Conditional and continuous electrical stimulation increase cystometric capacity in persons with spinal cord injury

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Abstract

Aims—Individuals with spinal cord injury (SCI) exhibit neurogenic detrusor overactivity (NDO) causing high intravesicle pressures and incontinence. The first aim was to measure changes in maximum cystometric capacity (MCC) evoked by electrical stimulation of the dorsal genital nerve (DGN) delivered either continuously or conditionally (only during bladder contractions) in persons with SCI. The second aim was to use the external anal sphincter electromyogram (EMG_{EAS}) for real-time control of conditional stimulation.

Methods—Serial filling cystometries were performed in nine volunteers with complete or incomplete supra-sacral SCI. Conditional stimulation was delivered automatically when detrusor pressure increased to 8–12 cmH_2O above baseline. MCCs were measured for each treatment (*continuous*, *conditional*, and *no stimulation*) and compared using post- ANOVA Tukey HSD paired comparisons. Additional treatments in two subjects used the EMG_{EAS} for automatic control of conditional stimulation.

Results—Continuous and conditional stimulation increased MCC by 63±73 mL (36±24%) and 74±71 mL (51±37%), respectively (p<0.05), compared to no stimulation. There was no significant difference between MCCs for conditional and continuous stimulation, but conditional stimulation significantly reduced stimulation time (174±154 s, or 27±17% of total time) as compared to continuous stimulation (469±269 s, 100% of total time, p<0.001). The EMG_{EAS} algorithm provided reliable detection of bladder contractions (six of six contractions over four trials) and reduced stimulation time (21±8% of total time).

Conclusions—Conditional stimulation generates increases in bladder capacity while substantially reducing stimulation time. Furthermore, EMG_{EAS} was successfully used as a real-time feedback signal to control conditional electrical stimulation in a laboratory setting.

Keywords

Neurogenic detrusor overactivity; Electromyogram; Neural prosthesis; Neuromodulation; Overactive bladder; Urinary incontinence; Biofeedback

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1 Introduction

Urological complications following spinal cord injury (SCI), including neurogenic detrusor overactivity (NDO), bladder-urethral sphincter dyssynergia, and urinary retention, can result in frequent urinary tract infections, severe urinary incontinence, kidney infections, and long-term renal damage (1,2). Common management of NDO, including intermittent self-catheterization and anticholinergic medication, remains inadequate due to recurrent urinary tract infections and dose-limiting side effects (3–5).

Neuromodulation is an alternative treatment for NDO. Electrical activation of pudendal afferents suppresses bladder activity and promotes continence (6–13). Continuous stimulation of afferents in the dorsal genital branch (DGN) of the pudendal nerve increases maximum cystometric capacity (MCC) in persons with SCI (9,11,13). Conditional stimulation, applied only during bladder contractions, may be more effective than continuous stimulation by minimizing habituation of spinal reflexes (9, 14,15), and in cats, MCC was significantly larger with conditional stimulation than with continuous stimulation (16). Despite previous studies of the efficacy of conditional stimulation (6, 9, 23, 24), there are few data directly comparing conditional and continuous stimulation. Kirkham and colleagues compared conditional and continuous stimulation, but only one protocol directly compared the two types of stimulation on the same day in the same patient (n=3) and the use of serial, rather than randomized trial order may have influenced the results (9). The current study tested for a significant difference between continuous, conditional, and no stimulation using a randomized trial order study design in human participants with SCI. Further, the potential benefit of conditional stimulation is counterbalanced by the requirement for a control signal to determine when the bladder is contracting. Previous studies used bladder pressure, electroneurogram, or electromyogram (EMG) to detect nascent bladder contractions (16–19).

The long term goal of our research is to develop a fully implanted electrical device to treat NDO and restore continence in persons with SCI. The first objective of this study was to quantify the effects of continuous and conditional electrical stimulation of pudendal dorsal genital afferents (DGN) on MCC in persons with SCI. The second objective was to demonstrate real-time closed-loop control of conditional stimulation using the EMG from the external anal sphincter (EMG_{EAS}) as the control signal.

2 Methods

2.1 Subject Selection

The study protocol was approved by the Institutional Review Board, and written informed consent was obtained. Inclusion criteria were neurologically stable complete or incomplete suprasacral SCI >1 yr and documented NDO; exclusion criteria were implanted electronic device, history of pelvic surgery, acontractile bladder, urethral stricture/obstruction or severe prostatic hypertrophy determined by their urologic physician, perineal inflammation, or low bladder compliance.

