



# Overactive bladder (OAB) in streptozotocin (STZ)-induced diabetic rats

## A MODEL OF DIABETIC BLADDER DYSFUNCTION

### Model

Diabetes mellitus is a metabolic disorder that results in a state of persistent hyperglycemia. This is most simply mediated by the autoimmune destruction of the insulin producing beta cells of the pancreas (type I diabetes).

Bladder dysfunction is one of the most important clinical features in poorly controlled diabetes mellitus. In fact, 43 to 85% of patients with type I diabetes have a wide variety of voiding complaints from overactive bladder (OAB) and urge incontinence to decreased bladder sensation and over flow incontinence.

We developed a model of OAB in streptozotocin (STZ)-induced type 1 diabetes mellitus in rats.

### Specie

Rats

### Interest

- This model is suitable for compounds acting on C-afferent fibers innervating bladder.
- This model is validated by clinically relevant compound mirabegron used in the clinic.
- Compounds that produce positive effects in this model include  $\beta_3$  adrenoceptor, glutamate receptor antagonists, COX inhibitors, prostacyclin receptor antagonists and P2X3 receptor antagonists.

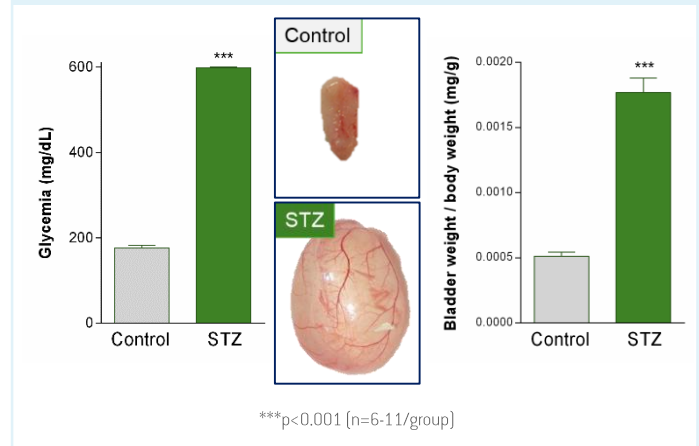
### Model Description

- STZ is injected intravenously at 50 mg/kg. Control rats are injected with STZ vehicle.
- Eight weeks after diabetes induction, an intravesical catheter was inserted into the dome of the bladder, under isoflurane anesthesia.
- Blood glucose concentration (glycaemia) is measured to assess diabetes induction.
- 2 days after surgery, cystomanometry is performed in conscious rats to assess bladder dysfunction.
- Test compounds can be administered via various routes (i.v., i.p., s.c., p.o.) in preventive or curative treatment.

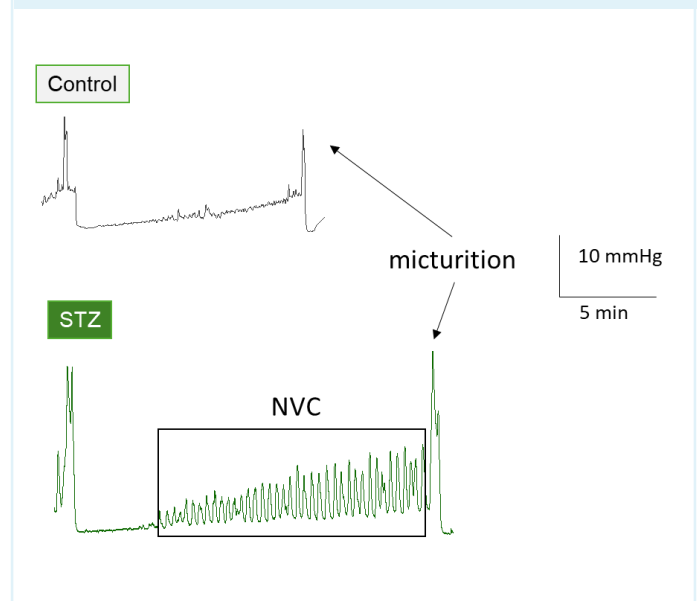
### Parameters evaluated

- Glycaemia (mg/dL)
- Bladder weight relative to body weight (mg/g)
- Bladder capacity (BC; mL)
- Amplitude of micturition (AM; mmHg)
- Amplitude of non-voiding contractions (NVC; mmHg)
- Frequency of NVC (nbr/min)

### STZ induces hyperglycaemia and bladder hypertrophy in rat



### Representative cystometric recording in STZ diabetic rats



### STZ diabetic rats exhibit bladder dysfunction (increase in bladder capacity as well as NVC amplitude and frequency)

