

INVOLVEMENT OF 5-HT7 RECEPTORS IN DETRUSOR SPHINCTER DYSSNERGIA OF CHRONIC SPINAL CORD INJURY RATS

Hypothesis / aims of study

To examine the effects of 5-HT7 selective agonist, LP44 on micturition in chronic spinal cord injury (SCI) rats, and compare the SCI rats' 5-HT7 receptors expression in L6-S1 spinal cord with normal rats. Furthermore, to testify the hypothesis that 5-HT7 receptors mostly express in the neurons related to the neural pathway of external urethral sphincter activity through retrograde neural tracing by Pseudorabies virus (PRV).

Study design, materials and methods

Thirty female Sprague–Dawley rats underwent either sham operation (n=10) or spinal cord transection at T10 level (n=20). Six weeks after operation, half of the rats were used for functional experiments, where a 5-HT7 selective agonist, LP44, was given intrathecally. Continuous cystometry was taken after the rats anesthetized by urethane. The remaining rats were injected with PRV in external urethral sphincter and killed 3 days later for immunofluorescence.

Results

Intrathecally administered 5-HT7 receptors agonist LP44 showed no effect in sham-operated rats. In SCI rats, LP44 (0.003–0.1mg/kg) induced significant dose-dependent increases in micturition volume ($P<0.05$), significant dose-dependent decreases in residual volume ($P<0.05$), resulting in significant increases in voiding efficiency. CMG measurements showed a dose-dependent increase of the high-frequency oscillation (HFO) activity, evident as an increased number of small oscillation per voiding. 5-HT7 receptors antagonist SB-269970 (0.1 mg/kg) partially or completely reversed LP44-induced changes. 5-HT7 receptors were found in L6-S1 spinal cord segments with an accumulation in the ventral horn and onuf's nucleus in both control and experimental rats. There was a significant increase of 5-HT7 receptors expression in onuf's nucleus in SCI rats. Besides, neurons expressed 5-HT7 in onuf's nucleus simultaneously expressed PRV,.

Interpretation of results

HFOs seems to reflect external urethral sphincter (EUS) bursting activity during voiding. 5-HT7 receptor agonist can enhance HFO activity, thereby improving voiding efficiency in SCI rats. 5-HT7 receptors are present in rat L6-S1 spinal cord, and are significantly up-regulated in onuf's nucleus after SCI, meanwhile these neurons related to the external urethral sphincter activity.

Concluding message

Up-regulated 5-HT7 receptors in onuf's nucleus might involve the detrusor sphincter dyssnergia (DSD) after SCI in rats.

Disclosures

Funding: National natural science foundation of China Grant 30872568 **Clinical Trial:** No **Subjects:** ANIMAL **Species:** rat
Ethics Committee: the animal care and use committee of Shanghai Sixth People's Hospital