2.2 Instrumentation

A Foley catheter (Bardex Foley, 12 Fr, 5 cc balloon, Coude tipped, C.R. Bard, Inc., Covington, GA) was placed into the bladder, inflated to occlude the bladder neck, and the bladder was drained. A pressure catheter (BPC-4L, Life-Tech, Inc., Stafford, TX), inserted with the Foley, was connected to an external pressure transducer (Deltran I, Utah Medical Products, Inc., Midvale, UT). A balloon catheter (Life-Tech RPC-9) was placed in the rectum and connected to a second pressure transducer, and detrusor pressure (P_{det}) was calculated as intravesicle pressure minus rectal (abdominal) pressure. Pressure signals were

amplified (1000x) and low-pass filtered (f=40Hz, ETH-255, iWorx/CB Sciences, Inc., Dover, NH), and sampled (5kHz, DAQPad-6016, National Instruments, Austin, TX). The EMGEAS was recorded using a bipolar pair of wire electrodes (1512A-M, Life-Tech) inserted ~ 2–3 cm deep into the EAS, both on the same side ~ 2 cm lateral to the anal opening, and a self-adhesive reference electrode (Empi 9000 series, 1.25 in round) placed on the outer thigh. The EMG_{EAS} was pre-amplified (50x, C-ISO-255, iWorx), further amplified (1000x) and band-pass filtered (3Hz-1kHz, ETH-255), and sampled (5kHz, DAQPad-6016). All data were further processed, displayed, and recorded on a computer (Dell Latitude D610, 1.86 GHz) using custom software developed with LabVIEW (National Instruments). For stimulation, a self-adhesive surface electrode patch (Empi 9000, 1.25 in diameter, St. Paul, MN) was placed over the genital branches of the pudendal nerve (dorsal base of penis in males (20), just cranial to clitoris in females (21)), with the counter electrode (Empi 5000, 2.75×4 in rectangle) on one hip. Charge-balanced biphasic regulated current 200 μs rectangular stimuli were delivered using an isolated, battery-powered electrical stimulator (300PV, Empi).

2.3 Experimental Protocol

The bladder was filled at 10–40 mL/min (dependent on maximum capacity in prior urodynamic evaluations and held constant for each subject) until MCC was reached (defined as infused volume at time of sustained bladder contraction, urine leakage, or 700 mL infused). In this study, a contraction was considered sustained if P_{det} was ≥ 40 cmH$_2$O for 20 s.

Two repetitions of three treatment types (*no stimulation*, *continuous stimulation*, and *conditional stimulation*) were performed, with the first treatment always *no stimulation* to determine baseline MCC and check for exclusion criteria (e.g., low compliance), the second treatment always *continuous stimulation* or *conditional stimulation*, and the remaining trials conducted in random order. If time permitted, additional trials were performed with newly randomized treatments. Stimulation amplitude was set at twice the pudendo-anal (PA) reflex threshold, or at 80 mA if no reflex was observed (22). During *continuous stimulation* treatments, low frequency (10 or 15 Hz) continuous stimulation was applied. Stimulation during conditional treatments was applied automatically when P_{det} increased to 8–12 cmH$_2$O, or when the EMG_{EAS}, acting as a surrogate detector for detrusor contractions, exceeded a threshold (see below). Stimulation remained *on* for ten seconds then turned *off* for two seconds, and this cycle continued while P_{det} remained above the threshold. An additional ten seconds of stimulation were delivered after P_{det} decreased below threshold. At least five minutes elapsed between trials.

In two subjects, two additional conditional stimulation treatments were conducted using the EMG_{EAS} to control the delivery of stimulation. The EMG_{EAS} signal was rectified, low-pass filtered, and compared with an adaptive threshold determined from an offset and time-lagged version of the rectified EMG_{EAS} (18). The parameters of the adaptive threshold algorithm including the signal low-pass filter time constant (0.5 s), the threshold low-pass filter time constant (2.0 s), and the threshold offset (2x) were determined by running the algorithm during the *no stimulation* cystometries performed earlier in each subject.

