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Poster presentation

In vitro and in vivo studies on the importance of the soluble gyanylyl cyclase alpha 1 subunit in penile erection

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Background

Penile erection is a highly regulated physiologic event in which the NO-cGMP pathway plays a pivotal role. NO derived from both non-cholinergic non-adrenergic nerves and endothelial cells diffuses to the arterial and corporal smooth muscle cells to bind and activate its target soluble guanylyl cyclase (sGC). The following increase in cGMP induces a cascade of events eventually leading to smooth muscle relaxation and penile erection. Because of its central role sGC seems to be an attractive and promising new target for the treatment of erectile dysfunction. Structurally, sGC is a heterodimer consisting of an α and a β subunit. Of both subunits, two isoforms have been characterised, however only the $sGC\alpha_1\beta_1$ and $sGC\alpha_2\beta_1$ heterodimers are functionally active.

Materials and methods

In order to elucidate the functional role of the $sGC\alpha_1\beta_1$ heterodimer in the mechanism of erection, experiments were performed in vivo and on isolated corpora cavernosa (CC) using $sGC\alpha_1^{-/-}$ mice. For the in vivo study the responses to electrical stimulation of the nervus cavernosus and intracavernosal injection of different sGC-dependent and -independent vasodilatory agents were investigated. For the in vitro study isolated CC tissues from $sGC\alpha_1^{-/-}$ and $sGC\alpha_1^{+/+}$ mice were mounted in organ baths for isometric tension recording and the responses to different sGC-dependent and -independent vasorelaxing agents were examined.

Results

The responses in $sGC\alpha_1^{-/-}$ to administration of sodium nitroprusside (1 – 4 μg/kg or 10^{-9} – 10^{-5} mol) and spermine/NO (10 – 20 μg/kg or 10^{-9} – 10^{-5} mol) and to electrical stimulation (5 – 15 Hz, 8 V, 60 s or 1 – 8 Hz, 80 V, 20 s) are significantly reduced although not completely abolished. Responses to sGC-independent vasorelaxing agents are similar between $sGC\alpha_1^{-/-}$ and $sGC\alpha_1^{+/+}$ mice suggesting that the decreased potential of smooth muscle relaxation is not related to structural changes or changes in the pathway downstream sGC.

Conclusion

This study clearly illustrates the importance of the $sGC\alpha_1\beta_1$ heterodimer, however the results also provide evidence that besides activation of $sGC\alpha_1\beta_1$ also other mechanisms are involved in penile erection such as $sGC\alpha_2\beta_1$ and/or sGC-independent mechanisms.