J. Physiol. (1978), **277**, *pp.* 91–102
With 6 text-figures
Printed in Great Britain

A STUDY OF THE CANINE GASTRIC ACTION POTENTIAL IN THE PRESENCE OF TETRAETHYLAMMONIUM CHLORIDE

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(*Received 26 April 1977*)

SUMMARY

1. The effects of tetraethylammonium (TEA) ion on the action potential of isolated longitudinal muscle of the dog antrum were used to gain some insight into the mechanism of generation of the plateau potential of the action potential complex. The double sucrose gap was used.

2. In concentrations of TEA up to 5 mM, the amplitude of the upstroke potential was increased. In 10 mM-TEA there was also an increase in the amplitude of the plateau potential and in the maximum rate of rise of the upstroke potential.

3. Concentrations of TEA (3 mM and greater) increased the duration of the action potential. Five mM-TEA produced spike potentials which occurred only during the plateau potential of the action potential. Each spike caused a contraction.

4. The steady-state voltage–current relation was studied in normal Krebs solution and in TEA containing Krebs solution. In normal Krebs solution the voltage response was not a linear function of the applied current when outward current pulses were used. In TEA solution the voltage response was a linear function of the entire range of applied depolarizing current.

5. In low concentrations of TEA (2–4 mM), when the steady-state voltage–current relation was linear, constant current pulses were applied between action potentials and during the plateau potential to determine if there were a decrease in membrane slope resistance during the plateau. It was found that the amplitude of the electrotonic potential recorded during the plateau was significantly less than the amplitude of the electrotonic potential recorded between action potentials.

6. The rate of repolarization of the plateau potential was studied in normal Krebs solution and in 2 mM-TEA Krebs solution. The rate of repolarization of the plateau potential was slowed in TEA Krebs solution.

7. It is concluded that there is an increase in the membrane conductance during the plateau potential. The repolarization following the plateau potential is due to a TEA-sensitive outward current.

INTRODUCTION

In previous papers (Szurszewski, 1975, 1976) the spontaneous action potential of the longitudinal muscle of the antrum of the canine stomach was described. Each

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action potential consisted of an upstroke potential followed by a plateau potential. In this smooth muscle, agonists such as acetylcholine and pentagastrin produced phasic contractions by increasing the amplitude and duration of the plateau potential. No spike potentials occurred during any portion of either the spontaneous action potential or during the stimulatory action of acetylcholine and pentagastrin.

In gastro-intestinal smooth muscle, slow wave potentials occur which are similar in shape to the plateau potential of the gastric action potential. There are two divergent hypotheses regarding the underlying mechanism of the intestinal slow wave. One hypothesis suggests that the slow wave potential is due to a cyclic turning-on and turning-off of an electrogenic sodium pump (Connor, Prosser & Weems, 1974). The other suggests that the slow wave is due to a cyclic increase in membrane conductance (Bolton, 1971; Mills & Taylor, 1971; Magaribuchi, Ohba, Sakamoto & Yamamoto, 1972; El-Sharkawy & Daniel, 1975). However, the slow wave occurs in the non-linear region of the voltage–current relation thus making it difficult to decide if the increase in the membrane conductance results from the increase in conductance to potassium which is known to occur in the region of delayed rectification or to an increase in conductance to other ions. In the circular muscle of the guinea-pig stomach, a plateau potential occurs which is quite similar to the one present in canine gastric muscle (Ohba, Sakamoto & Tomita, 1975). Using the double sucrose gap method Ohba *et al.* (1975) found that the amplitude of the plateau was reduced by depolarization and increased by hyperpolarization. They concluded that the plateau depended upon a voltage-dependent increase in membrane conductance. The mechanism underlying these potential changes in gastro-intestinal smooth muscle has not been entirely resolved.

There are no comparable studies dealing with the mechanism of generation of the plateau potential in canine gastric smooth muscle. Thus, experiments were designed to determine if a membrane slope resistance change occurs during the plateau potential. Since tetraethylammonium (TEA) ion suppresses outward-going rectification in smooth muscle (Ito, Kuriyama & Sakamoto, 1970; Kroeger & Stephens, 1975), experiments were done in TEA containing Krebs solution and constant current pulses were applied between action potentials and during the plateau potential. It should be emphasized that in these experiments, the change in voltage due to the applied current is a measure of the membrane slope conductance. If an increase in membrane slope conductance occurs during the plateau potential, then the amplitude of the steady-state electrotonic potential recorded during the plateau potential should be less than that recorded between action potentials. If the increase in conductance is only to potassium, then TEA should abolish the difference in the size of the electrotonic potentials. It will be shown that in TEA Krebs solution there is an increase in membrane conductance during the plateau potential. Further, it will be shown that repolarization of the plateau potential may be due to an increase in membrane conductance to potassium.

