Effects of Gastrectomy on Motility, Perfusion Pressure, and Caerulein-Induced Relaxation of Sphincter of Oddi in Dogs

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Abstract

The effects of subtotal-gastrectomy (gastrectomy) on the spontaneous motility and caerulein-induced relaxation of the sphincter of Oddi (SO) were investigated in the dog. The spontaneous motility and the response to caerulein of the SO were recorded using perfusion method.

The basal perfusion pressure (5.1\(\pm\)0.5 cmH\(_2\)O) and the frequency of phasic contractions (6.1\(\pm\)0.5 cycles/min, c/min) of the SO increased to 8.2\(\pm\)0.6 cmH\(_2\)O (p<0.05) and 9.3\(\pm\)0.4 c/min (p<0.05) after gastrectomy, respectively. They were observed one month after operation (7.8\(\pm\)0.5 cmH\(_2\)O and 9.1\(\pm\)0.9 c/min, p<0.05), but did not change by vagotomy with sympathectomy (vagosympathectomy).

In the spontaneous motility of the SO, the motility index increased to 143.7\(\pm\)18.7\% (p<0.05) at 4 hrs and 135.0\(\pm\)9.1\% (p<0.05) at one month after gastrectomy, but did not increase after vagosympathectomy.

Caerulein had an inhibitory effect on the SO motility in the normal animal (48.0\(\pm\)4.2\%). Gastrectomy reversed to the excitatory effect from the inhibitory effect to caerulein at 4 hrs (127.6\(\pm\)5.3\%, p<0.05) and at one month (126.6\(\pm\)5.3\%, p<0.05) after operation, but not reversed by vagosympathectomy and sham gastrectomy. The excitatory response to caerulein after gastrectomy was not effected by vagosympathectomy. It is concluded that gastrectomy induced the SO dysfunction, an increase of the perfusion pressure and the frequency of phasic contractions of the SO, and a change of the response to caerulein of the SO. These alterations suggests that one of the mechanisms of the regulation of the SO motility exist as the reflex from the stomach and/or uppermost duodenum through intrinsic nervous pathways.

Key words: caerulein, excitatory response, gastrectomy, inhibitory response, perfusion pressure, phasic contraction, sphincter of Oddi
Introduction

It is reported that caerulein and cholecystokinin (CCK) induced a relaxation of the sphincter of Oddi (SO) in humans (Liedberg and Halabi 1970; Carrtù et al., 1975; Corrazziari et al., 1982; Ryan 1987), dogs (Lin and Spray 1969; Mizutani et al., 1978; Sarles 1986), and cats (Behar and Biancani 1980; Sarles 1986) and an excitatory response in dogs (Mizutani et al., 1978) and cats (Behar and Biancani 1980). The relaxation response of the SO to caerulein was induced via nonadrenergic noncholinergic inhibitory neurons in the intrinsic nervous system, and the excitatory response was induced by the direct action on the smooth muscle of the SO (Mizutani et al., 1978; Behar and Biancani 1980). Wyatt (1967) reported that a gastric contraction decreased the SO perfusion resistance, and Rolny et al., (1986) observed a change to an excitatory response from an inhibitory response of the SO to caerulein in patients with biliary dyskinesia after cholecystectomy. Hopton (1978) described that the reflexly responses to the SO from the gallbladder were terminated by transection of the common bile duct with its surrounding nerve plexus and suggest that the reflex to the SO from the gallbladder was induced by mediating the nerve plexus in the common bile duct. However, it has not been clear whether a regulation of the SO motility from the stomach is mediated by the extrinsic or the intrinsic nervous pathway.

This work was carried out to determine whether the reflex regulation of the SO motility from the stomach was induced by mediating the intrinsic or extrinsic neural pathway in dogs using the methods of gastrectomy and sectioning of the extrinsic nerve supply and, in addition, the response to caerulein of the SO.

Material and Methods

General procedures

Thirty-six adult mongrel dogs of both sex weighing 7-11 kg were used. The animals were fasted for 24 hr but had free access to water. Dogs were anesthetized by pentobarbital sodium (25 mg/kg, i.v., Abott Lab., Chicago, USA). A tracheal cannula was inserted. The systemic blood pressure was monitored through a cannula placed into the femoral artery. The end tidal CO₂ pressure was monitored by a capnometer (Hewlett Packard, model 47210A). The external junghar vein was cannulated for systemic administration of Ringer’s solution containing 5% dextrose to composite for loss of body fluid and for administration of drugs. The systolic pressure was kept over 120 mmHg under artificial ventilation (17-20 cycles/min and appropriate volume), the endo tidal CO₂ pressure was kept at 37-42 mmHg. The body temperature was maintained at 36-38°C using a heating pad placed under the body.