2.4 Data Analysis

For each subject, MCCs were averaged within each treatment (at least two per treatment), and the average cystometric capacities (ACC) were compared using ANOVA (level of significance α=0.05) with subject as a random factor to remove inter-subject variation in absolute bladder volumes (6,9). Post-ANOVA pair-wise comparisons were made using Tukey's Honestly Significant Differences test with protected level of significance α=0.05.

Spearman's Rank was used to test for a correlation between MCC and trial order. Student's t-tests were used to compare stimulation times and to test for effects of stimulation carry-over (see Results). All *p*-values less than 0.05 were considered significant.

3 Results

3.1 Subject Characteristics

Informed consent was obtained from 13 subjects (11 male) who met medical and demographic criteria (Table I). Subjects had a mean age of 55 ± 11 yr at the time of study, and injury levels ranged from C5 to L2. Four of 13 subjects were excluded after completing the initial control cystometry (Subjects P1, P7, and P10 for acontractile bladders; Subject P9 for low bladder compliance). The remaining nine subjects completed the study, and there were no episodes of autonomic dysreflexia or other adverse events during the study.

3.2 Cystometric Capacity

Example cystometrograms recorded during *no stimulation*, *continuous stimulation*, and *conditional stimulation* trials are shown in Figure 1. During bladder filling without stimulation, P_{det} remained low until a sustained bladder contraction occurred at 271 mL. With continuous stimulation, P_{det} remained low for a longer period of time before a sustained contraction occurred, resulting in a larger MCC of 483 mL. Conditional stimulation applied at the onset of each contraction suppressed three of four contractions and increased MCC to 534 mL.

For each subject, MCCs were averaged within each treatment type (at least two per treatment), and these averages (ACC) were compared. Mean ACCs $\pm$ SD were 149 ± 131 mL (*no stimulation*), 211 ± 200 mL (*continuous*), and 223 ± 193 mL (*conditional*) from a total of 58 trials among nine subjects (Fig. 2). Compared to *no stimulation* treatments, continuous stimulation increased mean ACC by 42%, while conditional stimulation increased mean ACC by 50% over no stimulation and by 6% over continuous stimulation. Among the 12 *conditional stimulation* trials displaying one or more suppressed contractions, mean volume increase between the first contraction and MCC was 70 ± 63 mL (129 ± 196%). ACC was dependent on trial type ($p<0.05$, ANOVA with subject as a random factor). Furthermore, ACCs from *continuous* and *conditional stimulation* were significantly larger than those from *no stimulation*, but ACCs from *continuous* and *conditional stimulation* showed no significant difference (post hoc Tukey HSD pair-wise comparisons with $\alpha=0.05$).

ACC during continuous stimulation was greater than ACC during no stimulation in all nine subjects. One subject displayed a decrease in *conditional stimulation* ACC compared to *no stimulation* (-3%), and the remaining eight displayed increases (range 8–113%). In six of nine subjects, ACC during *conditional stimulation* trials was greater than ACC during *continuous* trials by an average of 31 ± 25% (range 2–60%), but this proportion (67%) was not different than chance ($p=0.25$, Sign test).

Compared to continuous stimulation, conditional stimulation decreased stimulation time from 469 ± 269 s or 100% of total time to 174 ± 154 s or an average of 27 ± 18% (two-tailed t-test on stimulation time, $p<0.001$). In five of the 15 *conditional stimulation* trials triggered by pressure, stimulation remained on during the latter part of the trial because detrusor pressure remained above threshold.

Trial order could have confounding effects on MCC including an increase in capacity during repeated baseline cystometries and/or "carry-over" effects of prior stimulation (9). Trial order was randomized, and did not correlate with MCC (Spearman's rank, $p=0.749$ for all trials, $p=0.802$ for *no stimulation* trials only; Fig. 3). Further, a two-tailed t-test comparing

MCCs of the first baseline trials to all other *no stimulation* trials was not significant (p=0.331), as were similar tests comparing trials of the same type preceded by either *continuous* or *conditional stimulation* trials (trial k+1 = *no stimulation: p*=0.106; *continuous: p*=0.860; *conditional: p*=0.152).