METHODS

Seventy-five dogs ranging in weight from 10 to 22 kg were used. The method used to remove patches of smooth muscle from the gastric antrum has been described (Szurszewski, 1975). The double sucrose gap and intracellular micro-electrode techniques were used in this study. When

the double sucrose gap technique was used, strips of isolated longitudinal muscle 700–800 μm in width and 3·5 cm in length were used. In these experiments, the test node width was adjusted to equal the width of the strips. The description of the double sucrose gap technique has been previously described (Szurszewski, 1975). In this study, this technique was the primary method used.

When the intracellular technique was used, isolated longitudinal muscle strips were prepared in exactly the same way as previously described for use in the double gap (Szurszewski, 1975). These strips were securely pinned down to the floor of the recording chamber with the serosal surface facing upwards. The transmembrane potential was recorded with glass micropipettes filled with 3 M-KCl. The usual apparatus was used for amplification and displaying of the signal.

In both the double sucrose gap and intracellular recording techniques, Krebs solution containing (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, glucose 11·5 was used and equilibrated with 97% O_2 + 3% CO_2, pH 7·3–7·4. All experiments were done at 37 ± 0·5 °C. TEA Krebs solution was similar to normal Krebs solution except the sodium chloride was replaced by an osmotically equivalent amount of TEA chloride.

RESULTS

General observations

Fig. 1*A* shows an example of an intracellular recording of a gastric action potential recorded from a muscle fibre bathed in normal Krebs solution. In ten longitudinal muscle strips removed from five dogs, recordings were made from twenty-three cells. In any single preparation when successful impalements were made, each cell recorded from produced action potentials. When the preparation was bathed in Krebs solution containing TEA chloride, marked changes occurred in the action potential. Fig. 1*B* shows the effect of a 13 min soak in 5 mM-TEA. Bursts of spikes occurred on top of the plateau potential. There was also a significant prolongation of the action potential. It was not possible to record the entire action potential from any longitudinal muscle cell soaked in TEA containing Krebs solution because of the strong twitches associated with each spike. To characterize better the effects of TEA on the gastric action potential and to be able to use TEA to analyse the mechanism which causes the plateau potential and its repolarization, the double sucrose gap was used. All the data which follow were obtained with this technique using isolated longitudinal muscle.

When the muscle was placed in Krebs solution containing TEA chloride, marked changes in the action potential occurred. The amplitude of the upstroke increased, the plateau potential increased, there was a marked prolongation of the duration of the action potential, repetitive spike bursts occurred on top of the plateau potential for high concentrations of TEA chloride and there was a suppression of the rectifying property of the active membrane.

The first three mentioned effects are illustrated in Fig. 2 and summarized for the whole series of experiments in Fig. 3. It can be seen in these Figures that TEA produced an increase in the peak amplitude of the upstroke potential which was concentration dependent. TEA also increased the amplitude of the plateau but this increase was not as marked as the increase in the upstroke. In Krebs solution containing 10 mM-TEA or greater, there was a significant increase in the maximum rate of rise of the upstroke. For example, in 20 and 30 mM-TEA, the maximum rate of rise was, respectively, 1·8 ± 0·25 V/sec (S.E. of mean, n = 15) and 2·0 ± 0·3 V/sec

(S.E. of mean, $n = 5$). In normal Krebs solution, the maximum rate of rise was 0·9 V/sec ± 0·1 (S.E. of mean, $n = 37$).

In concentrations ranging from 1 to 5 mM-TEA the membrane potential was not altered. In concentrations of 5 and 10 mM-TEA, the membrane depolarized by a mean of 0·2 ± 0·26 mV (S.E. of mean, $n = 7$) and 0·4 ± 0·2 mV (S.E. of mean, $n = 7$),

