

**EFFECT OF NBQX, A NON-COMPETITIVE  $\alpha$ -AMINO-3-HYDROXY-5-METHYLISOXAZOLE-4-PROPIONIC ACID RECEPTOR ANTAGONIST, ON THE SNEEZE-INDUCED ACTIVE URETHRAL CONTINENCE REFLEX IN RATS**Hypothesis / aims of study

Urinary continence during stress conditions such as sneezing or coughing is mediated by activation of Onuf's nucleus in the sacral spinal cord, which induces contractions of striated muscles of the urethral sphincter and pelvic floor. Previous studies demonstrated that noradrenergic and serotonergic pathways were involved with the active urethral closure mechanism during sneezing in rats. However, the effect of glutamatergic pathways, which is known to be the major excitatory system controlling the lower urinary tract system, on the urethral continence reflex during sneezing is not known. To clarify the role of glutamine pathways on the sneeze-induced urethral closure reflex in rats, the effects of NBQX, a non-competitive  $\alpha$ -amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) receptor inhibitor, and nisoxetine, a noradrenergic re-uptake inhibitor, were investigated.

Study design, materials and methods

Normal female rats were used. Sneezes were induced by inserting a rat whisker into the nostril. The urethral responses during sneezing caused by active reflex contractions of the mid-urethra were examined. Sneeze-induced leak point pressure (S-LPP) measurements and urethral microtip transducer catheter methods that measure the amplitude of the urethral response during sneezing (A-UPR) and the urethral baseline pressure (UBP) were performed. The effects of intrathecal (i.t.) application of NBQX on the sneeze-induced continence reflex were examined.

Results

NBQX dose-dependently (1, 10, and 100 nmol) inhibited A-UPR by approximately 60% without affecting UBP. NBQX (50 nmol) caused stress urinary incontinence (SUI) during sneezing in normal rats, which did not have SUI before NBQX injection.

Interpretation of results

NBQX (i.t.) dose-dependently attenuated A-UPR and caused SUI in normal rats. These results suggest that the glutamatergic pathway plays an important role as an excitatory system at the spinal level, affecting the urethral continence reflex during sneezing. Moreover, the results suggest that the glutamatergic pathway may be a major pathway of this continence reflex.

Concluding message

The glutamatergic pathway plays a crucial role in the active urethral closure mechanism at the spinal level during sneezing.

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<b><i>What were the subjects in the study?</i></b>	<b>ANIMAL</b>
<b><i>Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?</i></b>	<b>Yes</b>
<b><i>Name of ethics committee</i></b>	<b>the University of Tohoku Graduate School Institutional Animal Care Committee</b>