3.3 Suppressed Contractions

Of the 23 *conditional stimulation* trials using either pressure or EMG_{EAS}, 12 trials displayed one or more suppressed contractions (52%). Among these, the median number of suppressed contractions per trial was three (range one to seven). Figure 4A displays a *conditional stimulation* trial in which four distension-evoked detrusor contractions were suppressed with conditional stimulation. A fifth contraction was suppressed during stimulation and then developed into a sustained contraction after stimulation was switched *off*. Bouts of stimulation during the contraction resulted in phasic relaxations of the detrusor, but were unable to reduce P_{det} below 40 cmH_2O. There were two transient contractions during 19 *no stimulation* trials and three transient contractions during 20 *continuous stimulation* trials (Fig. 4B).

Mean peak P_{det} during suppressed contractions was 22 ± 12 cmH_2O (range 10–50 cmH_2O). The five suppressed contractions with peak pressures between 40 and 50 cmH_2O subsided within 20 seconds, did not cause leakage, and therefore did not constitute reaching cystometric capacity.

3.4 Closed-Loop Control Using EMG_{EAS}

EMG-based *conditional stimulation* trials were conducted twice in each of two subjects (P12, P13). An adaptive threshold algorithm was used to detect nascent hyper-reflexive detrusor contractions from the EMG_{EAS} in real-time and trigger conditional stimulation of the DGN. The adaptive threshold algorithm successfully detected all true contractions. After each detection, the stimulator turned on automatically for 20 s, then turned off for a time-out no-stimulation period of 5 s. An example is shown in Figure 5: four false positive detections occurred before two true positive detections and this resulted in 27% stimulation time during the 6.5 minute trial. Stimulation delivered in response to the first true detection reduced P_{det} to below 10 cmH_2O and suppressed the contraction, but a subsequent detrusor contraction began within the time-out period and the second contraction was not suppressed by stimulation and resulted in MCC. Detection of the contraction successfully occurred immediately after the time-out expired, but stimulation was unable to arrest the contraction. Across all trials, a total of six true positive and 26 false positive detections occurred over 28 minutes of cumulative trial time, resulting in 22% stimulation. Delay from the time P_{det} reached 10 cmH_2O to detection was -4.3 ± 2.2 s (detection occurred first in all five cases) and P_{det} at detection was 2.4 ± 1.9 cmH_2O. The detection of a sixth contraction was delayed by 5.9 s, due to the time-out, and P_{det} at detection was 55 cmH_2O.

4 Discussion

Serial cystometries were conducted in persons with SCI to quantify the effects of continuous and conditional electrical stimulation of the DGN on cystometric capacity. Average cystometric capacities (ACC) were significantly greater with both conditional stimulation (50% increase) and continuous stimulation (42% increase), and although conditional stimulation reduced stimulation time by 73% compared to continuous stimulation, it was not less effective at increasing ACC. In contrast to previous studies in humans (6,9,19), this study directly compared the efficacy of conditional stimulation to both continuous and no stimulation within the same subjects and sessions. The results provide further evidence that conditional stimulation is effective in increasing cystometric capacity in persons with SCI.

Conditional stimulation increased cystometric capacity by 50% over no stimulation. Although absolute increases in volumes were small (74 ± 71 mL), a large percentage increase in bladder capacity should translate to a proportional increase in time between necessary bladder evacuations. Similar increases of 66% (6) and 53% (23) were reported by Dalmose et al. and Hansen et al., respectively. In contrast, Kirkham et al. reported a 144% increase using 60 s stimulus trains (9). Shorter stimulation durations in the Dalmose study and stimulation cycling in the present study may explain the differences in efficacy.

Although some investigators have used physiologic filling (23,24), they were only able to perform two or three trials per experiment due to the slow rate of natural diuresis (8 mL/min, range 2–14 mL/min (24); 8.7 ± 4.2 mL/min (23)). In this study, a physiologic fill rate was traded for randomly ordered repeated measures, and the rate of 10–40 mL/min used was lower than used in other studies employing serial cystometries (6,11). Carry-over effects of repeated fills or stimulation can affect subsequent MCCs (9) but our analysis revealed that trial order was not a significant factor determining MCC.

