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Original Article

The acute effects of continuous and conditional neuromodulation on the bladder in spinal cord injury

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Study design: Laboratory investigation using serial slow-fill cystometrograms.
Objectives: To examine the acute effects of different modes of dorsal penile nerve stimulation on detrusor hyperreflexia, bladder capacity and bladder compliance in spinal cord injury (SCI).
Setting: Spinal Injuries Unit, Royal National Orthopaedic Hospital, Stanmore, Middlesex, UK.
Methods: Fourteen SCI patients were examined. Microtip transducer catheters enabled continuous measurement of anal sphincter, urethral sphincter and intravesical pressures. Control cystometrograms were followed by stimulation of the dorsal penile nerve at 15 Hz, 200 μs pulse width and amplitude equal to twice that which produced a pudendo-anal reflex. Stimulation was either continuous or in bursts of one minute triggered by a rise in detrusor pressure of 10 cm water (conditional). Further control cystometrograms were then performed to examine the residual effects of stimulation.
Results: Bladder capacity increased significantly during three initial control fills. Continuous stimulation ($n=6$) significantly increased bladder capacity by a mean of 110% ($\pm$Standard Deviation 85%) or 173 ml ($\pm$146 ml), and bladder compliance by a mean of 53% ($\pm$31%). Conditional stimulation in a different group of patients ($n=6$) significantly increased bladder capacity, by 144% ($\pm$127%) or 230 ml ($\pm$143 ml). In the conditional neuromodulation experiments, the gap between suppressed contractions fell reliably as bladder volume increased, and the time from start of stimulation to peak of intravesical pressure and 50% decline in intravesical pressure rise was 2.8 s ($\pm$0.9 s) and 7.6 s ($\pm$1.0s) respectively. The two methods of stimulation were compared in six patients; in four out of six conditional neuromodulation resulted in a higher mean bladder capacity than continuous, but the difference was not significant.
Conclusions: Both conditional and continuous stimulation significantly increase bladder capacity. The conditional mode is probably at least as effective as the continuous, suggesting that it could be used in an implanted device for bladder suppression.
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Keywords: male; detrusor hyperreflexia; spinal cord injury; electric stimulation therapy; reflex physiology; penis, innervation

Introduction

Over the last 30 years, the effects on the bladder of stimulating the pudendal afferent nerves have been studied in some detail. Penile squeeze,[1] anal stretch,[2] electrical stimulation by anal or vaginal plug electrodes,[3–5] dorsal penile nerve[6–9] stimulation and magnetic[10] or electrical[11] stimulation of the sacral roots have all been shown to suppress bladder activity. The effect is seen in normal subjects,[12] spinally injured patients[5,7–11] and those with idiopathic bladder instability.[6,13,14]

Such stimulation can be termed neuromodulation, in which 'activity in one neural pathway modulates the pre-existing activity in another through synaptic interaction'.[15] Neuromodulation in spinally injured patients has the potential to suppress the detrusor hyperreflexia that is the result of lesions of the spinal cord above the cauda equina, and if untreated may contribute to incontinence, vesicoureteric reflux and renal failure. It may be a better tolerated alternative to

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anticholinergics, drugs which many patients are reluctant to take in high doses and which are not always effective.[16]

In the last 20 years three centres have shown that continuous dorsal penile nerve (DPN) stimulation almost always increases bladder capacity acutely in spinal cord injured patients.[7–9] Shah *et al*[18] have demonstrated that DPN stimulation can reliably suppress provoked hyperreflexic detrusor contractions and have used this technique to define optimum stimulation parameters. Recently, stimulation of the sacral roots has been used successfully to increase bladder capacity in the long term in patients with detrusor hyperreflexia.[19–21]

Neuromodulation can be applied in two fundamentally different ways: (1) conditionally, where it is started as intravesical pressure begins to rise at the beginning of a hyperreflexic contraction, or (2) continuously where it is applied throughout bladder filling. Current systems for long term stimulation use the continuous mode,[19–21] but a conditional system that detects the start of unstable bladder contractions and then suppresses them has theoretical advantages.[22]

Work in animals on a conditional system has shown encouraging early results,[22,23] and it is vital that the technique is evaluated in humans as it becomes technically feasible. DPN stimulation is ideal for these tests because it is simple, effective and non-invasive. For these reasons, it is also a convenient screening test for the response to neuromodulation before considering an implanted device.

