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MODULATION OF SINGLE VAGAL EFFERENT FIBRE DISCHARGE BY GASTROINTESTINAL AFFERENTS IN THE RAT

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SUMMARY

1. A single fibre dissection technique was used to record activity from efferent fibres in the left cervical vagus nerve of urethane anaesthetized rats.

2. The efferent discharge, in all units, was modulated by gastric inflation, gastric contractions or compression of the stomach wall. The receptors mediating these effects are the slowly adapting 'in-series' tension receptors in the gastric musculature with afferent fibres in the vagus nerves.

3. Efferent units were classified according to their response to passive gastric distension and active gastric contractions.

4. Four distinct types of efferent unit were isolated. Type I units were excited and Type II units were inhibited by gastric distension and contraction. Type III units were excited at low or moderate levels of inflation and inhibited at high levels of inflation or during gastric contractions. Type IV units were inhibited by low levels of inflation but excited at higher levels.

5. Since there is clearly a reciprocal organization at least of some neurones in the vagal nucleus the possibility of reciprocal control of antagonist, cholinergic and 'purinergic' vagal pathways is discussed.

INTRODUCTION

Harper, Kidd & Scratcherd (1959) observed the effects on gastric motility and secretion of electrically stimulating the central and peripheral ends of the severed abdominal vagus in cats whose splanchnic nerves also had been sectioned. They concluded that the vagal innervation of the upper gastrointestinal tract contained both inhibitory and excitatory motor pathways which could be reflexly excited by vagal afferent fibres from the abdominal viscera. The physiological importance of these vago-vagal reflexes was not known at this time and the need to record and identify the nervous traffic in the abdominal vagus nerves during digestion was stressed.

As the importance of these vago-vagal reflexes in the regulation of normal gastrointestinal function has become more apparent (Grossman, 1968; Jansson, 1969) the need for the electrophysiological support has become increasingly important. Electrophysiological studies in which gastrointestinal activity is correlated with activity in individual vagal nerve fibres has concentrated on the afferent innervation of the upper alimentary canal (Paintal, 1973; Davison, 1972; Leek, 1977). There has been

far less work on vagal reflexes, particularly on the way in which vagal afferent discharge modulates vagal efferent activity.

Paradoxically, whereas most studies on vago-vagal control of gastric function have been made on the simple mammalian stomach, the only electrophysiological analysis of vagal reflexes has been in the compound ruminant stomach (Iggo & Leek, 1967*a*, *b*; Harding & Leek, 1972, 1973). It is clear from such studies that the extrinsic nervous regulation of the compound stomach is different in many respects from that of the simple stomach at least with regard to motility.

The aim of the present investigation, therefore, was to observe the way in which vagal efferent discharge was modulated by afferent fibres from receptors in the simple mammalian stomach. The rat was chosen because an analysis of the afferent innervation has been made previously (Clarke & Davison, 1974, 1975, 1976; Davison & Clarke, 1977) and it was possible therefore to determine the influence of specific receptor types, from different regions of the upper alimentary canal, on vagal efferent activity. A preliminary report of this work has been presented to the Physiological Society (Davison & Grundy, 1976, 1977).

METHODS

The experiments were performed on female Sprague-Dawley rats, weighing between 175 and 300 g. After an overnight fast, the animals were anaesthetized with urethane (1500 ml./kg body wt. I.P.) and the abdomen opened along the mid line. A cannula was introduced into the fundic region of the stomach via the greater curvature and any gastric contents washed out with warm isotonic saline. A second cannula was introduced into the stomach via the duodenum. The fundic cannula was attached to a 10 ml. syringe filled with isotonic saline and used for inflating the deflating the stomach. The pyloric cannula was attached to a Palmer pressure transducer (CFP 8138) and used to record intragastric pressure.

A pool was made in the neck and filled with liquid paraffin. A plastic dissecting platform was placed under the left vagus nerve and the nerve desheathed. The central ends of fine filaments, dissected from the surface of the nerve, were placed on a fine silver electrode. To the other electrode was attached a fine strand of connective tissue, thus providing differential recording facilities. Each strand dissected was tested for its response to gastric inflation and when suitable units were obtained, their activity was recorded on magnetic tape for further analysis. In order to ensure that the results obtained were from single fibres a Neurolog spike trigger (NL 200) was used to identify spikes of uniform size and wave form. The output from the spike trigger was then relayed to a Neurolog Log Display unit (NL 700) for instantaneous frequency analysis or to a Neurolog Integrator (NL 600) whose output represents total spike counts per unit time. The choice of method of analysis was determined by the level and pattern of activity. In general the integrator was most suitable at low levels of spontaneous activity. In some experiments, a conventional pre-trigger averaging technique (Unimac, Datalab 400) was used to estimate conduction velocities. The ability to do this can be taken as further evidence for single unit activity.