A median of three suppressed contractions occurred among 52% of conditional stimulation trials. Dalmose et al. reported a mean of 7.8 inhibited contractions per trial in ten conditional stimulation trials performed in a similar study (6). One possible reason for the low number of inhibited contractions in the present study is that stimulation did not always remain on until the contraction had fully subsided (see Fig. 4A, arrowhead). The two-second pause in stimulation that occurred periodically when the pressure remained high (5 s during EMG detection time-out) may have allowed P_{det} to continue to increase. Using one minute closed-loop stimulation durations, Kirkham and colleagues reported that contractions took an average of 41 seconds to return to 10% of the pre-contraction baseline pressure (9). It is likely that cycling diminished the effectiveness of conditional stimulation for trials in which contractions did not decrease below the pressure threshold within the stimulation duration (10–20 s). Cycling was included to mimic the behavior of the closed-loop EMG algorithm, since due to large stimulation artifacts, the EMG_{EAS} was not monitored during stimulation. Lengthening the minimum stimulation duration may further increase cystometric capacity by increasing the number of successfully inhibited contractions. Another possible reason for the low number of inhibited contractions is that inadvertent automatic stimulation due to fluctuations in abdominal pressure during some conditional treatments (i.e., false positives) may have delayed the occurrence of distension-evoked contractions. Therefore, both short-term inhibitory carry-over effects (9) and suppressed nascent contractions may have contributed to increases in MCC during *conditional* treatments.

Conditional stimulation increased ACC by 6% compared to *continuous stimulation* trials while using 73% less stimulation, and two-thirds of subjects exhibited increases in ACC of up to 60% during conditional versus continuous stimulation. A similar study also found a non-significant 5% increase in mean ACC with conditional stimulation, even though trial types were not randomized and the number of subjects was low (9). Furthermore, four of six subjects undergoing protocols designed to compare the two stimulation types displayed larger ACCs with conditional stimulation (9), and the present study revealed an equivalent ratio of six of nine subjects. Wenzel and colleagues reported a similar decrease in stimulation during closed-loop trials in cats (16), and conditional stimulation used less stimulation compared with the Medtronic Interstim, which employs a 70–90% duty cycle (25). Non-conditional intermittent stimulation may be an effective alternative to conditional stimulation to reduce stimulation time while preserving efficacy of continence control. Open-loop intermittent stimulation has the advantage of not requiring detection of a nascent bladder contraction and feedback control, but because inhibitory stimulation must be delivered soon after a hyper-reflexive contraction begins in order to be effective (16),

intermittent stimulation may not be effective at suppressing contractions that begin during the "off" phase."

Four of nine subjects exhibited a PA reflex (mean threshold 37 ± 11mA). Average percent increase in open-loop ACC over control for these subjects was 50% ($\pm$30%, range 15–87%), compared to 25% ($\pm$13%, range 8–42%) for those not exhibiting a reflex. Although not significant ($p<0.20$, Wilcoxon Rank-Sum Test), this difference reflects the expected increase in stimulation efficacy with robust sacral spinal reflexes. The PA reflex is not necessarily a physiological prerequisite for effective neuromodulation, but may be a convenient criterion for choosing subjects most likely to respond to pudendal nerve stimulation. In this study, the PA reflex was tested with 2 Hz stimulation, but lower frequency stimulation may have improved the response rate (26).

Given the variability of MCCs within subjects and assuming a true conditional stimulation effect size in the general SCI population of about 5% over continuous stimulation, this study was not adequately powered (low sample size) to detect a significant difference between the two treatments. Regardless of any true difference, an average increase of 5% is not clinically significant, and it remains unclear what factors (e.g., injury level, severity, baseline MCC, etc.) are predictive of the relative efficacy of conditional and continuous stimulation (6).

Persons with incontinence resulting from SCI also lose the ability to empty the bladder. Electrical stimulation of pudendal afferents can also facilitate efficient bladder emptying (27–29), and a future prosthesis may use pudendal nerve stimulation for both continence and micturition. Detrusor-sphincter-dyssynergia presents a challenge to producing efficient bladder emptying, and although pudendal afferent stimulation produces efficient voiding in chronic SCI cats (30), whether this will translate to humans with SCI remains uncertain. Conditional stimulation may reduce continence-promoting carry-over effects and allow more efficient voiding when stimulation is changed from continence-promoting (e.g., low frequency) to micturition-promoting (e.g., high frequency).

