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CARDIOVASCULAR CHANGES ELICITED BY VAGAL GASTRIC AFFERENTS IN THE RAT

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SUMMARY

Cardiovascular changes elicited by gastric distension in the urethane anaesthetized rat are described. Heart rate changes were mediated via a vago-vagal pathway with 'in-series' tension receptors in the stomach wall providing the afferent input and cholinergic cardio-inhibitory fibres forming the efferent pathway. Blood pressure changes occurred independently of the heart rate changes; the main afferent pathway was again vagal but the efferent outflow was non-cholinergic and probably sympathetic.

INTRODUCTION

Changes in blood pressure can be elicited by distension of the abdominal viscera. A fall in blood pressure following distension of the intestine and a rise in blood pressure following distension of the pyloric antrum and the duodenum were reported to be mediated by splanchnic afferents (Irving, McSwiney & Suffolk, 1937), while activation of vagal afferent fibres by electrical stimulation or by gastric distension results in an increase in blood pressure (Cragg & Evans, 1960). In both reports these haemodynamic changes occurred with no change in the heart rate. Heart rate and blood pressure changes have been described, however, in response to activation of gastric receptors by chemical irritation using capsaicin (Longhurst, Ashton & Iwamoto, 1980). Capsaicin injected into the gastric artery caused an 18% increase in blood pressure and a 4% increase in heart rate. These responses were markedly reduced by splanchnic nerve section and totally abolished by combined splanchnic and abdominal vagal section. The efferent limb of the reflex was not investigated.

Changes in heart rate and blood pressure have also been described during gastric endoscopic procedures (Fujita & Kumura, 1975). These authors reported that propranolol was effective in preventing changes in heart rate indicating a major role for the sympathetic innervation of the heart while Palmer (1976) concluded that atropine was effective in preventing the heart rate changes favouring a vagal efferent pathway.

There is clear evidence, therefore, that cardiovascular reflexes can be elicited from the gastrointestinal tract but the mechanisms involved in these reflexes remain ambiguous. The present paper describes marked changes in heart rate and blood pressure in response to gastric distension with isotonic saline, a procedure which readily activates vagal reflexes in the urethane anaesthetized rat (Davison & Grundy, 1978). The pathways involved in these cardiovascular reflexes were investigated.

METHODS

Eleven female urethane anaesthetized (1500 mg/kg) Sprague–Dawley rats weighing between 250 and 300 g were used.

The stomach was intubated via the pyloric sphincter and via a cannula introduced into the fundic region through an incision made in the greater curvature. The fundic cannula was used to inflate the stomach and the pyloric cannula attached to a Palmer pressure sensing device to record intragastric pressure. The system was therefore essentially isovolumetric. The left femoral artery was cannulated and attached to another Palmer pressure transducer to monitor blood pressure. The heart rate was monitored by a Devices heart rate meter, triggered by the e.c.g. recorded with bipolar leads II. Stainless steel hypodermic needles inserted subcutaneously were used as e.c.g. electrodes.

Vagotomy was performed just below the diaphragm. Atropine sulphate (1 mg/kg) was injected via the femoral artery.

RESULTS

The anaesthetized rats in the present study showed mean values for heart rate and systolic and diastolic arterial pressure of 310 ± 11 beats/min (range 270–396), $12{\cdot}25 \pm 0{\cdot}97$ kPa (range 7–15·4) and $10{\cdot}2 \pm 0{\cdot}85$ kPa (range 6·1–13·5) respectively (mean ± S.E. of mean, $n = 11$). Gastric distension caused marked cardiovascular changes in these animals the magnitudes of which are referred to in the text as percentage changes in mean arterial pressure and heart rate: a paired sample Student's t test was used to assess significance. Fig. 1 illustrates the results of these experiments. In all experiments step inflations of the stomach with 0·9% sodium chloride were followed, after a latency of approximately 350 ms, by a distinct bradycardia (Fig. 1 *A*). The level of gastric distension necessary to evoke this initial slowing of the heart rate varied from animal to animal but could be as low as 4 ml (corresponding to an intragastric pressure of 0·6 kPa). The threshold gastric volume in five experiments was $6{\cdot}8 \pm 0{\cdot}8$ ml. The magnitude of the bradycardia increased with increasing gastric volumes up to the maximum volume used which was 10 ml. A 10 ml inflation was subsequently used as the standard stimulus, giving a peak intragastric pressure of $3{\cdot}6 \pm 0{\cdot}3$ kPa. The fall in heart rate associated with this 10 ml inflation of the stomach was $17{\cdot}6 \pm 4\%$ (range 4·9–42%) ($P < 0{\cdot}001$) and was not dependent on the initial heart rate. The fall in heart rate adapted, at least partially, over a period of about 5–10 s, but distension of the stomach also evoked gastric contractions (Davison & Grundy, 1978) and when these occurred a further change in heart rate was observed. The most frequent response (eight animals) was a tachycardia during the contraction phase (Fig. 1 *A*) ($4{\cdot}7 \pm 1{\cdot}6\%$ increase in heart rate). On two occasions, however, the contractions were associated with an increase in the bradycardia. In either event, the heart rate fluctuated in phase with gastric motility. In one animal that showed no evoked gastric motility the heart rate remained below the predistension level until the stomach was deflated. The heart rate changes associated with both distension and contraction were completely abolished by abdominal vagotomy (five animals) and by injection of atropine (three animals) (Fig. 1 *B* and *D*). These procedures also abolished the gastric contractions associated with distension although the peak gastric pressure was not significantly altered.

