S 1-1

SIMULATION OF THE SPONTANEOUS ACTION POTENTIALS OF CARDIOMYOCYTE IN PULMONARY VEIN OF RABBIT

Chae Hun Leem, Chang Ahn Seol, Jeong Mi Ha, Won Tae Kim, Han Choe and Yeon Jin Jang
Department of Physiology, University of Ulsan College of Medicine, Seoul

Atrial fibrillation is the most prevalent arrhythmia. However, the mechanisms of development of atrial fibrillation are not yet clear. Recently the most frequent source (over 90%) of paroxysmal atrial fibrillation is located inside main pulmonary veins. We isolated the cardiomyocytes from the main pulmonary vein and found these cells could generate spontaneous action potentials. We checked the electrical characteristics of PV cardiomyocytes. Many different kinds of ionic currents were identified such as, I_{Na}, $I_{Ca,L}$, I_{Kr}, I_{ncx}, $I_{K,ATP}$, $I_{K,Ach}$, and $I_{Cl,Ca}$. I_{K1} and I_{Ks} were very minimal, even though the reasonable I_{Ks} could be identified in the presence of 10 μM forskolin. We could not identify $I_{Ca,T}$, I_{ST}, and If, which are main currents for pace making activity of sinoatrial node cells. We tried to make the model of these cardiomyocytes to identify what is the main cause of spontaneous action potential. We used and tried to reconstruct many experimental observations. The measured membrane area (3,907 μm^2) was well matched to the capacitance value (39.4±3.3 pF, n=30), which suggested no existence of t-tubular system. The cytosolic Ca^{2+} was highly compartmentalized (Leem et al., 2006). More interestingly, the increase of intracellular Na^+ or Ca^{2+} accelerated the beating frequency, compatible to atrial fibrillation (>5 Hz). As intracellular Na^+ was increased, Ca^{2+} activated Cl^- current was activated more and strongly affected the action potential shapes. Based on these experimental results, we reconstructed the spontaneous action potential of PV cardiomyocytes. From the simulation, the major contributing currents to the pace-making were Na^+-Ca^{2+} exchange, I_{Kr}, I_{CaL} and a background current. The Ca^{2+}-activated Cl^- current could be also important contributor depending on intracellular Cl^- concentration.

This work was supported by the grant (No. R01-2004-000-10374-0) from KOSEF.

S 1-2

ROLES OF SODIUM-CALCIUM EXCHANGE IN THE HEART

Denis Noble
Department of Physiology, Anatomy and Genetics, University of Oxford, Parks Road, OX1 3PT, UK

The sodium-calcium exchanger (NCX) plays multiple roles in the heart. In normal function, most of the time it operates in forward mode to pump calcium out of the cell, thus accounting for around 90% of calcium efflux. In this mode NCX carries an inward electric current that contributes to the net inward current during the plateau and possibly also to pacemaker depolarization. In diseased conditions, such as ischemia and heart failure, the calcium pumping function is impaired or even reversed. Calcium overload then occurs and this can trigger single or repetitive calcium release from the sarcoplasmic reticulum. Inward exchange current in response to such release can then generate ectopic beats and re-entrant arrhythmia. Despite the quantitative importance of these roles, cardiac-specific knockout of NCX in mice leads to relatively small changes in action potentials and calcium transients. Computer modelling of the heart has succeeded in reproducing all of these experimental results and in suggesting new experiments.