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Conduction of activity between muscles in the terminal region of the common bile duct and in the neighboring duodenum

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Abstract

The relationship between muscle activity at the terminal region of the common bile duct and the duodenal muscle was examined in rabbits. The rhythmic muscle activity in the terminal region was synchronous with duodenal muscle activity. The activity of the latter muscle preceded the former. The activity at the terminal region synchronous with the rhythmic activity of the duodenal muscle sometimes disappeared spontaneously. The muscle activity of the ampulla and the spincter at the terminal region was sometimes independently lost. The conduction of excitation from the duodenal muscle to the terminal region appeared to be performed at several sites. The existence of a "conduction-shunt path" between the terminal region and the duodenum, as well as between the ampulla and the sphincter appeared probably. Some quantitative differences were found between the spincter, ampulla and duodenum in inhibitory effects to stimulation of splanchnic nerves and reflex effects and to excitatory effects of cholecystokinin-pancreoxymin and caerulein. These results seem to indicate that the sympathetic nerves and the intramural cholinergic neurones controlling these region carry out activities quantitatively different from each other.

CONDUCTION OF ACTIVITY BETWEEN MUSCLES IN THE TERMINAL REGION OF THE COMMON BILE DUCT AND IN THE NEIGHBORING DUODENUM

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Abstract: The relationship between muscle activity at the terminal region of the common bile duct and the duodenal muscle was examined in rabbits. The rhythmic muscle activity in the terminal region was synchronous with duodenal muscle activity. The activity of the latter muscle preceded the former. The activity at the terminal region synchronous with the rhythmic activity of the duodenal muscle sometimes disappeared spontaneously. The muscle activity of the ampulla and the sphincter at the terminal region was sometimes independently lost. The conduction of excitation from the duodenal muscle to the terminal region appeared to be performed at several sites. The existence of a "conduction-shunt path" between the terminal region and the duodenum, as well as between the ampulla and the sphincter appeared probable. Some quantitative differences were found between the sphincter, ampulla and duodenum in inhibitory effects to stimulation of splanchnic nerves and reflex effects and to excitatory effects of cholecystokinin-pancreozymin and caerulein. These results seem to indicate that the sympathetic nerves and the intramural cholinergic neurones controlling these region carry out activities quantitatively different from each other.

It is a well known histological observations that the duodenum and muscles of the terminal region of the common bile duct of mammals are connected to each other (1, 2, 3, 4). Such a continuity was also reported in recent studies conducted with intracellular microelectorodes in guinea pigs by Creed and Kuriyama (5) and in rabbits by Nakayama, Tsuchiya and Yamasato (3). However, it is uncertain whether the movements of the terminal region of the common bile duct exist independently or are subservient to the movements of the duodenal muscle. For elucidation on this question, it becomes necessary to simultaneously record and analyze the activities of the various respective sites of both muscles. For assessment of the mutual relationships of such relatively small areas, electromyographic recordings would probably be the

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most appropriate method. Such recording methods have been being employed by research works in Japan, but a consistent concept has not evolved. Of these many concepts, two appear to be dominant. The first is that the terminal region of the common bile duct is not independent of the intestine because the two activities are synchronous and because the activity changes induced by the cholinomimetic drugs adrenaline and cholecystokinin occur in parallel in both muscles (2, 6, 7, 8, 9). The second concept is that the terminal region of the duct is independent of the duodenum, because the average rhythmic cycle of the terminal region is longer than that of the duodenum and because increased activity was observed only at stimulated sites on perfusing the duct with HCl solution or on expanding it with a balloon (10, 11, 12. 13).

The data presented by these two groups of Japanese investigators coincide on at least two points. Namely, (a) the rhythmic activities of the two muscles are sometimes synchronous, and (b) while a rhythmic activity is aroused in the intestine, activity is sometimes not present in the terminal region, where synchronous activity would be expected (an independent factor may cause a difference in the average rhythmic cycles between the two muscles). The data presented for point (a) indicate that the two muscles are connected functionally and coincide with the histological results and with the results of the intracellular electrode investigations. However, no synchronous activity is observable in some cases, but this may indicate that the conduction of excitation between the two muscles is sometimes functionally interrupted. Consequently, this suggests that the mechanism adjusting the conduction lies between the two muscles.

In these reported studies the electrode polar distances were over 2 mm and the recordings were all taken from a single point at the terminal region. Furthermore, the activity of surrounding duodenal muscles was recorded from a point more than 1.0 cm from the terminal region. By such recording methods the presence or absence of conduction between the two muscles can be confirmed, but it is not possible to analyze the manner of transmission.

In the present study, the distances between each pole of the recording electrode was less than 300 μ, which enabled us to record from more than two points on the terminal region of the common bile duct and to take recordings simultaneously from more than two points on the duodenal muscle around the terminal region. By such electorode placements it was possible to clarify the manner of conduction. The results suggest the presence of an active adjusting mechanism for conduction between the two muscles.