The EMG_{EAS} was used to detect hyper-reflexive bladder contractions and trigger conditional stimulation during real-time electrical control of conditional stimulation. An adaptive threshold algorithm successfully detected all true contractions, and five of six were detected before P_{det} rose above 10 cmH$_2$O. False positive detections also occurred, and some of these coincided with fluctuations in abdominal pressure or with coughing. Although a formal optimization of the adaptive threshold parameters was not performed, such optimization is feasible (18). Given the robust detection of hyper-reflexive contractions without formal parameter optimization, such optimization may reduce false positives and further reduce stimulation time. The similar performance of two different methods for real-time detection of hyper-reflexive contractions using EMG signals in this and a previous study (19) strongly supports the utility of this approach. Also, EMG signals can be accessed for clinical research using minimally invasive techniques, while a nerve cuff electrode implanted on the pudendal nerve may provide similar information for a fully implanted system (18).

5 Conclusions

Conditional and continuous stimulation were equally effective at increasing the MCC in persons with SCI, but conditional stimulation substantially reduced stimulation time compared to continuous stimulation. The benefit of conditional electrical control of urinary continence may be the ability to decrease the amount of stimulation needed to maintain continence. The combination of increased bladder capacity with reduced stimulation may prove to make closed-loop control of urinary continence the best therapeutic option in

persons with SCI. Furthermore, the demonstration of feasibility in using the EMG_{EAS} signal for real-time closed-loop control may support future efforts in developing a neural prosthesis for closed-loop electrical control of urinary continence.

