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# NERVE-MEDIATED EXCITATION OF THE TAENIA OF THE GUINEA-PIG CAECUM

By G. CAMPBELL

*From the Department of Zoology, University of Melbourne, Parkville N. 2, Victoria, Australia*

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SUMMARY

1. A study was made of the responses of the isolated taenia of the guinea-pig caecum to stimulation of the intramural nerves.

2. Four types of response are described, made up of a contraction and/or a relaxation occurring during stimulation and an after-contraction occurring when stimulation is stopped.

3. A delayed relaxation which sometimes occurred at the end of stimulation is also described.

4. Atropine usually abolished the contractions occurring during stimulation. After-contractions either appeared or were increased in amplitude in the presence of atropine, and delayed relaxations were abolished.

5. The anti-cholinesterase drug neostigmine could convert the response during stimulation from a relaxation to a contraction. After-contractions were often abolished by neostigmine and delayed relaxations appeared.

6. It is concluded that the contractions which occurred during stimulation were mediated by cholinergic nerves. The after-contraction appears to be a rebound phenomenon, following the hyperpolarization of the muscle caused by stimulation of the inhibitory nerves. It is suggested that the delayed relaxation is caused by the effects of persisting inhibitory transmitter substance on cells which do not undergo rebound excitation.

## INTRODUCTION

A study of the excitatory innervation of the taenia from the guinea-pig caecum has proved difficult, for two reasons. First, no drug has been found which abolishes specifically the responses to stimulation of the intramural inhibitory nerves (G. Burnstock, G. Campbell & M. J. Rand, 1966, and unpublished results). The effect of stimulation of the excitatory nerves as they run in the taenia must, therefore, be complicated by the simultaneous stimulation of the inhibitory nerves. Secondly, stimulation of the inhibitory nerves can cause hyperpolarization of the muscle, followed by

a rebound depolarization and acceleration of action potential firing (Bennett, 1966*a*). It is important to be able to distinguish between this rebound excitation and excitation resulting from the stimulation of excitatory nerves.

This paper is a study of the interaction between the effects of stimulation of the excitatory and the inhibitory nerves in the taenia. Various responses to stimulation are described and their interpretation in terms of electrical activity of the smooth muscle cells is discussed.

## METHODS

Guinea-pigs of either sex were stunned and bled to death. Taenia strip preparations and caecal wall preparations were dissected as described previously (Burnstock *et al.* 1966*a*). The preparations were suspended in a 40 ml. organ-bath filled with modified Krebs solution (Bülbring, 1953), bubbled with 95 % $O_2$ and 5 % $CO_2$. The temperature of the solution was maintained at between 35 and 37° C. Movements of the preparations were recorded with an isotonic frontal-writing lever, which exerted a load of about 1 g and recorded with approximately sixfold magnification on a smoked drum.

Taenia strips were stimulated through two platinum ring electrodes placed around the tissue, allowing free movement of the muscle. Caecal wall preparations were mounted on a Perspex holder, with the flap of caecal wall which is attached to the taenia in this preparation lying over two platinum wire electrodes in the holder. A Grass Model 5 stimulator was used to deliver monophasic square-wave pulses at various frequencies. The pulse duration was fixed at 1 msec throughout this work. Strengths of stimulation were used which caused approximately maximal responses. Bursts of stimulation lasting for 10 sec were given at intervals of more than 4 min.

The drugs used were: acetylcholine chloride; atropine sulphate; neostigmine methylsulphate.

## RESULTS

### *Types of response to stimulation of intramural nerves*

Stimulation of the nerves within the taenia or an attached flap of caecal wall caused a variety of responses of the taenia. The following description of the responses is based on observations made on taenia strip and caecal wall preparations which had not been treated with any drugs.

For ease of discussion, the responses are classified into four types. It must be emphasized that the types are not discrete, but are convenient divisions of a graded series of responses. As well as the four types, a delayed relaxation, which persisted for several minutes after stimulation, was seen. Since the delayed relaxation was not specifically associated with any of the four types of responses, it is described in a separate section.

