance of hormonal control, particularly of the secretory functions of the digestive system. More recently it has been suggested that local reflexes, mediated through the intrinsic plexuses, may be concerned in hormonal release. Little attention, however, has been paid to the possibility that 'long' reflexes through the visceral afferent fibres in the vagal and sympathetic nerves to the abdomen might, by arcs through the central nervous system returning through the efferent fibres in these same nerves, play a part in regulating gastro-intestinal secretions and movements.

Previous workers have attacked the problem either by studying the effects of extrinsic nerve section on the response to physiological stimulants in the lumen of the digestive tract, or by recording the secretory or motor responses to direct stimulation of the many afferent fibres, which have been shown to be present in the splanchnic nerves and abdominal vagus trunks (Bain, Irving & McSwiney, 1935; Harper, McSwiney & Suffolk, 1935; Agostoni, Chinnock, Daly & Murray, 1957).

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Most of the earlier work on the effects of direct central stimulation of the vagus nerves on the abdominal organs is casual and unsystematic, by ill-defined methods of stimulation applied to the cervical more often than the abdominal vagus branches, and with no dependable control of the reflex nature of the response. For these reasons a more systematic inquiry has been undertaken into the reflex effects on digestive secretions and gastro-intestinal motility of direct stimulation of the afferent fibres in the vagal supply to the abdomen. Preliminary reports of the results have already been published (Harper, Kidd & Scratcherd, 1955, 1956).

METHODS

The experiments were performed on 64 unfed cats. Anaesthesia was induced with ether and maintained by an intravenous injection of chloralose (0·075 g/kg) or of a mixture of chloralose (0·0375 g/kg) and urethane (0·45 g/kg). The splanchnic nerves were cut extraperitoneally. A soft rubber tube was passed through an incision in the cervical part of the oesophagus into the stomach, and the pylorus was occluded with a tape ligature. A tied-off duodenojejunal loop, some 6–8 in. (15–20 cm) in length, was similarly intubated and the stomach and intestinal loop were filled with 25 ml. 0·005 N-HCl and 10 ml. 0·9 % (w/v) saline, respectively. By replacing the stomach contents every 15 min it was possible to measure acid and pepsin responses to stimulation. The acid content, in m-equiv HCl, of each 25 ml. of gastric washings was determined by titration against 0·05 N-NaOH with phenolphthalein as indicator. Peptic activity was measured by the method of Hunt (1948).

Changes in tone and motility were recorded by connecting the fluid-filled viscera through water manometers to float recorders (Fig. 1). Conditions were standardized for successive 15 min periods by adjusting the fluid meniscus on the water manometers and the recording levers of the float recorders to reference levels by means of a syringe and 3-way tap at the beginning of each period.

The pancreatic duct was cannulated as it passed through the duodenal wall, and a flow of pancreatic juice was maintained throughout the experiment by injections of secretin prepared by the method of Crick, Harper & Raper (1949). The amylase content of the samples of pancreatic juice collected at 15 min intervals was determined by the modification of Nørby's method described by Lagerlöf (1942) and the results expressed as output of Nørby units $\times 10$.

The abdominal vagus trunks in the cat lie ventral and dorsal to the lower part of the oesophagus, and each receives contributions from the right and left vagus nerves (Fig. 2). The nerves were exposed by removing the 8th or 9th rib on one side, and one or other of the trunks or their contributory branches was cut and the central end stimulated through shielded bipolar silver electrodes. Fluid electrodes proved unsatisfactory in our hands, but in some experiments the electrode described by Schofield (1952) was used. The responses to centrifugal vagal stimulation were observed after stimulation of the peripheral end of the branch or trunk used for central stimulation, or of another branch divided later in the experiment. Square-wave pulses of variable width, frequency and voltage were applied from an electronic stimulator for ten 30 sec periods separated by 30 sec periods of rest. Respiration was maintained by a Starling Ideal pump.

The most easily elicited reflex response to stimulation of the central end of an abdominal vagus branch is violent vomiting movements. To eliminate these disturbing somatic effects the spinal cord was transected at the level of the second cervical vertebra or, in most experiments, small amounts of the di-iodide of tubocurarine dimethyl ether (75 μg/kg intravenously) were injected before each period of central stimulation. The effect of the drug in this dosage is to block transmission in motor nerves without affecting transmission in autonomic pathways (W. D. M. Paton, personal communication).

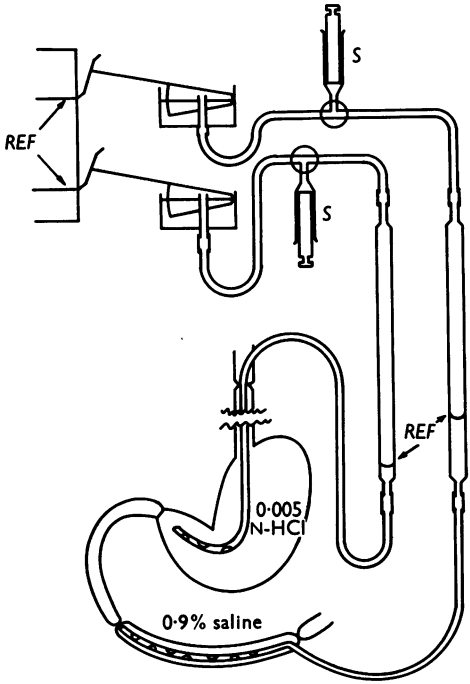

Fig. 1

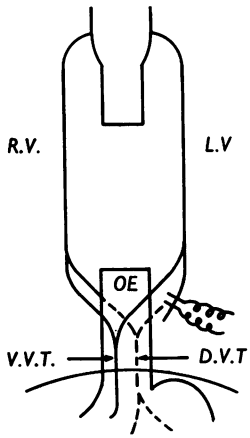

Fig. 2

Fig. 1. Diagram of apparatus. At 15 min intervals the contents of the stomach and intestinal loop were replaced, and the meniscus levels on the water manometers and position of the recording levers on the kymograph were adjusted to reference lines (*REF*) by means of the syringes (*S*) and 3-way taps.