The aim of this study was to determine the acute urodynamic effects of both conditional and continuous modes of DPN stimulation in patients with a spinal cord injury, and to compare them where possible.

Materials and methods

Fourteen consecutive male patients were studied. They had complete or incomplete traumatic lesions of the spinal cord, with neurological levels between C6 and L1, and were at least 1 year post injury. Anticholinergic medication was stopped at least 4 days before the tests. Local ethics committee approval and informed consent were obtained.

Urodynamics

Two different types of catheter were used. In the tests with continuous stimulation only, an 8 French bladder filling catheter and a standard water-filled bladder pressure line were used. In other studies a four channel microtip transducer catheter with a central filling channel (Gaeltech, Isle of Skye, UK) was used to allow filling, emptying and measurement of intravesical and urethral pressure simultaneously. Anal sphincter pressure was measured at the same time with a one channel microtip transducer. In some cases, it was not possible to measure bladder volume accurately because the position of the microtip catheter made complete aspiration of urine difficult. In these situations we reverted to a standard 8 French filling catheter and water filled pressure line. Patients were in the supine position.

Two or three control cystometrograms were always performed at the start of each study. Filling was always at 10 ml/min – this was chosen to be as close as possible to natural filling rates whilst enabling the necessary number of cystometrograms (CMGs) to be performed in 1 day. Cystometrograms with neuromodulation were then performed, followed (if time permitted) by final control CMGs. At the end of each CMG, total bladder capacity was calculated by adding the volume voided to the residual volume measured by aspiration.

In each test, filling was stopped when there was a sustained pressure rise of greater then 35 cm water, or voiding – 'firing off'. Compliance was measured as follows: (volume fired off + residual urine volume/ml)/(intravesical pressure before end-fill unstable contraction – starting intravesical pressure/cm H_2O). This parameter was measured in the continuous fill experiments only.

Neuromodulation was by stimulation of the dorsal penile nerve, using cutaneous self-adhesive siver-silver chloride electrodes and an electrically isolated stimulator (model DS7: Digitimer, Welwyn Garden City, Hertfordshire, UK). The frequency of stimulation was always 15 Hz, with a pulse width of 200 μs. The current was set between 20 and 60 mA, at a level equal to twice the threshold for contraction of the anal sphincter (the level which reliably gave a detectable contraction).

In the tests involving conditional neuromodulation, stimulation was triggered manually after a pressure rise of 10 cm water. Neuromodulation was applied for 1 min, and continued for a further minute if intravesical pressure was not suppressed to within 10 cm H_2O of the baseline.

Simultaneous measurements of anal sphincter and urethral sphincter pressure enabled a comparison of thresholds for the pudendo-anal and pudendo-urethral reflexes.

Protocols

Four protocols were used: (i) Continuous stimulation: Three control fills, followed by three fills with continuous neuromodulation, followed by two final control fills (six patients). (ii) Conditional stimulation: Two control fills, followed by two or three fills with conditional neuromodulation, followed by at least one control fill (six patients). To compare continuous and conditional modes: (iii) Alternating modes on the same day: two control fills, followed by alternating conditional and continuous fills (at least two of each type), followed by at least one final control fill (three patients). (iv) Two days of testing: on each day, two initial controls. Then two or three fills with either continuous or conditional neuromodulation (three patients).

Criteria for analysis
In the experiments with continuous neuromodulation (protocol i), analysis parameters were end fill bladder volume and bladder compliance.

In the experiments with conditional neuromodulation (protocols ii, iii, iv), parameters were end fill bladder volume and time between suppressed contractions. As secondary parameters, we noted time from start of neuromodulation to peak of suppressed contraction, time to 50% decay of suppressed contraction and time to return to within 10% of baseline intravesical pressure. The order of continuous and conditional fills in protocols iii and iv was not formally randomised, and the comparison between the two techniques was a secondary criterion for analysis.