Acknowledgments

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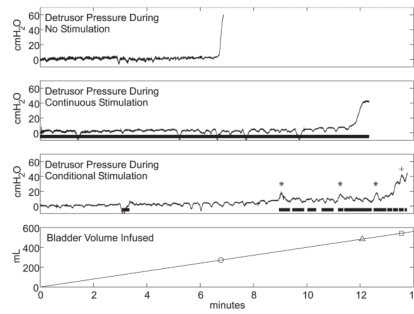
Fig. 1.
Cystometrograms in a person with spinal cord injury with no stimulation, continuous stimulation, and intermittent stimulation of the dorsal genital nerve. Top three traces display detrusor pressure during no, continuous, and conditional stimulation treatments, with cystometric capacities marked on the bottom trace of infused volume (circle: no stimulation, 271 mL; triangle: continuous stimulation, 483 mL; square: conditional stimulation, 534 mL). The thick horizontal lines denote the delivery of 15 Hz stimulation, asterisks denote stimulation-suppressed contractions, and cross denotes unsuppressed contraction during the conditional stimulation treatment. The transient dips in detrusor pressure were caused by fluctuations in abdominal pressure (not shown).
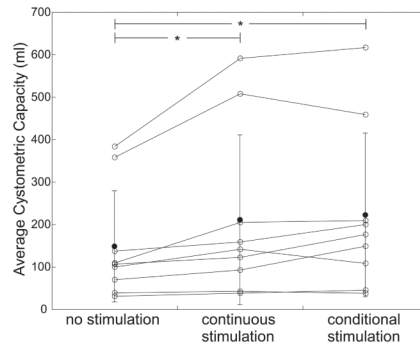
Fig. 2.
Average cystometric capacity during cystometry with no stimulation, continuous
stimulation, and conditional stimulation. Open points are individual subjects, solid points are
population means, and error bars show standard deviations. Asterisks denote significant
difference between groups.
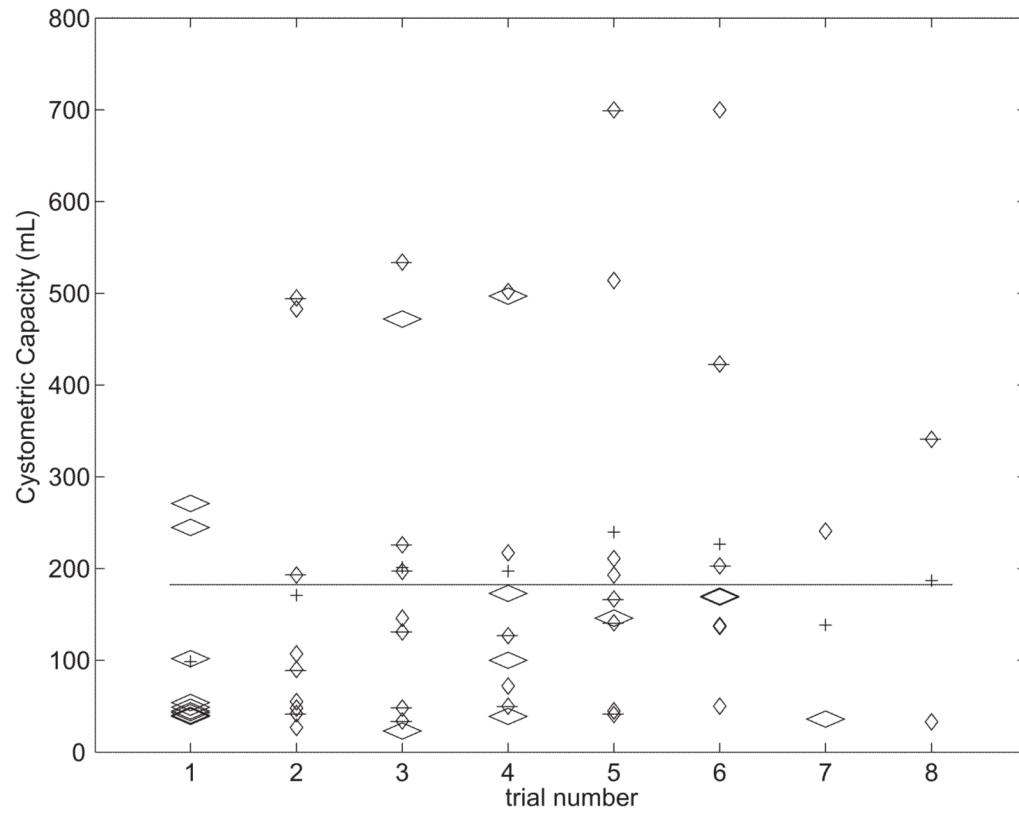
Fig. 3.
Analysis of cystometric capacity by trial number (1=first trial, 2=second trial, etc.). The plot displays cystometric capacities for each trial (diamonds: wide, no stimulation; narrow, continuous stimulation; barred, conditional stimulation), the mean cystometric capacity within each trial number group (crosses), and the overall mean (line). There was no significant correlation between cystometric capacity and trial number (Spearman's rank). Furthermore, the average cystometric capacity during the first trials (always baseline) was not significantly different from the average of other no stimulation trials (Student's t-test).
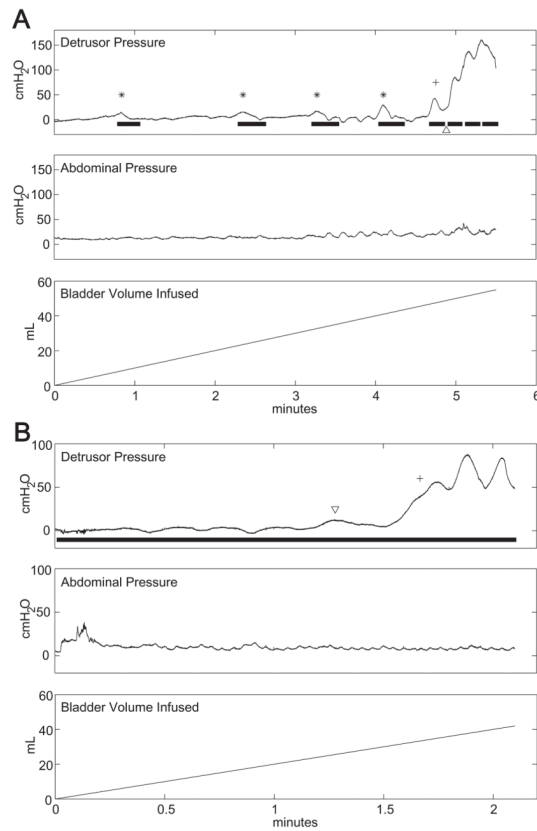
Fig. 4.
A: Example cystometrogram during a conditional stimulation treatment displaying four suppressed detrusor contractions (asterisks). The fifth contraction (cross) was not suppressed completely, possibly due to the pause in stimulation (arrowhead). **B:** Transient detrusor contractions (arrowhead) appeared in two of 20 continuous stimulation treatments and in one control treatment. An uncontrolled detrusor contraction (cross) determined the cystometric capacity (33 mL @ second 100).
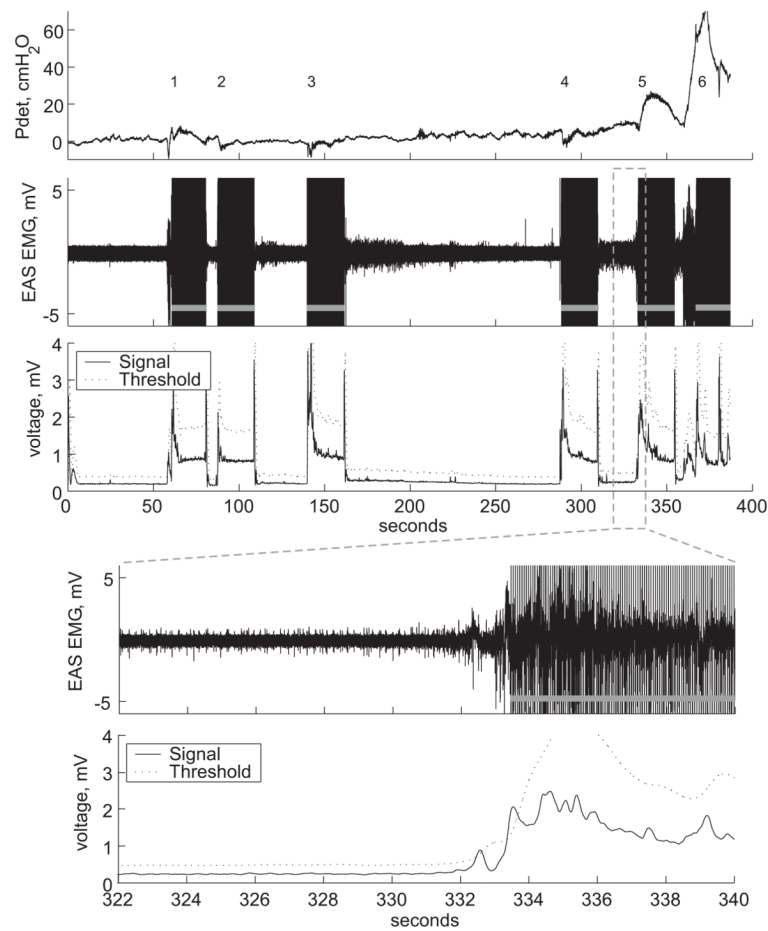
Fig. 5.
Closed-loop electrical control of continence. An adaptive threshold algorithm was used to detect hyper-reflexive detrusor contractions and trigger conditional stimulation (gray bars) in a real-time implementation of closed-loop control of urinary continence. Four false positive (1, 2, 3, 4) and two true positive detections (5, 6) were triggered by the algorithm. Magnification displays the external anal sphincter electromyogram (EAS EMG), detection signal, and adaptive threshold during the fifth detection. Pdet: detrusor pressure.