Fig. 2. Vagal nerve supply to the abdomen. The ventral vagus trunk (V.V.T.) and dorsal vagus trunk (D.V.T.) lie ventral and dorsal to the lower part of the oesophagus (*OE*), and receive branches from the right (R.V.) and left (L.V.) vagus nerves.

RESULTS

The pattern of the experiments was as follows. The responses, secretory and motor, to one or more periods of stimulation of the central end of a vagal branch or trunk were recorded. Increases over the control level of more than 0·05 m-equiv HCl, 40 u. pepsin or 1·5 u. amylase were regarded as significant. That the response had been a reflex one over afferent and efferent vagal pathways was demonstrated by the absence of response on repeating the stimulation after cutting the vagal connexions to the brain stem higher up in the thorax or in the neck. Finally, to show that the negative response was not due to diminished sensitivity of the animal the peripheral end of an abdominal vagus branch was stimulated. In a few experiments the responses of the stomach, pancreas and intestine were simultaneously recorded, but usually only two organs were studied in any one experiment.

Gastric secretion

A typical experiment is illustrated in Fig. 3. There was usually little or no secretion during the control period. Stimulation of the central end of a vagal branch resulted in a secretion of acid and pepsin which was maximal in the stimulation period and usually persisted for a further 15–30 min. No secretion occurred when the stimulation was repeated after section of the vagus nerves in the neck, but a well-marked increase in acid and pepsin followed stimulation of the peripheral end of a vagal branch. In twenty-six experiments the mean

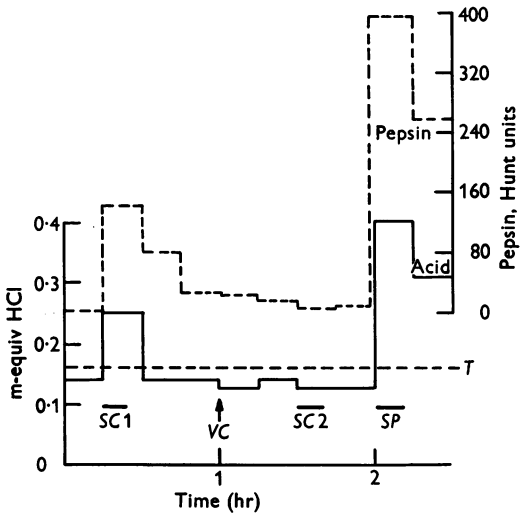

Fig. 3. Stimulation (*SC*1) of the central end of the branch of the right vagus to the dorsal vagus trunk (25 V, 10·0 msec, 50/sec) resulted in a secretion of acid and pepsin. Repetition of the stimulation (*SC*2) after section of the vagus nerves in the neck (*VC*) was ineffective, but stimulation (*SP*) of the peripheral end of the ventral vagus trunk produced a secretion of acid and pepsin. (The interrupted line, *T*, in this and other figures indicates the titration value of the 0·005 N-HCl put into the stomach.)

increase in secretion of acid was 0·13 m-equiv HCl (S.E. 0·013, range 0·50–0·63 m-equiv) in response to afferent stimulation, and 0·20 m-equiv (S.E. 0·026, range 0·05–0·68 m-equiv) in response to efferent stimulation. In thirty-seven animals the mean increase in pepsin was 227 u. (S.E. 23·5, range 40–920 u.) in response to afferent stimulation. The mean increase in response to efferent stimulation was also 227 u. (S.E. 26·5, range 40–630 u.).

Pancreatic secretion

The flow of pancreatic juice was maintained at a steady rate (usually about 1 ml./15 min) by intravenous injections of secretin. Neither central nor peripheral stimulation of any vagal branch had any consistent effect upon the

rate of flow. In most experiments stimulation of the efferent vagal fibres resulted in an increase in amylase output. In many animals stimulation of afferent vagal fibres produced a reflex increase in amylase secretion, but in a number of experiments in which gastric secretion was increased by afferent and efferent stimulation, and a well-marked rise in amylase output followed efferent stimulation, the pancreatic enzyme response to afferent stimulation was small

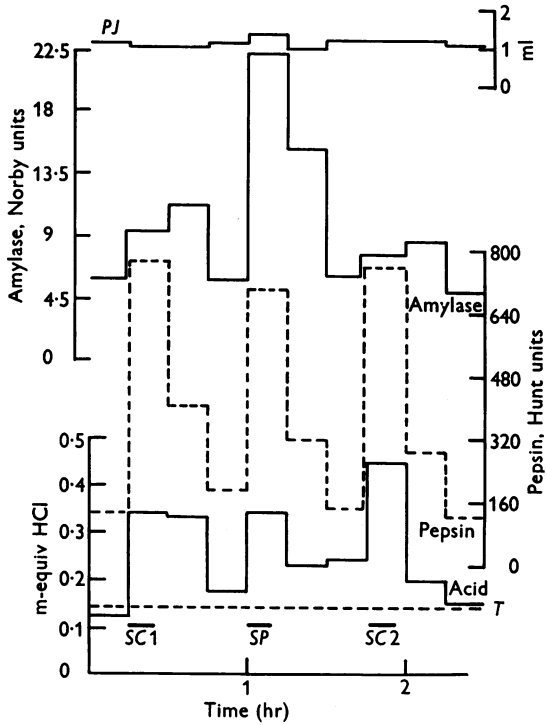

Fig. 4. Stimulations (*SC*1 and *SC*2) of the central end of the ventral vagus trunk (25 V, 10·0 msec, 50/sec) resulted in considerable increases in gastric acid and pepsin secretion, but very little effect on the output of pancreatic amylase. Stimulation (*SP*) of the peripheral end of the ventral vagus trunk had similar effects on gastric secretion, but a much greater effect on amylase output. None of the stimulations appreciably affected the rate of pancreatic secretion (*PJ*).