MATERIALS AND METHODS

Rabbits weighing 1.5-2.5 kg were used as experimental animals. The animals were anesthetized with an intravenous injection of urethane (0.7 g/kg) and

positioned with the right side up. The abdominal wall along the lower margin of the right terminal costa was opened, and the pylorus and the upper part of the duodenum were exposed. The stomach was ligated at the pylorus to stop movement of the stomach content to the duodenum. Then, the duodenum was severed at about 10 cm anal to the pylorus, and a vinyl tube (diameter 7 mm, length 50 cm) was attached to the oral cut-end. The other end of the vinyl tube was fixed at a level about 5 cm higher than the duodenum. This tube allowed maintenance of intra-duodenal pressure and outflow of secretion. The abdominal wound was opened widely by threads which were connected with poles fixed on the operating table. The peritoneal cavity was filled with liquid paraffin that was heated with a small electric lamps (6 W, 6 V) to maintain the paraffin temperature at 37-38°C. The cervical vagus and the major splanchnic nerve were stimulated at the neck and in the abdominal cavity, respectively. The common bile duct was isolated from the connective tissues and nerves at a point 2 cm from its entrance into the duodenal wall and severed carefully. For distension of the biliary ducts and gallbladder, a cannula was inserted into the hepatic side of cut-end of the common bile duct. The cannula was connected with a mercury manometer and syringe via a T-shape cannula. Distension of the lower duodenum was accomplished by inserting a cannula into the anal cut-end of the severed duodenum and by ligaton of the end part of the duodenum and connecting the cannula to the mercury manometer and the syringe, as described earlier.

The recording electrodes were stainless steel insect needles sharpened by electrolytic polishing to a tip several microns in diameter. Except for the tip 30-80 μ in length, the needles were coated with clear lacquer. Two such needles were fixed in parallel by Araldite (Ciba-Geigy) with the distance between them being 100-300 μ. An enamel wire (500 μ in diameter, 30 cm in length) was soldered to each needle. Bipolar recordings were taken usually from four points: two from the terminal region of the common bile duct and two from the duodenum.

For convenience of description the terminal region of the common bile duct was divided into the two parts: the ampulla and sphincter. The latter was located at the hepatic side from the ampulla and was 1-2 mm apart from the duodenal wall.

The activities were monitored with an oscilloscope and recorded by a pen recorder. The time constant of the A-C amplifier was set at 0.003-0.01 sec. For this experiments noradrenaline, phenylephrine, tetrodotoxin, pancreozymin (Boots) and caerulein were used. All these agents were injected into the auricular vein.

RESULTS

Relationship between rhythmic activities in the terminal region of the common bile duct and the adjacent duodenal muscle

The rhythmic activities of the terminal region of the common bile duct and the adjacent duodenum were usually synchronous. The activity of the
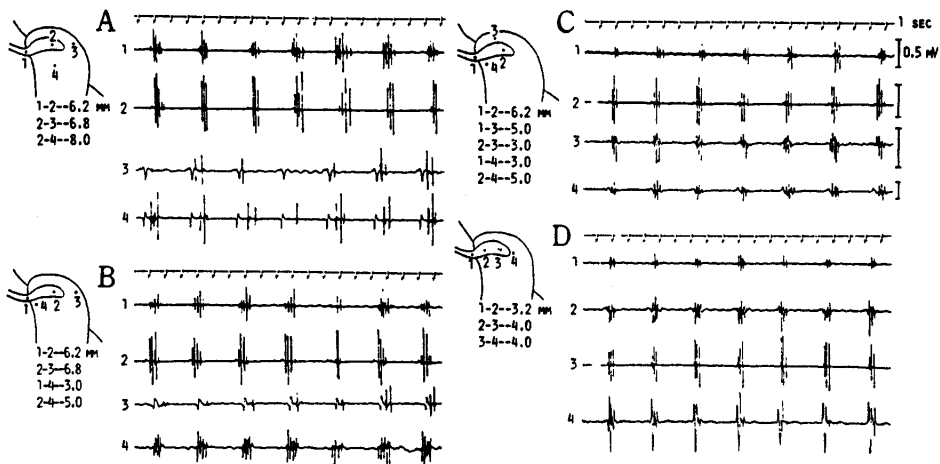
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Fig. 1. Spike potentials of the terminal region of the common bile duct and the neigh-
boring duodenal muscle of rabbits. Traces 1, 2, 3 and 4 were made from the sites 1, 2, 3 and
4, respectively. Recording sites and the distances between the recording sites are shown on
the left of each tracing. The same conventions are used for all subsequent figures. Identical
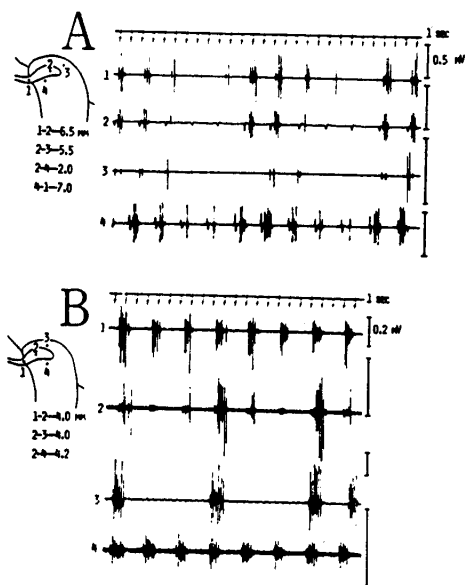time intervals are used for all figures except Fig. 10 and 12.

