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SLOW WAVE HETEROGENEITY WITHIN THE CIRCULAR MUSCLE OF THE CANINE GASTRIC ANTRUM

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SUMMARY

1. A cross-sectional preparation was designed in which multiple micro-electrodes can be precisely positioned to impale smooth muscle cells anywhere from the serosa to the submucosa.

2. Intracellular electrical recordings were obtained from gastric antral circular muscle cells from the myenteric plexus to the submucosa.

3. The resting membrane potential changed linearly as a function of distance from the myenteric plexus to the submucosa.

4. Slow wave upstroke dV/dt, upstroke potential amplitude, and plateau potential amplitude changed linearly as a function of distance from the myenteric plexus to the submucosa.

5. When slow waves were recorded simultaneously from a circular cell near the myenteric plexus and from a cell near the submucosa, the event always occurred first in the cell near the myenteric plexus.

6. Electrical differences did not appear to be caused by electrotonic decay of slow waves as they propagated through the circular muscle.

7. Electrical differences could not be explained on the basis of differences in intrinsic neural activity or prostaglandin synthesis.

8. Membrane polarization could not explain the differences in slow waves between myenteric and submucosal circular muscle cells.

9. The conclusion of this paper is that fundamental differences exist between the excitability mechanisms and/or passive membrane properties of cells near the myenteric plexus and the submucosa. These differences might be manifest in different motor performance of these two muscle cell populations.

INTRODUCTION

The circular muscle layer of the gastrointestinal tract is not anatomically homogeneous (Gabella, 1972; Gabella, 1974; Daniel, Daniel, Duchon, Garfield, Nichols, Malhotra & Oki, 1976; Taylor, Daniel & Tomita, 1976; Tomita, 1981). Studies on circular muscles of the canine small intestine have shown that gap junctions between muscle cells near the myenteric plexus are numerous, but much less frequent between muscle cells near the submucosa (Daniel *et al.* 1976). In several species (dog, cat, sheep,

guinea-pig, rat, and mouse) a special layer of smaller and more electron-dense circular muscle cells exists near the submucosa (Gabella, 1974). Quantitative evaluation of the innervation of the circular layer by Gabella (1972) showed that nearly two-thirds of the vesicle-containing axons in the guinea-pig ileum closely apposed muscle cells near the submucosa. The remainder of the circular muscle innervation was less dense and more uniformly distributed.

Electrical activity recorded at various sites within the circular muscle also appears to be heterogeneous. In rabbit jejunum (Taylor *et al.* 1976) and guinea-pig stomach (Tomita, 1981) larger amplitude slow waves were recorded from discrete regions of circular muscle near the myenteric plexus. These authors speculated that these areas were at or near the site of slow wave origin just beneath the longitudinal muscle layer. Other investigators (Hara & Szurszewski, 1981) have reported that electrical activities of circular muscle cells of canine jejunum varied when the muscle was trisected into the following layers: serosal, intermediate, and luminal. The serosal muscle generated spontaneous slow waves whereas the intermediate layer was quiescent. Slow waves were also absent from luminal muscle cells, but spike potentials were observed. *In situ*, the circular muscle probably functions as an electrical syncytium, and not as independent layers, so it is difficult to interpret the physiological significance of this study.

Although the electrical activity of canine gastric antral muscle has been recorded in several studies (Morgan & Szurszewski, 1980; El-Sharkawy, Morgan & Szurszewski, 1978; El-Sharkawy & Szurszewski, 1978; Sanders & Bauer, 1982), systematic investigations to determine whether electrical activity is homogeneous throughout the circular muscle have not been performed. All of the previous studies have employed preparations in which approximately three-fourths of the circular muscle layer was removed to reduce contractile force and increase the duration of intracellular impalements. Therefore, only the electrical activity of muscle cells near the myenteric plexus has been characterized. All of the studies have found a correlation between electrical slow wave activity and mechanical activity, so if electrical activity varies within the circular muscle then the mechanical responsiveness may vary as well. The present study investigates the hypothesis that electrical activity in the canine gastric antrum is not homogeneous throughout the circular layer. To test the hypothesis a cross-sectional preparation of the entire muscularis externa was used so that intracellular recordings could be made at precise distances from the myenteric plexus. Once the electrical activity was characterized, other experiments were designed to delineate possible mechanisms of these differences.