(Fig. 4), and sometimes absent. A similar relative insensitivity of the pancreas to afferent vagal stimulation was observed when the response to central vagal stimulation was compared with that to the injection of pancreozymin (Fig. 5). The mean increases in amylase output above the control level were 4·5 u. (S.E. 0·91, range 1·7–8·9 u., 14 observations) in response to afferent stimulation, and 7·9 u. (S.E. 2·02, range 1·5–30·8 u., 16 observations) in response to efferent stimulation.

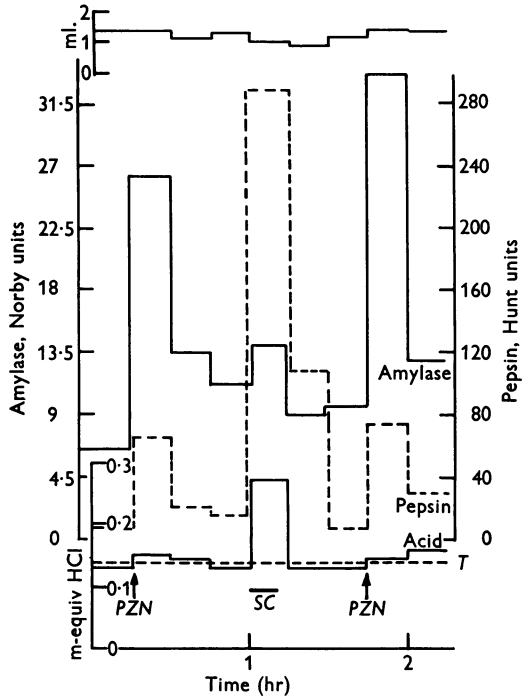

Fig. 5. Stimulation (*SC*) of the central end of the ventral vagus trunk (25 V, 10·0 msec, 50/sec) produced appreciable acid and well-marked pepsin secretion, but a negligible stimulation of amylase output. Compare the marked increase in amylase output in response to intravenous injections of 8·25 mg pancreozymin (*PZN*).

Gastric motility

The terms 'tone' and 'tonus' have often been used in descriptions of gastrointestinal motility without being clearly defined. In the sense of a 'fluctuating level of tension or length on which brief contractions may be imposed' (Bozler, 1948), the tone of the fluid-filled stomach or intestinal loop is related to the height of the meniscus in the water manometer. Slow increases or decreases in tone result in a decrease or increase in the volume of the viscus, which in turn is reflected in a rise or fall in the meniscus level. On these tonic changes shorter phasic contractions are superimposed. Our method of recording does not allow the nature of the phasic contractions to be determined, but from direct observation of the stomach both tonic changes and peristaltic waves occur in response to vagal stimulation.

There was usually little spontaneous motility of the phasic type in the control periods, and such activity as there was disappeared on vagal stimulation. The gastric responses to stimulation of the central end of an abdominal vagus branch were of two types. In 80 % of the records the reflex response was

predominantly a loss of tone which outlasted each period of stimulation, so that the response to the series of stimuli was a drop in tone to a level 1–6 cm below that of the control period. The original level of tone was gradually regained over a period of 15–30 min after the stimulation. In rather less than half the records of this type there was superimposed on the general loss of tone a very small contraction during each period of stimulation (Fig. 6). In 20 % of the records these slight contractions appeared without any background loss of tone. The latent period of the response varied between 5 and 10 sec and the

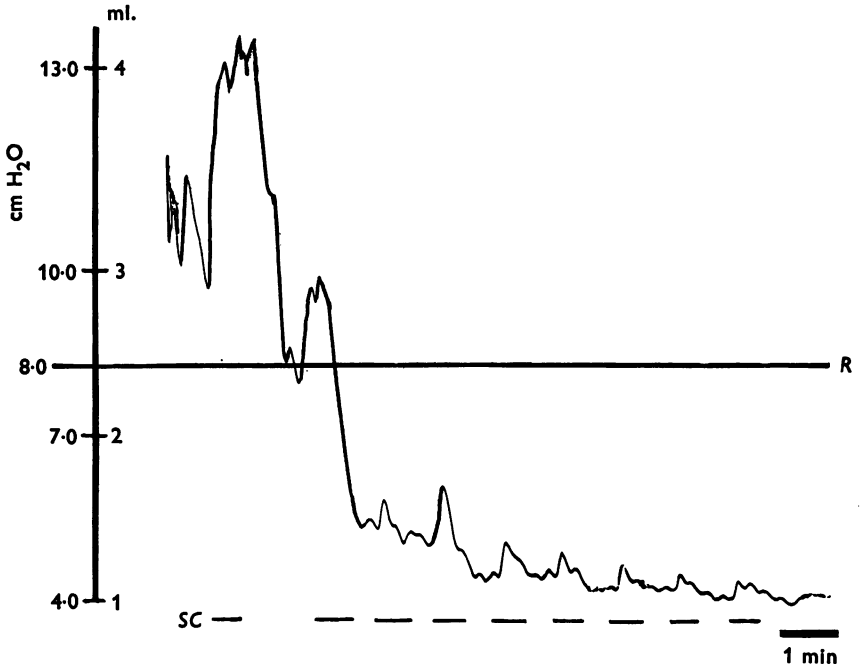

Fig. 6. Record (retouched) of gastric motility. Stimulations (*SC* – –) of the central end of the branch from the right vagus to the dorsal vagus trunk (25 V, 1·0 msec, 50/sec) resulted in a persistent loss of tone on which small contractions were superimposed during each stimulation period.

