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Effect of sex differences on the coupling between reactive oxygen species and prostanoids in perivascular adipose tissue-induced vasoconstriction of porcine coronary artery

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Introduction: Several mechanisms have been identified in the regulation of vascular tone by perivascular adipose tissue (PVAT)[1]. As there is a sexual dimorphism identified in the regulation of vascular tone by PVAT[2], the aim of this study was to determine the impact of sex differences on the coupling of reactive oxygen species (ROS) and prostanoids in PVAT-induced vasoconstriction of the porcine coronary artery (PCA).

Method: Isometric tension recording system was used to investigate the changes in porcine coronary arterial tone. ROS production was estimated in PVAT and PCA using lucigenin (5µmol/L)-enhanced chemiluminescence. Student's 2-tailed paired t-test or ANOVA was used to analyse the data depending on the number of factors analysed. Data are expressed as mean±S.E.M.

Results: Addition of PVAT stimulated a contraction in PCA from both sexes. Pre-incubation with ROS scavenger N-acetyl-L-cysteine (NAC) (10mM) significantly reduced PVAT-induced vasoconstriction in PCAs from both females and males. Neither the TXA_2 mimetic U46619 (100nM) nor $PGF_{2\alpha}$ (1µM) increased ROS production in PVAT. In contrast, both compounds stimulated ROS production in PCAs, but only in females (Table 1). Similarly, the Nox1 antagonist ML171 (100µM) only inhibited the contractile response to U46619 and $PGF_{2\alpha}$ in females with no effect in males (Table 2).

Table 1: Effect of prostanoids on superoxide anion production in PVAT and PCA from both sexes.

Drugs	PVAT (Female)	PVAT (Male)	PCA (Female)	PCA (Male)
U46619	108.3±24 vs 127.5±30.7 (n=14)	118.8±34.1 vs 97.4±19.9 (n=16)	44.6±8 vs 109.5±33.6 (n=11)*****	80±18 vs 67.7±12.2 (n=10)
$PGF_{2\alpha}$	308.6±53.7 vs 236.4±49.6 (n=8)	255±74.6 vs 266.2±56.1 (n=8)	71.3±33.9 vs 119.9±41.3 (n=7)*****	97±18.7 vs 122±43 (n=9)

*****P<0.05; mean±S.E.M. of photon emission/background photon count; control vehicle vs drug.

Table 2: Effect of ML171 on functional response of PCA to prostanoids in both sexes.

	U46619 (pEC50s)	$PGF_{2\alpha}$ (% KCl contraction)
PCA (Female)	8.3±0.12 vs 7.9±0.06 (n=6)*****	32±3.4 vs 18.2±3 (n=8)******
PCA (Male)	8±0.12 vs 8.1±0.05 (n=7)	25±4.6 vs 25.1±5.7 (n=7)

*****P<0.05,******P<0.01; mean±S.E.M., control vehicle vs ML171.

Conclusions: These data demonstrate that ROS have a functional role in the PVAT-induced vasoconstriction of PCA in both sexes. In females, but not males, ROS production appears to be downstream of the PVAT-derived prostanoids previously described[3].

References:

1. Brown *et al.* (2014). *Arterioscler Thromb Vasc Biol* **34**: 1621-1651.
2. Ahmad *et al.* (2017). *Br J Pharmacol* **16**: 2773-2783.
3. Ahmad *et al.* (2017). *J Physiol* (in press).