Spinal cord injury-induced neurogenic detrusor overactivity

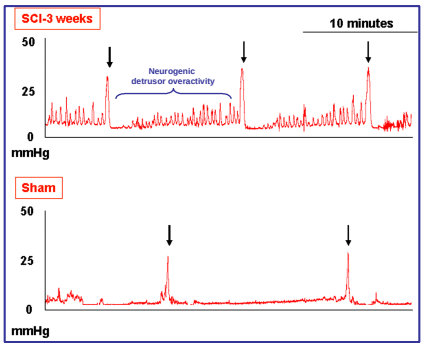
Model's advantages:

- 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 [1,2]
- 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)



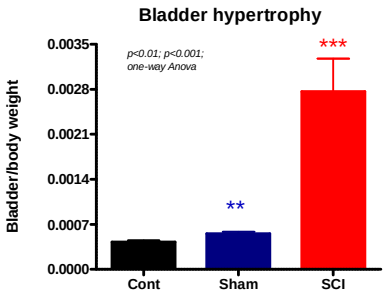


Figure 1: Representative cystometrograms in conscious 3 weeks SCI and sham rats. Arrows indicate the voiding contractions. Neurogenic detrusor overactivity occured in the SCI rat but not in sham rats. (Pelvipharm, internal data)

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.

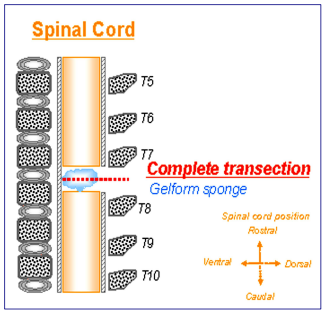


Figure 2: Complete transection between vertebral T7-T8

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:

- **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**