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THE AGE-RELATED CHANGE IN NITRIC OXIDE (NO) RELEASE AND NO SYNTHASE (NOS) IN THE HUMAN PROSTATE

Aims of study

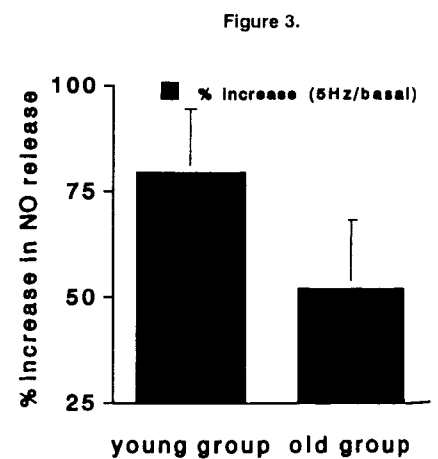
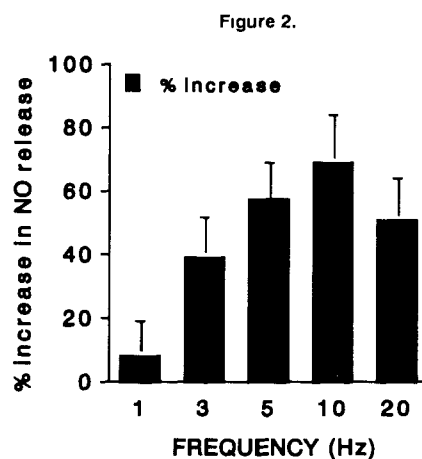
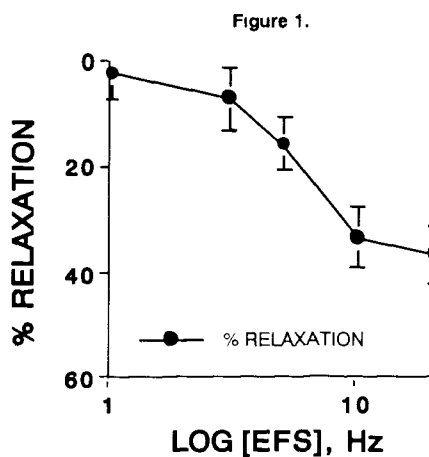
Nitric Oxide (NO) is suggested as a mediator involved in the regulation of smooth muscle tone in the genitourinary tract. The present study was designed to evaluate age-related NO releases induced by electrical field stimulation in human prostate strips using high-performance liquid chromatography (HPLC) coupled with microdialysis procedure. Furthermore, nicotinamide adenine dinucleotide phosphate diaphorase (NADPH-d) histochemistry and immunohistochemistry of neuronal NOS (nNOS) were also observed.

Methods

Human prostates were obtained from patients with cysturethrectomy due to bladder malignancy (n=25, mean age \pm S.E.M. ; 65.4 ± 7.1 years). The strips of human prostate were suspended in thermostatically controlled 20 ml muscle bath filled with oxygenated Krebs-Henselait solution for isometric tension recordings. Electrical field stimulation (main interval 60 s, supramaximal voltage, 2 msec duration, frequency 1-20 Hz and 3 sec train) was applied to prostate preparations precontracted with $1 \mu\text{M}$ phenylephrine in the presence of $10 \mu\text{M}$ guanethidine, $10 \mu\text{M}$ atropine and $10 \mu\text{M}$ indomethacine. Furthermore, the microdialysis probe was inserted into the strip, and Ringer's solution was perfused into the probe. The dialysate during electrical field stimulation was collected for 10 min ($20 \mu\text{l}$), and the amount of $\text{NO}_2^-/\text{NO}_3^-$ released in the dialysate was measured by HPLC and NOx analyzer based on the Greiss method. To evaluate NOS-positive neurons, NADPH-d staining and immunohistochemistry with nNOS antibody was performed in the same tissue.

Results

In all specimens, electrical field stimulation caused frequency-dependent relaxations of prostate strips (Figure 1). The amount of basal $\text{NO}_2^-/\text{NO}_3^-$ release before electrical field stimulation was 23.8 ± 2.1 pmol/g weight of prostate. The $\text{NO}_2^-/\text{NO}_3^-$ released by EFS increased in a frequency-dependent manner (Figure 2). The pretreatment with L-NNA (100 μM) completely inhibited NO release. The amount of $\text{NO}_2^-/\text{NO}_3^-$ release by EFS is significantly less in the old group (≥ 65 years, $n=11$) than in the young one (< 65 years, $n=14$) (Figure 3). In the prostatic tissue, NADPH-d staining and immunochemistry of nNOS revealed the existence of a dense nitrenergic innervation, which was weaker in the old group than in the young one.



Conclusions

The present data suggest there are age-related decreases in the releases of NO from nitrenergic nerve and nNOS activity in the human prostate, which may contribute to the prostatic urethral function in the aged.

References

1. J. Pathol , 189 : 224-229, 1999.
2. The Prostate , 33 : 1-8, 1997.