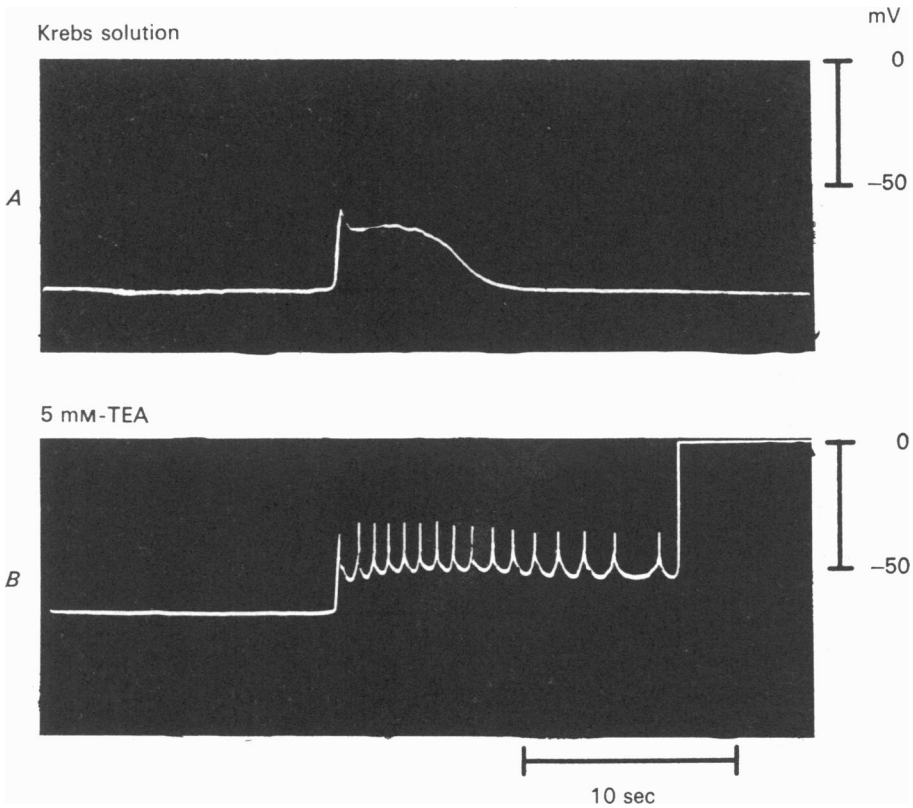

Fig. 1. Effect of 5 mM-TEA chloride on spontaneous action potential recorded intracellularly from a muscle fibre in longitudinal muscle. *A*, Krebs solution, *B*, 13 min after adding TEA. Note burst of spike potentials on top of plateau potential and prolongation of duration of action potential. In *B*, electrode dislodged from cell during spiking.

respectively. These changes were not statistically significant ($P > 0·05$). In 20 mM-TEA, the membrane potential depolarized at first by a mean of 3·5 mV ± 0·7 (S.E. of mean, $n = 15$, $P < 0·01$) but then repolarized in 4 min to near the original resting potential. The degree of repolarization in 20 mM-TEA seemed to depend upon the degree of spike activity associated with the plateau. The more vigorous the spike activity the quicker and greater the repolarization. In 30 mM-TEA, the membrane potential depolarized by a mean of 4·2 ± 1·3 (S.E. of mean, $n = 15$, $P < 0·01$) and in all but one preparation remained depolarized.

TEA Krebs solution also prolonged the action potential (Fig. 2). In 1 mM-TEA, the duration was not significantly different from that which occurred in normal

Krebs solution. Higher concentrations ranging from 2 to 20 mM-TEA greatly prolonged the action potential. Above 20 mM-TEA there was no further significant prolongation of the action potential; hence, there seemed to be a limit to the lengthening of the action potential by TEA.