METHODS

Mongrel dogs of either sex were anaesthetized with sodium pentobarbitone, and the abdomen of each animal was opened along a mid-line incision. The entire stomach was removed and placed in a dish containing a pre-oxygenated Krebs solution. The muscularis externa from the dorsal surface of the antrum was dissected from the mucosa and pinned, serosal side up, in a dissecting dish. From this antral muscle sheet, strips of muscle were obtained for electrophysiological experiments.

Electrophysiological experiments

Muscle strips for electrophysiological experiments were obtained by making two parallel cuts 10 mm long and 1 mm apart either parallel or perpendicular to the circular muscle fibres. The muscle strips were transferred to an electrophysiological recording chamber and pinned with several dissecting pins (0·14 × 10 mm) in cross-section to the Sylgard floor (Fig. 1). These cross-sectional preparations allowed precise placement of micro-electrodes to impale circular cells at any depth within the circular layer.

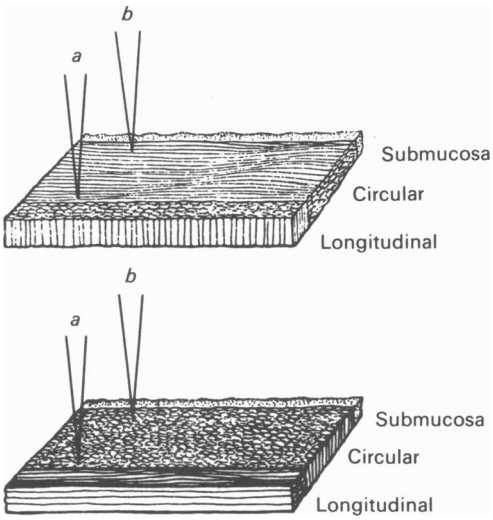

Fig. 1. Cross-sectional preparations of gastric antral muscle. Top panel shows a preparation cut parallel to the circular fibres and the bottom panel shows a preparation cut perpendicular to the circular fibres. Cells in the circular layer were impaled with micro-electrodes from the myenteric plexus (a) to the submucosa (b). In some experiments cells from both regions were recorded from simultaneously.

Muscles were maintained throughout dissection and recording by a constant perfusion of a pre-warmed, pre-oxygenated Krebs solution. The temperature was monitored constantly in the chamber by a thermistor probe submerged in the bathing solution near the muscle preparation and maintained at 37·5 ± 0·5 °C.

Once in the recording chamber, the antral muscle strip was allowed to equilibrate for one hour. Individual circular muscle cells were impaled with glass micro-electrodes filled with 3 M-KCl and having resistances ranging from 20 to 40 MΩ. Recordings were accepted when a sharp voltage drop of greater than 55 mV was observed, a steady resting membrane potential persisted, and spontaneous slow waves occurred. Simultaneous intracellular recordings from two cells within the same preparation were obtained by two rigidly mounted micro-electrodes suspended on independent micromanipulators. Transmembrane potentials were recorded by a multiple-channel high-impedance amplifier (WPI model 7000). The electrical signals were displayed on an oscilloscope (Tektronix) and recorded with an FM tape recorder (Hewlett–Packard 3964A) for off-line analysis.

