

# Observation on the Electrical and Mechanical Activities of the Monkey Ileum in Relation to Drug Actions

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## INTRODUCTION

Numerous electrophysiological studies on the intestinal smooth muscle were carried out from rodentia such as guinea-pig<sup>1,2)</sup>. Carnivora such as cat<sup>3,4,5)</sup> and dog<sup>6)</sup> was also used for the preparation of intestinal smooth muscle. Minor differences in the characteristics of intestinal smooth muscle have been reported. It is important to compare the characteristics of intestinal smooth muscle of primate to that of rodentia and carnivora for obtaining the information on the characteristics of the electrophysiological and pharmacological activity of human small intestine. In this experiment, monkey was chosen for comparison. The following study was made on the preparation of monkey ileum.

## METHODS

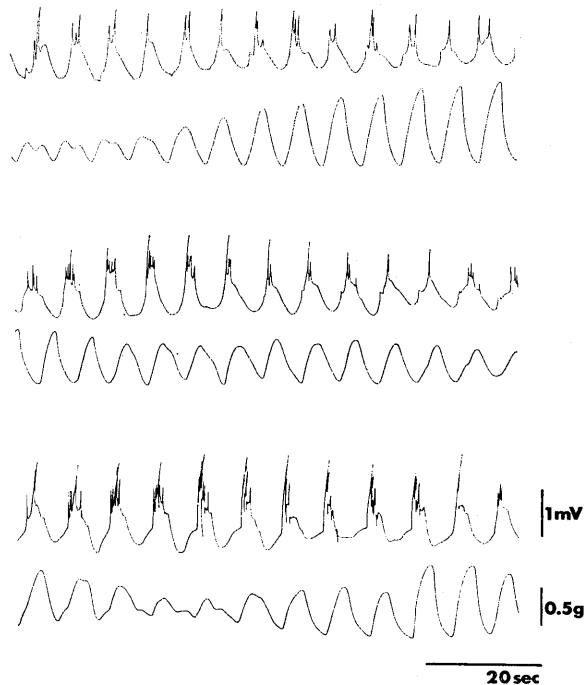
Segments of ileum were removed from adult monkey anaesthetized with nembutal and held for 1 hour or more before use in cooled Krebs solution. Segment, about 2 cm in length, of the ileum was used. The experimental procedures and the solution were same as those described in the previous paper<sup>7)</sup>. Electrical activity of the longitudinal muscle layer was recorded with pressure electrode. The following drugs were used; acetylcholine chloride, noradrenaline hydrochloride, atropine sulfate, phenoxybenzamine hydrochloride, propranolol, DCI, Adenosine triphosphate (ATP), adenosine monophosphate (AMP), 3',5'-cyclic AMP and 5-hydroxytryptamine.

## RESULTS

### *1) Spontaneous activity*

The longitudinal smooth muscle of the ileum exhibited the spontaneous,

rhythmic activity in normal solution. Electrical activity was consisted with slow wave and spikes. The slow waves generated rhythmically. Single or multiple spikes were superimposed near the peak of slow wave. Frequency of slow wave was ranged from 9/min to 12/min. The pattern of the electrical activity and its frequency were similar to those obtained from the longitudinal muscle layer of the cat small intestine. The slow wave with spikes was corresponded with phasic contraction along the longitudinal direction of the segment. Magnitudes of the phasic contraction were irregular in many preparations but some were regular. Simultaneous recordings of electrical and mechanical activities were shown in Fig. 1.

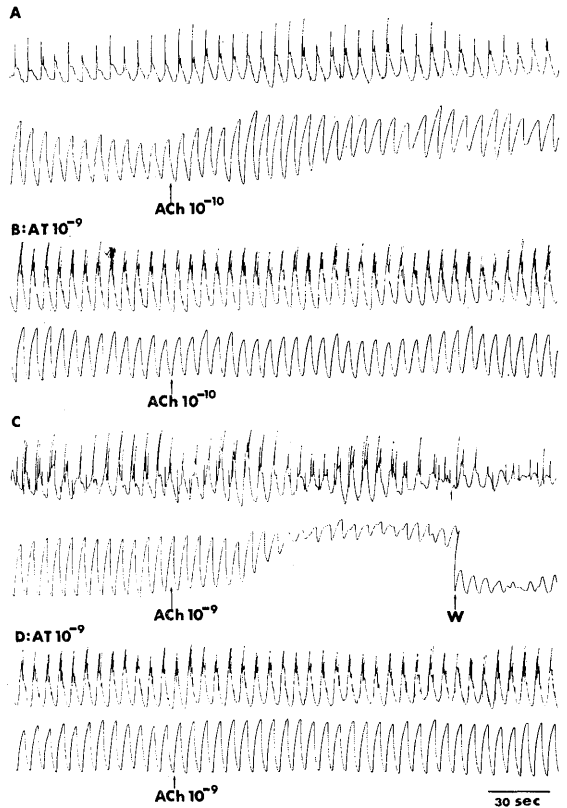


**Fig. 1.** Examples of simultaneous recordings of the electrical (upper) and mechanical (lower) activities of the monkey ileum.

