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SEROTONIN IN THE SPINE IS ASSOCIATED WITH BLADDER HYPERSENSITIVITY CAUSED BY ESTROGEN DEFICIENCY IN RATS

Hypothesis / aims of study

It has been considered that the changes in the bladder function such as overactive bladder and hypersensitive bladder, associated with postmenopausal state, are partially attributable to an estrogen deficiency. Also the change in the spinal 5-HT receptor system is suggested to be responsible for the bladder hypersensitivity. Using an ovariectomized animal model, we investigated whether serotonin and 5-HT receptor system in the spine related to the bladder hypersensitivity induced by estrogen deficiency.

Study design, materials and methods

Sprague-Dawley female rats were divided into 3 groups: sham operation (SO), bilateral ovariectomy (OVX), and ovariectomy plus β-estradiol (10μg/day) replacement (OVXe). Six weeks following the operation, cystostomy was created in advance of cystometry. On the 5th days after creating cystostomy, cystometry was performed using physiological saline or potassium chloride (3.3μM) as an infusion solution. Furthermore the effects of the intrathecal administration of tandospirone (5-HT_{1A} agonist) or serotonin on the bladder function were examined. After cystmetric evaluation, the urinary bladder and the sacral spinal cord tissues were removed, then the expression of mRNA of the 5-HT_{1A}, 5-$HT_{2A,}$ estrogen-alpha and estrogen-beta receptors, which obtained from the bladder and the sacral spinal cord tissues, were determined by real-time PCR.

Results

When cystometry was performed using potassium chloride (3.3μM), OVX rats showed much more decrease in bladder capacity compared to SO rats with statistically significance. Estrogen replacement (OVXe rats) restored the decreased bladder capacity seen in OVX rats.

Intrathecal administration of tandospiron increased bladder capacity in a dose-dependent manner in OVX rats (Fig.1). Intrathecal administration of serotonin 10^{-9} M increased bladder capacity in OVX rats but had no significant effect on bladder capacity in SO or OVXe rats.

The expressions of estrogen-alpha receptor mRNA were decreased in both bladder and sacral spinal cord of OVX rats, compared to SO and OVXe rats. In contrast, no significant differences were found in the expression of estrogen-beta. The expression of 5-HT_{1A} receptor mRNA were increased in the sacral spinal cord of OVX rats, compared to SO and OVXe rats, however no significant change was found in 5-HT_{2A} receptor mRNA.(Fig.2)

Interpretation of results

The present study showed that estrogen deficiency is closely related to the decrease in bladder capacity in OVX rats. Intrathecal administration of serotonin and 5-HT_{1A} agonist restored the decreased bladder capacity seen in OVX rats. Estrogen deficiency causes the decrease in the expression of estrogen-alpha receptor, and increase in the expression of 5-HT_{1A} receptor in the spinal cord.

Concluding message

Serotonin and 5-HT_{1A} receptor in the spine may be involved in the mechanism for the generation of hypersensitive bladder induced by estrogen deficiency.

Fig.1) Change in bladder capacity by intrathecal administration of 5-HT_{1A} agonist

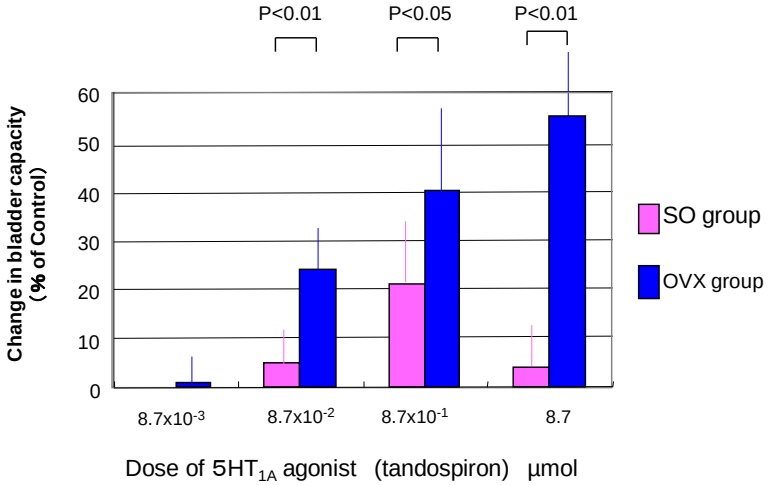
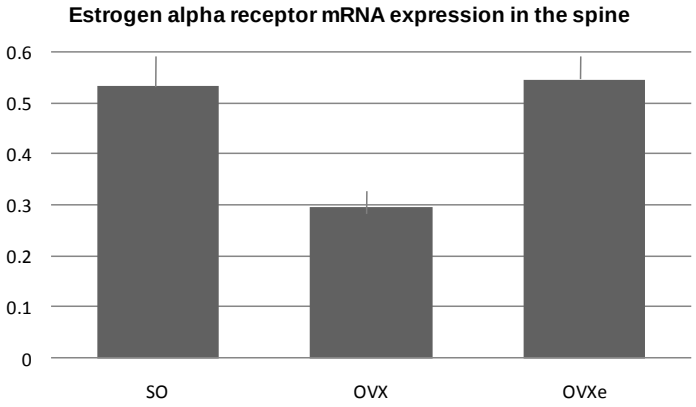
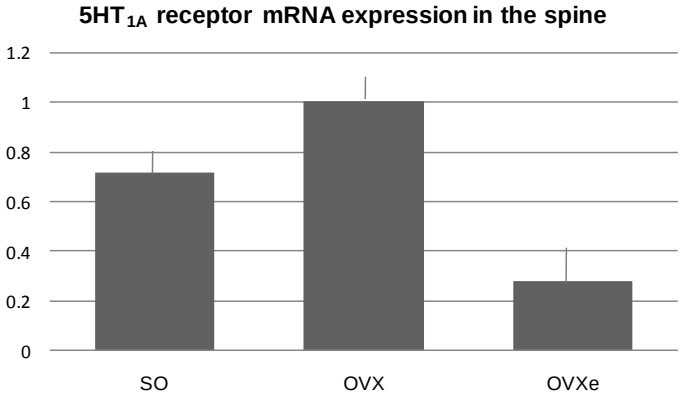


Fig.2) The expressions of estrogen-alpha and 5-HT_{1A} receptor mRNA





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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
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