

# Effects of Castration and Testosterone Replacement over Serotonin (Prostatic and Plasmatic): An in vivo study

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## BACKGROUND

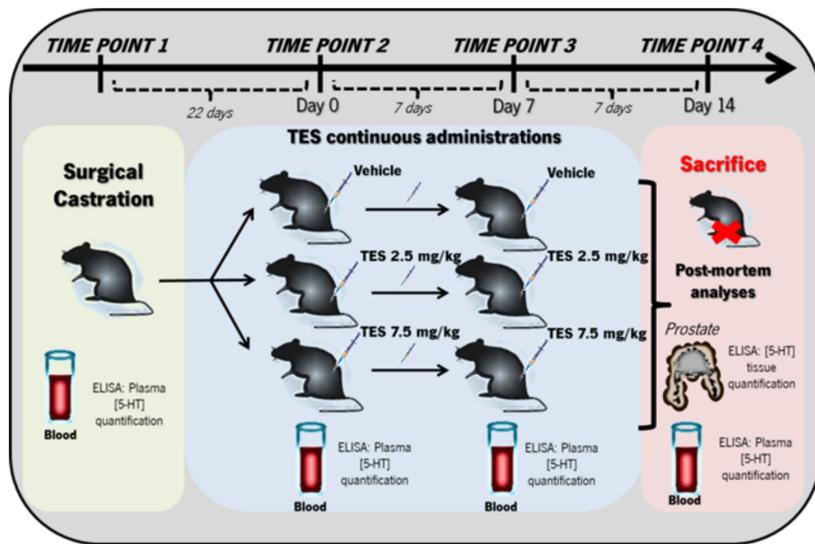
- Benign Prostate Hyperplasia is an extraordinarily prevalent disease, with enormous impact in patient's quality of life
- Its etiology remains unknown, despite the accepted impact of aging and testosterone (TES) in its pathophysiology
- Recent studies revealed that serotonin (5-HT) inhibits benign prostate growth through modulation of the androgen receptor.

## OBJECTIVE

- To investigate if castration and TES replacement regulate prostatic and plasmatic 5-HT concentration

## METHODOLOGY

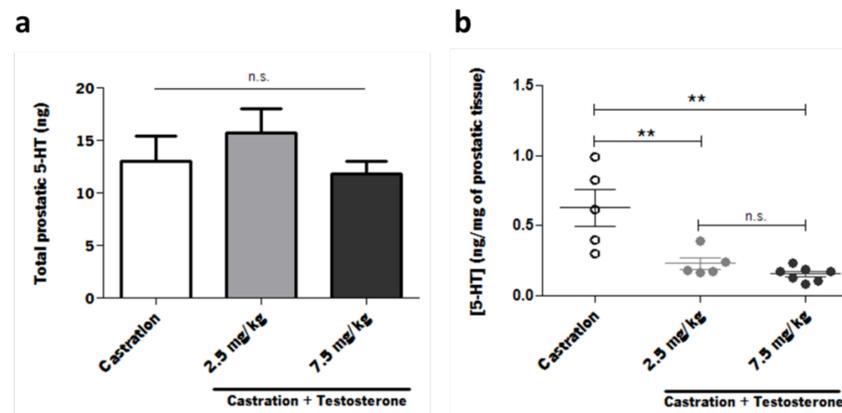
- C57BL/6 mice were submitted to surgical castration and divided into 3 Groups, Group 1: supplemented with vehicle; Group 2 and 3 supplemented with different TES concentrations, during 14 days. Prostatic and Plasmatic 5-HT concentrations were then determined in different time points (fig. 1).



**Fig. 1 - Experimental design.** Timeline of surgical castration, vehicle or TES continuous administration and sacrifice of C57BL/6 mice, with plasma and tissue samples analysis on each time point.

