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THE RESPONSE OF GASTRIC STRETCH RECEPTORS AND CERTAIN OTHER ABDOMINAL AND THORACIC VAGAL RECEPTORS TO SOME DRUGS

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The presence of gastric stretch receptors reported in detail in another paper (Paintal, 1954*b*) was revealed in the first instance by means of injection of phenyl diguanide into different vascular channels (Paintal, 1954*a*). This sensitivity is peculiar as the drug did not, in the same or somewhat higher doses, affect other visceral stretch receptors (Paintal, 1953). It, therefore, seemed worth while to study further the responses of gastric stretch receptors to this, and other drugs such as nicotine, lobeline and 5-hydroxytryptamine which are also known to produce reflex effects. An additional point was that in case these drugs did alter the activity of gastric stretch receptors the information so gained would help in the interpretation of the reflex effects of these drugs.

It is believed that the gastric stretch receptors with their afferent connexions are responsible for the immediate satiation of hunger and thirst (Paintal 1954*b*). Since some evidence exists to show that adrenaline and blood sugar level modify oral food intake (Mayer & Bates, 1952), the effects of these two drugs on gastric stretch receptors were also studied.

In the course of the investigation certain other abdominal and thoracic receptors sensitive to phenyl diguanide were also encountered. Two of these were located in the intestines and two were probably of pulmonary origin. The presence of pulmonary receptors sensitive to phenyl diguanide confirms the conclusions of Dawes, Mott & Widdicombe (1951).

METHODS

The experiments were performed on the same cats used in investigating the characteristics of gastric stretch receptors described in another paper (Paintal, 1954*b*). The afferent fibres studied and the methods of distending the stomach, recording intragastric pressure, etc., were, therefore, the same as those described in that paper.

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In the first thirteen experiments an aortic cannula 10·5 cm long and 2 mm external diameter, with its tip upstream from the coeliac artery, was inserted into the abdominal aorta. In the remaining six experiments a catheter was inserted into the right external jugular vein; the tip of this lay in the superior vena cava. The position of the cannula and catheter were confirmed post-mortem. Injections were made directly through these into the vessels.

The drugs used were dissolved in 0·9% NaCl (w/v), and the concentration in which they were injected were: phenyl diguanide, 5-hydroxytryptamine creatinine sulphate, and adrenaline hydrochloride (Parke Davis), 1 in 10,000; nicotine tartrate, lobeline and DL-amphetamine, 1 in 1000; and glucose, 20–50% (w/v). The usual doses of drugs injected were phenyl diguanide, 40–100 μg/kg; 5-hydroxytryptamine (base), 13–22 μg/kg; adrenaline, 20–55 μg/kg; nicotine, 80–550 μg/kg; lobeline, 350 μg/kg; amphetamine 0·5–1·5 mg/kg; and glucose 0·2–1·0 g/kg. Not all the drugs were injected when studying the responses of any particular fibre, and a few minutes were allowed to elapse before injecting the next drug. Usually, the effect of injecting 3–6 ml. 0·9% NaCl was noted before injecting the next drug; this never produced a discharge of impulses in any fibre. All the solutions were at room temperature which was about 30° C during the hot summer months when these experiments were performed.

Injections usually occupied about 1 sec and the response time was always reckoned from the beginning of the injection.

RESULTS

In Table 1 are summarized the responses of twenty-nine gastric stretch afferent fibres following injections into the abdominal aorta (fibres nos. 1–16) or the superior vena cava (fibres nos. 17–31) of phenyl diguanide, 5-hydroxytryptamine, nicotine, adrenaline and glucose. All the fibres except fibre no. 28 yielded an unmistakable slowly adapting discharge on distending the stomach with a balloon. Owing to the different circumstances of each experiment it was not possible to study the effect of all the above drugs on all the twenty-nine receptors. The responses of the fibres following injections of lobeline and amphetamine have not been included in the table owing to the small number of observations with these drugs.

Phenyl diguanide. The responses of twelve receptors to intra-aortic injections of phenyl diguanide were studied; ten of these yielded a discharge of impulses, two did not. Although the pattern and intensity of the response varied somewhat in different fibres, the discharge in all of them started within 1·2–2·4 sec after the beginning of the injection (average 1·5 sec). The duration of the response varied from 1·3 to 4·4 sec (average 1·8 sec). The peak frequency of discharge varied from 20 to 40/sec. A dose of 50–55 μg/kg was effective in stimulating the receptors, although the minimum effective dose was probably much less, and it is possible that the two receptors that failed to respond to this dose could have been stimulated by larger doses.

The pattern of discharge when plotted as the frequency of impulses/sec varied considerably (Fig. 1). In some fibres the discharge rose to a peak and gradually died away. In others, the impulses tended to form small groups at times, and in still others, near the end of the discharge, the frequency of impulses rose to a final peak to terminate in complete absence of any further impulses.