In all experiments, the threshold for the pudendo-anal reflex was recorded, and if possible, the threshold for the pudendo-urethral reflex.

Data analysis
In the results that follow, figures in brackets represent one standard deviation, with ranges (where stated) indicating minimum and maximum values. The statistical test used was a two-tailed Wilcoxon matched pairs test, except when comparing patients with incomplete and complete lesions. Here, a two-tailed Mann-Whitney U-test was used; in both cases a P value of <0.05 was considered significant.

Because the effects of neuromodulation often became larger with successive fills, in most cases we compared greatest (ie maximum) control fill volume (in all cases at least two controls were performed) with greatest neuromodulation fill volume. This gave the best indication of the potential effect of long term neuromodulation. The exception to this was the comparison between continuous and conditional fills in protocols iii and iv. Here, the mean for the conditional and continuous fills was calculated for the comparison (equal numbers of each type of fill were always compared).

Results from the conditional experiments were analysed in two ways: (i) Time method: a constant rate of filling was assumed – justified because the filling rate of 10 ml/min was likely to be much higher than the patient's urine output. The time to first unstable contraction (c in Figure 1) and time of successful conditional suppression (n in Figure 1) were measured. The fraction n/c then represented the proportional increase in bladder capacity with neuromodulation. Because of 'carry over' effects, this measurement was only justified in the first conditional neuromodulation fill of the day, before any continuous neuromodulation had taken place and (ii) Volume method: as in the continuous neuromodulation experiments, volume was measured by aspiration at the end of each fill.

The characteristics of the suppressed contraction (including time to peak, and time to return to within 50% and 10% of baseline – a, b and d in Figure 2) were measured from three suppressed contractions at the start, middle and end of the conditional neuromodulation period and the mean calculated for each patient.

Results

Pudendo-urethral (PU) and pudendo-anal (PA) reflexes
The catheter configuration enabled direct comparison of the PA and PU reflexes in seven patients. The P-U reflex was usually seen at a lower (but not significantly so) stimulation intensity than the P-A reflex (16.4 *vs* 20.6 mA, $P=0.12$).

Continuous fills (Figures 3 and 4)
The bladder capacity increased significantly during the control fills, with the third control fill higher than the first by a mean of 43% ($\pm$22%) ($P=0.03$).

The maximum volume with neuromodulation was greater than the maximum initial control volume by 110% ($\pm$85%, range 22–231%) or 173 ml ($\pm$146 ml, range 43–370 ml) ($P=0.03$). The persisting (but diminishing) effect of neuromodulation is demonstrated in Figure 3, with volume falling significantly in each of the final control fills ($P=0.03$ in each case).

The bladder compliance was also significantly ($P=0.03$) increased by neuromodulation, by a mean of 53% ($\pm$31%, range 16–104%) in the greatest neuromodulation fill compared to the greatest control.

Conditional fills (Figures 1, 2, 5 and 6)

Time method (six patients: protocol ii) The mean fractional increase in bladder capacity (n/c in Figure 1) was 125% ($\pm$103%, range 29 to 300%). In general, percentage increases were higher when the control volume was low. Because this method only measured the first conditional fill, it underestimated the potential increase with conditional neuromodulation: the increase in capacity with subsequent neuromodulation fills is clearly shown in Figures 3 and 5.

Volume method (six patients: protocol ii) The greatest volume with neuromodulation was a mean of 144% ($\pm$127%, range 41 to 385%) and 230 ml ($\pm$143 ml, range 97–420 ml) larger than the greatest control volume (Figure 5). In three remaining patients tested with the alternating protocol (iii), the mean increase in the conditional fills was 51% ($\pm$19%) or 90 ml ($\pm$6 ml) (Table 2).

The time between suppressed hyperreflexic contractions fell reliably with increasing volume in every patient (Figure 6), although the absolute time varied widely between patients.