*Type* 1 *responses.* The first response seen was a contraction, starting within 0·5–3 sec of the onset of stimulation. Stimulation with 1 pulse/sec or less caused an incompletely fused tetanus to appear (Fig. 1*a*). Stimulation with 2 pulses/sec or more caused a smooth contraction which was maintained throughout the 10 sec period of stimulation. In some pre-

parations, the contraction continued to increase throughout the period of stimulation (Fig. 1*b*). In other preparations, the contraction reached a maximal level after a few seconds of stimulation and this level was maintained until stimulation was stopped (Fig. 1*c*). In a few preparations, especially those with low tone, spontaneous contractions appeared during the contractions caused by stimulation.

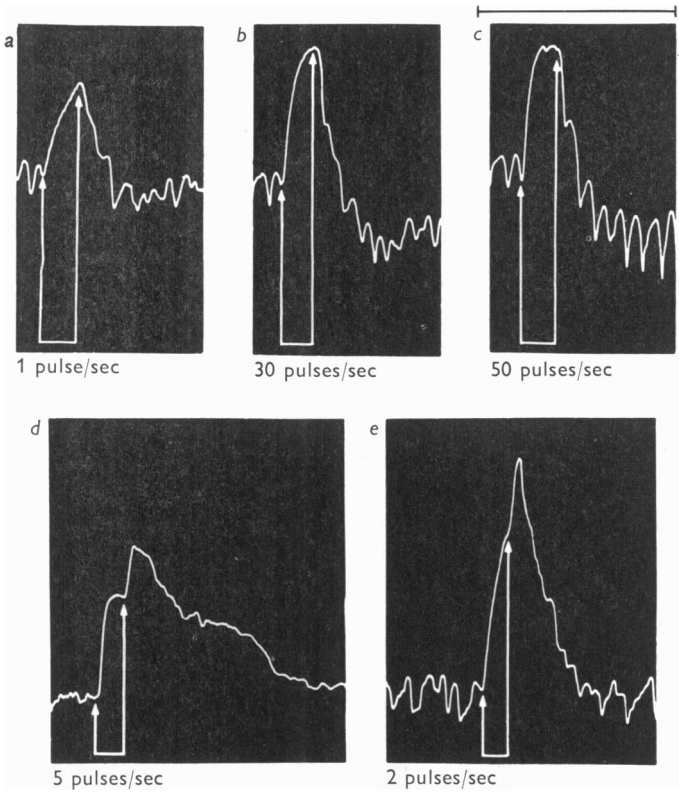


Fig. 1. Types 1 and 2 responses in taenia strip preparations. Type 1 responses are shown in panels *a*, *b* and *c*, type 2 in panels *d* and *e*. Note the partially fused tetanus in *a* and the delayed relaxation in *b* and *c*. For further explanation see the text. The periods of stimulation of the taenia with the frequencies indicated are shown by the arrows. Time marker, 1 min.

The muscle started to relax 1–2 sec after stimulation was stopped. The relaxation proceeded back to or below the control level of tone.

*Type 2 responses.* The first response to stimulation was a contraction which appeared 1–3 sec after the start of stimulation. The response differed from type 1 in one respect; 1 or 2 sec after stimulation was stopped, an after-contraction appeared (Fig. 1*d*). The amplitude of the

after-contraction was often greater than that of the contraction which occurred during stimulation.

In those preparations in which the contraction continued to increase throughout the period of stimulation, the after-contraction could still be distinguished because the rate of contraction increased at the end of stimulation (Fig. 1*e*). The after-contraction reached its maximal level within about 10 sec of the end of stimulation.

*Type 3 responses.* The first response to stimulation was a relaxation which started after about 1 sec of stimulation. After a further 1 sec or more of stimulation, the muscle started to contract. An after-contraction, as described for type 2 responses, was invariably seen.

