REALTIME AND COMPLETE (RE)SHAPING OF CARDIAC ACTION POTENTIALS ON A MULTICELLULAR LEVEL BY OPTO-ELECTRONIC DYNAMIC PATCH CLAMPING

Tim De Coster, Shanliang Deng, Sven O. Dekker, Cindy I. Bart, Antoine A.F. de Vries, Daniël A. Pijnappels, Balázs Ördög

Laboratory of Experimental Cardiology, Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands

All living cells possess a membrane potential (Vm), which has been implicated in the regulation of diverse biological processes, e.g. cell cycle, proliferation and volume control. In cardiomyocytes, dynamic Vm changes give rise to action potentials (APs) spreading throughout the heart to regulate contractions. Little is known, however, about the role of cardiac Vm in maintaining cardiomyocyte homeostasis or driving pathological conditions. To gain insight into such matters, one needs to meticulously control cardiac Vm on a multicellular level. To acquire such control, we developed an adaptive, feedback loop-controlled experimental system (APqr) using dynamic patch clamping and optogenetics. To exploit its novel research possibilities, we applied APqr to realize instant restoration of disturbed AP morphology. We show that under optimized conditions, drug-prolonged (4AP) AP durations (APD80, CTL: 228±41ms → 4AP: 325±19ms, $p<0.05$, $n=4$) were restored immediately using APqr (232±49ms) in monolayers of immortalized human atrial myocytes. APD20 and APD50 values were similarly corrected. Furthermore, the average Vm difference over one AP was as high as 33±6mV when comparing drug-prolonged APs to CTL, which was reduced to 5±3mV by our APqr method ($n=4$, $p<0.05$), indicating accurate AP reshaping. In conclusion, our data show that APqr is able to restore and maintain AP morphology in the presence of disturbance. APqr may be at the root of taking full control of the cardiac Vm in various conditions, including multicellular preparations from acute to chronic settings, to not only unravel the role of Vm in homeostatic regulation, but also in disease mechanisms and treatment.

Keywords: action potential, dynamic patch clamping, optogenetics, human immortalized atrial myocytes, cellular electrophysiology

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