Electrical Stimulation of Somatic Afferent Nerves in the Foot Increases Bladder Capacity in Healthy Human Subjects

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Purpose: We determined whether electrical stimulation of somatic afferent nerves in the foot could delay bladder filling sensations and increase bladder capacity in healthy humans without overactive bladder.

Materials and Methods: Eight subjects underwent 90-minute foot stimulation using skin surface electrodes connected to a transcutaneous electrical nerve stimulator. The electrodes were attached to the bottom of the foot. Subjects completed a 3-day voiding diary, during which foot stimulation was applied on day 2. Stimulation parameters were pulse frequency 5 Hz, rectangular waveform pulse width 0.2 milliseconds and intensity 2 to 6 times the minimal stimulation current necessary to induce toe twitch. Stimulation intensity was set by each subject to a maximal level without causing discomfort. Subjects were provided with 500 to 1,000 ml of water to drink during stimulation.

Results: Average ± SE volume per void was 350 ± 22 ml during the 24 hours before foot stimulation. This voided volume increased to a mean of 547 ± 52 ml for up to 5 hours after stimulation ($p < 0.01$). Average voided volume returned to 363 ± 21 ml within 36 hours after stimulation. There were no adverse events.

Conclusions: Foot stimulation can delay bladder filling sensations and significantly increase bladder capacity in healthy humans without overactive bladder. Although the study group was small, our results support moving forward with clinical trials of foot neuromodulation in patients with overactive bladder.

Key Words: urinary bladder; neurons, afferent; electrical stimulation; foot; urination

Abbreviations and Acronyms

OAB = overactive bladder

T = stimulation intensity threshold

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Study received University of Pittsburgh institutional review board approval.

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OVERACTIVE bladder is a syndrome characterized by urinary urgency with or without urge incontinence, often with frequency and nocturia.[1] Patients with OAB have significantly impaired quality of life.[2] First line therapy involves behavioral treatments such as fluid management, pelvic floor muscle physical therapy and bladder training.[3] Pharmacotherapy is offered concomitantly or subsequently if behavioral strategies fail. Antimuscarinics are the most common drugs used for OAB.[4] However, because drug therapy often has low efficacy and significant adverse effects, 70% of patients discontinue therapy within the first year of treatment.[4]

Food and Drug Administration approved treatment in patients in whom behavioral and antimuscarinic therapies fail include intradetrusor injection of onabotulinumtoxinA, or

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sacral or tibial neuromodulation. OnabotulinumtoxinA requires repeat injections every 6 to 12 months and results in adverse events such as urinary tract infection and urinary retention.[5,6] Sacral neuromodulation is invasive, requiring surgery to implant the electrodes and the neurostimulator.[7] Furthermore, the costs associated with sacral neuromodulation limit this option to some patients with OAB. Tibial neuromodulation is a minimally invasive, office based procedure that involves inserting a needle electrode near the ankle to stimulate the tibial nerve. The tibial nerve is stimulated for 30 minutes each week for 12 consecutive weeks, followed by 1 stimulation per month to maintain efficacy.[8] Although tibial neuromodulation is as efficacious as antimuscarinic drugs and has no major side effects,[8] the inconvenience of frequent office visits can be prohibitive for elderly as well as employed patients. Thus, a noninvasive, convenient OAB treatment with no major adverse effects would be attractive to many patients.

Our previous studies in cats demonstrated that transcutaneous electrical stimulation of somatic afferent nerves in the foot using skin surface electrodes could inhibit reflex micturition and significantly increase bladder capacity.[9,10] Foot stimulation is noninvasive and can be performed conveniently at home without major adverse events. It could be an attractive treatment for a large number of patients with OAB if proved to be effective. However, to our knowledge the effect of foot stimulation on bladder sensation in human subjects is currently unknown. We determined whether foot stimulation could delay bladder filling sensations and increase bladder capacity in healthy humans without OAB.