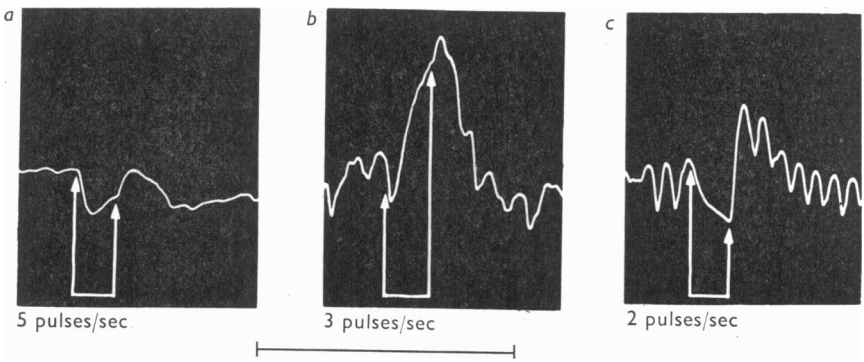


Fig. 2. Types 3 and 4 responses in taenia strip preparations. Type 3 responses are shown in panels *a* and *b*, type 4 in *c*. Note the small delayed relaxation in *a*. For further explanation see the text. The periods of stimulation of the taenia with the frequencies indicated are shown by the arrows. Time marker, 1 min.

The relative amplitudes of the relaxation and the contraction which occurred during stimulation and the time at which the contraction started were variable. In some cases, the contraction was not large enough to restore the muscle to its former length during stimulation (Fig. 2*a*). In other cases, the contraction was much larger than the relaxation (Fig. 2*b*).

*Type 4 responses.* The muscle relaxed throughout the period of stimulation after a latent period of about 1 sec. When stimulation was stopped, the muscle contracted rapidly. This after-contraction usually proceeded to a level above the control tone (Fig. 2*c*), but did not do so in preparations with very high tone. Generally, the higher the tone of the preparation, the more rounded and less pronounced the after-contraction became. In muscles with very low tone, type 4 responses consisted of a cessation of the spontaneous activity, but a marked relaxation was not possible. In these preparations, the only marked response to stimulation was the after-contraction. This is shown for an atropinized preparation in the first two

panels of Fig. 3. The amplitude of the after-contraction increased as the frequency of stimulation was increased (Fig. 3).

*Occurrence of the response types.* Of all the untreated taenia strip preparations used, about 60% gave type 3 or type 4 responses to stimulation with all frequencies between 1 and 50 pulses/sec. Type 4 responses were uncommon in the higher portion of this frequency range. The remaining preparations showed type 1 or type 2 responses over at least a part of the range of frequencies. Types 1 and 2 responses were most common when preparations were stimulated with 1 or 2 pulses/sec or with frequencies greater than about 20 pulses/sec.

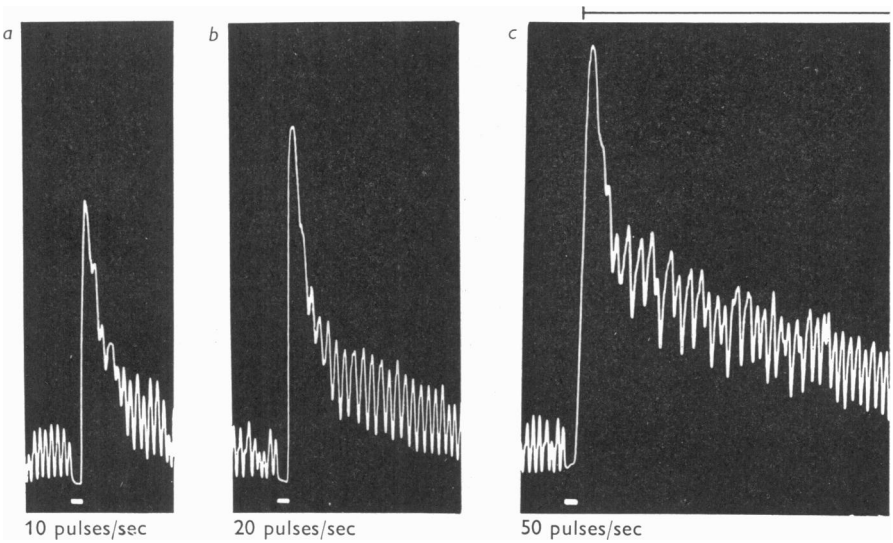


Fig. 3. Responses to stimulation of a taenia strip preparation with low tone. Stimulation with 10 pulses/sec in *a* and 20 pulses/sec in *b* causes type 4 responses. Stimulation with 50 pulses/sec in *c* causes an inhibition of the spontaneous activity but there is a slight contraction during stimulation, the response being type 3. Note the very large after-contractions. Since the preparation was treated with atropine ($10^{-7}$ g/ml.), the after-contractions are probably not caused by acetylcholine. The periods of stimulation of the taenia are shown by the white bars. Time marker, 5 min.

