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THE ELECTRICAL BASIS FOR CONTRACTION AND RELAXATION IN CANINE FUNDAL SMOOTH MUSCLE

BY KATHLEEN G. MORGAN, T. C. MUIR* AND J. H. SZURSZEWSKI

From the Department of Physiology and Biophysics, Mayo Medical School, Rochester, MN 55901, U.S.A.

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SUMMARY

1. Mechanical and intracellular electrical activities were recorded simultaneously from canine fundal and antral smooth muscle preparations.

2. Most fundal preparations displayed no spontaneous electrical or mechanical activity. The tissue had a space constant of 1·5 mm and a time constant of 189 msec and showed outward rectification in response to depolarizing current.

3. Transmural nerve stimulation of fundal preparations demonstrated the presence of cholinergic excitatory and non-cholinergic, non-adrenergic inhibitory neural inputs to the tissue. The cholinergic nerve response consisted of a small, graded depolarization accompanied by a slow graded contraction; the inhibitory nerve response consisted of a graded hyperpolarization accompanied by a slow relaxation.

4. The excitatory fundal nerve response was abolished or greatly diminished by D_{600} and Mn^{2+}. D_{600} and Mn^{2+} also decreased basal tone. The inhibitory nerve response was unaffected by either agent.

5. The excitatory nerve response in the fundus was contrasted with the excitatory nerve response in the antrum. In the fundus, stimulation of cholinergic motor nerves produced a depolarization which always produced a contraction. In the antrum, stimulation of cholinergic motor nerves between action potentials produced graded depolarizations of antral cells; however, there were no associated contractions. Stimulation of cholinergic motor nerves during spontaneous action potentials increased the amplitude and duration of the plateau phase of the action potential; this was associated with an augmentation of the spontaneous contractions.

6. Voltage–tension curves were determined for antral and fundal preparations using K^+ depolarization as a means of controlling membrane potential. Antral preparations displayed a voltage threshold for contraction at a membrane potential approximately 30 mV positive to the resting potential. In contrast, fundal resting potentials were at or more positive than their voltage thresholds.

7. These differences in electromechanical coupling provide an explanation for the marked differences in the responses of fundal and antral smooth muscles to nerve stimulation and account for their physiologic function *in vivo*.

* Present address: Department of Pharmacology, the University Glasgow G12 8QQ.

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INTRODUCTION

The fundus of the stomach is cephalad to the oesophago-gastric junction. It is capable of large variations in size and plays an important role in regulating gastric emptying (Kelly, 1977). By 'receptive relaxation' (Cannon & Lieb, 1911) the fundus acts as a reservoir during ingestion of food (Code & Carlson, 1968); but the physiological basis for such activity in the fundus is unknown. Unlike the corpus and antrum of the stomach, the fundus shows no spontaneous phasic contractions and no spontaneous electrical activity (El-Sharkawy, Morgan & Szurszewski, 1978). The gastric action potential which originates in the orad corpus, does not propagate into the fundus *in vivo* (Kelly, Code & Elveback, 1959). Since the space constant of the guinea pig fundus is greater than that of the antrum (Osa & Kuriyama, 1970; Kuriyama, Osa & Tasaki, 1970), differences in cable properties of the membrane cannot account for differences in motility between them. On the other hand, the electrical excitability of guinea-pig fundal muscle, as measured by the application of outward current pulses, was less than that of the antrum (Osa & Kuriyama, 1970). This difference in excitability could cause decremental conduction and minimize the occurrence of spontaneous activity thus accounting for the quiescent nature of the fundus. The absence of spontaneous activity and the decremental conduction of excitation raises the question as to how fundal smooth muscle regulates its contractility.

The present experiments were undertaken to investigate the physiological basis for the differences in motility between the fundus and the antrum of the stomach and to try to account for the functional characteristics of the former. It was found that very small membrane depolarizations produced significant contractions in the fundus but not in the antrum. This finding could be explained by differences in the resting membrane potential and in the voltage–tension characteristics of the two tissues.

A preliminary account of this work has been communicated (Muir, Morgan & Szurszewski, 1979).

METHODS

In sixty-one anaesthetized dogs of either sex (10–22 kg), the entire stomach was removed (El-Sharkawy *et al.* 1978) and a piece of the external muscularis was taken either from the fundus (the area cephalad to the oesophagogastric junction) or the antrum. Strips (2 × 6 mm) of the fundus were dissected from the centre of the fundus taking care to exclude fibres of sling muscle (Torgessen, 1942). The long axis of the preparation was parallel to the axis of the outermost layer of fibres. Muscle strips with the serosal surface uppermost were pinned to the floor of a Sylgard-coated bath. The technique for dissecting circular antral strip has been described previously (El-Sharkawy *et al.* 1978). For simultaneous measurement of tension and intracellular potentials, a 4 × 2 mm flap was left unpinned and attached to a force transducer. In experiments using the technique described by Abe & Tomita (1968), strips were cut slightly longer (4 mm) to allow the end of the preparation opposite the transducer to be pulled through holes in the stimulating plates. Glass micro-electrodes filled with 3 M-KCl and having resistances ranging from 30 to 80 MΩ were used to measure membrane potentials intracellularly. The standard electrophysiological techniques, employed throughout, have been described previously (El-Sharkawy *et al.* 1978). Nerve stimulation was effected either by Pt plates placed parallel or perpendicular to the preparation using pulses of 200–500 μsec duration. No qualitative differences between results from either method were noticed.