RESULTS

Response of vagal efferents to gastric inflations and contractions

The degree of gastric motility was an important consideration in the classification of efferent responses. In the first place, afferent nerve activity evoking the reflex responses is dependent upon the level of motility. Secondly, the gastric motility in the rat appeared to be influenced by the level of anaesthesia which may influence the central processes being studied. For this reason a summary of the different types of efferent unit isolated from the cervical vagus at different levels of gastric motility has been made (Table 1). Three levels of motility were recognized: (1) no gastric motility,

(2) small gastric contractions in response to gastric inflation (< 2·5 mm Hg), (3) well developed gastric contractions evoked by distension (> 2·5 mm Hg) (Fig. 1). The reason for this separation becomes particularly important when dealing with efferent units which show differential high and low threshold responses to gastric inflations and contractions (Types III and IV).

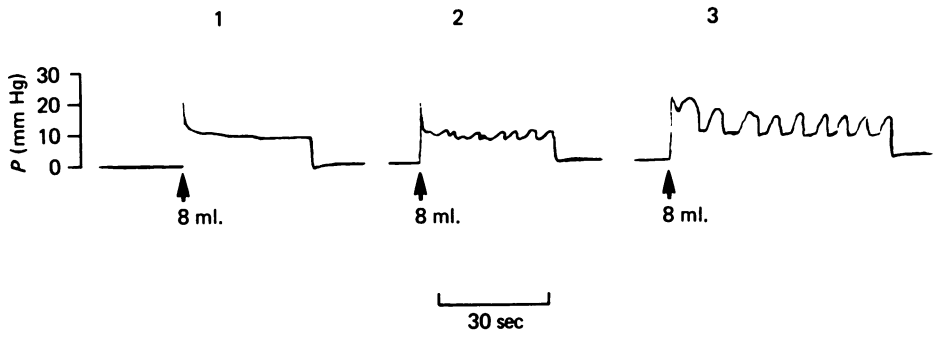

Fig. 1. Intragastric pressure (*P*) rises associated with a sudden inflation of the empty stomach to 8 ml. Note the different levels of motility recorded in the three different animals.

TABLE 1. Classification of efferent responses

Degree of gastric motility	No. of efferent units isolated				
	Type I				
	Type I	Type Ic	Type II	Type III	Type IV
1	14	—	13	(2)	(4)
2	23	10	15	6+(2)	3+(1)
3	15	26	18	10+(2)	4+(1)
Total	52	36	46	22	13

High thresholds were considered reached (*a*) during the contraction phase of an isometric contraction and (*b*) immediately after a sudden inflation when the dynamic phase of the gastric pressure, and therefore intramural tension, was exceptionally high for a short period (Fig. 1). Of these two situations, the isometric contraction appeared to be most effective in evoking the high threshold effects. Accordingly, in Table 1, the figures in brackets represent the units with differential inputs whose high threshold components can be distinguished by differential levels of distension, in addition to during isometric contraction, whereas the remaining units only show their high threshold responses during isometric contractions. The significance of the high and low threshold effects and the influence of gastric motility on these will become more apparent during the description of the classification of units which follows.

From Table 1 it can be seen that four different types of efferent unit have been isolated and classified. This classification is based on their response to gastric inflation and contraction.

Type I efferents

Type I units have been subdivided into two groups. The first group (Type I proper) were all tonically active, firing at variable rates (0·07–12 Hz) with no observed rhythm

when the stomach was completely deflated. In particular, respiratory and cardiovascular rhythms were not detected. On slowly inflating the stomach with isotonic saline these Type I efferents all increased their rate of firing with increasing intragastric volumes (Fig. 2). Thresholds for this response varied from less than 1 to 10 ml. gastric inflation, the latter volume being considered close to the physiological limit of the rat stomach. After inflation, the units all showed adaptation, in the case of the high threshold units, to the predistension frequency. If the inflation was sufficient to

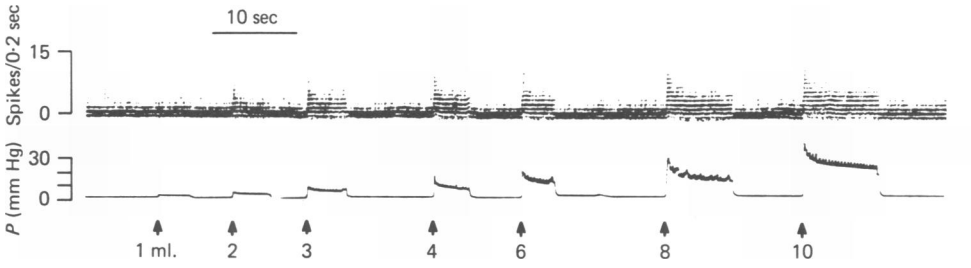

Fig. 2. Response of Type I unit to step inflations of the stomach. Lower trace shows the intragastric pressure associated with each inflation, the volume of which is shown below each arrow. The upper trace is the integrated response of a single efferent unit and represents the total count during successive 0·2 sec intervals.