Stimulation of a flap of caecal wall caused type 3 or type 4 responses of the taenia over the whole frequency range in less than a quarter of the preparations examined. Most of the remaining preparations showed type 2 or, more rarely, type 1 responses over the whole range. A few preparations showed type 1 or type 2 responses over only part of the frequency range.

*Delayed relaxations*: When type 1, 2 or 3 responses of the taenia were obtained with frequencies of stimulation of less than 5 pulses/sec, the recovery from the contraction or after-contraction usually proceeded only as far as the former tone of the muscle (Fig. 1*d*, *e*). When

frequencies greater than 5 pulses/sec were used, the relaxation during recovery usually passed below the former level of tone (Figs. 1*b*, *c*; 4; 5*b*). This relaxation is termed a delayed relaxation since inhibitory responses of such a long duration were not observed in atropinized preparations of taenia (Burnstock *et al.* 1966*a*). Delayed relaxations were also seen following some type 4 responses. For instance, the response shown in the second panel of Fig. 5*c*, recorded from a preparation treated with neostigmine, consists of a type 4 response followed by a small after-contraction and then a delayed relaxation. The delayed relaxation reached its maximum within 40 sec of the end of the period of stimulation. The muscle then contracted back towards the control level of tone. Up to 4 min elapsed before the former tone was attained. The amplitude and the duration of the delayed relaxation generally increased as the frequency of stimulation was raised.

### *The effects of drugs on the response types*

*Atropine.* The application of atropine ($10^{-8}$–$10^{-7}$ g/ml.) to preparations showing type 1 or type 2 responses converted their responses to type 3 or type 4. The conversion was too rapid to allow close examination of the changes which occurred in the form of the responses. Figure 4 illustrates the conversion of a type 2 response of a taenia strip preparation, caused by stimulation with 30 pulses/sec, to a type 4 response. Burnstock *et al.* (1966) did not observe responses of types 1 or 2 in atropinized preparations.

In those preparations which normally showed type 3 or type 4 responses, the addition of atropine usually increased the amplitude of the relaxation during stimulation. The greatest observed increase in amplitude of a type 4 response was 45%, but in two preparations atropine caused no change in the response amplitude. Type 3 responses were often, but not always, converted to type 4 by atropine. Type 3 responses in the presence of atropine usually consisted of a large relaxation with only a relatively small amount of contraction occurring during stimulation. However, in a few preparations the relaxation was small compared with the contraction during stimulation. Increasing the concentration of atropine to $10^{-6}$ g/ml. did not affect these contractions. Contraction of atropinized preparations during stimulation was more common when the preparations were stimulated with frequencies greater than about 10 pulses/sec. Such a response in the presence of atropine has been illustrated previously (Fig. 4*d* of Burnstock *et al.* 1966).

When the amplitude of the relaxation in types 3 and 4 responses was increased by atropine, the amount by which the after-contraction passed above the control level of tone was also increased. It should also be noted that the conversion of type 1 responses to type 3 or type 4 by atropine is accompanied by the appearance of an after-contraction.

Delayed relaxations were always abolished by atropine. The abolition occurred whether the final response was type 3 or type 4. Figure 4 illustrates such an abolition in a preparation, the responses of which were converted to type 4.

*Neostigmine.* Neostigmine ($10^{-8}$ g/ml.) increased the amplitude and the duration of contractions of the taenia caused by acetylcholine (Fig. 5*a*).

In the presence of neostigmine ($5 \times 10^{-9}$–$10^{-8}$ g/ml.), inhibitory responses which occurred during stimulation of taenia strip or caecal wall preparations were usually reversed to contractions during stimulation (Fig. 5*b*). Type 4 responses were converted, in sequence, to type 3, type 2 and then type 1 responses. The time taken for reversal to occur and the degree of reversal (i.e. the nearness of the ultimate response to type 1) were variable.

