612.328:612.898

THE SYMPATHETIC INNERVATION OF THE STOMACH.

II. The effect of stimulation of the peri-arterial nerves on the stomach and small intestine.

By B. A. McSWINEY and J. M. ROBSON.

(*Department of Physiology, University of Leeds.*)

McSwiney and Robson [1929 *a*] reported preliminary experiments demonstrating the response of the smooth muscle of the stomach to stimulation of the peri-arterial nerves. In a recent paper Brown, McSwiney and Wadge [1930] described the effects on the stomach of stimulation of the thoracic sympathetic trunk. They showed that stimulation with a weak faradic current at a frequency of 1 per sec. caused contraction, while stimulation with a tetanizing current brought about relaxation. These authors concluded that the body of the stomach receives motor and inhibitor fibres from the sympathetic chain, which can be influenced to a greater or lesser degree by the varying types of stimulation. Finkleman [1930] has recently described an inhibitory nerve smooth muscle preparation, and points out that parallel effects are produced by nervous and chemical inhibition.

This paper deals with the effects of stimulation of the vagus and peri-arterial nerves supplying smooth muscle preparations, and affords further evidence to demonstrate that motor and inhibitor effects may be obtained from the smooth muscle of the stomach on stimulation of sympathetic nerves.

Method.

Rabbits and cats were used. Rabbits were killed by a blow on the occiput, while cats were anæsthetized with ether. The stomach was removed from the animal, the coronary artery identified and dissected free from the surrounding tissue. The division supplying the body of the stomach was separated from the main artery, and the strip of muscle supplied removed free of mucous membrane. A strip of fundic muscle supplied by the main artery was also obtained. Preparations of small intestine with the mesenteric arteries have also been made.

The preparations obtained were placed in warm oxygenated solution and then suspended in a bath of Ringer-Locke or Tyrode solution. Experiments were made at 37° C., bubbling and hydrogen-ion concentration of the bath being kept constant.

Optical methods of registration were employed to obtain accurate measurement of the latent periods, but the majority of records were made on smoked paper, using light balanced levers. A Lewis contact breaker and induction coil were used, and the rate of stimulation varied from one break shock in 2 sec. to fifty make and break shocks per sec. The duration of the stimulus was regulated by an oil dash pot: time intervals shown on tracings, except Fig. 4, equal 10 sec.

Experimental results.

To stimulate the peri-arterial nerves the artery was laid on platinum electrodes. The response of the stomach muscle to faradization (fifty make and break shocks per sec.) was not constant, as in some experiments the muscle contracted, while in others relaxation was recorded. These effects were clearly not related to the region from which the strips were obtained, as similar results were recorded with preparations of the body and fundic regions of the stomach.

In view of these results further experiments were made to determine the effects of frequency and strength of current on the response of the muscle. It was observed that, if the muscle relaxed on stimulation of the peri-arterial nerves with a faradic current, contraction could usually be obtained by reducing the rate of stimulation. In Fig. 1 relaxation was obtained with frequencies varying from fifty make and break shocks to twenty break shocks per sec., but on stimulation of the peri-arterial nerves with four break shocks per sec. the muscle contracted. In Table I the results of some of the experiments are tabulated. The table shows the number of stimuli required to produce contraction and relaxation in different experiments.

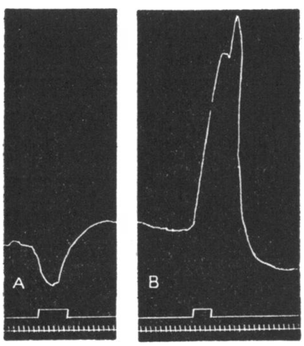

Fig. 1. Cat, fundus. A. Twenty break shocks per sec. cause relaxation. B. Four break shocks per sec. cause contraction.

It will be observed that in Exp. 7 four stimuli per sec. caused relaxation, while one break shock produced contraction.

TABLE I. Effect of frequency of stimuli.

No.	Contraction Break shocks per sec.	Relaxation Break shocks per sec.
1	12	20
2	12	45
3	4	21
4	4	45
5	4	12
6	4	45
7	1	4

Decreasing the strength of the current while keeping the frequency constant was also found to reverse the response of the muscle. The following example demonstrates the effect. Stimulation of the peri-arterial nerves with twelve break shocks per sec. using 1 ampere in the primary circuit caused contraction. Further stimulation of the nerves, using the same strength of current but with twenty break shocks per sec., caused relaxation. On reducing the current in the primary circuit from 1 to 0·4 ampere, using twenty break shocks per sec., contraction was again recorded. Reversal of the response could therefore be obtained by varying the frequency or strength of current.

