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Abstract

Effects of stimulation of the small intestine upon the gastric, small intestinal and colonic motility have been studied in dogs. The results are summarized as follows. 1. The movements of the stomach, small intestine, and proximal colon are always inhibited by the distension or the contracture of the muscular coats of the small intestine but no responses are produced by a mechanical or chemical stimulation of the mucosa; and those of the distal colon are in most cases also inhibited, whereas in rare instances are they augmented. 2. The afferent impulses are transmitted through the great and small splanchnic nerves and the lumbar sympathetic nerves to the inhibitory as well as the excitatory (pelvic nuclei) centers of the intestinal movements located within the spinal cord, whereas the vagal nuclei remain unaffected. The efferent impulses are transmitted through the thoraco-lumbar sympathetic nerves as well as through the pelvic nerves. The latter are involved in the augmentative effect produced in the distal colon. 3. The threshold producing the extrinsic muscular reflex is higher than that eliciting the intrinsic muscular reflex.

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ON THE INTESTINAL EXTRINSIC REFLEXES ELICITED FROM THE SMALL INTESTINE

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The movements of the stomach, small intestine and colon are regulated in situ by the intrinsic and extrinsic reflexes. On the small intestine we have verified recently that the intrinsic reflex consists of two reflexes i. e., the mucosal and muscular reflexes, whose receptors and reflex mechanism are quite different from each other[7]. The problem to be solved is whether or not these receptors are also concerned with the extrinsic reflex. Moreover, as regard to the extrinsic reflexes elicited from the small intestine there are some discrepancies among the results obtained by various authors. In the following studies, therefore, we stimulated differentially the mucosa and the muscular coats of the small intestine to observe the effects produced extrinsically upon the movements of the stomach, small intestine and colon.

METHODS

Twenty-one dogs are selected as the experimental animals. The animals are anesthetized with 0.5g/kg of urethane and 3 mg/kg of morphine. The movements of the stomach, small intestine and colon are simultaneously recorded by means of the balloon-method on the smoked paper. In order to produce the extrinsic reflex various stimuli are applied to an isolated intestinal loop of 5—10 cm. in length. The loop is distended by an abrupt injection of Ringer's solution, warmed up to about 37 °C, into the lumen of the loop. The muscular coats of the loop from which the mucosa and serosa has been completey removed are stretched by pincettes and the muscular contraction is produced by applying a small piece of filter paper (3 × 10 mm) moistened with 0.001—1% acetylcholine, 1% pilocarpine and 1% histamine, or the lumen of the loop is perfused by 0.1—1N HCl or olive oil, etc., taking care not to produce the rise in the intraluminal pressure.

The mucosal surface is in some cases exposed by means of longitudinal

incision along the anti-mesenteric border of the intestinal wall and is stimulated on the one hand mechanically by brushing with a tooth-brush as well as by rubbing with a clot of cotton-wool, and on the other hand, chemically by applying 0.1—1 N HCl, 5% $CuSO_4$ or mustard paste.

RESULTS

1. *The extrinsic reflexes are elicited only from the intestinal muscle.* When the small intestinal loop is distended by the procedure described above, the movements of the stomach, small intestine and proximal colon are always inhibited with a latent period of a few seconds (Figs. 1A and 2A), while those of the distal colon are in most cases inhibited (Fig. 2A) but in some cases augmented.

The minimal intraluminal pressure effective to evoke the small intestino-small intestinal reflex, i. e., the threshold of distension stimulus, is about 10 mmHg in an isolated intestinal loop of about 10 cm in length, irrespective of the level of the loop in the small intestine, while the threshold in the small intestino-gastric and the small intestino-colonic inhibitory reflexes is somewhat higher than that in the reflex described above and

