Impaired Vasorelaxation to Anandamide in Aortae from Zucker Diabetic Fatty Rats

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We have reported that the endocannabinoid 2-Arachidonylglycerol (2-AG) has heterogeneous actions throughout the vasculature of an animal model of type 2 diabetes, Zucker Diabetic Fatty rats. 2-AG is more likely to cause vasoconstriction in some arteries compared to comparable arteries taken from the lean control strain (Wheal et al. 2010). Therefore, we investigated whether the prototypical endocannabinoid anandamide would behave in a similar fashion.

Third-order mesenteric arteries, femoral arteries and thoracic aortic rings were taken from male, Zucker Diabetic Fatty rats (319 – 360g) and their related lean controls (275 – 311g). Preparations were set up in a wire myograph and left to equilibrate in warmed (37°C), gassed (95% O\textsubscript{2}/5% CO\textsubscript{2}) modified Krebs’-Henseleit buffer. Following this, methoxamine was used to raise vessel tone, and then concentration-response curves to anandamide were constructed.

In both Zucker Diabetic Fatty rats and their lean controls, anandamide caused full concentration-dependent vasorelaxations in third-order mesenteric arteries ($\rho EC_{50}$ Lean = 5.52 ± 0.32, n=5; Diabetic = 4.98 ± 0.35, n=4; mean ± s.e.mean), whilst in segments of femoral arteries anandamide was without effect. In thoracic arteries, the maximal percentage relaxation to anandamide was blunted in the diabetic rats compared to the lean controls ($R_{max}$ Lean = 31.4 ± 4.1 %, n=6; Diabetic = 10.6 ± 2.8 %, n=5; P<0.05, unpaired Student’s t-test).

Anandamide behaves differently to 2-AG in the vasculature of Zucker Diabetic Fatty rats. No vasoconstriction to anandamide was observed. However, blunted vasorelaxation in the aortae may be a sign of endothelial dysfunction in this model. Additional work is needed to investigate whether this is due to altered nitric oxide signalling.

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Wheal et al. (2010). BPS Winter meeting poster presentation.