Intestinal Pain

Experimental observation of the mesenteric nerve in a pain producing effect of intestinal contraction by acetylcholine

by

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It is inculcated in text books that there are slow and fast pains in the pain of the somatic region, and that the slow pain or intractable pain is carried in the non-myelinated afferent axons. Of intractable pains, visceral pain as well as vascular pain are considered to be representatives.

Acetylcholine-injection in the intestinal wall produces intestinal pain like an intestinal colic (KIMURA C., 1950).

In the following, afferent impulses in the mesenteric nerve and pain responses were experimentally investigated during intestinal contraction by administration of acetylcholine.

I. INTESTINAL PAIN AND NON-MYELINATED AXONS.

Which is the carrier of the mesenteric afferent during intestinal contraction by acetylcholine (Ach), myelinated or non-myelinated axons? Here the antidromic occlusion technique was used (DOUGLAS and RITCHIE, 1956).

i) Methods

Five adult cats (2.5-3.0kg) were used, anaesthetized with Nembutal (50mg/kg) and immobilized with succinylcholine chloride. The respirator was administered.

The cat was laid on the left side and the right abdominal wall was removed. A catheter was inserted into the duodenal part of the mesenteric artery for Ach-injection to the other part of the intestine and a rubber balloon connected to a vinyl tube (5 mm of inside diameter) was set in the canal of an intestinal segment for recording intraluminal pressure of the intestine.

After these procedures the nerve plexus along the mesenteric artery was exposed and cut near the mesenteric ganglion. The peripheral stump was held on the recording and stimulating electrode arranged in the way illustrated in Fig. 1. As a recording electrode a platinum wire (0.2 mm in diameter), as an indifferential electrode a platinum plate (1 × 1 cm) were used. The nerve was stimulated supramaximally with the square pulse synchronized with the oscilloscope time base. During repeated recordings (0.3-0.5 cps) of the antidromic evoked potentials, Ach (0.2 mg, 1 cc) was injected through the catheter.

An isolated electronic stimulator and a dual beam oscilloscope with 4-stage, differential C-R amplifier were used.

ii) Results

Antidromic evoked potentials in the mesenteric nerve (upper right in Fig. 1) contained two components, fast (over 2 m/sec) and slow (below 1 m/sec). The slow component consisted of some groups. It was not in the fast but in one or two groups of the slow that the height of the potential varied with each stage of intestinal contraction after Ach-injection. Traces in Fig. 1 illustrate changes of the heights of the potentials (The big line was from the fast component of one case. The fine ones were of the most fluctuating group of the slow component of the different cases.). The fast varied scarcely in all cases and the slow contained a group in the potential decreasing in the height during intestinal contraction.

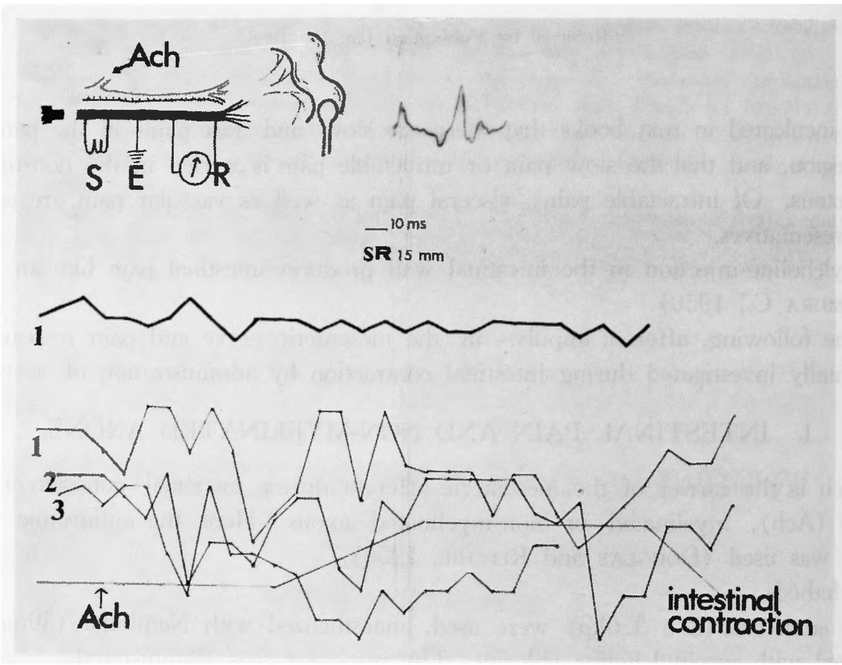

Fig. 1 The upper : Diagram showing an arrangement of electrodes and an antidromic evoked potential of the mesenteric nerve.
The middle : Change in the height of the fast component in the potential (cat No. 1).
The lower : Change in the height of the most fluctuating of the slow component in the potentials (cat No. 1, 2, 3).
The abscissa for these four changes is indicated by the course of internal pressure of the intestinal canal (intestinal contraction).

