

Improvement of bladder and urethral dysfunction by the early intervention with anti-BDNF antibody after spinal cord injury in mice

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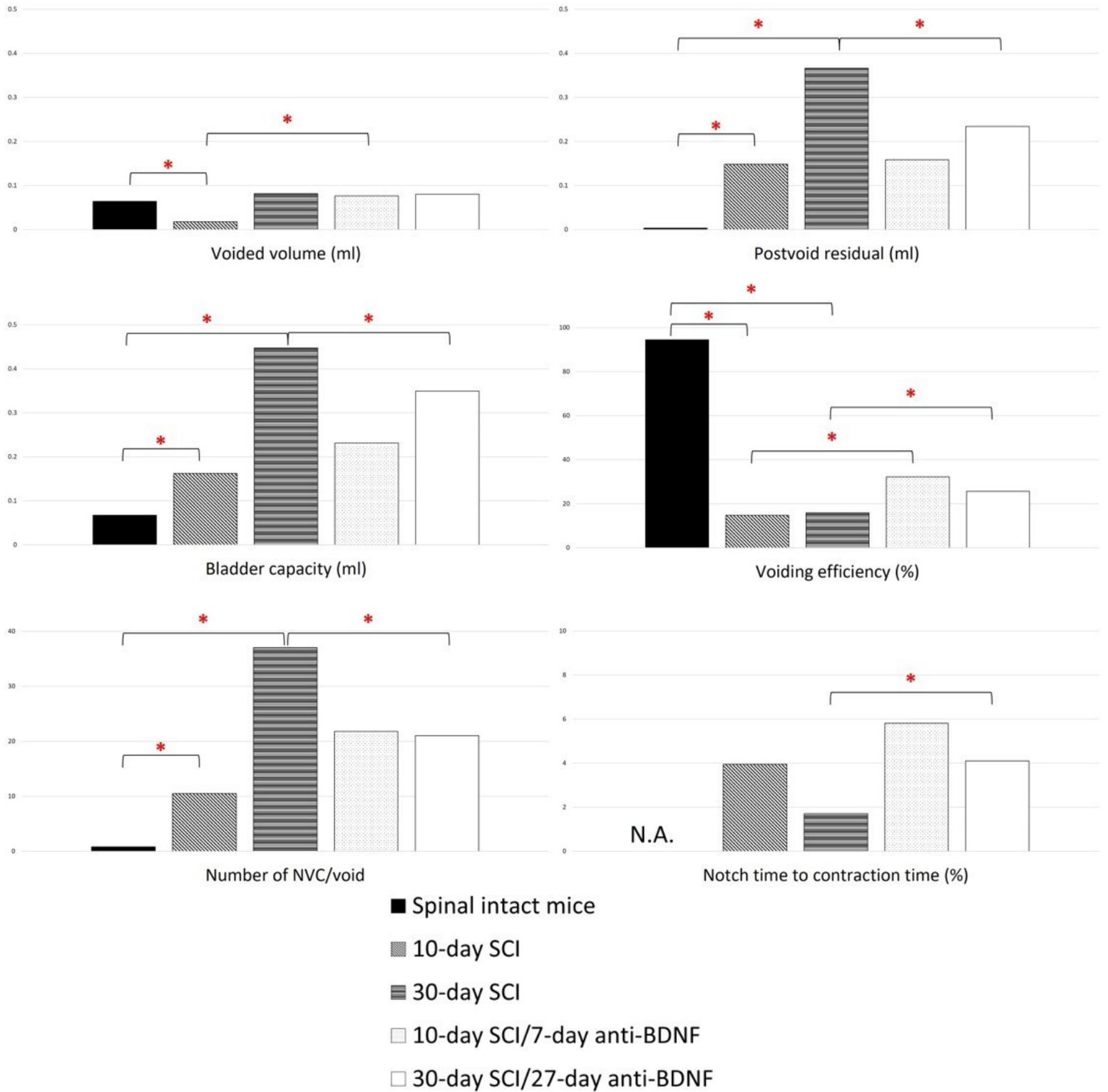
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Introduction & Objectives: We previously reported that, in chronic spinal cord injured mice, the short-term inhibition of BDNF improved voiding efficiency without changes in non-voiding contractions (NVC), and inhibited urethral sphincter hyperactivity detected by external urethral sphincter electromyograms, the reduction of which was coincided with 'notch' on cystometry traces during voiding. We therefore examined the time course of urodynamic changes and the effect of the long-term inhibition of BDNF from the early phase after spinal cord injury (SCI) in mice.

Materials & Methods: Using female C57BL/6N mice, their spinal cords were completely transected at level of Th8/9. Single-filling cystometry was performed under an awake condition at 10, 20 and 30 days after SCI. Bladder BDNF was measured by ELISA at 5, 10, 20 and 30 days after SCI. In a separate group of mice, osmotic pumps containing anti-BDNF antibody (10 µg/kg/h) were placed under the back skin at 3 days after SCI. Single-filling cystometry was then performed at 10 (7 days of administration) or 30 days (27 days of administration) after SCI.

Results: Compared to spinal intact mice, bladder mucosal BDNF was increased at each time point after SCI with the maximum level at 5 days after SCI. Voiding efficiency was lower at each point after SCI than that of spinal intact mice while voided volume was decreased only 10 days after SCI. Postvoid residual (PVR) and bladder capacity were increased at 20 and 30 days after SCI. The number of NVC was gradually increased with time (Figure). In 10-day SCI mice with 7-day inhibition of BDNF, voiding efficiency was improved by increasing voided volume, and the 'notch' duration to the voiding contraction time tended to be prolonged. In 30-day SCI mice with 27-day inhibition of BDNF, voiding efficiency was improved by decreasing PVR, the 'notch' duration to the voiding contraction time was significantly prolonged, and the number of NVC was significantly decreased (Figure).



Conclusions: Overexpression of bladder BDNF is associated with the deterioration of voiding efficiency with urethral hyperactivity (i.e. detrusor sphincter dyssynergia: DSD) after SCI. The early, long-term inhibition of BDNF improves voiding dysfunction due to DSD and is also effective to reduce the later-phase development of detrusor overactivity after SCI.