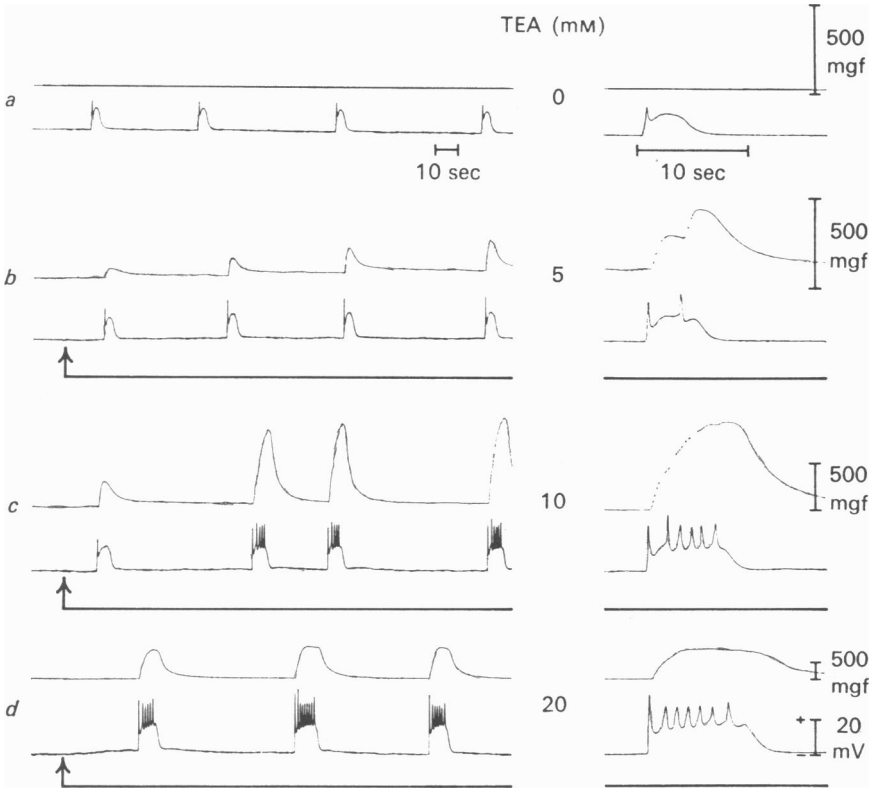

Fig. 2. Effect of three concentrations of tetraethylammonium (TEA) chloride on electrical and mechanical activity of isolated longitudinal muscle of the dog. Double sucrose-gap recordings. Records taken from the same preparation. Left-hand side, effect of applying TEA; right-hand side, effect after 3·5 min exposure. Top tracing, isometric tension; bottom tracing, electrical potential. On 20 mV calibration bar, + indicates depolarization is upward, − indicates hyperpolarization is downward. For further explanation see text.

TEA solutions (5 mM or greater) caused spike potentials to occur on top of the plateau potential (Fig. 2). Each spike produced an increase in twitch tension. Repetitive spiking was most pronounced in 20 and 30 mM-TEA. A few muscle strips were quite sensitive and showed repetitive firing in 4 mM-TEA.

According to Hille (1970), TEA can act on two sites in the membrane: sites that normally interact with acetylcholine and sites that normally interact with potassium ions. When tested (n = 10), atropine (1×10^{-4} g/ml.) had no effect on the action of TEA. Apparently, in this smooth muscle the second site of action is its only one.

To be sure the effects observed with TEA were not due to the reduction in the

external sodium concentration, five control experiments were performed in which 33 mM external sodium chloride were replaced with an osmotically equivalent amount of Tris chloride (hydroxymethylaminomethane). In all five experiments, none of the above effects occurred.

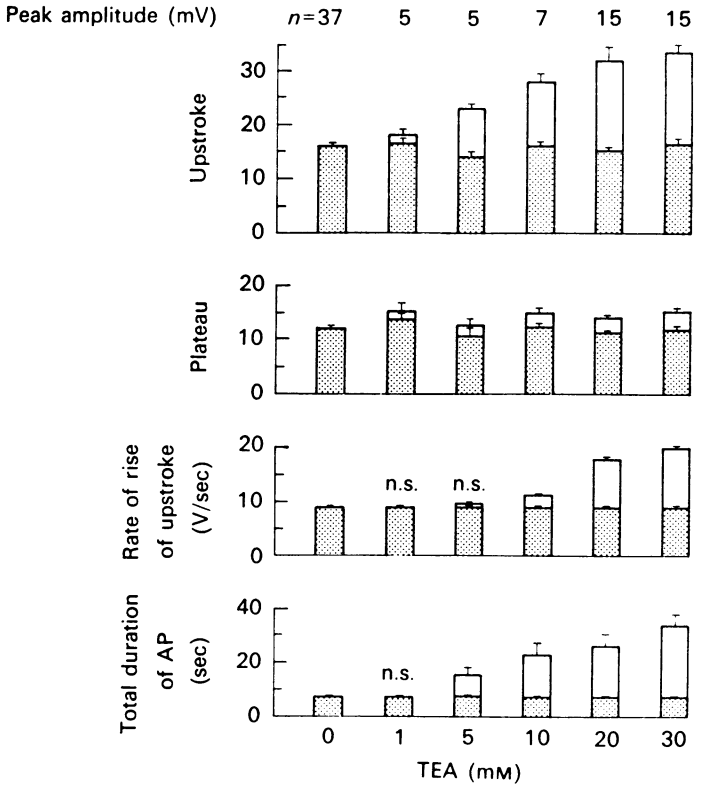

Fig. 3. Summary of changes in gastric action potential in different concentrations of TEA. Hatched bars on extreme left indicate mean ± S.E. of mean for four variables of action potential in Krebs solution in thirty-seven muscle strips. In each different concentration of TEA, hatched bar represents control value (± S.E. of mean) and clear bar value (± S.E. of mean) for the same muscle strip in the designated concentration of TEA. Number of muscle strips used indicated at top of the bars. Mean ± S.E. of mean indicated by height of column. N.S. = not statistically significant, $P > 0{\cdot}5$. All others significant at $P < 0{\cdot}05$. Further details, see text.