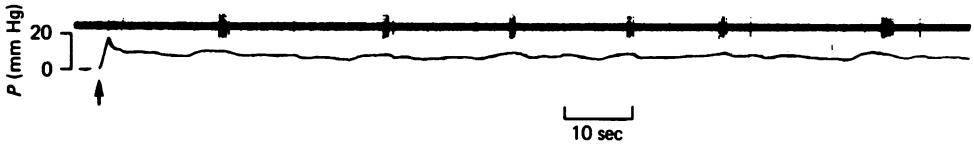

Fig. 3. Response of a Type Ic unit to a rapid 8 ml. inflation of the stomach. Lower trace – intragastric pressure. Upper trace – action potentials. Note lack of any response during the high pressure rise associated with the dynamic phase of inflation. Spikes occur at the peak of the pressure rise associated with gastric contraction during sustained inflation.

stimulate gastric contractions, then a further increase in gastric pressure was accompanied by an increase in frequency of firing of these Type I units unless, as occurred in some cases, the range of gastric pressure over which the unit was responsive was exceeded by the inflation.

On deflation of the stomach the frequency of firing of all the units returned to the predistension frequency unless it had already done so during the phase of adaptation. However, some units showed a transient period of reduced activity or even a distinct silent period when the stomach was deflated. These responses to deflation were seen more readily in the lower threshold units and in some cases the silent period continued for several seconds. At no point did gastric inflation or contraction produce inhibition in these Type I units.

The second group of Type I units (Type Ic) showed no spontaneous activity and only fired during active contractions of the stomach (Fig. 3). An inflation of 4–6 ml. was usually necessary to evoke contractions of the stomach and hence result in the discharge from these efferent fibres. If the gastric distension was increased, then the resulting gastric contractions differed from the contractions at the lower gastric

volumes and the frequency and pattern of the efferent discharge would also change. In general, the frequency increased with increasing gastric volumes due to the bigger contractions. However, with extreme distension, the size of the contractions decreased and were sometimes abolished. When this occurred, the response to the contractions varied in individual units. In some units, with smaller contractions at the higher inflations, the frequency of discharge associated with each contraction was greater. In other units it was lower. When the contractions were abolished by severe inflation none of the units showed any rhythmic modulation of activity.

The period of the gastric contraction during which the efferent fired was different for different units. These differences in phase were not considered to be merely threshold effects since the units did not continue firing throughout the pressure rise. If it is assumed that the pressure wave is a propagated wave of contraction then a better explanation for this observation is based on the location of the sensory endings mediating the reflex excitation. Units firing later in the phase must be excited by sensory endings situated more caudally than those exciting units firing early in the phase. As the wave of contraction passes beyond the receptive field, the sensory endings, and hence the efferent neurones, will no longer be excited, even though the pressure continues to rise as the wave propagates more caudally. Unfortunately it was not possible to check the location of the receptive fields of these endings since they do not respond to compression or probing (see later).

The discharge in these Type Ic units, which are considered to receive a very high threshold input since they are excited only by contractions, was shown to be due to reflex activation by gastric afferents by abolishing gastric motility using probanthine hydrochloride (1 mg). With no gastric contractions there was no discharge from these efferents. It is because these Type Ic efferents are reflexly excited by gastric contractions that they are grouped with the Type I units, even though at high levels of inflation the discharge in these efferent fibres may be reduced due to inhibition of motility.

Two Type Ic units were tested under both 'isotonic' and 'isometric' conditions. 'Isometric' contractions were achieved by connecting the fluid filled stomach directly to the fluid filled pressure transducer. 'Isotonic' conditions were achieved by connecting the stomach-pressure transducer system, via a tap, to an open reservoir of large cross-sectional area. In these experiments the initial inflation was determined by the height of the reservoir. Contractions under 'isometric' conditions resulted in a greater peak frequency and more spikes per contraction than under 'isotonic' conditions (Fig. 4). However it is difficult to obtain pure isotonic and isometric contractions (Leek, 1977), and hence the difference in response to contractions under these two conditions was only small, although significant.

Type II efferents

Efferents classified as Type II units responded in a reciprocal manner manner to Type I units. When the stomach was deflated, all but one of the Type II units fired spontaneously at variable rates (0·2–12·5 Hz) and with no detectable rhythm. On inflating the stomach, the rate of firing of all these units decreased (Fig. 5). Again a range of thresholds from 1 to 10 ml. was seen with the lower threshold efferents being completely inhibited by moderately high inflations (4–7 ml.). These units

showed adaptation in that the frequency of firing progressively increased during main tained inflations. However during active contraction of the stomach the efferent discharge showed further inhibition. After a period of adaptation, the discharge frequency during the relaxation phase following contraction could be higher than the resting level. When the stomach was deflated, a transient period of increased frequency of discharge was occasionally seen in some units. In other units, particularly the higher threshold ones, on deflation the activity simply returned to the predistension frequency.

