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INWARD RECTIFICATION IN RAT CEREBRAL ARTERIOLES; INVOLVEMENT OF POTASSIUM IONS IN AUTOREGULATION

BY F. R. EDWARDS, G. D. S. HIRST AND G. D. SILVERBERG*
From the Department of Zoology, University of Melbourne, Parkville, Victoria 3052, Australia

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SUMMARY

1. The resting membrane potentials of proximal and distal segments of the arterioles which arise from the rat middle cerebral artery were determined. Proximal segments had stable membrane potentials with a mean value of −69 mV. The membrane potentials of distal segments were less negative and often unstable.

2. When the extracellular concentration of potassium ions ($[K^+]_o$) was increased proximal segments of arteriole were depolarized whereas distal ones were hyperpolarized. When $[K^+]_o$ was decreased both proximal and distal segments were depolarized, the changes being more marked in proximal arterioles.

3. The membranes of proximal segments of arteriole displayed inward rectification at potentials near rest; inward rectification in distal segments of arteriole, when detected, was less pronounced.

4. The activation curve for inward rectification in proximal segments of arteriole was changed by changing the extracellular concentration of K^+. A reduction in $[K^+]_o$ caused the activation curve to move to such negative potentials that the inward rectifier no longer contributed to the resting conductance.

5. Increasing $[K^+]_o$ changed the activation curve for inward rectification in distal segments of arteriole so that more K^+ current flowed at potentials near resting. At the same time the membrane potential hyperpolarized.

6. The results are discussed in relation to autoregulatory changes which occur following changes in the K^+ concentration of cerebrospinal fluid.

INTRODUCTION

Blood flow through many organs is influenced by sympathetic nerve activity, circulating hormones and by the local production of metabolites. In the cerebral circulation the larger distributing arteries receive a dense sympathetic innervation but the innervation pattern of finer vessels is more variable (Heistad & Kontos, 1983). In many species, the decrease in cerebral blood flow that occurs in response to sympathetic nerve stimulation is only poorly maintained (see as example, Sercombe, LaCombe, Aubinea, Mamo, Pinard & Reyneir-Rebuffel, 1979). It is generally held

* Permanent address: Department of Neurosurgery, Stanford Medical Center, Stanford, CA 94305, U.S.A.

that this results from the accumulation of metabolic products around cerebral arteries and arterioles. The metabolites are considered to act directly on arterial smooth muscle and cause dilatation. A number of substances may be involved in autoregulatory escape. These include a fall in pH due to an increase in the partial pressure of carbon dioxide (Heistad & Kontos, 1983), the release of products of purine metabolism (Wahl & Kuschinsky, 1976) and an elevation of local extracellular K^+ concentration (Kuschinsky, Wahl, Bosse & Thurau, 1972).

This paper is concerned with the effects of changing extracellular potassium concentration ($[K^+]_o$) on the excitability of isolated cerebral vessels of the rat. It has been suggested that during neuronal activity, sufficient potassium is released to increase its local concentration in the cerebrospinal fluid (CSF) (Heinemann, Lux & Gutnick, 1977; Heistad & Kontos, 1983). Most arteries depolarize and contract when $[K^+]_o$ is increased (see Casteels, Kitamura, Kuriyama & Suzuki, 1979). However, pial arteries show a concentration-dependent dilatation when $[K^+]_o$ is increased in the range 0–20 mM (Kuschinsky *et al.* 1972). During a study of the ionic currents which underlie the action potential of rat pial arterioles it was found that these arterioles became devoid of sympathetic innervation at variable distances from their origin on the middle cerebral artery (Hirst, Silverberg & van Helden, 1986; Hill, Hirst, Silverberg & van Helden, 1986). It would seem likely that the fine non-innervated arterioles would respond to the application of autoregulatory substances. In this paper we describe experiments where the membrane potential of short segments of arterioles was measured. The effects of small changes in $[K^+]_o$ on membrane potential and electrical properties of arteriolar segments of different locations were then examined. It was found that very distal arteriolar segments had low membrane potentials and that an increase in $[K^+]_o$ caused membrane hyperpolarization. The responses to changes in $[K^+]_o$ were related to the states of activation of an arteriolar inward rectifier (Edwards & Hirst, 1988).