An adequate level of anesthesia was maintained by supplemental administration of pentobarbital sodium (25 mg/kg, i.v.) when the systemic blood pressure and/or the endo tidal CO₂ pressure started to fluctuate. By this, animals did not respond to pain stimulus throughout the experiment.
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Motility recording of the sphincter of Oddi

After a midline laparotomy, the gallbladder and biliary tree were identified. A small longitudinal incision was made in the common bile duct 1 cm from the choledochoduodenal junction and the duct was then cannulated with two cannulae (external diameter, 2.0 mm). One was directed distally with its tip placed at 5 mm proximal to the choledochoduodenal junction to perfuse the SO. The other was directed proximal to siphon off the hepatic bile. To prevent leakage from the proximal and distal segments of the common bile duct, they were tied off around the cannula. These two cannulae were placed in the common bile duct in a manner that prevented the occlusion of the orifice of the cannula.

The SO was perfused through the cannula with warmed Tyrode’s solution (36-37°C) at a rate of 0.12 ml/min using a low compliance infusion system. When the orifice of the cannula was abruptly occluded, the rise in post-occlusion pressure was 1,600 mmH$_2$O (about 120 mmHg) per second. The pressure changes were recorded on a pen-oscillograph (San-Ei, Recticorder 8S) through a pressure transducer which was placed between an infusion pump and the cannula.

Experimental design

In order to study the effects of gastrectomy and vagosympathectomy on the SO motility and on the inhibitory response of the SO to caerulein administered intravenously, the dogs were divided into three groups. Group 1 comprised acutely gastrectomized animals which underwent gastrectomy during the experiment (n=10), and chronically gastrectomized dogs which underwent gastrectomy 1 month prior to the experiment (n=5), Group 2 comprised acutely and chronically sham-operated dogs (both n=5) which underwent sham gastrectomy at the corresponding times. Group 3 comprised acutely vagotomized plus sympathectomized (vagosympathectomized) dogs with (n=6) or without gastrectomy (n=5). These operations were carried out under pentobarbital sodium anesthesia (25 mg/kg, i.v.).

Gastrectomy

The stomach and the upper duodenum were pulled out in view. After the lesser and greater omentum was carefully removed, the distal branches of the left gastric and gastroepiploic vessels were ligated. The gastric branches of the gastroduodenal vessels were also ligated. The stomach, distal to the level at which the gastric and gastroepiploic vessels were ligated, and the uppermost duodenum, 1-2 cm distal to the pylorus, were resected after clamping of the wall at the sectioning levels (dotted area shown in Fig. 1). Billroth I anastomosis was then completed. The level of SO was at 4-6 cm distal to the anastomosis. Gastrectomy was performed in approximately 30 min.

Sham gastrectomy was performed using the same procedure as gastrectomy except for the resection of the stomach and duodenum. The stomach and duodenum were pulling and crumpling during the corresponding times with gastrectomy.

Vagotomy and sympathectomy (vagosympathectomy)

The bilateral vagus nerves were severed at the neck and the celiac branches of the splanchnic nerves protruding from the celiac ganglion were also severed intraperitonially.
This operation was done only in the acute experiments.

**Application of caerulein**

It is known that caerulein has a similar structure to cholecystokinin (CCK) and the effects of caerulein on the sphincter of Oddi was also the same as CCK (Anastasi et al., 1967). Caerulein was therefore used instead of CCK in this experiment. Caerulein (Ceosunin®, Kyowahakko Kogyo Co. Ltd.) was diluted with Ringer's solution just before application and injected intravenously in a dose of 10 ng/kg as a bolus of 1 ml volume. Caerulein induced an inhibitory response in most animals (9/10 dogs in normal dogs). Thus, 10 ng/kg caerulein was used to determine whether the effect of cholecystokinin-like peptide on the SO motility is modulated by the gastrectomy and/or the vagosympathectomy.

