Tolerance of male and female rat papillary muscles to acute metabolic compromise

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The presence of functional oestrogen receptors within cardiac myocytes identifies the heart as a target organ for oestrogen, and raises the possibility that sex hormone effects on the heart may contribute to sex differences in the incidence of heart disease. We have previously reported that, under comparable conditions, the amplitude of the intracellular Ca^{2+} ($[Ca^{2+}]_i$) transient is larger in male as compared to female rat cardiac myocytes (Curl *et al.*, 2001). It has also been suggested that oestrogen can protect the heart against ischemia-reperfusion injury by limiting the associated increase in $[Ca^{2+}]_i$ (Zhai *et al.*, 2000). The aim of the present study was to determine whether there is a sex difference in the decline and recovery of function, and ability to maintain $[Ca^{2+}]_i$ homeostasis, in intact cardiac muscle subjected to acute metabolic compromise.

Left ventricular papillary muscles were dissected from the hearts of adult (300 – 350g) male and female Wistar rats that had been killed by chloroform overdose and decapitation. The muscles were mounted in a chamber located on the stage of an inverted fluorescence microscope to allow for simultaneous recording of force and tissue fluorescence. For monitoring of $[Ca^{2+}]_i$ the muscles were loaded with fura-2 by 3 hr incubation with fura-2/AM. Muscles were equilibrated in HEPES buffered physiological saline solution containing 2.5 mM Ca^{2+}, 10 mM glucose, and aerated with 100% O_2. They were then subjected to 20 min of metabolic inhibition followed by 60 min of recovery. To achieve metabolic inhibition 2 mM NaCN was added to the PSS, and glucose and O_2 were omitted. The temperature was maintained at 30^{o}C and the muscles were stimulated at 0.25 Hz throughout.

Following 20 min of metabolic inhibition developed force had declined to 10.8 ± 1.6 and 12.1 ± 1.8 % of the preceding steady-state control level in male (n = 12) and female (n = 14) papillary muscles respectively. In contrast, the amplitude of the Ca^{2+} transient only decreased to around 75% of the control amplitude in both sexes. Muscles from both sexes recovered with a similar time course, with developed force returning to approximately 90% of control by 60 min. There were also increases in passive force and diastolic $[Ca^{2+}]_i$ during metabolic inhibition, however, the increase in resting force was considerably less than might have been expected from the increase in diastolic $[Ca^{2+}]_i$. Overall, there were no significant differences between the sexes in either the decline in contractile force, increase in resting force, or changes in $[Ca^{2+}]_i$, during 20 min of metabolic inhibition.

Addition of 1×10^{-6} M 17β -oestradiol to the solutions resulted in a slight decrease (around 10%) in contractile force and amplitude of the Ca^{2+} transient in both male and female papillary muscles. The acute presence of oestradiol, however, had no significant effect on the changes in force or $[Ca^{2+}]_i$ that occurred during metabolic inhibition.

The results demonstrate that there are no apparent differences in the tolerance of isolated male and female rat papillary muscles to 20 min of metabolic inhibition. In addition, the acute presence of a high concentration of 17β -oestradiol did not provide any protection against the effects of metabolic inhibition in either sex. In muscles of both sexes there appeared to be some dissociation of force and $[Ca^{2+}]_i$ during metabolic inhibition.

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