METHODS

All experiments were carried out either on rat middle cerebral arteries or on the arterioles which originated from this or the internal carotid artery. Rats (Sprague–Dawley, male or female, weight 170–200 g) were anaesthetized with sodium pentobarbitone (50 mg/kg body weight, I.P.) and exsanguinated. The brain was rapidly removed and transferred to a dissecting chamber containing gassed physiological saline. An area of pia bounded by the internal carotid, the posterior communicating and middle cerebral arteries, was dissected free of the underlying brain tissue. Care was taken to remove as large an area of pia as possible so that long lengths (4–7 mm) of branching arterioles originating from the middle cerebral artery were obtained. The preparations were pinned out in a recording chamber (bath volume 0·1 ml) with the pial surface downwards. Warmed (37 °C) physiological saline (composition (mM): NaCl, 120; KCl, 5·0; $CaCl_2$, 2·5; $MgCl_2$, 2·0; NaH_2PO_4, 1·0; $NaHCO_3$, 25; glucose, 11); which had been bubbled with 95% oxygen–5% carbon dioxide, was perfused through the recording chamber at 5 ml/min. This solution had a pH in the range 7·38–7·42 when measured locally (at 37 °C) in the tissue bath with a miniature pH electrode (MI-408, needle pH electrode, Microelectrodes, Inc.). After allowing the preparation to equilibrate for some 30–40 min the arteriolar trees were cut into short segments (100–200 μm) using a fragment of razor blade. In many experiments $[K^+]_o$ was varied in the range 1·0–15 mM; this was done without osmotic compensation. In a few experiments $BaCl_2$ (0·5 mM) was added to the physiological saline.

Intracellular recordings were made using microelectrodes filled with 0·5 M-KCl; suitable electrodes had resistances in the range 90–110 MΩ. Membrane potentials and membrane currents

were collected using a single-electrode current clamp/single-electrode voltage clamp (Axoclamp-1, Axon Instruments Inc.). For details of the use of the single-electrode clamp and precautions taken with smooth muscle preparations see Finkel, Hirst & van Helden (1984). Data were filtered (cut-off frequency 300 Hz), digitized and stored on disc for later analysis using an IBM AT computer. Data acquisition and analysis routines were programmed using the DAOS (Laboratory Software Associates) software package (version 7).

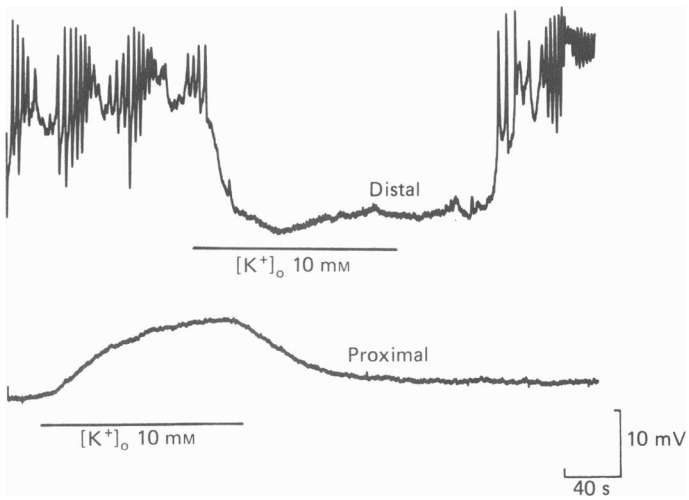

Fig. 1. Effect of changing $[K^+]_o$ on the membrane potentials of two different segments of cerebral arteriole. In both records $[K^+]_o$ was increased from control (5 mM) to 10 mM (continuous line). The membrane potential record shown in the upper trace was obtained from a distal segment of arteriole. Its resting potential in control solution was ~ -40 mV, the potential record was unstable and the segment constricted spontaneously. When $[K^+]_o$ was increased the membrane hyperpolarized and the preparation stopped constricting. The membrane potential record shown in the lower trace was obtained from a proximal segment of the same arteriole. Its resting potential in control solution was -69 mV, and when $[K^+]_o$ was increased the membrane depolarized. The calibration bars apply to both records.