II. PATTERN OF THE IMPULSES IN THE MESENTERIC AFFERENT NERVE ACCOMPANIED BY THE INTESTINAL CONTRACTION USING ACH.

What pattern of the afferent impulses does appear in the mesenteric nerve during intestinal contraction by Ach?

i) Methods (Fig. 2)

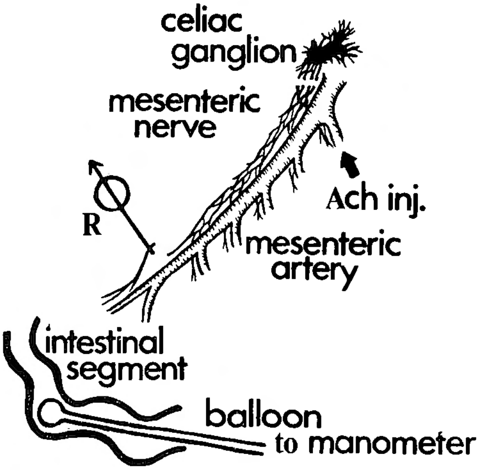

Fig. 2 Diagram showing an arrangement of the arterial canule for Ach-injection, the recording electrode (R) and the balloon in an intestinal segment.

Five adult cats (2. 0–3. 0 kg) were used. The mesenteric nerve was exposed and cut in the same way as in I. At the intestinal segment where the balloon was inserted, a branch of the nerve was exposed and cut. The peripheral stump was freed from the connective tissue or the mesenterium towards the intestinal wall. The cut end was divided into some functional single fibers, each of which was placed on the recording electrode (the same as in I.) for recording of the the afferent response of each fiber to the Ach-injection into the mesenteric artery, simultaneously with the recording of the intraluminal pressure of the intestine (Fig. 3). This investigation was repeated for all segments of the intestine.

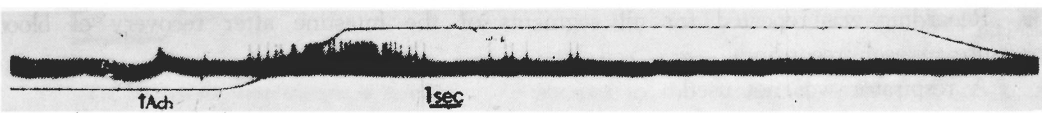

Fig. 3 Afferent discharges in a functional single fiber of the mesenteric nerve and the change in the intraluminal pressure of the intestinal segment supplied by the nerve.

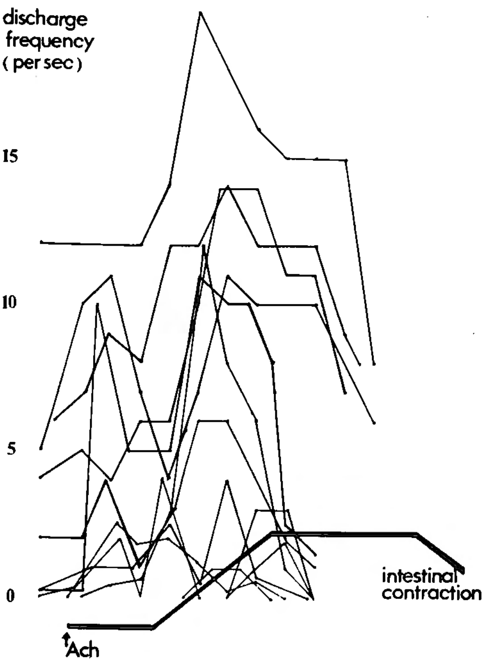

Fig. 4 Relation between discharge frequency of the mesenteric afferent and each state of the intraluminal pressure of the intestine.

ii) Results

By the injection of Ach, the intestine began to contract, and finally after continued constriction (spasm) became relaxed. This phenomenon was recorded as change of internal pressure of the balloon in the intestinal canal, which was indicated as intestinal contraction.

It were both fibers of slow and fast conducting velocity which discharged with intestinal contraction by Ach, and each was recorded without distinction. Both showed the same pattern of change in frequency of discharge. Relation between change in frequency of the discharge and change in intraluminal pressure of the intestine is illustrated in Fig. 4, in which increase in frequency is seen at the time of the injection of Ach and/or contracting state, not in spastic state.