Effect of TEA on the steady-state voltage–current relation

The effect of TEA on the steady-state voltage–current relation was determined by applying hyperpolarizing and depolarizing current pulses *between* spontaneous action potentials. Extracellularly applied inward current (3–5 sec duration) produced an electrotonic potential. Outward current pulses produced an action potential complex when the membrane was depolarized by 4–6 mV. When action potentials were produced by an outward current pulse, the pulse duration was increased to 15–20 sec. In this instance, the steady-state depolarization was obtained by measuring the membrane potential between action potentials. Fig. 4*A* shows the total voltage–

current relation in Krebs solution and in 2 mM-TEA and Fig. 4*B* in Krebs solution and 30 mM-TEA. In this Figure, the applied current is plotted on the abscissa as the independent variable and the steady-state voltage plotted on the ordinate as the dependent variable. The voltage values represent the amplitude of the electrotonic potential when a steady state was reached. In all muscle strips tested (n = 14) in normal Krebs solution there was a limited portion of the relation over which the voltage response was a linear function of the applied current. At either end of this linear region the slope resistance decreased with further increments in the strength of the applied current. In 2 mM-TEA Krebs solution the voltage response was a linear function for the entire range of applied depolarizing current (Fig. 4*A*).

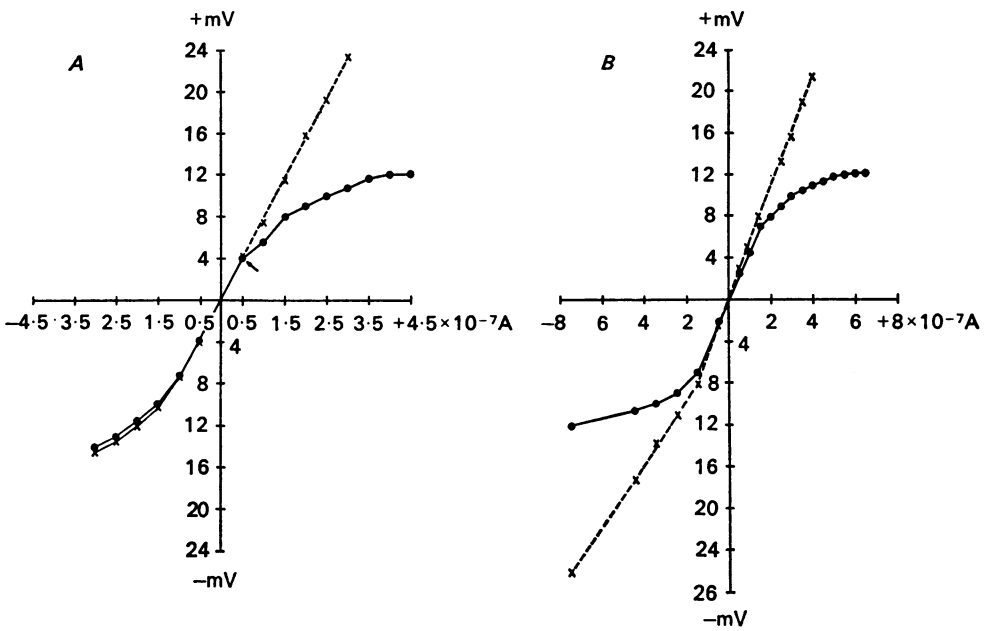

Fig. 4. Voltage–current relations from longitudinal smooth muscle from the canine antrum in Krebs solution (●—●, panels *A* and *B*) and during treatment with 2 mM-TEA (×---×, panel *A*) and 30 mM-TEA (×---×, panel *B*) solution. Effects of TEA observed after 5 min soak. Steady-state voltage values obtained *between* action potentials. Arrow marks electrotonic potentials analysed in Fig. 6.

Similar voltage–current relations were observed for concentrations of up to 10 mM. However, in 30 mM-TEA there was an increase in the slope resistance to both depolarizing and hyperpolarizing current pulses (Fig. 4*B*). This observation is in agreement with those recently made by Kroeger & Stephens (1975) for the canine tracheal smooth muscle and is in general agreement for the effects of high concentration of quaternary ammonium ions on steady-state voltage–current relations in other excitable membranes (cf. Hille, 1970; Narahashi, 1974).

Effect of TEA on the electrotonic potential recorded during the plateau potential

To determine if the membrane slope resistance changes during the plateau potential, the amplitude of the electrotonic potential between action potentials was compared to the amplitude of the electrotonic potential recorded during the plateau potential. If the steady-state electrotonic potential is smaller during the plateau potential, this can be taken as evidence that the membrane resistance is decreased during the plateau potential. In normal Krebs solution, the plateau potential is in the non-linear region of the voltage–current relation. However, in the presence of TEA, the current–voltage relation is linear (Fig. 4). Thus, comparison of the amplitude of the electrotonic potential between action potentials to the