Fig. 2. Spike potentials of the ter-
minal region of the common bile duct and
the neighboring duodenum.

terminal region was preceded by rhy-
rhmic activity of the duodenal muscle
(Fig. 1, A, C and D). However, the
activity at the terminal region some-
times preceded the recording site of
the duodenum (Fig. 1, B). In some
cases the activity of the ampulla pre-
ceded the sphincter (Figs. 1, B, C and
D-2) or in reverse order (Fig. 1, A).

The activity of the terminal
region synchronous with the rhythmic
activity of the duodenum sometimes
disappeared (Fig. 2, A). The losses
in the ampulla and sphincter some-
times occurred independently (Fig. 2,
A and Fig. 7). The large spike poten-
tial in terminal region sometimes de-
creased stepwise in amplitude (Fig. 2,
B and Fig. 6).

Effect of nerve stimulation on conduction activity between the two muscles

Effect of stimulation of the vagus. Stimulation of the vagus enhanced the rhythmic activity of the terminal region and the duodenum (Fig. 3, A, B and C). In addition, the loss of activity in the terminal region decreased as the frequency of stimuli was increased. Furthermore, stimuli administered at high frequency resulted in lengthening the rhythmic activities of both muscles, finally resulting in persistent activity (Fig. 3, D). Such persistent activity was observable most markedly in the sphincter. When the stimulus frequency
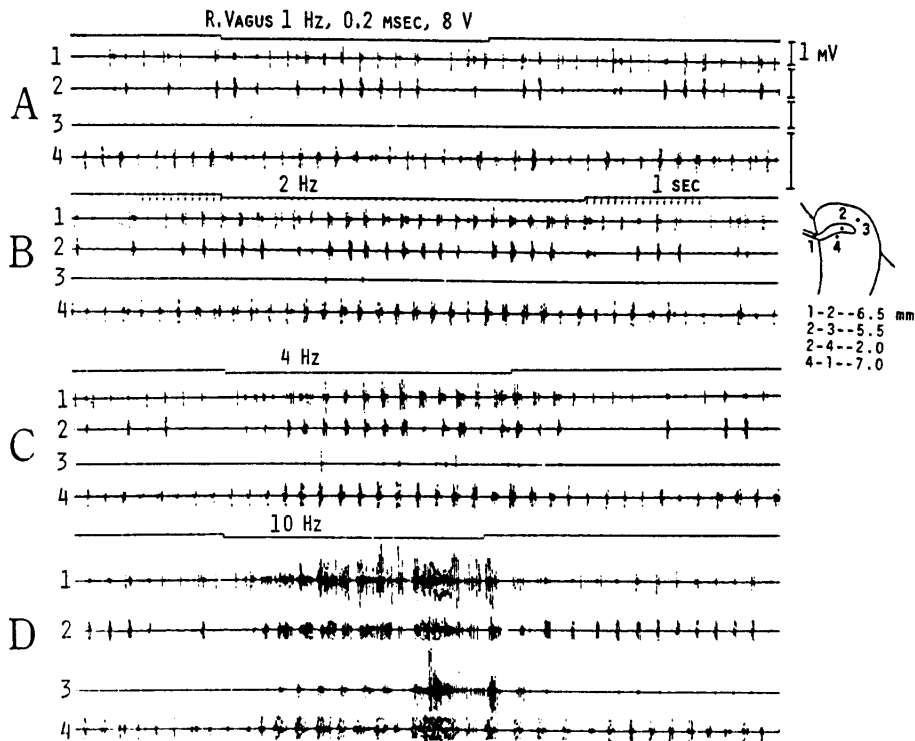

Fig. 3. Effects of vagus stimulation. Stimulation of the right cervical vagus.

was increased further (20 Hz, 40 Hz) the excitatory effect decreased, and finally the activity of the terminal region and the duodenum was suppressed (Fig. 4, B and C). It seemed that such an inhibitory effect was brought about by the synaptic connection of the vagus to the non-adrenergic inhibitory neurones in the wall (14, 15, 16).

