Chronic 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.
IC/BPS is induced by successive intraperitoneal injections of cyclophosphamide (CYP). Animals were observed up to 14 days after CYP first injection. This chronic model of inflammation-induced visceral pain and bladder dysfunction is reproducible and reliable to test therapeutic approaches for the treatment of IC/BPS.

Specie

Rat

Interest

- This chronic model recapitulates the 3 hallmark symptoms of IC/BPS (visceral pain, bladder inflammation and overactivity).
- Visceral pain and bladder function can be evaluated by non invasive techniques allowing repeated monitoring (from D1 to D14 in this model).
- As in clinic, severe visceral pain occurred whereas only sparse inflammation is observed (edema, focal urothelium damages and absence of massive infiltrate).
- Our chronic model showed persistent symptoms.
- This model allows curative or preventive therapy.
- This model is validated by clinically relevant compounds: non-steroidal anti-inflammatory drug (ibuprofen) and the gabapentin.

Model Description

- The pelvic sensitivity to mechanical stimuli is assessed using 8 von Frey filaments that are applied to the pelvic area.
- Bladder function is assessed in conscious animals by cystomanometry or metabolic cage.
- Tested compounds can be administered *via* various routes (i.v., i.p., s.c., p.o., intravesical).

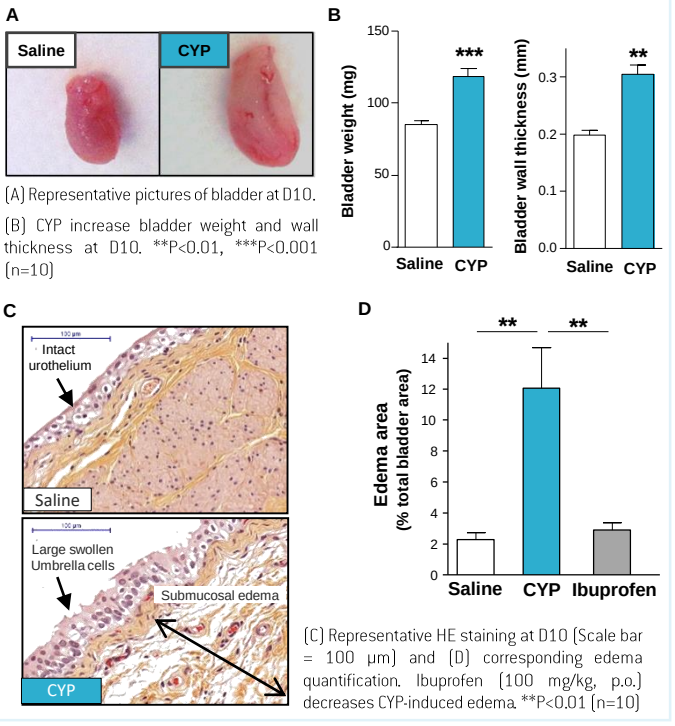
Parameters evaluated

- 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...), vascular permeability (Evans blue)
- Function: bladder capacity, intercontraction intervals (ICI), micturition pressure and micturition behavior

References

- Augé *et al.*, Front. Pharmacol. 11:1305. 2020
- Augé *et al.*, Front. Pain Res. 2:642706. 2021

CYP induces chronic bladder inflammation

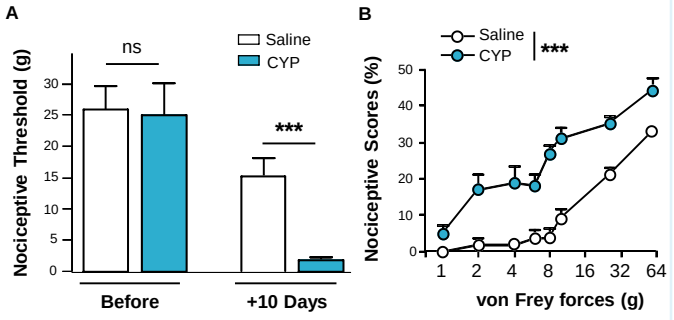


(A) Representative pictures of bladder at D10.

(B) CYP increase bladder weight and wall thickness at D10. **P<0.01, ***P<0.001 (n=10)

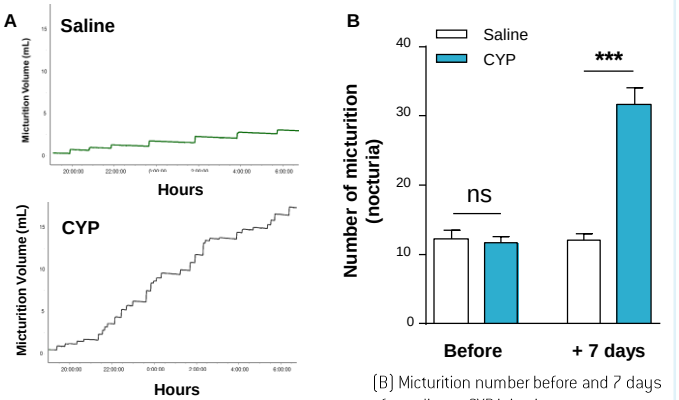
(C) Representative HE staining at D10 (Scale bar = 100 µm) and (D) corresponding edema quantification. Ibuprofen (100 mg/kg, p.o.) decreases CYP-induced edema. **P<0.01 (n=10)

CYP-induced chronic visceral pain



(A) Nociceptive threshold and (B) scores at D10. ns P>0.05, *** P<0.001 (n=11-12/group)

CYP induces chronic bladder hyperactivity



(A) Representative micturition profiles recorded during the night (metabolic cage) at D7.

(B) Micturition number before and 7 days after saline or CYP injection.

ns P>0.05, *** P<0.001 (n=9-10)