RESULTS

General observations

Stable resting membrane potentials were recorded from middle cerebral arteries and from isolated segments of arteriole if they lay close by (1–3 mm). The mean resting potential of the proximal arteriolar segments was 68·6 mV (S.E.M. $\pm$0·9 mV, $n = 25$). Recordings were also made from segments of arteriole cut out of the pial arterioles at greater distances (5–8 mm) from the middle cerebral artery. Their membrane potentials were often low in the range -35 to -50 mV and unstable. In many preparations rhythmical small amplitude (about 10 mV) oscillations were superimposed on the resting potential (Fig. 1) and such preparations constricted rhythmically. The distance from the middle cerebral artery at which arteriolar segments showed low resting membrane potentials varied between preparations. In some preparations low potentials were detected in segments cut as near as 4 mm from the origin of the pial arteriole; in others they were detected from segments cut 6 mm or more from the main artery. To make a comparison we have arbitrarily divided experimental observations into two groups. The first comprised observations from proximal segments of arteriole, taken 1–2 mm from the middle cerebral artery. The

second group comprised observations from distal arterioles, cut more than 5 mm from their origin, provided that their membrane potential was less negative than −50 mV. The mean membrane potential of the distal segments of arteriole which met these criteria was $-42{\cdot}7 \pm 1{\cdot}1$ mV ($n = 32$).

We do not think that the low values of resting potential resulted from damage during the dissection or during the impalement of the segment. The preparations had high input resistances and their responses to changes in $[K^+]_o$ fitted into a consistent pattern. Moreover, after making an appropriate reduction in $[K^+]_o$ low resting potentials were recorded from proximal segments of arteriole.

Effect of changing the external concentration of potassium ions on resting potential

Proximal segments of arteriole were depolarized when $[K^+]_o$ was increased. An example is shown in Fig. 1; it can be seen that when $[K^+]_o$ was increased from control (5 mM) to 10 mM the membrane potential fell from its resting value of −68 mV to −56 mV, a depolarization of some 12 mV. The membrane potential also fell when $[K^+]_o$ when reduced to 3 mM. A further reduction in $[K^+]_o$ caused a further fall in membrane potential; frequently the membrane potential became unstable and spontaneous rythmic constrictions could be detected visually. Qualitatively similar observations have been made on systemic arterioles of the guinea-pig (Hirst & van Helden, 1982). Grouped data from proximal segments ($n = 6$) are shown in Fig. 2. It can be seen that the most negative resting potentials ($-69{\cdot}1 \pm 2{\cdot}1$ mV) were recorded with a $[K^+]_o$ of 5 mM and that in solutions containing 1 mM-K^+ the resting potentials were $-37{\cdot}7 \pm 1{\cdot}6$ mV.

In contrast, the membrane potentials of distal arterioles became more negative when $[K^+]_o$ was increased in the range 7–15 mM (Fig. 1). In the preparations that generated action potentials in control solution, the increased membrane negativity prevented the discharge of action potentials; visual observation indicated that at the same time spontaneous mechanical activity was suppressed. During the change-over to solutions containing $[K^+]_o$ in the range 7–10 mM, only hyperpolarization to a new steady level was observed. When $[K^+]_o$ was increased above 10 mM the membrane potential changes were no longer monotonic. When the test solution arrived in the chamber the membrane potential hyperpolarized by some 20 mV, i.e. to the same level as reached during exposure to 10 mM-K^+. Thereafter the membrane potential depolarized to a steady level which was still negative of the control potential. During wash-out of the solution containing the increased concentration of K^+, the membrane potential first became more negative than depolarized to its initial control value. When constant current pulses were passed through the recording electrode it was apparent that input resistances of the preparations fell each time $[K^+]_o$ was increased. A reduction in $[K^+]_o$ produced only a small membrane depolarization. The relationship between $[K^+]_o$ and the steady potential of distal segments ($n = 7$) is shown in Fig. 2. It can be seen that the most negative membrane potentials were recorded when $[K^+]_o$ was 7–10 mM. The general forms of the relationships between membrane potential and K^+ concentration for the two different regions of the arteriolar tree are similar but much of the distal segment curve is shifted to the right. At high $[K^+]_o$ the two curves coincide.