Krebs solution at 37 ± 0·5 °C flowed through the chamber at 5–10 ml./min. The solution

contained (mM): Na^+, 137·4; K^+, 5·9; Ca^{2+}, 2·5; Mg^{2+}, 1·2; Cl^-, 134; HCO_3^-, 15.5; $H_2PO_4^-$, 1·2; dextrose, 11·5; was equilibrated with a 97 % O_2 and 3 % CO_2 gas mixture and had a pH of 7·3–7·4. K-rich Krebs solution was used to construct voltage–tension curves. The desired K concentration was achieved by replacing part of the NaCl with an isosmotic equivalent of KCl. Between K-rich solutions, the preparation was washed with normal Krebs solution for 10–30 min to allow the resting potential and tone to return to control levels. Membrane potentials were measured intracellularly from the same cell through the experiment.

The following drugs were used (concentrations in the text refer to bath concentrations): acetylcholine hydrochloride (Sigma), atropine sulphate (Sigma), eserine salicylate (Sigma), guanethidine sulphate (kindly donated by Smith, Kline and French), hexamethonium bromide (Sigma), ±methoxyverapamil (D_{600}) (Knoll), ±phentolamine tosylate (Ciba), and ±propranolol hydrochloride (Sigma).

RESULTS

Resting activity. Muscles were stretched by 0·5–1·0 mm increments until the contraction caused by acetylcholine (ACh 10^{-6} M) was maximum. The passive tension at which the contraction was maximum was maintained throughout the experiment (Szurszewski, 1975). At this optimal length, 90 % of the preparations showed no spontaneous electrical or mechanical activity. The mean resting membrane potential in these quiescent preparations was $-52 \pm 0{\cdot}39$ mV (mean ± SE. of mean, $n = 351$). In the remainder, slow spontaneous rhythmic fluctuations in membrane potential (5–10 mV), without spike-like action potentials, occurred which had a periodicity of 20–25 sec and were accompanied, frequently, by small (approximately 0·5 g) increases in tone. These rhythmic changes in membrane potential were unaffected by atropine (10^{-6} M). The passive electrical properties of the tissue were measured using the method devised by Abe & Tomita (1968). Current–voltage relationships for both hyperpolarizing and depolarizing current pulses (1–2 sec duration) were obtained in nine preparations. A typical current–voltage relationship is shown in Fig. 1. In this and all other preparations, there was outward rectification in the depolarizing direction. Outward current pulses did not trigger spike-like action potentials in any preparation. The time to reach the half amplitude of the electronic hyperpolarizing potential was plotted against the distance of the recording micro-electrode from the stimulating plate. The slope of this plot is equal to $\tau/2\,\lambda$ (Hodgkin & Rushton, 1946) where λ is the space constant of the tissue. λ was calculated as the distance at which the electrotonic potential decremented to 1/e of the value at zero distance from the plate. The values of λ and τ obtained were $1{\cdot}5 \pm 0{\cdot}2$ mm and 189 ± 30 msec (mean ± S.E. of mean, $n = 7$) respectively.

Responses to transmural nerve stimulation. In the fundus, transmural nerve stimulation produced small e.j.p.s (1–7 mV) without spike-like action potentials. The e.j.p.s produced contractions. Fig. 2 shows the response of a typical cell to nerve stimulation. A single shock (panel *A*) produced a barely detectable electrical response, which was accompanied by a weak contraction. The mean (±S.E. of mean) latent period to the beginning of depolarization following a single stimulus was 215 ± 28 (range 120–400) msec. The mean (±S.E. of mean) time constant of decay of the e.j.p. was 402–23 msec, $n = 11$. In comparison, the membrane time constant (τ), as measured by hyperpolarizing current pulses was 189 ± 30 msec ($n = 7$), indicating that the decay of the e.j.p. was not due simply to the passive decrement along the

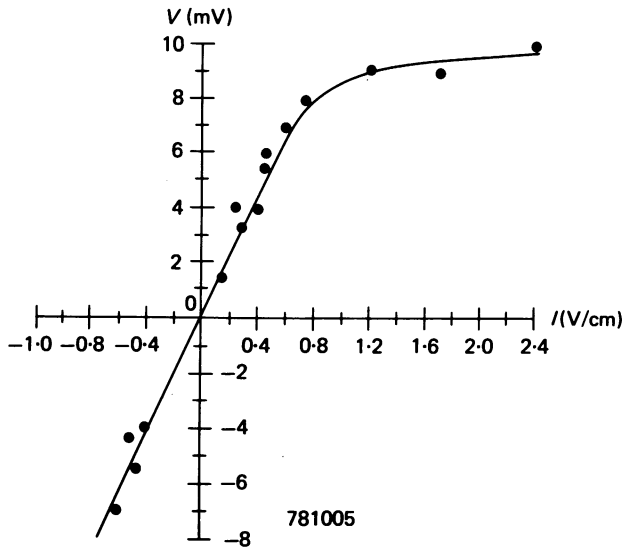

Fig. 1. Current–voltage relationship from fundus smooth muscle. All data points were taken from the same cell. Note linear relationship in the hyperpolarizing direction and outward rectification in the depolarizing direction.