In this and other motility records the ordinate scale shows the manometer pressures in cm H_2O on the left and the volume change in the recorder on the right. *R* is the reference level to which the recording lever of the water manometer was adjusted at the beginning of each recording period.

responses were consistent and repeatable in any one animal. The tone of the stomachs was assessed as 'high' or 'low', on an arbitrary standard of whether the fluid level in the manometer was more or less than 7 cm above the level of the operating table during the control period preceding stimulation. The type of response to stimulation bore no consistent relationship to the pre-existing level of tone in the stomach, assessed in this manner.

In the responses of the gastric muscle to efferent vagal stimulation there was less evidence of the inhibitory effects which dominated 80% of the reflex responses. In rather more than half the records there was a loss of tone in response to the series of stimulations, but in very few records was this the only effect of stimulation. In nearly all the responses, during each period of stimulation, there was superimposed on the general loss of tone a contraction, which was characteristically much greater in amplitude than those recorded in response to stimulation of afferent fibres (Fig. 7). The tone of the stomach recovered gradually during the 15 min period following stimulation. In rather

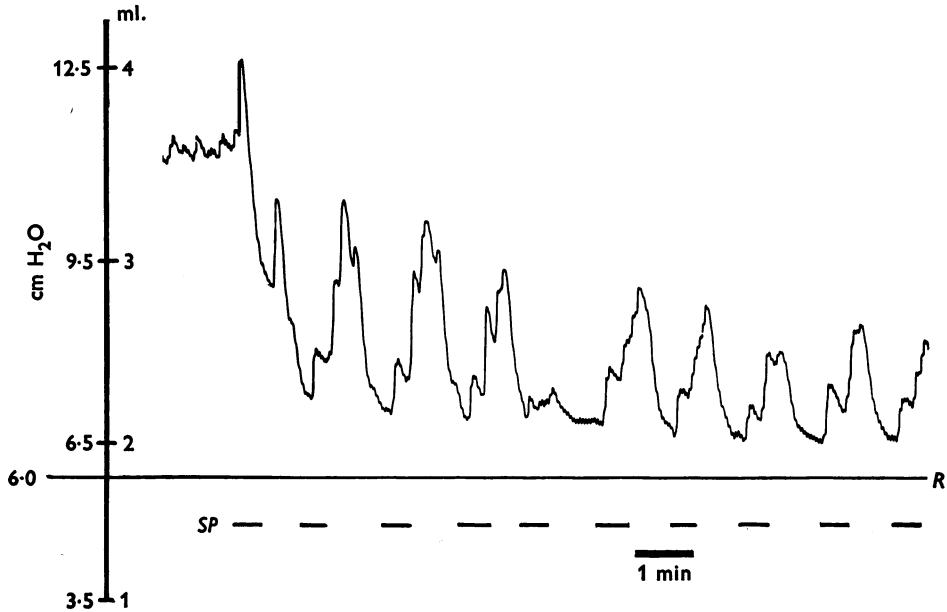

Fig. 7. Record of gastric motility. During a series of stimulations (*SP* – –) of the peripheral end of the branch from the right vagus to the dorsal vagus trunk (25 V, 0·5 msec, 50/sec) there was a sustained decrease in tone on which contractions in response to each period of stimulation were superimposed.

less than half the total number of records the contractions occurred without any appreciable loss of tone (Fig. 8). The latent period of the responses varied between 3 and 7 sec. There was a greater likelihood that efferent vagal stimulation would produce a fall in tone if the tone of the stomach before stimulation was 'high', but this relationship was by no means invariably found.

Intestinal motility

Similar effects were produced on the motility of a duodenojejunal loop by afferent and efferent vagal nerve stimulation. During each stimulation there was a well-marked contraction of the loop after a latent period of about 5 sec.

In many experiments the intestinal muscle relaxed rather slowly after the end of stimulation and the record did not return to the original base line before the next stimulation. As a result in many records there is a probably fallacious appearance of a rise in tone in the gut throughout the series of stimulations (Fig. 9). In none of the experiments did afferent or efferent stimulation produce the inhibition of tone during or after stimulation which was so frequently observed in gastric responses.