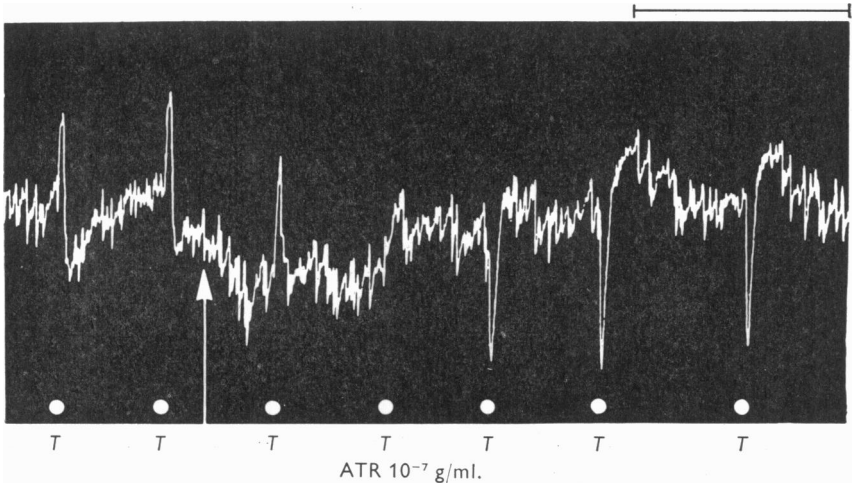


Fig. 4. Effects of atropine on responses to stimulation of a taenia strip preparation. Stimulation of the taenia with 30 pulses/sec (*T*, at the dots) initially caused type 2 responses with a slight after-contraction. After the application of atropine (ATR, $10^{-7}$ g/ml.), the responses are converted to type 4, with a slow after-contraction. Note the abolition of the delayed relaxation. Time marker, 10 min.

The responses of the taenia strip preparation illustrated in Fig. 5*b* to stimulation with 15 and 30 pulses/sec were reversed from type 4 to 2 within 20 min of the application of neostigmine ($5 \times 10^{-9}$ g/ml.). However, in some preparations the relaxations during stimulation were only reduced in amplitude by this concentration of neostigmine. Figure 5*c* illustrates one of these preparations. In this taenia strip preparation, the type 4 responses were converted, over the course of 1 hr, to type 3 responses. In similar preparations, reversal of the response during stimulation was not seen until the concentration of neostigmine was raised to $5 \times 10^{-8}$g/ml. At this concentration of neostigmine, the tone of the preparations was increased considerably.

Type 1 responses were not clearly increased in amplitude by neostigmine. However, it appeared that the rise of tone caused by neostigmine tended to depress excitatory responses. Certainly, high concentrations of

neostigmine ($5 \times 10^{-8}$ g/ml.) caused large tone rises and depressed type 1 responses.

The main effect of neostigmine on type 2 responses was to decrease the amplitude of the after-contraction. In many preparations, the after-contraction disappeared entirely and the response became type 1.