Effect of stimulation of the splanchnic nerve. Stimulating the splanchnic nerve inhibited the rhythmic activities of the terminal region and the duode-
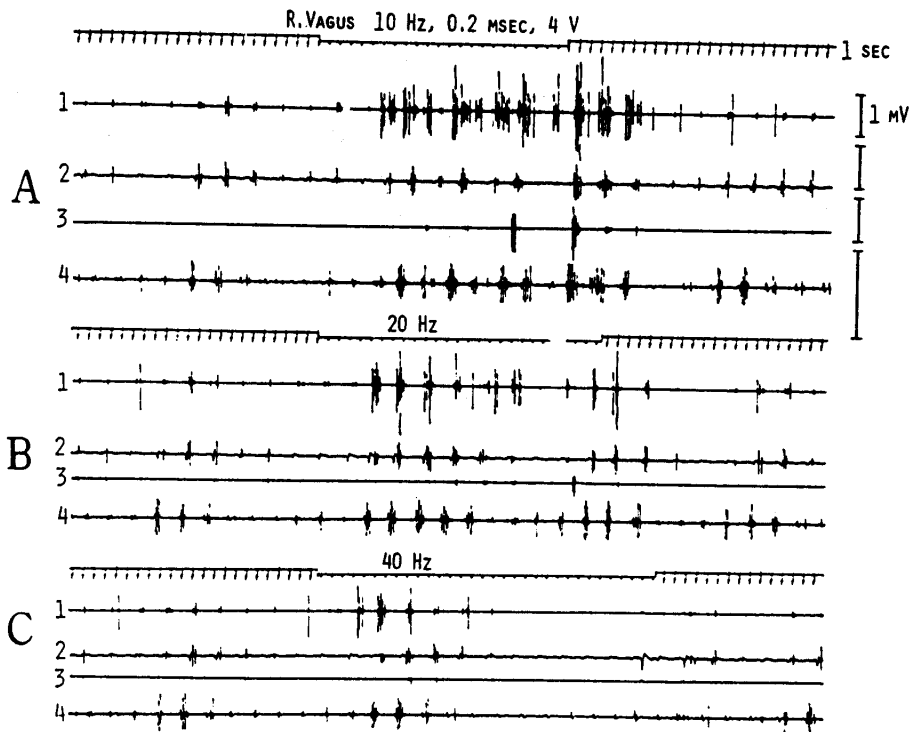
Fig. 4. Effects of vagus stimulation. The same animal and recording sites were used as those in Fig. 3.

num. However, the degree of inhibition often differed in the two regions. The rhythmic activity of the duodenum was weakened but the subsequent activity of the terminal region was not greatly weakened and there was no loss of activity (Fig. 5, A), and more frequent loss of activity occurred in the terminal region (Fig. 5, B, C and D). Likewise, even in the terminal region the degree of inhibition differed at different sites; namely, even when the activity of the sphincter was lost, activity was sometimes found in the ampulla (Fig. 5, D) or conversely (Fig. 5, C). Furthermore, when the activity of the duodenum itself was slightly inhibited, the activity of the terminal region was sometimes markedly inhibited (Fig. 5, E).

Effect of reflex

When the biliary tracts including the gallbladder were distended, the activity of the intestine was weakened. This was followed by the frequent loss of terminal region activity. However, no weakening of activity was found in the terminal region where loss had not occurred (Fig. 6).
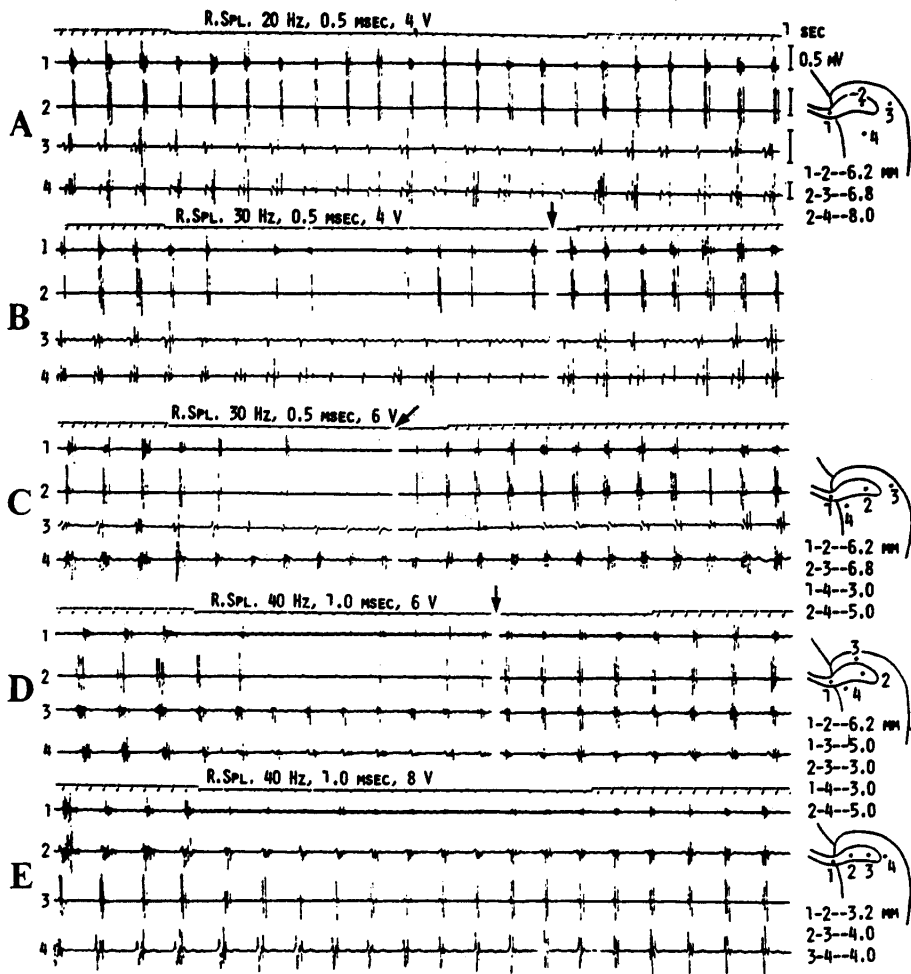
Fig. 5. Effects of stimulating the major splanchnic nerve. All tracings were recorded from the same animal. Arrows in recordings B, C and D, indicate interrupions for 15, 13 and 9 sec., respectively.

