

MECHANISM OF URINARY FREQUENCY CAUSED BY NORADRENALIN INJECTION INTO THE MEDIAL FRONTAL LOBE IN RATS

Hypothesis / aims of study

Micturition is primarily functions of the autonomic nervous system mediated by the spinobulbospinal reflex pathway passing through a coordination center located in the rostral brainstem, and this reflex pathway is modulated by the upper center in the cerebral cortex (cerebral micturition center). It has been reported that medial frontal lobe (MFL) neurons excited by glutamate inhibited the micturition reflex via activation of the rostral pontine reticular formation (RPRF) which promotes the inhibitory glycine neurons in the spinal cord (1). On the other hand, injection of noradrenalin into the MFL shortened the interval between bladder contractions in rats, and we thought that this model may be used as a nervous urinary frequency. In this study, therefore, we investigated the mechanism of urinary frequency caused by noradrenalin injection into the MFL in rats.

Study design, materials and methods

Twenty-eight female Sprague-Dawley rats were used. Rats were anesthetized with 2% isoflurane, and a polyethylene catheter (PE50) was inserted into the bladder through the urethra. Then three small holes (rostral: bregma +3.5 mm, R 0.8 mm, caudal: bregma -9.5 mm, R and L 1.0 mm) were made in the skull for injection of drugs into the MFL or the RPRF. For the continuous cystometry, each rat was placed in a restraining cage and was allowed to recover from anesthesia for about 30 minutes. Cystometry was done at least after 1 hour after the animal had been placed in the cage. The catheter in the bladder was connected via polyethylene tubing to an infusion pump and the bladder was filled with physiological saline at a rate of 0.05 ml/min. After bladder contraction had shown stability for over 30 min, 1 µl of noradrenalin (10 µM) was injected into the MFL by using a microsyringe. After confirming the shortening of the interval between bladder contraction caused by noradrenalin injection into the MFL, additional injection of glutamate or flavoxate (each 10 µM, each n = 7) into the RPRF or intravenous injection of flavoxate or propiverine (an anti-cholinergic agent)(each 1 mg/kg, each n = 7) was performed. Cystometry was continued for at least 60 min after injection and the changes of bladder activity were recorded.

Results

Injection of noradrenalin into the MFL significantly shortened (24% decrease) the interval between bladder contractions, but injection of glutamate into the RPRF just after noradrenalin injection into the MFL did not change the cystometric parameters. When flavoxate was injected into the RPRF just after noradrenalin injection into the MFL, the interval between bladder contractions significantly prolonged (42% increase) compared with that before noradrenalin injection into the MFL. Intravenous injection of flavoxate, but not propiverine, just after noradrenalin injection into the MFL also significantly prolonged (21% increase) the interval between bladder contraction compared with that before noradrenalin injection into the MFL. Significant changes of intravesical baseline and the maximum bladder contraction pressure were not observed by each agent administration.

Interpretation of results

It is reported that glutamate injection into the RPRF inhibit the micturition reflex by facilitating the RPRF descending neurons which activate the inhibitory glycine neurons in the spinal cord in rats (2). It is also reported that injection of flavoxate into the RPRF inhibits the micturition reflex by activating the inhibitory glycine neurons in the spinal cord in rats (2). Flavoxate shows affinity for adenosine A1, dopamine D2, or adrenergic alpha 2 receptors (3), and these receptors commonly mediate the inhibitory action. Therefore, flavoxate may inhibit the inhibitory interneurons which inhibit the RPRF descending neurons. In the present study, injection of noradrenalin into the MFL shortened the interval between bladder contractions, and its function was blocked by injection of glutamate or flavoxate into the RPRF. These results suggest that injection of noradrenalin into the MFL promotes the activity of inhibitory interneurons suppressing the RPRF descending neurons, and injection of glutamate or flavoxate into the RPRF directly or indirectly activates the RPRF descending neurons and inhibits micturition reflex. Moreover, urinary frequency induced by noradrenalin injection into the MFL did not blocked by intravenous propiverine (an anti-cholinergic agent). Therefore, the model showing the urinary frequency caused by noradrenalin injection into the MFL may reflect a nervous urinary frequency.

Concluding message

Injection of noradrenalin into the MFL promotes the activity of inhibitory interneurons suppressing the RPRF descending neurons, and injection of glutamate or flavoxate into the RPRF directly or indirectly activates the RPRF descending neurons and inhibits micturition reflex. This urinary frequency model by noradrenalin injection into the MFL may be used as a nervous urinary frequency model.

References

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Disclosures

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