A reversal of the response could also be obtained by varying the duration of faradic stimulation. Faradic stimulation of the nerves for periods of 0·07 to 2 sec. was found to cause contraction, but, as previously shown, prolonged faradic stimulation produced relaxation. A single contraction lasted 20 to 50 sec. If the nerve was again tetanized towards the end of the rising phase of the contraction, the contraction was prolonged, while repeated tetanization of the nerve at intervals of 20 to 50 sec. caused the contraction to be sustained.

A sustained contraction is demonstrated in Fig. 2, the nerve fibres being stimulated with a faradic current for periods of 1 sec. at intervals of 15 to 20 sec.

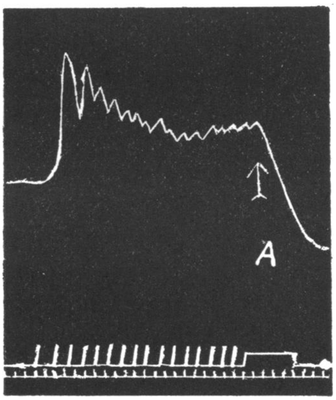

Fig. 2. Cat, fundus. Stimulation with a faradic current for periods of 1 sec. at intervals of 15 to 20 sec. At A continued faradic stimulation causes relaxation.

In order to obtain further information of the character of the response to stimulation of the peri-arterial nerves, the latent periods have been recorded and compared with the latent period obtained on stimulation of the vagus nerve.

TABLE II. Latent periods.

	Average	Longest	Shortest	No. of observations
Peri-arterial stimulation:				
Contraction	4·8	9·2	1·4	36
Relaxation	3·3	4·2	2·3	24
Vagus stimulation:				
Contraction	0·79	1·2	0·4	60

It will be seen that the latent period of contraction resulting from stimulation of the peri-arterial nerve varies between 1·4 and 9·2 sec.: the average of twelve experiments being 4·8 sec. The latent period of the response to vagus stimulation in the same preparation was much lower, and compared favourably with the results previously recorded by McSwiney and Robson [1929 *b*]. The rate and duration of stimulation appeared to have no appreciable effect on the latent period, as is seen in an experiment where the period of stimulation varied between 0·1 and 1·7 sec., the latent period remaining constant at a value of 5·5 sec. The latent period of relaxation was also determined and ranged between 2·3 and 4·2 sec., the average of eight experiments being 3·3 sec.

Further information of the character of augmentor and inhibitor responses was obtained from the action of the drugs, ergotoxine and atropine. Addition of ergotoxine, 0·6 to 1 mg., to the bath (250 c.c.) abolished the motor response, but relaxation could still be obtained by appropriate stimulation of the peri-arterial nerves. It must be mentioned that it was usually necessary to employ large doses of the drug, 5 to 10 mg., to obtain reversal, and occasionally it was found impossible to obtain complete motor paralysis even with these doses. Addition of 0·1 mg. of atropine was also found to inhibit the contraction of the muscle, which agrees with the findings previously recorded by Carlson, Boyd and Pearcey [1922].

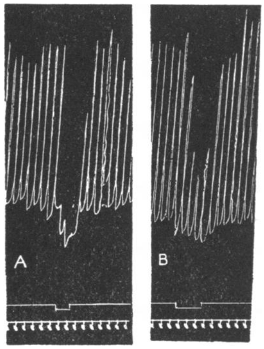

Fig. 3. Rabbit, jejunum.
A. Faradic stimulation.
B. Fifteen shocks per sec.

In order to study and compare the reactions of smooth muscle of different organs, a preparation of a strip of small intestine supplied by a branch of the superior mesenteric artery was made. Faradic stimulation of the peri-arterial nerves caused inhibition of rhythmic movement and relaxation of the muscle. It was observed that the frequency, strength and duration of stimuli did not affect the nature of the response; inhibition being recorded if the stimulus was adequate. Increase in rate or strength of stimulus over minimal value was found, however, to prolong the duration of the inhibition. Finkleman [1930] occasionally obtained contraction when the preparation was first set up by stimulating the mesentery with two to four induction shocks per sec.

Discussion.

The experiments described with isolated mammalian preparations of smooth muscle agree with the observations made by Brown, McSwiney and Wadge [1930] of the effect on the stomach of stimulation of the thoracic sympathetic trunk in the intact animal. Contraction, inhibition of rhythmic movement or relaxation of the muscle have each been recorded on appropriate stimulation of the peri-arterial nerves. Care was taken in the experiments to demonstrate that the response of the muscle was due to excitation of nerve fibres, and not to spread of current from the point of stimulation. After application of a thread ligature to the artery between the electrodes and the muscle, stimulation had no further effect.

