Abstract

Individuals with spinal cord injury or neurological disorders may develop involuntary bladder contraction at low volumes (bladder hyper-reflexia), which can lead to significant health problems. Current devices can eliminate nascent contractions through continuous stimulation of inhibitory pathways. The objective of this study was to determine whether conditional stimulation, with stimulation delivered only at the onset of nascent bladder contractions, allows the bladder to fill to greater volume before continence is lost than continuous stimulation. The pudendal nerve electroneurogram (PNT ENG) was used to detect bladder contractions and as the input to an event-triggered control system that regulated inhibitory stimulation to maintain continence. Conditional inhibitory stimulation controlled by the PNT ENG allowed the bladder to fill to greater volume before continence was lost than either continuous stimulation or no stimulation. The event-triggered control system had a 67% reduction in stimulation time as compared to continuous stimulation. These results support the use of an event-triggered control system to maintain urinary continence.

1. INTRODUCTION

The goal of this project is to develop a neural prosthesis to restore urinary continence in individuals with spinal cord injury or other neurological disorders. The objective of this study was to determine whether conditional stimulation, with stimulation delivered only when the bladder was contracting, enabled the bladder to fill to a larger volume than continuous inhibitory stimulation.

The lower urinary tract has two main functions: the accumulation of urine (continence) and the elimination of urine at an appropriate time (micturition). Neurological disease or spinal cord injury (SCI) can result in loss of voluntary control of bladder evacuation and bladder hyper-reflexia. Bladder hyper-reflexia is the involuntary reflex contraction of the bladder at small fluid volumes, and can result in loss of continence and/or high bladder pressure during bladder-urethral sphincter dyssynergia [1]. During dyssynergia the bladder and the urethral sphincter co-contract preventing or inhibiting the flow of urine down the urethra while increasing the bladder pressure. Loss of voluntary control, hyper-reflexia, and dyssynergia can result in long term renal damage, frequent urinary tract infections, and infections of the kidneys [2].

Electrical stimulation has been used to maintain continence, but each of the current methods continuously stimulates the nerve of interest to inhibit the bladder. Conditional stimulation, when stimulation is applied only when a hyper-reflexive contraction occurs, has several potential advantages over continuous stimulation to inhibit the bladder. First, conditional stimulation at the beginning of the contraction can completely abolish the contraction [3, 4]. Second, conditional stimulation may allow the bladder to fill to a greater volume before an uncontrollable contraction occurs [3, 5] by minimizing habituation resulting from repetitive activation of spinal reflexes [6-9]. Conditional stimulation to inhibit the bladder requires detection of the onset of nascent hyper-reflexive contractions. The activity in the pudendal nerve increases during reflex bladder contractions, and the pudendal electroneurogram can be used as a trigger to control conditional stimulation [10].

We hypothesized that conditional stimulation, using electrical activity of the pudendal nerve as a control signal, would allow the bladder to fill to a larger volume before continence was lost than would continuous stimulation. Experiments were conducted to compare the maximum bladder capacity under three conditions: no stimulation, unconditional (continuous) inhibitory stimulation, and conditional inhibitory stimulation (event-triggered) delivered only when the bladder was contracting.
2. METHODOLOGY

Intact adult male cats (n=6, 3.0–4.6 kg) were anesthetized with ketamine HCl, and anesthesia was maintained with alpha-chloralose. The ureters were located, ligated, and cut proximal to the ligation. A suprapubic catheter was used to fill the bladder and to monitor bladder pressure using a solid state pressure transducer. A tripolar silicone nerve cuff was placed around the pudendal nerve trunk (PNT) to measure the electroneurogram (ENG). The nerve cuff was a split silicone tube tripolar nerve cuff which had three platinum bands spaced 5 mm apart and an inner diameter between 1.0 and 1.5 mm [11]. The bladder was slowly filled (0.9 ml/mn) with warm saline until continence was lost. Electrical stimulation of the contralateral pudendal nerve with a bipolar hook electrode was used to inhibit bladder contractions (5-15 Hz, 400 µA, 15 seconds).