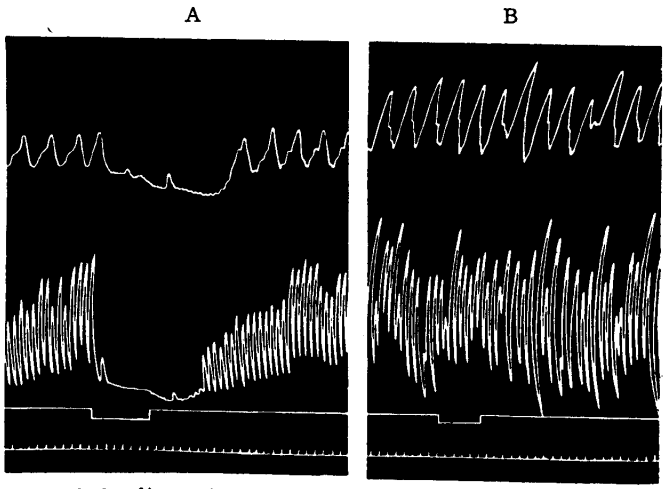

Fig. 1 Effects of the distension of the jejunal loop upon the gastric and duodenal movements.

Dog (8 kg) anesthetized with urethane and morphine. Tracing from above downwards are gastric movements, duodenal movements, signal and time in 3 sec. intervals. A: The spinal cord is transected at the level of the 4th thoracic segment. The movements of the stomach and duodenum are inhibited, when the jejunal loop of 10 cm length is distended with the intraluminal pressure of 140 mmHg. B: The spinal cord caudal to the 5th thoracic segment is pithed. No reflex response is obtained, when the jejunal loop is distended with pressure of 150 mmHg.

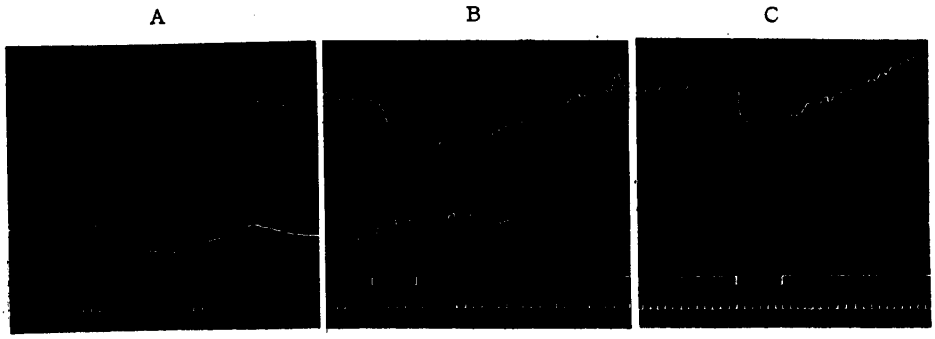

Fig. 2 Effects of distension of the jejunal loop upon the movements of proximal and distal colons.

Dog (14 kg) anesthetized with urethane and morphine. Tracings from above downwards are the movements of the proximal colon and of distal colon, signal and time in 3 sec. intervals. A : The extrinsic nerves of the colons intact. The jejunal loop distended with the pressure of 40 mmHg. B : After severing the colonic and the hypogastric nerves, the jejunum distended with the pressure of 60 mmHg. C : Following the previous procedures, pelvic nerves divided. The jejunum distended with pressure of 40 mmHg. Explanations in the text.

is about 15 mmHg and 25 mmHg respectively.

The inhibitory reflexes mentioned above are also elicited when the localized contracture is produced by applying the filter paper moistened with acetylcholine, pilocarpine or histamine on the surface of the small intestine. After stripping the mucosa, submucosa and serosa off the muscular coats concerned, the same effect can be obtained.

Even when acetylcholine produces, because of lower concentration (0.001 %), only an inconsiderable reflex response in the small intestine except for the stimulated loop (Fig. 3A), the movements of the loop itself are significantly inhibited, the inhibition being more remarkable below the stimulated region than that above (Fig. 3 B and C). It is quite natural to suppose that the influence of extrinsic reflex upon the loop itself is in this case also neglegible. It may be then possible to consider that the inhibitory response observed in the loop is due mainly to the intrinsic muscular reflex the mechanism of which was already reported in the previous paper (7), and that the threshold in the intrinsic muscular reflex is far lower than in the extrinsic reflex.

