522

Su X[1], Nickles A[1], Nelson D[1]
1. *Medtronic*

INHIBITION OF THE BLADDER RHYTHMIC CONTRACTION BY STIMULATION OF THE DORSAL NERVE OF THE CLITORIS IN RATS

Hypothesis / aims of study

Stimulation of the dorsal nerve of the penis/clitoris to inhibit bladder contractions has been reported in cat and humans. We have quantified the parameter effects of electrical stimulation of the dorsal nerve of the clitoris (DNC) using the rhythmic bladder contraction model in the rat.

Study design, materials and methods

In anesthetized female rats (urethane, i.p. 1.2g/kg), a wire electrode was placed under the DNC bilaterally and sealed with Kwik-Cast Sealant (WPI). A cannula was placed into the bladder via the urethra and the urethra was ligated to ensure an isovolumetric bladder. The cannula was linked with a pressure transducer (ADI MLT844D), and the signal was amplified through a DC amplifier (ADI, ML228). Saline infusion (50 microliter per min followed by 10 microliter per min) induced rhythmic bladder contractions. Two needle electrodes were inserted into the external anal sphincter through the skin just outside the anocutaneous junction. Action potentials of myoelectric activities (EMG) evoked by electrical stimulation of the DNC were initially amplified through a low-noise alternating current (AC) differential amplifier (ADInstrument; EC4-400) and displayed in a storage oscilloscopes (DPO4034, Tektronix).

Results

Electrical stimulation of the DNC evoked a reflex anal sphincter contraction with EMG latency of 14 (± 2) ms; stimulation currents were adjusted for each animal as a function of anal sphincter EMG threshold (T). The mean threshold was 1.04 ± 0.06 mA (n=43). Stimulation using 0.8 fold threshold (0.8*T) pulses (0.1 ms pulse-width) for 10 minutes at different frequencies (0.01, 0.1, 1, 10, 50, 100 and 500 Hz) was tested on the isovolumetric rhythmic contractions. Only 10 Hz stimulation significantly inhibited or decreased frequency of rhythmic bladder contractions. Neurostimulation decreased the frequency of contractions during treatment to 42 (± 13)% of controls (n=7, vs. control, n=9, $p<0.05$, two-way ANOVA). Stimulation did not significantly alter bladder contraction amplitude. Inhibitory effects of electrical stimulation (10 Hz) were dependent upon current intensity. Stimulation intensities of 0.2*T and 0.4*T were ineffective for reducing contraction frequency while 1*T and 2*T caused significant inhibition on frequency of bladder contractions to 56 (± 16)% of controls (n=8) and 4 (± 2)% of controls (n=5), respectively ($p<0.05$, two-way ANOVA).

Interpretation of results

Electrical stimulation of DNC attenuated the frequency of urinary bladder contractions in the rat with a stimulation frequency of 10 Hz. Attenuation of the bladder contraction frequency was stronger with increases in the current intensity. Compared with responses to spinal nerve stimulation (accompanying abstract), the absolute currents required to reduce rhythmic bladder contractions using DNC stimulation appear to be higher (0.18 mA for spinal nerve stimulation and 0.89 mA for DNC using 10Hz stimulation). The slower onset responses to threshold level spinal nerve stimulation were not observed during DNC stimulation. This result is consistent with the hypothesis that different mechanisms/nerve pathways may underlie the bladder quieting responses to these different stimulation sites.

Concluding message

Results from this study using the rat rhythmic bladder model demonstrate a significant effect of DNC stimulation in reducing the micturition reflex. It will be important for future studies to further elucidate the responses to DNC stimulation and compare the relative responsiveness to other nerve targets as potential treatments for overactive bladder.

Specify source of funding or grant	**Medtronic research funding**
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	**The Institutional Animal Care and Use Committee of Medtronic, Minneapolis, MN.**