17β-oestradiol attenuates phenylephrine-induced hypertrophy in male neonatal rat cardiac myocytes

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Cardiac hypertrophy is a major risk factor for cardiovascular related morbidity and mortality, and there is evidence for sex differences in the incidence of cardiac hypertrophy. The presence of oestrogen and androgen receptors in cardiac myocytes raises the possibility that sex hormones may influence how the heart responds to hypertrophic stimuli. The aim of the present study was to examine the role of oestrogen in modulating the hypertrophic response of cardiac myocytes. Male neonatal rat pups were humanely killed and the hearts removed, cardiac myocytes were isolated by enzymatic digestion and established in culture. The study protocol involved a 24h pre-treatment period exposing the cells to medium with or without 17β-oestradiol (1nM). This was followed by a 48h period where hypertrophy was induced by exposure of cells to phenylephrine (PE, 20μM) with or without 17β-oestradiol (1nM) in [^{3}H]-phenylalanine containing medium. Hypertrophy was assessed by [^{3}H]-phenylalanine incorporation (an indicator of protein synthesis), and normalised to total DNA to account for differences in cell numbers between cultures. Results were expressed as % of paired control, mean ± SEM. PE treatment increased protein synthesis (166 ± 25% of control n=10); cells exposed to 17β-oestradiol only during the 24h pre-treatment period showed an attenuated protein synthesis response to PE (113 ± 3% of control n=3) in the subsequent 48h treatment period. The PE response was also attenuated by co-incubation with 17β-oestradiol during the 48h treatment period only (122 ± 11% of control n=3). However, if the cells were exposed to 17β-oestradiol during the 24h pre-treatment period and exposure was continued throughout the 48 hour PE treatment period, 17β-oestradiol no longer attenuated the PE response (213 ± 45% of control n=10). These results indicate that 17β-oestradiol may directly act at the cardiac myocyte to modulate the hypertrophic response. 17β-oestradiol treatment may transiently up-regulate anti-hypertrophic pathways such that there is initially an attenuation of the hypertrophic response that is however, not seen with continued 17β-oestradiol exposure.