When the anal part of duodenum was distended, the rhythmic activities in both regions were weakened and the frequency of loss of terminal region activity increased (Fig. 7).

Raising the intraluminal pressure of the oral region of the duodenum including the terminal region enhanced the activities of both muscles (Fig. 8); this was followed by a decrease in the loss of terminal region activity.
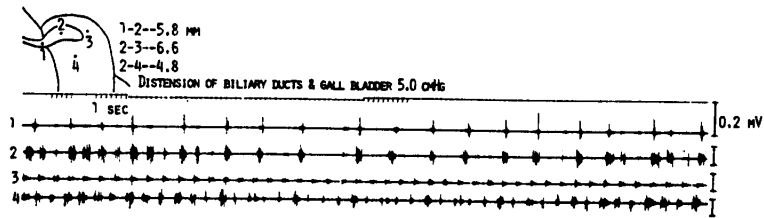
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Fig. 6. Effect of increasing intraluminal pressure of bile duct and gall bladder (5.0 cm Hg).
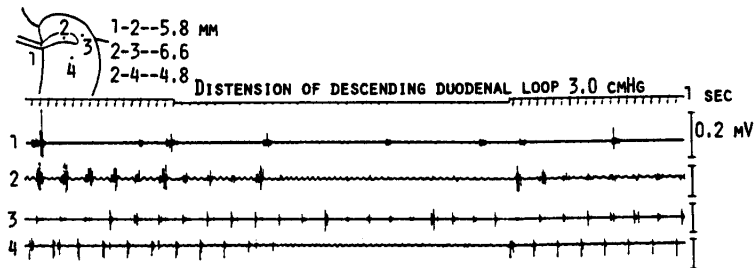

Fig. 7. Effect of increasing intraluminal pressure of lower duodenum (3.0 cmHg).
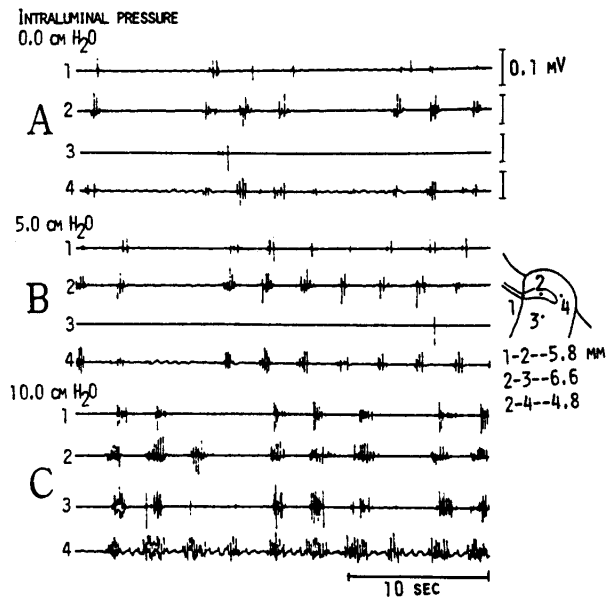

Fig. 8. Effects of increasing intraluminal pressure of duodenum including bile duct orifice.

Effects of drugs

When phenylephrine (0.01–0.1 mg/kg), which is a stimulant of the α-adrenergic receptor, was intravenously injected, an enhancement was found in the activities of the terminal region and the duodenal muscle (Fig. 9). The injection of isoprenaline (0.01–0.1 mg/kg), which is a stimulant of the β-adrenergic receptor inhibited both muscles (Fig. 10). The effects of these two drugs have already been described by many investigators (17, 18).

The excitatory effect of phenylephrine was especially marked on the sphincter: an increase in the amplitude, an elongation of the period of rhyth-
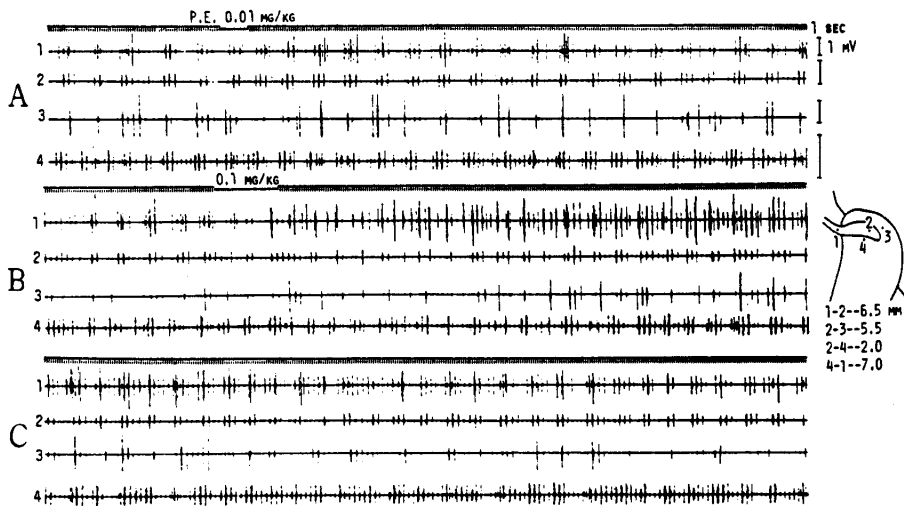

