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MICTURITION INHIBITORY MECHANISM OF THE ROSTRAL PONTINE RETICULAR FORMATION AND THE SPINAL GLYCINERGIC NEURONS IN RATS WITH OR WITHOUT CEREBRAL INFARCTION

Aims of study

In the central nervous system (CNS), glutamate which is the major excitatory amino acid plays a role in the facilitation of bladder contractions, and gamma-amino butyric acid (GABA) inhibits micturition reflex activity. Glycine has been also identified as another important inhibitory neurotransmitter in the CNS, and intrathecal injection of glycine inhibits bladder contractions. Recently, it has been reported that injection of a cholinergic agent into the rostral pontine reticular formation (RPRF) induced atonia and the increase of the spinal glycine level in cats. In rats, injection of carbachol (a cholinergic agent) or flavoxate hydrochloride into the RPRF inhibited bladder contractions and increased the spinal glycine levels. In our previous study, the spinal glycine level significantly decreased at acute term after cerebral infarction (CI) in rats with urinary frequency, but urinary frequency improved and the spinal glycine level recovered to the baseline level at 2-4 weeks after CI. Therefore, in order to clear the role of the RPRF for lower urinary tract function in intact CNS and CI conditions, we examined the effect of RPRF stimulation on bladder activity and the spinal glycine level in rats with or without CI.

Materials and methods

Fifty female Sprague-Dawley rats were used. The rats were divided into four groups; 1) 10 intact rats for cystometry, 2) 15 intact rats for amino acid analysis, 3) 10 CI rats for cystometry, and 4) 15 CI rats for amino acid analysis. Rats from the CI group were anaesthetized with 2% halothane, and a 4-0 nylon thread was inserted into the right middle cerebral artery to make CI. At 3 days after surgery, intact and CI rats were anaesthetized with urethane, and a small hole was made in the cranial born (bregma -9.5 mm, R 1.0 mm). In 20 rats for cystometry, a polyethylene catheter was inserted into the bladder through the urethra. The urethra was ligated to the catheter near the external urethral meatus, and bladder was filled with physiological saline (0.05 ml/min) to above the threshold volume to induce isovolumetric rhythmic contractions. After the bladder contractions had become stable, 0.5 μl of physiological saline, carbachol (0.3 μM) and flavoxate chloride (0.3 or 3 μM) were injected into the RPRF by a microsyringe, and the change of bladder activity was recorded. In 30 rats for amino acid analysis, 0.5 μl of physiological saline, carbachol (0.3 μM) and flavoxate chloride (0.3 or 3 μM) were injected into the RPRF. After 5 min, these rats were sacrified and the spinal glycine level was measured. Data were expressed as means±standard deviation.

Results

In intact rats, injection of physiological saline did not influence any parameters of bladder contractions and the spinal glycine level. When carbachol (0.3 μM) was injected, bladder contractions disappeared over 30 min and the spinal glycine level was significantly increased (44% increase compared with controls). Injection of flavoxate (0.3 μM) also transiently abolished bladder contraction for 12.4±3.3 min, and the spinal glycine level was significantly increased (29% increase compared with controls). In CI rats, the frequency and amplitude of bladder contractions were significantly increased (69% and 56% increase, respectively), while the spinal glycine level was significantly decreased (34% decrease) compared with those in intact rats. When carbachol was injected, bladder contractions were transiently abolished, but bladder contractions were recovered after 10 min. The spinal glycine level did not change after carbachol injection. Injection of physiological saline and flavoxate (0.3 μM) did not influence any parameters of bladder contractions and the spinal glycine levels. However, high dose of flavoxate (3 μM) transiently abolished bladder contractions for 4.9±1.3 min although the spinal glycine level did not change.

Interpretation of results

In intact rats, activation of the RPRF by local injections of carbachol or flavoxate may inhibit the micturition reflex by activation of spinal glycinergic neurons. In CI rats with urinary

frequency, the spinal glycine level was decreased compared with intact rats. The effects of injections of carbachol or flavoxate into the RPRF on bladder activity and the spinal glycine level were weaker in CI rats than intact rats. These results suggest that activity of the RPRF is weak in CI rats, and that weak activity of the RPRF is due to the decrease of excitatory projection from the upper CNS to the RPRF after CI.

Concluding message

Urinary frequency after cerebral vascular diseases may be due to the decrease of excitatory projection from the upper CNS to the RPRF in addition to the decrease of inhibitory projection to the pontine micturition center. The RPRF plays an important role in the inhibition of the micturition reflex by activation of spinal glycinergic neurons.