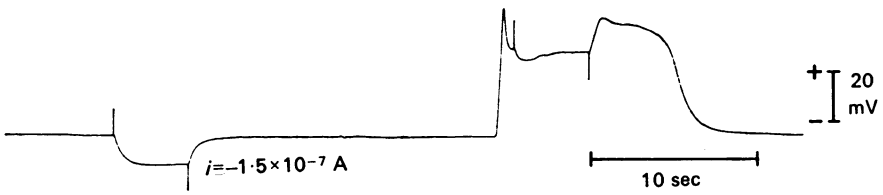

Fig. 5. Amplitude of electrotonic potential due to a constant current pulse ($-1{\cdot}5 \times 10^{-7}$ A) applied *between* action potentials (left) and *during* the plateau potential (right). Muscle soaked in 4 mM-TEA Krebs solution for 6 min. On 20 mV calibration bar, + indicates depolarization is upward, − indicates hyperpolarization is downward.

electrotonic potential during the plateau potential in TEA containing Krebs solution should indicate if the membrane resistance is decreased during the plateau potential. Using this rationale, experiments were performed in TEA Krebs solution. A concentration of TEA was used which did not produce spike potentials and which lengthened the duration of the plateau potential enough so that a long inward current pulse which reached steady state could be applied. Then an inward current pulse of the same strength and duration was applied between action potentials and during the plateau potential and the amplitude of the two electrotonic potentials were compared. The results from one of the six experiments are shown in Fig. 5. The voltage–current relation for this experiment was illustrated in Fig. 4*A*. The amplitude of the electrotonic potential recorded between action potentials is shown on the left in Fig. 5. The amplitude of the electrotonic potential recorded during the plateau potential is shown on the right in Fig. 5. The method of determining the maximum amplitude of the electrotonic potential during the plateau potential is worth special mention. The amplitude was determined by measuring the difference between the voltage just preceding the application of the current pulse (the reference potential) and the maximum change in voltage reached during the first few seconds following application of the current. This was necessary because when the current pulse was turned-off, the membrane voltage moved back to near a point on the plateau potential where it would have been had no current pulse been applied. This was always accompanied by an anode-break excitation which appeared as a small hump on top of the plateau potential (Fig. 5). Thus following the turning-off

of the current pulse, it is likely that other voltage and time dependent conductances might have occurred. When the amplitude of the electrotonic potentials between action potentials and during the plateau potential were compared to each other, the amplitude of the electrotonic potential during the plateau potential was smaller by 73% (Fig. 5). This demonstrates a decrease in slope resistance during the plateau potential even though the *steady-state* voltage–current relation was linear in this region.

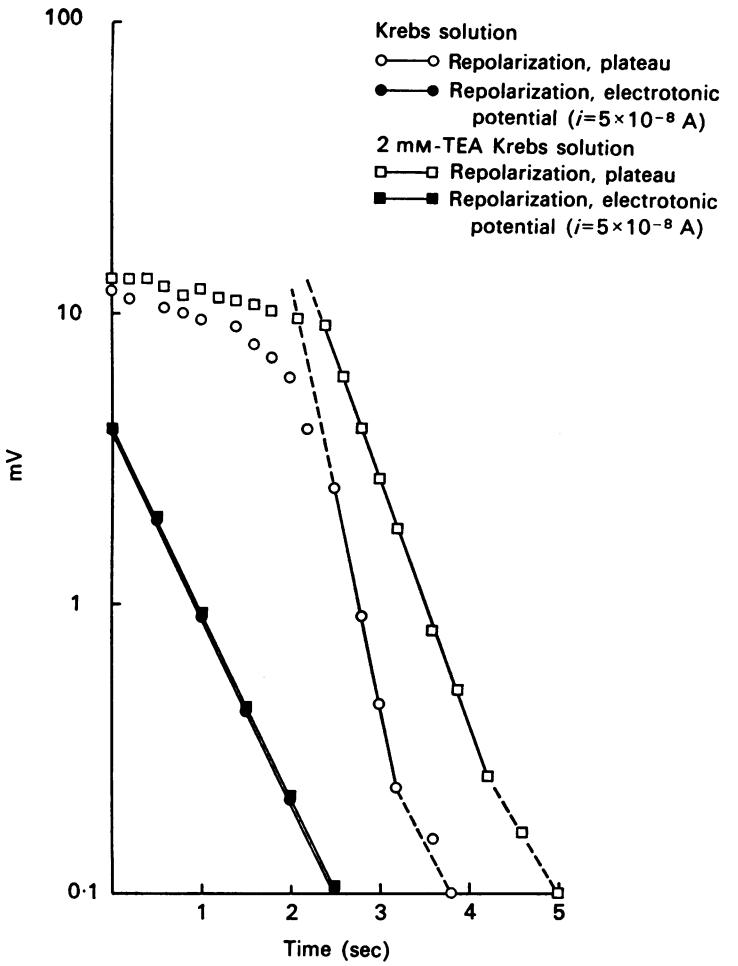

Fig. 6. Voltage–time relation for repolarization of the electrotonic potential and for repolarization of the plateau potential of the action potential in normal Krebs solution and in 2 mM-TEA Krebs solution. Continuous lines drawn by least-square analysis; bottom dashed lines drawn by eye. For details, see text.