**Experimental protocol**

In the acute experiments, recording of the SO motility was started 1 hr after termination of cannulation into the common bile duct, and continued for at least 2 hrs. Caerulein was administered 1 hr after beginning recording. After that, gastrectomy, sham-gastrectomy, vagosympathectomy or gastrectomy with vagosympathectomy was done. One hour after these operations, recording of the SO motility was again continued for 4 hrs. Caerulein was injected every 1 hr.

In chronic experiments, cannulation into the common bile duct was performed one month after sham-operation or gastrectomy. Recording of the SO motility started 1 hr after cannulation and then caerulein tests were repeated every 1 hr as in the acute experiments.

After termination of the experiment, the integrity of innervation of the SO in gastrectomized animals was tested by efferent stimulation of the cervical vagus and the major splanchnic nerves, which induced a contractile or relaxation response on the SO.

**Data analysis**

As seen on the tracing in figure 2, tonic contractions superimposed with a high frequency of phasic contractions. The number of phasic contractions that produced a pressure over 5 mmH₂O was counted and the mean frequency per minute was calculated. The pressure at the point just before development of each tonic contraction (shown with dots in Fig. 2) was measured on the tracing for 10 min and the mean ± standard error (SE) for measured values was
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Fig. 2. Diagram of the method for measuring the basal perfusion pressure. To determine the 0 cmH\textsubscript{2}O level, the tip of the perfusion cannula was placed on the same level as the sphincter of Oddi, and basal perfusion pressure was calculated as the distance from the two points during a 10 min period, and then determining the mean value of those measurements.

estimated in each animal as the basal perfusion pressure.

To evaluate the effects of caerulein on the SO, the square between the line of 0 cmH\textsubscript{2}O and the trace of the SO perfusion pressure changes used as a motility index, was measured using a planimeter every two minutes after application of caerulein up to 6 min. The motility index was expressed as the percentage to mean square per two minutes during 10 min of recording before caerulein application, and was again measured at 4 hrs and one month after gastrectomy using the same method which was used before caerulein application.

All data were represented as a mean±SE, and the paired and unpaired Student’s t test was used for statistical analysis. The data in the chronic experiments was compared with the data obtained from the preoperative animals in the acute experiments.

Results

1. Effects of gastrectomy, sham-gastrectomy and vagosympathectomy on spontaneous motility of SO

The spontaneous motility of the SO was recorded using perfusion method. The SO exhibited tonic contraction with superimposed phasic contractions of variable rates and amplitudes in the normal animals (Fig. 3). The phasic contractions and the basal perfusion pressure varied from animal to animal, but were relatively constant in each individual animal. The perfusion pressure and the frequency of phasic contractions of the SO in the preoperative animals of each group, except for chronic groups in which control experiments were not carried out, were not significantly different (Tables 1 and 2).

In the acute-gastrectomized group, the perfusion pressure and the frequency of spontaneous contractions were 5.1±0.5 cmH\textsubscript{2}O and 6.1±0.5 c/min in the preoperative animals, respectively. The gastrectomy significantly increased the perfusion pressure and the frequency of phasic contractions of the SO at 4 hrs (8.2±0.6 cmH\textsubscript{2}O, 9.3±0.4 c/min) and at one month (7.8±0.5 cmH\textsubscript{2}O, 9.1±0.9 c/min) after the operation (Tables 1 and 2). The motility index of the spontaneous motility significantly increased at 4 hrs (143.7±18.7%) and at one month (135.0±9.1%) after gastrectomy (Table 3).

In the animals without gastrectomy, the perfusion pressure and the frequency of phasic contractions of the SO were all either transitory increased (3/5 animals) or decreased (2/5
animals) by vagosympathectomy, but recovered to the control level at about 4 hrs (5.7±0.5 cmH₂O and 5.1±0.4 c/min, respectively) after the nerve section. The motility index did not change significantly from the control at 4 hrs after vagosympathectomy (Table 3). However, gastrectomy with vagosympathectomy increased the perfusion pressure (7.9±0.3 cmH₂O), the frequency of phasic contractions (8.7±1.1 c/min) and the motility index (134.2±6.6%) at 4 hrs after operation (Tables 1, 2 and 3). The increases in the perfusion pressure, the frequency of phasic contraction and the motility index were not significantly different from that in the gastrectomized animals (8.2±0.6 vs 7.9±0.3, p>0.05 in the pressure, 9.3±0.4 vs 8.7±1.1, p>0.05 in the frequency and 143.7±18.7 vs 134.2±6.6%, p>0.05 in the motility index), indicating that extrinsic denervation did not modulate the effect of gastrectomy on the perfusion pressure and