When the mucosa of the innervated jejunal loop is stimulated chemically (with 0.1—1 N HCl, 5 % $CuSO_4$ and mustard paste) or mechanically (with brush or cotton-wool), the movements of the loop are significantly augmented orad to the simulated spot and are inhibited anally (Fig. 4 C and D), while there is no changes in the movements of the stomach and the small intestine except for the loop (Fig. 4A and B). That the former

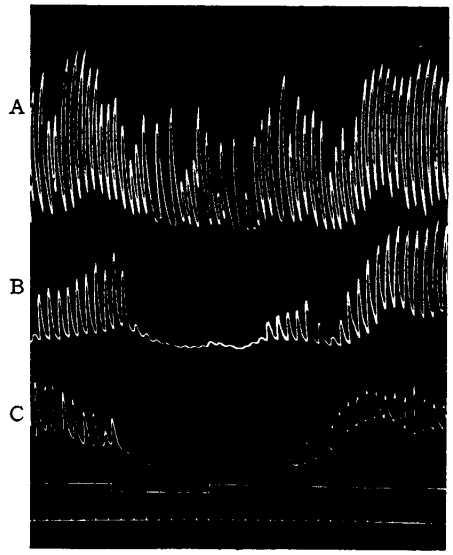

Fig. 3 The extrinsic and intrinsic reflex responses elicited by stimulating the intestinal muscle.

Dog (8 kg) decerebrated under ether anesthesia. When 0.1% acetylcholine solution is applied to the serosal surface of the jejunal loop, the duodenal movements are slightly inhibited (A), whereas the movements of the loop are significantly inhibited, the inhibition being more remarkable below (C) the stimulated region than that above (B). Time in 6 sec. intervals.

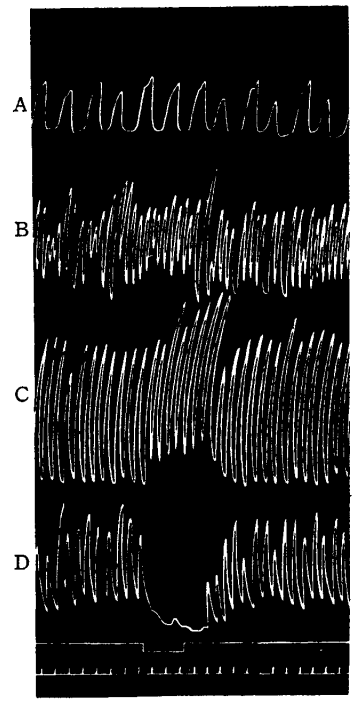

Fig. 4 The stimulation of the intestinal mucosa produces the intrinsic reflex, but no extrinsic reflex.

Dog (9 kg) anesthetized with urethane and morphine. The mucosa of the innervated jejunal loop is repeatedly stroked with a clot of cotton-wool. No change is observed in the gastric (A) and duodenal (B) motility, whereas in the jejunal loop there is to be seen the excitation above (C) and inhibition below (D) the stimulated region. Time in 6 sec. intervals.

is local responses, the occurrence of which should be attributed to the intrinsic mechanism, is already reported in the previous paper (7). From the results described above it may be concluded that any receptor related

with the extrinsic intestinal reflex does not at all exist in the mucous membrane.

2. *The afferent and efferent pathways of the small intestino-gastric and of the small intestino-small intestinal reflexes.* A series of experiments is performed in order to ascertain how the vagus nerves participate in the extrinsic inhibitory reflex described above. After the reflex effect has been ascertained with a certain degree of distension, the spinal cord is transected at the level situated between the 4th and the 5th thoracic segments. When the loop is then again distended with the same degree of the intraluminal pressure as before, the reflex is produced with the same degree of the inhibition (Fig. 1A). The reflex is completely abolished when the spinal cord caudal to the 5th thoracic segment is destroyed (Fig. 1B). From the results described above it may be said that the intestinal reflex of which reflex pathways pass through the vagi is not detectable.