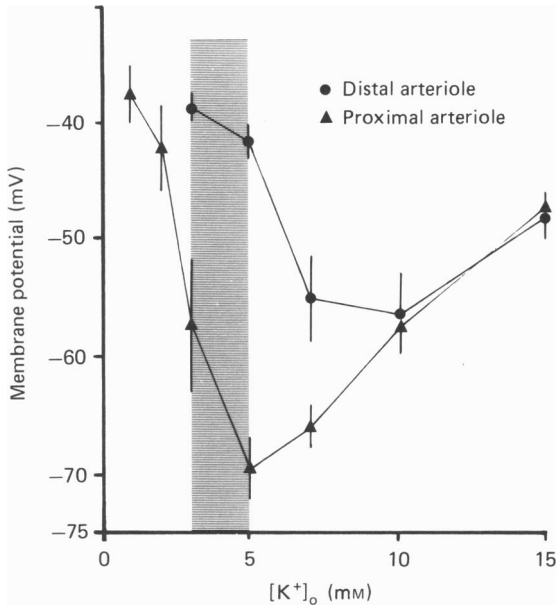

Fig. 2. Relationships between membrane potential and $[K^+]_o$ of proximal (▲) and distal (●) segments of cerebral arteriole. The vertical lines represent ±S.E.M. It can be seen that the forms of the two curves are similar but that higher concentrations of K^+ are required to give maximal membrane potentials of the distal segments. The hatched area indicates the K^+ concentration gradient between CSF and plasma (see Discussion).

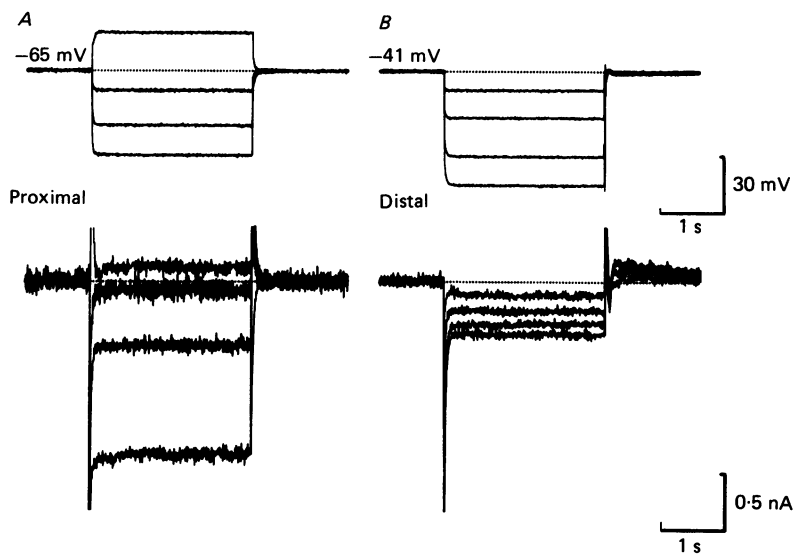

Fig. 3. Comparison of membrane potential changes and associated membrane currents recorded from proximal (*A*) and a distal segments (*B*) of cerebral arteriole. In each experiment the membrane potential was held at the recorded resting potential, −65 mV, for the proximal segment and −41 mV for the distal segment. Voltage command steps were applied and the membrane currents were recorded. The calibration bars apply to each set of records.

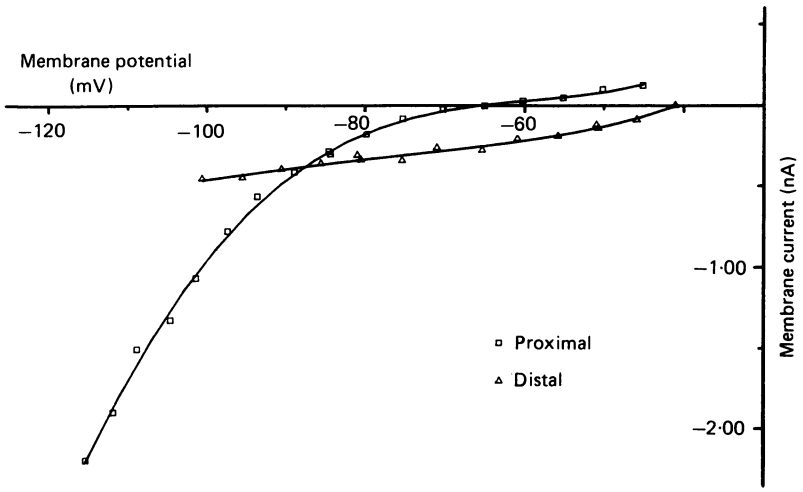

Fig. 4. Comparison of current–voltage relationships of proximal and distal segments of cerebral arteriole. The plots show the relationships between membrane potential and membrane current from the proximal (□) and distal (△) segments of arteriole (raw data shown in Fig. 3*A* and *B*). It can be seen that the relationship of the proximal segment is non-linear over the membrane potential range −55 to −90 mV. In contrast, the current–voltage relationship of the distal segment is linear over the same range of membrane potentials.

