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Noriaki Itano*

Toshiaki Neya†

*Okayama University,

†Okayama University,

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Noriaki Itano and Toshiaki Neya

Abstract

The effect of a change in cecal volume on gastric motility was studied in 24 h fasted rats anesthetized with urethane (0.8 g/kg, i.p.). A cecal volume increase from 1 to 10 ml (in 1 ml steps) produced a decrease in the basal tone of the stomach. The maximal inhibitory response was produced with an 8 to 10-ml increase in cecal volume. The gastric inhibitory response continued as long as the increased cecal volume was maintained. It was abolished by a combination of a splanchnicotomy and vagotomy, or only a splanchnicotomy in a few cases. The inhibition of gastric motility by increasing the cecal volume also occurred after severance of dorsal roots between T8 and L4 and gastric branches of vagus nerves. It is suggested that an increase in cecal volume induces gastric relaxation mainly via the splanchnico-splanchnic pathway and partly via the vago-vagal and vago-splanchnic pathways. Therefore, retardation in transit of the gastric contents in germ free rats having an enlarged cecum may be attributed to an enhancement of the ceco-gastric inhibitory reflex. The ceco-gastric inhibitory response mediated by the splanchnic pathway was abolished by guanethidine (3-5 mg/kg, i.v.), but the response mediated by the vagal pathway was resistant to guanethidine as well as to atropine (0.2 mg/kg, i.v.). This result indicates that splanchnic postganglionic efferents are adrenergic, while vagal postganglionic efferents are non-adrenergic and non-cholinergic.

KEYWORDS: cecum, gastric motility, autonomic nerves

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THE EFFECT OF CECAL VOLUME CHANGE ON GASTRIC MOTILITY IN RATS

Noriaki ITANO and Toshiaki NEYA

Department of Physiology, Okayama University Medical School, Okayama 700, Japan
(Director : Prof. S. Nakayama)

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Abstract. The effect of a change in cecal volume on gastric motility was studied in 24 h fasted rats anesthetized with urethane (0.8 g/kg, i.p.). A cecal volume increase from 1 to 10 ml (in 1 ml steps) produced a decrease in the basal tone of the stomach. The maximal inhibitory response was produced with an 8 to 10-ml increase in cecal volume. The gastric inhibitory response continued as long as the increased cecal volume was maintained. It was abolished by a combination of a splanchnicotomy and vagotomy, or only a splanchnicotomy in a few cases. The inhibition of gastric motility by increasing the cecal volume also occurred after severance of dorsal roots between T8 and L4 and gastric branches of vagus nerves. It is suggested that an increase in cecal volume induces gastric relaxation mainly via the splanchnico-splanchnic pathway and partly via the vago-vagal and vago-splanchnic pathways. Therefore, retardation in transit of the gastric contents in germ free rats having an enlarged cecum may be attributed to an enhancement of the ceco-gastric inhibitory reflex. The ceco-gastric inhibitory response mediated by the splanchnic pathway was abolished by guanethidine (3-5 mg/kg, i.v.), but the response mediated by the vagal pathway was resistant to guanethidine as well as to atropine (0.2 mg/kg, i.v.). This result indicates that splanchnic postganglionic efferents are adrenergic, while vagal postganglionic efferents are non-adrenergic and non-cholinergic.

Key words : cecum, gastric motility, autonomic nerves.

The rodent has a relatively large cecum whose motility *in vivo* has been studied by several authors (1-3). However, the role of the cecum in the regulation of gastrointestinal motility has not been studied sufficiently, although it has been reported that a change in cecal volume induced by alternating the microbial flora in the digestive tract or the cecectomy altered the gastrointestinal transit rate of the luminal contents (4-6). The authors of these reports considered the change in transit rate to be due to the change in microbial flora. We have suggested that gastrointestinal motility or transit rate of contents may be influenced by changes in sympathetic or parasympathetic nervous activity caused by an increase or decrease in cecal afferent discharges depending on an increase or decrease in cecal volume (7).

To better understand the reflex regulation of gastrointestinal motility from the cecum, the effect of cecal volume changes on gastric motility was studied in rats.