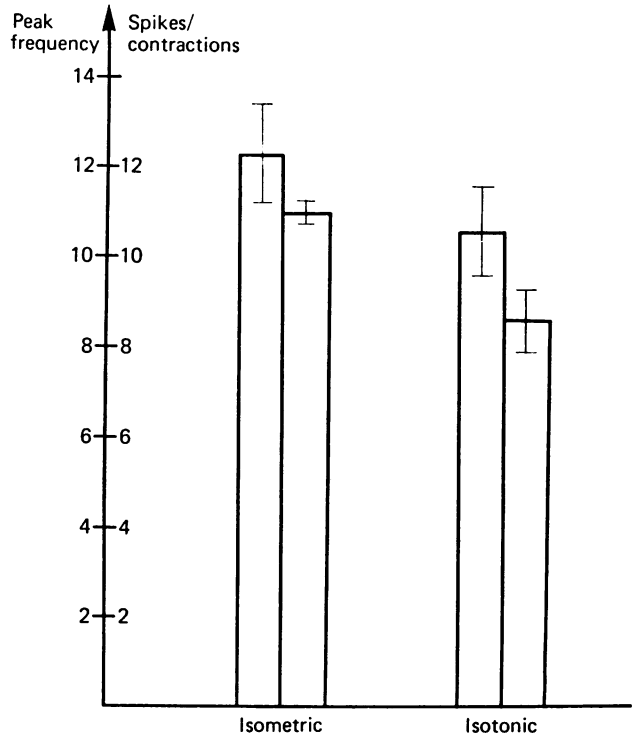

Fig. 4. Histogram showing the effect on peak frequency and the number of spikes per contraction in a Type Ic efferent when changing from 'isometric' to 'isotonic' conditions and vice versa. Mean ± S.E. For each pair of columns the left hand one refers to peak frequency and the right hand one to spikes/contraction.

The one unit which had no spontaneous activity represents an extreme example of a Type II efferent fibre. This unit remained silent throughout gastric inflation and contraction but gave a burst of activity on relaxation of the stomach after contractions.

At no point did excitation occur in Type II efferents when the stomach was inflated or when active gastric contractions occurred.

Type III efferents

As referred to earlier, Type III efferents showed differential high and low threshold responses to gastric inflation and contraction (Fig. 6). When the stomach was deflated, Type III units were all spontaneously active, firing at variable rates (0·2–30 Hz) and with no apparent rhythm. Inflating the stomach to low and moderate levels

(1–8 ml.) caused excitation in these units. In six of the twenty-two Type III efferent units (Table 1), further increases in the level of inflation caused inhibition during the dynamic phase of inflation and on two occasions even during the static phase of severe inflations. Inhibition also occurred during active contractions. In the remaining sixteen units, the inhibitory component only became apparent during contractions and no inflations up to the physiological limit of the rat stomach resulted in inhibition. In these units, therefore, if no contractions had occurred it probably would have been impossible to distinguish them from the Type I units.

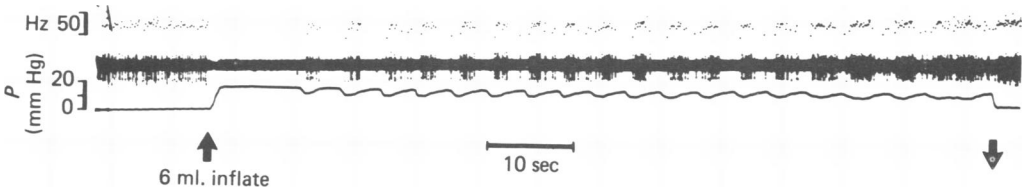

Fig. 5. Response of a Type II unit to a 6 ml gastric inflation. Lower trace, intragastric pressure; middle trace, action potentials; upper trace, instantaneous frequency analysis of efferent discharge. Note complete inhibition during the first 10 sec following inflation and during contraction. The degree of inhibition declines throughout the period of maintained inflation and on release of distension the frequency of the discharge rises to a higher level than the spontaneous activity. Although not shown, this increased activity eventually declines to the original spontaneous level.