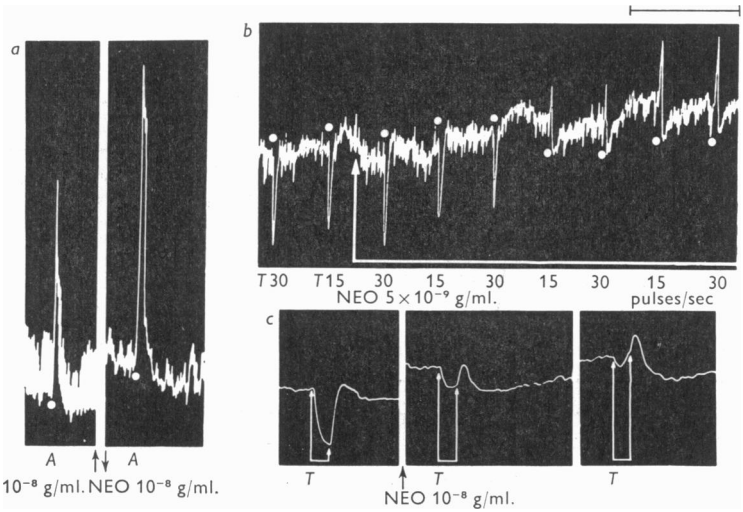


Fig. 5. Effects of neostigmine on responses of taenia strip preparations. (*a*) Neostigmine (NEO, $10^{-8}$ g/ml., left in the bath for 10 min and washed out 10 min before the start of the second panel) increased the amplitude of responses to acetylcholine (*A*, $10^{-8}$ g/ml., applied at the dots for 1 min). (*b*) Neostigmine (NEO, $5 \times 10^{-9}$ g/ml.) converted type 4 responses to stimulation of the taenia with 15 or 30 pulses/sec (T 15, T 30, at the dots) into type 2 responses. Note the appearance of delayed relaxations. (*c*) In the first panel, stimulation of the taenia with 15 pulses/sec (*T*, between the arrows) caused a type 4 response. Thirty minutes after the application of neostigmine (NEO, $10^{-8}$ g/ml.) the response was converted to type 3 and a delayed relaxation had appeared (second panel). Twenty minutes later (third panel), the contraction during stimulation had become larger. Time marker in *a*, 20 min; in *b*, 10 min; in *c*, 1 min.

Delayed relaxations were potentiated by neostigmine. The application of neostigmine to preparations showing type 4 responses with no delayed relaxation caused a reduction in the amplitude of the relaxation during stimulation. During this change, the preparations usually started to develop a delayed relaxation following each response, even before the response was converted to type 3. The final response to stimulation of the preparation shown in Fig. 5*c* was type 3, with only a brief after-contraction when stimulation was stopped followed by a delayed relaxation. In other preparations, the delayed relaxation became even more marked as the response changed towards type 1.

## DISCUSSION

The four types of responses of the taenia to electrical stimulation, which are described above, can each be broken down into three components. These components are a contraction which occurs during stimulation, a relaxation which occurs during stimulation and a contraction which appears at the end of the period of stimulation. Table 1 illustrates the contributions made by the three components to the four response types.

TABLE 1

| Components | Type of response | | | |
|---|---|---|---|---|
| | Type 1 | Type 2 | Type 3 | Type 4 |
| Contraction during stimulation | + | + | + | − |
| Contraction after stimulation | − | + | + | + |
| Relaxation during stimulation | − | − | + | + |

The table illustrates the manner in which the four response types can be made up from three components. + indicates that a component is discernible in a response type, − that the component cannot be distinguished.

The contractions which occur during stimulation are, in general, mediated by cholinergic excitatory nerves. This conclusion was also reached by Burnstock *et al.* (1966). Treatment of the taenia with the anticholinesterase, neostigmine, led to the appearance of such contractions in some preparations. After the application of atropine the contractions were usually greatly reduced or abolished. In some preparations, however, contractions of considerable magnitude did occur during stimulation of atropinized preparations. The nature of the latter contractions is considered below.

The relaxations occurring during stimulation are mediated by inhibitory nerves. Burnstock *et al.* (1966) have shown that there is a double inhibitory innervation of the taenia comprising intramural nerves and perivascular inhibitory nerves. No attempt has been made in the present study to distinguish between the relative contributions of these two sets of inhibitory nerves to the observed relaxations.

The contractions which occur at the end of the period of stimulation are clearly not mediated by cholinergic nerves, since they appear or increase in amplitude in the presence of atropine. Bennett (1966*a*) has studied the electrophysiological phenomena underlying the after-contractions and has concluded that they are rebound contractions. That is to say, hyperpolarization of the smooth muscle cell membrane, resulting from stimulation of the inhibitory nerves, initiates changes which tend to cause depolarization and accelerated spontaneous activity.

