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KEYWORDS: gastrocecal reflex, cecal motility, splanchnic nerve, vagus nerve, rat.

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ON THE GASTROCECAL INHIBITORY REFLEX IN THE RAT

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Abstract. In rats anesthetized with urethane, the effects of distention of the stomach upon cecal motility and neural mechanisms which generate this effect were studied. Cecal motility was inhibited when the pars glandularis of the stomach was distended by pressure ranging from 25 to 30 cm H_2O. This inhibitory reflex was not affected by bilateral cervical vagotomy, but completely abolished following bilateral severance of the greater splanchnic nerves or after intravenous administration of guanethidine. After transection of the spinal cord at the level of the 5th thoracic segment the inhibitory reflex remained intact, but was abolished following pithing of the 6th thoracic segment and below. It may be concluded that the afferent and efferent path of the gastrocecal inhibitory reflex mainly pass through the greater splanchnic nerves and the reflex center is located in thoracic segments caudal to the 6th thoracic segment.

Key words : gastrocecal reflex, cecal motility, splanchnic nerve, vagus nerve, rat.

The rodent has a relatively large cecum whose motility *in vivo* has been studied by several authors since 1904. Elliot and Barclay-Smith studied motility and extrinsic innervation of the cecum in rats (1). Masuda (2) observed through a transparent abdominal window that the ingestion of food caused increased motility of the cecum in conscious rabbit and guinea pig. MacEwen (3) and Hertz and Newton (4) reported that the taking of food or contrast medium produced augmented motility of the proximal colon and the cecum in conscious man. Hertz and Newton termed it the gastrocolonic reflex, but Welch and Plant (5) denied the existence of this reflex and considered it a feeding reflex. Subsequently many investigators (6-9) reported that eating increased colonic motility in man.

The present studies were carried out to examine whether distending the stomach produces any change in the cecal motility of the rat and, if there is any effect of distention, to determine the reflex pathways for this change.

MATERIALS AND METHODS

Fifty-three rats of either sex were used. They were fasted but were given tap water *ad libitum* 24 h before the experiment. The animal was anesthetized with urethane (1 g/kg, i.p.). Some animals were further immobilized with gallamine (6 mg/kg, i.v.) and artificially ventilated.

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A polyethylene cannula was inserted into the left external jugular vein for intravenous infusion of drugs.

Distention of the stomach. After abdominal incision, a small rubber balloon 2 cm long connected with a tube was inserted into the pars glandularis of the stomach through the pars proventricularis (12) and the tube was ligated with the latter.

The following two methods were used for recording cecal motility: 1. A small rubber balloon 2 cm long was inserted into the cecum through the ileocecal junction from the ileum 2 cm oral to the former. At the beginning of the experiment, the internal pressure in the recording balloon during the relaxation period was set up about 3 cmH_2O and cecal motility was recorded by a pressure transducer and a pen oscillograph. 2. An extraluminal strain gage transducer (12 × 3 mm) was sewn in a circular direction on the cecal wall just anal to the ileocecal junction with care taken not to injure blood vessels.

Section and stimulation of nerves. The cervical vagus nerves were sectioned bilaterally and the greater splanchnic nerves were sectioned intraperitoneally at the subdiaphragm. The parameters of electrical square pulses used for stimulation were 5 V, 10 Hz and 1-2 msec.

Transection and pithing of the spinal cord. After laminectomy was performed on the 5th, 6th and 7th thoracic vertabrae and the dura mater was incised longitudinally, the spinal cord was transected between the 5th and the 6th thoracic segments. For pithing of the spinal cord caudal to the transected level, a polyethylene tube 2 mm in diameter was inserted into the vertebral canal and the spinal cord was sucked through the tube by a vacuum pump. After the operation the animals were placed in a thermostatic box and the abdominal cavity was left open to prevent artificial mechanical disturbance produced by distention of the stomach. The wound edge was raised by connecting it to the upper edge of the thermostatic box with thread, and the abdominal cavity was filled with warm Tyrode solution. A lamp set over the abdominal area served as the heat source to maintain the temperature of the abdominal cavity at about 38℃.

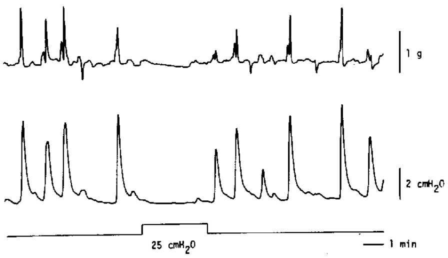
RESULTS

Usually, about 40 min after a termination of the surgical operation spontaneous rhythmic cecal contraction appeared. The contractions were 1 to 3 cmH_2O in amplitude and 0.5 to 3 c/min in rate, and between these contractions smaller contractions of 0.05-0.2 cmH_2O and of 4-6 c/min occurred. In a few case only the smaller contractions were recorded. Tracings of the cecal motility recorded by the balloon method and by the strain gage method were usually very similar, but there was occasionally some difference between them. For example, cecal motility could be recorded as a single contraction by the balloon method, when it was recorded as two contractions by the strain gage method. Moreover no motility was recorded by the former method in the same case, while by the latter method some contraction was recorded.