Two patients (MC and DS) were excluded from the analysis of conditional neuromodulation in Figure 2 because the tracings were not of sufficient quality, leaving eight patients who were investigated with protocols ii, iii or iv.

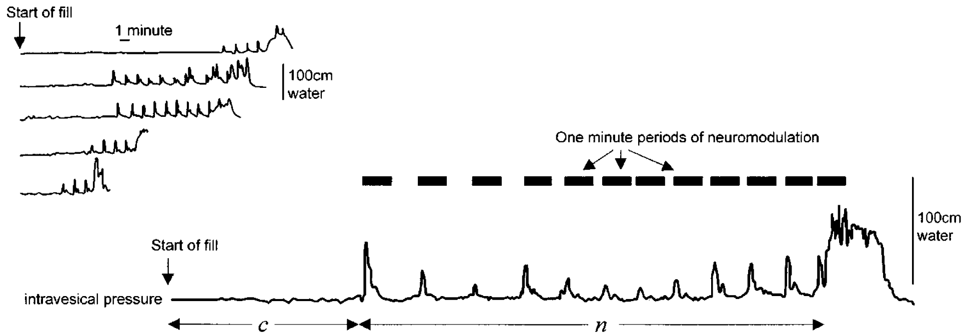

Figure 1 Sample conditional stimulation fill, starting with an empty bladder. *n* represents the additional bladder capacity from neuromodulation. Complete intravesical pressure traces in a further five patients during the first conditional neuromodulation fill are shown on the top left

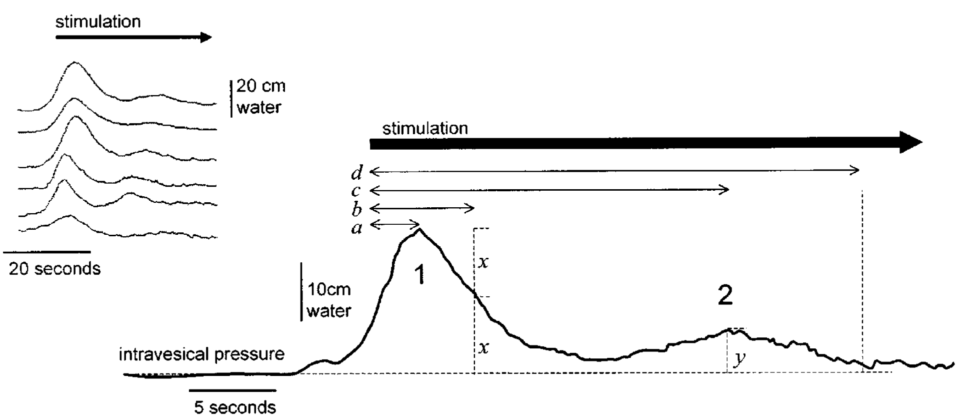

Figure 2 A suppressed contraction during conditional neuromodulation. Curves from the middle of the neuromodulation period in six further patients are shown on the top left

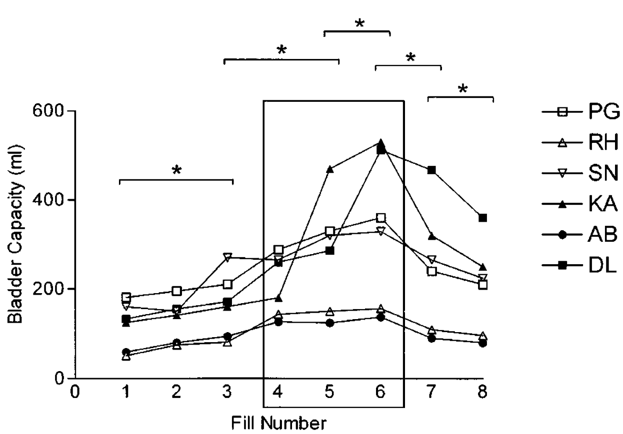

Figure 3 Individual results with continuous neuromodulation. The box encloses the fills with stimulation. Asterisks represent significant differences ($P<0.05$)