Table 1 shows that when phenyl diguanide was injected into the superior vena cava, half of the fibres examined yielded no responses, although the doses of the drug injected were often nearly twice those injected into the aorta. In those, where a response appeared (Figs. 1 and 2), the injection-response time

TABLE 1. Response of gastric stretch receptors to certain drugs. Drugs were injected into the abdominal aorta while studying responses of fibres nos. 1–16 and into the superior vena cava in the rest. Figures represent doses of drugs which yielded (+) or did not yield (−) a discharge of impulses in the fibres

Fibre no.	Phenyl diguanide (μg/kg)	5-Hydroxy-tryptamine (μg/kg)	Nicotine (μg/kg)	Adrenaline (μg/kg)	Glucose (g/kg)	Situation of receptors
1	+40	—	—	—	—	*C*
2	+70	—	—	—	—	*P*
3	+55	—	—	—	—	—
4	+55	—	—	—	—	*C*
5	+55	—	—	—	—	—
6	+55	—	—	+20	+0·1	*B*
7	+50	—	—	—	−0·5	*C*
8	+50	+22	+240	+50	+0·5	*B*
9	+50	+22	+500	−50	−0·2	—
11	+55	—	—	+55	+0·2	—
12	−60	—	—	—	−0·2	—
13	—	—	+150	+60	+0·2	—
14	−50	—	—	−50	+0·9	—
15	—	—	−250	−50	−0·2	*P*
16	—	—	−250	−50	−0·2	—
17	−90	—	−550	−55	−1·0	—
18	−100	—	−100	−50	−1·0	—
19	+80	+17	−80	+40	−0·8	*B*
20	+80	+17	−80	—	−0·8	—
21	−80	—	—	−40	−0·8	—
22	+80	—	—	+40	—	—
23	−60	—	—	—	—	*P*
24	+50	—	—	+30	—	—
25	+60	+13	—	—	+0·6	—
26	+60	+22	—	—	−0·6	*P*
27	−60	−22	—	—	−0·6	*P*
28	−100	—	—	—	—	*C*
30	+80	+22	—	+25	−1·0	—
31	−100	−22	—	—	—	*P*

+, positive response; −, negative response; *P*, pyloric end of stomach; *B*, body of stomach; *C*, cardiac end of stomach.

varied from 3·8 to 9 sec (average 5·6 sec). The duration varied from 3 to 8 sec (average 5·6 sec). This value is about 3 times the average value obtained following intra-aortic injections. The peak frequency was 15–35 impulses/sec. As in the case of intra-aortic injections considerable variations in the pattern of discharge were observed in this series as well.

In two fibres, after an initial clear response following an intra-aortic injection of phenyl diguanide, no further responses could be obtained by subsequent injection of the drug. Although in most of the fibres repeated injections at intervals of 5–10 min yielded undiminished responses, there were a few in which the peak frequency and duration of the discharge fell after subsequent

injections. For this reason the responses to vena caval and intra-aortic injections are not strictly comparable as these injections followed each other, but in spite of this, intra-aortic injections with few exceptions yielded a higher peak frequency of discharge. On the other hand, the duration of the discharge following intra-aortic injections was always less, being 10–90% of the duration following injection into the superior vena cava. This suggests that most of the drug was washed past the coeliac artery as the tip of the intra-aortic cannula was just upstream from this artery.

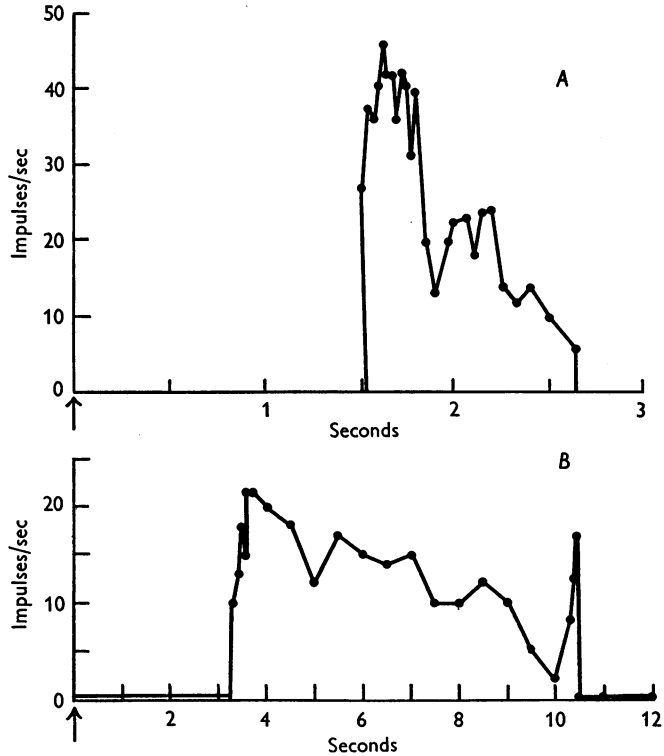

Fig. 1. Graph of responses in two gastric stretch fibres in the same cat to injection of phenyl diguanide at arrow. A, intra-aortic injection of 55 μg/kg; and B, injection of 80 μg/kg into the superior vena cava. Note the different injection-response times in the two cases.