Repolarization of the plateau. The preceding data suggest that an increase in membrane slope conductance caused the plateau potential. The question arises as to whether or not repolarization back to resting potential between action potentials is due only to turning-off of the inward current or to a turning-on of an outward current. A way to decide between these alternatives is to compare the rate of

repolarization of the plateau potential to the rate of repolarization of an electrotonic potential evoked by an outward current. If the rate of repolarization between the peak of the plateau and resting membrane potential is faster than the rate of repolarization of an electrotonic potential due to an outward current pulse, then a turning-on of an outward current would seem to be involved. An analysis of the repolarizations was made in Krebs solution and is illustrated in Fig. 6. The electrotonic potential used in this analysis was selected from the linear portion of the current–voltage relation shown in Fig. 4*A* and is marked with an arrow. The voltage–time relation for repolarization of the electrotonic potential is plotted using filled circles and repolarization of the plateau potential in normal Krebs solution is plotted using open circles. In normal Krebs solution during and just after the peak of the plateau when the membrane first began to repolarize, the slope of the voltage–time relation was steeper than the slope of repolarization of the electrotonic potential. This suggests that repolarization of the plateau was due to an outward current. However, the slope of the tail end of repolarization of the plateau potential (bottom dashed line, Fig. 6) approached the slope for repolarization of the electrotonic potential suggesting that during this later time of repolarization of the plateau, the outward current had turned off and the repolarizing process decayed across a resistance roughly equivalent to that for the resting membrane.

The effect of 2 mM-TEA on repolarization of the electrotonic potential (filled squares) and on repolarization of the plateau potential (open squares) is also plotted in Fig. 6. The rate of repolarization of the electrotonic potential in the presence of TEA was identical to that which occurred in normal Krebs solution. However, the initial rate of repolarization of the plateau was slower in TEA containing solution than in Krebs solution suggesting that repolarization of the plateau potential may be induced by a turning-on of an outward potassium current.

DISCUSSION

The major purpose of this study was to use the membrane effects of TEA to gain some insight into the mechanism of generation of the plateau potential of the action potential present in longitudinal muscle of the dog stomach. Using constant current pulsing techniques, others have shown that a conductance increase occurs during slow wave activity in other smooth muscle such as in guinea-pig ileal muscle (Bolton, 1971) rabbit intestine (Mills & Taylor, 1971) and guinea-pig gastric circular muscle (Magaribuchi *et al.* 1972). In these previous studies, however, TEA was not used and the peak voltage of the slow wave was in the non-linear region of the voltage–current relation.

In the present studies, non-linearity was a prominent characteristic of the current–voltage relation when the muscle was bathed in Krebs solution. In TEA solution, the voltage response was a linear function of the entire range of applied depolarizing current. Thus, in TEA solution it was possible to determine if there was a decrease in the membrane slope resistance during the plateau of the action potential. The data obtained indicate that a decrease in membrane slope resistance occurred during the plateau because the voltage change due to a current pulse applied during the plateau was smaller than the voltage change to the same current

pulse when applied between action potentials. While the present results are incompatible with a quantitative estimate of the change in conductance during the plateau, the results nevertheless lead to the qualitative conclusion that membrane resistance is much lower during the plateau than between action potentials.

In a previous study (Szurszewski, 1975) it was found that the amplitude of the plateau potential was reduced by depolarization suggesting a voltage-dependent membrane conductance produces the plateau potential. In addition, calcium was found to be important for the plateau potential of spontaneously occurring action potentials and was necessary for augmentation of the plateau by cholinergic agonists (Szurszewski, 1975). These past observations considered together with the presently observed increase in membrane slope conductance during the plateau strongly suggest that calcium ions might carry some of the depolarizing current.