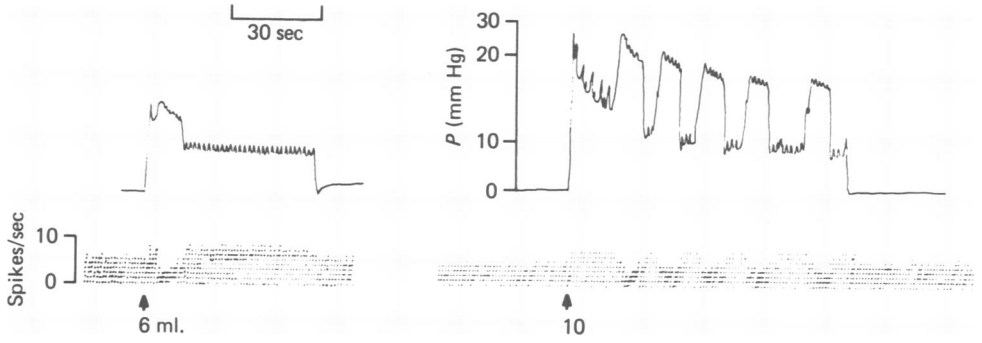

Fig. 6. Response of Type III unit to gastric inflation. Upper trace, intragastric pressure. Lower trace, integrated record of efferent discharge in a single unit, reset time 1 sec. Degree of inflation shown below arrows.

On deflation of the stomach, the firing rates of these Type III units generally returned rapidly to the predistension frequency, but in some units, especially those units with the lowest threshold excitatory component, a transient period of reduced activity occurred.

Type IV efferents

Type IV efferent units responded to gastric distension and contraction in a reciprocal manner to Type III units. Again these were spontaneously active (1·0–15·0 Hz) when the stomach was deflated, with no detectable rhythm. The response to gastric inflation in these units was inhibition at low and moderate levels of inflation and excitation at higher levels of inflation and/or during gastric contractions (Fig. 7).

Again the response showed adaptation to maintained inflation. On deflation of the stomach, these efferents generally returned rapidly to the predistension frequency of firing. In some units, however, an 'off' response occurred which depended on the rate of deflation and the volume preceding deflation.

Receptive fields

In later experiments an attempt was made to identify the receptive fields of sensory endings modulating individual efferent units by probing or compressing small regions of the stomach. Of the eighteen tested which responded to compression, only two units (Type I) showed a distinct and localized receptive field which was in the region of the antral-fundic junction (ventral surface). A further unit showed responses to compression of the antrum but not of the fundus. The remainder of the efferent

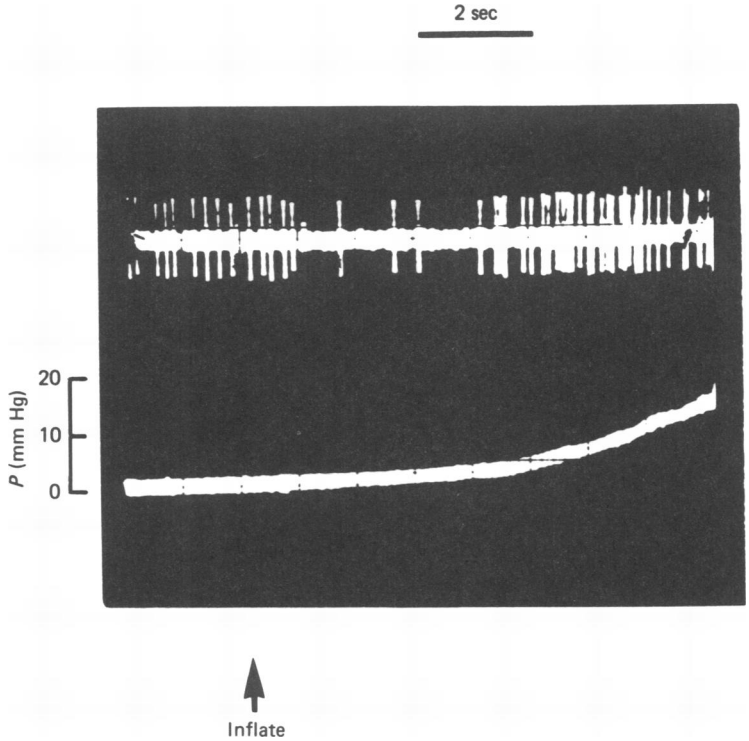

Fig. 7. Response of Type IV unit to very slow gastric inflation. Lower trace, intragastric pressure; upper trace, action potentials. Note the inhibition at very low intragastric pressure followed by excitation as the pressure rises further.

fibres did not have a specific receptive field as such but a response could be evoked by compressing small areas of the gastric wall (about 10 mm^2). In these units compression of these small areas over the whole of the stomach evoked a response; the larger the area, the greater being the response. However, some areas seemed more sensitive to compression than others. In one unit which showed low threshold inhibition and

high threshold excitation (Type IV) compression of areas of the fundus evoked excitation in the efferent and compression of the antrum had a small, but reproducible, inhibitory effect. Three Type Ic units were tested, but gave no response to compression of any part of the stomach.