| Table 1. Effects of gastrectomy, sham gastrectomy and vagosympathectomy on perfusion pressure of the sphincter of Oddi (cmH₂O) |
|-------------------------------------------------------------|
| Operation | Control | 4 hrs after operation | 1 month after operation |
|----------|---------|-----------------------|------------------------|
| acute gastrectomy (n=5) | 5.1±0.5 | 8.2±0.6<sup>ii</sup> | ... ... ...           |
| acute sham gastrectomy (n=5) | 4.9±0.3 | 4.7±0.5 | ... ... ...           |
| chronic gastrectomy (n=5) | ... ... | ... ... | 7.8±0.5<sup>iii</sup> |
| chronic sham gastrectomy (n=5) | ... ... | ... ... | 5.0±0.3 |
| acute vagosympathectomy (n=5) | 5.3±0.3 | 5.7±0.5 | ... ... ...           |
| acute gastrectomy plus vagosympathectomy (n=6) | 5.4±0.5 | 7.9±0.3<sup>iii</sup> | ... ... ... |

i, significantly different from the control; ii, significantly different from sham gastrectomy; iii, significant different from the control of acute gastrectomy.

| Table 2. Effects of gastrectomy, sham gastrectomy and vagosympathectomy on spontaneous phasic contractions of the sphincter of Oddi (cycles/min) |
|-------------------------------------------------------------|
| Operation | Control | 4 hrs after operation | 1 month after operation |
|----------|---------|-----------------------|------------------------|
| acute gastrectomy (n=5) | 6.1±0.5 | 9.3±0.4<sup>ii</sup> | ... ... ...           |
| acute sham gastrectomy (n=5) | 5.5±0.6 | 5.2±0.4 | ... ... ...           |
| chronic gastrectomy (n=5) | ... ... | ... ... | 9.1±0.9<sup>iii</sup> |
| chronic sham gastrectomy (n=5) | ... ... | ... ... | 5.3±0.2 |
| acute vagosympathectomy (n=5) | 5.4±0.3 | 5.1±0.4 | ... ... ...           |
| acute gastrectomy plus vagosympathectomy (n=6) | 5.6±0.4 | 8.7±1.1<sup>ii</sup> | ... ... ... |

i, significantly different from the control; ii, significantly different from sham gastrectomy; iii, significantly different from the control of acute gastrectomy.
Table 3. Effects of gastrectomy, sham gastrectomy and vagosympathectomy on the motility index of the sphincter of Oddi

| Operation                                      | 4 hrs after operation | 1 month after operation |
|------------------------------------------------|-----------------------|-------------------------|
| acute gastrectomy (n=5)                        | 143.7±18.7%¹         | ...                     |
| acute sham gastrectomy (n=5)                   | 97.9±2.8%            | ...                     |
| chronic gastrectomy (n=5)                      | ...                  | 135.0±9.1%¹           |
| chronic sham gastrectomy (n=5)                 | ...                  | 100.0±13.6%            |
| acute vagosympathectomy (n=5)                  | 104.9±13.6%          | ...                     |
| acute gastrectomy plus vagosympathectomy (n=6) | 134.2±6.6%²         | ...                     |

Data are expressed as a percentage to the control value (mean±SE). The control value of chronic gastrectomy and chronic sham gastrectomy was used as 100% of control value in the acute gastrectomy and sham gastrectomy, respectively.
I, significantly different from the control and acute sham gastrectomy ; ii, significantly different from chronic sham gastrectomy and control of acute sham gastrectomy ; iii, significantly different from control and acute vagosympathectomy.

Fig. 3. Effects of caerulein on the sphincter of Oddi (O) before operation and sham operation (A) and after gastrectomy (B). Aa and Ba, control; Ab and Bb, 3-4 hrs after sham operation and gastrectomy; Ac and Bc, one month after sham operation and gastrectomy; Caer, caerulein 10 ng/kg, i.v..
Aa and Ab were recorded in the same acute sham operated dog and Ac was recorded in a chronic sham operated dog. Ba and Bb were recorded in the same acute gastrectomized dog and Bc was recorded in another chronically gastrectomized dog.
the frequency of phasic contractions of the SO.