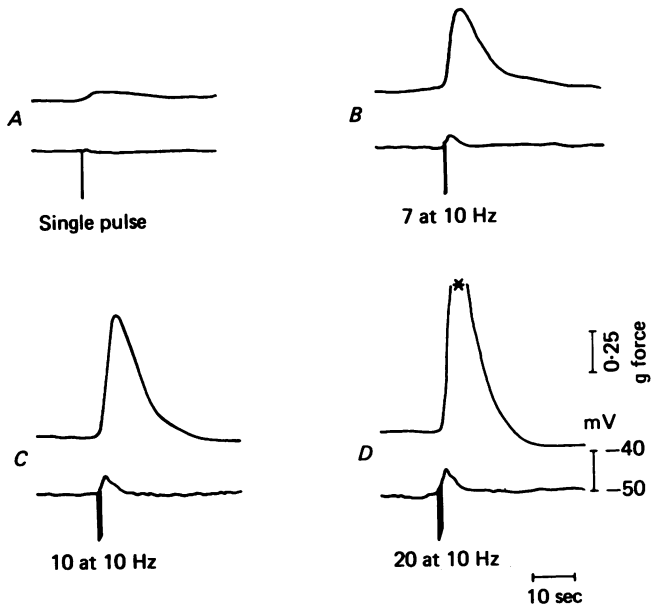

Fig. 2. E.j.p.s in fundal smooth muscle. Top trace in each panel, contraction. All electrical records (bottom trace) from the same cell. Nerves were stimulated transmurally with 1, 7, 10 or 20 pulses of 200 μsec duration at 10 Hz. The asterisk denotes an off-scale contraction.

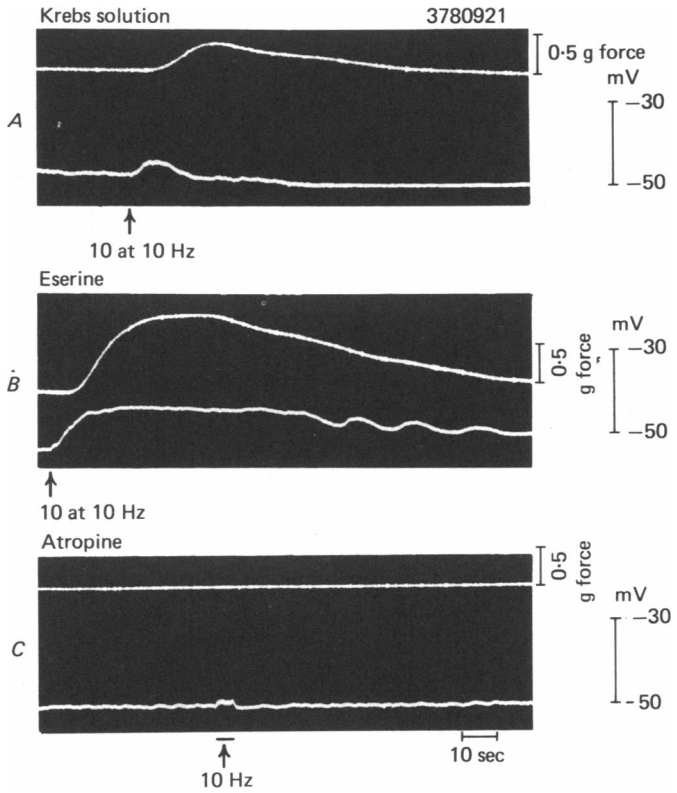

Fig. 3. Effect of eserine and atropine on summated e.j.p. in fundal smooth muscle. All electrical responses from the same cell. Intramural nerves stimulated with 200 μsec pulses at 10 Hz, same current intensity in all panels. Panel *A*: control intracellular electrical (bottom trace) and mechanical (top trace) recording. Panel *B*: 10 min exposure to 10^{-6} M-eserine. Panel *C*: 20 min after washing out eserine and adding 10^{-6} M-atropine.

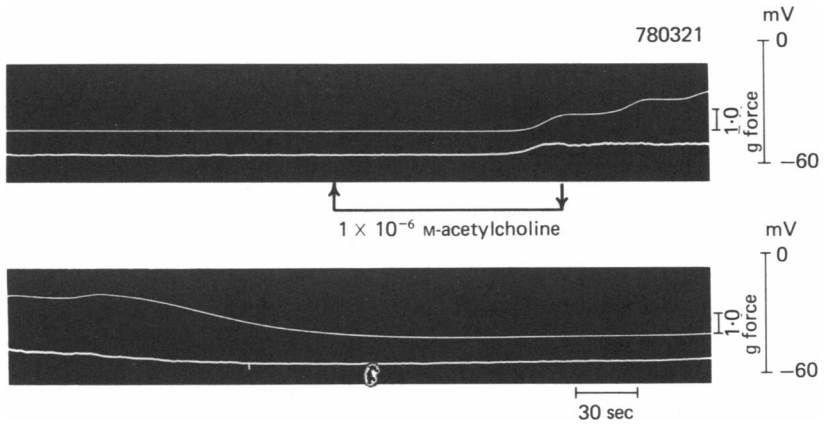

Fig. 4. Effect of acetylcholine on force and intracellular potential. Bottom panel continuous with top. Infusion of acetylcholine was begun at first arrow. At the second arrow, infusion of acetylcholine ceased and that of normal Krebs solution recommenced.

cable. Repetitive stimulation at 10 Hz produced larger responses which increased in a graded fashion with an increasing number of pulses (Fig. 2*B–D*). Although the contraction exceeded a gram of force in response to 20 pulses, the electrical response was less than 10 mV. Spike potentials were never seen in response to nerve stimulation. However, spike-like action potentials were produced in response to transmural nerve stimulation in the presence of tetraethylammonium (TEA 15 mM). TEA by itself produced no spontaneous spike potentials.

