Abstract: The role of T-type Ca2+ channels for cardiovascular physiology, in particular blood pressure regulation, is controversial. Selective blockade of T-type Ca2+ channels in resistance arteries has been proposed to explain the effect of the antihypertensive drug mibefradil. In the present study, we used a third generation, time- and tissue-specific conditional knockout model of the L-type Ca2+ channel Cav1.2 (Cav1.2SMAKO mice) to genetically dissect the effects of mibefradil on T- and L-type Ca2+ channels. Myogenic tone and phenylephrine-induced contraction in hindlimb perfusion experiments were sensitive to mibefradil in control mice, whereas the drug showed no effect in Cav1.2-deficient animals. Mean arterial blood pressure in awake, freely moving control mice was reduced by 38+/-2.5 mm Hg at a dose of 1.25 mg/kg bodyweight mibefradil, but not changed in Cav1.2SMAKO mice. These results demonstrate that the effect of the putative T-type Ca2+ channel-selective blocker mibefradil on blood pressure and small vessel myogenic tone is mediated by the Cav1.2 L-type Ca2+ channel.
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