ALTERED CONTRACTILE, ELECTROPHYSIOLOGICAL AND CA2+ RELEASE FROM LEFT ATRIA AND ISOLATED VENTRICULAR MYOCYTES FROM MDX MICE

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Cardiomyopathies reduce the average life expectancy of boys with Duchenne Muscular Dystrophy (DMD). The absence of dystrophin in cardiac myocytes is associated with calcium overload and is a major contributor to heart failure, muscle necrosis and fibrosis in DMD. The present study used hearts from mdx mice, an animal model for DMD to investigate the underlying mechanisms responsible for the development of cardiac myopathies in DMD. Mice (13-17 months) were anaesthetised with sodium pentobarbitone (70 mg/kg, ip) prior to euthanasia by excision of the heart. In left atrial (LA) contractility studies, mdx mice had a significant reduction in; basal contractility (P<0.05); time to peak force (P<0.05) and time to 50% and 90% relaxation (P<0.05). Microelectrode studies in the LA revealed that mdx mice had a significantly longer action potential duration (APD) at 50% repolarisation (P<0.05) but a shorter APD at 90% repolarisation (APD_{90}). Action potential recordings from isolated mdx ventricular myocytes in current clamp confirmed a shorter APD_{90} as observed in the LA studies. Ventricular myocytes from mdx mice had significantly impaired force-frequency responses at all stimulation frequencies from 0.25 to 3 Hz (P<0.05). Measurements of intracellular Ca^{2+} using FURA 2 revealed that mdx ventricular myocytes had significantly increased Ca^{2+} release following field stimulation (0.25 through to 2 Hz; P<0.05). In conclusion, both the atria and ventricles of mdx mice show altered electrophysiological, contractile and Ca^{2+} release properties all of which may contribute to the Ca^{2+} overload and impaired cardiac function.