Trains of stimuli (0·1–2·0 Hz) produced e.j.p.s which did not facilitate throughout the train but summated at approximately 1 Hz or greater. The optimal frequency was 15–20 Hz. Infrequently, small damped oscillations occurred on top of those e.j.p.s which were produced following longer trains of stimuli but action potentials were not observed. Both the e.j.p.s and the accompanying mechanical contractions were enhanced were enhanced in duration and amplitude by the anticholinesterase eserine. A typical response is shown in Fig. 3 where identical stimuli were applied before (panel *A*) and 10 min. after (panel *B*) eserine (10^{-6} M). The decaying phase of the e.j.p. showed oscillations in the presence of this drug. In other preparations, oscillations were also occasionally seen in the mechanical response. E.j.p.s were abolished by tetrodotoxin (TTX 1×10^{-6} M) and significantly reduced or abolished by atropine ($0{\cdot}5–1 \times 10^{-6}$ M) (Fig. 3*C*) confirming their neural cholinergic origin. The effect of exogenously applied ACh on this tissue was also studied. A typical response is shown in Fig. 4. At the arrow, a solution of 10^{-6} M-acetylcholine was infused into the bath at a relatively slow rate. After a lag time for the solution to traverse the tubing and mix into the bath, a small sustained depolarization and a tonic contraction were observed. Again, the contraction occurred in the absence of spike potentials. At the onset of the effects, the acetylcholine was washed out of the bath. It took some time to diffuse out of the bath but, the effects were reversible on washing. It was of interest that both the mechanical and electrical response to acetylcholine showed oscillatory behavior similar to that seen in response to nerve stimulation in the presence of eserine.

In 51 % of the preparations examined, nerve stimulation produced biphasic changes in membrane potential which consisted of an initial depolarization, (excitatory junction potential, e.j.p.) followed by a small, slow hyperpolarization (inhibitory junction potential, i.j.p.). This biphasic response was probably due to the effect of both excitatory and inhibitory transmitters. Accompanying these electrical changes were alterations in tone. A typical example of a biphasic response is shown in Fig. 5. The initial contraction of the muscle was followed by a decline in tone to below the original resting level. These changes in tone were associated with summated e.j.p.s and i.j.p.s. When only i.j.p.s (1–5 mV) were observed following a single stimulus, the latency was between 75 and 100 msec, the time to peak 2500 msec and the time to 50 % decay of the response was between 2000 and 2500 msec. The amplitude of the hyperpolarization increased with increasing numbers of pulses at a given frequency and with increasing frequency up to the optimum (10–15 Hz). I.j.p.s and the accompanying mechanical relaxation were unaffected by guanethidine (10^{-6} M), hexamethonium (10^{-6} M), phentolamine (10^{-6} M) or propranolol (10^{-6} M) but were abolished by TTX (10^{-6} M). These results suggested that the inhibitory phenomena obtained in response to transmural nerve stimulation were mediated by non-cholinergic, non-adrenergic nerves.

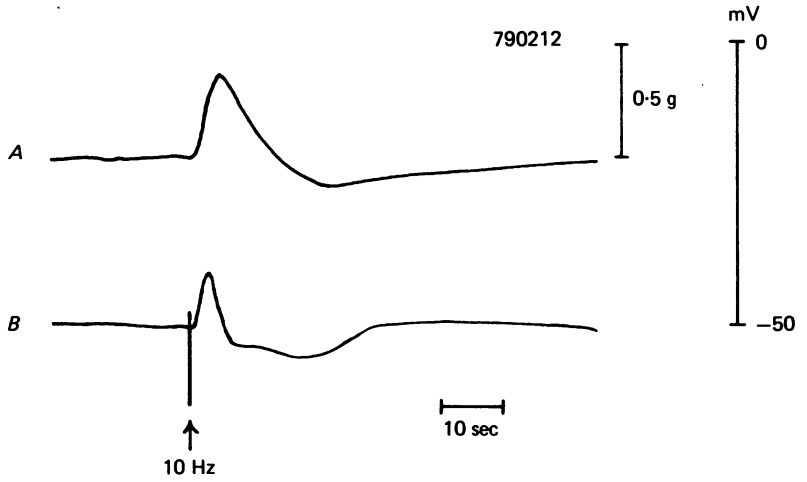

Fig. 5. Biphasic response of fundal smooth muscle to transmural nerve stimulation at 10 Hz. Top panel, mechanical; bottom panel, intracellular electrical record.