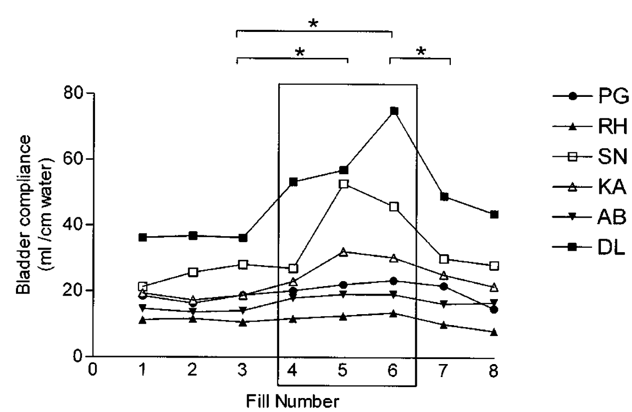

Figure 4 Change in bladder compliance with continuous neuromodulation in six patients. The box encloses the fills with stimulation. Asterisks represent significant differences ($P<0.05$)

The peak of the suppressed contraction ($2x$ in Figure 2) was on average 30 cm H_2O (± 8.7 cm H_2O) above baseline. Several parameters were strikingly similar between patients – the mean time from start of stimulation to peak of suppressed contraction, and time for the contraction to fall to 50% of peak were 2.8 s (± 0.9 s, range 2.3–3.2 s) and 7.6 s (± 1.0 s, range 6.6–8.7 s) respectively (a and b in Figure 2).

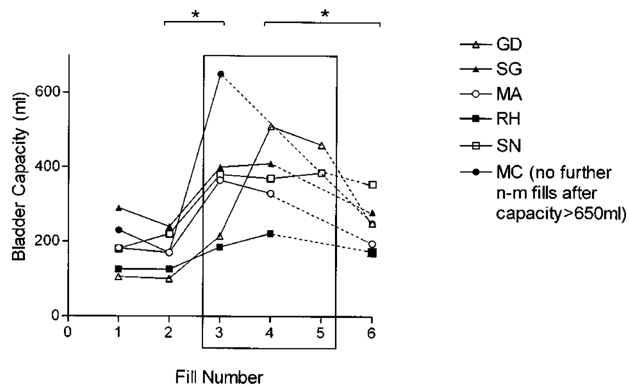

Figure 5 Increase in bladder volume with conditional neuromodulation in six patients. The box encloses the fills with stimulation. Asterisks represent significant differences ($P<0.05$)

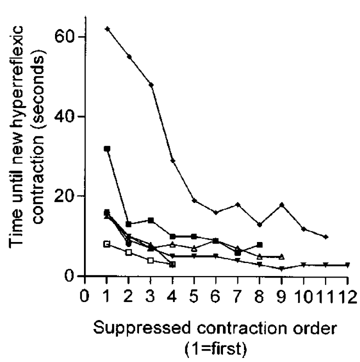

Figure 6 Time between suppressed hyperreflexic contractions during the first conditional neuromodulation fill in seven patients

The initial decay of the suppressed hyperreflexic contraction was approximately fitted by a single exponential function [$y=A+Be^{-t/k}$], with a time constant (k) of 6.9 s ($\pm$0.9 s).

In all cases, the first peak in intravesical pressure was followed by a second, smaller peak after 20.4 s ($\pm$3.0 s) (c in Figure 2). The rise in intravesical pressure over baseline at the height of this second peak (*y* in Figure 2) was on average 42.5% ($\pm$19.1%) of the size of the initial peak.

The mean time taken for the intravesical pressure to decline to within 10% of pre hyperreflexic contraction baseline (d in Figure 2) was 41 s ($\pm$14 s) with only one of 21 measurements longer than 1 min. The mean intravesical pressure during the neuromodulation period was 7.3 cm H_2O ($\pm$1.8 cm H_2O, range 5–10 cm H_2O) higher than the baseline before the onset of hyperreflexia.

Comparison of the two techniques
In the three patients in whom conditional and continuous fills were compared using the alternating protocol (iii), conditional was better than continuous in two out of three cases (Table 2).

