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Cardiovascular Reflexes Resulting from Capsaicin-Stimulated Gastric Receptors in Anesthetized Dogs

JOHN C. LONGHURST, JULIET H. ASHTON, AND GARY A. IWAMOTO

SUMMARY To determine whether significant cardiovascular reflexes can be generated from gastric receptor stimulation, we developed an autoperfused canine stomach preparation from a dog anesthetized with a-chloralose so that capsaicin, a C fiber agonist, could be injected into the left gastroepiploic artery (a) supplying the greater curvature of the stomach. Control injections were made into the inferior vena cava (IVC) to determine capsaicin's effects on areas downstream from the stomach. Significant cardiovascular reflexes were obtained in 37 of 42 dogs after ia injection and in 28 of 28 dogs after IVC injection. Capsaicin (25–500 µg) caused significant increases in systolic blood pressure (SBP) (15%), heart rate (HR) (4%), contractility (maximal dP/dt) (19%), and systemic vascular resistance (SVR) (18%), whereas there were no changes in left ventricular end-diastolic pressure (LVEDP) or aortic flow (AF). On the other hand, downstream IVC capsaicin injections caused significant decreases in SBP (28%), HR (34%), dP/dt (33%), and AF (41%), but no change in SVR or LVEDP. The dP/dt response to ia injection continued to occur after overdrive right atrial pacing. However, the responses of pressure, rate, and dP/dt were diminished to a large extent by diaphragmatic celiac nerve section and to a smaller extent by diaphragmatic vagus nerve section. We conclude that these results demonstrate that capsaicin, a potent C-fiber agonist, can stimulate gastric or perigastric receptors to induce a significant activation of the cardiovascular system. Thus, the potential of the stomach to function as a reflexogenic organ which regulates the cardiovascular system has been demonstrated.


THERE is considerable evidence to support the existence of several types of neural receptors in the stomach wall or in the vessels coursing over the wall of the stomach in several animal species (Davison and Grundy, 1977; Douglas and Ritchie, 1957; Iggo, 1955; Iggo, 1957a, 1957b; Nijima, 1964; and Paintal, 1954). There are receptors known to respond specifically to mechanical deformation which are innervated by small group IV or C fibers traveling in the vagus nerve (Davison and Grundy, 1977; Iggo, 1955; Iggo, 1957a; Iggo, 1957b; and Paintal, 1954). Some of these receptors respond both to stretch and to a variety of drugs which directly activate C fibers such as phenylidiguanide, 5-hydroxytryptamine, epinephrine, and acetylcholine (Iggo, 1957a, 1957b; Paintal, 1954).

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Other studies, mostly from the older Russian literature, have suggested that gastric stimulation by electrical, mechanical, and chemical stimuli may variably increase blood pressure and increase or decrease heart rate (Bykov and Chernigovskiy, 1947; Dmitrenko, 1916; Lapshin, 1950; Lapshin, 1951; Mayer and Pribam, 1872; Saphir and Rapaport, 1969; Simonovskiy, 1881). However, many of these studies did not account for the possibility of extragastric stimulation. In addition, interruption of the afferent pathways was not employed to demonstrate the reflex nature of their responses. Therefore, a canine preparation was developed to allow systematic investigation of cardiovascular reflexes resulting from selective pharmacological stimulation of the stomach and its vessels.

The primary goals of this study were to adequately stimulate afferent endings located in the stomach musculature and vessels and to accurately measure changes in cardiovascular parameters that occur as a result of this stimulation. Capsaicin, a decilenic acid amide of vanillylamine and a selective C-fiber agonist, was used in this study to stimulate the afferent nerve endings.