With regard to the contractions which occur during stimulation of atropinized preparations, the simplest view to take is that the cholinergic

nerves in these preparations possess some degree of atropine-resistance. One disadvantage of this view is that it would be necessary to propose that resistance is found in only some preparations, while others are extremely sensitive to the blocking action of atropine. An alternative view is that there is a fatigue effect in the intramural inhibitory nerves. Rapid stimulation of these nerves would cause an initial large hyperpolarization of the smooth muscle membrane. Then, as fatigue set in, the output of inhibitory transmitter substance would fall off and the membrane potential would return towards the resting potential, although stimulation was continued. Under these conditions, a rebound depolarization and acceleration of action potential firing could occur, resulting in a contraction during stimulation.

The conversion of excitatory to inhibitory responses and vice versa following the application of atropine or neostigmine indicates that there is an antagonism between the excitatory and inhibitory nerves in the taenia. Such an antagonism may occur in two ways. First, it may be that some cells are contracted during nerve stimulation while others are simultaneously relaxed. The net response would be the summation of the various changes of length. This situation appears to hold in type 2 responses. In these responses, the primary response to stimulation is a contraction. But it is clear that some cells are inhibited during stimulation, for an after-contraction occurs at the end of stimulation. Bennett (1966*b*) has shown that some cells of the taenia develop excitatory junction potentials on stimulation of the intramural nerves, while nearby cells respond to the same stimulus with inhibitory junction potentials.

Secondly, it appears that there is a direct antagonism between the effects of the excitatory and inhibitory transmitter substances on the membrane of a single cell. Thus Bennett (1966*b*) has recorded excitatory junction potentials from some cells in non-atropinized preparations, but Bennett, Burnstock & Holman (1966) recorded only inhibitory junction potentials from all cells in atropinized preparations of taenia. Bülbring (1957) has found that all muscle cells in the taenia can respond to both acetylcholine and adrenaline.

The nature of the delayed relaxation seen in this study is difficult to explain. The relaxation is clearly not of the same type as the inhibitory effects described by Cantoni & Eastman (1946), since it was seen after responses which did not include a large contraction. Nor is the relaxation due to an effect of the inhibitory fibres alone, since it is abolished by atropine and appears after treatment with neostigmine. This evidence clearly links the presence of a delayed relaxation with the presence of an active cholinergic innervation, although the relaxation obviously is not mediated by acetylcholine directly.

The occurrence of the delayed relaxation and its sensitivity to drugs could be explained in the following manner. In non-atropinized preparations, some cells would be depolarized by the excitatory transmitter substance even though they are exposed to the inhibitory trans-

mitter substance. At the end of a period of stimulation, the concentrations of both transmitters would decline. If the inhibitory transmitter persisted in the tissue for a much longer time than did acetylcholine, the cells would eventually become hyperpolarized and the spontaneous activity would be slowed. These cells would be contracted during stimulation and a delayed relaxation would occur after stimulation. Other cells would be hyperpolarized by the inhibitory transmitter substance during stimulation. The hyperpolarization would initiate the changes which are responsible for rebound excitation (Bennett, 1966*a*). At the end of stimulation, there would be an antagonism between the hyperpolarizing effect of the persisting inhibitory transmitter and the depolarizing effect of the rebound process. It is possible that the changes responsible for the rebound activity would overcome the declining effects of the inhibitory transmitter. The inhibition caused by the transmitter would then be curtailed. These cells would be relaxed during stimulation, but would contract rapidly at the end of stimulation.

In preparations treated with atropine, in which acetylcholine has no excitatory action, all cells affected by stimulation of the intramuscular nerves would be inhibited during stimulation and would contract rapidly at the end of stimulation. This would explain why delayed relaxations were not seen in atropinized preparations. In preparations treated with neostigmine, the proportion of cells which are contracted during stimulation, and which therefore do not develop a rebound contraction, would be increased. Neostigmine treatment would therefore increase the size of the delayed relaxation.

