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CONDITIONAL FUNCTIONAL ELECTRICAL STIMULATION FOR URINARY INCONTINENCE

Hypothesis / aims of study

Neuromodulation to treat idiopathic overactive bladder by activating afferent fibers in sacral and pudendal nerves has demonstrated clinical efficacy [1,2]. However, majority (54%) of the patients with urinary incontinence still have incontinence episodes at 3 years after implant [1]. We studied whether functional electrical stimulation (FES) designed to activate efferent fibers in the pudendal nerve to close the urinary sphincter applied only at the onset of nascent bladder contractions would increase bladder capacity and "warning" time from the first contraction to when continence is lost compared to continuous afferent stimulation (CAS).

Study design, materials and methods

CAS and FES were studied in five isoflurane anesthetized intact male dogs (24-32 kg). A tripolar cuff electrode was placed on the pudendal nerve trunk. A triple lumen catheter was inserted through the urethra into the bladder to both fill the bladder with a 0.4% acetic acid saline solution at 10 ml/min and to record bladder pressure (P_{bla}) and the urethral pressure at the level of the sphincter (P_{us}). The FES parameters were titrated at the frequency that generated the maximum sustained P_{us} while applying 40 s trains of current pulses of varying frequency (20-50 Hz) with the amplitude at the threshold of generating maximum urethral pressure. The CAS was titrated at a frequency of 14 Hz and amplitude at the level that elicited a threshold anal EMG response but did not generate a P_{us} response. The bladder filling and voiding tests were performed with no stimulation, CAS only (continuous afferent stimulation delivered throughout the duration of the filling), FES only (conditional FES delivered at the onset of a bladder contraction), and CAS plus FES (CAS is replaced with FES at the onset of a bladder contraction and resumed after the FES duration ended). The bladder capacity (filled volume when 1 ml fluid exited the meatus) and the warning time (time from the onset of the first contraction to when 1 ml fluid exited the meatus) were evaluated. The conditional FES was controlled using P_{bla} as the input to an event triggered system. The duration of the FES stimulation was 40 s, after which the system was allowed to retrigger if another bladder contraction was detected. There was a minimum of 2 filling trials of each type of stimulation per dog and the order of the stimulation conditions was randomized.

Results

The CAS parameters were selected as 14 Hz and 0.20±0.06 mA (mean±SD) and the conditional FES parameters were 40 Hz and 0.8 mA in all 5 dogs. At a frequency of 40 Hz, FES provided high peak P_{us} and high P_{us} at the end of stimulation duration of 40 s. An example of P_{us} due to FES at different stimulation frequencies is shown in Fig. 1.

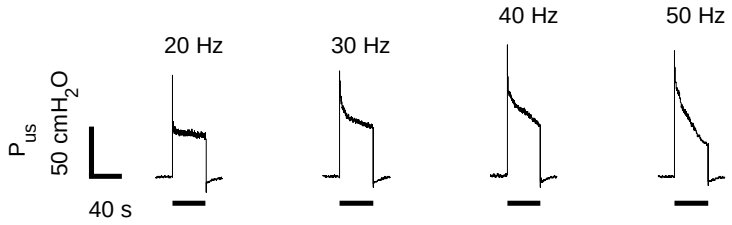

Fig. 1. Example of the P_{us} with different stimulation frequencies (amplitude 0.8 mA, pulse width 210 µs). Bars under pressure responses denote the duration of the stimulation pulse train.

The bladder capacity was 64±12 (mean±SD) ml with no stimulation, 70±16 ml with CAS only, 98±24 ml with FES only, and 103±17 with CAS plus FES (Fig. 2A). Conditional FES increased bladder capacity by 53% over no stimulation and by 40% over CAS only (one-way ANOVA and post hoc Fisher's pairwise comparisons, p=0.02 and p=0.04 respectively). CAS plus FES increased bladder capacity by 60% over no stimulation and by 47% over CAS only (p=0.008 and p=0.02, respectively). The bladder capacity with CAS only showed a slight trend of increase compared to that with no stimulation but it was not statistically significant. The bladder capacity with CAS plus FES did not differ significantly from that with FES only. The warning time was 9.1±4.9 s with no stimulation, 10.8±5.5 s with CAS only, 213.4±59.9 s with FES only, and 195.9±78.6 s with CAS plus FES (Fig. 2B). The warning time with FES only and CAS plus FES was 22 and 21 times longer than that with no stimulation ($p<0.0001$ for both) and 19 and 17 times longer than that with CAS only ($p<0.0001$ for both). There was no statistical significance between the warning time with no stimulation and that with CAS only and between the warning time with FES only and that with CAS plus FES.

