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Adipose tissue enhances nitrite-mediated vascular relaxation in conditions of hypoxia

Nitrite is an important source of nitric oxide (NO), particularly when production from endothelial cells (EC) is compromised e.g. during hypoxia (1). Adipose tissue, e.g. white (WAT) and perivascular (PVAT), modulates a variety of vascular parameters. Here we aim to determine if PVAT and WAT influence nitrite-mediated vascular reactivity.

Aortic rings from male C57BL/6 mice were denuded of EC. PVAT was maintained on some segments while removed from others, rings were then mounted for tension recording. Three groups of ring were created: smooth muscle cells alone (SMC), SMC+PVAT and SMC+PVAT+WAT (in which segments of inguinal WAT were cohabited with SMC+PVAT rings in the myograph bath). Tissues were gassed with 5% CO\(_2\) in oxygen (control) or 5% CO\(_2\) in nitrogen (hypoxia) for 2 h (2). Responses to sodium nitrite (1nM – 1mM) were generated following contraction with phenylephrine. Hydroxocobalamin (HXO; 1 mM) and 1H-[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one (ODQ; 10 µM) determined the influence of NO and soluble guanylyl cyclase (sGC), respectively. Statistical significance determined by two-way ANOVA.

In control oxygen, nitrite produced a concentration-dependent relaxation of SMC rings (maximum 69.9 ± 9.2%, n=6) that was not different from that found in either SMC+PVAT (80.0 ± 4.9%, n=6) or SMC+PVAT+WAT (80.9 ± 3.5%, n=6) groups. The relaxation produced in all groups was abolished (P<0.001) following treatment with either HXO or ODQ demonstrating that nitrite mediated relaxation was reliant on NO generation and sGC activation. In conditions of hypoxia, the magnitude of the nitrite-induced response was not changed in either SMC or SMC+PVAT groups compared to that found with control oxygen, however, the relaxation found in SMC+PVAT+WAT rings was substantially greater (97.5 ± 1.1%, n=5, P<0.001). In hypoxic conditions, HXO and ODQ continued to eliminate relaxation in SMC and SMC+PVAT tissues. In contrast, nitrite-induced relaxation in SMC+PVAT+WAT rings persisted in the presence of HXO although this was substantially impaired (39.0 ± 11.6%, n=5, P<0.01) compared to that found in control conditions. ODQ still obliterated the nitrite mediated relaxation in this group.

In conditions of abundant oxygen, adipose tissue (PVAT or PVAT+WAT) has no influence on the magnitude or character of nitrite-induced relaxation to SMC. However, in conditions of low oxygen the presence of PVAT+WAT both enhanced the scale and character of the response thus demonstrating that adipose tissue in hypoxic conditions does indeed modulate nitrite-mediated relaxation.