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Poster presentation

Nerve-induced release of nitric oxide from the rabbit corpus cavernosum is modulated by cyclic GMP

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Nitric oxide (NO) is a messenger of the autonomic nerves in the urogenital tract; in particular the release of NO in the cavernous tissue is of importance for maintaining erection. However, the regulation of NO formation in neurons of the corpus cavernosum is poorly understood. Here, we report, that upon electrical stimulation of isolated rabbit corpus cavernosum, NO/NO_2^- was formed and released in a reproducible fashion. The nerve-induced release of NO/NO_2^- was decreased upon application of the NO synthase inhibitor N^w-nitro-L-arginine methyl ester (L-NAME) and the neurotoxin tetrodotoxin (TTX). Further, the release of NO/NO_2^- was not modulated by inhibition of the adrenergic and cholinergic pathways. In smooth muscle, NO mediates its effects via soluble guanylate cyclase (sGC)/cyclic guanosine 3',5'-monophosphate (cGMP)-pathway. Hence, we applied modulators of the sGC/cGMP-pathway to study if and to what extent cGMP might affect the release of NO from the tissue. In the presence of the cGMP analogue 8-Br-cGMP and the sGC stimulator YC-1, the evoked release of NO/NO_2^- was increased. Further, inhibition of sGC by ODQ decreased the release of NO/NO_2^- whereas the unselective phosphodiesterase (PDE) inhibitor zaprinast did not significantly influence the nerve-induced release of NO/NO_2. Nitrergic neurons are important for erectile responses in the corpus cavernosum and impaired signalling may result in erectile dysfunction. At present, erectile dysfunction can be successfully treated by oral administration of the selective PDE 5 inhibitors sildenafil, tadalafil and vardenafil. We applied the selective PDE 5 inhibitors to the isolated rabbit corpus cavernosum and found that the selective PDE 5 inhibitors all decreased the evoked release of NO. Our results suggest that NO/NO_2^- is released by nitrergic neurons within the rabbit corpus cavernosum and that the nerve-induced release of NO/NO_2^- is subject to modulation by the sGC/cGMP-pathway. However, there seems to be a dual effect of cGMP in nitrergic neurotransmission. First there might be a general enhancing mechanism on neuronal excitability or on some other aspect of activation of the neurotransmission. Second, the formation and release of NO is probably under a direct local inhibitory control via cGMP.