MATERIALS AND METHODS

This study was approved by the University of Pittsburgh institutional review board. Foot stimulation was tested in 5 males and 3 females 25 to 60 years old who were healthy and without OAB (see table). Subjects were instructed to record daytime voided volumes during a 3-day period without restriction on daily food and water intake. They were also instructed to void in response to the usual bladder sensations and note any void that was withheld or induced early due to unexpected situations. Voiding volumes that resulted from unexpected situations were excluded from study.

Daytime volume per void before and after 90-minute foot stimulation

Subject—Sex—Age No.	Mean ± SE Vol/Void (ml) 24 Hrs Before	About 5 Hrs After (No. voids/hrs:mins)	About 36 Hrs After
1—M—46	368 ± 63	667 ± 106 (3/1:50)	465 ± 69
2—M—49	436 ± 25	755 ± 33 (3/2:50)	388 ± 18
3—F—41	206 ± 26	200 ± 0 (2/4:45)	175 ± 28
4—M—40	406 ± 71	577 ± 15 (3/5:00)	469 ± 55
5—M—25	444 ± 26	600 ± 25 (2)*	368 ± 30
6—F—48	173 ± 11	195 ± 15 (2/1:30)	238 ± 19
7—M—47	323 ± 54	530 ± 80 (2/2:10)	263 ± 26
8—F—60	538 ± 78	800 ± 0 (1/1:35)	581 ± 74

* One 30 minutes into and another 10 minutes after stimulation.

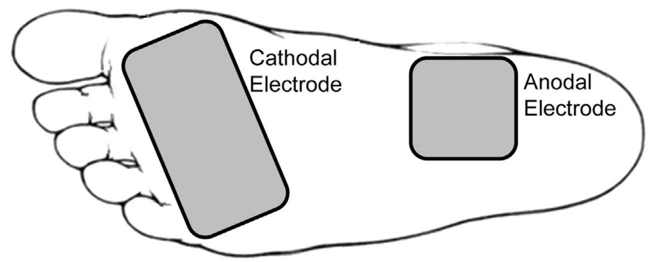

Figure 1. Sites on right foot where 2 pad electrodes were placed to stimulate somatic afferent nerves of foot.

Foot stimulation was applied for 90 minutes in the morning (10:00 to 11:30 a.m.) on day 2 with the subject sitting. During stimulation the subject was asked to drink 1 to 2 bottles of water (500 to 1,000 ml) so that a void could occur soon after stimulation. Two skin surface electrodes (LGMedSupply, Cherry Hill, New Jersey) were attached to the bottom of the foot. A large cathodal electrode (2 × 3.5 inches) was placed on the front of the foot to cover as much skin area as possible and a small anodal electrode (2 × 2 inches) was placed between the inner foot arch and the heel (fig. 1). The electrodes were connected to an LG TEC Elite™ transcutaneous electrical nerve stimulator, which provided constant current, rectangular pulses of 5 Hz frequency and 0.2 millisecond pulse width. The subject controlled the stimulator to determine the minimal current needed to induce a toe twitch. Stimulation intensity was then increased to the maximal level (25 to 60 mA) comfortable for the subject for the entire 90-minute stimulation, which ranged between 2 to 6 times the minimal intensity necessary to induce a toe twitch.

Volume per void was averaged among subjects during 3 periods, including 1) 24 hours before foot stimulation, 2) up to 5 hours after stimulation and 3) up to 36 hours after stimulation. The second period always included the first void after stimulation. However, if voided volumes remained increased in the following 1 to 2 voids, they were also included in the second period (see table). Therefore, the second period was variable, ranging up to 5 hours (see table). The third time period included voids up to 36 hours after stimulation, excluding voids counted in the second time period. One-way ANOVA followed by the Dunnett multiple comparison was used to detect statistically significant differences ($p < 0.05$) between voided volumes before and after stimulation.

RESULTS

Average ± SE volume per void was 350 ± 22 ml during the 24 hours before foot stimulation, which increased to 547 ± 52 ml for up to 5 hours after stimulation ($p < 0.01$, see table and fig. 2). Average