The problem is to decide whether the vagal nuclei are in any way influenced by the afferent impulses propagated through the splanchnic nerves and the lumbar sympathetic nerves. The ventral roots which originate in the 5th to the 13th thoracic segments are bilaterally severed, leaving the dorsal roots intact, and in addition, the spinal cord caudal to the lst lumbar segment is completely destroyed. By this procedure the efferent sympathetic pathways are eradicated whereas the afferent pathways left intact. When the loop is distended, no reflex effect can be recognized. From this it may be said that the vagal nuclei have no relation to the reflex. After cutting bilaterally the great and small splanchnic nerves the degree of the inhibitory response is diminished but is never completely abolished and the additional bilateral section of the lumbar sympathetic trunks is necessary to abolish the reflex.

From the results described above it may be considered that the reflex centers are localized in the thoracic and lumbar sympathetic nuclei in the spinal cord and their reflex pathways, i. e., the afferent and efferent pathways, are consisted of the splanchnic and lumbar sympathetic nerves, whereas the vagal nuclei and the afferent and efferent fibers involved in the vagi have no relation to the inhibitory reflex.

3. The small intestino-colonic reflex. AIBA (1) and MASUDA (11) have noticed that at the region of the colon where the branches of *A. colica sinistra* communicate with those of *A. colica media* a pulsating ring of constriction exists from which the antiperistaltic waves recurrently arise. From these findings the regions of the colon situated proximally and distally to the constriction ring have been named the proximal and the distal colon respectively.

The movements of the proximal colon are always inhibited by distension of the small intestine (Fig. 2A), and the severance of the hypogastric nerves exerts no influence upon the inhibitory response, whereas additional severance of the colonic nerves reduces moderately the inhibitory response (Fig. 2B). The vagus nerves may be severed without producing any change on the reflex. When the pelvic nerves are then bilaterally severed, the reflex inhibition becomes more remarkable than before (Fig. 2C); and the severance of the great and small splanchnic nerves abolishes the reflex completely. Consequently it may be considered that both the sympathetic and the pelvic nuclei are related to the reflex described above, the excitation of the former having predominance over that of the latter.

4. *On the reflex pathways in relation to the reflex movements of the distal colon.* Two kinds of the reflex responses, the excitatory and inhibitory, are produced by distension of the loop of the small intestine, the former being more frequently observed than the latter. It has been ascertained that when the distension of the jejunal loop produces the inhibitory response (Fig. 2A), the reversal of the response occurs, i. e., the excitatory response is produced when the colonic and hypogastric nerves are severed (Fig. 2B). When the bilateral pelvic nerves are subsequently severed, the reflex is completely abolished (Fig. 2C). On the other hand, the excitatory response reverts to the inhibitory, after the severance of bilateral pelvic nerves; and an additional severing of the colonic and hypogastric nerves abolishes the reflex completely. As regard to the inhibitory efferent pathways it is noteworthy that the severance of the inferior splanchnic nerves, which are considered to be the original roots of the colonic and the hypogastric nerves, can not completely abolish the inhibitory response and additional severance of the ascending branches of the inferior mesenteric ganglia (coeliac roots) is necessary to abolish the response concerned. It may, therefore, be considered that some inhibitory fibers which originate in the great splanchnic nerves pass through the colonic and the hypogastric nerves via the coeliac roots. Since the intestinocolonic inhibitory reflex is abolished by pithing the spinal cord caudal to the 5th thoracic segment, it may, therefore, be considered that the inhibitory reflex center is located in the spinal cord caudal to the 5th thoracic segment.

5. *Is the intestinal reflex elicited via prevertebral gaglia ?* After destroying the spinal cord caudal to the 4th thoracic segment, an unequivocal inhibitory response can never be observed even though the jejunal loop of 10 cm in length is distended with a very high intraluminal pressure of 200 mmHg. It may consequently be supposed that a more powerful

distension of longer loop than used in this experiment is necessary to obtain the same effect as that observed by KUNTZ.