Spontaneous electrical and mechanical activities were obtained from the longitudinal muscle layer of the segment.

## 2) Effects of drugs

Acetylcholine potentiated the mechanical activity. When lower concentrations of acetylcholine (final concentration;  $10^{-12}$ - $10^{-11}$  g/ml) added into the external media, no observable changes in electrical and mechanical activities were obtained. At a concentration of  $10^{-10}$  g/ml, small contracture was produced. Atropine ( $10^{-9}$  g/ml) blocked the potentiatory effect of acetylcholine ( $10^{-10}$ - $10^{-9}$  g/ml). Fig. 2 shows the excitatory effect of acetylcholine and the inhibition caused by atropine on acetylcholine action.



**Fig. 2.** Effect of acetylcholine on the electrical (upper) and mechanical (lower) activities of the monkey ileum.

A; Acetylcholine (ACh)  $10^{-10}$  g/ml. Drug was added at the arrow.

B; Acetylcholine  $10^{-10}$  g/ml after treatment with atropine (AT)  $10^{-9}$  g/ml.

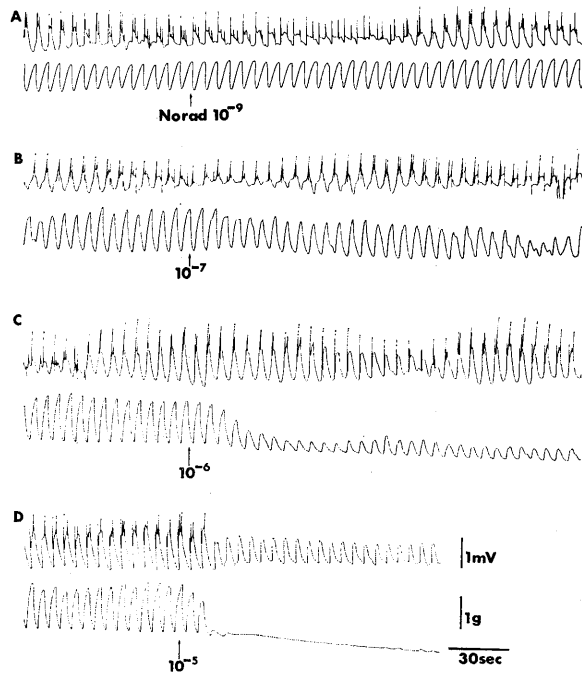
C; Acetylcholine  $10^{-9}$  g/ml. W indicates the washing out by normal solution.

D; Acetylcholine  $10^{-9}$  g/ml after treatment with atropine  $10^{-9}$  g/ml.

Calibration; 1mV and 1g.

Noradrenaline inhibited the spike and mechanical activities as shown in Fig. 3. Lower concentrations of noradrenaline (up to  $10^{-8}$  g/ml) had no considerable effect on the contractile activity. At a concentration of  $10^{-7}$  g/ml, phasic contraction was decreased gradually but the frequency was not changed. No observable change in the electrical activity was detected. Higher concentration of noradrenaline ( $10^{-6}$  g/ml) produced stronger inhibition on the phasic contraction, that is, immediate abolition of phasic contraction was produced and the tonus level was also decreased. In this solution, spikes were also abolished immediately. However slow waves were generated continuously as shown in Fig. 3.

Phenoxybenzamine ( $10^{-5}$  g/ml) and propranolol ( $10^{-5}$  g/ml) showed minor inhibitory effect on the phasic contraction. After 10-20 min in phenoxybenzamine ( $10^{-5}$  g/ml) or propranolol ( $10^{-5}$  g/ml), the inhibitory action of noradrenaline ( $10^{-6}$  g/ml) was partially depressed by these blockers. DCI ( $10^{-5}$  g/ml) also inhibited the depressor effect of noradrena-