MATERIALS AND METHODS

Fifty-three Wister rats of either sex, weighing 230 to 350 g, were used. They were fasted for 24 h before the experiments, but tap water was given *ad libitum*. The animals were anesthetized with urethane (0.8 g/kg, i.p.). A polyethylene cannula was inserted into the left external jugular vein for infusion of lactate-Ringer solution (Na^+ , 130; K^+ , 4; Ca^{2+} , 3; Cl^- , 109; lactate $^-$, 28 mEq/L; 2 ml/h) to compensate for loss of body fluid during the experiments and to administer drugs intravenously.

After abdominal incision, a 2-cm-long rubber balloon was inserted into the stomach through a small hole made at the *pars proventricularis*, and 1.5-2.0 ml of water was introduced into the balloon. Intraluminal pressure changes of the balloon, which represented gastric motility, were recorded by an ink-writing oscillograph through the pressure transducer. Intraluminal contents of the cecum were washed out with Tyrode solution through an opening made at its blind end, and then a 2-cm-long rubber balloon was inserted into the emptied cecum from the opening. To change cecal volume, water warmed to 37°C was introduced into the balloon, and the volume of water introduced into the balloon represented the cecal volume. The cecal volume increase was achieved in 1 ml steps from 0 to 10 ml at intervals of 2 min, or progressively up to a certain level between 1 and 10 ml which was maintained for 2 min. The cecal volume was kept 0 ml for 20 min of an interposing rest period between trials.

After the operation, the abdominal cavity was left open and covered with cotton wool and gauze humidified with warm Tyrode solution to prevent artificial mechanical disturbance produced by cecal volume change. A lamp set over the abdominal area served to maintain the temperature of the abdominal cavity at $37 \pm 0.5^\circ\text{C}$. If necessary, the cervical vagus nerves were bilaterally sectioned just caudal to the larynx, and the major and minor splanchnic nerves were bilaterally sectioned intraperitoneally. After a laminectomy, the spinal cord was transected at the 6th thoracic segment. Pithing of the spinal cord caudal to the 6th thoracic segment was performed with suction using a polyethylene tube. Atropine sulphate (Sigma), a cholinergic blocker, and guanethidine sulphate (Tokyo-Kasei), an adrenergic neuron blocker, were administered intravenously.

RESULTS

Spontaneous rhythmic contraction usually appeared in the stomach when the cecum was empty. When the cecal volume was increased stepwise up to 10 ml, the gastric motility was inhibited, that is, there was a decrease in the frequency of phasic contractions and basal tone which recovered a few minutes after the cecal volume was decreased (Fig. 1, A). The amplitude of contractions was also reduced just after each increase in cecal volume, and then recovered gradually. The cecal volume increase necessary to induce gastric inhibition was 1 ml. With an increase in the volume of the cecum over the 1-ml threshold, the basal tone of the stomach decreased. It was recognized that the response consisted of phasic and tonic components (Fig. 1, a and b). The former appeared just after prompt increase in the volume. The relationship of the magnitude of phasic and tonic inhibitory responses in the stomach to cecal volume increases in 6 animals is shown in Fig. 1, B. In this figure, the maximal inhibitory response obtained when the cecal volume increase was from 1 to 10 ml was taken as 100% response. Both

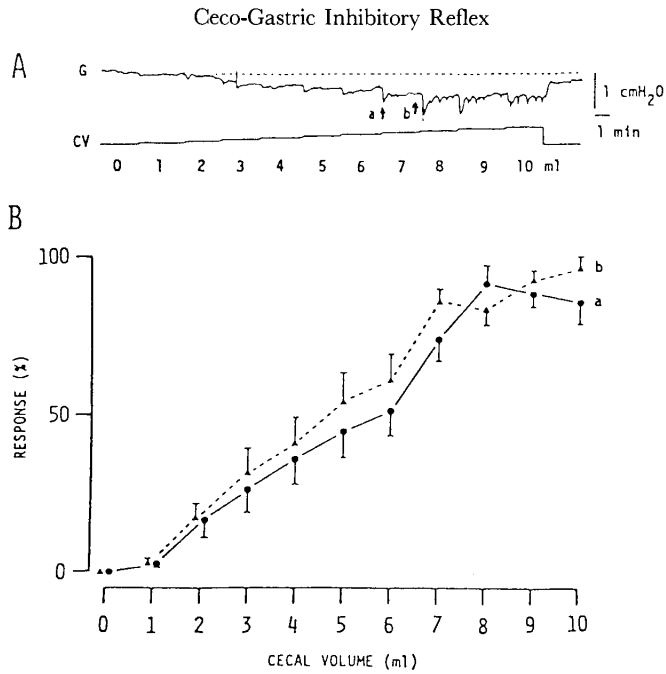


Fig. 1. Effects of cecal volume changes on gastric motility. A: Phasic (a) and tonic (b) inhibition of gastric motility (G) was produced when the cecal volume (CV) was increased stepwise. B: The responses were strengthened in parallel with increasing cecal volume.