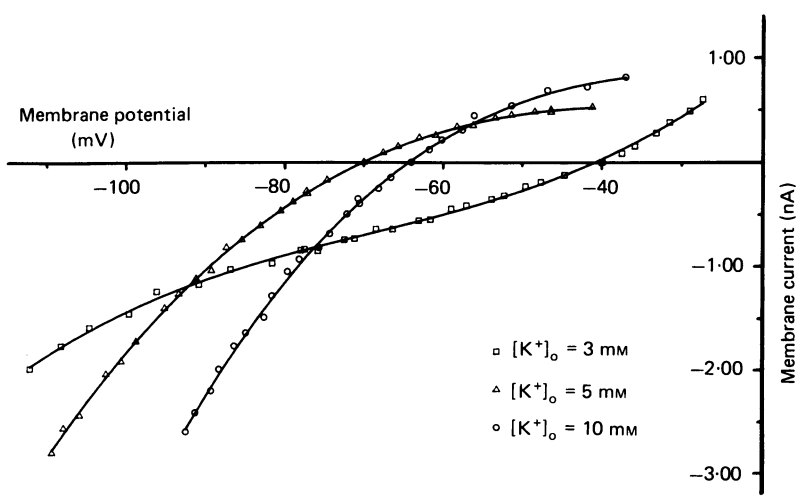

Fig. 5. Effect of changing $[K^+]_o$ on the current–voltage relationship of a proximal segment of cerebral arteriole. The current–voltage relationships determined with $[K^+]_o$ of 3 mM (□), 5 mM (△) and 10 mM (○) are shown. It can be seen that the resting potentials in the three solutions were −40, −70 and −64 mV respectively, and that the activation curves for inward rectification moved to more negative values as $[K^+]_o$ was reduced.

Current–voltage relationships of proximal and distal arterioles

In these experiments intracellular recordings were made from short segments of arteriole. The relationships between membrane current and membrane potential of preparations were examined using a single-electrode voltage clamp. Segments were

clamped at their individual resting potentials, voltage steps were applied and the associated currents were recorded. Examples from a proximal segment and a distal segment are shown in Fig. 3*A* and *B*. The relationships between membrane current and membrane potential for these two segments are plotted in Fig. 4.

The relationship between current and voltage obtained from the proximal segments was non-linear (Figs 3*A* and 4); it displayed a rectification similar to that detected in intestinal arterioles (Edwards & Hirst, 1988). Twelve proximal preparations were examined. For analytical purposes the current–voltage relationship was divided into three regions: an approximately linear region usually found at membrane potential positive of −60 mV, a region described by a single exponential which usually covered the range −60 to −100 mV and a second linear region usually first detected at potentials more negative than −100 mV (for further details see Fig. 7, Edwards & Hirst, 1988). The mean linear slope resistance in the depolarized quandrant was 185±35 MΩ; the mean voltage constant of the exponential was 22·6±1·3 mV and it was fitted over the membrane potential range −59·5±2·7 to −100·3±2·3 mV; the mean linear slope resistance in the hyperpolarized quadrant was 14·5±1·3 MΩ; the mean resting potential of this group was −66·2±1·3 mV ($n = 12$). These data indicate that the activation potential for the onset of rectification is at potentials positive of rest and that the membrane conductance increases by a factor of about 12 over the membrane potential range −60 to −100 mV.

In contrast, many of the current–voltage relationships obtained from distal segments of arteriole did not show rectification (Figs 3*B* and 4). A group of fifteen distal preparations were examined. In six of these preparations the current–voltage relationships over the membrane potential range −50 to −100 mV were linear. Their mean slope was 152±42 MΩ and mean membrane potential was −42·3±1·2 mV ($n = 6$). In the other nine preparations rectification was detected but only at potentials more hyperpolarized than resting (see Fig. 6). When analysed into three components, the mean linear slope resistance in the upper quadrant was 154±26 MΩ; the mean voltage constant was 28·5±6·2 mV, with the exponential being fitted over the membrane potential range −66·0±4·5 to −99·1±3·8 mV; the mean linear slope resistance in the hyperpolarized quadrant was 35·5±3·9 MΩ; the mean resting potential of this group was −42·7±1·2 mV ($n = 9$). Thus the activation potentials for rectification in distal segments of arteriole, when it occurred, although similar to those of proximal segments, were negative of resting potential. Moreover, the increase in membrane conductance of distal segments was less: over the membrane potential range −66 to −100 mV their conductance only increased by a factor of about 4.

