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AMP-activated protein kinase activation partially restores the anti-contractile effect of perivascular adipose tissue in male offspring of obese dams

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Introduction: Maternal obesity preprograms offspring to develop obesity and associated cardiovascular disease although the underlying mechanism is currently unknown. Perivascular adipose tissue (PVAT) reduces vascular contractility in healthy blood vessels and dysfunction has been demonstrated in male offspring of obese dams.

Purpose: We aimed to determine the mechanisms by which an obesogenic maternal diet pre-programmes detrimental vascular changes in her offspring.

Methods: 6 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, during pregnancy and lactation. At weaning, offspring were provided with the control 10% fat diet until sacrifice at 12 and 24 weeks of age. PVAT-denuded mesenteric arteries from pups, with or without exogenous PVAT, were mounted on a wire myograph and concentration-response curves were constructed to thromboxane A2 receptor agonist U46619 (10nM-3µM) in the presence or absence of 10µM A769662, an activator of AMP-activated protein kinase (AMPK), and/or glucosamine (an O-GlcNAcylator).

Results: Body weight and arterial blood pressure were significantly increased in HFD dams and their 24 weeks old offspring compared to controls but not in 12 weeks old offspring. Without PVAT, vessel contractions to U46619 were reduced in HFD dams’ offspring at both ages, effects mimicked in control arteries by preincubation with 10 mM glucosamine. When separately incubated, PVAT from control, but not from HFD offspring, exerted an anti-contractile effect on the corresponding PVAT-denuded arteries at both ages. Pre-incubation of PVAT with glucosamine diminished the anti-contractile effect of PVAT in vessels from control offspring at both ages. PVAT from HFD offspring pre-incubated with glucosamine had no effect on PVAT-denuded vessels but simultaneous AMPK activation within PVAT partially restored anti-contractile capability at both ages.

Conclusions: The diminished anti-contractile effects of PVAT in offspring of HFD dams can be mimicked by incubation of PVAT with glucosamine and partially restored by AMP-activated protein kinase activation within PVAT.