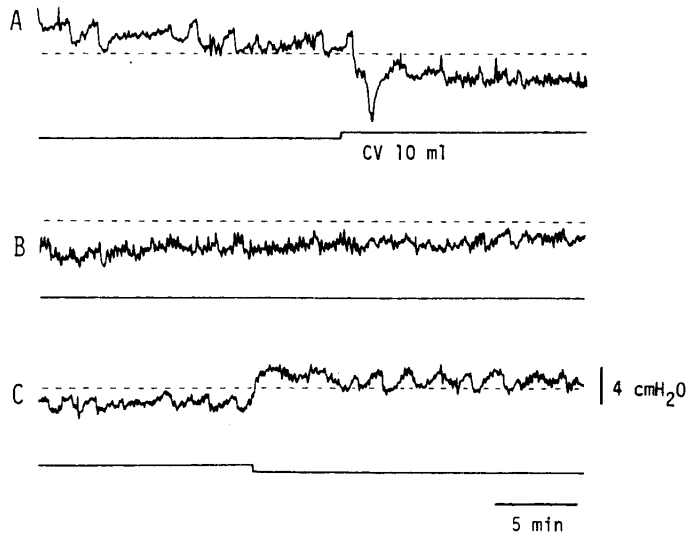


Fig. 2. Effect of a long-lasting volume increase of the cecum (CV) on gastric motility. A, B and C are continuous traces. Tonic inhibition persisted as long as the cecal volume increase was maintained. In this case, the volume was kept at 10 ml for 1 h.

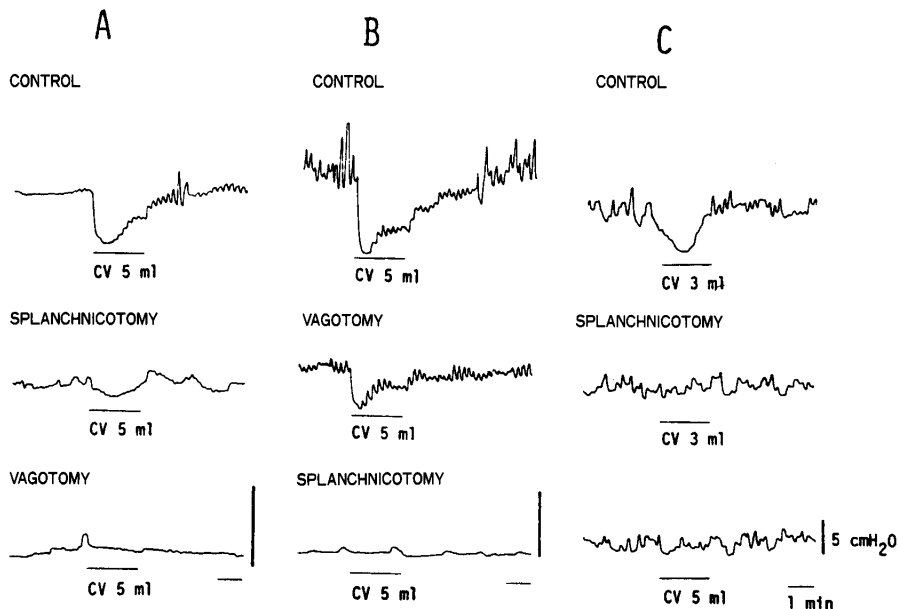


Fig. 3. Effect of a splanchnicotomy (sympathectomy) and vagotomy on ceco-gastric inhibitory response. A: The response to a cecal volume increase (CV) of 5 ml largely decreased after a splanchnicotomy and was abolished after a subsequent vagotomy. B: The response to a cecal volume increase (CV) of 5 ml was reduced after a vagotomy and abolished after a splanchnicotomy. C: The response to a cecal volume increase (CV) of 3 ml was completely abolished after a splanchnicotomy and was not produced by further increase in cecal volume (5 ml). A, B, and C were obtained in three different rats.