Fig. 9. Effects phenylephrine infused intravenously (i.v.). Doses administered were: condition A, 0.01 mg/kg and condition B, 0.1 mg/kg. Trace C is a continuation of trace B.
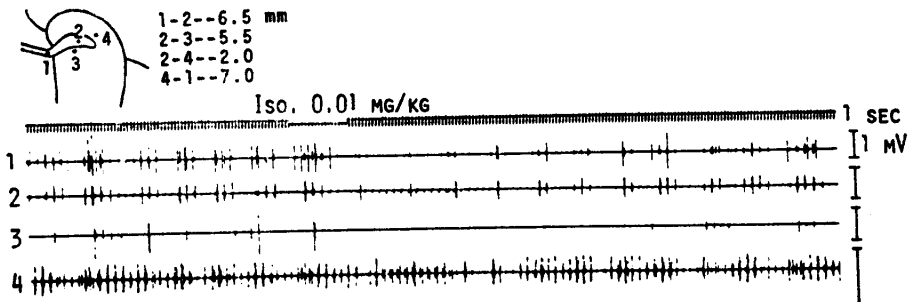

Fig. 10. Effect of isoprenaline administered i.v. at 0.01 mg/kg.

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mic activity, as well as a decrease in the frequency of loss of activity. The activities of the ampulla and the duodenum were accelerated, but the effects on the latter were usually minimal compared to the sphincter. The inhibitory effect of isoprenaline in most instances acted to markedly increase the frequency of loss of activity in the terminal region (Fig. 10).

Pancreozymin (0.5–2.0 U/kg) enhanced the activity of both muscles and decreased the frequency of loss of activity (Fig. 11). In the sphincter the prolongation of the activity period was marked.
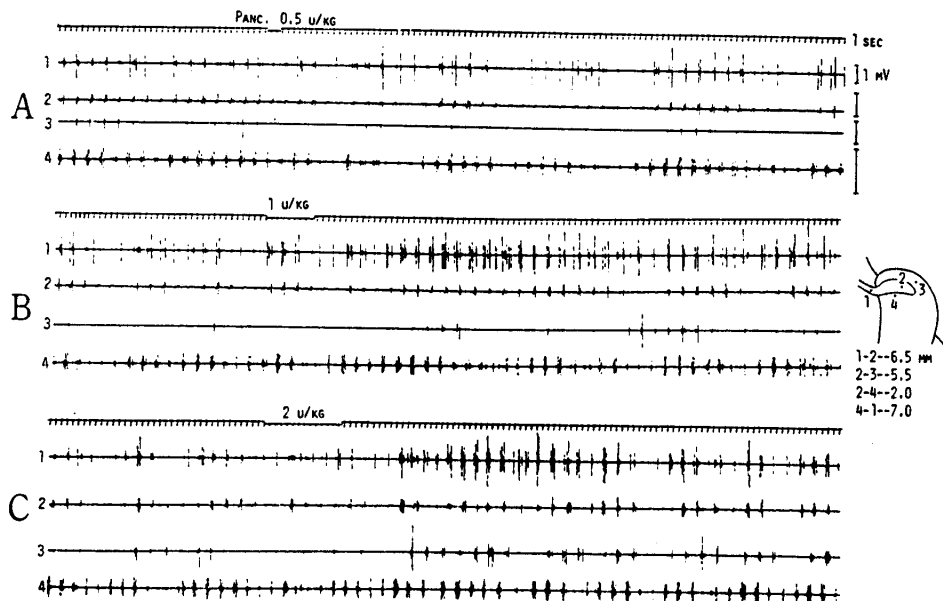

Fig. 11. Effect of pancreozymin infused i.v. Doses administered were: condition A, 0.5 U/kg; condition B, 1.0 U/kg; and condition C, 2.0 U/kg.

Similar effects were observed with caerulein (10–100 ng/kg). Such excitatory effects were suppressed when the excitatory effect of the vagus was weakened by atropine (3 mg/kg, Fig. 12, C, D, E and F), and they also disappeared when the excitatory effect of the vagus was abolished by application of tetrodotoxin (4 μg/kg, Fig. 12, H, I, J, K, L and M).