Data analysis

Various parameters of the electrical slow wave activity (Fig. 2) were quantitatively analysed: (i) resting membrane potential; (ii) time constant of the slow wave foot (τ_f); (iii) maximum rate of rise of the upstroke; (iv) upstroke amplitude; (v) plateau amplitude; (vi) duration of the slow wave to 90 % repolarization; and (vii) the integrated area of the slow wave to 90 % repolarization. Most of these parameters were calculated by computer. The time constant of the foot potential was calculated by digitally curve-fitting fifty points along the foot of the slow wave to an exponential

function. The time constant was then determined from the best exponential (average correlation coefficient was $r = 0{\cdot}997 \pm 0{\cdot}004$; $n = 42$). Maximum rate of rise of the upstroke potential (dV/dt) was calculated by digitally sampling the depolarization at 500 Hz and calculating the maximum rate of change. Slow wave duration was calculated as the time from 10% of the maximum upstroke amplitude to 90% repolarization of the slow wave. Area under the slow wave was calculated as the time integral of slow wave amplitude/duration. Amplitudes were calculated as the maximum depolarizations from resting membrane potential during the upstroke and plateau phases of the slow waves. Data were compiled as means ± S.D., and differences in slow wave parameters between cell populations were determined by a paired or unpaired t tests.

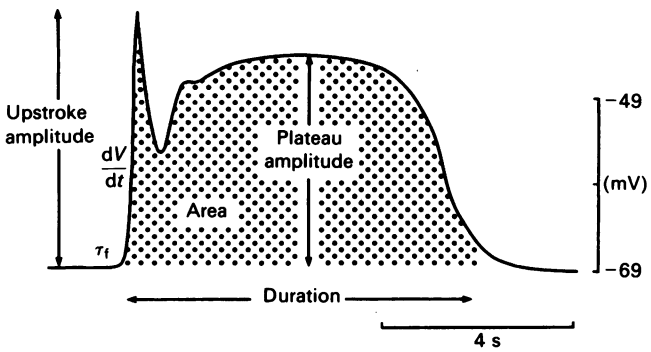

Fig. 2. Slow wave parameters measured from myenteric and submucosal circular muscle cells. (See text for details.)

Solutions and drugs

The modified Krebs solution used throughout these studies 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. When aerated with a 97% O_2–3% CO_2 gas mixture, the pH was 7·4 ± 1·0. Drugs used were: phentolamine, propranolol, tetrodotoxin (TTX; Sigma), and indomethacin (gift of Merck, Sharp and Dohme). The concentrations of the drugs reported in the results are those of the final concentration of the agent reaching the tissue.

RESULTS

Spontaneous electrical activity of circular muscle cells

Slow waves occurred spontaneously in all preparations at an average frequency of 1·6 ± 0·5 events min^{-1}. The characteristics of antral slow waves recorded from cells near the myenteric plexus have been described previously (El-Sharkawy *et al.* 1978; El-Sharkawy & Szurszewski, 1978), but briefly, slow waves consist of a relatively rapid upstroke depolarization followed by a partial repolarization and a prolonged plateau depolarization before the membrane repolarizes to its resting membrane potential (see Fig. 2). Fig. 3*A* shows a typical slow wave recorded from a circular cell within 0·5 mm of the myenteric plexus. These will be referred to as 'myenteric' circular cells. Slow waves recorded from this region were very consistent from cell to cell and from preparation to preparation. The averaged slow wave parameters measured are shown in Table 1. Slow waves recorded from preparations cut either parallel or perpendicular to the circular fibres were not significantly different. Therefore, a distinction of circular muscle orientiation will not be made throughout

the rest of the study, and only the recording position through the thickness of the circular layer will be noted.

In contrast to myenteric cells, circular muscle cells from within 0·5 mm of the submucosa, 'submucosal' cells, demonstrated electrical activities that were significantly different. The main differences were that submucosal cells were less polarized

