

A RAT MODEL FOR THE STUDY OF THE EFFECT OF TIBIAL NERVE STIMULATION ON AFFERENT NERVE ACTIVITY

Hypothesis / aims of study

The Overactive Bladder (OAB) is a symptom based syndrome, one symptom being “urgency”, often associated with increased bladder afferent sensation. Tibial Nerve Stimulation (TNS) has been advocated as a clinical treatment for OAB, although the underlying working mechanism is largely ambiguous. Only a handful of animal studies have been done to understand the basic science behind TNS. The aim of our study was to investigate the post stimulation effect of TNS on bladder afferent activity in an acetic acid (AA) rat model of OAB.

Study design, materials and methods

Experimental procedures

Male Wistar rats (n=4, 425 ± 52g) were anaesthetized with urethane (1 g/kg, i.p.). An abdominal incision was made to expose the bladder and the nerves. Afferent nerve activity was recorded by mounting one of the postganglionic pelvic nerve branches (crushed between major pelvic ganglion and electrode, to eliminate efferent nerve signals) on a bipolar electrode. A 23G needle was inserted at the top of the bladder for filling (0.06 ml/min) and measurement of bladder pressure (p_{ves}). p_{ves} and nerve activity (amplified and filtered) were both sampled at 25 kHz and recorded for 900s and 300s respectively. The tibial nerve was exposed through an incision on the medial side of the right hind limb and a bipolar cuff electrode was positioned around it.

Bladder filling and stimulation protocol

Step 1: Initially, the bladder was filled 2-3 times with saline until a voiding contraction occurred, to determine the control bladder capacity. Next, the bladder was irritated (to induce bladder overactivity) by repeatedly filling it with 0.5 % Acetic Acid (AA).

Step 2: The Bladder was emptied and the tibial nerve was stimulated for 30 min. with biphasic rectangular pulses of frequency =5 Hz, width = 200 μ s and intensity 2 to 3 times the threshold (T) to induce toe movement.

Step 3: Next a few measurements with AA infusion were done without stimulation to study the post stimulation effect of TNS, with the first measurement done ~15 min. after the end of stimulation.

Results

In four rats AA instillation reduced the mean bladder capacity (filled volume) and the threshold pressure (maximum pressure before a voiding contraction) by 3% and 15% respectively as compared to the control saline measurements (Table 1). 30-min of TNS (with amplitude 2–3 times the threshold intensity) with the bladder empty increased the bladder capacity and the threshold pressure by 23% and 15% respectively of the pre-stimulation level. Afferent activity was measured in 1 of the 4 rats and it was found to increase by 8% after AA instillation. 30-min of TNS decreased the afferent activity by 4% in the post stimulation measurements as compared to the pre-stimulation AA measurements (Table 1).

Interpretation of results

In our preliminary results, in a small sample of 4 rats, TNS showed a post-stimulation effect in form of increased bladder capacity and threshold pressure. However, there was no change in the post-stimulation afferent activity in the one rat in which it was measured. In cats an increased bladder capacity after a 30 min. TNS was found [1]. In a STEP (Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation) study, a monthly 30 min. percutaneous TNS was found to be effective as a long-term treatment for OAB patients [2]. These studies indicate that similar mechanisms of action for post-TNS inhibition might exist in different species.

Concluding message

Increased sensitivity of C fibers has been reported to play an important role in the pathology of the overactive bladder syndrome [3]. All previous animal studies have focussed only on the urodynamic effects of TNS, which does not provide an explanation of its working mechanism. Our animal model of TNS including afferent nerve activity along with urodynamic signals will be useful to reveal the underlying mechanism behind tibial nerve stimulation.

Parameter	Control (saline)	Prestimulation (Acetic acid)	Poststimulation (Acetic Acid)
Bladder capacity (filled volume, ml)	0.36 ± 0.26 (n=9)	0.35 ± 0.22 (n=11)	0.46 ± 0.26 (n=13)
Pressure before void, p_{thres} (cmH ₂ O)	33 ± 5 (n=9)	28 ± 5 (n=11)	33 ± 5 (n=13)
Afferent activity (μ V)	0.24 ± 0.01 (n=2)	0.26 ± 0.02 (n=3)	0.25 ± 0.01 (n=2)

Table 1: mean ± SD of the estimated parameters. n=total number of measurements.

References

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Disclosures

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