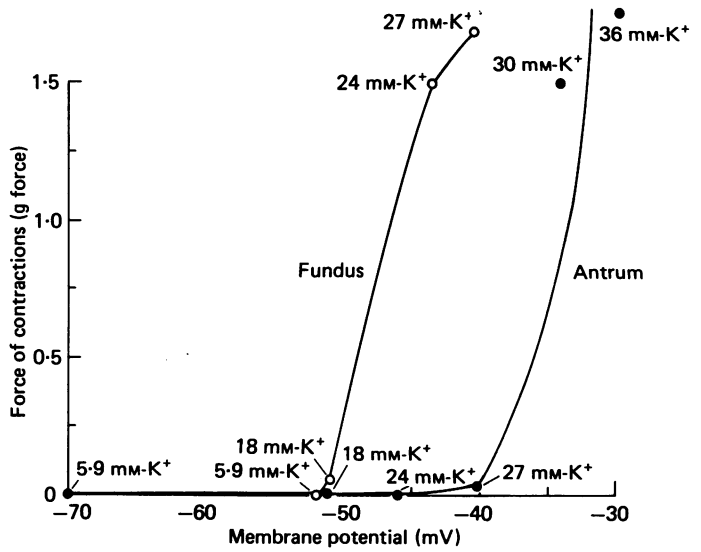

Fig. 6. Effect of K^+ depolarization on contractile force. Two voltage–tension curves are shown: one from a fundal preparation, the other from an antral preparation. For each curve, all membrane potentials were recorded in the same cell and the preparations were washed 20–30 min in normal Krebs solution (5·9 mM-K) between each K-rich solution. Note an inflexion in the antral curve at approximately −40 mV and in the fundal curve at approximately −52 mV.

Excitation–contraction coupling. The relationship between excitation and contraction in fundus smooth muscle was examined and compared with that in the antrum. Two different techniques were used. In the first technique, the voltage–tension relationship of each tissue was established by the stepwise increase in external $[K^+]$. In each elevated K concentration, the steady-state membrane potential was plotted against

the steady-state increase in tone (Morgan & Szurszewski, 1980). A typical voltage–tension curve for fundal and antral smooth is shown in Fig. 6. In the example shown in Fig. 6 and in all antral preparations, small depolarizations produced no increase in tone, but measurable (arbitrarily defined as > 0·05 g force) increases in tone occurred when the membrane potential became more positive than −40 mV. Thus, antral preparations displayed a voltage threshold for contraction. We have previously reported similar threshold behaviour in corporal preparations (Morgan & Szurszewski,

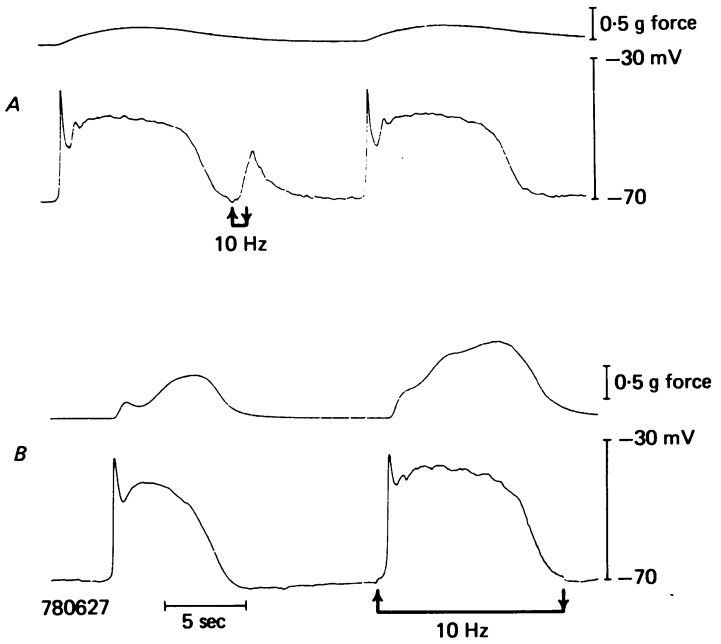

Fig. 7. Response of antral smooth muscle to transmural nerve stimulation. In panel *A*, nerves were stimulated briefly at 10 Hz between two spontaneous action potentials producing a depolarization but no contraction. In panel *B*, nerves were stimulated during a spontaneous action potential producing an increase in the size of the contraction and in the amplitude and duration of the plateau of the action potential. Panels *A* and *B* are from different preparations.

1979). In contrast, in all fundal preparations, measurable increases in tone occurred whenever the membrane potential became more positive than −52 mV (Fig. 6). Indeed, in the majority (five out of six) of preparations investigated, no voltage threshold for mechanical activity was apparent because all depolarizations were accompanied by measurable increases in tone. However, in one fundal preparation, an inflexion was demonstrable (at 18 mM-K, Fig. 6). This prompted us to investigate the effect of hyperpolarization on other fundal preparations in which there was no apparent voltage threshold for contraction. Hyperpolarization was achieved by using the technique described by Abe & Tomita (1968). Hyperpolarizations caused a decrease in tone. However, there was a membrane potential beyond which further hyperpolarization produced no further decrease in tone. This suggested that fundal muscle has a mechanical threshold, but that the resting membrane potential in most

fundal muscles is more positive than the mechanical threshold. In the second technique, the response of each tissue to small depolarizations of membrane potential (e.j.p.s) produced by transmural nerve stimulation were compared. In the antrum, the mean resting potential is −68 mV (El-Sharkawy *et al.* 1978) and the mechanical threshold is approximately −40 mV (Fig. 6). These data suggest that depolarizations less than approximately 30 mV would not be expected to elicit a contraction. To test this concept, transmural nerve stimulation was timed to occur either between or