Effect of changing the external concentration of potassium on current–voltage relationships of proximal and distal arterioles

It has been shown that submucosal arteriolar membranes exhibit inward rectification. The inward rectifier is selective to K^+, its activation voltage determined by the $[K^+]_o$ and it provides the dominant resting K^+ conductance (Edwards & Hirst, 1988). It seemed possible that the observed differences in resting potential in different regions of the cerebral vasculature could reflect regional differences in the K^+ requirement for rectifier activation. Therefore the effects of changing $[K^+]_o$ on the

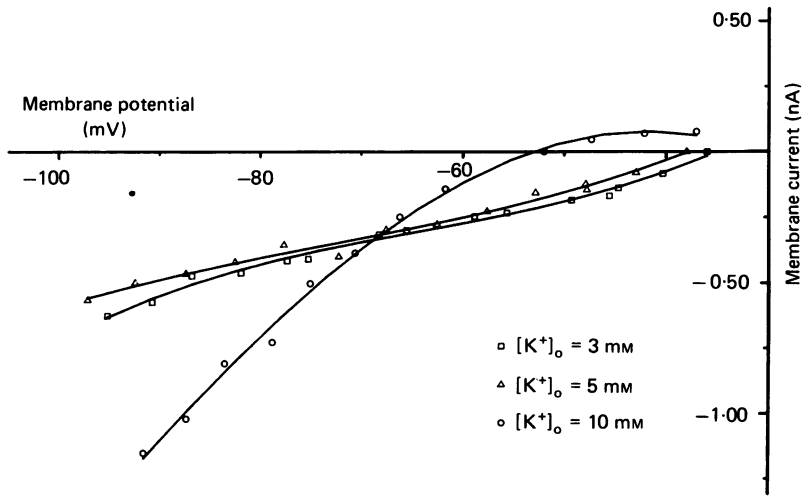

Fig. 6. Effect of changing $[K^+]_o$ on the current–voltage relationships of a distal segment of cerebral arteriole. The current–voltage relationships were determined with $[K^+]_o$ of 3 mM (□), 5 mM (△) and 10 mM (○). The resting potentials in the three solutions were −36, −38 and −54 mV respectively. It can be seen that the current–voltage relationships in 3 and 5 mM-K^+ were similar but that inward rectification was readily detected in 10 mM-K^+ solution.

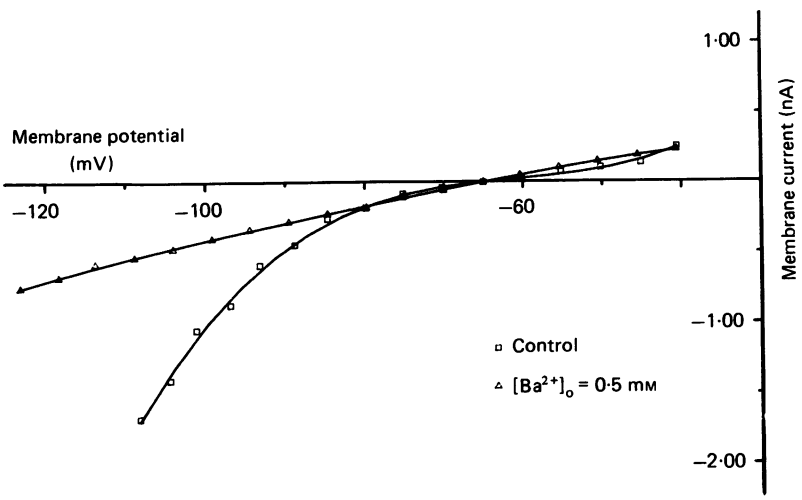

Fig. 7. Effect of Ba^{2+} on the current–voltage relationship of a proximal segment of cerebral arteriole. The current–voltage relationships are shown when determined in control solution (□) and again after the addition of 0·5 mM-Ba^{2+} (△) to the perfusion fluid. The curves were determined over the same membrane potential range; the addition of Ba^{2+} caused the appearance of a holding current ~ 0·1 nA, which was required to maintain the membrane potential at −65 mV.

current–voltage relationships of proximal and distal arterioles were examined. Again the voltage clamp technique was used. After each solution change the holding current was adjusted to zero, i.e. the segments were clamped at their true resting potentials in the test solutions. Current–voltage relationships were then determined by applying the appropriate hyperpolarizing and depolarizing command steps.

