Acute cystitis induced by cyclophosphamide

A MODEL FOR INTERSTITIAL CYSTITIS / BLADDER PAINFUL SYNDROME (IC/BPS)

Model

Interstitial cystitis / bladder painful syndrome (IC/BPS) is a chronic inflammatory disease characterized by visceral pain and urinary symptoms such as urinary frequency.
IC/BPS is induced by a single injection of cyclophosphamide (CYP). This acute model is a rapid, reliable and widely used model to test therapeutic approaches on visceral pain, bladder inflammation and dysfunction.

Specie

- Rat

Interest

- This model recapitulates the 3 hallmark symptoms of IC/BPS (visceral pain, bladder inflammation and hyperactivity).
- Visceral pain and bladder function can be evaluated by non invasive techniques allowing repeated monitoring (from 1 to 24h).
- Visceral pain includes allodynia and hyperalgesia that can be independently analyzed.
- This model is validated by clinically relevant compounds: non-steroidal anti-inflammatory drugs (aspirin and ibuprofen) and opioid receptor agonist (morphine).

Model Description

- Visceral pain is assessed by von Frey testing using 8 filaments of increasing forces that are applied to the pelvic area.
- Bladder dysfunction is characterized by increase in micturition frequency and urinary leakage. Evaluation is performed in conscious animals by cystomanometry or metabolic cages.
- Bladder inflammation is characterized by structural changes of the bladder (weight, edema, permeability...), cells infiltration and mediators releases (MCP-1, IL-1β...).

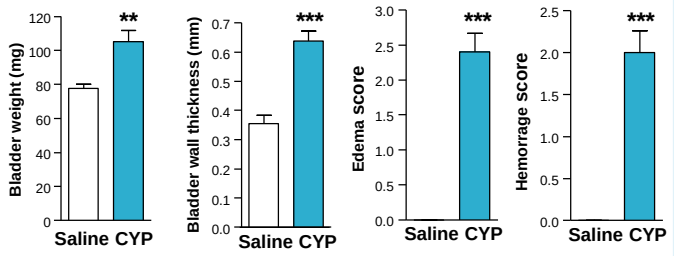
Parameters evaluated

- Pain: nociceptive threshold, scores and area under the curve (AUC) by plotting scores against von Frey forces
- Inflammation: macroscopic evaluation (weight, thickness, edema / hemorrhage scores), histological analysis (HE, CD45, uroplakin...), mediators dosage in urines, blood or tissue (ELISA, multiplex assays), urothelial and vascular permeability quantification (Evans blue)
- Function: bladder capacity, intercontraction intervals (ICI), micturition pressure and micturition behavior

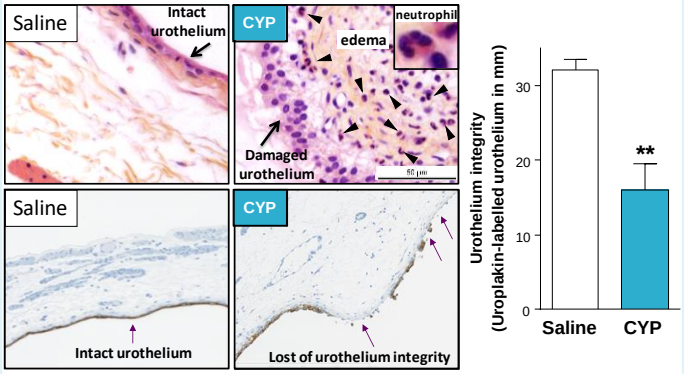
Reference

Auge *et al.*, Eur J Pharmacol. 707:32-40, 2013

CYP induces acute bladder inflammation



Bladder inflammatory macroscopic evaluation at 4h. ** P<0.01, *** P<0.001 (n=10)

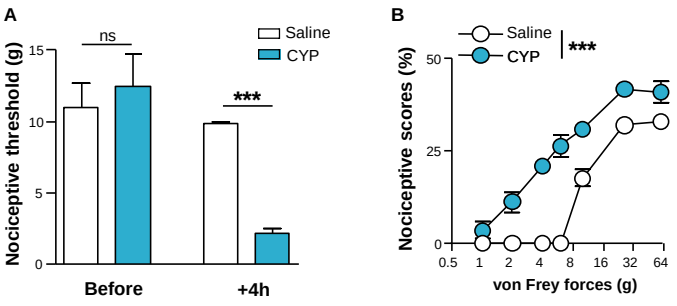


Top: representative HE staining at 4h. Arrowheads indicate neutrophils (Bar = 50 µm)

Bottom: uroplakin staining and quantification (graph) at 4h. Quantification was performed using digitized slides of the whole bladder. Results were expressed as uroplakin-labelled urothelium in mm.

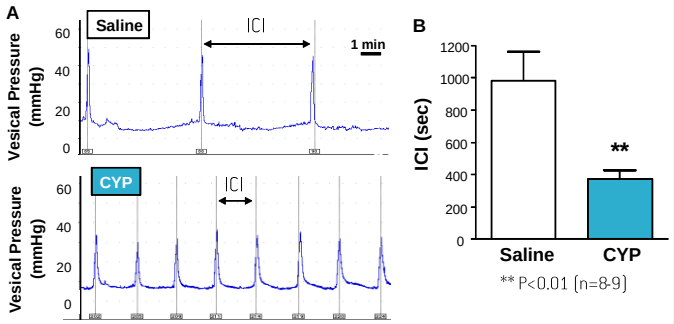
** P<0.01 (n=6-8)

CYP-induced acute visceral pain



(A) Nociceptive threshold and (B) nociceptive scores at 4h.
ns P>0.05, *** P<0.001 (n=10)

CYP induces bladder hyperactivity



(A) Representative cystometric recordings in conscious rat and (B) ICI quantification at 4h

** P<0.01 (n=8-9)