As already pointed out by many investigators, these drugs seem to elicit an excitatory effect via the intramural cholinergic neurons and the atropine-resistant nervous elements (19, 20, 21, 22). However, in the present study inhibitory effects by these drugs were not observed on terminal region activity as reported in experiments with dogs (17).
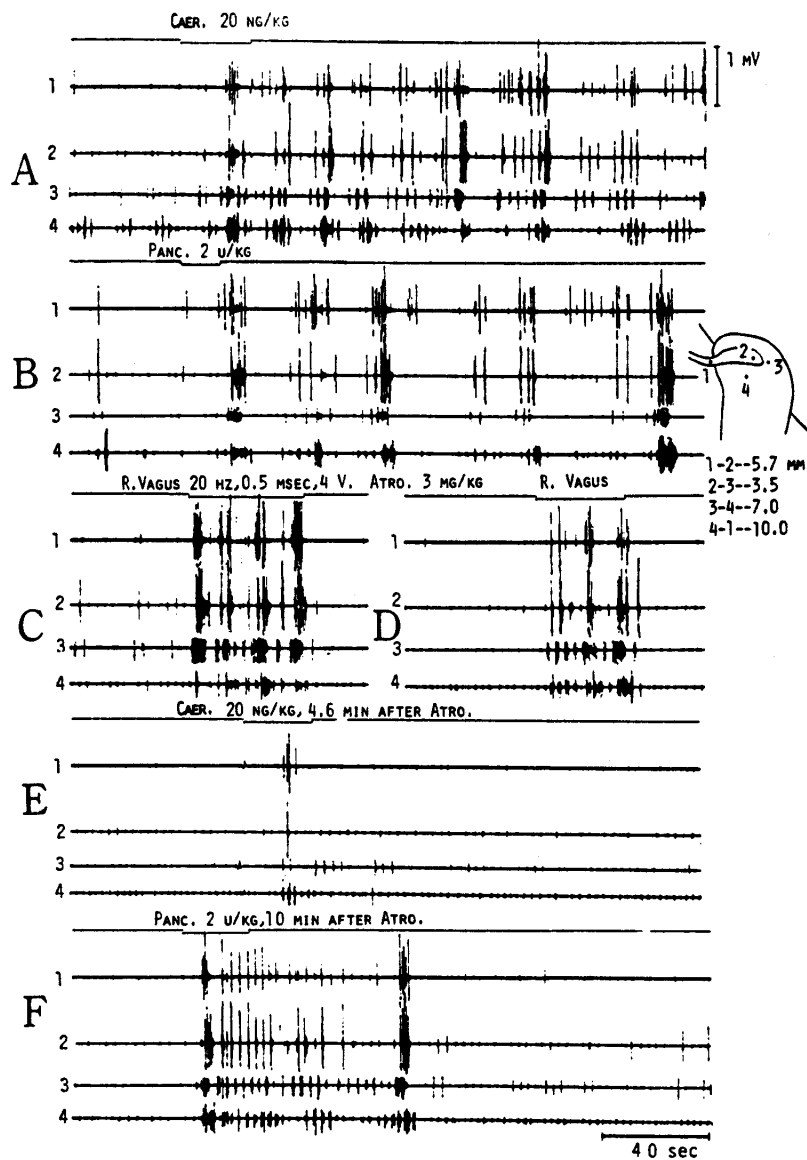
Fig. 12-I. Effects of CCK-PZ and caerulein. A, caerulein at 20 ng/kg, i. v.;
B, CCK-PZ at 2.0 U/kg, i. v.; C, effects of vagal stimulation. Atropine at
3 mg/kg was infused i. v. between recording periods C and D. D, vagal stimu-
lation; E, caerulein i. v. at 20 ng/kg 4.6 min after atropinization; F, CCK-PZ
at 2 U/kg, i. v. 10 min after atropinization.
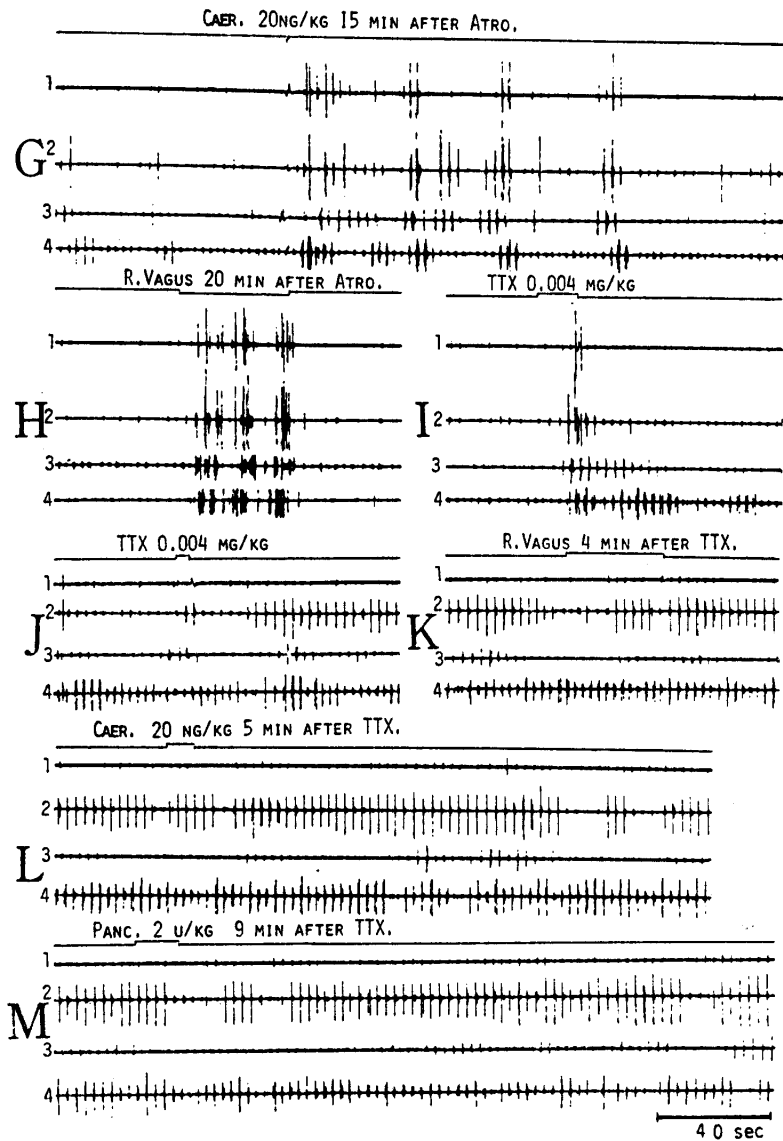
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Fig. 12-II. Effects of CCK-PZ and caerulein. G, Caerulein at 20 ng/kg, i. v. 15 min after atropinization; H, vagal stimulation 20 min after atropinization; I and J, tetrodotoxin at 0.004 mg/kg; K, vagal stimulation 4 min after TTX; L, caerulein at 20 ng/kg, i. v. 5 min after TTX; M, pancreozymin at 2.0 U/kg, i. v. 9 min after TTX.