DISCUSSION

In the experiments so far described we observed that in the extrinsic reflexes produced by the stimulation of the muscular coats of the small intestine the movements of the stomach, small intestine and proximal colon are always inhibited, whereas those of the distal colon may in most cases be inhibited but in rare cases excited, and that the vagus nerves are not concerned with the small intestino-gastric and the small intestino-small intestinal inhibitory reflexes.

MCCLURE, REYNOLDS and SCHWARTS[12], BÁRSONY and EGAN[2], and BRAUCH[3] state that the reflex inhibition of gastric motility is elicited by the injection of various chemical substances into the duodenum. In these cases we are of the opinion that the reflex inhibition might be mainly due to the distension of the duodenal muscular coats rather than to the chemical stimulation of the mucosa, since, according to our results, the receptors concerned with the extrinsic reflexes do not exist in the mucosa but in the muscular coats. THOMAS, CRIDER and MOGAN[16] state that the injection of moderate dose of HCl solution (20 cc of N/10 HCl) into the duodenum produces the inhibition of the gastric movements, and that the sections of both splanchnics and both vagi do not abolish the inhibitory response, though the response is less marked. BRUNEMEIER and CARLSON[4] obtained also similar results under similar experimental conditions as of the authors mentioned above. Such an inhibitory response as observed after sectioning the extrinsic nerves might be due to the muscular intrinsic reflex[7]. LALICH, MEEK and HERRIN[10] state that the lumbar sympathetic chains are not involved in the small intestino-gastric inhibtoriy reflex and that the vagi contain both afferent and efferent pathways for the reflex. Our results are, however, diametrically opposed to their results. The cause of this discrepancy is yet to be solved. As regard to the small intestino-gastric reflex, MORIN and VIAL[13], and as regard to the small intestino-small intestinal reflex YOUMANS, MEEK and HERRIN[17] and HERMANN and MORIN[6] and FREUND and SCHEEHAN[5] agree with us in that the vagus nerves contain neither afferent nor efferent pathways for the reflexes concerned. As to the small intestino-colonic reflex PEARCY et al[15] and MORIN and VIAL[14] observed only an inhibitory effect and IVY and MCILVAIN[8] observed only an excitatory effect, but it may be probable that they observed a part of the reflexe effects.

That the stimulation of the mucous membrane of the small intestine does not produce any extrinsic reflexes appears to have not been noticed by these investigators. It may be advantageous for the living body to have no extrinsic reflex of the mucosal origin. If such a reflex did exist, it would result in the retardation of transportation or stagnation of the intestinal contents, since the mucous membrane is considered to be continuously exposed to mechanical and chemical stimuli.

KUNTZ[9] postulated a sort of the intestino-intesinal reflex, the center of which was supposed to be located in the prevertebral ganglia. Such a reflex can never play an important role in regulating the intestinal movements, even if it existed, since, according to our experiments, conclusive results have not been obtained even by raising an intraluminal pressure as high as 200 mmHg.

SUMMARY

Effects of stimulation of the small intestine upon the gastric, small intestinal and colonic motility have been studied in dogs. The results are summarized as follows.

1. The movements of the stomach, small intestine, and proximal colon are always inhibited by the distension or the contracture of the muscular coats of the small intestine but no responses are produced by a mechanical or chemical stimulation of the mucosa; and those of the distal colon are in most cases also inhibited, whereas in rare instances are they augmented.

2. The afferent impulses are transmitted through the great and small splanchnic nerves and the lumbar sympathetic nerves to the inhibitory as well as the excitatory (pelvic nuclei) centers of the intestinal movements located within the spinal cord, whereas the vagal nuclei remain unaffected. The efferent impulses are transmitted through the thoraco-lumbar sympathetic nerves as well as through the pelvic nerves. The latter are involved in the augmentative effect produced in the distal colon.

3. The threshold producing the extrinsic muscular reflex is higher than that eliciting the intrinsic muscular reflex.

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