In the three patients tested on separate days with each technique (protocol iv), neuromodulation gave greater volume rises in all three patients, and greater percentage rises in two out of three (Table 3).

In five out of the six patients in whom both types of stimulation were compared, the maximum bladder volume achieved with neuromodulation was with the conditional stimulation mode.

Comparison by Frankel grade
The maximum percentage increase in bladder volume using any type of neuromodulation was significantly higher in the group of patients with Frankel D grade lesions compared to the three patients in the incomplete group (mean 143% *vs* 56%, $P=0.028$).

Discussion

The efficacy of neuromodulation
In every patient examined, continuous stimulation increased bladder capacity. The consistency of these results may reflect the benefits of basing stimulation parameters on values derived from optimisation work using provoked contractions.[18] The continuous stimulation results also demonstrate that the order and number of fills must be taken into account when evaluating the effects of neuromodulation. The rise in bladder volume during the three initial control fills in our six patients was significant – this effect has been noted before.[24,25]

The persisting (but diminishing) effect following neuromodulation in the final control fills has also been found before,[7,8] and was probably due to two main factors. Firstly, an initial mechanical distension is likely to diminish afferent discharge from the bladder at a given volume during subsequent fills; such an effect has been shown directly in cats.[23] Secondly, the effects of neuromodulation at the spinal level may persist, consistent with the observation that the beneficial effects of 'maximal electrical stimulation' of the pelvic floor may last for hours or days.[26] However, such maximal stimulation has mainly been used in patients with intact sensation, and two studies of its use in spinal injury showed that it was of limited efficacy at best,[27,28] suggesting that the residual neuromodulatory effect of penile nerve stimulation diminishes rapidly in the first hour. Experiments with provoked contractions confirm this finding.[29]

The largest rises in bladder capacity during this study occurred in patients who had required a high dose of anticholinergics to maintain a high bladder capacity. On stopping these drugs for the study, they often had hyperreflexia at low bladder volumes during control fills. This was effectively suppressed by neuromodulation, enabling them to return to their

Table 1 Patient details

Initials	*Age/y*	*Level*	*Frankel Grade*	*Date of injury*	*Bladder management*	*Daily dose of oxybutinin*	*Protocol used*
PG	38	T10	D	Jan 1995	ISC, condom	15 mg	i
RH	34	T6	D	Jun 1995	ISC	30 mg	i, ii, iv
KA	37	C6	D	Nov 1996	ISC, condom	30 mg	i
SN	36	T6	D	Oct 1995	ISC	30 mg	i, ii, iv
AB	21	C6	D	Apr 1997	SPC	30 mg	i
DL	34	T4	D	Oct 1995	ISC	30 mg	i
GD	46	T3	D	Jun 1995	ISC	30 mg	ii, iv
MF	20	T6	C	Oct 1998	ISC	30 mg	iii
DS	48	L1	B	1973	ISC, condom	none	iii
SG	29	T2	B	1990	ISC	none	ii
MA	32	T3	D	1994	ISC, condom	15 mg	ii
DQ	29	T4	D	Jul 1998	ISC	7.5 mg	iii
DH	29	T7	D	Apr 1999	ISC	22.5 mg	(ii)*
MC	37	T5	D	Mar 1999	ISC, condom	4 mg Tol.	ii

ISC = intermittent self catheterisation; SPC = suprapubic catheter; Tol = Tolterodine; (ii)* = one conditional fill only

Table 2 Results using protocol iii

Patient, protocol	*Control fill volumes/ml*	*Volumes with continuous/ml*	*Volumes with conditional/ml*	*Mean increase with continuous/ml (%)*	*Mean increase with conditional/ml (%)*
MF iii (continuous first)	190, 210, 210	340, 265	310, 285	**99 (49)**	**94 (46)**
DS iii (conditional first)	380, 380	460, 470, 405	470, 500, 450	**65 (17)**	**93 (25)**
DQ iii (continuous first)	160, 170	190, 260	215, 280	**60 (36)**	**83 (50)**

