**Nerve-mediated responses in isolated myogenic and non-myogenic arteries.**

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Small arteries and arterioles of the resistance vasculature can exhibit a basal level of vasoconstriction, or myogenic tone in response to an increase in intraluminal pressure,. Myogenic tone occurs without influence from perivascular nerves and the endothelium, and is most likely dependent on stretch-activated receptors which mediate depolarization and smooth muscle contraction. The aim of the current investigation was to compare nerve-mediated responses in myogenic and non-myogenic arteries, as data on modulation of myogenic tone by neurotropic factors is lacking.

To address this aim, rat mesenteric and cremasteric arteries were excised and studied as non-myogenic and myogenic arteries, respectively. A combination of immunohistochemistry, wire and pressure myography was employed to evaluate the effect of perivascular nerve activation by electrical field stimulation (EFS).

Both artery types are innervated by sympathetic nerve fibres, as confirmed with staining for tyrosine hydroxylase observed only in the adventitial layer. Furthermore, both mesenteric and cremasteric arteries exhibited vasomotor responses to exogenously added norepinephrine (NE), phenylephrine, and adenosine triphosphate (ATP). The sensitivity of the tissue to these agents was greater in the pressure myograph compared with the wire myograph, indicating the importance of considering data using EFS in pressurized arteries as well as from arteries under isometric tension.

EFS (10 V, 50 pulses, 7 Hz, 1 ms pulse width) caused vasoconstriction of mesenteric arteries ($27.5 \pm 1.3$ %) which was attenuated by the voltage-gated $Na^+$ channel blocker tetrodotoxin (TTX, to $6.6 \pm 0.8$ %). Furthermore, EFS-induced vasoconstriction was reduced by the $\alpha_1$-adrenoceptor antagonist prazosin ($18.7 \pm 1.5$ %), the $P2X_1$ receptor antagonist NF 449 ($17.5 \pm 3.5$ %), and a combination of the two ($10.9 \pm 1$ %). The L-type $Ca^{2+}$ channel blocker nifedipine also attenuated the response ($11.0 \pm 2.8$), and in combination with TTX almost completely abolished it ($1.4 \pm 1.0$ %). Propranolol had no effect on the vasoconstriction ($25.3 \pm 2.9$ %) despite presence of β-adrenoceptors mediating vasorelaxation to exogenous norepinephrine. Most interestingly, EFS failed to elicit any response in cremasteric arteries – an observation with some similarities to data from myogenically-active rat tail arteries[1].

This investigation highlights the importance of conducting experiments with EFS on pressurized arteries. EFS of mesenteric arteries confirmed a synergistic role for NE and ATP released from perivascular nerves, and suggests an additional direct effect on L-type voltage-gated $Ca^{2+}$ channels. Our data raise the question, why are arteries with a basal level of spontaneous tone insensitive to EFS, while non-myogenic arteries are activated. Explaining these observations may be important for our understanding neural control of blood flow *in vivo.*

[1] S. Anschütz, R. Schubert, Modulation of the myogenic response by neurogenic influences in rat small arteries., Br. J. Pharmacol. 146 (2005) 226–33. doi:10.1038/sj.bjp.0706323.