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Review

Role of stretch-activated channels on the stretch-induced changes of rat atrial myocytes

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Abstract

The role of stretch-activated channels (SACs) on the stretch-induced changes of rat atrial myocytes was studied using a computer model that incorporated various ion channels and transporters including SACs. A relationship between the extent of the stretch and the activation of SACs was formulated in the model based on experimental findings to reproduce changes in electrical activity and Ca^{2+} transients by stretch. Action potentials (APs) were significantly changed by the activation of SACs in the model simulation. The duration of the APs decreased at the initial fast phase and increased at the late slow phase of repolarisation. The resting membrane potential was depolarised from −82 to −70 mV. The Ca^{2+} transients were also affected. A prolonged activation of SACs in the model gradually increased the amplitude of the Ca^{2+} transients. The removal of Ca^{2+} permeability through SACs, however, had little effect on the stretch-induced changes in electrical activity and Ca^{2+} transients in the control condition. In contrast, the removal of the Na^{+} permeability nearly abolished these stretch-induced changes. Plotting the peaks of the Ca^{2+} transients during the activation of the SACs along a time axis revealed that they follow the time course of

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the Na_i^+ concentration. The Ca^{2+} transients were not changed when the Na_i^+ concentration was fixed to a control value (5.4 mM). These results predicted by the model suggest that the influx of Na^+ rather than Ca^{2+} through SACs is more crucial to the generation of stretch-induced changes in the electrical activity and associated Ca^{2+} transients of rat atrial myocytes.

Keywords: Mechano-electric feedback; Stretch-activated channels; Stretch; Rat atrial myocytes

Contents

1. Introduction

Mechanical stimulation such as stretch or dilation of the heart is known to modulate the electrical activity of myocytes, which suggests that there is a feedback system in the heart, in addition to excitation–contraction coupling, whereby mechanical stimuli modulate electrical activity (Lab, 1982; Nazir and Lab, 1996). This feedback system is often referred to as mechano-electric feedback (Lab, 1996; Kohl and Ravens, 2003). The stretch-induced modulation of electrical activity includes after-depolarisation (Lab, 1978; Franz et al., 1989; Hansen, 1993), depolarisation of the resting potential (Boland and Troquet, 1980; Franz et al., 1992) and alteration of the action potential (AP) duration (Dean and Lab, 1989; Franz et al., 1989; Taggart, 1996). In severe cases, these changes are found to be arrhythmogenic. There is an increasing body of evidence that major events of mechano-electric feedback are mediated by the activation of stretch-activated channels (SACs) (Bustamante et al., 1991; Craelius, 1993; Hoyer et al., 1994;