It has been pointed out by McCrea [1924] that the sympathetic nerves to the muscle are derived from the splanchnic nerves and take origin from the cœliac plexus. The majority of nerve twigs accompany the branches of the cœliac artery, though a few run with the inferior phrenic arteries. Thus, the main nerves associate themselves with the left gastric or coronary artery, and are reinforced in the neighbourhood of the cardia by twigs which accompany the inferior phrenic artery. Sympathetic and vagal fibres are stated to be intermingled in the peripheral distribution, and it is possible that the effects described might be due to stimulation of mixed fibres.

It is suggested, however, that the response of the muscle is due to stimulation of sympathetic nerve fibres, as in the first place the muscle will only contract if the appropriate stimulus is applied. This however does not apply to the vagus as, in previous experiments, McSwiney and Robson [1929 *b*] have shown that contraction of the muscle is recorded when the vagus nerve is stimulated with frequencies ranging from one break shock in 2 sec. to fifty make and break shocks per sec. Secondly, inhibition of movement and relaxation of the muscle were only obtained in vagus nerve preparations after addition of atropine. Thirdly, the latent periods recorded for two sets of nerves are of different orders: with vagal stimulation the average latent period equalled 0·8 sec., with sympathetic stimulation the period varied from 1·4 to 9·2 sec. for contraction, and 2·3 to 4·2 sec. for relaxation. Again, if the vagus and peri-arterial nerves are stimulated simultaneously two contractions were obtained (Fig. 4). Owing, apparently, to the different latent periods, the contraction due to stimulation of the vagus nerve was followed by a contraction resulting from stimulation of the peri-arterial nerves. Lastly, the evidence obtained with ergotoxine lends support to the conclusions.

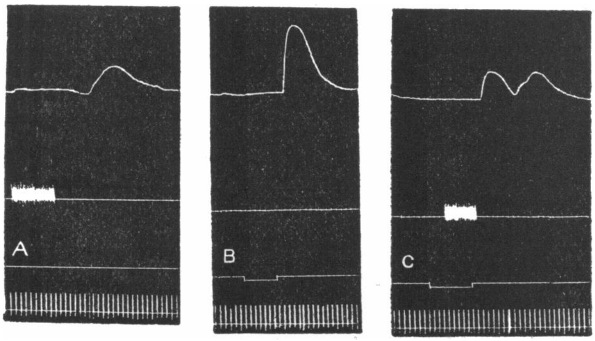

Fig. 4. Cat, fundus. A. Faradic stimulation of peri-arterial nerves for a period of 0·5 sec. B. Stimulation of vagus nerve with single break shock. C. Simultaneous stimulation of peri-arterial and vagus nerves. Time intervals = 1 sec.

It would appear, therefore, that it is possible to demonstrate in the isolated muscle preparations, as in the intact animal, that the smooth muscle of the stomach, fundus and body receive fibres which may cause contraction or relaxation of the muscle. It is clear that the response to sympathetic stimulation is not due to vasomotor changes nor dependent on the existing state of tonus, as relaxation and contraction have been repeatedly demonstrated in the same muscle strip without any apparent change of condition. There are many points of analogy between these findings and those recently described by Dale and Gaddum [1930], but it is hardly profitable to discuss the points at length at this stage of the investigations.

Summary.

Isolated strips of the smooth muscle of the stomach and small intestine innervated by peri-arterial nerves were prepared. The reaction of the gastric muscle depended on the type of stimulation employed. Stimulation of the nerves with frequencies of one to twelve break induction shocks per sec. caused contraction of the muscle; with twenty to fifty shocks per sec. relaxation was obtained. Reversal effects were also recorded by varying either the strength of current or the duration of

faradic stimulation. The motor response was abolished by addition of ergotoxine or atropine. The movements of the intestine were inhibited by all types of stimulation. The latent periods of contraction and relaxation have been recorded and compared with the latent periods obtained on stimulation of the vagus nerve. Evidence is put forward to show that the motor and inhibitor response is due to stimulation of sympathetic fibres conveyed in the peri-arterial nervous network.

The expenses of the researches described in Part I and Part II have been defrayed in part by a grant from the Government Grant Committee of the Royal Society.

REFERENCES.

Brown, G. L., McSwiney, B. A. and Wadge, W. J. (1930). *J. Physiol.* **70**, 253.
Carlson, A. J., Boyd, T. E. and Pearcey, J. F. (1922). *Amer. J. Physiol.* **61**, 14.
Dale, H. H. and Gaddum, J. H. (1930). *J. Physiol.* **70**, 109.
Finkleman, B. (1930). *J. Physiol.* **70**, 145.
McCrea, E. D. (1924). *J. Anat.* **59**, 18.
McSwiney, B. A. and Robson, J. M. (1929 *a*). *Amer. J. Physiol.* **90**, 450.
McSwiney, B. A. and Robson, J. M. (1929 *b*). *J. Physiol.* **68**, 124.