In view of the failure of some receptors to respond to repeated doses of the drug it became obvious that an attempt to determine the threshold amounts of the drug effective in stimulating the receptors would be accompanied by considerable difficulties. However, it is conjectured that 30 μg/kg of phenyl diguanide intravenously would probably be effective. Lesser doses would probably suffice if injected into the abdominal aorta.

Bathing the peritoneal surface of the stomach or the mucous membrane with phenyl diguanide solution particularly at the site of the receptor located digitally, yielded no responses. Thus, if the drug did affect the smooth musculature in any way this had apparently nothing to do with the stimulation of the receptors. The fact that bathing the stomach in a dilute solution of acetylcholine did not affect the receptors but gave rise to powerful gastric contractions suggested that phenyl diguanide could satisfactorily act on the smooth musculature if it was poured on to the stomach. In one experiment, submucous infiltration of phenyl diguanide at the site of the receptor, such that a large vesicle was formed, did not give rise to any impulses.

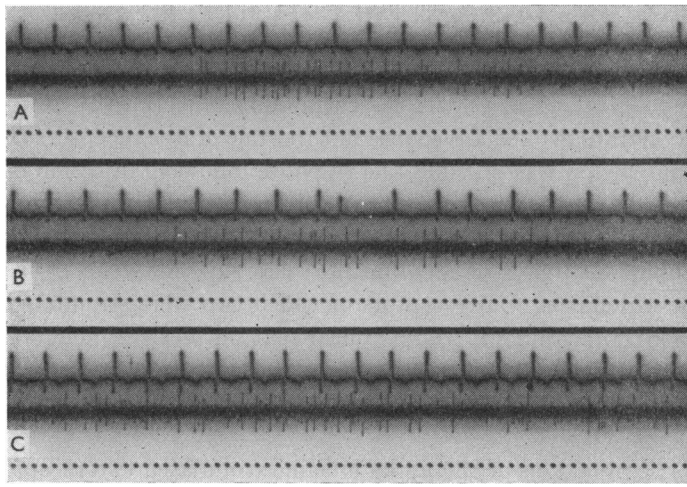

Fig. 2. Impulses in a gastric stretch fibre. A, B and C are the responses to phenyl diguanide, 60 μg/kg; 5-hydroxytryptamine, 13 μg/kg; and glucose 0·6 g/kg respectively. The injection-response times were, respectively, 8·9, 8·9 and 11·6 sec. From above downward in each e.c.g., impulses in fibre; and time in $\frac{1}{10}$ sec.

Receptors sensitive to and insensitive to phenyl diguanide were found in all cats. An analysis of the results showed that there is apparently no correlation between the sensitivity of a receptor to phenyl diguanide and (*a*) the nature of its response to gastric distension, (*b*) the presence or absence of spontaneous activity and (*c*) the situation of the receptor in the stomach.

5-*Hydroxytryptamine* (HT). The effect of intra-aortic injections of HT on the activity in two fibres was determined. In both, a discharge of impulses appeared 1·8 and 2·0 sec respectively after the injection. These values, though slightly lower, were not significantly different from those following injection of phenyl diguanide. The duration and peak frequency of discharge were, however, greater in both.

Injection of the drug into the superior vena cava evoked a discharge in five out of seven fibres examined (Fig. 2). The injection-response times varied between 3·5 to 9·0 sec, being the same as that following phenyl diguanide. The duration of the evoked discharge varied from 1·8 to 8·0 sec, and in all but one fibre, the durations were greater than those seen in the same fibres after injection of phenyl diguanide. As can be seen in Table 1, doses of 13–22 μg/kg were effective in stimulating the receptors. As in the case of phenyl diguanide, the pattern of discharge varied considerably in different fibres.

Both the receptors that were insensitive to HT were also insensitive to phenyl diguanide. This observation was confirmed in a number of other fibres studied purely on the screen of the cathode-ray tube. As in the case of phenyl diguanide the sensitivity of a receptor to HT apparently bore no relation to either the exact situation of the receptor in the stomach or to the presence of spontaneous activity in it.