It was shown that stimulation of the intrinsic nerves in some preparations caused a small primary relaxation followed by a very large rebound contraction. If the burst of stimulation was applied for only a brief period, it would be easy to confuse this response with a primary contraction. A study of the literature suggests that this may have happened on a number of previous occasions. Thus, Munro (1953) reported that stimulation of the wall of the guinea-pig terminal ileum normally caused a primary contraction. After the addition of atropine, the primary contraction was virtually abolished, but a large, prolonged contraction occurred at the end of stimulation. This was probably a rebound contraction, and not a contraction caused by the release of a non-cholinergic excitatory transmitter substance as thought by Munro. Tweeddale (1963) found that stimulation of strips of circular muscle from the rabbit ileum caused a large contraction which had a latency of at least 5 sec and sometimes did not appear until the ends of a 15 sec period of stimulation. This also was possibly a rebound contraction.

In addition, the contractions of the gastro-intestinal tract in response to vagal stimulation which were recorded by a number of early workers (Bunch, 1899; Bayliss & Starling, 1899, 1900; May, 1904; Veach, 1925) resemble rebound contractions, presumably resulting from the stimulation of inhibitory vagal fibres. Perhaps it is these rebound contractions which are the contractions referred to by Dale & Gaddum (1930) as atropine-resistant. Since recent workers have denied that there is any atropine-resistant excitatory influence of the vagi on the stomach (Greeff & Holtz, 1956) it would be interesting to examine under what conditions, if any, the vagi cause rebound contractions of the gut.

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## REFERENCES

BAYLISS, W. M. & STARLING, E. H. (1899). The movements and innervation of the small intestine. *J. Physiol.* **24**, 99–143.

BAYLISS, W. M. & STARLING, E. H. (1900). The movements and innervation of the small intestine. *J. Physiol.* **26**, 125–138.

BENNETT, M. R. (1966*a*). Rebound excitation of the smooth muscle cells of the guinea-pig taenia coli after stimulation of intramural inhibitory nerves. *J. Physiol.* **185**, 124–131.

BENNETT, M. R. (1966*b*). Transmission from intramural excitatory nerves to the smooth muscle cells of the guinea-pig taenia coli. *J. Physiol.* **185**, 132–147.

BENNETT, M. R., BURNSTOCK, G. & HOLMAN, M. E. (1966). Transmission from intramural inhibitory nerves to the smooth muscle of the guinea-pig taenia coli. *J. Physiol.* **182**, 541–558.

BÜLBRING, E. (1953). Measurements of oxygen consumption in smooth muscle. *J. Physiol.* **122**, 111–134.

BÜLBRING, E. (1957). Changes in configuration of spontaneously discharged spike potentials from smooth muscle of the guinea-pig taenia coli. The effect of electrotonic currents and of adrenaline, acetylcholine and histamine. *J. Physiol.* **135**, 412–425.

BUNCH, J. L. (1899). On the vaso-motor nerves of the small intestine. *J. Physiol.* **24**, 72–98.

BURNSTOCK, G., CAMPBELL, G. & RAND, M. J. (1966). The inhibitory innervation of the taenia of the guinea-pig caecum. *J. Physiol.* **182**, 504–526.

CANTONI, G. L. & EASTMAN, G. (1946). On the response of the intestine to smooth muscle stimulants. *J. Pharmac. exp. Ther.* **87**, 392–399.

DALE, H. H. & GADDUM, J. H. (1930). Reactions of denervated voluntary muscle, and their bearing on the mode of action of parasympathetic and related nerves. *J. Physiol.* **70**, 109–144.

GREEFF, K. & HOLTZ, P. (1956). Über die Natur des Überträgerstoffes vagalmotorischer Magenerregungen. *Arch. exp. Path. Pharmak.* **227**, 559–565.

MAY, W. P. (1904). The innervation of the sphincters and musculature of the stomach. *J. Physiol.* **31**, 260–271.

MUNRO, A. F. (1953). Effect of autonomic drugs on the responses of isolated preparations from the guinea-pig intestine to electrical stimulation. *J. Physiol.* **120**, 41–52.

TWEEDDALE, M. G. (1963). The electrically stimulated circular muscle strip of the rabbit ileum. *J. Pharm. Pharmac.* **15**, 846.

VEACH, H. O. (1925). Studies on the innervation of smooth muscle. I. Vagus effects on the lower end of the esophagus, cardia and stomach of the cat, and the stomach and lung of the turtle in relation to Wedensky inhibition. *Am. J. Physiol.* **71**, 229–264.