Methods

Anesthesia and Physiological Monitors

Mongrel dogs weighing 21 ± 1.5 kg (mean ± SEM) (range, 11–33 kg) were initially anesthetized with sodium thiopental (35 mg/kg). α-Chloralose (100...
mg/kg) was subsequently administered, followed by supplemental doses as necessary for maintenance of anesthesia. The animals were intubated and artificially ventilated with a respirator (Harvard Apparatus Co, model 607). End-tidal carbon dioxide was continuously monitored (Beckman, model LB-2) and kept within a range of 30-45 mm Hg. Arterial blood gases (Po2 and PCO2) and pH were frequently monitored (Instruments Laboratory, model 313) to keep these variables within the physiological range (Po2: ≥90 mm Hg; PCO2: 35-45 mm Hg, pH: 7.35-7.45). Corrections in acid-base balance were made by administering a 1.5% bicarbonate solution (volume sufficient to restore the pH to physiological range), changing the ventilatory rate or volume, or enriching the inspired air with 100% oxygen. Rectal temperature was continuously monitored (Yellow Springs, model 41TD) and maintained at 36-40°C using a circulating water heating pad (Gormon-Rupp, model K-1-3) and heating lamps. The estimated blood loss due to surgery was approximately 150 ml or 8.4% of the dog's total blood volume (assuming 85 ml/kg total blood volume).

Surgical Preparation

Catheters were inserted into the brachial vein for fluid and drug administration, the brachial artery for arterial pressure measurement, the right femoral artery for the proximal portion of the autoperfusion circuit, the right femoral vein for injection into the inferior vena cava (IVC), and the left ventricle via the left common carotid artery (Fig. 1). In certain dogs, a left jugular catheter was inserted and the tip advanced to the mid or lower portion of the right atrium (confirmed by palpation) for blood withdrawal.

Median sternotomy and midline abdominal incisions were made to expose the heart and the stomach. A splenectomy was performed, and the vessels between the greater omentum and the stomach were ligated. Additionally, the right gastroepiploic artery at the level of the antrum was ligated. The main left gastroepiploic artery was ligated and cannulated toward the stomach. This procedure completed an autoperfusion circuit from the femoral artery to the greater curvature of the stomach through a variable speed perfusion pump (Cole Parmer, Masterflex, model 7565). The average flow to the gastroepiploic artery ranged from 10-30 ml/min. Perfusion pressure was monitored from a sidearm tubing placed in the circuit, and injections could be made into the circuit through a stopcock (Fig. 1). In each preparation, the area of perfusion was visually determined to include only the greater curvature of the stomach by rapid injection of 5 ml of indocyanine green dye.

In 10 experiments, the ascending aorta was cleared for placement of a flow transducer. In other experiments, the dorsal and ventral (right to left) esophageal vagus nerves just superior to the diaphragm and the celiac nerves at the level of origin of the celiac artery were carefully isolated by loose ligatures for later sectioning. In certain experiments, a bipolar epicardial electrode was sutured to the right atrium for overdrive pacing with a stimulator (Grass, model S4CR).

Instrumentation

Aortic and perfusion blood pressures were measured with Statham pressure transducers (model P23ID). A catheter-tipped micromanometer (Millar Instruments, model PC350) was used to measure left ventricular pressure. Four needle electrodes were placed, one in each limb, to monitor the electrocardiogram (ECG). Aortic flow was measured by an electromagnetic flow transducer and meter (Zapeda Instruments, model SWF-4RD). The flow transducers were calibrated by an in vitro system consisting of a saline reservoir connected to dialysis tubing and an outlet valve. Multiple timed collections at steady state flow rates were made into a graduated cylinder. Calibration curves were linear over the entire range of flows.

Arterial pressure, perfusion pressure, left ventricu-
ular pressure, ECG, and aortic flow were recorded either on a direct writing thermal stylus recorder (Hewlet Packard, model 7758A) or a photographic recorder (Electronics for Medicine, model DR-8) with a rapid developing system. The left ventricular end-diastolic pressure (LVEDP) was amplified and recorded on a 0–20 mm Hg scale. The first derivative of the left ventricular pressure, the dP/dt, was obtained from the left ventricular pressure channel through a derivative amplifier (Hewlett Packard, model 8814A). The developed pressure for calculation of dP/dt at a developed pressure of 40 mm Hg was determined by subtracting the LVEDP from the total left ventricular pressure during systole in three to six cardiac cycles recorded at a paper speed of 100 or 200 mm/sec. This ratio is thought to be more independent of filling pressure changes in anesthetized preparations (Mason et al., 1971). The instantaneous heart rate was computed by a cardi-otachometer triggered by the ECG or pressure sig-