Distention of the Stomach

The stomach was distended by a pressure ranging from 0 to 35 cmH_2O. Distention by pressure over 7 cmH_2O always inhibited cecal motility. There was some relationship between the distention pressure and the amount of inhibition.

A distention pressure of 25 to 30 cmH_2O caused the most marked inhibitory



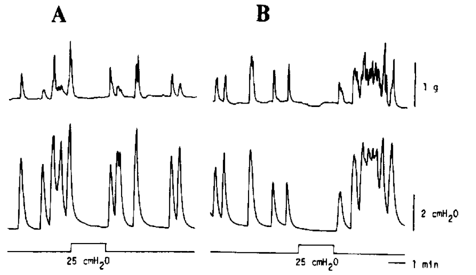


Fig. 1. *(left)* The effect of distention of the pars glandularis of the stomach on cecal motility. Cecal motility was markedly inhibited by distention of the stomach. The upper and lower tracings of this and following figures indicate cecal motility recorded by strain gage and balloon, respectively.

Fig. 2. *(right)* The effect of bilateral vagotomy on the gastrocecal inhibitory reflex. A: Vagus nerve intact. B: After bilateral vagotomy.

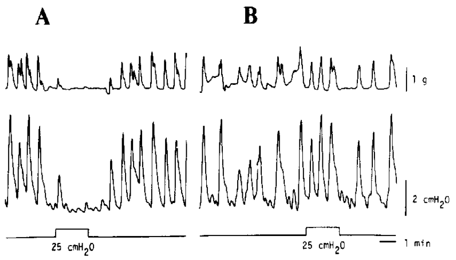
response. When the stomach was distended by the pressure of 25 to 35 cmH_2O, after a latency of about six seconds, cecal motility was remarkably inhibited in rate and in amplitude accompanied by a slight decrease or no change in tone in 29 out of 31 cases. An example is shown in Fig. 1. In 17 out of 29 cases, after termination of stimulation the inhibitory response continued for a little while and then gradually returned to the same motility as before distention, and in the remaining 12 cases immediately after interruption of distention a transitory excitatory response occurred. There was no purely excitatory response in any case. When cecal motility before distention of the stomach was feeble, the inhibitory response was not clear.

Reflex Pathways

Section and efferent stimulation of the vagus nerve. Section of bilateral vagus nerves caused transient decrease in motility of the cecum in both rate and amplitude. After motility returned to that before the nerve section, the stomach was again distended. In 5 out of 6 cases, the inhibitory response to gastric distention was almost the same as before vagus nerve section (Fig. 2).

Electric efferent stimulation (5 V, 10 Hz, 1 msec) of the vagus nerve produced increased cecal motility accompanied by elevation of tone after a latency of about six seconds. Immediately after interruption of the stimulation the excitatory response disappeared and the cecal motility returned to that before stimulation. The excitatory response to electric stimulation was incompletely inhibited by administration of atropine (1 mg/kg, i.v.).

Section and efferent stimulation of the greater splanchnic nerve. After the right greater splanchnic nerve along with its adrenal branch were sectioned, the inhibitory gastrocecal response remained unchanged, but additional cutting of the left greater splanchnic nerve almost completely abolished the inhibitory response. An example is shown in Eig. 3. Efferent stimulation (5 V, 10 Hz, 2 msec) of the greater splanchnic nerve markedly inhibited the rhythmic contractions of the cecum in rate, in



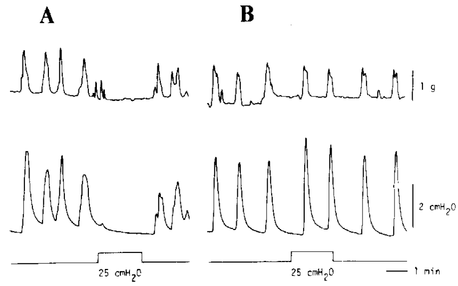


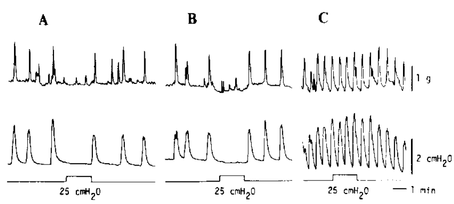
Fig. 3. *(left)* The effect of bilateral splanchnicotomy on the gastrocecal inhibitory reflex. A: After unilateral (right) splanchnicotomy the inhibitory reflex response was not affected. B: After bilateral splanchnicotomy the respose was completely abolished.

Fig. 4. *(right)* The effect of intravenous injection of guanethidine on the gastrocecal inhibitory reflex. A: Before injection. B: After injection of guanethidine the inhibitory response was abolished.

amplitude and in tone in all 7 cases tested. After interruption of the stimulation a transitory excitatory response appeared and then cecal motility returned to that before stimulation. The results described above suggest that the efferent pathways of the gastrocecal inhibitory reflex are contained mainly in the splanchnic nerves.

