

IMPROVING VOIDING EFFICIENCY IN THE SCI RAT BY A 5-HT₇ SEROTONIN RECEPTOR AGONIST

Hypothesis / aims of study

To better understand the effects of the selective 5-HT₇ receptor agonist LP44 on micturition in SCI rats.

Study design, materials and methods

Female SD rats weighing 200-275 g were used. SCI was produced in 7 of the 15 rats by transection at the T₁₀ level; cystometric study occurred 8-12 weeks post-transection. Intravesical pressure was monitored in urethane-anesthetized animals via a transvesical catheter. The Selective 5-HT₇ antagonist SB-269970 was administered after each LP44 dose-response curve (all drugs were administered intravenously, i.v).

Results

Compared to controls, SCI rats had a higher bladder capacity and residual volume, and a lower peak bladder pressure and voiding efficiency. In SCI rats, LP44 (3-300 µg/kg, i.v) induced significant dose-dependent increases in micturition volume, significant dose-dependent decreases in residual volume, resulting in significant increases in voiding efficiency. There was also a dose-dependent increased phasic EUS activity. This was correlated with the improved voiding efficiency. SB-269970 (100 µg/kg, i.v) partially or completely reversed all LP44-induced changes.

Interpretation of results

Spinal cord injury disrupts phasic activity of the EUS, resulting in decreased voiding efficiency and increased residual volume. 5-HT₇ receptor agonist LP44 induced a dose-dependent decrease in bladder capacity, with an increase in micturition volume and decrease in residual volume, resulting from improvement in voiding efficiency. It is mainly due to the partial restoration of the function of EUS, which relaxes during voiding, reducing the outlet obstruction.

Concluding message

5-HT₇ receptor agonist improves the bladder voiding contraction, and promotes periodic EUS activity, thereby improving voiding efficiency. In addition, this study adds to the growing evidence of the importance of the 5-HT₇ in the control of micturition reflex. Whether or not these results may have implications for the future treatment of voiding dysfunction in SCI patients remains to be studied.

Disclosures

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