Altered contractile, electrophysiological and Ca^{2+} 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.