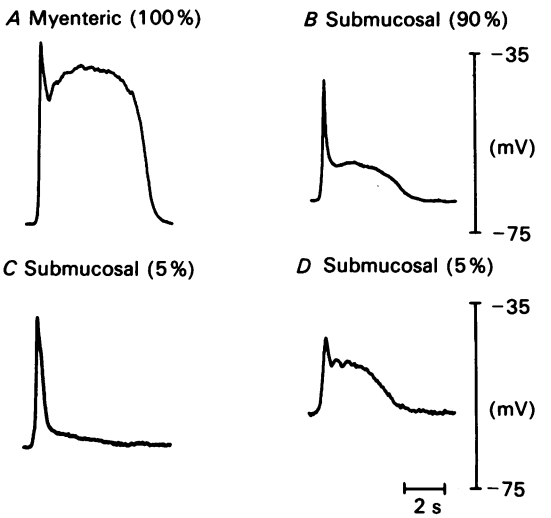

Fig. 3. Slow waves recorded from myenteric and submucosal circular cells. *A* shows an example of the robust slow waves recorded from muscle cells near the myenteric border of the circular muscle. Electrical activity from this region was similar in all preparations. The shape of slow waves from submucosal cells was more variable. *B–D* show the types of slow wave activity and the relative size (%) of cell populations displaying each type of activity. Table 1 summarizes the differences in slow wave parameters between myenteric and submucosal cells.

TABLE 1. Comparison of slow wave parameters measured from myenteric and submucosal circular muscle cells

	Myenteric circular	Submucosal circular	Significance
R.m.p. (mV)	−73·3±4·4	−64·1±5·3	$P < 0·001$
τ_f (ms)	48·1±12·4	84·0±25·2	$P < 0·001$
dV/dt (V s^{-1})	0·64±0·23	0·32±0·12	$P < 0·001$
U_{amp} (mV)	32·2±4·5	22·1±5·1	$P < 0·001$
P_{amp} (mV)	26·1±5·4	10·1±2·3	$P < 0·001$
Duration (s)	6·6±1·4	5·6±1·3	$P < 0·05$
Area (mV s)	147·9±56·0	44·9±15·9	$P < 0·001$
Preparations	30	29	

R.m.p., resting membrane potential; τ_f, time constant of the slow wave foot; dV/dt, maximum rate of rise of the upstroke; U_{amp}, upstroke amplitude; P_{amp}, plateau amplitude.

than myenteric cells, and the slow waves recorded from submucosal cells were of a different configuration, which also occasionally varied from cell to cell. Approximately 90% of cells demonstrated slow waves consisting of an upstroke depolarization followed by a small plateau potential (Fig. 3*B*); 5% of the slow waves consisted of a slow wave which repolarized without a plateau potential (Fig. 3*C*); and 5% of the

cells were quite depolarized (average $-58{\cdot}2 \pm 2{\cdot}6$ mV; $n = 13$) and had slow waves of a greatly reduced amplitude (Fig. 3*D*). In some preparations all three types of slow wave activities were observed. But from the majority of preparations slow waves like those shown in Fig. 3*B* were recorded from all cells. Table 1 compares several parameters of the electrical activity of the myenteric and submucosal circular muscle cells.

One explanation of the differences in slow wave configuration might be that slow waves arise in the longitudinal muscle or near the myenteric plexus and spread passively toward the submucosa (Bortoff & Sachs, 1970; Bortoff, Michaels & Mistretta, 1981). If submucosal cells lack the capacity to regenerate activity and propagation is electrotonic, one would expect: (i) approximately an exponential decay in the voltage response as a function of distance and (ii) nearly simultaneous occurrence of the slow waves through the thickness of the circular muscle syncytium. To test this hypothesis two cells were impaled within the same muscle strip and simultaneous recordings of transmembrane potential were made. In twenty-seven preparations in which dual intracellular recordings were made, slow waves always occurred first in the myenteric cells. The time required for the slow waves to spread from the impaled myenteric cell to the impaled submucosal cell varied from event to event, but had an average latency of $0{\cdot}32 \pm 0{\cdot}21$ s. Fig. 4 shows an example of simultaneous recordings from myenteric and submucosal circular cells. These data demonstrate that time is required for slow wave propagation from the site of origin (which is apparently on the serosal half of the muscularis externa) through the circular muscle.