Effect of vagotomy and electrical vagal stimulation

The effect of vagotomy was investigated in twenty-one efferent units covering all types. In some cases the procedure was carried out in two stages. The right cervical vagus was first severed and the effect on efferent discharge and the gastric response

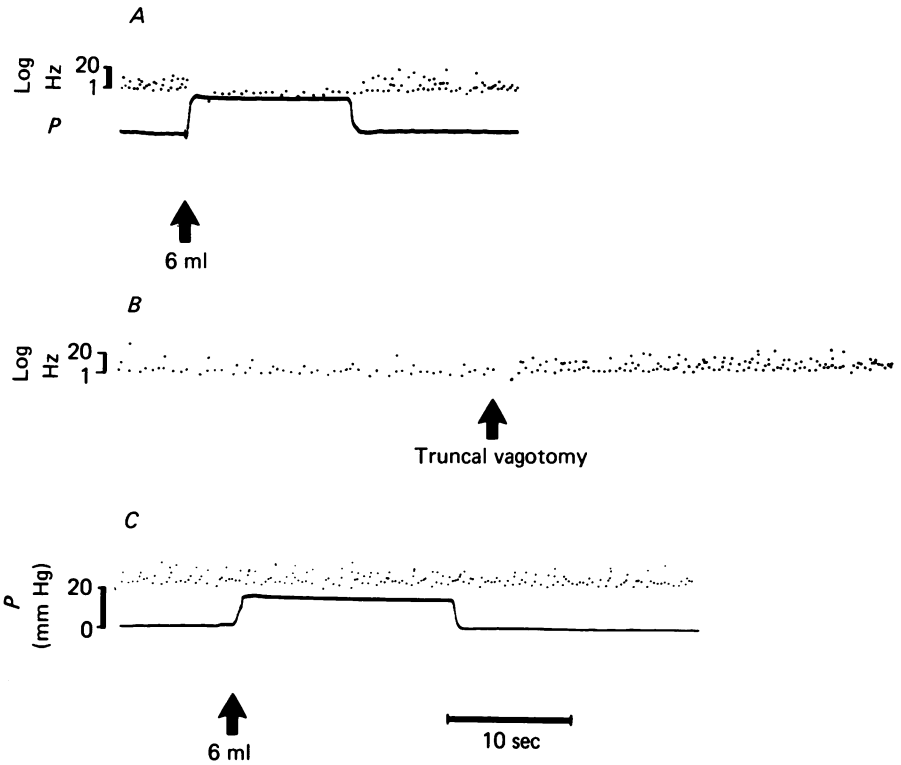

Fig. 8. Effect of vagotomy on a Type II unit. This is the same unit as in Fig. 5. Lower trace, intragastric pressure; upper trace, instantaneous frequency analysis. *A*, response to a 6 ml. gastric inflation after contralateral vagotomy, *B*, effect of vagotomy on the spontaneous discharge, *C*, gastric inflation following vagotomy.

noted. Complete truncal vagotomy was then produced at the level of the abdominal plexus. In the remaining cases complete abdominal vagotomy only was tested. In most cases right cervical vagotomy reduced the response to gastric inflation (compare Figs. 5 and 8), but the degree to which the response was reduced varied from unit to unit. Some efferent units showed very little reduction in their response to gastric inflation while in other units the response was greatly reduced. In all cases truncal vagotomy completely abolished the response to gastric inflation (Fig. 8). It also abolished the contractions which were usually evoked by gastric inflation.

In addition to the effect on the efferent response to gastric inflation, vagotomy affected the spontaneous activity of these efferents, particularly of the lower threshold units. The first effect of vagotomy is a brief response (an increased discharge in Type I units and a decreased discharge in Type II units) caused possibly by an afferent volley evoked by cutting the nerve. After this the spontaneous activity adjusted to a new frequency of firing which was higher or lower than the original spontaneous frequency depending on the type of efferent (Fig. 8*B*). In Types I and III efferents, interruption of the vagal afferent pathways generally caused a decrease in the spontaneous frequency whereas in Types II and IV units the spontaneous frequency usually increased.

The effect of electrical stimulation of the central cut end of the right cervical vagus was tested on eight units (one Type I, five Type II and two Type III). The Type I unit was only excited by electrical stimulation (5 V, 1 msec, 1-50 Hz for 1–10 sec) and the Type III efferents showed no definite response to stimulation even when the stimulus parameters were varied. However, the response of the Type II units to electrical stimulation showed marked divergence, ranging from long lasting inhibition to long lasting excitation. Of the five Type II units tested by electrical stimulation, three were excited and only two inhibited. Of these two, one was a low threshold unit which on electrical stimulation showed long lasting inhibition. The other was a high threshold unit which was inhibited only during the period of electrical stimulation.