Nicotine, lobeline and amphetamine. Intra-aortic injections of 150–500 μg/kg of nicotine tartrate evoked a response in three out of five receptors (Fig. 3, C). Where a comparison was possible, the response following injection of nicotine was always much greater than that resulting after phenyl diguanide, the duration of the discharge in these fibres being 4·3, 12·0 and 16·5 sec respectively.

Injections of 80 μg/kg of nicotine into the superior vena cava were ineffective in stimulating four receptors of which two were stimulated by both HT and phenyl diguanide; it would appear that the doses of 80 μg/kg were too small. A fifth receptor, which was not stimulated by 90 μg/kg phenyl diguanide injected into the superior vena cava, also failed to respond to 550 μg/kg nicotine (Table 1).

Intra-aortic injections of 350 μg/kg lobeline stimulated two receptors which were also stimulated by nicotine. The duration and peak frequency of the discharges were much less, but the injection-response times were identical.

Injections of amphetamine into the superior vena cava yielded no responses from four receptors on which it was tried. Two of them were stimulated by both phenyl diguanide and HT but were unaffected by 4 mg/kg amphetamine. A third that was stimulated by phenyl diguanide and adrenaline was unaffected by 1 mg/kg amphetamine.

Adrenaline. Intra-aortic injections of 20–60 μg/kg adrenaline yielded a discharge of impulses in four out of eight fibres after an injection-response time varying from 1·2 to 1·8 sec in three fibres and 3·2 sec in the fourth (Fig. 3, D and E). Where a comparison was possible, the injection-response times were identical with those following intra-aortic injection of phenyl diguanide thereby suggesting that the mechanism of stimulation of the receptors may be identical in both cases. The duration of the discharge varied from 1 to 14 sec, being clearly longer than that following phenyl diguanide or HT; the peak frequencies attained were also higher. The doses of adrenaline used were high

when compared to the small doses that are effective in producing a considerable rise in blood pressure. Often, obvious changes in the e.c.g. accompanied injection of adrenaline. Some receptors sensitive to phenyl diguanide were unaffected by adrenaline.

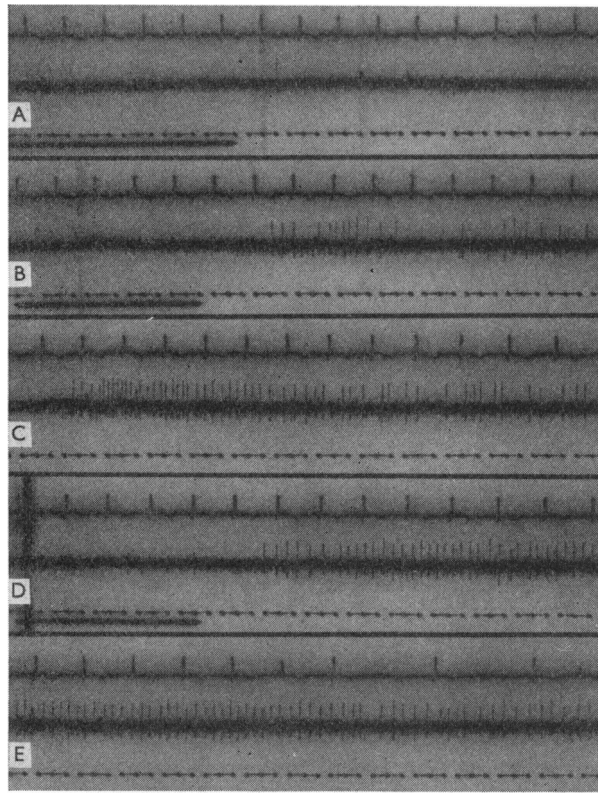

Fig. 3. Impulses in a gastric stretch fibre. In A, B and C 1·3 ml. of 0·9% NaCl, 0·2 g/kg glucose, and 150 μg/kg nicotine respectively were injected into the aorta. D and E, which are continuous, show the response of the fibre to intra-aortic injection of 60 μg/kg adrenaline. From above downwards in each record e.c.g. impulses in a fibre; time in $\frac{1}{10}$ sec and injection signal. There is no signal in E. The injection-response times in B and D are identical.

Four phenyl diguanide-sensitive receptors were stimulated by 25–40 μg/kg adrenaline injected into the superior vena cava (Fig. 4). Two receptors unaffected by phenyl diguanide were also unaffected by adrenaline (Table 1). In one fibre a discharge appeared 12·5 sec after the injection. This was believed to be secondary to other changes since the discharges following phenyl diguanide and HT appeared 3·5–3·8 sec after injection of these drugs into the superior vena cava.

In a few instances injection of adrenaline was followed by a low frequency persistent discharge some minutes later in receptors not active spontaneously. In others where spontaneous discharges were present to begin with, the activity was enhanced. These changes usually lasted for several minutes. No attempt was made to correlate these changes with any occurring in the smooth muscle of the stomach. They were particularly marked in one fibre described elsewhere (Paintal, 1954*b*).