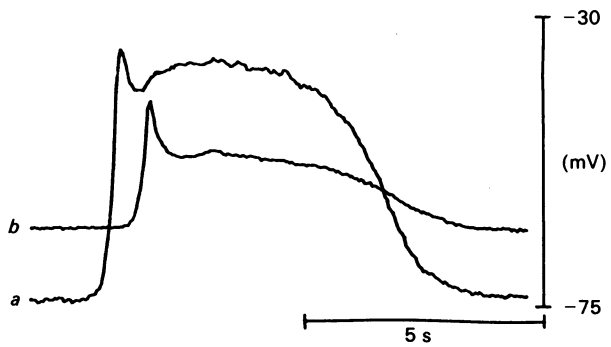

Fig. 4. Propagation of a slow wave from a myenteric circular muscle cell (a) to a submucosal muscle cell (b). These recordings were made simultaneously from two cells at the approximate positions depicted in Fig. 1. Spontaneous slow waves were always observed first near the myenteric plexus and then later at the submucosa.

Another means to test the hypothesis that the slow waves propagate passively is to consider the generation of slow waves near the longitudinal border as a brief inward 'current injection' and the resulting slow wave as the transmembrane voltage response. If propagation is passive, cable theory for a long cable would predict that the upstroke, which is the transient voltage response to an impulse of inward current, would decay exponentially with distance from the site of origin (Abe & Tomita, 1968). Therefore, in nine preparations several circular muscle cells were impaled at various

distances from the myenteric plexus and slow wave activity was recorded. These recordings showed that the upstroke dV/dt, upstroke potential amplitude and plateau potential amplitude decayed generally in a linear manner with distance with average slopes of $-10{\cdot}0 \pm 4{\cdot}5$ V s^{-1} mm^{-1}, $-6{\cdot}5 \pm 3{\cdot}1$ mV mm^{-1}, $-7{\cdot}4 \pm 3{\cdot}0$ mV mm^{-1}, respectively and average correlation coefficients of $-0{\cdot}87 \pm 0{\cdot}11$, $-0{\cdot}89 \pm 0{\cdot}15$, $-0{\cdot}96 \pm 0{\cdot}03$, respectively. Data from one representative experiment are plotted in Fig. 5. The data from these experiments also demonstrated that all of the slow wave parameters displayed in Table 1 change gradually as a function of distance from the myenteric plexus.

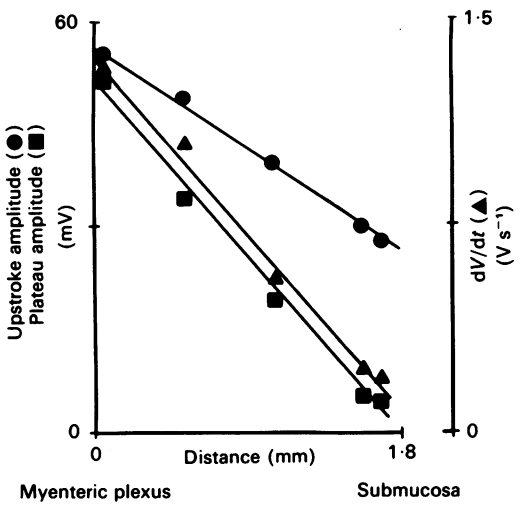

Fig. 5. Upstroke depolarization velocity (dV/dt), upstroke amplitude, and plateau amplitude decay linearly as a function of distance from the myenteric plexus to the submucosa (1·8 mm). The Figure shows data recorded from five cells of one preparation at various distances from the myenteric plexus. The values of slow wave parameters at each site were fitted to straight lines by linear regression analysis. The results are representative of nine similar experiments; for mean values see text.

Effects of TTX and receptor antagonists on electrical activity of submucosal cells

The enteric nervous system is known to modulate the activity of gastrointestinal smooth muscles (Wood, 1981). Others have reported that antral muscle near the myenteric plexus is not tonically affected by nerves (El-Sharkawy *et al.* 1978). But Gabella (1972) has found a higher axonal density in the circular muscle near the submucosa, so it is possible that the differences in electrical activity in cells near the submucosa were caused by tonic neural activity. To test this hypothesis muscles were treated with neural blockers and receptor antagonists, including atropine (10^{-6} M), TTX (10^{-7} M), phentolamine (10^{-6} M), and propranolol (10^{-6} M). In these experiments after recording control slow wave activities from cells near the submucosa in nine preparations, the muscles were treated with TTX and atropine (five muscles) or phentolamine and propranolol (four muscles). None of these agents had discernible effects on the spontaneous slow wave activity of the submucosal circular cells. These

data suggest that the gradient in electrical activity recorded through the thickness of the circular muscle was not due to a gradient in neural activity.

