Progesterone signaling mechanisms and functional effects in the male and female rat urinary bladder

Progesterone exerts a strong and reversible anti-contractile effect in both male and female rat bladder, with no apparent sex difference and no evidence of involvement of PR or PGRMC1.

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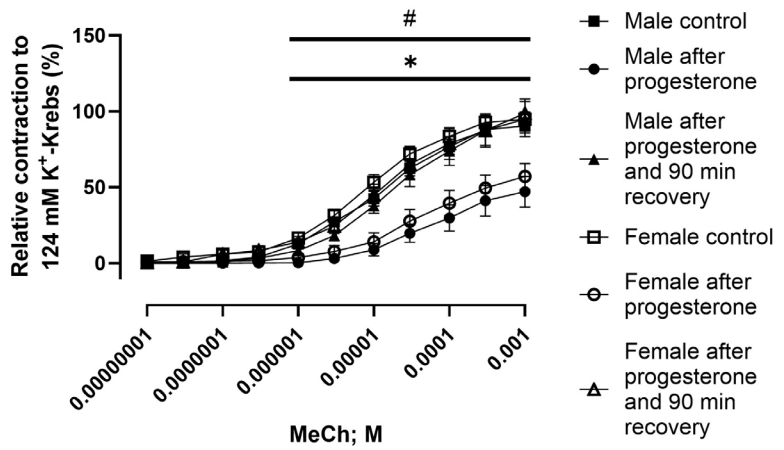

Figure 1. *Contractions to MeCh of bladders from male and female rats in the absence (control; ■, □), after progesterone treatment (●, ○), and after 90 min recovery post treatment (▲, △). Statistical comparisons made with male control strips: * denotes p<0.05 for male control vs. male progesterone-treated preparations, and # denotes p<0.05 for male control vs female progesterone-treated preparations. (Identical outcomes were obtained when comparisons were instead made with female control strips.) n= 8-10 for each sex, bars represent SEM, 2-way ANOVA with Dunnett's multiple comparison test.*

Background

Hormonal effects on bladder contractility remain understudied. We previously showed that progesterone reduces methacholine (MeCh)-induced contractions in male rat bladder, but the underlying mechanism and possible sex differences remain unclear.

Aim

To investigate progesterone's anti-contractile effect on subsequent MeCh responses in male and female rat bladder and to assess functional involvement of progesterone receptor (PR) and progesterone receptor membrane component 1 (PGRMC1).

Methods

Full-thickness bladder strips from male and female Sprague-Dawley rats (n=10 rats per sex) were mounted in organ baths.

MeCh concentration-response curves were recorded at baseline, 10 min after washout following a 10-min progesterone exposure (5×10^{-4} M), and after 90 min recovery. Total conc. of the vehicle DMSO was <3 %.

Separate preparations received the PR antagonist mifepristone (10^{-4} M) or the PGRMC1 modulator AG-205 (10^{-5} M) 30 min before progesterone.

Results

- Control MeCh responses were similar between sexes.
- Progesterone reduced maximal contractions in males from 90.4 ± 4.6% to 47.1 ± 10.1% and in females from 94.8 ± 4.8% to 57.2 ± 8.4%.
- Responses recovered after 90 min to 94.9 ± 11.6% in males and 98.7 ± 9.6% in females.
- Mifepristone and AG-205 did not prevent progesterone's anti-contractile effect. PR or PGRMC1 involvement was thus not demonstrated under the conditions tested.

Conclusion

Progesterone (5×10^{-4} M) produces a strong, reversible anti-contractile effect on MeCh-induced contractions in male and female rat bladder, with no apparent sex difference. This effect was not prevented by mifepristone or AG-205 under these conditions, suggesting possible involvement of an alternative signaling mechanism.