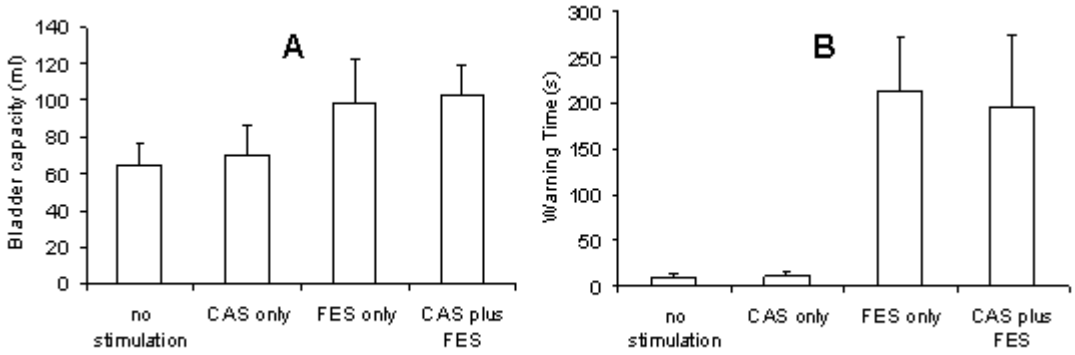

Fig. 2. Bladder capacity (A) and warning time (B) with no stimulation, CAS only, FES only, and CAS plus FES.

Among the bladder contractions in all dogs to which FES was applied (n=132), 57% of them (n=75) were inhibited by the FES (defined as P_{bla} returning to baseline within 10 s of FES) and the remaining contractions (n=57) were not. There was no statistical significance between the peak P_{bla} of contractions not inhibited by the applied FES (86±16 cmH_2O) and that of the contractions without FES (84±14 cmH_2O), although the peak P_{bla} of contractions inhibited by FES (45±7 cmH_2O) was significantly smaller than the peak P_{bla} of contractions without FES (p=0.001).

Interpretation of results

In a previous study conditional stimulation (5-15 Hz, 2 to 4 times the pudendo-anal reflex threshold) designed to activate the afferent inhibitory pathways to suppress bladder contractions increased bladder capacity compared with continuous stimulation of the same parameters [3]. In our study the conditional FES was optimized to activate efferent pathways to close urethral sphincter temporarily to prevent incontinence. Nevertheless the inhibition of 57% of the bladder contractions by FES suggested possible dual functions of activating both afferent inhibitory pathways and closing the urinary sphincter. With no stimulation and CAS we observed leakage upon the first bladder contraction in all dogs but one (reflected by the mean warning time of about 10 s), whereas with FES the leakage was usually much delayed due to the sphincter closure upon contractions (reflected by the mean warning time of > 3 min). FES repetitively triggered upon bladder contractions may be susceptible to sphincter muscle fatigue especially when the time intervals between the bladder contractions were small. Incontinence may still be prevented if there is enough warning time to allow a delayed voluntary voiding during which the FES is deactivated. It is worthy to note that the peak bladder pressure during bladder contractions did not increase during FES compared to no FES in this data set, which suggests that closing the urinary sphincter temporarily upon contractions may not impose a safety concern. It is unknown whether the sensation due to the FES in awake subjects is tolerable.

Concluding message

Functional electrical stimulation (FES) designed to activate efferent pathways to close the urinary sphincter applied only at the onset of bladder contractions increased bladder capacity and the “warning” time from the first contraction to when continence is lost compared to continuous afferent stimulation on the pudendal nerve in dogs. Further studies on the clinical safety and efficacy of this treatment are warranted.

References

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Specify source of funding or grant	**Medtronic Inc.**
Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**The Institutional Animal Care and Use Committee at Medtronic Physiological Research Laboratories, Minneapolis, USA.**