The current–voltage relationships obtained from a proximal segment of arteriole in three different concentrations of K^+ are shown in Fig. 5. In the control solution (5 mM-K^+) the resting potential was −70 mV; the current–voltage relationship shows a characteristic non-linearity over the membrane potential range −55 to −100 mV. After reducing $[K^+]_o$ to 3 mM, the membrane potential fell to −40 mV and inward rectification was only detected at potentials more negative than −80 mV. When $[K^+]_o$ was increased to 10 mM the membrane potential fell to −64 mV and the activation voltage for the rectifier moved to a more positive potential. Complete sets of observations with the same range of K^+ concentrations were made on two other proximal segments of arteriole.

A similar series of experiments was carried out on five separate distal arteriolar segments. In control solution the current–voltage relationships of two were linear; in the others slight rectification was apparent. When $[K^+]_o$ was increased in the range 7–10 mM pronounced rectification and membrane hyperpolarization were detected in all five preparations. The current–voltage relationships obtained from a distal segment which showed a degree of inward rectification in control solution ($[K^+]_o$ = 5 mM) is shown in Fig. 6. Also shown are the relationships obtained in solutions containing reduced (3 mM) and increased (10 mM) K^+. In control solution the membrane potential was −38 mV. Reducing $[K^+]_o$ to 3 mM caused a small membrane depolarization (2 mV) with no clear change in the current–voltage relationship. When $[K^+]_o$ was increased to 10 mM the membrane potential increased to −52 mV and the current–voltage relationship displayed rectification over the membrane potential range −40 to −80 mV.

These observations suggest that distal segments of cerebral arteriole require a higher $[K^+]_o$ for the inward rectifier to supply sufficient K^+ current to influence the membrane potential than do proximal segments. It would seem unlikely that the changes in membrane potential which accompanied changes in $[K^+]_o$ of either proximal or distal arterioles resulted directly from altered Na^+ pump activity. Changes in the amount of pump current flowing across the arteriole membranes would shift the membrane potential along a fixed current–voltage relationship, whereas changing $[K^+]_o$ changed the forms of the current–voltage relationships (see Figs 6 and 7).

The inward rectifier of submucosal arterioles is inactivated by Ba^{2+} (Edwards & Hirst, 1988). In three segments of distal arteriole, each bathed in 10 mM-K^+, Ba^{2+} (0·5 mM) caused membrane depolarization and abolished the rectification over the membrane potential range −40 to −80 mV. Similarly, in three proximal segments Ba^{2+} (0·5 mM) caused membrane depolarization and abolished the rectification detected in control K^+ solution (Fig. 7).

DISCUSSION

The membrane potential of cerebral arterioles showed regional variations. Arteriolar segments which lay close to the middle cerebral artery had stable membrane potentials in the range −60 to −70 mV. However, segments of the same arterioles which lay distant from their points of origin on the middle cerebral artery had less negative, often unstable membrane potentials. The membrane potential change which accompanied a change of the $[K^+]_o$ also showed regional variations.

Proximal arterioles were depolarized when $[K^+]_o$ was increased from 5 to 10 mM. In contrast, distal segments of arteriole were hyperpolarized when $[K^+]_o$ was increased in this range. Both distal and proximal segments of arteriole were depolarized when $[K^+]_o$ was reduced. Thus the relationships between $[K^+]_o$ and membrane potential for the two different regions were U-shaped but with different K^+ requirements for maximal polarization.

It should be pointed out that the physiological concentration of K^+ in the extracellular fluid of the arteriolar muscle layer is not known. The K^+ concentration in CSF is lower than that in plasma. In mature rats, plasma $[K^+]$ is in the range 3·8–5·0 mM whilst that of CSF is about 3·0 mM (Amtorp & Sørensen, 1974; Jones & Keep, 1987). Presumably some diffusion of K^+ across the walls of cerebral arteries and arterioles occurs. The mean concentration in the walls of these vessels might therefore be about 4 mM. This implies that moderate increases in CSF K^+ concentration *in situ* will hyperpolarize all of the vessels examined. However, the more distal the arteriole the more likely it will be that large increases in CSF K^+ concentration will cause sustained hyperpolarizations (see Fig. 2).