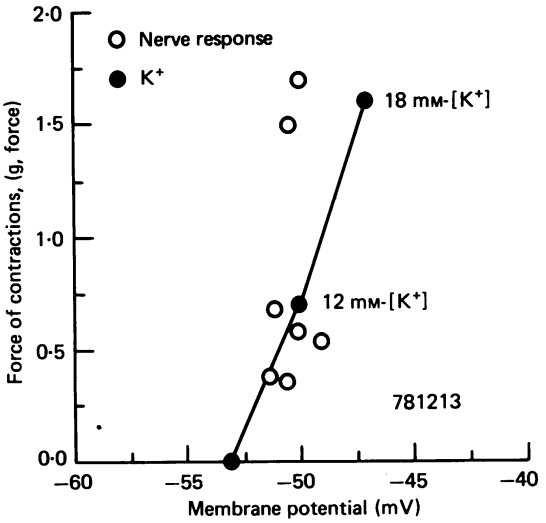

Fig. 8. Comparison of effects of K^+-depolarization and transmural, cholinergic nerve stimulation in fundal smooth muscle. The line was drawn to connect the points for K depolarization. All electrical responses were recorded in the same cell.

during a spontaneous action potential. When nerve stimulation occurred between spontaneous action potentials, large e.j.p.s (5–20 mV) failed to cause contraction (Fig. 7*A*). However, when repetitive nerve stimulation was timed to occur during spontaneous action potentials (Fig. 7*B*), there was an increase in both the amplitude and duration of the plateau phase of the action potential. This increase in the size of the plateau potential was associated with an increase in the force of the phasic, antral contraction. This association of an increase in the size of the plateau potential with an increase in the force of contraction has been seen previously in response to exogenous acetylcholine (Szurszewski, 1975). In the fundus the mean resting potential is −52 mV and the mechanical threshold is approximately −52 mV. Thus, in the fundus the proximity of the voltage threshold for mechanical contraction to the resting membrane potential explains how small e.j.p.s (1–3 mV) could initiate contractions (cf. Fig. 2). To further test this concept, we determined in the same cell, the magnitude of the K-induced depolarization, the nerve-induced depolarization due to supramaximal nerve stimulation and the associated increases in tone and plotted the amplitude of the depolarizations against the increase in tone (Fig. 8). Although caution must be used in interpreting these results because all cells in the preparation may not be equally innervated, the data indicate that most nerve responses fit the

voltage–tension relationship predicted by the K^+ line. The two largest nerve responses deviate slightly from the K^+ line. Perhaps at higher acetylcholine concentrations, a non-voltage-dependent mechanism was involved.

Effects of methoxyverapamil (D_{600}) *and of* Mn^{2+}. To determine if the changes in membrane potential and contractile force in the fundus involve external Ca^{2+}, Ca^{2+} antagonists D_{600} and Mn^{2+} were used. Two series of experiments were performed. In

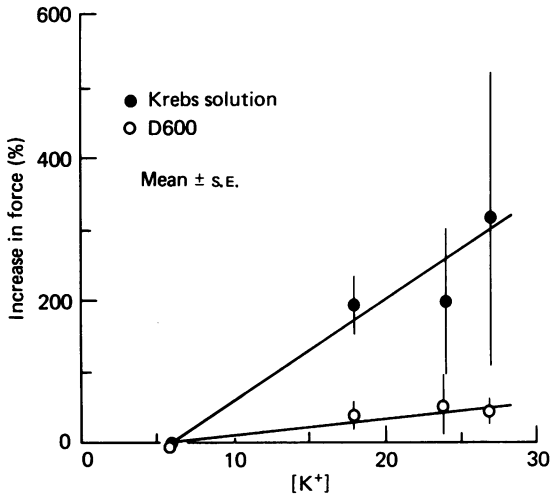

Fig. 9. Effect of D_{600} on K^+-induced contractions of fundal muscle. Ordinate: percent of resting tone by which force was increased by the $[K^+]$; abscissa: $[K^+]$ in mM. Each data point represents the mean response ± S.E. of mean from five preparations. All preparations were pretreated with TTX (10^{-6} M) and atropine (10^{-6} M).

the first, the effects of D_{600} (2×10^{-6} M) on the increase in tone produced by graded increase in K^+ were examined. In these experiments, TTX (10^{-6} M) were present to eliminate the effects of K-induced release of neurotransmitter. In all K-rich solutions, D_{600} significantly reduced the ability of K^+ to increase tone (Fig. 9). This suggests that K-induced increases in tone were due, at least in part, to increases in Ca permeability.

In the second series, the effects of D_{600} ($1–3 \times 10^{-6}$ M) on the intracellular electrical response to transmural nerve stimulation were examined. D_{600} either abolished or reduced the amplitude of the e.j.p. In Fig. 10, D_{600} abolished the excitatory response to nerve stimulation at 5 Hz and unmasked the inhibitory response, the persistence of which suggests that presynaptic nerve elements were functional. TTX (10^{-6} M) abolished all responses to nerve stimulation. In seven preparations, D_{600} (3×10^{-6} M) decreased the amplitude of the excitatory response to nerve stimulation (5–10 Hz, 0·5 msec for 0·5–1 sec; held constant in any one experiment) by $58 \pm 7{\cdot}9\%$ (mean ± S.E. of mean) of control and caused a marked decline in resting tone. Support for the view that D_{600} acted by blocking Ca^{2+} channels and not by other mechanisms was obtained by the use of Mn^{2+}. In five fundal preparations, Mn^{2+} (0·5 mM) decreased the amplitude of the e.j.p.s in response to transmural nerve stimulation (20 Hz 0·5 msec for 0·5–1 sec) by $39 \pm 3\%$ (mean ± S.E. of mean).