Table 3 Results using protocol iv

Patient, protocol	*Control fills (continuous day)/ml*	*Volumes with continuous stimulation/ml*	*Control fills (conditional day)/ml*	*Volumes with conditional stimulation/ml*	*Mean increase with continuous/ml (%)*	*Mean increase with conditional/ml (%)*
RH iv	75, 81	143, 150	125, 125	185, 222	**69 (88)**	**79 (63)**
SN iv	160, 150, 270	265, 320, 329	182, 180, 220	380, 370, 385	**111 (58)**	**184 (95)**
GD iv	146, 170	280, 320, 480	105, 100	215, 510, 460	**202 (128)**	**309 (301)**

previously high bladder capacity. As expected, patients who were not previously on anticholinergics had less impressive increases, as there is a limit to the distension that can be achieved in a chronically small bladder during 1 day. However, it is possible that neuromodulation over weeks or months would gradually increase capacity beyond the modest acute rises seen here, in a similar way to the gradual increase in capacity seen after posterior rhizotomy.[30] The smaller bladder capacity in our group of patients with incomplete injuries may be accounted for by differences in medication: two out of three of them were not on anticholinergics, while all of the patients with complete lesions were. It is clear that the selection of patients critically affects the results of neuromodulation studies and means that caution is necessary in comparing results from different centres.

Although continuous neuromodulation is an effective and simple way to increase bladder capacity in spinally injured patients, in many situations it is not ideal. The need for constant current delivery would shorten both battery and electrode life in a completely implanted device, and stimulation of sacral afferents has reflex effects on the anal and urethral sphincters. A device which stimulated the mixed sacral nerves for neuromodulation would cause both reflex and direct activation of the sphincters and skeletal muscles. Conditional stimulation might reduce such unwanted effects, and although it requires a method for detecting intravesical pressure, a major possible benefit of this would be the possibility of feedback to the patient about bladder fullness.

Experiments in cats[23] and pigs[22] have shown that it is possible to detect hyperreflexic bladder contractions by recording from the mixed sacral nerve roots, and that these contractions can be suppressed by stimulation of the same roots. Recently, signals have been recorded from a human sacral nerve using a cuff electrode suitable for long term use.[31] This work suggests that an implanted conditional neuromodulation device is feasible, but it will be considerably more complex than a simple stimulator.

Conditional neuromodulation

The combination of slow fill rates and the ability to rapidly switch on stimulation is essential for establishing how effective conditional neuromodulation might be in everyday use; these conditions have not been present in most previous studies, which have used conventional (and more provocative) filling rates of around 50 ml/min.

Filling at 10 ml/min, conditional neuromodulation in this study increased bladder capacity in every patient tested. As with continuous stimulation, the range of increases was wide, so that conditional and continuous modes should ideally be examined in the same patients to compare efficacy. Although the number of patients was too small to answer the question definitively, the results suggest that conditional stimulation is at least as effective as continuous. It was difficult to devise an adequate protocol for comparing the two modes of stimulation: the alternating continuous/conditional strategy for comparison is flawed because it is impossible to eliminate the effects of 'carry over' in a series of CMGs, and comparing results from two different days' testing eliminates the carry over effect but introduces other sources of variation – in particular, varying capacity on the control CMGs, and differing electrode position and stimulation parameters.

The gap between suppressed unstable contractions almost always decreased progressively with increasing bladder volume. This effect resembles the finding that unstable contraction frequency increases with volume in the spinal cat,[32] and may well be useful for the estimation of bladder volume in an implanted system for conditional neuromodulation, because intravesical pressure often rises only a small amount during the stable phase of filling.

Although bladder volume increases with neuromodulation varied widely, the time to peak of suppresssed contractions and time to 50% decline were strikingly similar between patients, suggesting a common mechanism. A mean of 2.8 s from start of stimulation to contraction peak is consistent with a previous observation that the effects of neuromodulation occur after a latency of '1 – 3 s'.[33] The time constant of 6.9 s ($\pm$0.9 s) for the decay of the suppressed pressure is less than the figure of 9.9 s ($\pm$2.6 s) seen with magnetic stimulation of the sacral roots in healthy men,[12] but in the latter study stimulation was for 2 s only. The mean rise in intravesical pressure of 7.3 cm water during conditional neuromodulation suggests that this technique will be safe: in no patient was the rise greater than 10 cm water.