Effects of indomethacin on electrical activity of submucosal cells

Previous studies have shown that endogenous prostaglandins are local regulatory substances in gastric muscles, and the dominant effect of these compounds in antral circular muscle is inhibitory (Sanders & Szurszewski, 1981; Sanders, Bauer & Publicover, 1983; Sanders, 1984). Many of the slow wave parameters shown to differ

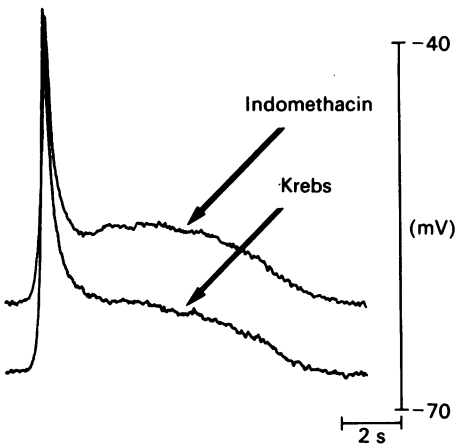

Fig. 6. Effect of indomethacin on submucosal slow waves. The Figure shows an example of the changes in slow waves caused by indomethacin (10^{-5} M) for 45 min. After indomethacin the membrane potential was less polarized, dV/dt and upstroke amplitude decreased, and plateau amplitude increased. (See text for details.)

in the submucosal cells could be the result of higher local prostaglandin E_2 concentrations (Sanders & Szurszewski, 1981). Therefore experiments were conducted in which muscles were treated with indomethacin, a cyclo-oxygenase inhibitor, to determine whether decreasing prostaglandin production would cause the electrical activity in submucosal cells to approach that observed in myenteric cells. In three preparations electrical activity was recorded from submucosal cells, and then while maintaining the impalements, the muscles were treated with indomethacin (10^{-5} M) for 45 min. During this period the following changes in submucosal slow waves were noted: (i) the resting membrane potential depolarized from $-68{\cdot}0 \pm 5{\cdot}3$ mV to $-63{\cdot}3 \pm 2{\cdot}1$ mV; (ii) dV/dt decreased from $0{\cdot}27 \pm 0{\cdot}16$ V s^{-1} to $0{\cdot}16 \pm 0{\cdot}08$ V s^{-1}; (iii) upstroke amplitude decreased from $31{\cdot}3 \pm 4{\cdot}3$ mV to $26{\cdot}3 \pm 3{\cdot}2$ mV and (iv) plateau amplitude increased from $6{\cdot}0 \pm 1{\cdot}0$ mV to $8{\cdot}3 \pm 4{\cdot}0$ mV. These changes were similar to those previously documented in myenteric circular muscle (Sanders & Szurszewski, 1981). In these experiments indomethacin treatment failed to convert the activity of submucosal cells to activity similar to myenteric cells (Fig. 6). In fact the resting potential, dV/dt and upstroke amplitude deviated further from myenteric slow wave values. These data strongly suggest that a gradient in endogenous prostaglandin concentration cannot explain the gradient in electrical activity through the thickness of the circular muscle.

