

**Spinal cord injury-induced neurogenic detrusor overactivity**

**Model's advantages:**

- The most commonly utilised and highly informative model of a central lesion with respect to lower urinary tract function
- used for the evaluation of drugs targeting **neurogenic detrusor overactivity** (NDO) but also overactive bladder whatever its etiology<sup>1,2</sup>
- useful to investigate the effect of mechanisms known to act on **C-fiber** afferents
- useful to investigate an effect on the **external urethral sphincter** activity

**Species:** rat

**Pathophysiological features:**

- Mimics the voiding patterns of patients with **neurogenic detrusor overactivity** due to spinal cord injury
- Display neurogenic detrusor overactivity characterized by non-voiding contractions during the filling phase with increased maximal micturition pressure and increased micturition duration.
- Reduced voiding efficiency and large residual urine volume associated with **detrusor-sphincter dyssynergia**
- Bladder hypertrophy
- Increase in bladder afferent nerve activity, in particular through C-fibers
- BBB score impairment altered locomotor activity (reduced BBB score)

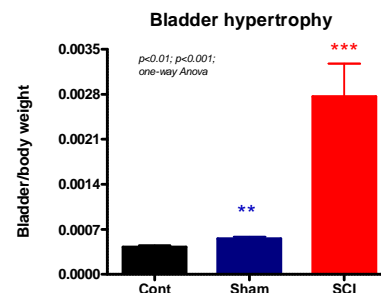
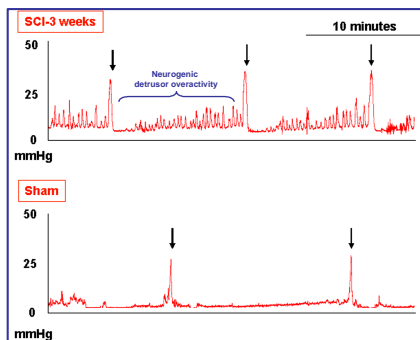


Figure 1: Representative cystometrograms in conscious 3 weeks SCI and sham rats. Arrows indicate the voiding contractions. Neurogenic detrusor overactivity occurred in the SCI rat but not in sham rats. (Pelvipharm, internal data)

**Summarized methodology:**

A T7-T8 laminectomy is performed and the spinal cord is cut between T7 and T8 vertebrae. A sterile gelform sponge is placed between the cut ends of the spinal cord. NDO progressively develops over time until 3-4 weeks where it is stabilized.

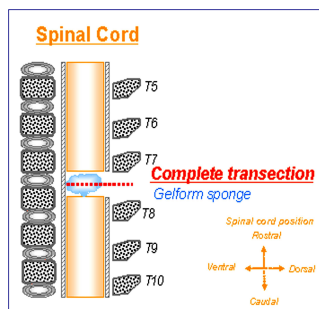


Figure 2: Complete transection between vertebral T7-T8

**Related Pelvipharm bibliography:**

Broqueres-You, D. et al. **Basic & Clinical Pharmacology & Toxicology**, 107 (Suppl. 1), 192 (WorldPharma 2010)  
 Behr-Roussel, D. et al. **J Urol** (2010) : 183(4),supl1:e391 (AUA, 2010)  
 Broqueres-You, D. et al. **J Urol** (2010) : 183(4),supl1:e76-e77 (AUA, 2010)  
 Behr-Roussel, D. et al. **Eur Urol Suppl** (2010) : 9(2):73 (EAU, 2010)  
 Broqueres-You, D. et al. **Eur Urol Suppl** (2010) : 9(2):112 (EAU, 2010)  
 Broqueres-You, D. et al. **Neurourol Urodyn** (2009) : 28(7):695 (ICS, 2009)  
 Broqueres-You, D. et al. **J Urol Abstract** (AUA, 2008) : 179(4) : 348-349

**NB:** Pelvipharm will gladly study the feasibility to fit this experimental model in order to meet its client's needs.

**Links to applicable experimental skills:**

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- **Administration routes / regimen**
- **Plasma / urine / tissue collection**
- **In vivo experiments – conscious animals**
  - \* Urodynamic evaluation (conscious)
  - \* Urine collection - Metabolic cages
  - \* Eye wipe test
  - \* Locomotor activity evaluation (BBB score)
- **In vivo experiments – anesthetized animals**
  - \* Bladder blood flow
  - \* Neural firing recording
- **Organ bath studies (EFS / Pharmacological studies)**
  - \* Animal tissues
  
- **Biochemistry (Plasma / Urine / Tissue)**
  - \* Spectrophotometric assays
  - \* Protein expression and activity
- **Histology**
  - \* Histomorphology
  - \* Histomorphometry
  - \* Oxydative fuorescence
- **Immunohistology / Confocal microscopy**
  - \* Protein expression – immunohistochemistry / immunofluorescence
  - \* Confocal microscopy
- **Neuro-anatomical tracing techniques**
- **Electrophysiology**