2. Effects of gastrectomy, sham-gastrectomy and vagosympathectomy on caerulein-induced response

Caerulein (10 ng/kg, i.v.) inhibited the SO motility, reducing the perfusion pressure and the frequency of phasic contractions over 2-3 min in the pre-operated animals (Figs. 3Aa, Ba). The motility index decreased to 48.0±4.2% (n=10, p<0.05 compared with that at pre-injection period) at 2 min after caerulein and then was restored to control level with time (97.6±4.6% at 6 min after caerulein) (Fig. 4). This response was used as the control response to caerulein in chronic sham-gastrectomized and gastrectomized animals, since the control response did not test in chronic sham gastrectomized and gastrectomized animals.

The inhibitory effect of caerulein was abolished 1 hr after gastrectomy, and at 3 and 4 hrs after gastrectomy caerulein induced the excitatory response in 10 out of 11 animals (Fig. 3Bb). The motility index increased to 127.6±7.5% (n=10, p<0.05 compared with the control response) by gastrectomy at 2 min after application of caerulein. This value was gradually restored to the control value at 6 min after caerulein application (Fig. 5). Caerulein induced a weak inhibitory effect in the remaining one animal. One month after gastrectomy, the motility index increased to 126.6±5.3% (n=5, p<0.05 compared with the control response in the pre-operative animal) at 2 min after application of caerulein. This value decreased to control value at 6 min after caerulein application (Figs. 3Bc and 5).

In the animals at 4 hrs after sham-gastrectomy, the motility index decreased to 54.5±5.0%
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Fig. 6. Effects of vagosympathectomy on caerulein-induced relaxation and caerulein-induced contraction after gastrectomy; ○, control response (n=10); ●, after vagosympathectomy (n=5); ▲, 4 hrs after gastrectomy; ■, 4 hrs after gastrectomy plus vagosympathectomy (n=6); ▲, caerulein 10 ng/kg, i.v.; *, p<0.05, compared with vagosympathectomized animals.

(n=5, p<0.05 compared with the control response in the preoperative animals) at 2 min after application of caerulein, and was gradually restored to the control value at 6 min after caerulein application (Figs. 3Ab and 4). One month after sham-gastrectomy, the motility index decreased to 52.7±6.3% (n=5, p<0.05 compared with the control response in the preoperative animals) at 2 min after caerulein. This was gradually restored to the control value at 6 min after caerulein application (Figs. 3Ac and 5).

In the vagosympathectomized animals, caerulein had an inhibitory effect on the SO similar to that in normal animals. The motility index decreased to 47.6±6.2% (n=5, p>0.05) at 2 min after caerulein (Fig. 6). In the gastrectomized animals with vagosympathectomy, the motility index increased to 135.3±8.6% (n=5, p>0.05 compared with gastrectomy) at 2 min after caerulein application (Fig. 6). This value restored to control value at 10 min after caerulein application.

Discussion

Early work by Wyatt (1967; 1969) showed that gastric peristaltic contractions decreased the SO perfusion resistance and a Polya type of gastrectomy ceased this coordination but did not cause biliary hypertension reflecting an increase in the SO resistance in the dog. Although the coordination of the gastric contraction and the SO motility was not observed in the present experiment, the perfusion pressure of the SO, an indicator of its resistance, and the frequency of phasic contractions of the SO increased significantly after gastrectomy (from the level at the gastric and gastroepiploic vessel to the uppermost duodenum), but not after sham-gastrectomy or vagosympathectomy. It is therefore indicated that continuity of the bowel wall, including the muscle layers and intrinsic nerve plexus from the uppermost duodenum and/or stomach to the SO, is one of the factors essential to maintain the SO resistance in the normal animal. It is suggested that an elevation of the SO perfusion pressure after gastrectomy is due to an
interruption of the tonic inhibitory inputs from the stomach and/or the uppermost duodenum to the SO passing through the intrinsic nerve pathway, rather than through the muscular connection from the stomach to the SO, though continuity of the longitudinal muscles from the antrum to the duodenum exist over the pylorus (Yamagami, 1955) and no invasion of the duodenal muscles into the SO (Boyden, 1965) have been clearly demonstrated in the dog. Vagosympathectomy did not change the SO perfusion pressure and phasic contraction. These findings indicate that the increased perfusion pressure and phasic contraction of the SO were not induced by denervation of the vagosympathetic nerves, but caused by disconnection of the intrinsic nerves from the uppermost duodenum and/or stomach. This change in the SO perfusion pressure may persist for an extended time. In this case, these behaviors of the SO were observed even one month after gastrectomy.