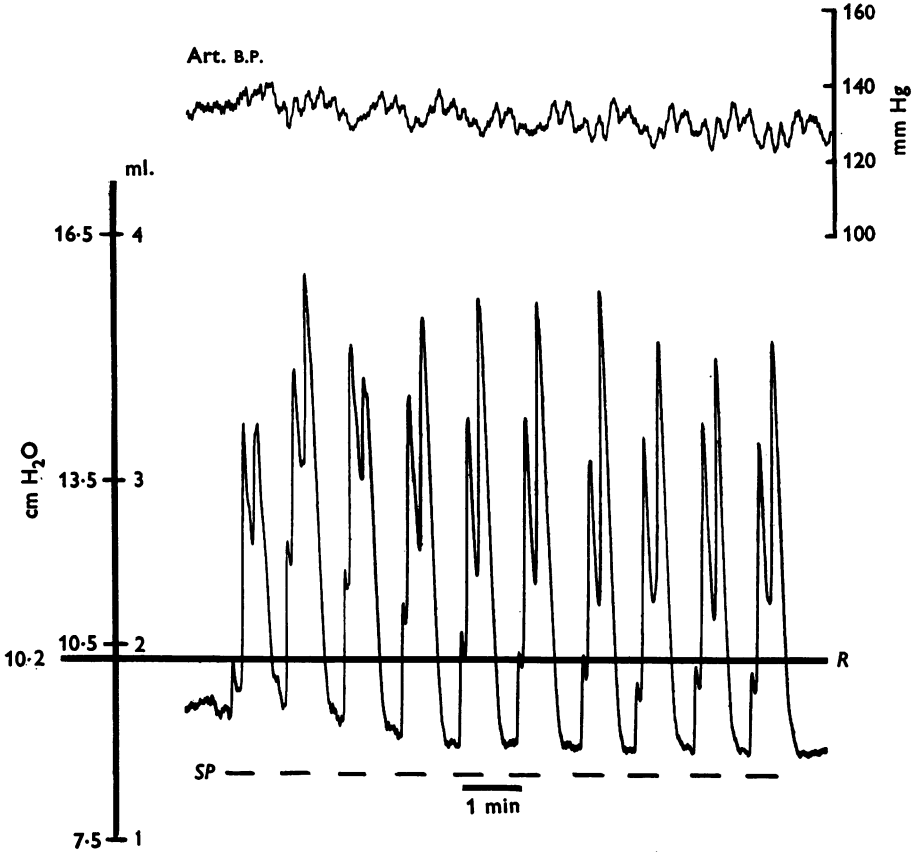

Fig. 8. Records of carotid arterial blood pressure and gastric motility. Gastric contractions were produced by each stimulation (*SP* – –) of the peripheral end of the ventral vagus trunk (15 V, 1·0 msec, 50/sec), with no appreciable alteration in the tone of the stomach.

Effects of section of the splanchnic and vagus nerves

In nine experiments section of the splanchnic nerves, which was usually done during preparation of the animal, was delayed until after the first afferent stimulation. Cutting the splanchnic nerves at this stage had no effect on the control levels of acid and pepsin secretion, but in a number of experiments spontaneous motility became apparent and the background tone in the stomach

showed a moderate increase. When the afferent stimulation was repeated after section of the splanchnic nerves there was usually some increase in the amount of acid secreted and a more striking increase in the output of pepsin (Fig. 10). No consistent effect on pancreatic amylase output was observed in the few experiments of this type in which pancreatic juice was collected. The tone of the intestinal loop and its response to stimulation was unaltered by splanchnic nerve section, and the character of the gastric motor responses was unaffected by splanchnic nerve section or adrenalectomy.

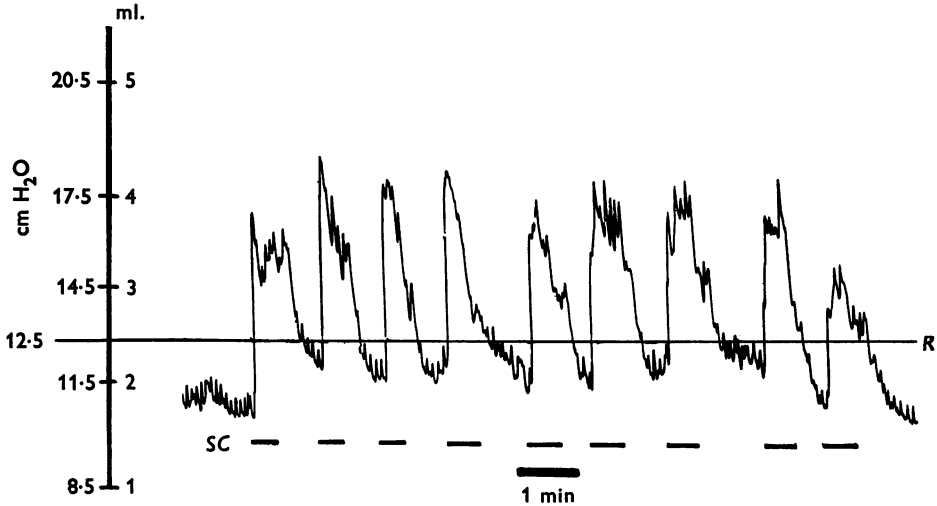

Fig. 9. Record of intestinal motility. Intestinal contractions were produced by each stimulation (*SC* – –) of the central end of the branch of the right vagus to the dorsal vagus trunk (10 V, 1·0 msec, 50/sec).

After the vagus nerves were cut, either in the thorax or in the neck, there was no alteration in basal secretion of acid, but in one-third of the experiments the amount of pepsin in the gastric washings increased for some 30–45 min. Thereafter it usually declined to its previous level, but in a number of experiments the high pepsin secretion was maintained. In two-thirds of the animals there was a gradual progressive increase in gastric tone, associated with the appearance of spontaneous contractions, after vagal section (Fig. 11). No alteration in the tone of the intestinal loops was observed after vagal section. In eight of the fourteen experiments in which the output of pepsin increased after the vagus nerves were cut there was no concomitant increase in gastric tone and motility.

Arterial blood pressure

In five animals, in addition to the observations on secretion and motility, the arterial blood pressure was recorded from the carotid artery. During each 30 sec afferent vagal stimulation there was a slight fall in pressure, varying

between 5 and 15 mm Hg, and slight rises of a similar magnitude coincided with each efferent vagal stimulation (Fig. 8). There was no alteration in the general level of arterial pressure over the 10 min periods during which the series of stimulations were applied. The blood pressure level was unchanged after cutting the vagi in the thorax or, except briefly at the time of section, in the neck.

