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PELVIC AND PENILE DORSAL NERVE STIMULATION EVOKE BLADDER PRESSURE CHANGES; THE EFFECT OF UNILATERAL HYPOGASTRIC NERVE TRANSECTION

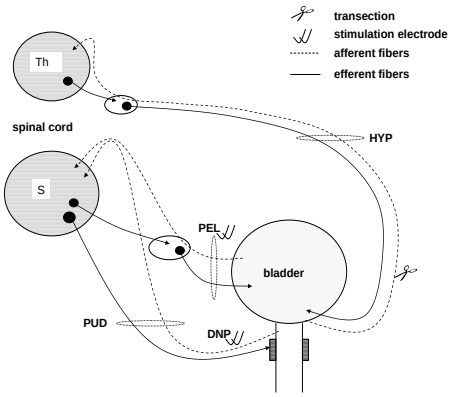
Hypothesis / aims of study

The lower urinary tract is innervated by the autonomic pelvic and hypogastric nerves and by the somatic pudendal nerve. During the filling/voiding cycle these nerves are active in a coordinated fashion. In patients suffering from detrusor overactivity, this coordination may be impaired, for instance due to damaged connections in the spinal cord. In order to restore normal function, neurostimulators are implanted to stimulate the sacral roots or the pudendal nerves. Stimulation of the dorsal nerve of the penis, an afferent branch of the pudendal nerve, has also been attempted. This alternative is less invasive and appears to have less side effects. In order to unravel the role of the hypogastric nerve, the rat dorsal nerve of the penis was stimulated during filling-evoked bladder contractions before and after unilateral transection of the hypogastric nerve. The pressure increase evoked by stimulation of the pelvic nerve was also quantified before and after transection of the hypogastric nerve. A better understanding of the detailed function of the neural network will contribute to optimizing neurostimulation protocols.

Study design, materials and methods

Intact male Wistar rats (454 ± 61 g) were anesthetized with urethane (1.2 g/kg, ip). The animals were kept warm on a heated pad. The abdomen was opened and the urinary bladder, the left side hypogastric (HYP), pelvic (PEL) and dorsal nerve of the penis (DNP) were dissected. A catheter was inserted into the bladder to both fill the bladder with saline at 0.11 ml/min using an infusion pump and to record pressure. PEL and DNP were mounted on bipolar platinum electrodes connected to stimulators. The abdominal cavity was filled with paraffin oil to prevent the tissue from drying out and for electrical isolation purposes. The bladder was filled to volumes ranging from 0.2 – 1.1 ml. Three stimulation protocols (P_{1-3}) were applied. In P_1 the PEL was stimulated (15Hz, 2-6V, 400μs bipolar pulses), in P_2 the PEL was first stimulated alone and subsequently in combination with DNP (respectively 15Hz, 4/6V, 400μs bipolar pulses and 3 or 30Hz, 4/6V, 400μs bipolar pulses) and in P_3 the DNP was stimulated during filling-evoked contractions (3 or 30Hz, 4V, 400μs bipolar pulses). All protocols were applied before and after unilateral transection of the HYP. Stimuli on/off and bladder pressure were read into a PC using Labview®. Data were analyzed using Matlab®. The Mann- Whitney-U test was used to compare means.

Fig. 1
Schematic drawing of the nerves innervating the lower urinary tract



Results

Stimulation of PEL (P_1) always resulted in a pressure rise reaching a plateau. The unilateral transection of HYP had no significant effect on that pressure increase. When DNP and PEL were stimulated simultaneously (P_2), pressure increased to a plateau which was not different from the plateau reached by stimulation of PEL only. In one animal, DNP+PEL and PEL stimulations were performed before and after transection of HYP (Fig. 2). No significant difference was found. Stimulation of DNP at 3 or 30Hz during filling-evoked contractions (P_3) resulted in a pressure decrease to base line (Fig. 3). The filling-evoked pressure increase divided by the DNP-stimulated decrease was the same before and after transection of HYP.

Table

Mean pressure change ± standard deviation before and after unilateral transection of the HYP

Protocol	Intact			After unilateral HYP transection			
	Pressure ↑ (cm H_2O)	**n**	**p**	**Pressure ↑ (cm H_2O)**	**n**	**p**	**p**
P_1	36 ± 9	31(5)		42 ± 9	26(5)	ns	
P_2 PEL only	44 ± 7	7(1)	}ns	43 ± 3	7(1)	ns	}ns
P_2 DNP+PEL	41 ± 7	6(1)		44 ± 3	6(1)	ns	
	Pressure↑/↓ (%)			**Pressure↑/↓ (%)**			
P_3 3Hz	96 ± 7	8(2)	}ns	95 ± 6	5(2)	ns	}ns
P_3 30Hz	93 ± 6	11(2)		97 ± 9	5(2)	ns	

P_1: stimulation of PEL
P_2: stimulation of PEL followed by stimulation of DNP+PEL in the same animal
P_3: (filling evoked pressure increase/DNP stimulated decrease)

HYP is hypogastric nerve, PEL is pelvic nerve, DNP is dorsal nerve of the penis, n is number of measurements (..) number of animals. The Mann-Whitney-U-test was used to compare means, p>0.05 is not significant (ns)

Fig. 2

P_2: Pressure increase during stimulation of DNP+PEL before and after transection of the HYP

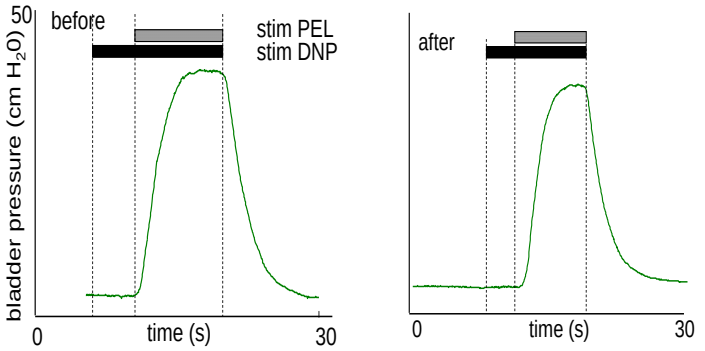
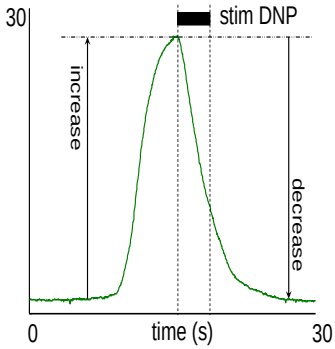


Fig. 3

P_3: Pressure increase during filling-evoked contraction and subsequent decrease during stimulation of DNP at 3Hz



Interpretation of results

- The bladder pressure increase caused by stimulation of the pelvic nerve did not depend on the bilateral integrity of the hypogastric nerve.
- Simultaneous stimulation of the pelvic nerve and the dorsal nerve of the penis caused the same pressure increase as stimulation of the pelvic nerve only. This was not affected by unilateral transection of the hypogastric nerve.
- Stimulation of the dorsal nerve of the penis at 3 or 30Hz during a filling-evoked bladder contraction caused a decrease in pressure to base line. This inhibition was not affected by unilateral transection of the hypogastric nerve.

Concluding message

Unilateral transection of the hypogastric nerve does not change pelvic nerve evoked bladder contractions nor the inhibition of filling-evoked contractions by stimulation of the dorsal nerve of the penis.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Approval for the animal experiments was obtained from the local Dier Experiment Commissie (Animal Experiment Committee)**