In five experiments, right atrial blood was sampled for the appearance time of indocyanine green dye with a densitometer (Waters Instruments, model COR-100A) after ia gastric injection in a manner identical to capsaicin injection. The appearance time was defined as the time from injection to initial appearance in the densitometer minus the catheter transit time (i.e., time required for dye to travel from the right atrial catheter tip to the densitometer). The mean arterial pressure was cal-
culated as one-third of the pulse pressure added to the diastolic pressure. The systemic vascular resis-
tance was calculated as the ratio of the mean arterial pressure to aortic flow.

Capsaicin

Capsaicin was dissolved by heating it to 55°C in a solution of normal saline, 0.1 ml of absolute alco-
hol, and a drop of Tween 80 at an initial concentra-
tion of 1000 µg/ml. Further dilutions were made with normal saline at room temperature. Receptor stimulation was accomplished by briefly interrupting the perfusion flow and injecting 1 ml of capsaicin solution. After injection, the perfusion pump was rapidly restarted, flushing the drug into the stom-
ach. Control injections of saline or the saline, alco-
hol, and Tween 80 solution (in a procedure identical to that used for capsaicin injection) produced no cardiovascular reflex responses. Inferior vena caval capsaicin injections were made into the femoral vein catheter and flushed with 5 ml of saline. Injec-
tions were made at 15-minute intervals.

Statistics

The control or resting hemodynamic conditions in dogs found to be responsive to capsaicin were compared to the peak responses (Fig. 2) by the paired Student's t-test. If phasic alterations oc-
curred from respiratory afferent stimulation (i.e., sinus arrhythmia), the average of the variation was used for data calculation. The cardiovascular re-
sponses in which repetitive responses to similar-
capsaicin doses were compared over time were an-
alyzed for nonrandom variation by a two-way analy-

FIGURE 2 Examples of cardiovascular responses to 100 µg of ia capsaicin—unpaced—(IA CAP) and 100 µg of inferior vena caval capsaicin (IVC CAP) injections. Pa-

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Results

Protocols

Fifty-two dogs received ia gastric and/or IVC capsaicin injection. Specifically, 26 dogs received only ia gastric injections, nine received only IVC injections, and 17, received both ia gastric and IVC injections. In the first few dogs, the dose of capsaicin eliciting maximal cardiovascular alterations was de-
termined to be 50–100 µg. Thereafter, these doses were employed to investigate the cardiovascular reflexes. Lower doses caused smaller cardiovascular responses. Higher doses (＞500 µg) usually caused responses similar to those induced by 100 µg of capsaicin, although an overriding depressor re-
sponse, possibly of pulmonary origin, was occasion-
ally observed after 10–12 seconds.

From the 52 dogs, there were several subgroups that underwent additional studies. In five dogs, we com-
pared over time the hemodynamic responses to an initial and two repeated ia gastric capsaicin in-
jections using similar dosages. In another sub-
group of five dogs, the appearance time of indocy-

anine green dye from ia gastric injection to the right

atrium was measured. Seven dogs were paced at a rate sufficient to overdrive the reflex tachycardia
before and during IA gastric capsaicin injection. Ten dogs comprised a fourth subgroup, in which vagus section was performed. Celiac nerve section was performed in a subgroup of five dogs. Both pathways were sectioned in four animals.

To use all available data, the sample sizes of the parameters varied (Fig. 3–5). For instance, in Figure 3, mean and diastolic pressures could not be measured in 16 dogs because aortic pressure was not determined. In two, there was equipment malfunction so that peak dP/dt could not be determined. In seven additional dogs, dP/dt at 40 mm Hg developed pressure could not be accurately calculated. In eight, mean arterial pressure and aortic flow were

**Figure 3** Average cardiovascular responses in 37 reactive dogs to IA gastric capsaicin (IA CAP) injection. Means and standard errors (brackets) are given for control, preinjection periods, and for peak responses after IA CAP injection. Significance levels comparing control values to response values are listed.