For comparison, the effect of D_{600} (3×10^{-6} M) was also determined on the electrical and mechanical responses to transmural nerve stimulation in antral preparations. In contrast to the fundus, D_{600} (3×10^{-6} M) produced little or no (4·4 ± 4·9 %; mean ± S.E. of mean, $n = 5$) decrease in the amplitude of summated e.j.p.s and no noticeable decrease in resting tone.

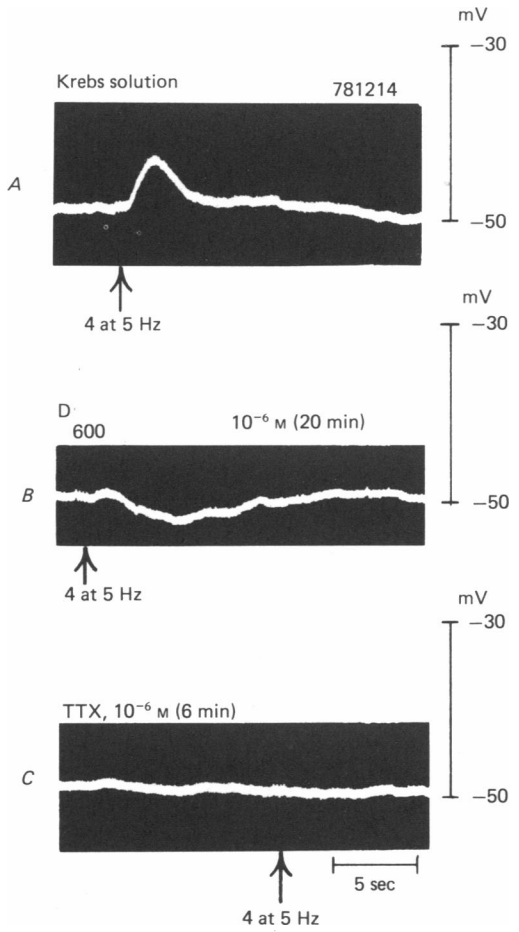

Fig. 10. Effect of D_{600} on response to transmural nerve stimulation in fundal smooth muscle. All responses from same cell.

DISCUSSION

In contrast to circular muscle of the antrum and corpus, fundal smooth muscle is not spontaneously active and possesses the ability to contract in the absence of action potentials. Two features of the present results underlie these characteristics. The first feature is the low resting membrane potential of fundal smooth muscle cells which may inactivate the action potential mechanism present in both the antrum (El-Sharkawy *et al.* 1978) and corpus (Morgan & Szurszewski, 1980). The second important feature is the relationship which exists between the resting membrane

potential and the voltage threshold for mechanical activity as revealed by the voltage–tension curves. In this study, the voltage-tension curves for antral and fundal smooth muscle have been determined. In a previous study we determined voltage–tension curves for corporal smooth muscle (Morgan & Szurszewski, 1979). In fundal smooth muscle, the voltage threshold for mechanical activity occurred at a more negative potential and was closer to (or even more negative than) the resting membrane potential than were those of the antrum and corpus. In consequence, the fundus is predisposed to contract in response to relatively small depolarizations (such as those produced by nerve stimulation) which in antral and corporal smooth muscles would fail to exceed the mechanical threshold. Hence the ability of the fundus to contract in response to small depolarizations stems at least in part from the promixity of the resting membrane potential to the voltage threshold for mechanical activity. The fact that the mechanical threshold was negative to the resting potential in most fundal preparations may also explain the presence of resting 'tone' in fundal smooth muscle.

An important implication is that Ca^{2+} channels may be at least partially open at the resting membrane potential giving fundal preparations active tone, even at 'rest'. The following observations are consistent with this view. First, in the fundus but not in the antrum, muscle tone was increased with each increment of K^+ depolarization no matter how small the latter. Secondly, the Ca^{2+} antagonist D_{600} significantly reduced resting tone in the fundus but not in the antrum supporting the involvement of Ca^{2+}.

Since in most cases the resting membrane potential of the fundus lies above the voltage threshold for contraction, the muscle is normally tonically contracted and hyperpolarisation, for example manifested by i.j.p.s, reduces basal tone. The fundus is therefore a truly tonic muscle. This is in marked contrast to the antrum, where the resting membrane potential is far below the mechanical threshold. In consequence, as expected, the antrum has no 'resting tone'. Neither i.j.p.s nor the passage of hyperpolarizing current reduced tone in the antrum (unpublished data). The antrum only contrasts phasically when the action potential exceeded the mechanical threshold. Thus, by virtue of their electromechanical coupling characteristics, fundal and antral smooth muscles are well suited to perform their physiologic function *in vivo*. The 'tone' of the fundus determines the volume of the stomach and regulates the reservoir function of the stomach. The antrum, in contrast, resists changes in volume and its phasic contractions serve to mix and grind the gastric contents.