DISCUSSION

All the units isolated in this study were modulated by gastric mechanoreceptors whose afferent fibres projected centrally in both vagi. Only two types of gastric receptors, with afferent fibres in the vagus nerves, have been identified electrophysiologically in the rat. These are rapidly adapting mucosal mechanoreceptors (Clarke & Davison, 1974) and the slowly adapting mucosal mechanoreceptors (Clarke & Davison, 1975, 1976; Davison & Clarke, 1977).

Most of the patterns of modulation are adequately explained by the known behaviour of these slowly adapting mechanoreceptors and it seems probable that they are mainly responsible for the reflex responses described in this report.

The following properties of the slowly adapting gastric mechanoreceptors with vagal afferent fibres have been described.

(1) They are spontaneously active. The effects of vagotomy confirm that the efferent neurones receive a tonic excitatory drive (Type I) or a tonic inhibitory input (Type II). Types III and IV units showed a variable response to vagotomy, possibly reflecting the reciprocal nature of the afferent input. The effects of vagotomy also suggest that the level of spontaneous activity in the sensory inputs is greatest in the lower threshold afferents.

(2) The afferents produce a graded response to distension, the threshold varying from 0·1 to 10 ml. This accounts for the graded reflex response in the efferents to gastric inflation and explains the variations in the thresholds for reflex responses. The question of whether a central mechanism or a peripheral receptor mechanism is responsible for differences in threshold is important, particularly when considering the more complex Type III and Type IV responses. While it is impossible to discount a

central mechanism for the differential effects of high and low tensions in the stomach wall, a simple mechanism involving two populations of receptors, one of high threshold and the other of low threshold, provides an adequate explanation. Certainly, receptors with a wide range of thresholds exist (Clarke & Davison, 1976; Davison & Clarke, 1977). Moreover, in one Type IV unit there was a separation of the receptive fields of the receptors producing excitation and those producing inhibition. In these types of unit, electrical stimulation of the central end of the contralateral vagus produces no clear-cut response, suggesting that both inhibitory and excitatory inputs are being stimulated simultaneously. Finally, vagotomy has little effect on the level of spontaneous activity and this may reflect the duality of the tonically active afferent input.

(3) The vagal afferents are slowly adapting to maintained inflation. This would explain the adaptation seen in the efferent discharge.

(4) The slowly adapting mechanoreceptor is excited by distension and contraction thus behaving as an 'in series' tension receptor which would account for the gastric rhythms seen in the efferent discharge.

(5) On deflating the stomach, or when the stomach relaxes after a contraction, vagal afferent units show a period of reduced activity or even a distinct silent period. This was also reflected in the efferent discharge patterns, particularly in the lower threshold Types I and II units. This particular property of the afferent nerves also accounts for the exceptional behaviour of some units. For example, one non-spontaneously active unit, which was excited only during the relaxation phase following an isometric contraction, was regarded as a simple Type II unit which was released from tonic inhibition only during these phases of reduced afferent activity. The same property explains the rise in frequency of discharge above the resting level in Type II units during relaxation following isometric contraction. A corresponding pattern was occasionally observed in Type I units.

(6) Tension receptors respond more readily to isometric contractions rather than isotonic contractions (Leek, 1977) and this property has been confirmed in the slowly adapting mechanoreceptors of the rat stomach (Clarke, 1977). The reflex responses of the Type Ic units reflect this pattern. Moreover, the fact that the response is slight is consistent with the marginal effect on the afferent activity and presumably reflects the fact that conditions in the experimental set-up are far from ideal.

From a consideration of these details of the reflex modulation of vagal efferent fibre discharge by gastric mechanoreceptors it seems probable that the 'in-series tension receptors' described previously are mainly responsible for all the effects described. However, the possibility of some involvement of mechanoreceptors with afferent fibres in the splanchnic nerves (Floyd & Morrison, 1974) should not be entirely discounted since the splanchnic nerves were left intact, though such a pathway would be of minor importance judging from the effects of vagotomy.

It is clear that there is some degree of convergence of vagal afferents since the majority of efferent units tested receive afferents from a large area of the stomach yet individual vagal mechanoreceptors innervate a very limited receptive field (Clarke, 1977). Moreover, afferents modulating single efferent fibres project centrally in both vagi, and since Type III and IV responses are dependent upon different threshold afferent endings as discussed above, this too suggests convergence.

The electrical stimulation experiments show that convergence may occur from afferents other than those stimulated by gastric inflation and contractions since in several Type II units, electrical stimulation of the central end of the contralateral vagus produced excitation rather than inhibition. In preliminary observations (Davison & Grundy, 1978) these same efferent types have shown some response to both duodenal and/or oesophageal inflation.

