

CORRELATION OF STRUCTURAL AND FUNCTIONAL CHANGES IN THE ACUTE AND CHRONIC SPINAL CORD INJURED RAT BLADDER

Hypothesis / aims of study

Neurological insults including spinal cord injury (SCI) lead to disturbances in bladder function which include an acute areflexic phase followed by chronic bladder overactivity or underactivity. We previously investigated cellular changes in the SCI rat bladder, 5 weeks after injury and reported altered distribution of interstitial cells (IC), smooth muscle hypertrophy and patchy denervation (1). These changes were correlated with an underactive, hypercompliant phenotype (2).

The purpose of the present study was to investigate structural and functional changes in the SCI rat bladder at selected time points after injury.

Study design, materials and methods

Female Sprague Dawley rats underwent spinal cord transection at T8/T9. Animals underwent in vivo cystometry under anaesthesia by subcutaneous injection of urethane (1.2g/kg) at selected time-points post-SCI before being humanely sacrificed. Bladders were removed and processed for histology, immunofluorescence and confocal imaging. Histological and immunofluorescence studies were carried out on 4 tissue samples from at least 3 animals.

Results

Cystometry demonstrated a loss of voiding and non-voiding contractions in acute SCI bladders at 2h (N=5) and 24h (N=4). Overactivity later developed and was characterised by an increased frequency of voiding contractions from $0.43 \pm 0.1 \text{min}^{-1}$ (mean \pm SEM) in spinal-intact animals (N=5) to $1.4 \pm 0.64 \text{min}^{-1}$ (N=3; $p < 0.05$) at 4wk, and $1.84 \pm 0.33 \text{min}^{-1}$ (N=3; $p < 0.05$, ANOVA, post-hoc Dunnett's) at 8wk. Chronic SCI bladders also exhibited urinary retention and incomplete emptying.

Histological evaluation showed that initial loss of the urothelial layer in the acute phase was accompanied by inflammation throughout the bladder wall, which was repaired by 2wk post-injury. Notable smooth muscle hypertrophy occurred from 1wk.

Platelet-derived growth factor receptor alpha (PDGFR α)⁺-IC networks in the lamina propria were disrupted in the acute phase, but recovered in the later stages. PDGFR α ⁺-IC in the detrusor were disrupted as early as 24h with marked loss of cellular morphology. This was correlated with partial denervation. In the chronic phase, the morphology of detrusor IC did not return to normal. Interestingly, α -smooth muscle actin⁺-myofibroblasts which were not present in controls, were detected in the bladder wall at 1wk and 2 wk post-SCI.

Interpretation of results

The acute SCI bladder is associated with loss of voiding and non-voiding contractions along with initial disruption of lamina propria PDGFR α ⁺-IC networks. Cellular remodelling throughout the overactive chronic phase appears to restore lamina propria IC but the detrusor layer is typified with persistent hypertrophy, patchy denervation and disrupted IC.

Concluding message

Significant cellular remodelling of urothelium, smooth muscle, IC and nerves are correlated with the acute, areflexic and the chronic, overactive SCI-rat bladder.

References

1. Johnston L et al. 2012. J Cell Mol Med. 16(7):1533-43.
2. Young JS et al 2013. BJU Int. 111(2):355-61.

Disclosures

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