Home use of a wirelessly controlled stimulator to deliver dorsal genital nerve stimulation for suppressing bladder overactivity following SCI

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Abstract: *Incontinence is prominent in neurological patient populations such as Spinal Cord Injury. Electrical stimulation of pudendal afferents can increase bladder capacity and suppress reflex contractions. Presented is a single case study of an SCI subject using surface genital nerve stimulation at home over one week, using a wirelessly controlled stimulator and Android app based diary logger. An increase in voided volumes and time between voids was recorded, though incontinence, characterised by leak event rate and ICIQ score, remained unchanged.*

Keywords: *Bladder, Spinal Cord Injury, Incontinence, Dorsal Genital Nerve Stimulation, Neuromodulation*

Introduction

Following spinal cord injury (SCI), neural control of the Lower Urinary Tract (LUT) becomes aberrant. This leads to the development of Neurogenic Detrusor Activity (NDO) and Detrusor-Sphincter-Dyssynergia (DSD) affecting the LUT's ability to store and void urine. During storage, high intra-detrusor pressures and urinary incontinence become common, therefore urological management goals for storage of urine are to enable low pressures and maintain continence [1].

Electrical stimulation of sacral afferents can acutely inhibit NDO, reducing pressures and maintaining continence. This may be achieved superficially by stimulating the Dorsal Genital Nerve (DGNS), a purely afferent and superficial branch of the pudendal nerve, by applying electrodes to the dorsum of the penis or over the clitoris. DGNS is thought to both stimulate the striated sphincter and project onto autonomic pathways at a spinal level to inhibit detrusor activity [2]. It has been shown in standard cystometry studies to increase bladder capacity by 131 ± 101 ml, from 212±131 ml without DGNS to 343±159 ml with DGNS [3].

DGNS may be applied continuously or conditionally, having been shown to be equivalent in acute urodynamic study [4]. Continuous stimulation raises potential issues with habituation and device battery life, therefore a robust conditional stimulation paradigm is viewed as the gold standard option. Conditional stimulation requires knowledge of bladder activity to be fed back to appropriately trigger stimulation. This feedback may be provided automatically in a closed loop system utilising a means of physiological monitoring, or through a user's preserved sensation.

Numerous efforts have been made to enable physiological detection of NDO in a manner suitable for chronic implementation, recent options include implantable vesical pressure measurement combined with context aware thresholding of bladder events [5], use of external anal sphincter EMG [6] and implantable devices capable of measuring sacral afferent ENG [7]. However, none have yet been implemented as a viable option for chronic treatment and there are questions regarding chronic use of DGNS, such as the appropriateness of using sensation as a trigger or of electrode configurations and whether reflex inhibition is habituated with long term use, that may already be investigated using available techniques.

To date, the majority of chronic studies using DGNS have recruited sensate patients, able to trigger their own stimulation conditionally [8-10]. This has predominantly been shown to be a valid approach [8-10], however issues with easy access to stimulation trigger in some patients may be a limiting factor [11]. Further to this, whilst there is a large proportion of persons with SCI who possess some degree of pelvic sensation, there is a portion of these for whom the ability to detect unwanted bladder contractions may be too late to trigger conditional neuromodulation and further proportion who have no sensation at all [11, 12].

We hypothesised that by implementing stimulator control on an easily accessible User Interface (UI) we may increase acceptability of the technique and reduce problems associated with access to stimulation triggers. The design of this system has been outlined previously [13].

We present a case study of DGNS use in the home environment over one week using the described device, with a participant who had some preserved sensation.

Methods

Ethical approval was obtained from our local ethics board and the study was conducted in accordance with the Declaration of Helsinki.

System used

The stimulation system used consists of four components. Commercially available 2.5cm round electrodes (PALS®, Axelgaard Manufacturing Co., Ltd.) were used along with commercially available Odstock Medical Pace stimulator (Odstock Medical Ltd.) modified to deliver 15 Hz stimulation. The traditional foot switch has been replaced with

a Bluetooth low energy (BLE) connected switch, consisting of a MOSFET switch controlled by a BLE microcontroller with power source. This switch receives a stimulation profile and switching updates from a custom Android application. To stimulate the DGN electrodes were placed on the dorsum of the penile shaft. Electrodes were placed approximately 2cm apart, the cathode was placed proximally. Stimulation was set to 200µ S pulse width and biphasic.