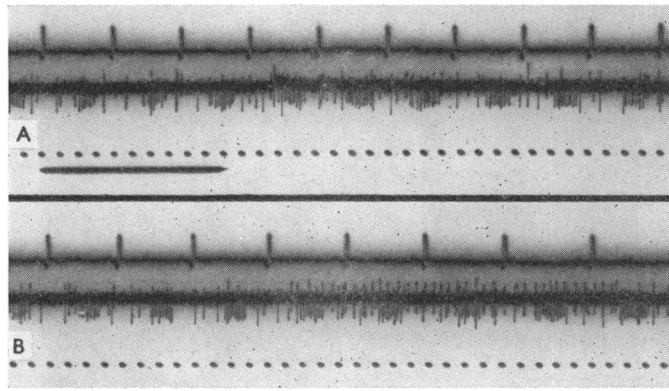

Fig. 4. Response of a gastric stretch fibre (small spikes above base-line in B) to injection of 30 μg/kg adrenaline into the superior vena cava. From above downwards e.c.g. impulses in vagal fibres; time in $\frac{1}{10}$ sec and in A, injection signal. Adrenaline was injected at signal in A and the response appeared in B after 5·6 sec. A and B are continuous. Impulses with a cardiac rhythm are from atrial type B fibres.

Glucose (Figs. 2, 3). The discharges following injections of glucose were seldom as dramatic as the responses to other drugs. In doses shown in Table 1, intra-aortic injections evoked positive responses in five out of ten receptors. The injection-response time varied from 1·3 to 3·8 sec, being usually identical with those following injections of other drugs. The duration of the discharge varied from 2 to 3 sec and the peak frequency in every case was below 20 sec (Fig. 3, B).

As with other drugs, injection of glucose into the superior vena cava yielded a response in a smaller proportion of receptors—only two out of nine receptors giving a clear cut discharge. In one of these (fibre no. 25, Fig. 2, C), for no obvious reason, the injection-response time was 2·7 sec more than those following phenyl diguanide and HT. So far no case has been encountered where a receptor was insensitive to phenyl diguanide but sensitive to glucose.

In one fibre (fibre no. 15, Table 1), although an intra-aortic injection did not yield a response after the usual interval, a persistent discharge at about 8 impulses/sec appeared about 1 min later and lasted for several minutes. This

fibre had previously shown no spontaneous activity and was insensitive to both adrenaline and nicotine. The discharge was not associated with any change in intragastric pressure.

A significant observation was that repeated injections of glucose as a rule did not produce responses as strong as that following the first injection.

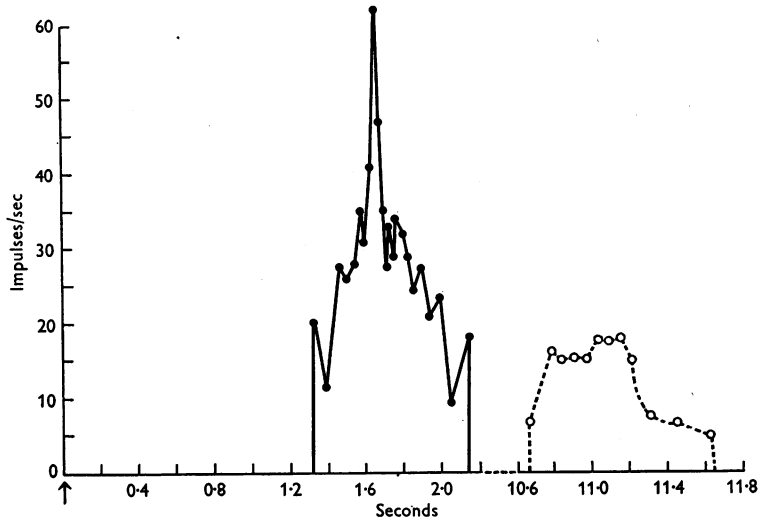

Fig. 5. Graph of response of a gastric fibre unaffected by gastric distension to injection at arrow of phenyl diguanide into the aorta, –●–●–, and superior vena cava, –○–○–. The responses are similar to those seen in gastric stretch fibres. The receptor was localized in the cardiac end of the stomach.