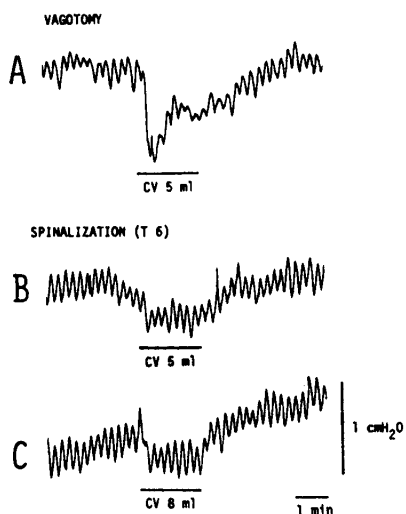


Fig. 4. Ceco-gastric inhibitory response (A) produced in a vagotomized animal was reduced after transection of the spinal cord at the 6th thoracic segment (B, C). The cecal volume increase (CV) was 5 ml in A and B and 8 ml in C.

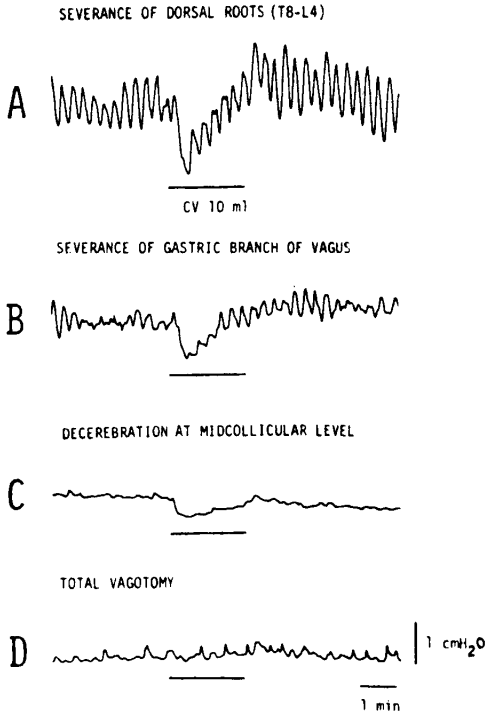


Fig. 5. Gastric inhibition was elicited by a cecal volume increase of 10ml after severance of dorsal roots between T8 and L4 (A). This response could still be induced after severance of gastric branches of the vagus nerve (B) and decerebration at the intercollicular level (C). After total vagotomy below the larynx, the inhibitory response terminated (D).

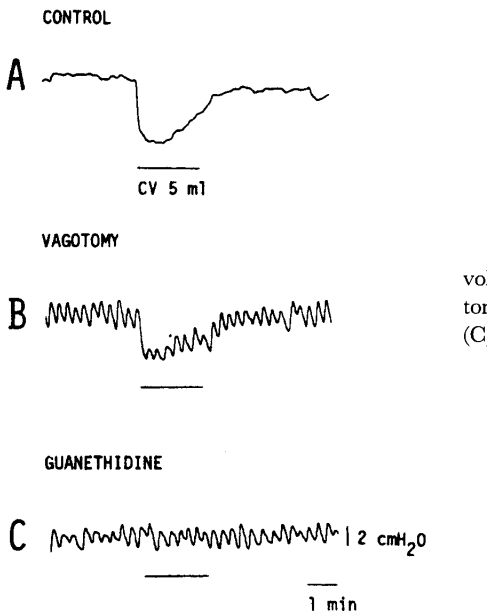


Fig. 6. The gastric inhibitory response to a cecal volume increase of 5 ml (CV) produced after a vagotomy (B) was abolished by guanethidine (3 mg/kg, i.v.) (C)

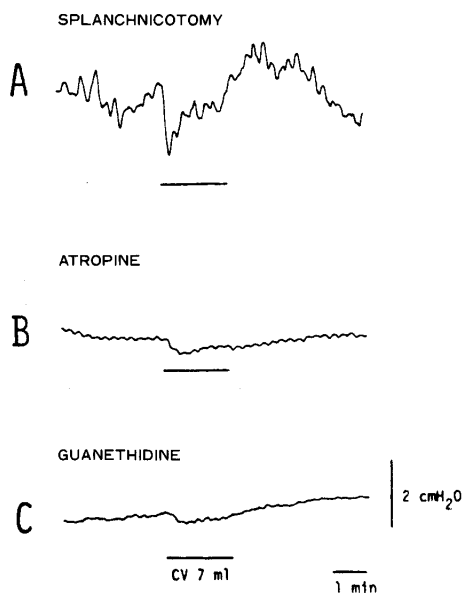


Fig. 7. The gastric inhibitory response to a cecal volume increase of 7 ml after a splanchnicotomy (sympathectomy) (A) was resistant to atropine (0.2 mg/kg, i.v.) (B) and guanethidine (3 mg/kg, i.v.) (C).

