

THE EFFECT AND MECHANISM OF CHANGE IN NEURORECEPTORS IN THE BLADDER AND SKIN WITH OVARECTOMISED RATS.

Hypothesis / aims of study

Menopause is a condition that almost all women experience in their lifetime. Decreased secretion of estrogen from the ovary influences the whole body and causes many symptoms. Osteoporosis, arteriosclerosis is a major concern and are treated heavily. However, symptoms that influence their quality of life have not yet been focused enough. Menopause women experience hot flash, which causes major sweat, but they sometimes experience hypersensitivity to cold environment, which causes Lower urinary tract symptoms (LUTS), such as urinary urgency, frequency, and nocturia. Cold stress produced by sudden change or continuous exposure to low temperature exacerbates LUTS. The mechanism of such symptoms have been proven to appear due to activation of the c-fibers in the bladder and TRPM8 channels in the skin. From this theory, we hypothesised that menopause women's neural receptors in the bladder and skin has a difference compared to premenopausal women. The aim of this study is to discuss cold stress related LUTS in ovariectomized rats and to see the neural receptor expression in the bladder and skin.

Study design, materials and methods

A total of 24 female spontaneously hypertensive rats (160-180g) and 12 female Sprague-Dawley(SD) rats at postnatal week 10 were used for the experiments. Each type of rats were randomly divided into two groups, which were ovariectomy (ovx) operation or sham operation under anesthesia (sevoflurane 3%). Four weeks later, the rats were anesthetized and the urinary bladder was exposed and incised at the center of the dome. A polyethylene catheter was inserted and the free end was tunneled subcutaneously and exteriorized at the back of the neck. Three days after cannulation, the rats underwent cystometry (CMG) unanesthetized. CMG was first performed in room temperature (RT, median 25 celsius) for 20 minutes. Rats were then put into low temperature (LT, median 4 celsius) for 20 minutes. After LT, rats were put into RT again for 20 minutes. Basal pressure and micturition pressure of the bladder were measured. Voiding volume and interval were also measured to see the change rate between RT and LT. After CMG, the whole bladder and dermis of the skin of 10 week old SHR rats were removed for real time PCR and immunohistochemistry to see the effect of ovx against neuromechanism in the bladder and skin.

Results

Basal pressure and micturition pressure did not show a difference between control rats and ovx rats. Voiding interval and micturition volume did not show any difference between both rats. However, the bladder volume in RT was larger in the ovx rats, so change rate of voiding interval and micturition volume when exposed to cold stress showed a significant increase in ovx rats. Results of real time PCR of the bladder are shown in Fig 3. Up-regulation of TRPV1, and TRPM8 was seen in ovx rats. However, neurotransmitter materials such as substance P (SP), neurokinin A (NKA) and B (NKB) did not show any difference between both groups. Immunohistochemistry of the dermis showed a correlation of increased HIF-1 and increased TRPM8 channels.

Table1

	RT			LT		
	control	ovx	p value	control	ovx	p value
basal pressure (mmHg)	9.3	7.1	N.S	7.9	6.8	N.S
micturition pressure (mmHg)	32.7	25.6	N.S	30.3	22.3	N.S
voiding interval (sec)	349	370	N.S	266	260	N.S
micturition volume (ml)	1.08	1.24	N.S	0.789	0.952	N.S
<u>change rate in cold stress</u>						
	control	ovx	p value			
voiding interval (%)	19	49	0.01			
micturition volume (%)	27	37	0.04			

Fig 1

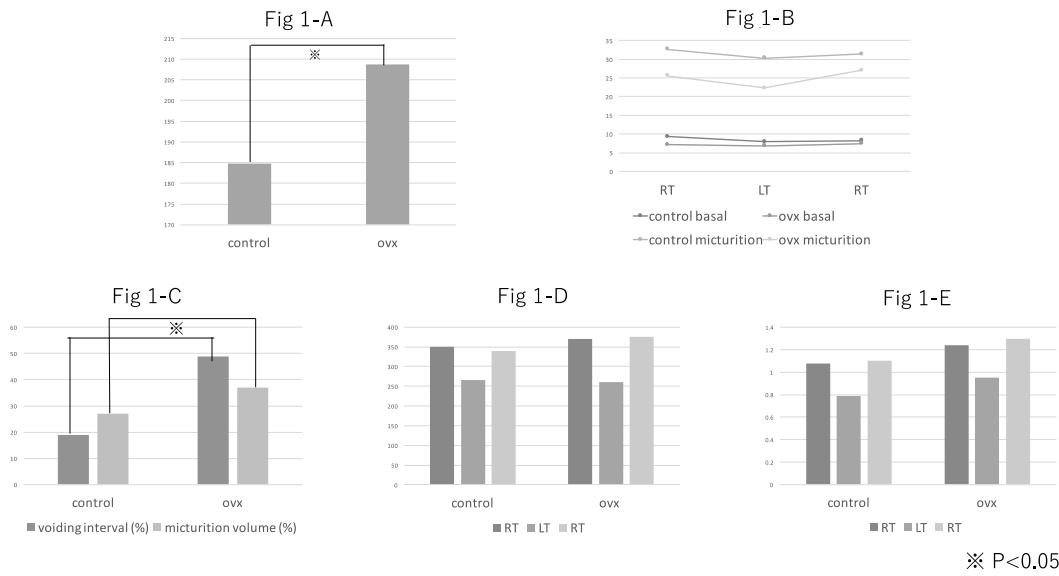
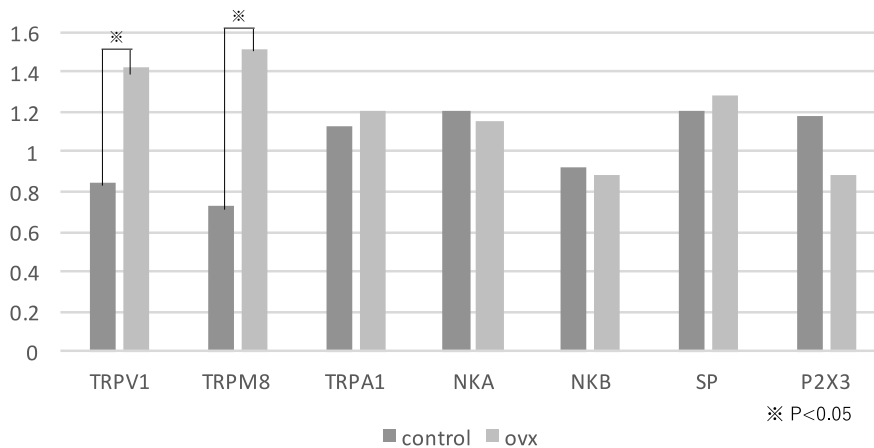


Fig1-A: body weight. Fig 1-B: bladder pressure. Fig 1-C: change rate with cold stress. Fig 1-D: voiding interval. Fig 1-E: micturition volume.

Fig 2



Interpretation of results

From this study, ovx showed a significant exacerbation with cold stress induced LUTS in 10 week old SHR rats without changing voiding pressure and patterns. The mechanism of this improvement may be explained by upregulation of the c-fiber receptors such as TRPV1. The correlation of upregulated HIF-1 and TRPM8 may mean that micro blood flow impairment causes change in neruroreceptors.

Concluding message

SHR ovx rats showed increased sensitivity to cold. Thus may be explained by micro blood flow impairment which causes upregulation of TRP channels in the skin and bladder.

References

1. W.Noguchi et al. J Urol. 2013; 189 (5): 1975-81

Disclosures

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