Androgens positively regulate NO-mediated relaxant pathway in rat clitoris

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Testosterone/Estradiol Ratio Regulates NO-Induced Bladder Relaxation and Responsiveness to PDE5 Inhibitors

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Rat clitoris shows the same pattern of expression of NO/cGMP signalling related genes as the male penis, although at a significantly lower level (qRT-PCR).

\*p<0.05, \**p<0.01 vs. female clitoris
Female clitoris expresses high level of AR (similar to PR), but lower than that observed in male CC

**p<0.05 \*p<0.05 and **p<0.01 vs. male bladder

°° p<0.01 vs. female clitoris
Female Sprague Dawley rats

- No surgery/Intact group
- Bilateral ovariectomy/OVX group

17-β estradiol 10 µg/Kg, daily subcutaneous injection

Hormone replacement (for 6 weeks)

- Progesterone 10 mg/Kg, daily subcutaneous injection
- Testosterone 30 mg/Kg, weekly intramuscular injection
- Letrozole 2.5 mg/Kg, daily in drinking water

Recovery period (3 weeks)

No further treatment

Vignozzi et al., J Sex Med Oct 11 2012
Effect of the treatments on circulating sex steroids

Effect of the treatments on two ER-dependent genes: PR & OTR
TESTOSTERONE normalizes OVX-induced down-regulation of genes related to NO/cGMP signaling

*p<0.05, **p<0.01 vs intact female
*p<0.05; ***p<0.001 vs ovx
§p<0.05, §§§p<0.001 vs OVX+T
TESTOSTERONE normalizes OVX-induced down-regulation of α smooth muscle actin

αSMA

mRNA/18S

Female  Ovx  Ovx+T  Ovx+E  Ovx+P  Ovx+T+letrozole

*p<0.05, **p<0.01 vs intact female
*p<0.05; ***p<0.001 vs ovx
§p<0.05, §§§p<0.001 vs OVX+T
ESTRADIOL normalizes OVX-induced down-regulation of genes related to RhoA/ROCK pathway

*estradiol normalizes OVX-induced down-regulation of genes related to RhoA/ROCK pathway

*p<0.05, **p<0.01 vs intact female
*p<0.05; ***p<0.001 vs ovx
§p<0.05, §§§p<0.001 vs OVX+T
RELAXANT EFFECT OF Y27632 ON RAT CLITORAL STRIPS PRECONTRACTED BY PHENYLEPHRINE (100 μM)

shared IC50= 1.7±0.7μM
Estradiol positively regulates RhoA/ROCK-dependent cell migration (Boyden chamber assay) in rat clitoris smooth muscle cells.
Conclusions:

• TESTOSTERONE normalizes, OVX-induced downregulation of NO/cGMP signaling-related genes

• ESTRADIOL normalizes, OVX-induced downregulation of RhoA/ROCK pathway-related genes

Either Testosterone and estradiol are important regulators of clitoris relaxant and contractile mechanisms.

Vascular smooth muscle
Relaxation/ vasocongestion

nNOS  cGMP  PDE5  eNOS

RhoA/ROCK

PKG1