MATERNAL OBESITY ATTENUATES THE ANTI-CONTRACTILE EFFECT OF PERIVASCULAR ADIPOSE TISSUE IN RAT OFFSPRING.

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Objective: Maternal obesity pre-programmes offspring to develop obesity, glucose intolerance and associated cardiovascular disease later in life although the underlying mechanism is currently unknown. This study investigated the effect of a rat maternal high fat diet on perivascular adipose tissue (PVAT) regulation of resistance artery tone in 24-week old offspring.

Design and method: 8-week old female Sprague Dawley rats were fed a 10% fat diet (controls) or an obesogenic, high fat diet (HFD; 45% fat) for 12 weeks before mating and during pregnancy and lactation. At weaning, male offspring were provided with the 10% fat diet and were killed at 24 weeks of age. PVAT-intact (+PVAT) or -denuded (-PVAT) segments of mesenteric artery were mounted on a wire myograph and cumulative concentration-response curves were constructed to the thromboxane A₂ receptor agonist U46619 (10nM-3µM) in the presence or absence of A769662, an activator of AMP-activated kinase (AMPK), and/or L-NMMA, a nitric oxide synthase (NOS) inhibitor.

Results: Body weight was significantly increased in 24-week old offspring of HFD dams (672 ± 14g, n=21) compared to controls (633 ± 10g, n=23, p<0.05) and systolic and diastolic blood pressure were each approximately 20 mm Hg higher in the HFD offspring (p<0.0001). In artery segments from control offspring, contractions to U46619 were greater in the absence than in the presence of PVAT (p<0.05). In contrast, PVAT had no effect on responses to U46619 in vessels from HFD offspring, and contractions were similar to those of -PVAT control vessels. A769662 (10µM) decreased contractility of PVAT-denuded vessels from offspring of both control (p<0.01, n=8) and HFD (both p<0.01, n=8) dams and there was no additional effect in the presence of PVAT. L-NMMA (100µM) increased contractility of PVAT-intact control and HFD vessels (p<0.0001, each n=8) and responses to U46619 were similar to those of their corresponding PVAT-denuded counterparts in the presence of L-NMMA. Interestingly, in the absence of PVAT the contractions to U46619 in the presence of L-NMMA were significantly greater in HFD than in control vessels (p<0.05, n=8).

Conclusions: There was no evidence for the loss of NO function or modification of the AMPK-NO pathway in PVAT from the 24-week old offspring of HFD dams. Nevertheless, the anti-contractile effect of PVAT was lost and endothelial control of vascular tone appeared to be modified. The findings suggest that contractile factors may be released from the PVAT and/or endothelium. Further experiments are in progress to test this possibility.

Acknowledgements: This study was funded by the British Heart Foundation (FS/12/68/30006).