

EFFECTS OF CHEMICAL STIMULATION OF THE MEDIAL FRONTAL LOBE ON THE MICTURITION REFLEX 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 known as the pontine micturition center. This reflex pathway is, in turn, modulated by the upper center in the cerebral cortex which is involved in the voluntary control of micturition. It has been reported that cerebral infarction due to occlusion of the internal carotid and middle cerebral arteries induces urinary frequency in rats [1]. In human, urinary frequency and urgency are common in patients with cerebrovascular disease, and the activity in the medial frontal lobe correlates positively with daytime incontinence frequency and urine loss in the functional magnetic resonance imaging test [2]. However, it is not yet known enough how important this area is for the micturition or urine storage. Therefore, we examined the function of the medial frontal lobe on micturition by chemical stimulation such as excitatory agents and their antagonists. Moreover, we also examined the relationship between the medial frontal lobe and the rostral pontine reticular formation (RPRF) which is known as a site inhibiting micturition strongly [3].

Study design, materials and methods

Thirty 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 +2.5 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 medial frontal lobe 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 physiological saline, glutamate, MK-801 (a glutamate receptor antagonist), noradrenaline, or naftopidil (an alpha 1-adrenergic receptor antagonist) (each 10 µM, n = 4-7) was injected into the medial frontal lobe using a microsyringe. In case of glutamate injection into the medial frontal lobe, MK-801 was also injected into the RPRF, because it is reported that glutamate projection to the RPRF neuron inhibits micturition and that its effect is blocked by MK-801 [3]. Cystometry was continued for at least 60 min after injection and the changes of bladder activity were recorded.

Results

Injection of glutamate into the medial frontal lobe significantly prolonged (45% increase) the interval between bladder contractions, and injection of its antagonist MK-801 into the medial frontal lobe significantly shortened (14% decrease) the interval between bladder contractions. Injection of noradrenaline into the medial frontal lobe significantly shortened (42% decrease) the interval between bladder contractions, and injection of its antagonist naftopidil into the medial frontal lobe significantly prolonged (47% increase) the interval between bladder contractions. There was no significant change in the maximum contraction pressure and the baseline pressure before and after injection of such agents. Injection of glutamate into the medial frontal lobe just after MK-801 injection into one side of the RPRF also prolonged (41% increase) the interval between bladder contractions. However, in case of the pre-injection of MK-801 into the bilateral RPRF, glutamate injection into the medial frontal lobe did not change the cystometric parameters.

Interpretation of results

When the glutamate was injected into the medial frontal lobe, the micturition reflex was inhibited. On the other hand, injection of MK-801 into the medial frontal lobe facilitated the micturition reflex. In case of the pre-injection of MK-801 into the bilateral RPRF, but not one side RPRF, glutamate injection to the medial frontal lobe did not inhibit the micturition reflex. These results suggest that the medial frontal lobe neurons are glutamate neurons projecting to the bilateral RPRF neurons which inhibit the micturition reflex. When the noradrenaline was injected into the medial frontal lobe, the micturition reflex was facilitated. On the other hand, injection of naftopidil into the medial frontal lobe inhibited the micturition reflex. These results suggest that the activation of medial frontal lobe neurons presenting alpha-1 adrenergic receptors facilitate the micturition reflex.

Concluding message

It is suggested that the medial frontal lobe neurons excited by glutamate inhibit the micturition reflex via RPRF neuronal activity by glutamate projection. The medial frontal lobe neurons also excited by noradrenaline facilitate the micturition reflex. Therefore, it is thought that the medial frontal lobe is an important integration center for micturition and urine storage mechanisms, and voluntarily regulates the micturition reflex depending on the situation.

References

1. Biomed Res 24: 173-180, 1995.
2. J Urol 183: 221-228, 2010.
3. Life Sci 85: 732-726, 2009.

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none

Is this a clinical trial?

No

What were the subjects in the study?

ANIMAL

*Were guidelines for care and use of laboratory animals followed
or ethical committee approval obtained?* Yes

Name of ethics committee

The Institute for Animal Experiments, Faculty of Medicine,
University of the Ryukyus.
