Functional Mapping of the Bladder Regulatory System: Communication between the Lower Urinary Tract and the Central Nervous System

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Introduction

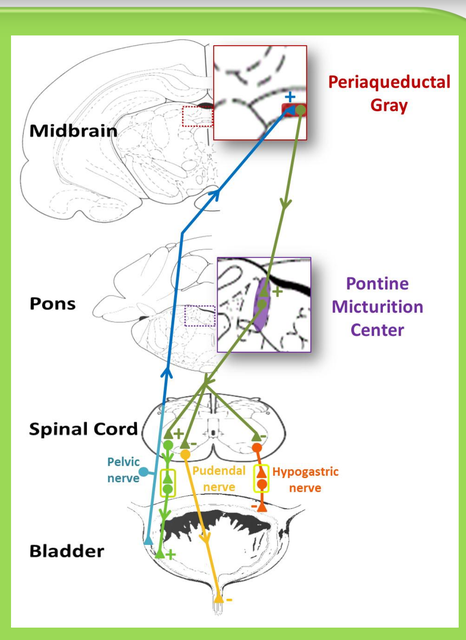
The literature on urinary symptoms describes an incidence about 16 % among people over 50 years that increases with age. In this context, it is necessary to understand the physiological and pathological processes involved in the micturition and the urinary continence for the development of new and more specific treatment options.

The functions of the lower urinary tract are controlled by complex pathways in the central nervous system that act like switching circuits to voluntarily or reflexly shift the activity of various pelvic organs (bladder, urethra, urethral sphincter, and pelvic floor muscles) from urine storage to voiding.

Incontinence is often related to an overactive bladder and the assumptions put forth to explain the increased activity of the detrusor muscle could be related to the deregulation of these efferent or afferent pathways.

The juxtacellular recording-labeling technique is a powerful tool achieving single-cell structure/function correlation studies in living animal. This non-invasive single-cell filling procedure allows to keep alive the extracellularly recorded and stimulated neuron and so to reveal the overall picture of the smallest neurons, including interneurons and to investigate the physiological and architectural bases of cell-cell communication.

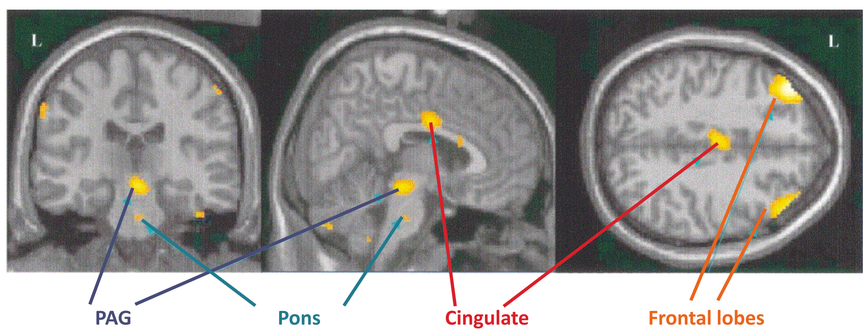
In this project, the juxtacellular recording – labelling technique in combination with *in vivo* cystometry in rat will be used to map the neural innervation in the periaqueductal gray (PAG) and to understand the sensory perception and the processing during bladder filling.



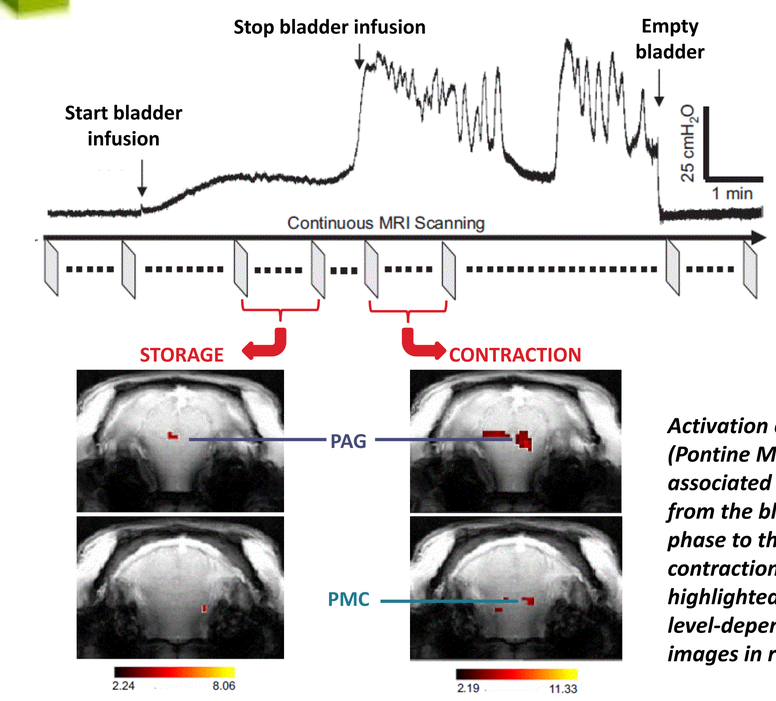
Periaqueductal Gray (PAG)

Neural control of the bladder in humans [1]

Increases in brain activity with increases in bladder volume in the PAG, pons, cingulate and frontal lobes highlighted by PET scan sessions in healthy men



Neural control of the bladder in rats [2]



