Fructose-fed mice exhibit myocardial growth and calcium handling abnormalities associated with oxidative stress

K.M. Mellor,[1] I.R. Wendt,[2,1] R.H. Ritchie[3] and L.M.D. Delbridge,[1] [1]Department of Physiology, University of Melbourne, VIC 3010, Australia, [2]Department of Physiology, Monash University, VIC 3800, Australia and [3]Baker IDI Heart and Diabetes Institute, PO Box 6492, St Kilda Road Central, VIC 8008, Australia.

Recent increase in the prevalence of insulin resistance has coincided with a marked elevation in dietary fructose intake. There is emerging evidence that insulin resistance impacts on the heart and the specific cardiac consequences of excess fructose intake require definition. The aim of this study was to determine the cardiac effects of a 12 week high fructose dietary intervention (60% energy intake) in C57Bl/6 male mice. Hyperglycemia (19% increase) and impaired glucose tolerance were observed coincident with normal plasma insulin levels. Hypertension and obesity were not contributing factors in this study. Hearts were collected for measurement of ventricular weight index (VWI) and myocardial production of superoxide (lucigenin chemiluminescence). Expression levels of signalling proteins (western blot) and cardiac hypertrophic genes (rtPCR) were analysed. Ca^{2+} handling (fura-2, 360:380nm ratio) and cell shortening (edge detection) properties of cardiomyocytes from fructose- and control-fed mice were analysed. A 22% increase in VWI in the fructose fed mice was associated with elevated superoxide production (fructose, 553 ± 28 counts/s/mg *vs* control, 489 ± 11 counts/s/mg, $p < 0.05$). Surprisingly, fructose fed mice exhibited suppressed expression of cardiac hypertrophic markers. Calcium transient amplitude was decreased in cardiomyocytes from fructose-fed mice associated with a slower calcium transient decay rate. Fructose feeding suppressed myocardial phosphorylation of Akt and S6. These findings demonstrate that a 12 week dietary fructose intervention induces cardiac hypertrophy associated with calcium handling dysregulation and oxidative stress. Specific signalling alterations may play a role in fructose induced cardiac pathologies. Further mechanistic studies are required to identify the basis of abnormal cardiac growth in this model.