The PNT ENG was rectified and low pass filtered (τ = 250 ms), and was the input to an event-triggered control system (Fig 1). The control system was implemented using custom software created using Labview (National Instruments, Inc). A CUSUM algorithm was used by the control system to detect hyper-reflexive bladder contractions from the PNT ENG and had three adjustable parameters: the time constant of the low pass filter cut-off for the ENG signal, the window size for initial mean and standard deviation of the signal, and the number of data points used in the cumulative sum. The detection parameters were determined by collecting a trial run at the beginning of the experiment.

The volume at which continence was lost was recorded for each trial, and there were three trial types: no stimulation, continuous stimulation, and event-triggered stimulation. Incontinence occurred when 1 ml of fluid was expelled out of the urethra or when a bladder contraction lasting longer than 25 seconds occurred.

3. RESULTS

The volumes at which continence was lost were 28 ± 14 ml (mean ± SD) for no stimulation, 33 ± 14 ml for continuous stimulation, and 38 ± 13 ml for event-triggered stimulation (Fig 2; N=74 trials across 6 cats with a minimum of 9 trials per cat). The volumes at which continence was lost for continuous and event-triggered stimulation were statistically greater than the volume at which continence was lost for no stimulation (p=0.029 and p<0.001, respectively). The volume at which continence was lost for event-triggered stimulation was significantly greater than the volume at which continence was lost for continuous stimulation (p=0.027). Conditional inhibitory stimulation using the event-triggered control system reduced the stimulation time by 67 ± 21% as compared to unconditional continuous stimulation (Fig 2).

The average delay from the start of a bladder contraction to the time of detection for the event-triggered control system was 4.1 seconds. The average increase of bladder pressure above baseline at the time of detection was 10.8 cmH2O. The sensitivity (number of detected contractions divided by the total number of contractions) was 89% and the selectivity (number of detected contractions divided by the number of detected contractions plus the number of false positives) was 97%.

4. DISCUSSION

The objective of the present studies was to determine whether an event-triggered control system could be used to maintain continence by detection and abolition of reflex bladder contractions. We compared the maximum bladder volumes achieved with no stimulation, continuous stimulation, and event-triggered inhibitory stimulation delivered only when the bladder was contracting. The maximum bladder volume achieved by event-triggered control was greater than continuous stimulation and no stimulation. The event-triggered control system also significantly reduced the total stimulation time.
This study showed that conditional stimulation, regulated by an event-triggered control system using electrical activity of the pudendal nerve as a control signal, allowed the bladder to fill to a larger volume before continence was lost than did continuous stimulation. This study supports using event-triggered control system to maintain urinary continence.

The performance of continence control with the event-triggered control system may have been limited by the performance of the detection algorithm. The average delay was 4.1 seconds, and the average increase in the pressure was 10.8 cmH2O. The detection parameters were not optimized, and previous results with optimized parameters yielded earlier detection (2.1 s) and smaller increases in bladder pressure (9.5 cmH2O) [10]. Preliminary results show that detecting a bladder contraction closer to its onset increases the ability for the inhibitory stimulation to arrest the contraction. Thus, modifications to improve the detection algorithm of the event-triggered control system should improve the performance of the control system.

This study showed that conditional stimulation, regulated by an event-triggered control system using electrical activity of the pudendal nerve as a control signal, allowed the bladder to fill to a larger volume before continence was lost than did continuous stimulation. This study supports using event-triggered control system to maintain urinary continence.

Figure 2. The volumes at which continence was lost for no stimulation, continuous stimulation, and event-triggered stimulation. The maximum volumes achieved with continuous and event-triggered stimulation were significantly greater than those achieved with no stimulation (p=0.029 and p<0.001), and the volumes achieved with event-triggered stimulation was significantly greater than continuous stimulation (Black bars on left axis). The stimulation time was normalized such that continuous stimulation was 1 and no stimulation was 0 (Grey bars on right axis).

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Reference