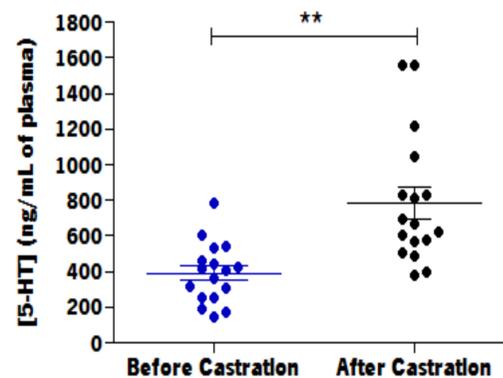
## RESULTS

- Prostatic mice 5-HT seems not to be regulated by the presence or absence of androgens (Fig. 2).
- Plasmatic 5-HT concentration significantly increases after castration (Fig. 3).
- Plasmatic 5-HT concentration significantly decreases after TES supplementation of castrated animals (Fig. 4).



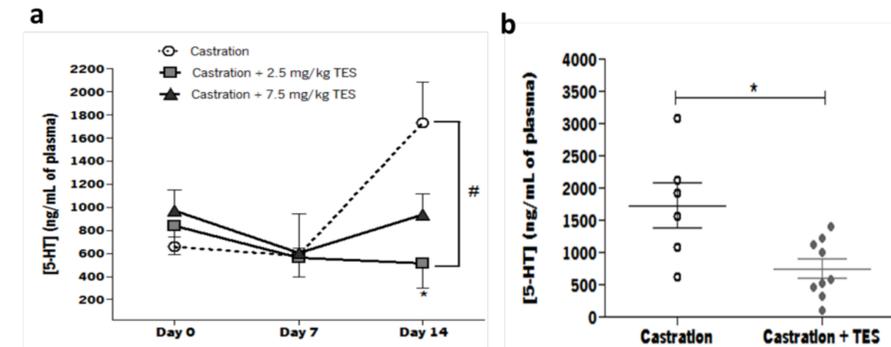
**Fig. 2. - 5-HT is present in high levels in normal mice prostate. The total amount of prostatic 5-HT is not dependent of the presence of testosterone.**

(a) After 14 days of vehicle or different dosages of TES administrations, animals were sacrificed and prostate was isolated and then total 5-HT amount was measured by ELISA (n=5-7). Data is represented by mean and error bars indicate SEM; n.s. – non significant. (b) After 14 days of vehicle or different dosages of TES administrations, animals were sacrificed and prostate was isolated and total 5-HT concentration was measured by ELISA (n=5-7). Data is represented by mean and error bars indicate SEM; \*\*p=0.006, 2.5 mg/kg vs. castration; \*\*p=0.001, 7.5 mg/kg vs. castration; n.s. - non-significant.



**Fig. 3 - Castration increases plasmatic 5-HT concentration.**

C57BL/6 male mice were bilaterally orchidectomized and 5-HT plasma concentration was measured by ELISA, before surgery and after 22 days (n= 17). Data is represented by mean and error bars indicate SEM; \*\*p=0.001.



**Fig. 4 - TES re-supplementation reduces plasmatic 5-HT concentration.**

C57BL/6 mice were submitted to surgical castration and divided into 3 groups, continually exposed to vehicle or to different TES doses, during 14 days. (a) 5-HT plasma concentration was measured by ELISA previously to the first administration and after 7 and 14 days (n=4-6). Data is represented by mean and error bars indicate SEM; \*p=0.043, Day 14 vs. Day 0 to castration+2.5 mg/kg group; #p=0.038, castration vs. castration+2.5 mg/kg at Day 14. (b) 5-HT concentration at Day 14 of follow-up was compared between the castration group (n=6) and castration + TES group (n=9). Data is represented by mean and error bars indicate SEM; \*p=0.012.

## CONCLUSIONS

- ❖ In accordance with previous findings, the normal mice prostate produces high levels of 5-HT independently of androgens. This prostatic 5-HT might counteract the stimulatory action of TES in prostatic growth, maintaining the normal organ size.
- ❖ This new finding that androgens strongly regulate plasmatic 5-HT concentration remains completely unexplained, but raises the question of a possible relationship between extra-prostatic organs and the regulation of prostatic growth.