The function of these efferent fibres cannot be determined from the results of the present study. One crucial piece of missing information is the precise destination of the fibres isolated by dissection. However, it appears probable, for the following reasons, that most, if not all, of the efferent fibres described in this account innervate the upper gastrointestinal tract:

(1) They are all believed to be C-fibres on the basis of the size and duration of the spikes (75–250 μV amplitude and 3–6 msec duration). The conduction velocity has been measured in 3 units using a pre-trigger averaging technique and all three were slowly conducting C-fibres (0·5, 0·54, 1·4 $msec^{-1}$ respectively). Since the majority of non-myelinated efferent fibres in the cervical vagus are abdominal (Agostini, 1957) then there is a high probability that the units described here are also abdominal.

(2) All the efferent discharge patterns showed gastric rhythms. This is considered to be an important criterion in identifying gastric efferents though other criteria have also been used (Iggo & Leek, 1967*a*). However, by itself gastric rhythm is considered to be an inadequate criterion (Davison & Grundy, 1977).

(3) They show no other rhythms detectable by our methods. In particular there were no observed cardiovascular or respiratory rhythms. Conventional cardiovascular efferents, with distinct cardiovascular and respiratory rhythms, were isolated in this study and were easily distinguishable from the four types of efferent described here. Thus it appears unlikely that they are cardiovascular or respiratory efferents and are more likely to be gastrointestinal. It would be desirable therefore to confirm this by tracing the destination of these efferents but this is impossible using the present dissection technique. The method of recording from the vagal nucleus of the medulla with microelectrodes clearly has advantages in this respect (Harding & Leek, 1971, 1972). Preliminary studies in the dog with a similar technique has revealed the distribution of abdominal vagal efferent fibres to the upper gastrointestinal tract and adjacent structures (Andrews, Duthie, Fussey & Mellersh, 1977).

The four types of vagal efferent units described in this account are quite distinct from those described previously (Iggo & Leek, 1967*a*, *b*). Although the Type Ic units resemble those in the sheep in that they show phasic activity consisting of bursts of discharge during each gastric contraction, they show fundamental differences in their mode of activation. In the sheep the rhythm was determined by central 'rate and amplitude centres' which could be modified by gastric afferent inputs. Thus blocking of rhythmic gastric contractions with probanthine did not abolish the phasic rhythms of the efferent discharge. The Type Ic units in this study, however, were reflexly activated by high threshold gastric tension receptors so that only gastric contractions were capable of exciting them. Hence, when gastric contractions were abolished by probanthine, the rhythmic discharge also ceased.

Another superficial point of similarity is the behaviour of the Type Ic units in response to extreme levels of distension. As in the sheep, there was a reduction in the

magnitude of the gastric contractions and the associated efferent discharge. In the case of the sheep this was attributed to a high threshold inhibitory effect asserting itself at the higher inflations. The Type Ic units, on the other hand, showed no evidence of any inhibitory input. The reduced efferent discharge is a consequence of the reduced gastric motility and not vice versa as in the sheep. The differential effects of high and low levels of gastric inflation on efferent discharge described by Iggo & Leek (1967*b*) in the sheep were attributed to either a central mechanism or to the existence of two populations of receptors with different thresholds. No evidence was presented in support of either of these possibilities. In the present work, reasons for favouring the peripheral mechanism, utilizing different threshold receptors, has already been presented above.

Micro-electrode recordings from the vagal nucleus of the medulla in the sheep (Harding & Leek, 1971, 1972, 1973) have revealed some patterns of neuronal activity similar to those described in this report. Apart from Type Ic patterns, two other types of neurone resembling Types I and II have been described. Both these neurone types were shown to be interneurones since they did not respond directly to antidromic or orthodromic electrical stimulation of the vagal nerves. The patterns of motoneurone activity, however, were quite different from the patterns described in this report.

Although in this study the responses have been classified into four distinct types, the boundary between one type and another may be blurred. Moreover the proportion of the four different patterns of response may not have been accurately assessed. For example, an overestimation of Type I units may have occurred by failing to reach threshold for activation of the inhibitory input. The ability to convert a Type III response to a Type I by blocking gastric contractions with probanthine would support this contention. For a similar reason Type II responses may also have been overestimated.

Nevertheless the four types of efferent unit described in this report can be arranged into two reciprocal pairs, Types I and II being reciprocally modulated and Types III and IV likewise. The presence of inhibitory and excitatory vagal pathways to the upper gastrointestinal tract is well documented (Burnstock, 1972). These pathways may be excited by vagal afferent fibres as for example in reflex receptive relaxation of the stomach (Jansson, 1969). The present observation of reciprocally modulated pairs of vagal neurones suggests the possibility that activation of a vago-vagal reflex, be it excitatory (cholinergic) or inhibitory (purinergic), may involve the reciprocal inhibition of the antagonist pathway. Such a mechanism has been proposed to explain receptive relaxation of the dog stomach (Miolan & Roman, 1974) and this would be supported by the present findings.

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