

SALINE LOADING CAUSED THE CHANGE OF THE EXPRESSION OF α_1 -ADRENOCEPTOR SUBTYPES AND ANGIOTENSIN II TYPE1 RECEPTORS IN THE PROSTATE OF SPONTANEOUSLY HYPERTENSIVE RATS

Hypothesis / aims of study

Spontaneously hypertensive rats (SHRs) have been used as animal models of benign prostate hypertrophy (BPH) and detrusor overactivity. To clarify the mechanism of lower urinary tract symptoms (LUTS) associated with BPH and the effects of saline-loading, we investigated the change of the morphology and expression of α_1 -adrenergic receptor (AR) subtypes and angiotensin II (AT II) type1 receptors within the prostate of SHRs.

Study design, materials and methods

Twelve male 25-week-old SHRs were randomly separated into two groups (n=6 each). One group was given orally 20 ml 0.9% saline per kg-body weight daily for one week. The other group received no treatments. After 7 days of the saline loading, systolic blood pressure (SBP) and prostate weight were measured. The prostates were excised and analyzed for the presence of dividing cells, α_1 -AR subtypes, and AT II type 1 receptors by the immunohistochemical methods.

Results (Table 1, Fig. 1-4)

After 7 days, the SBP and prostate weight of saline-loaded SHRs tended to increase, but was not significantly different compared to the non-treated rats. The prostate ventral lobes of both groups had numerous proliferating cell nuclear antigen (PCNA)-positive epithelial cells. The lateral-dorsal lobes of the saline-treated SHRs more PCNA-positive cells than did the non-treated ones. The expression of α_1 -AR subtypes and AT II type 1 receptors within the prostates of saline-loaded SHRs was higher than the non-treated ones.

Interpretation of results and concluding message

Increased numbers of α_1 -AR subtypes and AT II type 1 receptors in the prostate of the saline-loaded SHRs might play important roles in the development of LUTS associated with BPH.

Table 1. PCNA-positive cells, epithelial α_1 -AR subtypes, and ATII receptors in the ventral and lateral-dorsal lobes

cells/ μm^2 or spots/ μm^2	Ventral lobe		Lateral-dorsal lobe	
	Non-treated	Saline-loaded	Non-treated	Saline-loaded
PCNA positive cells	0.30±0.03	0.31±0.03	0.01±0.002††	0.03±0.01**§§
α_{1A} adrenergic receptor	2.05±0.51	5.27±1.15*	0.58±0.11†	1.53±0.24**§
α_{1D} adrenergic receptor	1.49±0.25	7.80±1.39**	1.47±0.21	6.03±1.95*
α_{1B} adrenergic receptor	1.31±0.19	2.73±0.27**	1.81±0.18	6.08±1.24**§
AT II type 1 receptor	0.35±0.03	0.58±0.11*	1.09±0.23†	6.20±2.54*§

*P < 0.05, **P < 0.01, compared with non-treated control SHRs

†P < 0.05, ††P < 0.01, compared with ventral prostate of non-treated control SHRs

§P < 0.05, §§P < 0.01, compared with ventral prostate of saline-loaded SHRs

Fig. 1. Ventral lobes in non-treated control and saline-loaded SHRs. At 7 days after saline loading, there were no obvious differences between the prostate ventral lobes of the non-treated (A) and saline-loaded SHRs (B) when viewed and analyzed by image processing. H&E stain, x40. Both the control (C) and saline-loaded (D) SHRs had numerous proliferating epithelial cells that were positive for PCNA antibody (red). Bar = 50 μm . Apoptotic cells induced by caspase-dependent or -independent pathways (green, arrow) were rarely present in the (E) control or (F) saline-loaded SHRs. Bar = 10 μm Blue: nuclei.

Fig. 2. α_1 -AR subtypes and AT II type 1 receptors within the ventral lobes. There were fewer α_{1A} -, α_{1D} -, and α_{1B} -ARs (A, C, and E, green, arrows) within the epithelial cells of the ventral lobes in the non-treated control SHRs than in the saline-loaded ones (B, D, and F, green, arrows). Similarly, the expression of the AT II type 1 receptor (A, C, and E, red, arrowheads) within the epithelial cells of the ventral lobes of the control SHRs was also lower than in the saline-loaded ones (B, D, and F, red, arrowheads). Bars = 10 μm , Blue: nuclei.

