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Receptor-Independent Effects of Endocannabinoid Anandamide on Contractility and Electrophysiological Properties of Rat Ventricular Myocytes

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Abstract : A role for anandamide (N-arachidonoyl ethanolamide; AEA), a major endocannabinoid, in the cardiovascular system in various pathological conditions has been reported in earlier studies. In the present work, we have hypothesized that the antiarrhythmic effects reported for AEA are due to its negative inotropic effect and altered action potential (AP) characteristics. Therefore, we tested the effects of AEA on contractility and electrophysiological properties of rat ventricular myocytes. Video edge detection was used to measure myocyte shortening. Intracellular Ca2+ was measured in cells loaded with the fluorescent indicator fura-2 AM. Whole-cell patch-clamp technique was employed to investigate the effect of AEA on the characteristics of APs. AEA (1 µM) caused a significant decrease in the amplitudes of electrically-evoked myocyte shortening and Ca2+ transients and significantly decreased the duration of AP. The effect of AEA on myocyte shortening and AP characteristics was not altered in the presence of pertussis toxin (PTX, 2 µg/ml for 4 h), AM251 and SR141716 (cannabinoid type 1 receptor antagonists) or AM630 and SR 144528 (cannabinoid type 2 receptor antagonists). Furthermore, AEA inhibited voltage-activated inward Na+ (INa) and Ca2+ (IL,Ca) currents; major ionic currents shaping the APs in ventricular myocytes, in a voltage and PTX-independent manner. Collectively, the results suggest that AEA depresses ventricular myocyte contractility, by decreasing the action potential duration (APD), and inhibits the function of voltage-dependent Na+ and L-type Ca2+ channels in a manner independent of cannabinoid receptors. This mechanism may be importantly involved in the antiarrhythmic effects of anandamide.

Keywords : action potential, anandamide, cannabinoid receptor, endocannabinoid, ventricular myocytes
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