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Resumo	6-Nitrodopamine (6-ND) modulates vas deferens, seminal vesicles, and corpus cavernosum contractility; however, its role on the lower urinary tract organs has not been evaluated. Investigations of isolated urinary bladders from wild-type (WT) mice revealed 6-ND release was comparable to that of dopamine and adrenaline, whereas noradrenaline was hardly detected, as assessed by liquid chromatography coupled to tandem mass spectrometry. In vitro, 6-ND induced concentration-dependent relaxations in carbachol pre-contracted bladders with high potency (pEC50: 8.04 ± 0.86), independently of eNOS/sGC activity. Co-incubation of 6-ND (1-10 μM) antagonizes the contractile effects of acetylcholine ($p < 0.05$). Experiments using nitric oxide synthase (NOS) knockout mice demonstrated that 6-ND release from isolated urinary bladder was significantly reduced by neuronal NOS (nNOS-/-) deletion and abolished by triple NOSs deletion (n/i/eNOS-/-), while no significant changes were observed in endothelial (eNOS-/-) or inducible (iNOS-/-) knockout mice. Incubation with tetrodotoxin resulted in a significant decrease in 6-ND release in bladders obtained from WT, but not in nNOS-/- mice. The bladders from nNOS-/- and n/i/eNOS-/- mice exhibited significantly higher contractile responses to electric field stimulation (EFS), compared to eNOS-/-, iNOS-/-, or WT bladders. The hyperreactivity observed in triple NOS knockouts was reversed by the incubation with bladder mucosal layer obtained from a donor WT mice, but not with the muscular layer. These findings clearly demonstrate 6-ND is the most potent endogenous relaxing agent of urinary bladder, and inhibition of its release is associated with bladder hyperreactivity.
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