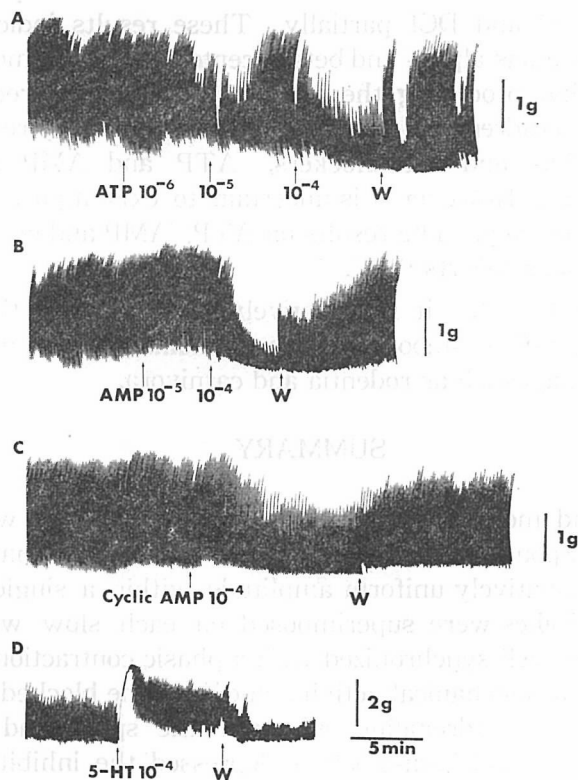
**Fig. 3.** Effect of noradrenaline on the electrical (upper) and mechanical (lower) activities of the monkey ileum.

- A; Noradrenaline (Norad)  $10^{-9}$  g/ml. Drug was added at the arrow.  
 B; Noradrenaline  $10^{-7}$  g/ml, C; Noradrenaline  $10^{-6}$  g/ml  
 and D; Noradrenaline  $10^{-5}$  g/ml.

line ( $10^{-6}$ g/ml) partially.

ATP and AMP exhibited the inhibitory action on the phasic contraction (Fig. 4). At concentration of  $10^{-4}$  g/ml of ATP, the magnitude of phasic contraction was gradually decreased. AMP at a concentration of  $10^{-4}$  g/ml also inhibited the phasic contraction. When cyclic AMP ( $10^{-4}$  g/ml) added into the external media, weaker inhibition on the contractile activity was observed, that is, slower decrease in the magnitude of phasic contraction was obtained.

5-hydroxytryptamine ( $10^{-7}$ - $10^{-4}$  g/ml) was also examined. Higher concentration ( $10^{-4}$  g/ml) of 5-HT produced the contracture (Fig. 4). However, phasic contractions superimposed on the contracture were still observed. This contracture was gradually reduced and returned to the original level after 15 min.



**Fig. 4.** Effects of ATP, AMP, cyclic AMP and 5-HT on the mechanical activity of the monkey ileum.

A; ATP  $10^{-6}$ - $10^{-4}$  g/ml. Each drug was added at the arrow. W indicates the washing out by normal solution. B; AMP  $10^{-5}$  and  $10^{-4}$  g/ml

C; Cyclic AMP  $10^{-4}$ g/ml and D; 5-HT $10^{-4}$  g/ml.

## DISCUSSION

Slow wave and spike type potential was obtained by using pressure electrode. This pattern was very similar to that of cat intestinal smooth muscle.<sup>3,5,7,8)</sup> Frequency of slow waves was also similar to that of cat small intestine<sup>3,5,7,8)</sup>. Since the longitudinal muscle layer of ileum of monkey was thinner, leading the electrical activity by using pressure electrode was a little difficult. Phasic contraction of the longitudinal muscle layer recorded simultaneously was good synchronized with spike activity. The effects of some drugs on the electrical and mechanical activities were also similar to that obtained by other animals<sup>9,10)</sup>. Acetylcholine induced the potentiation of the activity and atropine blocked the response to acetylcholine. However it seems that the longitudinal muscle very sensitive to acetylcholine. Catecholamine such as noradrenaline produced the inhibitory action and this action was blocked by phenoxybenzamine, propranolol and DCI partially. These results indicate that the longitudinal muscle has alpha- and beta-receptors as usual smooth muscles. It is interesting that producing the inhibitory action was required higher concentration of noradrenaline and that weaker inhibitory responses were observed in alpha- and beta-blockers. ATP and AMP inhibited the mechanical activity. However it is uncertain to exist a purinergic fiber in the ileal wall of monkey. The results on ATP, AMP and cyclic AMP also agreed with previous reports<sup>5,11,13)</sup>.

From obtained results, it is tentatively concluded that the characteristics of the longitudinal smooth muscle of monkey ileum was similar to that of other animals such as rodentia and carnivora.

## SUMMARY

Electrical and mechanical activities of monkey ileum were recorded simultaneously. Spontaneous, rhythmic slow waves which have a duration of seconds and a relatively uniform amplitude within a single preparation were obtained. Spikes were superimposed on each slow wave and the spike activity was well synchronized with a phasic contraction. Acetylcholine potentiated the mechanical activity and atropine blocked the response to acetylcholine. Noradrenaline inhibited the spike and mechanical activities and alpha- and beta-blockers depressed the inhibitory action of noradrenaline. ATP, AMP and cyclic AMP produced the inhibitory action on the mechanical activity. 5-HT rised the contactile activity. The results of this study indicate that the electrical activity of the longitudinal muscle of the monkey ileum was similar to those obtained from the intestinal

muscle of rodentia and carnivora. Evidences for the presence of both type receptors were available.

#### ACKNOWLEDGEMENT

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