TEA had other effects which are of interest because they also shed some light on the mechanism of repolarization of the action potential. First, TEA initiated repetitive spikes which were grouped as bursts and restricted to the occurrence of the plateau potential. If the non-linearity of the voltage–current relation observed in normal Krebs solution in this smooth muscle is indicative of outward-going rectification observed in other smooth muscles (Ito *et al.* 1970; Kroeger & Stephens, 1975), then inhibition of the outward-going rectification, as one possible action of TEA, occurred only during the plateau potential or the spike currents it unmasked only occurred during the plateau potential. Except for very high concentrations of TEA (30 mM or greater), TEA failed to produce a significant depolarization of the resting membrane potential and failed to produce a change in membrane resistance between action potentials as measured by inward current pulses. These observations further support the conclusion that a TEA-sensitive outward potassium current occurred only during the plateau potential. This is quite unlike other smooth muscles where TEA induces repetitive spike activity which occurs continuously as long as TEA is present in the bathing medium (Suzuki, Nishiyama & Inomata, 1963; Osa & Kuriyama, 1970; Ito *et al.* 1970; Mekata, 1971; Kroeger & Stephens, 1975; Creed, Gillespie & Muir, 1975). Secondly, TEA produced a significant prolongation of the plateau potential. Similar effects were observed in small medullated fibres of the frog (Lorente de Nó, 1949) crustacean muscle (Fatt & Katz, 1953) and crustacean nerve (Burke, Katz & Machne, 1953) and in guinea-pig antrum (Ito *et al.* 1970) and taenia coli (Suzuki *et al.* 1963). In squid axon and frog myelinated fibres, it has been shown using voltage-clamp techniques that the potassium permeability is selectively blocked by TEA and that this block leads to the prolongation of the action potential (Hille, 1970; Armstrong & Hille, 1972). And thirdly, the rate of repolarization of the plateau potential in TEA solution was slower than the rate of repolarization in normal Krebs solution. These three observations indicate the occurrence of a TEA sensitive outward potassium current during the plateau potential.

This work was done during the tenure of an Established Investigatorship of the American Heart Association and was supported by Research Grant AM 17238 from the National Institutes of Health, Public Health Service.

REFERENCES

ARMSTRONG, C. M. & HILLE, B. (1972). The inner quaternary ammonium ion receptor in potassium channels of the node of Ranvier. *J. gen. Physiol.* **59**, 388–400.

BOLTON, T. B. (1971). On the nature of oscillations of the membrane potential (slow waves) produced by acetylcholine or carbachol in intestinal smooth muscle. *J. Physiol.* **216**, 403–418.

BURKE, W., KATZ, B. & MACHNE, X. (1953). The effect of quaternary ammonium ions on crustacean nerve fibers. *J. Physiol.* **122**, 588–598.

CONNOR, J. A., PROSSER, C. L. & WEEMS, W. A. (1974). A study of pace-maker activity in intestinal smooth muscle. *J. Physiol.* **240**, 671–701.

CREED, K. E., GILLESPIE, J. S. & MUIR, T. C. (1975). The electrical basis of excitation and inhibition in the rat anococcygeus muscle. *J. Physiol.* **245**, 33–47.

EL-SHARKAWY, T. Y. & DANIEL, E. E. (1975). Ionic mechanisms of intestinal electrical control activity. *Am. J. Physiol.* **229**, 1287–1298.

FATT, P. & KATZ, B. (1953). The electrical properties of crustacean muscle fibres. *J. Physiol.* **120**, 171–204.

HILLE, B. (1970). Ionic channels in nerve membranes. *Prog. Biophys. molec. Biol.* **21**, 1–32.

ITO, Y., KURIYAMA, K. & SAKAMOTO, Y. (1970). Effects of tetraethylammonium chloride on the membrane activity of guinea-pig stomach smooth muscle. *J. Physiol.* **211**, 445–460.

KROEGER, E. A. & STEPHENS, N. L. (1975). Effect of tetraethylammonium on tonic airway smooth muscle: initiation of phasic electrical activity. *Am. J. Physiol.* **228**, 633–636.

LORENTO DE NÓ, R. (1949). On the effect of certain quaternary ammonium ions upon frog nerve. *J. cell. comp. Physiol.* **33**, suppl. 1–231.

MAGARIBUCHI, T., OHBA, T., SAKAMOTO, Y. & YAMAMOTO, Y. (1972). Some electrical properties of the slow potential changes recorded from the guinea pig stomach in relation to drug actions. *Jap. J. Physiol.* **22**, 333–352.

MEKATA, F. (1971). Electrophysiological studies of the smooth muscle cell membrane of the rabbit common carotid artery. *J. gen. Physiol.* **57**, 738–751.

MILLS, R. G. & TAYLOR, G. S. (1971). Studies of intestinal slow wave activity with a double sucrose gap apparatus. *Life Sci. Oxford* **10**, 347–353.

NARAHASHI, T. (1974). Chemicals as tools in the study of excitable membranes. *Physiol. Rev.* **54**, 813–889.

OHBA, M., SAKAMOTO, Y. & TOMITA, T. (1975). The slow wave in the circular muscle of the guinea-pig antrum. *J. Physiol.* **253**, 505–516.

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

SUZUKI, T., NISHIYAMA, A. & INOMATA, H. (1963). Effect of tetraethylammonium ion on the electrical activity of smooth muscle cell. *Nature, Lond.* **197**, 908–909.

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

SZURSZEWSKI, J. H. (1976). Neural and hormonal determinants of gastric motility. In *Physiology to Smooth Muscle*, ed. BÜLBRING, E. & SHUBA, M. F., pp. 379–384. New York: Raven.