TABLE I

Subject Characteristics

ID	Sex	Age (yr)	Injury Level, Severity	Injury Date	Injury Cause	Normal Voiding Method	Medications (stopped>48 h)
(P1)	M	34	T10, Complete	1983	Gunshot	CIC	None
P2	F	41	T8/T9, Complete	1986	Fall	CIC	None
P3	F	37	T12/L1, Incomplete	2001	TM/CES	Straining	Oxytrol patch
P4	M	57	T4, Complete	1996	Accident	CC	Baclofen
P5	M	63	T2, Incomplete	1998	Iatrogenic	CIC	Oxybutinin
P6	M	59	T8, Complete	1984	Gunshot	CIC	Oxybutinin
(P7)	M	62	C5, Incomplete	1986	Accident	CIC	None
P8	M	62	T10/T12, Complete	1999	Fall	CIC	None
(P9)	M	57	T10, Complete	1995	Accident	CIC	None
(P10)	M	53	T3, Complete	2005	Gunshot	IC	Diazepam
P11	M	66	L1, Complete	1966	Accident	CC	None
P12	M	71	T12/L1, Incomplete	1965	Accident	CIC	Ditropan
P13	M	51	T12/L2, Complete	1977	Accident	CC	None

TM/CES - Transverse Myelitis with Cauda Equina Syndrome; CIC - clean intermittent catheterization; CC - condom catheter; IC - indwelling catheter. Parentheses around subject ID denote subject exclusion (see text).