PRECONDITIONING BY THE β-ADRENOCEPTOR AGONIST, ISOPRENALINE, IN THE RAT ISOLATED ATRIUM BUT NOT VENTRICLE

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Ischaemia and reperfusion (IR) have a deleterious effect on myocardial function. This can be abrogated by short periods of IR prior to a longer insult (ischaemic preconditioning, PRE) or by modified reperfusion (ischaemic postconditioning, POST). We sought to investigate reports that PRE can be mimicked pharmacologically by activation of β-adrenoceptors (Moolman *et.al*. 2006, Yates *et.al.*2003), and to examine whether POST could also be elicited by β-adrenoceptor activation.

Male Sprague-Dawley rats (250-350g) were killed and left atria and right ventricular strips set-up in Krebs-Henseleit buffer at 37ºC gassed with 95% O_2 /CO_2. An initial resting tension of 1g (±0.1g) was applied. Tissues were electrically paced at 2 Hz with threshold voltage + 50%. Tension developed during each electrical stimulus was recorded. All preparations were left for 60 min before undergoing experimental procedure. Ischaemia was simulated for 30 minutes by replacing glucose in the buffer with choline chloride (7 mM) and gassing with 95% N_2/CO_2. Reperfusion was simulated by return to oxygenated, glucose–containing buffer. Effects of exposure to isoprenaline (ISO, 10^{-7}M) before ischaemia for 5 or 10 min (PRE) or at reperfusion (10 min, POST) were examined. Tension was measured at 60 min of reperfusion and expressed as the % of pre-ischaemic baseline (Table 1). Mean (±SEM) values were compared statistically by ANOVA and the Student-Newman-Keuls *post hoc* test.

	Control	5 min ISO PRE	10 min ISO PRE	10 min ISO PRE + propranolol	ISO POST	Propranolol only
Atria	59.2 ± 2.7 (n=11)	75.8 ± 9.9 (n=6)	106.6 ± 18.5* (n=9)	51.5 ± 3.9 (n=5)	59.2 ±5.5 (n=9)	71.4 ±7.2 (n=6)
Ventricle	52.2 ± 5.5 (n=11)	71.2 ±12.5 (n=6)	53.8 ± 6.3 (n=9)	52.6 ± 4.3 (n=5)	40.4 ±5.3 (n=9)	52.7 ±4.5 (n=5)

Table 1: Contractile function at one hour post-reperfusion expressed as % of pre-ischaemic value. * indicates significant difference from control values ($P < 0.05$).

In atria, ISO, when given as a PRE stimulus for 10 min significantly improved post-ischaemic cardiac function with respect to controls. This effect was β-adrenoceptor mediated, as it was blocked by propranolol (10^{-6} M), which alone had no effect. In contrast, ISO preconditioning was unable to protect ventricles. When administered immediately after reperfusion (POST), ISO did not exert any protective effect in either tissue. Thus, β-adrenoceptor stimulation can exert preconditioning but not postconditioning in isolated atria. No protection was seen in ventricular muscle.

Moolman, J. *et.al*. (2006) *Cardiovascular Drugs and Therapy* **20,** 13-25
Yates, L *et.al.* (2003). *Autonomic & Autacoid Pharmacology* **23,** 246

This work was funded by a studentship to PEP from the British Heart Foundation.