Different vasodilator mechanisms in intermediate- and small-sized arteries from the hindlimb vasculature of the toad, *Rhinella marina*

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In this study, myography was used to determine the vasodilatory signalling pathways, with a focus on nitric oxide (NO) signalling, in the intermediate-sized iliac artery and the smaller-sized sciatic artery of the toad, *Rhinella marina*. Toads were anaesthetized by immersion in a 1% solution of tricaine methanesulfonate (MS222) until no toe pinch or jaw reflex was observed. All experiments involving *R. marina* were approved by the Deakin University Animal Ethics Committee. Immunohistochemical analysis showed NO synthase 1-immunoreactivity (NOS1-IR) in perivascular nitrergic nerves in the iliac artery, and only a sparse distribution of NOS1-IR in the sciatic artery. Furthermore, NOS3-IR was observed in the vascular smooth muscle of the sciatic artery but not in the endothelium. Acetylcholine (ACh) was used to facilitate intracellular Ca signalling in order to activate vasodilatory pathways. In the iliac artery, ACh-mediated vasodilation was abolished by blockade of both the NO and prostaglandin (PG) signalling pathways with the soluble guanylate cyclase inhibitor, ODQ (1H-[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one (10^{-5} M), and indomethacin (10^{-5} M), respectively. Furthermore, removal of the endothelium had no effect on the ACh-mediated vasodilation in the iliac artery, and generic inhibition of NOS with L-NNA (N^{ω}-nitro-L-arginine, 3×10^{-4} M) significantly inhibited the vasodilation. In contrast to the iliac artery, ACh-mediated vasodilation of the sciatic artery was mostly endothelium-dependent and was not significantly affected by NOS inhibition. However, ODQ and indomethacin, alone and in combination, significantly inhibited the vasodilation, but did not abolish it. It is proposed that PGs and a signalling molecule other than NO, possibly carbon monoxide, are vasodilators in the sciatic artery. This study showed that the mechanisms of vasodilation in the hindlimb are dependent on vessel size, and the endothelium may become more important as vessel size diminishes.