**Figure 4** Average cardiovascular responses in seven dogs to pacing and IA CAP injection. Means and standard errors (brackets) are given for preinjection, control unpaced, control paced, and peak responses during pacing after IA CAP injection. Significance levels comparing two control periods and control paced period with IA CAP paced period are listed.
simultaneously measured for calculation of systemic resistance.

**Gastric Arterial Capsaicin Injection**

Typical recordings of cardiovascular changes occurring in one dog after injection of 100 μg capsaicin (ia) to the stomach and into the IVC are shown in Figure 2. There was a significant pressor response and tachycardia as well as an increase in maximal dP/dt when capsaicin was injected into the stomach vasculature. However, large depressor responses and bradycardia as well as a decrease in maximal dP/dt occurred when capsaicin was injected into the IVC.

Significant cardiovascular changes occurred in 37 of 42 dogs after ia gastric capsaicin injections (average dose = 95 ± 15 μg, range 25–500 μg). (Fig. 3). There were increases of 15, 17, and 17% respectively, in systolic, mean, and diastolic arterial pressures (Fig. 3, A–C). Maximal dP/dt and dP/dt at a developed pressure of 40 mm Hg both increased by 21% (Fig. 3, E and F). The heart rate increased by 6%, and the total systemic vascular resistance increased by 20% (Fig. 3, G and I). On the other hand, there was no increase in the left ventricular filling pressure or the ascending aortic flow (Fig. 3, D and H).

The time of appearance of green dye in the right atrium after ia injection in five dogs was 23 ± 3 seconds, well after the time of initial onset of the cardiovascular responses to ia gastric capsaicin injection of 5.6 ± 0.9 seconds. The peak of the cardiovascular response after gastric capsaicin injection was 16 ± 1.5 seconds, and the duration of response was 1–2 minutes. Of the five dogs that yielded no response or a depressor response to gastric capsaicin injection, a depressor response occurred in four after an average of 9 ± 1.9 seconds (peak depressor response = 19 ± 4.6 seconds).

**Contractility Changes**

An increase in cardiac contractility was observed after ia gastric injections of capsaicin as demonstrated by increases in both maximal dP/dt and dP/dt at a developed pressure of 40 mm Hg (Fig. 3, E and F). Pacing the heart increased heart rate but did not change systolic pressure or LVEDP (Fig. 4, A–C). Pacing caused small increases in maximal dP/dt, dP/dt at 40 mm Hg developed pressure, and aortic flow (Fig. 4, D and E). Gastric capsaicin injection during pacing did not further change heart rate, LVEDP, or aortic flow (Fig. 4, A, C, and F). However, gastric capsaicin significantly increased systolic blood pressure (11%), maximal dP/dt (14%), and dP/dt at 40 mm Hg developed pressure (13%) during overdrive pacing (Fig. 4, B, D, and E).

**Reproducability of Capsaicin Response**

In six dogs, three sequential ia gastric capsaicin injections (30 ± 8 μg, 32 ± 8 μg, and 50 ± 11 μg,
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**Figure 6** Effects of sectioning the sympathetic celiac (top 3 panels) the parasympathetic vagus (bottom 3 panels) nerves on change in systolic blood pressure, heart rate, and maximal \( dP/dt \) in response to gastric capsaicin injection. Means and standard errors (brackets) are given for maximal responses during control period, just before nerve section and maximal responses after nerve section. Significance levels comparing control changes to post-section changes are listed.

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doses not significantly different) with an interval of 37 ± 20 minutes separated the first and second and 60 ± 19 minutes separated the second and third injections and caused similar cardiovascular responses. Thus, the initial capsaicin increased systolic arterial pressure by 19 ± 5 mm Hg, heart rate by 8 ± 2 beats/min, and maximal \( dP/dt \) by 500 ± 148 mm Hg/sec. The second injection of capsaicin increased systolic pressure by 21 ± 9 mm Hg, heart rate by 10 ± 3 beats/min, and maximal \( dP/dt \) by 417 ± 198 mm Hg/sec. The third injection of capsaicin increased systolic arterial pressure by 25 ± 7 mm Hg, heart rate by 11 ± 2 beats/min, and maximal \( dP/dt \) by 463 ± 123 mm Hg/sec.