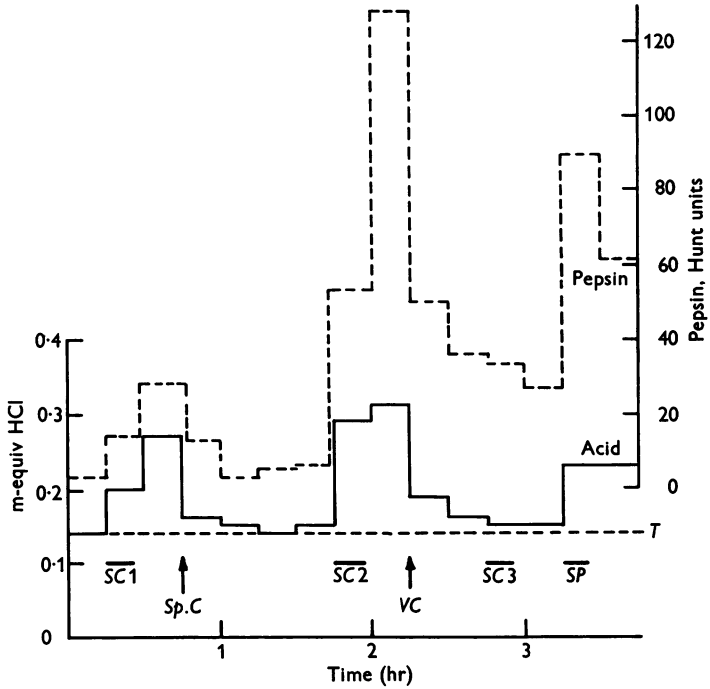

Fig. 10. Stimulation of the central end of the branch of the right vagus to the dorsal vagus trunk (30 V, 10·0 msec, 50/sec) had a more marked effect on acid and pepsin secretion after (*SC*2) than before (*SC*1) section of the splanchnic nerves (*Sp.C*). Repetition of central stimulation (*SC*3) after section of the vagus nerves (*VC*) was ineffective, but an increase in acid and pepsin secretion followed stimulation (*SP*) of the peripheral end of the branch of the right vagus to the dorsal vagus trunk.

General observations

In experiments of the type described in this paper there are two main difficulties in comparing the responses to stimulation of the different vagal branches and trunks which supply the abdomen. The responsiveness of the organs to stimulation may vary, generally in the direction of a progressive reduction in sensitivity; and since the secretory response to one period of afferent stimulation may last 45 min there can be only two or at the most three such stimulation periods before the reflex nature of the response is proved by complete vagal section and subsequent afferent and efferent stimulations. From an

examination of the results of 260 afferent and 255 efferent periods of stimulation it is clear that reflex and efferent responses can be elicited by stimulation of the ventral and dorsal trunks and the branches of the right and left nerves which form the dorsal trunk. There was no consistent difference in the size of the responses nor, with one exception, in the percentage of positive responses from any branch or trunk. The exception was the ineffectiveness of stimulation of the peripheral end of the ventral vagus trunk on intestinal motility in the majority of experiments.

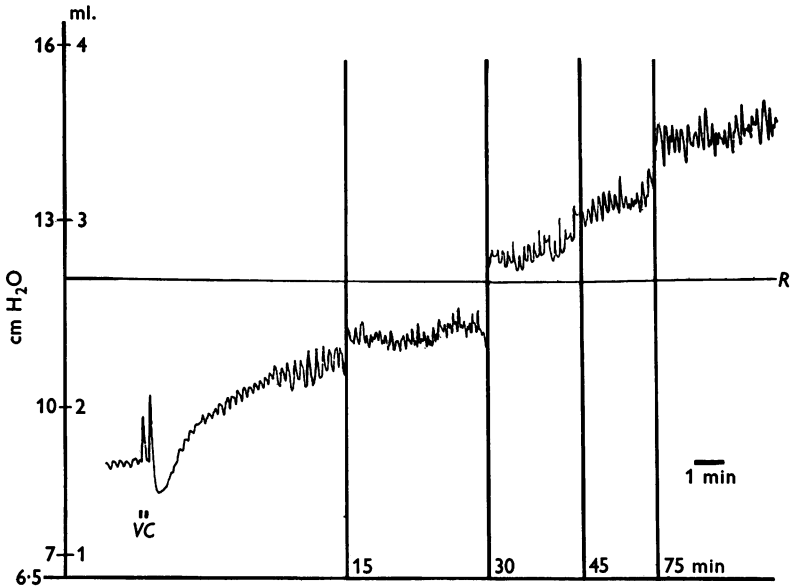

Fig. 11. Records (retouched) of gastric motility. After section of the vagus nerves in the neck (*VC*) there was a progressive increase in gastric tone. The second, third, fourth and fifth records commence at the 15th, 30th, 45th and 75th minutes, respectively, after vagal section.

For the same reasons it was impossible to assess in any quantitative fashion the effects of varying the voltage or pulse duration of the electrical stimulation. Remarkable changes were produced in the motor responses by variations in the frequency of stimulation, and these are described in another paper (Blair, Harper, Kidd & Scratcherd, 1959). In the present series of experiments secretory and motor responses were obtained with a range of intensity from 5 to 40 V, of pulses from 0·1 to 10·0 msec, and frequencies between 30 and 50 per second.

DISCUSSION

Except for the few experiments in which the splanchnic nerves were left intact, all the reflex effects described were mediated over arcs containing approximately a quarter to half the afferent fibres and half to three-quarters of the efferent fibres in the abdominal vagus nerves, depending on whether one of the

branches to the dorsal trunk or an entire trunk was used for the afferent stimulation, leaving intact either a branch and a trunk or only one trunk respectively for the efferent pathway. From the results of Agostoni *et al.* (1957), who showed that 90 % of the 31,000 fibres in the abdominal vagus nerves of the cat are afferent, it can be calculated that the afferent pathways contained some 7000–14,000 fibres, and the efferent pathways 1500–2000 fibres.

Although no measurements were made of splanchnic blood flow, it seems unlikely that the reflex effects on secretion and motility are secondary to vasomotor changes, as the alterations produced in the arterial blood pressure level by stimulation of the abdominal vagus nerves are slight and evanescent. Against the view that these reflexes may occur in normal digestion it might be argued that they are merely part of the vomiting reflex, of which the somatic manifestations were suppressed by high spinal section or tubocurarine. Undoubtedly some of the effects observed, such as the inhibition of gastric motility and increased intestinal motility have been described in nausea and vomiting. On the other hand the stimulation of gastric and pancreatic secretion and the gastric motor responses which followed afferent vagal stimulation in these experiments have not been described in vomiting, with which they clearly have no functional connexion.

