NO-MEDIATED VASCULAR SMOOTH MUSCLE RELAXATION IN SGCA\textsubscript{1} KNOCK-OUT MICE
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Soluble guanylyl cyclase (sGC) is composed of one $\alpha$ and one $\beta$ subunit, each existing in 2 isoforms ($\alpha_1/\alpha_2$ and $\beta_1/\beta_2$). The aim of our study was to investigate the functional importance of the sGC$\alpha_1$-subunit in several sGC-mediated vasorelaxations. Therefore, we studied blood vessels from mice lacking the sGC$\alpha_1$ subunit. From mice of both genders, segments of the thoracic aorta and femoral artery were mounted in a small vessel myograph for isometric tension recording. Concentration-response curves were established on acetylcholine (ACh) (1 nM–10 $\mu$M), sodium nitroprusside (SNP) (1 nM–10 $\mu$M), NO gas (1 $\mu$M–100 $\mu$M), BAY 41-2272 (1 nM–10 $\mu$M), and levomakalim (Lev) (1 $\mu$M–100 $\mu$M) in control conditions and/or in the presence of ODQ. The relaxing influence of endogenous NO (released from the endothelium in response to ACh), exogenous NO (delivered by the NO-donor SNP and NO gas) and BAY 41-2272 (an NO-independent sGC-activator) was significantly reduced in the arteries of the sGC$\alpha_1$ knock-out mice. However, preparations from sGC$\alpha_1$ knock-out mice still showed a substantial relaxation in response to exogenous NO and BAY 41-2272. The sGC-inhibitor ODQ strongly diminished the remaining effect of exogenous NO and BAY 41-2272. The sGC$\alpha_1$ knock-out mice and their wild type littermates showed a similar response to the $K_{\text{ATP}}$-channel opener Lev, indicating that the reduced NO- and BAY 41-2272-induced responses are not aspecific. All observations were similar in both sexes. Taken together, these findings indicate that the sGC$\alpha_1\beta_1$ isoform is involved in the vasorelaxing effect of both endogenous and exogenous NO. However, the substantial relaxation response to exogenous NO still observed in the sGC$\alpha_1$ knock-out mice suggests the contribution of the sGC$\alpha_2\beta_1$ isoform or other ODQ sensitive mechanism. The vasorelaxing effect of BAY 41-2272 in the sGC$\alpha_1$ knock-out mice, indicates that both sGC isoforms are present in the blood vessels studied.