TABLE 2. Response to drugs of receptors unaffected by gastric distension

Fibre no.	Drug	Route	Dose (μg/kg)	Injection-response time (sec)	Duration of discharge (sec)	Impulses/sec	Spontaneous discharge	Situation of receptors
1	Phenyl diguanide	Aorta	55	1·4	3·1	16	Groups	?
2	Phenyl diguanide	Aorta	55	1·3	0·9	35	Nil	Stomach
3	Phenyl diguanide	Aorta	55	2·3	1·4	20	Single impulse	Stomach
4	Phenyl diguanide	Aorta	60	1·9	1·6	20	Nil	Intestine
5	Phenyl diguanide	Aorta	50	1·4	3·9	25	Nil	Not attempted
	Adrenaline	Aorta	11	1·7	2·0	22	—	—
6	Phenyl diguanide	S.V.C.	90	1·6	1·8	40	Nil	Lungs
	Nicotine	S.V.C.	550	1·2	3·0	35	—	
7	Phenyl diguanide	S.V.C.	90	6	7·0	25	Single impulses	Intestines
	5-Hydroxytryptamine	S.V.C.	20	5·2	3·1	20		
8	Phenyl diguanide	S.V.C.	80	2·6	3·2	?	Nil	Lungs

S.V.C., superior vena cava.

Responses of other gastric, intestinal and thoracic visceral receptors. In this investigation eight afferent fibres were encountered with phenyl diguanide-sensitive receptors, which were unaffected by rapid or slow maximal disten-

sion of the stomach. In five of them a discharge appeared within 1·4–2·3 sec after intra-aortic injection of 50–60 μg/kg phenyl diguanide, leaving no doubt that these receptors were located in the abdominal viscera. In the case of one of these receptors (fibre no. 5, Table 2) no attempts at digital localization were made. This was, however, stimulated by 11 μg/kg adrenaline and was unaffected by HT and glucose. Two were localized in the stomach—one of them, no. 2, accurately at the cardiac end of the stomach (Fig. 5). The other yielded inconsistent responses, and, therefore, could not be accurately localized. This fibre showed a spontaneous low frequency discharge at 1 to 2 impulses/sec. Several futile attempts were made to localize the receptors of fibre no. 1, Table 2. This fibre showed an interesting spontaneous discharge (Fig. 6) which occurred in groups of impulses lasting about 16 sec—the groups appearing regularly at about 3/min. The peak frequency of discharge in the groups was about 25 impulses/sec.

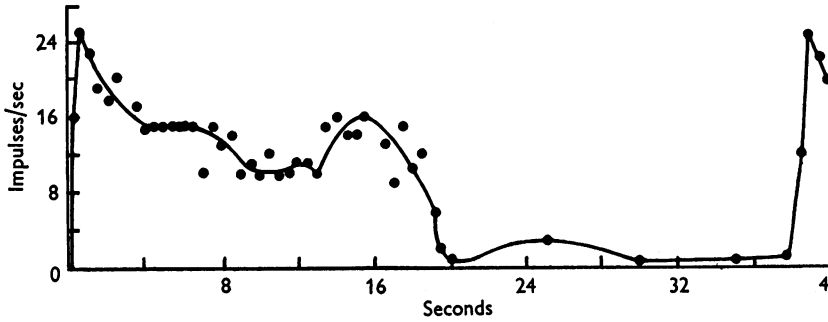

Fig. 6. Graph of spontaneous activity in a vagal fibre from an abdominal visceral receptor. The receptor was stimulated by intra-aortic injections of phenyl diguanide but could not be accurately localized.

The receptor of fibre no. 4, Table 2, was unequivocally localized at the attachment of the mesentery to the jejunum. Distension of this part of the intestines failed to produce a discharge of impulses but light digital pressure was effective in doing so. This intestinal receptor was unaffected by an intra-aortic injection of 26 μg/kg HT.

In fibre no. 7 a discharge of impulses appeared 6 sec after injection of 90 μg/kg phenyl diguanide into the superior vena cava and 5·2 sec after 20 μg/kg HT (Fig. 7); the receptor was situated in the intestines. This receptor was unaffected by intravenous injection of 45 μg/kg adrenaline and 0·55 mg/kg amphetamine. Spontaneous discharges in the form of bursts of impulses at about 8/sec, which were interspersed with a lower frequency of discharge were present.

Fibres nos. 6 and 8 were believed to be of pulmonary origin. In these a discharge appeared 1·6 and 2·6 sec respectively after injecting phenyl diguanide

into the superior vena cava. This was an unusual observation since, for abdominal receptors the minimum injection-response time had been found to be 3·5 sec in twenty observations with various drugs. It was, therefore, thought that these receptors were located in the lungs. Fibre no. 6 (Fig. 8) also yielded a discharge 1·2 sec after injecting 0·55 mg/kg nicotine into the superior vena cava but none after injecting glucose, 1 g/kg; adrenaline, 55 μg/kg; and amphetamine 0·55 mg/kg. The other (no. 8) was unaffected by glucose 1 g/kg, and adrenaline 40 μg/kg. The effect of nicotine was not tried on this one. It