In the gastric secretory response the amounts of pepsin in the gastric contents after afferent and efferent stimulation were considerable, but the acid secretion was small, particularly in response to afferent stimulation. All the animals were receiving artificial respiration, and the pump stroke was adjusted until the animals were just attempting to breathe. Nevertheless, some of them may have been overventilated, with a consequent reduction in the responsiveness of the oxyntic cells to vagal stimulation (Browne & Vineberg, 1932). Some of the pepsin recovered in the gastric contents after stimulation may have accumulated in the glandular tubules during the pre-operative fasting period and been washed out by the flow of acid, but there are several reasons for regarding the increases in pepsin after afferent stimulation as evidence of a real secretion by the chief cells of the glands. If the pepsin recovered were merely washed out from the tubules one would expect the amount to be progressively reduced on subsequent stimulations. There was in fact usually no reduction in the pepsin output in response to repeated afferent stimulation, and in experiments in which the splanchnic nerves were cut after the first afferent stimulation the pepsin response to a subsequent stimulation was often considerably enhanced. The mean pepsin output elicited by afferent stimulation was the same as the mean response to stimulation of the efferent fibres, which has been shown by other workers to produce a discharge of pepsinogen granules from the chief cells (Bowie & Vineberg, 1935). Finally, the ratio of pepsin to acid in these experiments was much greater than in the gastric secretion produced by histamine, which is thought to stimulate only the oxyntic cells.

Although the effects of electrical stimulation of efferent vagal fibres on acid and pepsin secretion are well established (Pavlov, 1902; Bowie & Vineberg, 1935; Heslop, 1938; Linde, 1950, 1953) there appears to be no previous work on the gastric secretory response to direct stimulation of afferent fibres in the abdominal vagus nerves. There is clear evidence that humoral agents are concerned in the gastric secretory response to mechanical or chemical stimulation of the gastric and intestinal mucosa (see Grossman, 1950), but the possibility that the secretion may in part be reflexly excited through afferent and efferent fibres in the abdominal vagus nerves has received little consideration. The abolition of the cephalic phase of gastric secretion by vagotomy is well established, but much less attention has been paid to its effect on the gastric and intestinal phases. It has been shown that the response to gastric distension (Bezborodko & Voronova, 1938), to meals or meat extracts introduced through a gastrostomy (Orbeli, 1907; Ferguson, 1953) or to caffeine instilled through a stomach tube (Meyer, Rosi & Stein, 1948) is reduced by vagal denervation. Since, however, the response to direct stimulants of the glandular cells, such as histamine, pilocarpine and gastrin, was also reduced, these results do not support the concept of a reflex element in the gastric and intestinal phases of secretion. The only previous observation which might be regarded as evidence of a secretory reflex is that of Code & Watkinson (1955), who showed that the acid gastric secretion produced by intraduodenal instillation of 0·1 N-HCl or 0·9% (w/v) NaCl solutions was dependent on the vagal innervation of the stomach.

The ineffectiveness of afferent vagal stimulation in altering the volume of secretin-stimulated pancreatic juice is not surprising, as it has been shown, both in the present experiments and by other workers, that stimulation of efferent vagal fibres in the cat does not affect the volume of pancreatic secretion, although the enzyme content of the juice is increased (Korovitsky, 1923; Sergeyeva, 1938; Harper & Vass, 1941; Harper & Mackay, 1948). The increased enzyme secretion which followed afferent vagal stimulation in a number of our experiments was not observed by Harper & Vass (1941), who found that the enzyme output was unaffected or diminished by stimulation of the central end of the ventral vagus trunk. In their experiments, however, only weak stimulation was applied to the nerve, to avoid vomiting movements. The demonstration of fibres in both vagus trunks which on stimulation increase enzyme output contradicts Harper & Vass's statement that such fibres are present only in the dorsal vagus trunk. A possible explanation of the discrepancy is the use by these workers of *induction coils*, which may have provided stimuli insufficient in intensity and pulse width to excite the small non-myelinated fibres in the ventral trunk.

The extrinsic nerves to the pancreas provide the efferent pathway for a psychic reflex which Pavlov considered of little importance, but otherwise their

role in normal digestion is unknown. As the result of many observations in the last 50 years on the response of the pancreas to intestinal extracts and excitants in the intestine there is general agreement that the hormones secretin and pancreozymin play a dominant part in regulating pancreatic secretion (Wang & Grossman, 1951), with a caveat from Thomas and his associates about the possible importance of a local reflex control (Thomas, 1950). The demonstration that the efferent fibres to the pancreas may be reflexly excited through afferent vagal fibres from the abdomen must also be borne in mind in identifying the mechanism of the pancreatic response to intestinal excitants.

Both afferent and efferent vagal stimulation excited intestinal muscle and produced a mixture of excitor and inhibitor effects on gastric motility, the reflex effects being predominantly inhibitor and the efferent mainly excitor. By our method of recording it was not possible to determine whether the phasic intestinal contractions were normal peristaltic waves or antiperistaltic movements. We have been unable to confirm the observations of earlier workers that the nature of the gastric response is determined by the frequency or intensity of the stimulation (Veach, 1925), or by the degree of pre-existing muscle tone (McCrea, McSwiney & Stopford, 1925; McSwiney & Wadge, 1928). There have been a number of reports (Bayliss & Starling, 1899; Wertheimer, 1892; Veach, 1925; Hodes, 1940; Babkin & Kite, 1950) of reflex stimulation or inhibition of gastric and intestinal motility elicited by stimulation of the central end of a vagus nerve in the neck, a procedure vigorously criticized by Whitteridge (1952). A vagal reflex contraction of the reticulum of the ruminant stomach on stimulation of the central end of the abdominal vagus has recently been described (Iggo, 1956; Titchen, 1958).