**Inferior Vena Caval Injection of Capsaicin**

When compared to the effects from arterial gastric capsaicin injection, most of the hemodynamic changes occurring after IVC capsaicin injection were in the opposite direction. (Fig. 5). Thus, systolic, mean, and diastolic arterial pressures decreased by 28, 41, and 42%, respectively (Fig. 5, A–C), after an initial response time of 10 ± 1.4 seconds (peak depressor response = 19 ± 1.8 seconds; duration 1–2 minutes), the maximal \( dP/dt \) and \( dP/dt \) at a developed pressure of 40 mm Hg decreased by 28 and 27%, respectively (Fig. 4, E and F), and the heart rate and aortic flow decreased by 33 and 39%, respectively (Fig. 5, G and H). The left ventricular filling pressure did not significantly change (Fig. 5D). Also, the total systemic vascular resistance (Fig. 5I) did not significantly change (in three animals, this value decreased, and in two, it increased).

**Gastric Denervation**

Sympathetic (celiac) and parasympathetic (esophageal vagus just superior to the diaphragm) afferent denervation was performed in 11 dogs to evaluate the reflex nature of the response to gastric capsaicin injection and to determine the afferent limb of the reflex. The hemodynamic responses just prior to nerve section (control period) were compared with the responses occurring just after nerve section (Fig. 6). Sympathetic section to a large extent diminished the change in systolic blood pressure, heart rate, and peak \( dP/dt \) (Fig. 6, A–C). Parasympathetic section significantly, but to a smaller extent than sympathetic section, reduced the change in systolic blood pressure, heart rate, and peak \( dP/dt \) (Fig. 6, D–F). Combined section in four dogs totally eliminated the cardiovascular response to gastric capsaicin injection. After afferent denervation, each dog demonstrated a pressor response of 10–30 mm Hg during hindlimb ia gastric capsaicin injection. This response is comparable to that elicited in other studies (Crayton, 1975; Toh et al., 1955).

**Discussion**

This study demonstrates that the stomach of the dog contains receptors that can be activated by capsaicin to cause significant cardiovascular reflex responses. These responses include an increase in blood pressure, heart rate, myocardial contractility, and total systemic vascular resistance but no change in LVEDP or ascending aortic flow. Further, the afferent pathways appear to course to a major extent with the splanchnic sympathetics and to a lesser extent with the thoracic parasympathetics.

In this study, capsaicin, an extract of paprika, was the pharmacological agent used to elicit these cardiovascular responses. As a control for the ia gastric injection, the cardiovascular effects of cap-
Capsaicin injected downstream from the stomach, in the IVC, were determined in this preparation under similar conditions. The effects of intravenous injection of capsaicin included a profound depressor response, a bradycardia, a decrease in contractility, and a decrease in ascending aortic flow. These effects were directionally opposite to the effects that occurred after gastric capsaicin injection. It is likely that the depression of the cardiovascular system from venous injection of capsaicin was elicited by stimulation of pulmonary C fiber afferents which course in the vagus (Coleridge et al., 1964; Coleridge et al., 1965; Toh et al., 1955). The opposite nature of the cardiovascular response to gastric and vena caval injections of capsaicin suggests that the effects from gastric injection are specific to the stomach or the vessels or mesentery immediately adjacent to the stomach. This conclusion is reinforced by the appearance time of indocyanine green dye in the right atrium which was well after the onset of the hemodynamic responses to gastric capsaicin injection. The results of nerve section also suggest that the reflexes are limited to the stomach or regions adjacent to the stomach. Further, it is possible that the pulmonary depressor effects may have reduced the gastric pressor response since the time course of both responses overlapped.

The five dogs not analyzed in this study either gave no response or depressor responses to gastric capsaicin injection. Although it is possible that the afferent pathways may have been disrupted by manipulation, it is also possible that these responses may have occurred as a result of an overriding pulmonary depressor reflex since the onset of this response occurred later than the pressor response. Also, these animals may have demonstrated the biological variation of the cardiovascular response from gastric capsaicin stimulation.