The blood pressure response to gastric inflation involved two components. Following gastric inflation there was a slight, but significant, transient depressor effect which reversed to a much larger pressor effect. Again the threshold intragastric volume necessary to evoke these blood pressure responses could be as low as 4 ml and the magnitude of the response increased with increasing gastric volume. Following a 10 ml inflation the maximum fall in mean arterial pressure was $8{\cdot}4 \pm 1{\cdot}4\%$ (range 4–18·3%, $P < 0{\cdot}01$) and the maximum increase in arterial pressure was $40{\cdot}2 \pm 7{\cdot}2\%$ (range 10·9–75%) ($P < 0{\cdot}001$). When no gastric

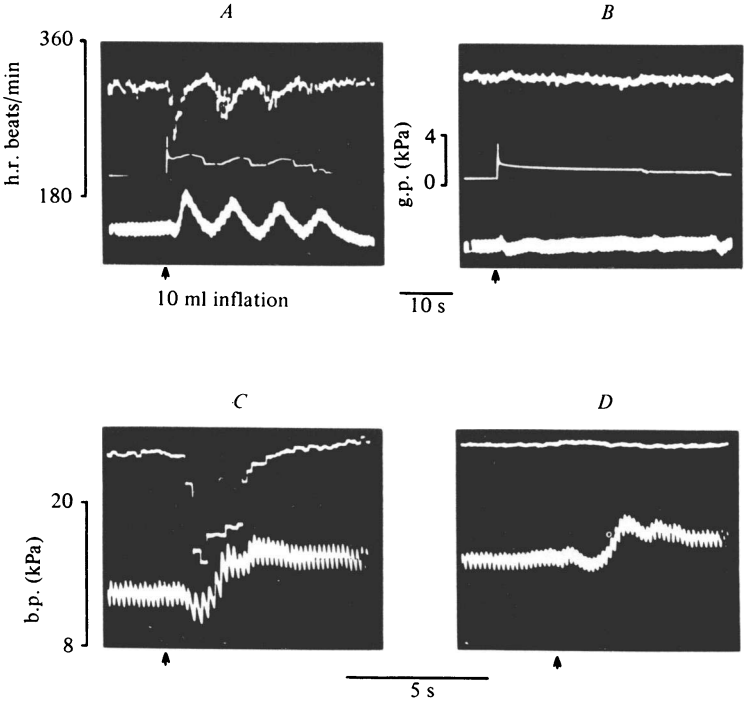

Fig. 1. Cardiovascular response to gastric inflation; effect of abdominal vagotomy (*A*, before; *B*, after) and atropine (*C*, before; *D*, after). Upper trace, heart rate (h.r.); middle trace (top record only), intragastric pressure (g.p.); lower trace, arterial pressure (b.p.). 10 ml gastric inflations shown by arrows.

contractions occurred the blood pressure remained elevated until the stomach was deflated. However, when the gastric motility was present then each gastric contraction and relaxation was accompanied by a fall and rise in blood pressure such that blood pressure fluctuated in phase with gastric motility. After abdominal vagotomy the pressor response was completely abolished while the slight depressor effect persisted (Fig. 1 *B*). The blood pressure response was still present after atropine and was therefore independent of any heart rate changes. The sympathetic supply to the heart was still intact, however, and therefore may have contributed to the blood pressure changes by affecting myocardial contractility.