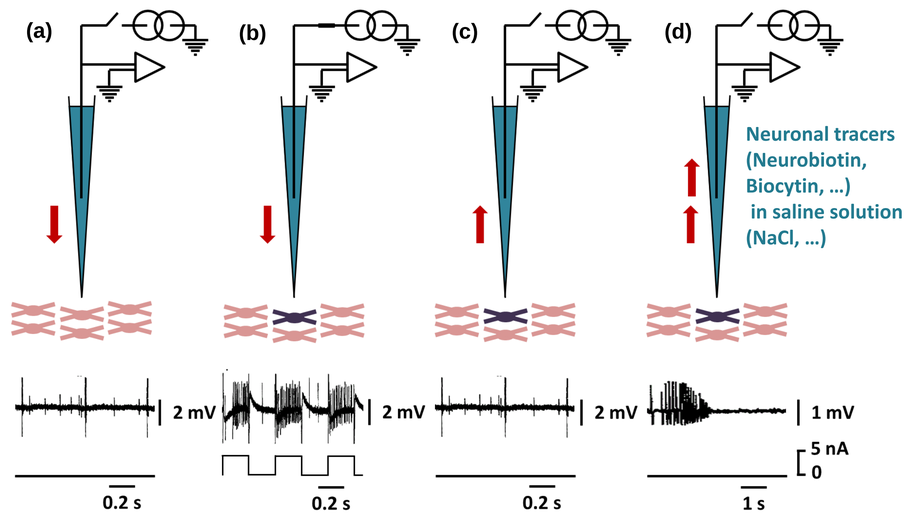
Activation of PAG and PMC (Pontine Micturition Center) associated with switching from the bladder storage phase to the bladder contraction phase highlighted by blood oxygen level-dependent (BOLD) images in rat.

- **Role in the transition between storage and voiding**
- **Integrator center of informations from both higher centers and bladder afferents**
- **Similar organization of the central control of micturition and urinary continence in humans and rats**

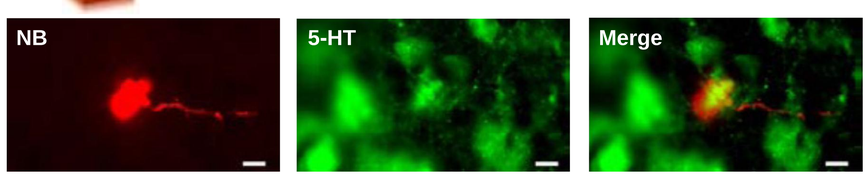
Juxtacellular recording & labeling

Procedure of juxtacellular filling

(a) Extracellular recording of a single nerve cell
(b) Juxtacellular recording, Nano-stimulation and Iontophoresis.
(c) Back to the extracellular configuration.
(d) Leaving the recorded/stimulate d neuron



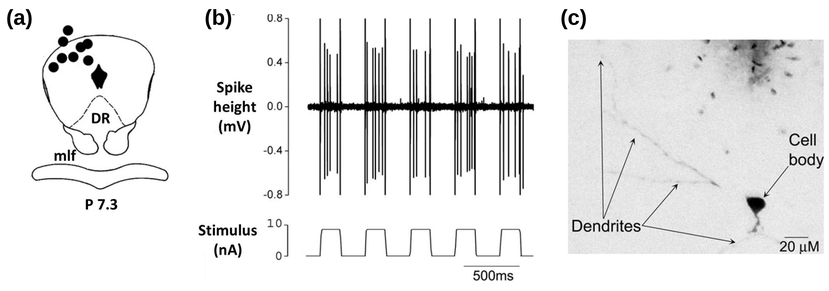
Combination of juxtacellular labeling with immunohistochemistry [3]



Photomicrographs of neurobiotin (NB) labelled dorsal raphe nucleus neuron immunopositive for 5-HT

Juxtacellular labeling of neuron in the PAG [4]

(a) Location of recorded neurons in the PAG
(b) Recording of a neuron after entrainment using a 200 ms on 200 ms off positive current of 9 nA
(c) Photomicrograph of a section containing the soma and some proximal dendrites of a neurobiotin-filled neuron

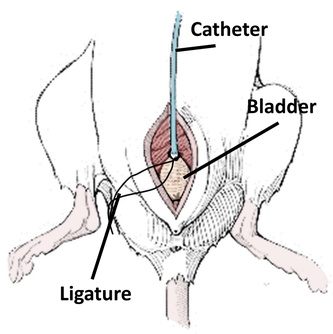


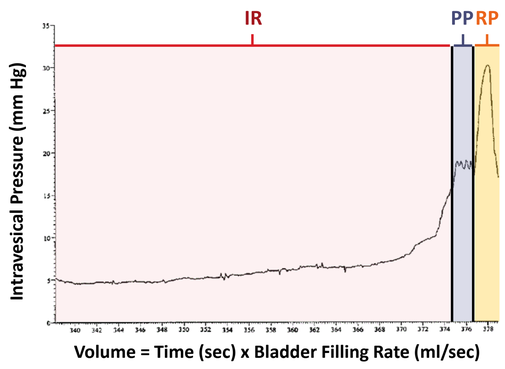
- **Highlighting of electrophysiological activity, location and type of neurons**

In vivo cystometry

Method of cystometry in rat [5]

- ✓ **Insertion of the catheter through the apex of the bladder dome and fixation with a suture**
- ✓ **Connection of the cannula to a warm saline reservoir put under pressure to infuse the bladder**
- ✓ **Connection of the tubing to a pressure transducer and amplifier to record the intravesical pressure**





Normal cystometric pattern in rat [6]

- ✓ **Initial rise of intravesical pressure (IR)**
  No emission of fluid
- ✓ **Plateau phase with series of phasic contraction (PP)**
  Several drops of fluid
- ✓ **Rapid fall of intraluminal pressure (RP)**

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Conclusion

- ❑ **Highlighting of the PAG innervation in rats**
- ❑ **Highlighting of neural networks between PAG and PMC, thalamus in rats**
- ❑ **Functional mapping of the PAG during rat bladder filling to understand the sensory perception and processing**