Capsaicin is also known to reflexly activate the cardiovascular system and produce pressor responses when it is injected regionally into skeletal muscle (Crayton, 1975; Toh et al., 1955) or into superior mesenteric arteries (Baraz et al., 1968). However, this pharmacological agent has never been previously used to stimulate gastric receptors. Other agents, including nicotine, acetylcholine, histamine, peptone solutions, a solution saturated with carbon dioxide, and bradykinin, have been reported to cause pressor changes when they were injected into an artery supplying the stomach (Bykov and Chernigovskiy, 1947; Guzman et al., 1962; Saphir and Rapaport, 1969). The heart rate, myocardial contractility, filling pressure, and aortic flow responses were not examined in any of these studies.

Since capsaicin is an irritant and stimulates fibers known to carry nociceptive reflexes (Toh et al., 1955; Coleridge et al., 1965), it is possible that the reflexes elicited by its injection into the stomach may represent a pseudoaffective response similar to that described by Guzman et al. (1962).

Other studies have demonstrated response properties of receptors in the abdominal viscera considered to be potentially reflexogenic. For instance, Paintal (1954) and Iggo (1957a, 1957b) showed that gastric stretch receptors (specifically, the "in-series tension receptors") could be stimulated by phenyl-diguanide, serotonin, nicotine, lobeline, acetylcholine, adrenaline, and glucose. No observations of the cardiovascular system were made during these injections.

Capsaicin selectively stimulates the finely myelinated (A8 fibers) or unmyelinated (C fibers) nerve endings (Coleridge et al., 1964; Coleridge et al., 1965; Coleridge et al., 1973; Douglas and Ritchie, 1957; Iggo, 1957a). Iggo (1957a) and Douglas and Ritchie (1957) demonstrated that C fiber vagal afferents from the abdominal viscera, especially from the in-series tension gastric receptors, could be stimulated by phenyl-diguanide, serotonin, adrenaline, and acetylcholine. Further, several histological studies have shown that small fibers constitute a large proportion of the afferent pathways in the abdominal vagus and splanchnic nerves (Agostoni et al., 1957; Foley and DuBois, 1937; Ranieri et al., 1973; Saphir and Rapaport, 1969). In the vagus at least 65% (Foley and DuBois, 1937) and in some studies more than 90% (Agostoni et al., 1957) of the total number of fibers were afferent. These studies further showed that the majority (80-90%) of these abdominal sensory fibers either were fine myelinated or unmyelinated nerves (Ranieri et al., 1975). Another study has suggested that the splanchnic nerves contain proportionately more small myelinated fibers than the vagus, although, relatively, the C fibers probably were more abundant in both afferent systems than the myelinated sensory fibers (Ranieri et al., 1970; Ranieri et al., 1973).

The lack of significant attenuation of the response to repeated capsaicin injection was an important feature to demonstrate, since some authors (Toh et al., 1955) have suggested that a tachyphylaxis develops when it is repeatedly injected into the superior mesenteric artery. The differences between these two studies may have been due to the longer period of equilibration between each dose of capsaicin (at least 15 minutes) and the careful maintenance of physiological acid-base and blood gas values throughout each experiment in the present study. The lack of progressive attenuation of the cardiovascular responses to gastric capsaicin injection after the initial dose is also an important feature to demonstrate when one attempts to elicit a cardiovascular reflex. First, this feature allows one to demonstrate that the reflex is repeatable, at least over several hours. Second, a repeatable reflex allows one to do successive studies such as pacing, dye injection, and celiac and vaginal deafferentation.

Although several groups have demonstrated blood pressure increases (Dmitrenko, 1916; Mayer and Pribram, 1872; Simanovskiy, 1881), others have
noted both pressor and depressor reactions during gastric stimulation (Lapshin, 1950; Lapshin, 1951). Many studies, however, did not carefully isolate the exciting stimulus to the stomach. There are receptors in areas adjacent to the stomach, and their stimulation can cause pressor reactions (Irving et al., 1937; Moore and Singleton, 1933; Niijima, 1964; Saphir and Rapaport, 1969). The present experiments localize the effect of the pressor response to the stomach, the vessels associated with the stomach, or the mesenteric borders of the stomach. More specific location of the reflex must await neural recording experiments with careful probing to locate receptors.