Figure **1**: Wireless version of Odstock Pace stimulator with custom Android app

Experimental protocol

The experiment was carried out in 3 phases: a screening assessment where the participant underwent cystometry (CMG) to test for NDO and test the suppressive effect of DGNS, a control week completing a bladder diary whilst continuing usual care and an experimental week completing a bladder diary whilst using DGNS on top of usual care.

To assess the effectiveness of DGNS the participant first underwent CMG [14] to record baseline and "with stimulation" bladder pressures and capacity. During these tests the participant was supine. A 10.5 Ch catheter was placed urethrally and used to fill the bladder with room temperature saline at 60ml/min. Pressure was measured using Medex (Smiths Medical) pressure transducers placed at the level of the pubic synthesis, through 4.5Ch water filled catheters placed urethrally to measure vesical pressure (P_{ves}) and rectally to measure abdominal pressure (P_{abd}). Detrusor pressure was calculated as Eq. 1.

$$P_{det} = P_{ves} - P_{abd} \qquad (1)$$

Infused volume was measured using a weight transducer. Signals were amplified using a CED 1902 isolated amplifier, digitised through a CED 1401 and recorded on Spike 2 software (Version 4, Cambridge Electronic Devices, UK) used to display data and trigger stimulation. To threshold stimulation amplitude, 15Hz bursts of one second were given in increasing amplitudes until 2x the threshold for contraction of the external anal sphincter (EAS_{thresh}), detected visually, was reached. Stimulation was monophasic and delivered by a constant current stimulator (DS7, Digitimer, UK).

CMG was performed without stimulation, with DGNS applied at a rise of 10 cm_{H2O} and again without stimulation. First Detrusor Contraction Volume (FDCV), Maximum Cystometric Capacity (MCC) and Maximum Detrusor Pressure (MDP) were used for analysis.

A baseline bladder diary was then completed using the smartphone app. Leakage events, volume voided, urgency sensations and fluid intake was recorded over 6 days in the participant home. From this diary, the time between Clean Self Intermittent Catheterisation (CSIC) was calculated, excluding overnight periods.

Following the control week, the participant was set up with the Pace stimulator and wireless controller. The amplitude was set to as close to 2 x EAS_{thresh} as was tolerable. Stimulation was biphasic, 15Hz and set to 200µS pulse width. The stimulation mode was then set to User Controlled only, based on the participant having sensation of bladder activity. The participant then used DGNS at their discretion, to suppress bladder overactivity, over the following week at home whilst recording the same diary.

The International Consultation on Incontinence Urinary Incontinence Short Form (ICIQ UI-SF) was used as an additional measure, completed at the end of the control week and the end of the DGNS week. The ICIQ-UI Short Form is a brief patient-completed questionnaire for evaluating the frequency, severity and impact on quality of life of urinary incontinence in men and women.

Results

Participant characteristics

One 69-year-old male with a C5, ASIA D, SCI was recruited. Current bladder management was CSIC on urge, with chronic incontinence managed using pads and 10mg Oxybutinin od. Previous intra-detrusor botulinum type-A injections had been administered, though none in the preceding 12 months.

Baseline cystometry

Stimulation amplitude was set to 45mA, the maximum tolerable level, at 1.5 x EAS_{thresh}. Baseline CMG without stimulation had a mean volume from onset of NDO to MCC of 18ml, this increased to 125ml when DGNS was applied at onset of NDO. Results are shown in Tab. 1 and raw CMG traces in Fig. 2 below. No decrease in MDP was found, although two detrusor contractions were suppressed with increasing P_{det}.

Table 1: Standard CMG results. Including volume infused at first detrusor contraction (FDCV), Maximum Cystometric Capacity (MCC) and Maximum Detrusor Pressure (MDP)

Fill	FDCV/ml	MCC/ml	MDP/cm_{H2O}
Control 1	92	109	67
DGNS 45mA	71	196	60
Control 2	95	114	45