DISCUSSION

These results demonstrate that afferent fibres from receptors in the stomach sensitive to distension and contraction can modulate both the heart rate and the blood pressure of anaesthetized rats. Two types of gastric mechanoreceptors have been identified electrophysiologically. Those with afferent fibres in the splanchnic nerves are generally associated with receptors in the mesenteric attachments of the viscera and respond to distortion of the visceral organs (Floyd & Morrison, 1974; Morrison, 1977) while vagal afferent fibres have receptors which respond as if they are 'in-series' with the smooth muscle elements (Iggo, 1957; Davison & Clarke, 1977), i.e. they respond to both passive distension and active contraction of the stomach. The nature of the heart rate and pressor responses to both distension and contraction of the stomach and the observation that these responses were abolished by abdominal vagotomy suggests that it is activation of these 'in-series' tension

receptors that are mediating these reflex changes. The transient depressor response, however, still persisted after abdominal vagotomy and was presumably mediated by splanchnic afferents.

The efferent limb for the heart rate effects was atropine sensitive and presumably vagal. The blood pressure effects, however, were not abolished by atropine and occurred independently of the changes in heart rate. These results demonstrate, therefore, a gastro-cardiac reflex mediated via a vago-vagal pathway, a reflex increase in blood pressure mediated via a vago-sympathetic pathway and a splachno-sympathetic reflex mediating a fall in blood pressure.

The mechanisms by which gastric distension evokes a bradycardia and rise in blood pressure while gastric contractions result in a tachycardia and fall in blood pressure are unclear. One possible explanation would be that these two responses represent a differential afferent input from low and high threshold tension receptors. Certainly receptors with a wide range of thresholds exist (Clarke & Davison, 1976), and moreover, the higher threshold receptors would be more readily activated by tension developed during isometric gastric contractions. Carlson (1916), after describing vasomotor changes during hunger contractions in man, concluded that they may be due to the close association between the 'vasomotor centre' and the 'gastric centre' or due to a direct action of gastric afferents on the 'vasomotor centre'. The present observation of differential effects of distension and contraction of the stomach would favour the latter. However, the functional significance of these reflexes remains unknown.

REFERENCES

CARLSON, A. J. (1916). *The Control of Hunger in Health and Disease.* Chicago: The University of Chicago Press.

CLARKE, G. D. & DAVISON, J. S. (1976). Response of distension sensitive, vagal afferent nerve endings to controlled inflation of the rat stomach. *Journal of Physiology* **256**, 122–123*P*.

CRAGG, B. G. & EVANS, D. H. L. (1960). Some reflexes mediated by the afferent fibres of the abdominal vagus in the rabbit and cat. *Experimental Neurology* **2**, 1–12.

DAVISON, J. S. & CLARKE, G. D. (1977). Electrophysiological analysis of vagal afferent innervation of the muscle of the upper gastrointestinal tract. In *Physiology & Pharmacology of Smooth Muscle*, ed. PAPASOVA, M. & ATANASSOVA, E., pp. 102–107. Sofia: Bulgarian Academy of Sciences.

DAVISON, J. S. & GRUNDY, D. (1978). Modulation of single vagal efferent fibre discharge by gastrointestinal afferents in the rat. *Journal of Physiology* **284**, 69–82.

FLOYD, K. & MORRISON, J. F. B. (1974). Splanchnic mechanoreceptors in the dog. *Quarterly Journal of Experimental Physiology* **59**, 361–366.

FUJITA, R. & KUMURA, F. (1975). Arrythmias and ischemic changes of the heart induced by gastric endoscopic procedures. *American Journal of Gastroenterology* **64**, 44–48.

IGGO, A. (1957). Gastrointestinal tension receptors with unmyelinated afferent fibres in the vagus of the cat. *Quarterly Journal of Experimental Physiology* **42**, 130–143.

IRVING, J. T., MCSWINEY, B. A. & SUFFOLK, A. S. (1937). Afferent fibres from the stomach and small intestines. *Journal of Physiology* **89**, 407–420.

LONGHURST, J. C., ASHTON, J. H. & IWAMOTO, G. A. (1980). Cardiovascular reflexes resulting from capsaicin-stimulated gastric receptors in anaesthetised dogs. *Circulation Research* **46**, 780–788.

MORRISON, J. F. B. (1977). The afferent innervation of the gastrointestinal tract. In *Nerves and the gut*, ed. BROOKS, F. P. & EVERS, P. W. C.B.S.

PALMER, E. D. (1976). The abnormal upper gastrointestinal vago-vagal reflexes that effect the heart. *American Journal of Gastroenterology* **66**, 513–522.