In the present experiment, the caerulein-induced SO relaxation in the preoperative dog is converted to the contraction after gastrectomy with or without vagsosympathectomy, but not after vagsosympathectomy alone. Its is, therefore, suggested that the SO relaxation to caerulein in normal dogs was induced by activation of the intrinsic inhibitory pathway from the stomach and/or the uppermost duodenum to the SO.

Intravenous injection of caerulein or CCK with bolus produced the relaxation of the SO (Lin and Spray, 1969; Carrazziari et al., 1975; Sarles, 1986; Ryan, 1987) which is mediated by nonadrenergic noncholinergic inhibitory motor neurons in the enteric plexus in the dog (Mizutani et al., 1978) and cat (Behar and Biancani, 1980). It is supposed that the reversed response in the gastrectomized dog was produced by direct action on the SO muscles or by indirect action on the intrinsic cholinergic neurons.

Caerulein induced the SO contraction by stimulating the CCK receptors on the smooth muscles of the SO in the dog and cat after application of TTX (Sarles, 1986; Lin, 1975; Bertaccini et al., 1968). The excitatory response was induced by stimulation of the cholinergic neurons in the myenteric plexus of the guinea-pig ileum (Nemeth et al., 1984). Stimulation of the vagus nerve induced the atropine-sensitive excitatory response on the canine SO (Satler et al., 1972).

In the present study, although the cannulae inserted in the common bile duct were tied with its wall containing the neurons on the serosa (Hopton, 1973), caerulein induced the relaxation response on the SO in the preoperative and sham operated dogs. That the excitatory response of the SO to caerulein was only induced by gastrectomy indicates that the SO motility was reflexly controlled by the neuronal regulation from the stomach and/or uppermost duodenum. If the reversed response to caerulein was induced by cholecystectomy alone (Rolny et al., 1986) and sectioning of the nerves surrounding the common bile duct (Hopton, 1973), the reversed response should have been indicated after tying the common bile duct with cannula in the normal and sham operated dogs in the present experiment. However, caerulein induced the relaxation response on the SO after tying the cannulae with its wall of the common bile duct. The reversed response of the SO is reflexly induced from the stomach and/or the uppermost duodenum rather than the gallbladder, a finding which is supported by our previous work (Mizutani et al., 1978).

Rolny et al. (1986) have demonstrated that, in patients with biliary dyskinesia after
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cholecystectomy, intravenous application of caerulein with bolus induced an increase in basal perfusion pressure and the amplitude of phasic contractions of the SO, but Mizutani et al. (1978) reported that cholecystectomy had no effects to the caerulein-induced inhibitory response of the canine SO. Hopton (1973) described that the reflex from the gallbladder to the SO was terminated by transection of the common bile duct with its surrounding nerve plexus.

Wyatt (1967) reported that electrical or mechanical stimulation of the antrum sometimes decreased the SO perfusion pressure, and suggested that these responses were probably induced by the intrinsic nervous pathway from the stomach.

It has been reported that vagotomy does not affect the SO motility and the effect of CCK on the SO of cats (Liedberg and Halabi, 1970) and dogs (Funch-Jensen et al., 1981) and synthetic block in man has no effect on the perfusion pressure and motility of the SO (Schein et al., 1970).

In the present experiment, vagosympathectomy transiently either increased or decreased the perfusion resistance and the frequency of phasic contractions of the SO. These results suggest that the spontaneous activity and tone of the SO are partly regulated by extrinsic nerves. However, persistent change of the basal tone of the SO may be controlled by the enteric nervous system since the long-term change of the SO dynamics was not affected by extrinsic nerve sectioning.

In summary, motility of the SO may, at least in a part, be controlled by the intrinsic inhibitory reflex from the stomach and/or the uppermost duodenum, and the caerulein-induced inhibition of the SO may be mediated via the descending inhibitory pathway from the stomach and/or the uppermost duodenum.

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