Effect of membrane depolarization on electrical activity of myenteric cells

The membranes of submucosal cells were approximately 5 mV less polarized than myenteric cells. All of the electrical differences between myenteric and submucosal cells described in Table 1 might be due to the less polarized state of submucosal cells. The greater foot potential time constant and lower upstroke velocity of submucosal slow waves might be explained by a lower input resistance resulting from the depolarized state. A smaller driving force on ions carrying inward currents and an inactivation of potential-dependent ion channels (Morgan & Szurszewski, 1980) might result in lower upstroke and plateau potential amplitudes. To test this hypothesis,

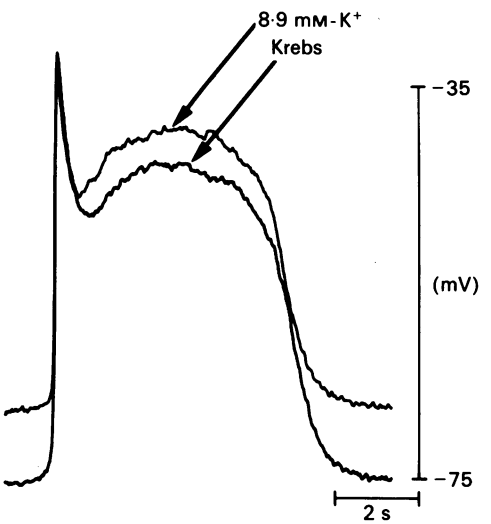

Fig. 7. Effects of elevated external potassium on myenteric slow waves. External potassium was increased from 5·9 mM (regular Krebs solution) to 8·9 mM to test the hypothesis that differences in slow wave activity were due to differences in membrane polarization. Elevating external potassium to 8·9 mM depolarized membrane potentials of myenteric cells to the average level of submucosal cells. This depolarization increased τ_f, decreased dV/dt and upstroke amplitude, and increased the maximum level of depolarization achieved during the plateau depolarization. These changes made the myenteric slow waves somewhat more similar to the submucosal slow waves, but differences in polarization alone could not fully explain the differences in electrical activity between these two populations of cells.

the electrical activity in myenteric cells from six preparations was recorded in Krebs solution containing 5·9 mM-K^+ (regular Krebs solution) and while maintaining the impalement exposed to an isotonic Krebs solution containing 8·9 mM-K^+. This concentration of external potassium was found to depolarize myenteric cells to an average of $65{\cdot}7 \pm 3{\cdot}7$ mV, approximately the resting membrane potential of mucosal cells. Depolarization increased τ_f of the myenteric slow waves from $36{\cdot}2 \pm 12{\cdot}3$ ms to $54{\cdot}6 \pm 28{\cdot}8$ ms, decreased dV/dt from $0{\cdot}74 \pm 0{\cdot}14$ V s^{-1} to $0{\cdot}64 \pm 0{\cdot}14$ V s^{-1}, and also decreased upstroke and plateau amplitudes from $38{\cdot}6 \pm 4{\cdot}4$ to $35{\cdot}5 \pm 4{\cdot}5$ mV and from $32{\cdot}0 \pm 5{\cdot}6$ to $29{\cdot}4 \pm 5{\cdot}4$ mV respectively ($n = 5$, $P > 0{\cdot}05$) (see Fig. 7). These changes in myenteric electrical activity due to depolarization changed some of the myenteric

slow wave parameters toward submucosal parameters, but depolarization alone could not account for the differences between the electrical activities of myenteric and submucosal circular cells.

DISCUSSION

These experiments have demonstrated that a gradient exists in the electrical activities of circular muscle cells within the wall of the canine antrum. Cells near the myenteric plexus were more polarized and generated robust slow wave depolarizations. In contrast cells near the submucosa were less polarized and generated much weaker and less prolonged slow waves. These findings are potentially physiologically significant because others have demonstrated that a relationship exists between the magnitude and duration of the electrical slow wave and the magnitude and duration of the subsequent mechanical activity (El-Sharkawy *et al.* 1978; El-Sharkawy & Szurszewski, 1978; Morgan & Szurszewski, 1980). In order for excitation–contraction to occur in antral muscles, slow waves must exceed a 'mechanical threshold' voltage, which in myenteric cells of canine muscles has been reported to be approximately −40 mV (Morgan & Szurszewski, 1980). In the present study slow waves recorded from myenteric cells depolarized to approximately −45 mV, which was close to the reported mechanical threshold. Low levels of excitatory stimulation would be capable of generating large contractile responses in these cells. In contrast slow waves of submucosal cells depolarized to approximately −55 mV. This level of depolarization is well below the mechanical threshold. Therefore, this finding suggests that either submucosal muscle cells are mechanically inactive in the absence of massive excitatory input, or excitation–contraction coupling is dependent upon a different mechanical threshold in submucosal cells.