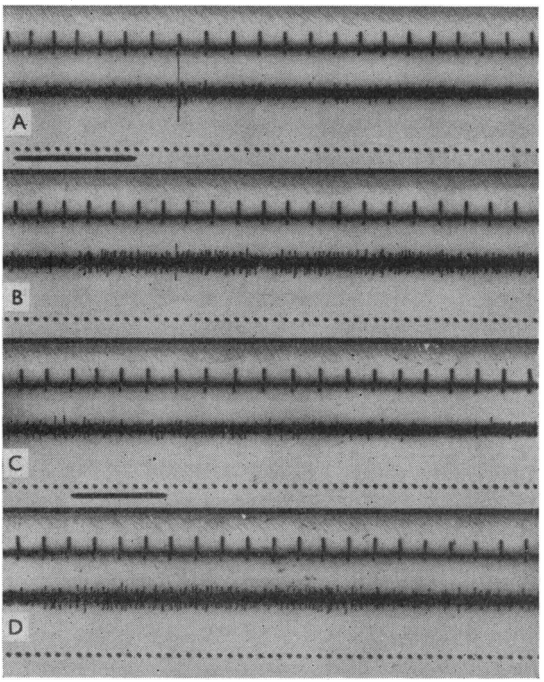

Fig. 7. Impulses in a fibre from the intestines. A and B (continuous records) show the response to injection of 90 μg/kg phenyl diguanide into the superior vena cava; injection response time is 6 sec. C and D (continuous records) show the response to 20 μg/kg, 5-hydroxytryptamine injection. Response time is 5·2 sec. Compare the injection-response times with those seen in the pulmonary fibre obtained in the same cat in Fig. 8. From above downwards e.c.g.; impulses in fibres; time in $\frac{1}{10}$ sec; and in A and C, injection signal.

was confirmed that the small injection-response times were genuine and not due to a faulty injection signal. In both experiments abdominal visceral afferent fibres were encountered and in these there was the usual injection response time of 6 sec thus lending strong support to the view that the receptors mentioned above were located in the lungs. Further experiments (to be published) have confirmed the existence of such receptors.

Pulmonary stretch fibres. Phenyl diguanide, HT (in doses of 17–44 μg/kg), glucose, adrenaline, nicotine and lobeline, did not affect the activity in different experiments of five, three, three, four, one and one pulmonary stretch fibres respectively, thus confirming some of the conclusions of earlier work (Mott & Paintal, 1953; Paintal, 1953).

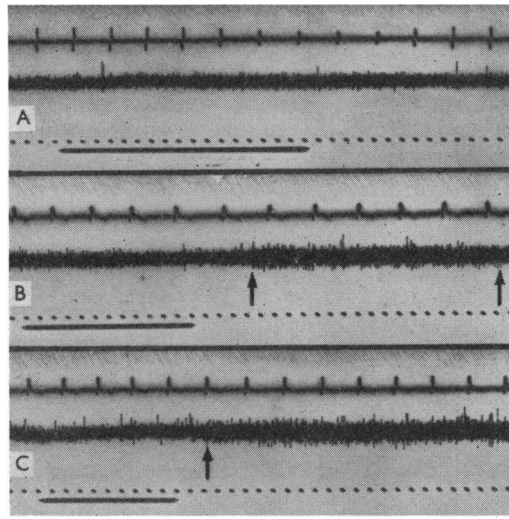

Fig. 8. Impulses in fibres from phenyl diguanide-sensitive receptors presumably in the lungs. In A, 1 g/kg glucose was injected into the superior vena cava. There is no response. In B a response appeared 1·6 sec after the injection of 90 μg/kg phenyl diguanide into the superior vena cava. In C a response appeared 1·2 sec after injecting 0·55 mg/kg nicotine. Compare these injection-response times with those seen in Fig. 7 which are records of response in an intestinal fibre from the same cat.

DISCUSSION

The results of these experiments show that there are several different types of vagal visceral receptors that are stimulated by one or more drugs such as phenyl diguanide, HT, nicotine, adrenaline. The existence of intestinal vagal receptors has been shown unequivocally. None of the four types of receptors, i.e. gastric stretch receptors, gastric receptors unaffected by distension of the stomach, intestinal and thoracic receptors, showed any specificity towards any of the drugs studied, and it is highly probable that other drugs of the guanidine and isothiourea groups would also stimulate them. The fact that any one drug can stimulate several functionally different receptors emphasizes the need for interpreting cautiously the reflex effects produced by drugs.

Although the conduction velocities of intestinal and thoracic afferent fibres with phenyl diguanide-sensitive receptors have not been determined, it is

believed that like gastric stretch afferent fibres, they belong to the 2–14 m/sec group. This means that it would not be possible by cooling the vagus to a suitable temperature to block one type of fibre with phenyl diguanide-sensitive receptors and not the others.