phasic and tonic inhibitory responses increased linearly against cecal volume increases from 1 to 7 ml and reached maxima at 8 to 10 ml. Furthermore, the tonic inhibitory response in the stomach continued as long as the cecal volume increase was maintained. An example is shown in Fig. 2. In this case, the cecal volume increase was kept at 10 ml for 1 h. A large phasic response appeared as soon as the cecal volume was changed and then the tonic response appeared and continued until the cecal volume was returned to the control level.

The gastric inhibitory response to a cecal volume increase was largely reduced after bilateral section of the major and minor splanchnic nerves and was abolished after a bilateral cervical vagotomy following the section of the splanchnic nerves (Fig. 3, A). In 3 of 9 animals, the gastric inhibitory response was abolished after a splanchnicotomy alone (Fig. 3, C). On the other hand, when the vagotomy was carried out first, the decrement in the inhibitory response to the cecal volume increase was smaller than that observed after the splanchnicotomy alone. After a splanchnicotomy following a vagotomy, the remaining inhibitory response was completely abolished (Fig. 3, B). From these results, it is concluded that the gastric inhibitory response to cecal volume increase is mediated by both vago-vagal and splanchnico-splanchnic pathways but mainly by the latter.

In vagotomized animals, the inhibitory response was reduced, but remained after transection of the spinal cord at the 6th thoracic segment (Fig. 4). The response was abolished after a splanchnicotomy or pithing of the spinal cord below the transected level. In rats whose dorsal roots between the 8th thoracic and 4th lumbar segments were severed previously, gastric inhibition could be

induced by an increase in cecal volume. This response, though reduced by severance of gastric branches of the vagus nerve, remained after decerebration at the intercollicular level, but was completely abolished by a cervical vagotomy (Fig. 5).

The gastric inhibitory response to an increase in cecal volume was largely reduced by intravenous administration of guanethidine (3-5 mg/kg, i.v.). The residual response was not affected by additional application of atropine (0.2 mg/kg, i.v.), but was completely abolished by a vagotomy. The ceco-gastric inhibitory response observed in vagotomized animals was abolished by guanethidine (Fig. 6), but was not affected by atropine. The inhibitory response in rats whose bilateral splanchnic nerves were previously severed was resistant to atropine and guanethidine (Fig. 7), but abolished by a vagotomy.

DISCUSSION

It has been revealed that the transit rate of the luminal contents through the gastrointestinal tract in cecectomized rats was faster than in intact rats (6), and that in germ free rats having an enlarged cecum it was slower than in normal rats due to the absence of microbial flora (4, 5). However, the ceco-gastric inhibitory reflex demonstrated in this study may also regulate the transit rate of the luminal contents through the gastrointestinal tract since an increase in cecal volume reflexly caused sustained inhibition of gastrointestinal motility. Thus, transportation of the luminal contents through the upper digestive tract is augmented in cecectomized rats, while it is retarded in germ free rats. It is, therefore, suggested that the cecum in herbivora having a large cecum may play an important role in the regulation of motility of the upper digestive tract.

The ceco-gastric inhibitory response was abolished by a combination of a splanchnicotomy and vagotomy, or only a splanchnicotomy in some cases. In vagotomized rats, the response was maintained after decerebration or spinalization at the upper thoracic segment. Therefore, this reflex probably occurs mainly via the splanchnico-splanchnic spinal pathway and partly via the vago-vagal pathway. Furthermore, vagal afferents arising from the cecum may facilitate the splanchnico-splanchnic reflex inhibition of gastric motility since the ceco-gastric inhibitory reflex was obtained even after severing the dorsal roots involving splanchnic afferents and the gastric branches of the vagus nerve involving vagal efferents to the stomach.

Splanchnic efferents of postganglionic neurons related to the ceco-gastric inhibitory reflex are adrenergic, and vagal efferents are non-adrenergic and non-cholinergic, because the splanchnico-splanchnic reflex was blocked by guanethidine, while the vago-vagal reflex was resistant to atropine and guanethidine.

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