Impulses have been recorded in the vagus nerves from afferent endings in the gastro-intestinal tract sensitive to tension and pH changes (Iggo, 1957*a*, *b*; Paintal, 1954). When, however, one seeks parallels between the reflex effects of stimulating such endings and the responses to nerve stimulation, the picture is far from clear. It is generally accepted that the inhibition of gastric tone and motility in vomiting is reflex (Borison & Wang, 1953) but the gastric inhibitory effects of distending, or putting acid in, the duodenum have been variously attributed to long vagal reflexes (the enterogastric reflex), to local reflexes or to a mixture of the two (Thomas, Crider & Morgan, 1934; Brunemeier & Carlson, 1915). The increased intestinal motility following ingestion of a meal, the gastro-ileal reflex of Hertz (1913), has also been explained on a basis of long reflexes, local reflexes or a mixture of the two (Douglas & Mann, 1939; Gergory, 1950). We did not observe the vagally-mediated inhibition of intestinal tone and motility which has been found to accompany nausea and vomiting produced in dogs by small doses of apomorphine (Gregory, 1946, 1947).

With the exception of the predominantly inhibitor effects on gastric motility the reflex responses to stimulation of the abdominal vagus nerves were always

excitor. There was usually little or no background secretion of acid pepsin or amylase to be inhibited, but in a few experiments there was spontaneous gastric secretion or a high level of amylase output, and in none of these was a reflex inhibition observed. Nevertheless, the effects which followed section of the splanchnic or vagus nerves in the course of experiments indicate the removal of inhibitory influences. The increase in tone and appearance of spontaneous movements in the stomach and the increased output of acid and pepsin on stimulation after section of the splanchnic nerves were not unexpected, and may have been in part secondary to effects on the splanchnic circulation. More surprising was the increase in pepsin secretion and gastric tone and motility after all the abdominal vagus supply was cut. The increased pepsin output was not secondary to the increase in motility, since these two effects were dissociated

TABLE 1

	Type of stimulation					
	Afferent			Efferent		
	Total no. of trials	No. of positive responses	Mean response	Total no. of trials	No. of positive responses	Mean response
Gastric acid	63	36	0·13 m-equiv HCl	61	37	0·20 m-equiv
Gastric pepsin	63	44	227 u.	63	45	227 u.
Pancreatic volume	35	0	—	29	0	—
Pancreatic amylase	35	14	4·5 u.	29	16	7·9 u.
Motility, gastric	56	43		65	52	
Motility, intestinal	43	35		48*	28*	
				34†	25†	

* All branches. † Omitting ventral vagus trunk.

in many experiments. This inhibitory vagal influence on the cat's stomach resembles the vagally mediated inhibition of gastric secretion in the dog observed by Code & Watkinson (1955) and Sircus (1958) when acid was put in the duodenum. Increases in gastric tone immediately after vagal section have also been noted by Carlson, Boyd & Pearcey (1922) and Veach (1926).

For each of the gastric, pancreatic and intestinal functions investigated the proportions of the total responses to afferent stimulation which were positive have been compared with one another, and with the corresponding figures for efferent stimulation. The figures, with the mean secretory responses, are set out in Table 1. The low proportion of intestinal responses to efferent stimulation is due to the failure of most ventral-vagus-trunk stimulations to produce any effect. This may indicate that the ventral trunk is distributed mainly to the stomach, but is more likely to be the result of its intestinal branches being damaged by the ligature round the pyloric sphincter. With these results excluded it can be seen that the reflex motor effects are the most frequently elicited. Of the secretory responses the reflex effect on pancreatic amylase was the most difficult to demonstrate, and the mean response was less than that

produced by efferent stimulation. These facts, coupled with the observation that the pancreas responds much less to afferent stimulation than to pancreozymin, suggest that the vago-vagal reflex is of little importance in the regulation of pancreatic secretion.

The experiments described establish that vago-vagal reflex effects can be produced by direct stimulation of afferent fibres. Many of the effects on secretion and motility are those which occur in normal digestion rather than mere accompaniments of a vomiting reflex, but by their nature such experiments cannot establish the importance or indeed the existence of these reflexes in the regulation of digestion. The digestive system can function when the vagus and splanchnic nerves are cut, and it has been illogically assumed that these nerves, apart from affording an efferent pathway for cephalic reflexes and an afferent pathway for visceral pain, play little part in regulating digestive functions in the intact animal. It is claimed that certain motor effects depend at least in part on reflex pathways through the central nervous system, but the usual textbook account of digestive secretions stresses hormonal control almost exclusively, and ignores any nervous regulation other than cephalic. To establish the physiological importance of vago-vagal reflexes it would be necessary to record and identify the nervous traffic in the abdominal vagus nerves during digestion. Until such an investigation becomes technically feasible the present work may serve to remind gastroenterologists of the existence of these reflex pathways which could be a means of regulating the activities of the digestive system.

SUMMARY

1. Stimulation of the central end of an abdominal vagus branch in the cat resulted in a reflex secretion of acid and pepsin by the stomach and, less frequently, amylase by the pancreas.

2. Stimulation of efferent fibres in the abdominal vagus nerves resulted in well-marked increases in acid and pepsin secretion by the stomach and amylase by the pancreas.

3. The response of gastric muscle to afferent nerve stimulation was of two types. 80% of the responses consisted of a loss of tone which outlasted stimulation, and in half of these small contractions were superimposed on the fall of tone. In the remaining 20% small contractions occurred without the fall in tone.

4. During each period of stimulation of efferent vagal fibres there was a considerable gastric contraction, which in about half the experiments was superimposed on a background of diminished tone produced by and outlasting the series of stimulations.

5. Contractions of a loop of small intestine were produced by either afferent or efferent vagal stimulation.

6. The reflex secretory and motor changes were abolished after section of the vagus nerves in the neck or thorax.

7. After vagal section there was a progressive increase in gastric tone associated with the appearance of spontaneous contractions in two-thirds of the experiments, and an increase in the basal output of pepsin in one-third of the experiments. The increase in enzyme output was independent of the motility changes.

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