The observations on membrane potentials are in accord with those of Kuschinsky *et al.* (1972) who showed that moderate increases in external K^+ concentration (range 1–20 mM) led to dilatation of fine pial arteries. In our experiments as the K^+ concentration was increased in the range 1–15 mM the membrane potential became more negative. Thus the membrane potential moves to values negative of the threshold for voltage-dependent Ca^{2+} entry (about −50 mV, Casteels *et al.* 1979; Hirst *et al.* 1986). Our observations do not prove that K^+ ions are involved in vascular autoregulation *in vivo*, but they do show that an increase in CSF K^+ concentration would cause a decrease in distal arteriolar excitability.

The membranes of the proximal cerebral arterioles demonstrate inward rectification at membrane potentials near resting when $[K^+]_o$ is higher than 3 mM. A similar rectification has been described in peripheral arterioles of the guinea-pig (Edwards & Hirst, 1988). In each tissues the current–voltage relationships are non-linear, the membrane resistance falling at more negative membrane potentials. Like the K^+-selective inward rectification of skeletal muscle, starfish egg and submucosal arterioles (Hagiwara, Miyazaki, Moody & Patlak, 1978; Standen & Stanfield, 1978; Edwards & Hirst, 1988), the rectification shown by cerebral arterioles is prevented by Ba^{2+}. The activation voltage of K^+-selective inward rectifier channels (inward rectifier K^+ channels), unlike other voltage-dependent K^+ channels, are shifted when $[K^+]_o$ is changed (Katz, 1949; Hagiwara & Takashi, 1974; Standen & Stanfield, 1978; Hille, 1984; Hirst & Edwards, 1988). This is also the case for cerebral arterioles (Fig. 5).

Most inward rectifier K^+ channels are activated only at membrane potentials negative of the K^+ reversal potential (E_K) unless E_K is changed by reducing the $[K^+]_i$ (Hagiwara & Yoshi, 1979; Leech & Stanfield, 1981). In contrast, inward rectification is detected in submucosal arterioles at potentials positive of E_K with normal internal and external K^+ concentrations. As a consequence, virtually all the resting K^+ conductance at normal resting potential (−70 mV) results from activated inward rectifier K^+ channels (Hirst & Edwards, 1988). This appears to be the case with the proximal segments of the cerebral arterioles examined in this study.

Barium, which prevented inward rectification, caused membrane depolarization. When $[K^+]_o$ was reduced, the activation curve for inward rectification moved to more negative potentials and membrane depolarization occurred (Fig. 5). That is, although E_K became more negative, the fall in K^+ conductance led to membrane depolarization.

Clearly there is a regional variation in the $[K^+]_o$ required to activate inward rectifier K^+ channels of cerebral arterioles at a given membrane potential. All proximal segments showed inward rectification when $[K^+]_o$ was normal. In contrast, many distal segments of arteriole failed to show inward rectification in control solution. When present, the conductance increase with hyperpolarization was slight. However, when $[K^+]_o$ was increased, inward rectification was readily detected. This was associated with membrane hyperpolarization. We suggest that, as $[K^+]_o$ is increased, the K^+ conductance provided by inward rectifier K^+ channels in these vessels becomes appreciable at potentials positive of E_K. Although E_K will become less negative, the increase in relative permeability to K^+ will dominate the membrane potential and result in hyperpolarization. With a further increase in $[K^+]_o$ the fall in E_K will start to dominate and the membrane potential changes will no longer be monotonic. The observation that the membrane potentials of both regions are the same in high $[K^+]_o$ suggests that $[K^+]_i$ does not vary along the arteriolar vessels. Thus in normal K^+ solutions the fine distal vessels, which lack a sympathetic innervation (Hill *et al.* 1986), will be likely to generate myogenic activity (see Fig. 1). This activity will be suppressed should the local concentration of K^+ increase and the vessels will dilate.

Fine distal rat cerebral arterioles lack a sympathetic innervation when examined with fluorescence microscopic techniques (Hill *et al.* 1986), a finding routinely reconfirmed during this present study. The data given in this report provide another example of differences in arteriolar properties that can be related to the presence of absence of sympathetic innervation. Non-innervated vessels have previously been shown to undergo only a small increase in Ca^{2+} conductance during membrane depolarization as compared to innervated segments (Hill *et al.* 1986). The present report suggests that the inward rectifier K^+ channels of non-innervated vessels require a higher $[K^+]_o$ to activate them, at membrane potentials near -60 mV, than do those of innervated segments. Presumably the sympathetic innervation has a trophic influence on the properties of the vascular muscle.

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