211

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CONDITIONAL NEUROMODULATION USING TRANS-RECTAL STIMULATION IN SPINAL CORD INJURY

Hypothesis / aims of study

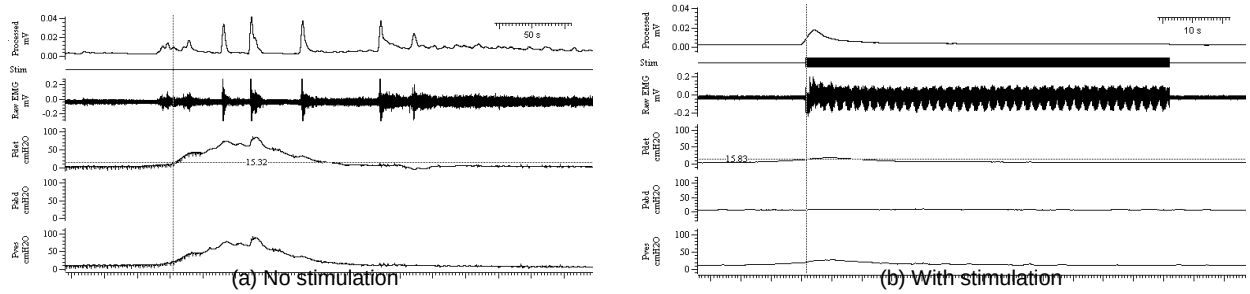
A supra-sacral spinal cord injury (SCI) invariably results in neurogenic detrusor overactivity (NDO). NDO is often exacerbated by detrusor-sphincter dyssynergia (DSD) to cause seriously high detrusor pressures which may compromise renal function. However, NDO can be suppressed using relatively high doses of anti-muscarinic drugs, which also improves bladder capacity, but these drugs have some bothersome side-effects including dry mouth and constipation. Recently, a novel "conditional neuromodulation (CN)" device (1) for wearing in the anal canal has been developed. The device was designed to suppress NDO automatically by applying electrical stimulation trans-rectally to the mixed pudendal nerves in response to dyssynergic electromyographic (EMG) activity detected in the external anal sphincter (acting as a surrogate for the striated urethral sphincter). The aim of this study was to test the efficacy of the device in a preliminary clinical study on people with spinal cord injuries.

Study design, materials and methods

With Research Ethics Committee approval and informed consent six male subjects aged 18-75 with complete or incomplete supra-sacral SCI and proven NDO were included. Each subject was requested to stop their anti-cholinergic drugs for up to 5 days prior to the tests. Following insertion of the device into the anal canal/rectum a standard cystometrogram (CMG) at 10ml/min was recorded while monitoring rectified-smoothed sphincter EMGs through the device's electrodes. This CMG provided a control NDO with DSD from which a threshold was set to deliver stimulation (constant current at 15 pulses/s for 60s) at a pre-determined level through the device's rectal electrodes to produce a good anal sphincter contraction. This became the level used for repeated CN of NDO. Suppression of maximum detrusor pressure and the increase in bladder capacity following repeated CN were the outcome measures compared with those during non-stimulated controls and tested for significance using a Wilcoxon Signed Rank test.

Results

All six subjects demonstrated successful CN of NDO. Figure 1 shows a typical result in one subject (AA) with and without CN during a single NDO contraction.



(a) No stimulation (b) With stimulation

Figure 1: Pves, Pabd and Pdet represent the bladder, abdominal and detrusor pressure respectively. EMG of the anal sphincters represents in "Raw EMG" and the rectified-smoothed EMG used for triggering is shown as the "processed" signal. (a) shows NDO contraction; (b) shows CN through the device using a threshold of 0.04mV in the processed signal to trigger the stimulation.

Figure 2 shows the effect of conditional stimulation in the same subject repeatedly suppressing a series of NDO

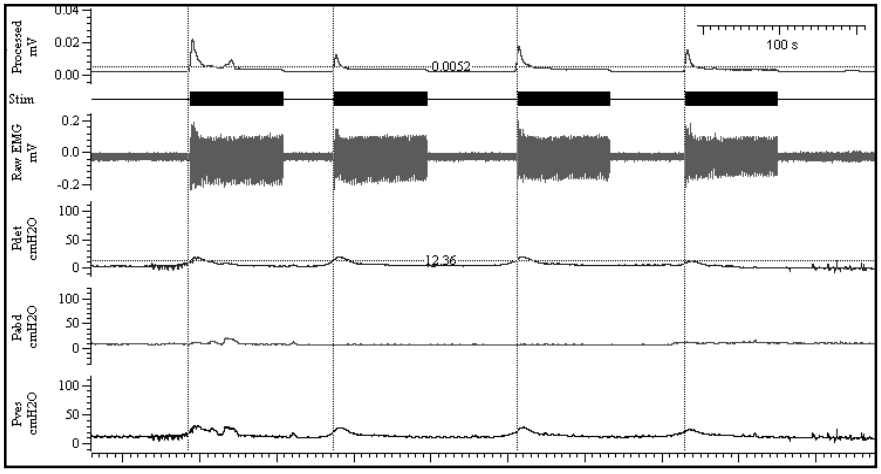


Figure 2. Four repeated conditional neuromodulations in subject (AA) consistently suppressing NDO. An EMG threshold was set as shown in Figure 1.

Table 1 Shows the results of CN on maximum Pdet and bladder capacity changes compared with control values across all six subjects.

Table 1.

Subject	Control P_{det} max (cm of H_20)	P_{det}max with CN. (cm of H_20)	Control bladder capacity (ml)	Bladder capacity with CN (ml)
RG	72	13	110	418
BB	120	17	128	358
ES	147	46	105	331
CC	60	29	115	333
PK	83	57	87	381
AA	89	27	150	500
Mean	95.2	31.5	115.8	386.8
S.D.	29.6	15.5	19.6	58.7
p	**≤0.001**		**≤0.001**	

Interpretation of results

EMG threshold proved to be a reliable source for triggering stimulation.

In all six subjects repeated conditional neuromodulation both significantly suppressed NDO (Pdetmax) and increased bladder capacity. Across the subjects the mean maximum detrusor pressure was reduced from 95 cmH_2O to 31 cmH_2O ($p \leq 0.001$)and the mean bladder capacity increased from 115ml to 380ml ($p \leq 0.001$).

In these subjects continence was achieved as a result of both suppression of NDO and activation of the sphincter during trans-rectal stimulation of the mixed pudendal nerves bilaterally.

Concluding message

These results have demonstrated the utility of a novel wearable device for conditional neuromodulation of NDO in spinal cord injury. It remains to be seen if such results are repeatable over the longer term. Tests are now planned to assess the device's performance and durability in activities of daily living. This device could be a suitable alternative for those patients not wishing to have an implantable device and by delivering stimulation in a conditional way is less likely to show reduced efficacy through habituation of spinal reflex pathways.

References

1. Craggs MD (WO/2007/101861) Neuromodulation device for pelvic dysfunction. Patent 6 March. 2006

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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Royal National Orthopaedic Hospital NHS Trust/ National Research Ethics System, UK**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**