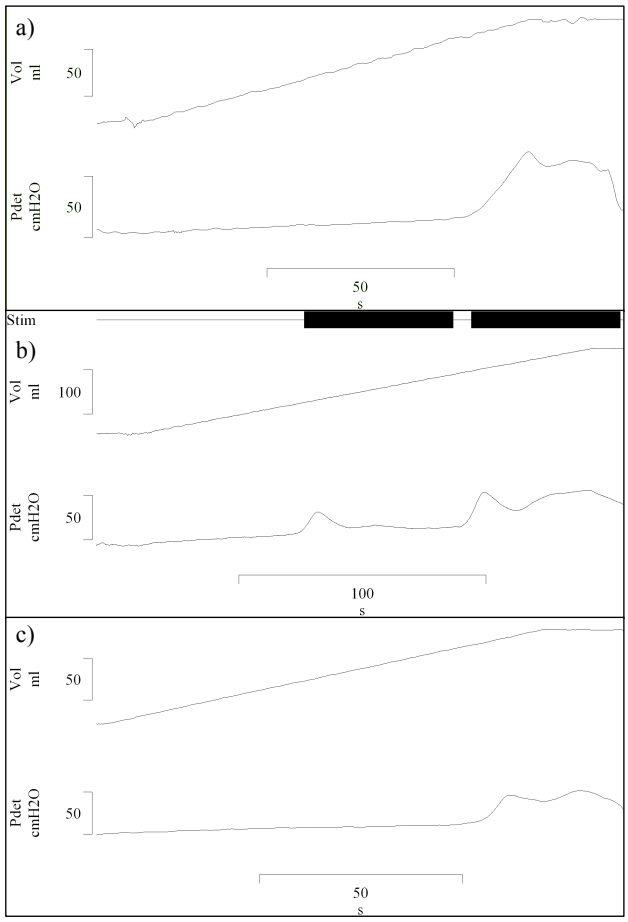

Figure 2. a) Control CMG performed prior to use of stimulation b) DGNS CMG, where stimulation was triggered at a rise in P_{det} for 60 seconds c) Control CMG performed following the with stimulation CMG.

Control week

Recordings were made on 6 days, volume output ranged from 150 to 660ml, mean 298ml. Fluid intake was not recorded. There was a range of 2-5, mean 3, reported episodes of incontinence a day and the ICIQ UI-SF score following this week was 14.

DGNS week

Stimulation amplitude was set to 50mA on the Pace, only 1.25x EAS_{thresh} recorded on the day. DGNS was used on 4 days, with a voiding volume range over this period of 250-600ml, mean 371ml. Fluid intake was not recorded. Reported incontinence events and the ICIQ UI-SF score remained at 3/day (range 2-4) and 14 respectively.

Table 2: Diary results including: volume voided expressed as mean ± standard deviation; incontinence events recorded per day expressed as mean; time between CSIC expressed as mean ± standard deviation, calculated excluding overnight periods; ICIQ UI-SF score

	Vol (ml)	Leak/day	Time between CSIC	ICIQ
Control	298 ±128	3	2hr04 ± 1hr14	14
DGNS	371±112	3	5hr33 ± 2hr20	14

Discussion

The increase in void volume reported here of 73ml, or 25%, is a modest improvement. Acute studies have seen a mean increase of 131 ± 101 ml (62%) [3], whilst previous studies of DGNS use at home have reported increased void volumes of 145ml (72%) [8], and of 12% [10]. There was a large increase in time between voids whilst using DGNS of 3 hours 29 minutes, compared with 42 minutes reported in another case study [8].

Despite the increased volume and time between CSICs the leak event rate and ICIQ score remained unchanged. We know stimulating the pudendal nerve has a limited capacity to suppress ongoing NDO, average number of detrusor contractions suppressed has been 3 [15] and 4 [6]. One contributing factor may be an insufficient amplitude of stimulation, which was set to 1.25 x EAS_{thresh}, below what we consider to be optimal. It may be that the incontinence episodes were offset but not avoided or the case that the participant delayed time between voids for as long as possible, to test the DGNS. As reported by Martens et al. [11], better assessment of the reliability of individual's sensation as a trigger would be valuable.

Stimulation was tolerated well by the participant and no side effects were reported. Autonomic Dysreflexia (AD) remains a risk for SCI patients, generally it has not been reported [8-10] and sharp rises in blood pressure found during NDO have been decreased previously using DGNS [16]. Symptoms of AD were not reported in the presented case.

The application of surface electrodes to the skin of the penis/clitoris has been problematic in previous reports, understandably. This was not reported as a problem by the participant.

Sensation of bladder activity may be present in a majority of SCI patients, one study reporting partial or totally preserved sensation in 77% of the population tested, including in 67% of the 52 complete SCI patients included [12]. To use non-continuous stimulation in SCI persons with no sensation, it may be possible to delay the onset of NDO, triggering DGNS following a set interval based on a preceding bladder diary so as to cover periods of time where incontinence events occur. This functionality is in the developed system [13].

The system was found to trigger stimulation reliably and to provide an accessible UI for a tetraplegic to trigger stimula-

tion. It is necessary to test the system further and as such further case studies of DGNS are planned. The reported results are, of course, limited as this is a single case study and all measures were self-reported. Patient controlled, transcutaneous DGNS remains an intriguing possibility for treatment.

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