

INHIBITION OF BLADDER CONTRACTIONS BY ELECTRICAL STIMULATION OF THE TIBIAL NERVE

Hypothesis / aims of study

Both spinal nerve (1) and dorsal nerve of the clitoris (2) stimulation have been shown to modulate bladder activities in a rat model of the bladder rhythmic contraction (BRC). In this study we use the BRC model to characterize the effect of tibial nerve stimulation on bladder micturition functions. Stimulation parameter ranges of frequency (1-50 Hz) and intensity (1-4.7 fold relative to motor threshold) were tested.

Study design, materials and methods

In anesthetized female rats (urethane, i.p. 1.2g/kg, n=43), a wire electrode was placed under the tibial nerves 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 urethral cannula was linked with a pressure transducer, and the signal was amplified through a DC amplifier. Saline infusion induced rhythmic bladder contractions.

Results

Electrical stimulation of tibial nerves evoked hind-toe twitches and leg muscle contractions; stimulation currents were adjusted for each animal as a function of the motor threshold (T_{mot}). The mean T_{mot} was 0.16 ± 0.02 mA (n=43).

There was no significant change in isovolumetric bladder contraction during 45 min recording when no electrical stimulation was applied. Stimulation of tibial nerves using 3*T_{mot}, 10 Hz for 10 min either abolished the contractions or reduced contraction frequency during the time of electrical stimulation. The inhibitory effect of stimulation is frequency-dependent (Figure 1A); 10 Hz stimulation produced the strongest inhibition while 1, 20 and 50 Hz stimulation produced smaller or no attenuation of the BRC.

Inhibitory effects of electrical stimulation were also dependent upon current intensity. Stimulation intensities of T_{mot}, 2*T_{mot} and 0.6 mA, which was equivalent to 4.7*T_{mot}, were ineffective for reducing contraction frequency while 3*T_{mot} and 4*T_{mot} using 10 Hz significantly decreased the frequency of rhythmic bladder contractions to 23 ± 13% (mean, SEM, n=6) and 55 ± 13% (n=7), of controls, respectively (P<0.05, Student's t-test, vs control at 108% ± 9%, n=10). 3*T_{mot} stimulation produced a stronger inhibition of bladder contractions than 4*T_{mot} (Figure 1B).

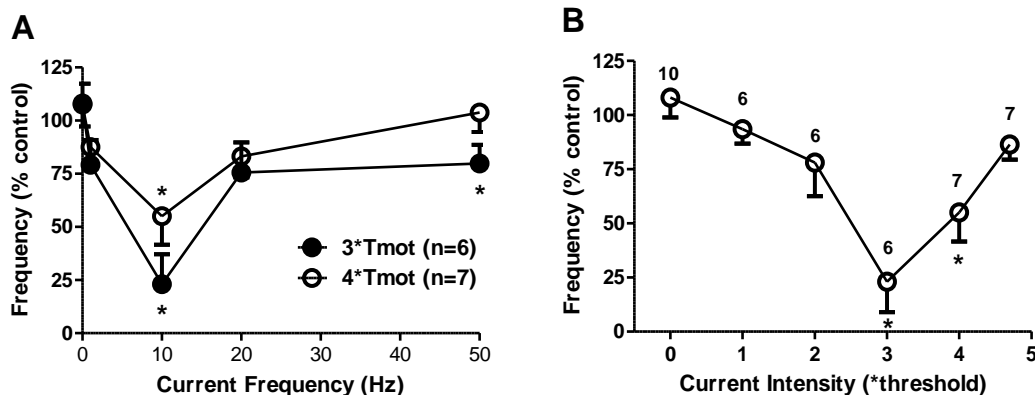


Figure 1. Current frequency- (A) and intensity- (B) dependent inhibition of the bladder rhythmic contraction by tibial nerve stimulation for 10 min. * P<0.05, vs control, Student's t-test. Animal numbers are shown above each symbol (B).

Interpretation of results

In the rat BRC model, electrical stimulation of tibial nerves attenuated the frequency of urinary bladder contractions in a frequency and intensity dependent manner. 10 Hz and 3 fold motor threshold intensity produce the strongest inhibition of bladder contractions. Increasing or decreasing of frequency or intensity produces less or no inhibition on bladder contractions.

Compared with stimulation of the spinal nerve (1) and the dorsal nerve of the clitoris (2), tibial nerve stimulation causes similar frequency-dependent bladder quieting effects: 10 Hz appears to be the optimal frequency of stimulation for all three nerve targets. Tibial nerve stimulation, however, is associated with very different intensity-dependence as bladder quieting effects of tibial nerve stimulation are directly dependent on relative intensity for stimulations smaller than 3*T_{mot}. Above 3*T_{mot} intensity, increasing intensity produces smaller bladder quieting responses. This "U-shaped" intensity-dependence differs from both spinal nerve stimulation and dorsal genital nerve stimulation which produce stronger inhibitory effects with increasing stimulation intensity.

The unique intensity-dependent effect of tibial nerve stimulation is supported by a study from Morrison and colleagues (3). They reported that stimulation of myelinated A afferent fibers of the tibial nerve elicited a strong reflex inhibition of efferent discharges in parasympathetic activity while stimulation of unmyelinated C afferent fibers with higher intensities produced both strong reflex inhibition and simultaneous excitation of pelvic efferents. Thus the final response of the bladder to tibial nerve stimulation may depend upon a balance of excitatory and inhibitory actions of stimulation. The maximal inhibitory effect of bladder contraction to 3* T_{mot} intensity of tibial nerve stimulation in this study may be due to the dominance of inhibitory parasympathetic activities over excitation caused by this optimal stimulation intensity.

Concluding message

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

References

1. Su X, Nickles A, Nelson, DE. Interstim® therapy in a rat model of rhythmic bladder contraction. ICS Annual Meeting, 2010a.
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3. Morrison JF, Sato A, Sato Y, Suzuki A. Excitatory and inhibitory A- and C-reflexes in pelvic parasympathetic afferent nerves elicited by single shock to A and C afferent fibers of perineal and limb somatic nerves in anesthetized rats. Neuroscience Letters 12: 25-28,1996.

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