DISCUSSION

The activity of the terminal region of the common bile duct was usually synchronous with the neighboring duodenum. Furthermore, the rhythmic activity was initiated first at a site of the duodenum, and then conducted to the terminal region and other duodenal sites (Fig. 1). This conduction actually appeared to pass through several "conduction-shunt paths", and the paths seemed to have a competitive relationship: (a) The activity of the ampulla of the common bile duct preceded the sphincter and the activity occurred in reverse order in one and the same specimen; (b) the rhythmic activities of the ampulla and the sphincter were sometimes independently lost; (c) the activity in the terminal region decreased sometimes stepwise (quantitatively) in amplitude; and (d) when the duodenal rhythmic activity was conducted to a duodenal site where it was not usually activated, a further increase in activity was elicited in the terminal region (Fig. 2).

When the rhythmic activity of the duodenal muscle was weakened spontaneously, by sympathetic nerve stimulation, by reflex due to the distension of the anal part of duodenum or biliary tract, or by drugs, such as isoprenaline and adrenaline, the corresponding rhythmic activity of the terminal region was frequently lost. This phenomenon can also be found in the results reported by Ishioka (10) and Kassai (11). These two investigators did not consider the synchronous nature and the loss of phenomenon in the rhythmic activity of the terminal region. Such a loss of rhythmic activity can often be observed independently at the ampulla and the sphincter (Fig. 3; Fig. 4; Fig. 5, C and D; Fig. 6; Fig. 8; Fig. 11). In contrast, when intestinal activity is enhanced spontaneously, by stimulation of the vagus or by administration of phenylephrine, pancreozymin or caerulein, the frequency of the activity loss in both regions decreased. However, the amplitude of the rhythmic activity in the terminal region depended on the width of the activated sphere in the neighboring duodenum, as shown in Fig. 2. These phenomena closely resemble the response observed in the atrio-ventricular node of the heart. The conduction block observed frequently in the node is explained on the basis of the fine branching of the muscle fibres of the node. In histological observations, many fine branches of muscle bundle were observed entering into the terminal region from the neighboring duodenal muscle layers (personal communication from Naitoh, and Yamasato).

The terminal region muscle and the duodenal muscle are, therefore, probably continuous, and frangible paths may exist that shunt conduction between the terminal region and the duodenal muscle, and between the ampulla and sphincter, so that the conduction may sometimes be interrupted in

some paths and consequently the activities in these regions may be elicited independently.

In cases where the inhibitory effect of stimulation of the splanchnic nerve is severe at the duodenum, a more marked inhibition was observable at the terminal region of the same specimen. In addition, the inhibitory effect of the reflex elicited by distension of the biliary tracts was always more marked at the terminal region. Moreover, cholecystokinin always induced a strong accelerative effect on the sphineter.

From these findings the sympathetic nervous system that controls the duodenum, and the nervous system that controls the cholinergic neurones in the intestinal wall, as well as the terminal region seem to be functionally differentiated. In other words, the nervous system that controls both parts seems to act independently to a certain extent.

Phenylephrine always accelerated the activities of the terminal region and the neighboring duodenum, but it inhibited the movement of the anal duodenum. The inhibitory effect of isoprenaline was also most marked on the terminal region. These findings seem to suggest that the muscle in the terminal region is differentiated and possesses properties which are different from the duodenal muscle. In addition, it has been assumed that the duodenal muscle layer adjacent to the terminal region is a conglomeration of the inherent duodenal muscle and the terminal region muscle.

The differentiation of this muscle property and nerve control seems to make the activity of the terminal region different from the activity of the duodenal muscle, at least quantitatively by virtue of the frangible conduction-shunt paths that exist between the duodenal muscle and the muscle at the terminal region, as well as between the ampulla and sphincter.

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