Previously, the heart rate has been noted to variably increase or decrease during gastric distension (Davison and Grundy, 1977; Dmitrenko, 1916; Lapshin, 1950; Lapshin, 1951; Mayer and Pribram, 1872; Simanovskiy, 1881). On the other hand, chemical stimulation by celiac artery injection caused no heart rate change, despite a blood pressure increase (Saphir and Rapaport, 1969). No data are available for injections directly into the stomach. Studies on conscious dogs and primates have demonstrated increases in heart rate and aortic systolic and diastolic pressures within 15 minutes of eating (Vatner et al., 1970; Vatner et al., 1974). The present data suggest that gastric receptor stimulation by capsaicin elicits similar heart rate and pressor responses.

There is little information on the myocardial performance response during stimulation. Saphir and Rapaport (1969) indicated that \( \frac{dP}{dt} \) increased after two of two injections of chemicals into the left gastroepiploic artery. However, they present no specific data. In addition, the heart rate (Bowditch effect) and filling pressure changes were not given, although both may change \( \frac{dP}{dt} \) when the myocardial performance is unchanged (Mahler et al., 1975; Mitchell et al., 1963). Stimulation of gastric receptors by capsaicin in the present study significantly increased the left ventricular performance above that caused by the increase in heart rate (Mitchell et al., 1963). Also, preload remained constant in the present study.

Despite the increased heart rate and myocardial contractility, mean aortic flow remained constant during gastric capsaicin stimulation. This was likely a result from the increase in systemic vascular resistance which would tend to limit the increase in cardiac output (Bugge-Asperheim and Kil, 1969). The electromagnetic flowmeter system showed that there were no transient cardiac output changes.

The afferent pathways of the gastric capsaicin reflex largely followed the sympathetic and to a lesser extent the thoracic parasympathetic efferent pathways. The importance of the parasympathetic pathway cannot be determined with certainty from the present experiments since thoracic sympathetic fibers are known to mix with the thoracic vagus for some distance above the diaphragm. These data are consistent with that from other sources and demonstrate that gastric sensory fibers are conducted through both pathways (Bykov and Chernigovskiy, 1947; Iggo, 1957b; Irving et al., 1937; Moore and Singleton, 1933; Morrison, 1973; Niijima, 1964). Injection of capsaicin into the greater curvature of the stomach may have caused selective stimulation of the celiac rather than the vagal afferent pathways.

After food ingestion, heart rate and mean arterial pressure increase at rest and during exercise (compared to fasted states) in some studies on humans (Dagenais et al., 1956; Jones et al., 1965). The lack of an increase in the heart rate or blood pressure in some studies may be attributed to ingestion of a small meal (Goldstein et al., 1971). Food ingestion either increases or does not change resting cardiac output (Dagenais et al., 1956; Jones et al., 1965). The similarity of the reflexes after gastric capsaicin injection to the hemodynamic alterations occurring after food ingestion is apparent. However, additional neurophysiological studies are required to establish a relation between capsaicin stimulation, food ingestion, gastric distension, and reflex cardiovascular alterations.

In conclusion, in an autoperfused canine stomach preparation, significant capsaicin-induced increases in blood pressure, heart rate, and myocardial contractility have been demonstrated. Filling pressure and cardiac output did not change. These alterations were reflex in nature and could be partially eliminated by sectioning afferent nerves coursing with either the sympathetic or the thoracic parasympathetic efferent nerves. The sympathetic pathway appeared to be relatively more important than the parasympathetic pathway. Combined section totally eliminated the cardiovascular reflex responses. Since capsaicin stimulates only fine myelinated and unmyelinated nerves, an argument has been made that these are the important afferent nerve fibers carrying this reflex. Although it is not possible to extrapolate this reflex to the cardiovascular changes occurring postprandially, these data do demonstrate, at least in the dog, that the potential for gastric-cardiovascular reflexes is present.

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