The mechanism of slow wave propagation in gastrointestinal circular muscles has been investigated before (Kobayashi, Nagai & Prosser, 1966; Bortoff & Sachs, 1970; Connor, Kreulen, Prosser & Weigel, 1977; Connor, Mangel & Nelson, 1979; Bortoff *et al.* 1981). Bortoff and co-workers, using volume recordings, reported that intestinal slow waves spread electrotonically through the thickness of the circular muscle. In sharp contrast, our data obtained from gastric antral muscles with more precise recording techniques indicate that propagation is an active, regenerative process because: (i) time is required for slow waves to spread through the circular muscle (see Fig. 4) and (ii) the depolarization velocity of the upstroke (dV/dt), the upstroke amplitude and the plateau amplitude decayed in an approximately linear manner with distance (see Fig. 5), rather than exponentially as predicted from cable theory if the slow wave propagated passively (Abe & Tomita, 1968). Connor and colleagues (1977; 1979) and Kobayashi *et al.* (1966) have also suggested that propagation in circular muscle of cat small intestine occurs actively. Clearly the precise mechanism of propagation in circular muscle is yet to be understood. However, the circular muscle of the stomach must contain regenerative mechanisms because circular muscle entirely free of longitudinal muscle is spontaneously active and depolarizing current can also evoke slow waves (A. J. Bauer & K. M. Sanders, unpublished observations).

The data in this study also demonstrate that a small voltage gradient exists within the circular muscle. Myenteric cells were on average 5 mV more polarized than

submucosal cells. Since the myenteric and submucosal cells appear to be electrically coupled this finding suggests that small currents may continually flow through the circular muscle layer. The magnitude of these currents is likely to be extremely small because of the large number of intercellular junctional resistances in the current pathway. Others who have measured cable properties in circular muscle in the direction perpendicular to the long axis of the circular cells have found length constants to be 0·5 and 0·3 mm (Connor *et al.* 1977; Elden & Bortoff, 1984). This suggests that internal resistance in this axis is high enough that a small voltage difference could be tolerated without excessive energy loss.

The more depolarized submucosal cells may have a lower input resistance which might explain the difference in slow wave activities in myenteric and submucosal cells. Morgan & Szurszewski (1980) have shown that at relatively low levels of depolarization, approximately 6 mV, a delayed rectification turns on in gastric corporal circular muscle. An increased membrane conductance in submucosal cells might, therefore, account for the greater 'foot' time constants, slower depolarization velocities, lower slow wave amplitudes, and shorter slow wave durations recorded. This hypothesis was tested by recording slow wave activity in myenteric cells before and in the presence of slightly elevated external potassium to determine if the activity in submucosal cells could be mimicked by depolarization of myenteric cells. These experiments demonstrated that the differences between myenteric and submucosal slow waves could not be explained solely on the basis of resting membrane potential. Depolarization probably increased membrane conductance by primarily increasing potassium conductance (delayed rectification) and this caused some of the slow wave parameters such as τ_f and upstroke velocity to approach the values obtained from submucosal cells. Perhaps the permeability of submucosal cells is also generally higher to ions such as sodium and chloride. This might explain the depolarized state and reduced slow waves in these cells. Experiments are in progress to test this hypothesis.

Differences in electrical activity of myenteric and submucosal muscle cells might also be explained by differences in excitability mechanisms. The membrane channels responsible for the active slow wave event might be more sparse in submucosal cells. Testing of this hypothesis will most likely depend upon analysis of channel density utilizing the patch-clamp technique.

In conclusion, the present study has demonstrated that a linear change in slow wave activity occurs within the antral circular muscle wall. The measured slow wave parameters diminished linearly with distance from the myenteric plexus to the submucosa. This finding is physiologically of interest because of the dependence of excitation–contraction coupling on membrane potential.

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