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ROLE OF SUPRASPINAL AND SPINAL A1-ADRENERGIC RECEPTOR SUBTYPES IN THE MICTURITION REFLEX IN CONSCIOUS RATS

Hypothesis / aims of study

The α_{1A}- and α_{1D}-adrenergic receptors are widely distributed in the central nervous system, including the spinal cord. In the previous studies in anesthetized rats, it was proposed that bulbospinal noradrenergic inputs to the sacral parasympathetic nucleus played an important role in micturition function. However, these findings were not confirmed in conscious rats. The aim of this study was to investigate the role of supraspinal and spinal α_1-adrenergic receptor subtypes in modulating the micturition reflex in conscious rats.

Study design, materials and methods

Female Wistar rats weighing 250–300 g were used. **Cystometrogram:** Rats were anesthetized with sevoflurane. After lower abdominal incision, a polyethylene catheter (PE-50) was inserted into the urinary bladder. The bladder catheter was connected to a pressure transducer and an infusion pump using a T-connector. The rat was placed in a Ballman restraining cage (Natsume, Tokyo, Japan). After recovery from anesthesia, saline was infused into the bladder at a rate of 2.4 ml/h. Vesical pressure was recorded on an AP-601 polygraph (Nihon Kohden, Tokyo, Japan) and digitized with a converter for recording on a PowerLab system, version 5.0. **Intracerebroventricular (i.c.v.) injection:** A guide cannula was stereotaxically implanted into the left cerebral ventricle (stereotaxic coordinates: 0.8 mm posterior to bregma, 1.5 mm lateral to midline, and 4.0 mm below the skull). The cannula was fixed in place by applying dental acrylic cement around the cannula and screws anchored to the skull. After the cement was completely dry and hardened, a stainless steel stylet was used to occlude the cannula during recovery and between drug injections. After the recovery from surgery, animals were individually housed and allowed to recover over 4–5 days following implantation of the cannula. For injections, the internal cannula (with 0.5 mm projection below the cannula) was connected to a polyethylene tube and a microinfusion syringe, was inserted into the cannula. **Intrathecal (i.t.) injection:** The i.t. cannula was made of silicon-coated polyethylene tubing which was previously tapered into an appropriate size by heating. Briefly, this involved inserting a length of polyethylene tubing following laminectomy between L1 and L2 and careful placing the catheter tip in the subarachnoid space of L5. The rats were allowed to recover over 4–5 days following implantation of the catheter filled with artificial cerebrospinal fluid (CSF).

Results

I.c.v. injection of the α_{1A}-adrenergic receptor antagonist tamsulosin, the selective α_{1A}-adrenergic receptor antagonist silodosin and the selective α_{1D}-adrenergic receptor antagonist BMY 7378 dose-dependently prolonged the intercontraction interval (ICI) during continuous infusion cystometrograms in conscious rats (Figure 1A). I.c.v. injection of tamsulosin (1-10 μg), silodosin (1-10 μg) and BMY 7378 (1-10 μg) significantly prolonged the ICI (Figure 1A), but did not alter the maximum voiding pressure (MVP) (Figure 1B). Although I.t. injection of BMY 7378 did not affect the ICI (Figure 2A), tamsulosin and silodosin prolonged the ICI in a dose-dependent manner (Figure 2A). The MVP was significantly decreased by i.t. injection of tamsulosin (10 μg) but not by silodosin and BMY 7378 (Figure 2B).

Interpretation of results

The present results indicate that supraspinal α_{1A}- and α_{1D}-adrenergic receptors are important for the regulation of reflex-bladder activity in conscious rats. Noradrenergic projections from the brainstem to the spinal cord could promote the afferent limb rather than the efferent limb of the micturition reflex pathway, and the main α_1-adrenergic receptors in the afferent limb of this reflex pathway may be α_{1A}- adrenergic receptors.

Concluding message

Supraspinal α_{1A}- and α_{1D}-adrenergic receptors or spinal α_{1A}-adrenergic receptors might play an important role in the micturition reflex pathway in conscious rats.

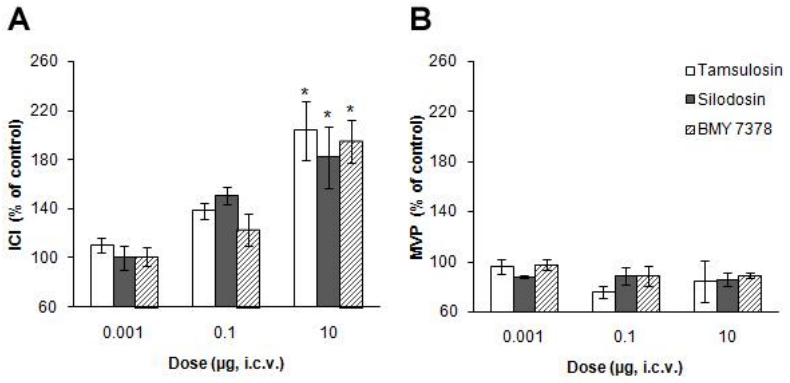

Figure 1. The effect of i.c.v. injection of tamsulosin, silodosin, or BMY7378 on cystometrogram in conscious rats. All drugs (10 μg) prolonged the ICI, but did not alter the MVP.

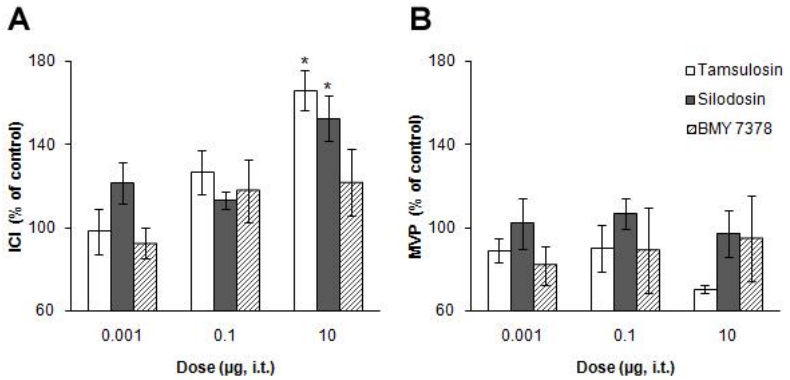

Figure 2. The effect of i.t. injection of tamsulosin, silodosin, or BMY7378 on cystometrogram in conscious rats. The ICI was prolonged by 10 μg of tamsulosin or silodosin, whereas only tamsulosin reduced the MVP. BMY7378 did not affect the ICI and the MVP.

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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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