ROLE OF THE SOLUBLE GUANYLYL CYCLASE α1 β1 (sGCα1β1) ISOFORM IN MICE CORPUS CAVERNOSUM SMOOTH MUSCLE RELAXATION

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As the major effector molecule for NO, soluble guanylyl cyclase (sGC) plays a key role within the NO/cGMP signalling cascade which participates in penile erection. The enzyme exist as an αβ-heterodimer, but only two isoforms have been reported to be active (sGCα1β1 and sGCα2β1). The functional importance of the α1-subunit in corpus cavernosum (CC) smooth muscle relaxation was assessed by mounting CC from male sGCα1$^{-/-}$ mice and wild type littermates in organ baths for isometric tension recording. The endothelium-dependent relaxation to acetylcholine (ACh) or bradykinin (BK) and the neurogenic response to electrical field stimulation (EFS) were nearly abolished in the sGCα1$^{-/-}$ CC. The relaxing influence of exogenous NO (from sodium nitroprusside (SNP) and NO-gas) was also significantly decreased in the sGCα1$^{-/-}$ mice. The remaining relaxation seen in the sGCα1$^{-/-}$ mice with exogenous NO, was strongly but not completely inhibited by the sGC-inhibitor ODQ. In the preparations of the sGCα1$^{-/-}$ mice, the response to BAY 41–2272 (NO-independent sGC-stimulator) and to T-1032 (phosphodiesterase type 5 inhibitor) were also significantly reduced. The specificity of the impairment of the sGC-related responses was demonstrated by the similar forskolin (adenylyl cyclase activator) and 8 pCPT-cGMP (cGMP-analogue)-induced responses. In conclusion, our findings indicate the involvement of an sGC isoform with the α1-subunit in NO-induced CC smooth muscle relaxation. However, the remaining relaxing influence of exogenous NO in the sGCα1$^{-/-}$ mice, suggests the contribution of (an) additional pathway(s).