



VAGINAL DISTENSION (VD) AND PUDENDAL NERVES CRUSH (PNC) INDUCES URINARY INCONTINENCE

IN VIVO MODEL FOR STRESS URINARY INCONTINENCE

Model

- Urinary incontinence affects 25-45% of women. Approximately 50% of all incontinent women are classified as having stress urinary incontinence (SUI). The SUI pathology is multifactorial and appears to be in part due to anatomic changes in urethral support and dysfunction of the intrinsic sphincteric mechanism of the urethra.
- These conditions are responsible of involuntary loss of urine during any activity that causes abdominal straining.
- We developed a model of stress urinary incontinence by vaginal distension associated with pudendal nerves crush in female rats. Urinary incontinence was evaluated by measure of the leak point pressure (LPP).

Species

Rat

Interest

- This model allows to evaluate the effect of selected compounds on LPP test in incontinence model induced by bilateral PNC and vaginal distension.
- LPP test is a rapid and relevant preclinical model to mimics abdominal contraction leading to stress urinary incontinence.
- This model is suitable for evaluation of:
 - compounds acting on external urethral sphincter (EUS) such as re uptake inhibitors of norepinephrine and serotonin
 - cell therapy on restoration of injured nerves and muscles.

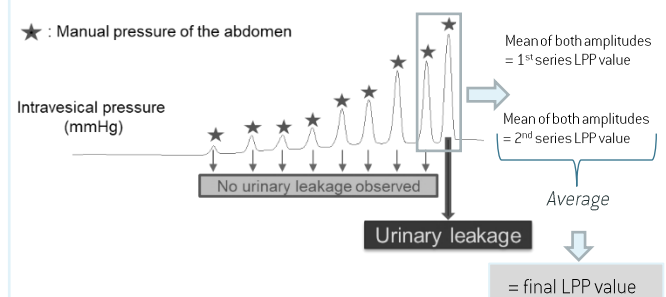
Model Description

- Pudendal nerves are crushed 30 sec bilaterally under isoflurane anesthesia. Then, a balloon is inserted into the vagina and inflated with 3 mL of saline for 4 hours. Vehicle is administered into the urethral wall after distension (2x50 µl). Sham groups underwent the same procedure without vaginal distention (*i.e.* 4 h anesthesia).
- 2 weeks after PNC and VD, animals are anesthetized with urethane (1.2 g/kg) and an intravesical catheter is inserted into the bladder through the dome for the evaluation of LPP.
- Bladder is first continuously infused with saline at the rate of 2 mL/h for bladder capacity determination.
- LPP test is then performed after filling bladder at around 30-50% of the bladder capacity. Successive and progressive manual abdominal pressures are applied until occurrence of urinary leakage. This procedure is performed twice.
- Rats are euthanized after LPP test.

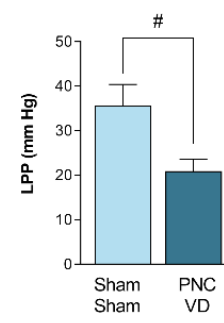
Parameters evaluated

- Leak point pressure (LPP; mmHg)
- Bladder capacity (BC; mL)
- Body weight (g)

Measurement of LPP in anesthetized rats



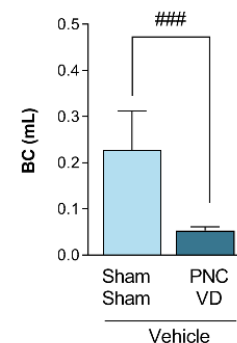
Effect of VD+PNC on LPP in anesthetized rats



Vehicle: 2x50 µL, peri-urethral, n=7-9, once

P<0.05, Mann-Whitney test

Effect of VD+PNC on BC in anesthetized rats



Vehicle: 2x50 µL, peri-urethral, n=7-9, once

P<0.001, Mann-Whitney test