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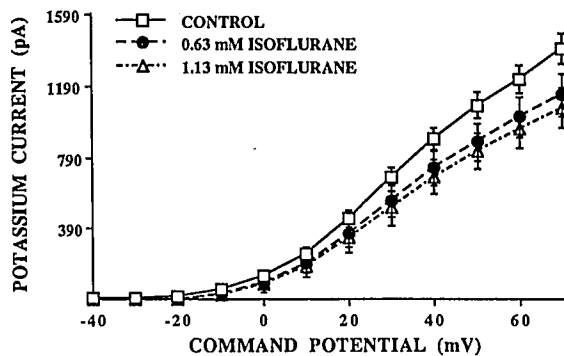
TITLE: EFFECTS OF VOLATILE ANESTHETICS ON TRANSIENT OUTWARD POTASSIUM CURRENT IN PURKINJE FIBERS
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Effects of halothane (H), isoflurane (I) and enflurane (E) were examined on the transient outward potassium current (I_{to}) using whole-cell patch-clamp technique. I_{to} has been described as having two components. One component is voltage dependent, responsible for the prominent phase 1 and the notch between phase 1 and the plateau of the action potential, fast, sensitive to 4-aminopyridine, and a second one which is voltage independent, much smaller, activated by Ca-release from the sarcoplasmic reticulum and is specifically blocked by ryanodine.¹⁻⁴

After institutional approval Purkinje fibers from mongrel dog hearts were incubated at 37°C for 3.5 hours in low calcium solution containing collagenase. The digested fibers were washed and placed in a perfusion chamber of the inverted microscope. In order to measure the magnitude of I_{to} , we blocked Ca^{2+} inward current by 2mM $MnCl_2$, intracellular Ca^{2+} by 10 mM EGTA (pipette sol), and sodium was replaced by N-methyl-D-glutamine 130 mM in external solution (pH=7.4). The glass pipettes were heat-polished and filled with a pipette solution containing (in mM): KCl 50, K-glutamate 60, $MgCl_2$ 2.6, HEPES 10, EGTA 10, K_2ATP 4 and glucose 10 (pH=7.4).

The current was generated by a computer system, amplified by a LIST EPC 7 patch-clamp amplifier, digitized and stored for later analysis. I_{to} was elicited by stepwise (10 mV increments) depolarizing pulses (200 msec) from a holding potential of -40 mV to a more positive membrane potential up to the voltage of +70 mV. The peak amplitude was analyzed within 5-15 msec after voltage pulse initiation before, during and after the administration of equianesthetic concentrations (in mM) of halothane (0.42 and 0.78), isoflurane (0.63 and 1.13) and enflurane (1.1 and 1.78).

The figure represents a current-voltage relationship of I_{to} in the presence of low and high concentration of isoflurane. All three anesthetics caused dose dependent decrease in the peak I_{to} current. This depression was in the range of 17-22% for low concentration and 19-30% for high concentration with no statistically significant difference between anesthetics. Therefore the inhalational anesthetics may decelerate the phase 1 repolarization due to a depression of I_{to} which may lead to altered calcium influx during plateau phase of action potential and change the contractile and refractory characteristics of the myocardium.



References:

1. *J Gen Physiology* 90:671-701, 1987.
2. *Circulation Research* 64:633-647, 1989.
3. *Circulation Research* 62:116-126, 1988.
4. *J Gen Physiology* 73:139-157, 1979.

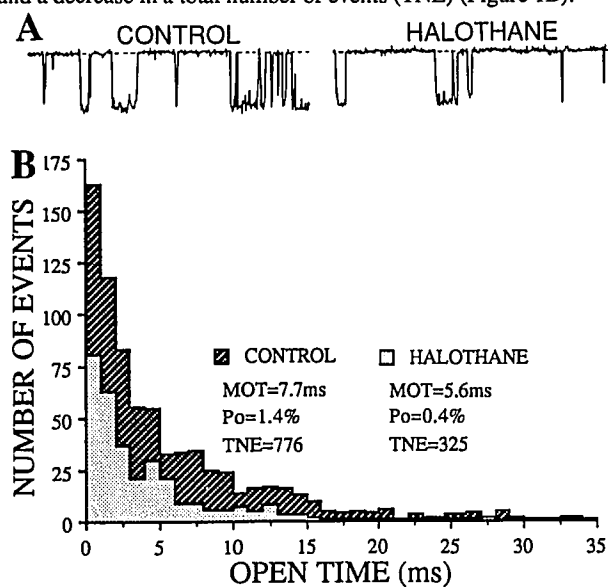
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TITLE: Effects of Halothane on Single Potassium Channels in Isolated Smooth Muscle Cells of Dog Coronary Arteries
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The purpose of this study was to examine the effect of halothane on the single channel K^+ current recorded from enzymatically isolated smooth muscle cells from the canine epicardial coronary arteries using a single-pipette voltage-clamp technique in a cell-attached mode. The potassium channels play an important role in regulating arterial smooth muscle tone by influencing membrane potential and therefore affecting the voltage dependent Ca^{2+} channels.¹ The majority of the sarcolemmal K^+ current is due to a high conductance Ca^{2+} -activated K^+ channels.²

The left circumflex coronary artery was carefully removed, cut into 2 mm rings, and placed into a small vial containing low Ca^{2+} enzyme solution of collagenase and papain at 37°C for 1-2 hours. Single channel currents were recorded using a patch-clamp amplifier (List EPC 7) at room temperature as described previously.³ Potassium channel current was isolated by using modifying external and pipette solution. Halothane was equilibrated in the bath solution at a final bath concentration of 0.85 mM (1.5% effective partial pressure at room temperature) as verified by gas chromatography.

Single potassium channels are shown in Fig. 1A, had high-conductance (96 pS) and were Ca^{2+} -activated [10.3 fold increase in probability of opening (P_o) by 10 μ M calcium ionophore A23187]. 1.5% halothane caused a decrease in P_o of I_K channels from 1.4 to 0.4% and mean open time (MOT) from 7.7 to 5.6 ms and a decrease in a total number of events (TNE) (Figure 1B).



Halothane may act directly on potassium channels or it may cause K^+ current depression by decreasing Ca^{2+} current. One of the other possibilities which could be responsible for these results, is an increase in $[cAMP]_i$ via adenylate cyclase stimulation⁴ which would decrease potassium current in the smooth muscle.⁵ On the other hand, it is possible that a decrease in $[cGMP]_i$ caused attenuation of K^+ current, although unlikely since halothane does not appear to interfere with cGMP-mediated relaxation in vascular smooth muscle.⁶ **References:** 1) *J Physiol (Lond)* 427:657,1990; 2) *Circ Res* 65:1718,1989; 3) *Mol. Cell. Biochem.* 93:69-96,1990; 4) *Anesthesiology* 40:162, 1974; 5) *Mol Cell Biochem* 80:59,1988; 6) *Anesthesiology* 68:31,1988.