Diet-induced obesity alters sensory nerve activity in rat small mesenteric artery

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A functional interaction between sympathetic nerve-mediated vasoconstriction and sensory nerve vasodilatory action has previously been demonstrated in mesenteric resistance vessels (Coffa & Kotecha, 1999). During obesity however, vasoconstriction due to sympathetic activity in pressurized mesenteric arteries is enhanced due to the upregulation of both adrenergic and purinergic neurotransmission (Haddock & Hill, 2011), while the role of vasodilatory sensory nerves remains unexplored.

In the present study, male Sprague-Dawley rats were fed either a normal or high fat diet. Small mesenteric arteries (343 ± 9.1 μm, n=60) were isolated and pressurized (80 mmHg) and sharp intracellular microelectrodes (120-185 MΩ) and computer tracking (Diamtrak) were used to simultaneously measure cell membrane potential and vessel diameter. Impaled cells were dye identified and sympathetic and sensory nerves were activated with electrical field stimulation. Immunolabelling and confocal microscopy were used to examine the density of perivascular nerves, while sympathetic adrenergic nerves were identified using the faglu method (Furness *et al.*, 1978).

Resting membrane potential in arteries exhibiting myogenic tone did not differ between diet groups (control:−40.5mV, n=20; obese: −41.0mV ± 0.6 mV, n=25), however obesity significantly increased the amplitude of the sympathetic nerve mediated constriction at 10Hz (P<0.05). Addition of αβ-methylene ATP (1μM) and prazosin (0.1μM) in combination, to inhibit the purinergic and adrenergic components of the sympathetic vasoconstriction (10 Hz), unmasked a nerve-mediated vasodilation in arteries from both control (−9.3 ± 2.0% D_{max}, n=6; P<0.05) and obese animals (−6.8 ± 3.1% D_{max}, n=5; P<0.05). This response was abolished in arteries taken from control but not obese animals following exposure to capsaicin to inhibit sensory neurotransmitter activity (10 μM; P<0.05). Capsaicin also significantly increased the amplitude of the nerve mediated vasoconstriction evoked by 10 Hz stimulation in arteries from both diet groups, although the effect was greater in control rats (control: 23.7 ± 2.0% D_{max}, capsaicin: 34.5 ± 2.6% D_{max}, n=5, P<0.05; obese: 33.4 ± 1.8% D_{max}, capsaicin: 36.2 ± 2.2% D_{max}, n=4, P<0.05). Excitatory junction potentials (EJPs) evoked by a single supramaximal stimulus were increased in amplitude in arteries taken from obese animals (P<0.05). Obesity also increased the amplitude of the transient hyperpolarization associated with EJPs (P<0.05). This hyperpolarization was abolished in arteries from both diet groups upon addition of capsaicin (P<0.05). Immunoreactivity showed that obesity increased the innervation density of perivascular nerves although plexuses of sensory and nitrergic nerves were similar in density between arteries from control and obese rats.

In conclusion, sensory nerve activity negatively modulates neurally evoked vasoconstriction in arteries from both control and obese animals. Although sensory and nerve density is not changed in obesity, negative modulation by sensory neurotransmitters is less effective in obesity leading to the augmentation of the amplitude of the sympathetic nerve mediated vasoconstriction which could contribute to the hypertension and global organ damage associated with diet-induced obesity.

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