The pressure rise of 10 cm water chosen as a trigger for conditional neuromodulation is necessarily somewhat arbitrary but is similar to the smallest intravesical pressure rises that can currently be detected in animals by recording from the sacral roots.[22,23]

The parameters used for neuromodulation via the dorsal penile nerve

The stimulation period of 1 min was sufficient to bring intravesical pressure to within 10% of baseline in almost all cases (the figure of 10% was chosen to allow for any rises due to low compliance or signal noise). This confirms the results of provocation experiments, where 60 – 70 s was found to be best for minimising the area under the intravesical pressure-time curve,[18] and suggests that 1 min is an appropriate 'on' time for conditional neuromodulation.

We based stimulation current strength on experiments with provoked contractions, and other groups have achieved good results at 2 to 3.5 times the threshold for the bulbocavenosus reflex[7] (which will be similar to the threshold for anal sphincter contraction[34]). One group has specifically examined the influence of current strength on bladder suppression, achieving their best results at twice the threshold and markedly reduced suppression when stimulating at a level equal to the threshold.[24] In the current study, the pudendo-urethral reflex had a lower threshold than the pudendo-anal reflex in a majority of patients, a point which should be borne in mind if using it to set the current level for neuromodulation.

The ideal frequency for bladder suppression is still a matter of debate. Experiments with provoked contractions in humans suggest that 15 Hz is optimal,[18] but in cats this frequency may be too high, with best results at 5 Hz.[35] In one study anal stimulation in humans was equally effective at 5, 10 and 20 Hz,[33] and others have used frequencies between 5 and 20 Hz.[5–9] The numbers of patients in these studies are too small to properly determine the ideal stimulation frequency, so that we relied on findings derived from repeated provocation of unstable contractions.

Dorsal penile nerve vs *sacral foramen stimulation*

One group has examined the acute increase in bladder capacity that occurs with unilateral sacral foramen stimulation in spinal cord injury.[11] The design of the study was different to the one here in several significant ways – in particular, half the subjects were female, there was a single fill with neuromodulation and it is not clear whether anticholinergic medication was continued during the tests. However, the mean increase in bladder volume at first uninhibited contraction reported by this group was 98% (or 207 ml), which is similar to the results described here.

In both cases, the pudendal afferent nerves are stimulated incompletely: sacral foramen stimulation because only one out of six roots that carry pudendal fibres is stimulated, and DPN stimulation because a fraction of S_2 fibres is stimulated bilaterally.

Both techniques stimulate pudendal afferents, and there are several pieces of evidence indicating that afferent stimulation is central to the mechanism of neuromodulation in spinal cord injury. Skeletal muscle paralysis does not abolish the inhibitory effect of pudendal nerve stimulation in cats,[36] and when pudendal afferents from the cat penis are identified and stimulated, marked inhibition of the bladder occurs, while stimulation of pelvic floor fibres has little effect.[37]

The similarity between the two techniques in mode of action and efficacy suggests that DPN stimulation can be used as a non-invasive screening test for the response to neuromodulation before implantation of a sacral root stimulator. It is also likely that conditional neuromodulation will be effective when applied via the sacral nerve roots.

In conclusion, both continuous and conditional dorsal penile nerve stimulation at twice the threshold for the pudendo-anal reflex reliably increased bladder capacity in spinally injured patients, and continuous neuromodulation significantly increased compliance. Conditional neuromodulation was more effective than continuous in the majority of patients, and never resulted in a rise in mean intravesical pressure of >10 cm water. During conditional neuromodulation, the time from start of stimulation to intravesical pressure peak and to fall to 50% of peak is similar between patients. The time between suppressed contractions falls as the bladder fills and might be used as a marker of bladder volume. These results suggest that conditional neuromodulation in a fully implanted device will be effective and is a goal worthy of pursuit.

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