Relaxin induces differential arteriolar dilations and gap junctionally mediated upstream arteriolar dilations

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Recently, we demonstrated the hormone relaxin causes vasodilation in the terminal microvasculature *in vivo* and identified mechanisms (nitric oxide, potassium channels, protein kinase A, phosphoinositide 3-kinase) that mediate this response. We have extended this study to elucidate whether relaxin equally vasodilates different branches of the terminal microcirculation in the blood-perfused, anaesthetized, hamster cremaster preparation. Relaxin (10^{-10}M) was applied by micropipette directly onto transverse, branch or module inflow (MI) arterioles and the local application site was observed (n = 8 in each case). For all experiments, n = 8 and statistical significance was accepted at $P < 0.05$. Relaxin caused a significant, transient vasodilation in transverse (TA) and branch but not MI arterioles. In order to determine if capillaries respond to relaxin, we applied relaxin (10^{-10}M) to capillaries and observed the upstream MI for possible vasodilation. Relaxin application significantly vasodilated upstream MI arterioles indicating capillaries are responsive to relaxin. To explore this transmitted upstream vasodilation further, we applied relaxin to a TA and observed ~1000μm upstream; significant vasodilation was observed in response to relaxin. Since gap junctions have been implicated in transmitting vasodilation and to investigate the mechanisms by which relaxin may stimulate upstream vasodilation, we placed one of two gap junction uncouplers [18-β-glycyrrhetinic acid (40×10^{-6}M) or halothane (0.07%)] midway between the local and upstream observation sites and tested the effect of relaxin. Both gap junction uncouplers significantly inhibited the transmitted vasodilation. Taken together, this study is the first to report differential vasodilatory responses to relaxin in the terminal microcirculation, the first to demonstrate relaxin's ability to transmit vasodilation, and the first to implicate gap junctions in this response.