Fig. 3. Lateral-dorsal lobes in non-treated control and saline-loaded SHRs. At 7 days after saline loading, there were no obvious differences between the prostate lateral-dorsal lobes of the non-treated (A) and saline-loaded SHRs (B) when viewed and analyzed by image processing. H&E stain, x40. (C) The control SHRs had few PCNA-positive epithelial cells (red). Bar = 50 μm . (D) In contrast, the saline-loaded SHRs had a more PCNA-positive epithelial cells than the controls (red). Bar = 50 μm . Apoptotic cells induced by caspase-dependent or -independent pathways (green, arrow) were rarely present in the (E) non-treated or (F) saline-loaded SHRs. Bar = 20 μm , Blue: nuclei.

Fig. 4. α_1 -AR subtypes and AT II type 1 receptors within the lateral-dorsal lobes. There were fewer α_{1A} -, α_{1D} -, and α_{1B} -AR (A, C, and E, green, arrows) within the epithelial cells of the non-treated control lateral-dorsal lobes than in the saline-loaded ones (B, D, and F, green, arrows). Similarly, the expression of the AT II type 1 receptor within lateral-dorsal lobe epithelium in the control SHRs (A, C, and E, red, arrowheads) was also lower than in the saline-loaded ones (B, D, and F, red, arrowheads). Bars = 10 μm , Blue: nuclei.

Fig. 1

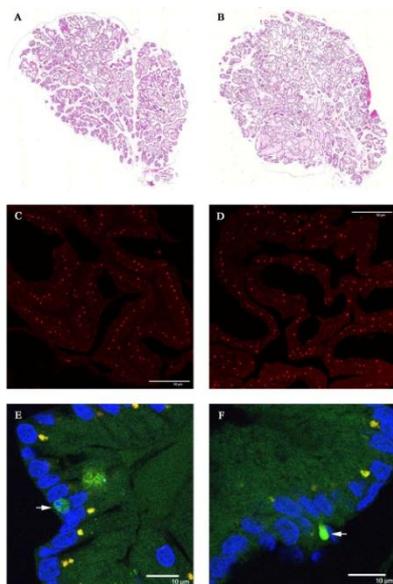


Fig.2

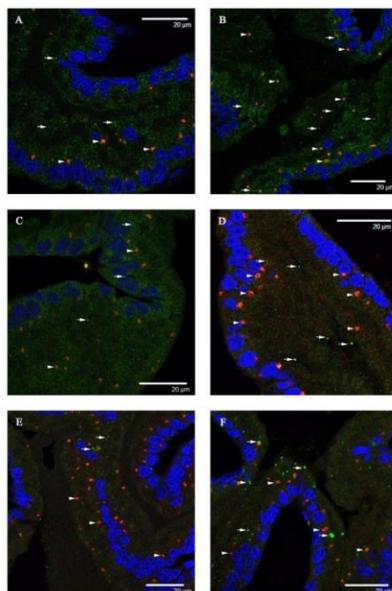


Fig.3

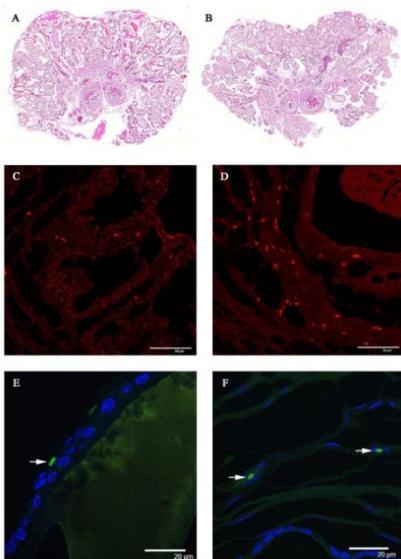
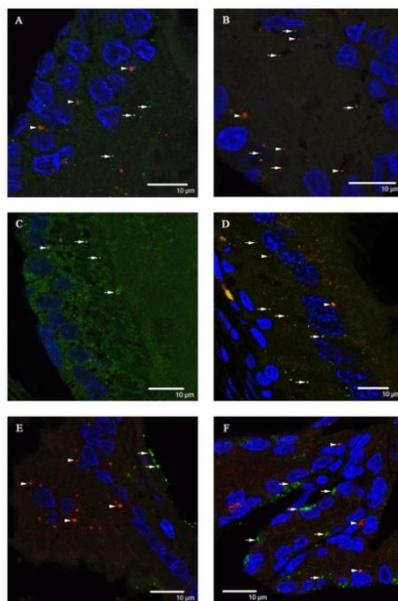


Fig.4



<i>Specify source of funding or grant</i>	none
<i>Is this a clinical trial?</i>	No
<i>What were the subjects in the study?</i>	ANIMAL
<i>Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?</i>	Yes
<i>Name of ethics committee</i>	The ethics committee of Shinshu University School of Medicine