III. PAIN RESPONSE BY INTESTINAL CONTRACTION.

Pain ; does it occur, not in the contracting state of the intestine but in the spastic state despite the peripheral afferent impulses decreasing or disappearing in the spastic state?

Of the responses of pain, change in blood pressure and respiration were investigated through the course of intestinal contraction.

i) Methods

Five adult cats (2.0-2.5 kg) were used, anaesthetized with Nembutal (20 mg/kg). The balloon and the catheter were set in the same way as in I., through the small incision of the abdominal wall with the utmost care against damaging the wall nerves. Closing of the incision was roughly done because the balloon must be removed to the next segment after every recording.

A T-type canule was set in the incised trachea, one end of which was connected to a manometer. A vinyl tube (2 mm of diameter) was inserted into the femoral artery and connected to a manometer.

Two hours after the above operations, the change in intraluminal pressure of an intestinal segment by Ach-injection was recorded simultaneously with blood pressure or respiration curve (Fig. 5).

Recording was repeated for all segments of the intestine after recovery of blood pressure in each recording.

A respirator was not used.

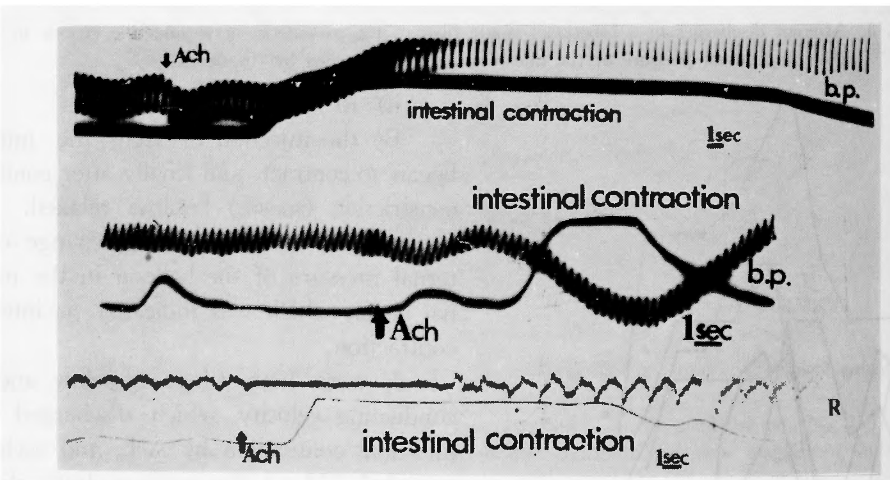

Fig. 5 Records of the intraluminal pressure of an intestinal segment with blood pressure (b.p.) or respiration curve (R).

ii) Results

Fig. 6 illustrates changes of blood pressure and respiration for every state of contraction. Each respiration curve is illustrated by drawing a line on which thick bars represent depth of the respiration by length and frequency by interval, while tiny circles indicate appearance of a deep valley in the respiration curve caused by movement or vomiting, etc.

It was observed in the figure that temporary interruption of breath or superficial

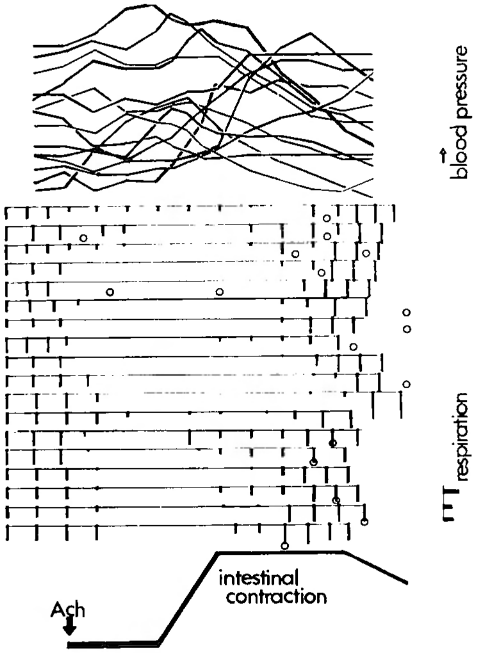

Fig. 6 Changes of blood pressure and respiration. The abscissa for these changes is indicated by each state of the intraluminal pressure of the intestine (intestinal contraction). Each state is severally named pre-contracting (the time of Ach-injection), contracting, spastic and relaxig state.

breath occurred during Ach-injection and/or contracting state while it was not produced in the spastic state.

The pattern of change in the blood pressure was rather variable.