The blood glucose concentrations, at which the receptors were stimulated following injection of glucose, must have been abnormally high. Even with these, the responses were of low intensity and so it seems unlikely that gastric stretch receptors will respond to the comparatively small changes in blood sugar levels found normally. The pulmonary phenyl diguanide-sensitive receptors must be surely concerned in the reflex effects produced by phenyl diguanide (Dawes *et al.* 1951). Like most other phenyl diguanide-sensitive receptors at least some of those in the thorax are also apparently normally inactive. As in the case of intestinal receptors and gastric receptors unaffected by distension of the stomach their normal functions remain to be determined.

The fact, that nicotine and lobeline stimulate gastric stretch receptors, has created the necessity of distinguishing the chemoreceptors from the former, when studying the impulses in vagal fibres. Both types of fibres may show low-frequency irregular spontaneous discharges, but the gastric stretch receptors are not affected by anoxia and the chemoreceptors are not likely to be affected by gastric distension so that differentiation of one from the other need not present a serious problem.

If the results obtained in cats are applicable to man then amphetamine does not inhibit hunger by stimulating the gastric afferent mechanism as the drug does not stimulate the gastric stretch receptors. Harris, Ivy & Searle (1947) believe that the action of the drug is a central one.

It would appear that these receptors are primarily sensitive to the drugs and that their stimulation is not secondary to contraction or relaxation of the smooth muscles. This is supported by the fact that both HT and adrenaline, which respectively stimulate (Rapport, Green & Page, 1948; Gaddum, 1953) and inhibit smooth muscle, stimulate the receptors. Further, pouring phenyl diguanide over the surface of the stomach or on the mucous membrane over a prolonged period does not stimulate the receptors. If stimulation had been secondary to smooth muscle changes, this procedure should have been effective in rousing the receptors. Douglas & Gray (1953) and Diamond (1953) reached a similar conclusion regarding the cutaneous and carotid baroreceptors respectively. Unlike these investigators no attempts were made here to study the responses of the receptors following the injection of acetylcholine, hexamethonium, or D-tubocurarine, since the main purpose was to study the possible role of various drugs in producing visceral reflexes. The mechanism of stimulation of these receptors by drugs is being studied in a further investigation.

There is no doubt that some gastric stretch receptors are not affected by any

of the drugs mentioned, but it is not possible to say whether these receptors are actually insensitive to the drugs or whether they fail to respond due to some other reason, e.g. the drugs not reaching the receptors owing to local vasoconstriction.

It has been shown that HT, when injected intravenously, does not stimulate pulmonary stretch receptors (Mott & Paintal, 1953) and having confirmed this fact in this investigation, we must consider the conclusion of Schneider & Yonkman (1953) to the contrary. In both the fibres illustrated by them (Figs. 6, 7), the enhanced activity appeared at least 9 sec following injection of HT, by which time the reflex effects had already set in, thus implying that the receptors responsible for these reflex effects had been stimulated long before. If, similarly, the pulmonary stretch receptors had been stimulated primarily, the increased activity should have appeared before 9 sec. Further, as positive pressure ventilation was used by these authors while recording the impulses, it is significant that no respiratory fluctuations in the frequency of discharge during periods of enhanced activity are visible in their records. This is strongly suggestive of blockage of the bronchioles connected with the receptors concerned which could be caused by a plug of mucous or broncho-constriction. This is not surprising as HT is a strong broncho-constrictor both directly and reflexly (Comroe, Lingen, Stroud & Roncoroni, 1953). It is, therefore, likely that the increased activity observed by them was due to secondary factors and not due to a direct action of HT on the receptors.

SUMMARY

1. Drugs were injected into the abdominal aorta and superior vena cava of anaesthetized cats and action potentials recorded from gastric stretch afferent fibres in the right vagus nerve.

2. Gastric stretch receptors were found to be stimulated by phenyl diguanide, 5-hydroxytryptamine, nicotine, lobeline, adrenaline and glucose. This was a primary stimulation and not secondary to smooth muscle changes. They were not stimulated by DL-amphetamine.

3. Phenyl diguanide-sensitive receptors unaffected by gastric distension were found in the stomach.

4. Receptors in the intestines sensitive to phenyl diguanide in addition to other drugs were observed; their normal function is not known.

5. Evidence was obtained of the existence of pulmonary phenyl diguanide-sensitive receptors whose normal functions are not known.

6. The injection-response time was found to be useful in determining the location of receptors. For abdominal receptors the minimum injection-response time following injection of drugs into the superior vena cava was found to be 3·5 sec.

7. It was confirmed that 5-hydroxytryptamine in doses of 17–44 μg/kg did not stimulate pulmonary stretch receptors.

8. Cautious interpretation of reflex effects of drugs is emphasized since several types of visceral receptors are affected by drugs.

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