The present results show that transmural nerve stimulations release two transmitters, one which is excitatory and inhibited by atropine and is presumably cholinergic. The other, inhibitory, is unknown. However, the slow time course of the e.j.p., the rebound excitation which follows the end of stimulation and the resistance to atropine and adrenergic antagonists indicate its non-adrenergic non-cholinergic nature (Campbell, 1968; Beani, Bianchii & Crema, 1971).

We have previously reported (Morgan & Szurszewski, 1980) for the canine orad corpus that small depolarizations in response to exogenous pentagastrin are accompanied by increases in tone. When we attempted to mimic these changes caused by pentagastrin with K^+-induced depolarization, we were unable to cause a contraction with less than 20 mV depolarization. We concluded that the increase in tone occurred

by a voltage-independent mechanism which may have also, coincidentally, produced the small depolarization. A similar voltage-independent mechanisms may also occur in the fundus for acetylcholine induced activity. This would be in addition to the voltage-dependent mechanisms described above. Indeed, the deviation of voltage and tension associated with large e.j.p.s from the K^+-induced voltage-tension curve supports this idea (cf. Fig. 8). However, the distinction between the two tissues is that in the fundus, small depolarizations do cause contraction through 'electro-mechanical coupling' mechanisms whereas in the corpus they do not.

The underlying ionic mechanisms of the e.j.p. in the fundus can only be partly derived from the present results. The effectiveness of D_{600} suggests that Ca^{2+} may carry part of the inward current or that it may regulate inward current of Na^+. The question arises as to the ionic basis of the D_{600}-resistant antral e.j.p.s and the function of the part of the fundal e.j.p. which was resistant to D_{600}. At least one other ion, perhaps Na^+ must be involved in these D_{600}-resistant depolarisations. Indeed the D_{600}-susceptible depolarization may not occur primarily as a result of transmitter activity but by another process resistant to D_{600}. On this basis, e.j.p.s in the fundus and antrum may, as in other smooth muscles, be the result of an increased Na^+ conductance (Kuriyama, 1970). The membrane depolarization so produced would then lead to a subsequent increase in Ca^{2+} conductance.

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REFERENCES

ABE, Y. & TOMITA, T. (1968). Cable properties of smooth muscle. *J. Physiol.* **196**, 87–100.

BEANI, L., BIANCHI, C. & CREMA, A. (1971). Vagal non-adrenergic inhibition of guinea-pig stomach. *J. Physiol.* **217**, 259–279.

CAMPBELL, G. (1966). The inhibitory nerve fibres in the vagal supply to guinea-pig stomach. *J. Physiol.* **185**, 600–612.

CANNON, W. B. & LIEB, C. W. (1911). The receptive relaxation of the stomach. *Am. J. Physiol.* **29**, 267–273.

CODE, C. F. & CARLSON, H. C. (1968). Motor activity of the stomach. In *Handbook of Physiology*, section 6, vol. IV, pp. 1903–1916. Washington: Am. Physiol. Soc.

EL-SHARKAWY, T. Y., MORGAN, K. G. & SZURSZEWSKI, J. H. (1978). Intracellular electrical activity of canine and human gastric smooth muscle. *J. Physiol.* **279**, 291–307.

HODGKIN, A. L. & RUSHTON, W. A. H. (1946). The electrical constants of a crustacean nerve fibre. *Proc. R. Soc.* B. **133**, 444–479.

KELLY, K. A. (1977). Vagotomy impairs pentagastrin-induced relaxation of canine gastric fundus. *Am. J. Physiol.* **232**, *E*504–509.

KELLY, K. A., CODE, C. F. & ELVEBACK, L. R. (1959). Patterns of canine gastric electrical activity. *Am. J. Physiol.* **217**, 461–470.

KURIYAMA, H. (1970). Effects of ions and drugs on the electrical activity of smooth muscle. In *Smooth Muscle*, ed. BÜLBRING, E., BRADING, A. F., JONES, A. W. & TOMITA, T., pp. 366–395. Baltimore: Williams & Wilkins.

KURIYAMA, H., OSA, T. & TASAKI, H. (1970). Electrophysiological studies of the antrum muscle fibres of the guinea pig stomach. *J. gen. Physiol.* **55**, 48–62.

MORGAN, K. G. & SZURSZEWSKI, J. H. (1980). Mechanisms of phasic and tonic actions of pentagastrin on gastric smooth muscle. *J. Physiol.* **301**, 229–242.

MUIR, T. C., MORGAN, K. G. & SZURSZEWSKI, J. H. (1979). Electrical and mechanical responses of canine fundic smooth muscle to nerve impulses produced by field stimulation. *Fedn Proc.* **38**, 958.

OSA, T. & KURIYAMA, H. (1970). The membrane properties and decremental conduction of excitation in the fundus of the guinea-pig stomach. *Jap. J. Physiol.* **20**, 626–639.

SZURSZEWSKI, J. H. (1975). Mechanism of action of pentagastrin and acetylcholine on the longitudinal muscle of the canine antrum. *J. Physiol.* **252**, 335–361.

TORGESSEN, J. (1942). *The Muscular Build and Movements of the Stomach and Duodenal Bulb.* Oslo: Fabritius & Sonners Boktrykken.