COMMENTS

Afferent nerve fibers responding during intestinal contraction by Ach were found in both A-δ and C fibers. According to the antidromic occlusion technique, the mesenteric afferent excitation during intestinal contraction by Ach was found predominantly generated in C fibers. If no stimulation more similar to an intestinal colic than Ach-stimulation is found, it may be proposed that the affernt C fiber plays a main role in an intestinal colic. However, the proposition has some defects Some other substances to the intestinal wall produce pain like an intestinal colic and have proved to provoke also excitations of A-δ and thicker fibers as well as C fiber, and intestinal contraction does not only excite the receptors in the intestinal wall but also, by traction, the receptors in the mesenterium and the retroperitoneal tissues. In addition, it is inadequate for poor contents of A fibers to be carried in comparison of quantity of excitation with rich C fibers.

This result alone is not able to contribute to any of theories of pain, after all.

The result in II. shows the afferent volley is not generated in spastic state but in the contracting state of the intestine. The same result has been reported on the course of intestinal contraction by Ach and frequency of the discharge in the M. rectus abdominis (TSUNEKAWA K., 1959) of which contraction is said to be a pain response of the viscera.

The result shows nothing but adaptations of the afferent units during intestinal contraction. In Fig. 4, a slow adaptation is seen in the units of considerable spontaneous activity, C fibers and the ones of low spontaneous activity, A-δ fibers tend to adapt rather rapidly.

General action of Ach indicated by fall of blood pressure appeared usually in the final course of the intestinal spasm, so the neural response accompanied by rise of blood pressure during growing contraction was considered to be due to local action of Ach. However, the pattern of the change in blood pressure was not constant (III), supposedly, because of participation of the pressor reflex from the pacinian body which was said to respond to rise of pressure in the mesenteric artery caused by injection, or to ischemia in the intestine by contraction. So, blood pressure was no satisfactory indicator of pain response.

As to respiration, if there were to consider any participation of Ach in a general action, there would appear a change also in respiration not earlier after injection than in blood pressure. Change in respiration at the contracting state may be considered a pain response. And it is proposed that the intestinal pain by Ach does not appear in the spastic state but in the contracting state of the intestine when the maximum firing is observed in the peripheral intestinal afferent.

Concerning pain, there are the specificity theory, the pattern theory and other new theories. The author has the opinion ; it should be more significant that pain is produced by strong excitation of all kinds of the peripheral afferent units, though some investigators put their main emphasis on the question which kind of afferent units is activated during pain and it is indeed suggested in I. that the afferent C fiber in the intestine is predominantly activated during intestinal contraction by Ach. So, II. has the significance in the point that A-δ and C fibers fired by volleys in the contracting state of the intestine.

It is seemingly opposed to the wide-spread belief that the pain is rather generated in the hypoxic intestine by spasm, that the pain response is found synchronized with the peripheral firing in the contracting state of the intestine. The significance of the fact or the peripheral mechanism of intestinal pain, is to be discussed in some other reports with findings on intestinal pain by other pain producing substances.

The investigation in this report was done as the preliminary for other reports on intestinal pain by Ach, in order to show that pain responses are indicated by the contracting state of the intestinal contraction.

SUMMARY

i) Cats were anaesthetized with Nembutal and immobilized with succinylcholine chloride. By the antidromic occlusion technique, afferent response in the mesenteric nerve was investigated during intestinal contraction produced by acetylcholine chloride and the C fiber was found as a main carrier of the afferent excitation in the intestine.

ii) Relation between change in frequency of the mesenteric afferent impulse and change in the intraluminal pressure of the intestine by acetylcholine was investigated with the same preparation of the cats, and the curve of frequency proved to show increase and peak in the contracting state of the intestine and decrease in the spastic state.

iii) Changes in blood pressure and respiration during intestinal contraction by acetylcholine were observed. Blood pressure showed variable patterns while interruption of respiration was found in the contracting state of the intestine, not in the spastic state.

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和文抄録

腸管痛：アセチールコリンによる腸管収縮発痛効果と腸間膜神経求心性興奮の実験的観察

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熊　田　馨

猫を用いて，アセチールコリンの腸間膜動脈内注入に関して若干の観察を行なつた．

1) 腸管収縮に際して腸間膜神経の求心性興奮は伝導速度1 m/sec 以下の線維に著明にみられる．

2) アセチールコリン注入によつて，腸管は間もなく収縮をはじめ，やがて痙縮期に達して後に弛緩する．この際，腸間膜神経求心性線維は，伝導速度を問わずいづれも，腸管収縮期に発火して，痙縮期には発火せず，放電の減弱がみられるのみである．

3) 腸管収縮と呼吸，血圧の変化とを浅麻酔の猫で観察すると，血圧には一定の傾向は認めがたいが，呼吸に関して，腸管の痙縮期ではなく収縮期を中心に，呼吸停止・浅薄呼吸などの反応がみられる．