Guanethidine administration. Spontaneous cecal motility was inhibited by guanethidine (6 mg/kg, i.v.) which blocks adrenergic nerves, and about twenty minutes after injection returned to that before administration. In some cases, immediately after the administration of guanethidine cecal motility was accelerated. After guanethidine administration the inhibition of cecal motility produced by gastric distention was completely abolished (Fig.4).

Spinal transection and pithing. After transection of the spinal cord between the 5th and 6th thoracic segments, gastric distention produced almost the same response as before transection (Fig. 5B). Pithing of the 6th thoracic segment and below completely abolished the gastrocecal inhibitory response (Fig. 5C).



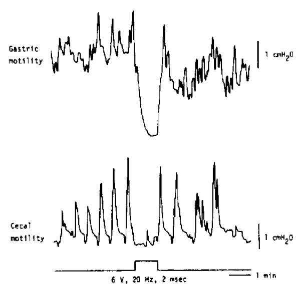


Fig. 5. *(left)* The effect of transection of the spinal cord and pithing on the gastrocecal inhibitory reflex. A: Spinal cord intact. B: The spinal cord transected between the 5th and 6th thoracic segment. C: After pithing of the 6th and lower thoracic segments the inhibitory response was abolished.

Fig. 6. *(right)* Inhibitory effect of afferent stimulation of the right cervical vagus nerve on the motility of stomach and cecum. The left vagus was intact.

DISCUSSION

Distention of the pars glandularis of the stomach always caused an inhibition of cecal motility in the rat. The inhibitory response was abolished by bilateral splanchnicotomy, guanethidine administration or pithing of the 6th thoracic segment and below, although transection of the spinal cord between the 5th and 6th thoracic segments did not abolish the inhibitory response. According to our anatomical observation of the rat, the greater splanchnic nerve passes through the 8th, 9th and 10th thoracic sympathetic ganglia. Therefore, the nerve probably arises from the 8th, 9th and 10th thoracic segments of the spinal cord. It is concluded from the above results that the inhibition of the cecal motility produced by distention of the stomach is a reflex response, that the inhibitory reflex center probably is situated in the lower thoracic segments (Th8-Th10), and that the afferent and efferent pathways are not contained in the vagus nerves, but in the splanchnic (sympathetic) nerves of which efferent nerve endings release noradrenaline as a transmitter.

It is well known that in conscious animals and in man the ingestion of food or contrast medium causes increased activity of the colon and cecum or defecation. Hertz and Newton (4) supposed that filling the stomach with food would elicit reflexively an excitatory response of colonic motility, and consequently they termed it the gastrocolonic reflex. The above investigators never examined the effect of stimulation of the stomach alone. Adachi (10) reported that gastric distention (40-120 mmHg) produced increased or decreased motility of the proximal colon in anesthetized dogs and that bilateral vagus nerve section abolished the fomer response while after bilateral splanchnicotomy the latter response became excitatory response, which was abolished by bilateral vagotomy. Therefore, the central neural activities for this inhibitory response seem to be mediated via the splanchnic nerves. Tansy *et al.* (11) reported that gastric distention produced augmented segmentation of the proximal colon in anesthetized dogs, but did not observe an inhibitory response. They found that after interruption of the lumbar sympathetic nerves or bilateral cervical vagotomy the excitatory response was abolished and also the increased activity of the proximal colon induced by afferent stimulation of the cervical vagus nerve was abolished by section of the lumbar sympathetic nerve. Therefore, they presumed that the afferent pathways of this excitatory reflex may be contained in the vagus nerves and the efferent pathways in the lumbar sympathetic nerves. Elliott *et al.* (1) observed that stimulation of the inferior mesenteric nerves relaxes the cecum as well as the colon in the rat. Although we did not explore the role of the inferior mesenteric nerve, it is considered from the present results that this nerve does not participate in the gastrocecal inhibitory reflex.

Regarding the splanchnic inhibitory reflex response, the present results correspond with Adachi's results (10). Additional results of the present experiment showed that the afferent stimulation of unilateral cervical vagus nerve caused decreased response of gastric and cecal motility (Fig. 6), and after a contralateral vagotomy the inhibitory response was abolished. Therefore, it is suggested that there must be a vago-vagal inhibitory reflex on gastric and cecal motility although efferent vagal stimulation causes accerelation of cecal motility.

The cervical vagus nerve contains afferent fibers originating from all the thoracic and abdominal organs. Therefore, the effect of afferent stimulation of this nerve is not necessarily the same as the effect of gastric distention though both induced similar result of cecal inhibitory response.

After the bilateral section of the vagus nerve, gastric distention was still effective in producing decreased cecal motility. It might be concluded, therefore, that the neural path for the gastrocecal inhibitory reflex mainly passes through the greater splanchnic nerves.

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