Neurographic recordings, electrical stimulation and new neural signal processing methods for closed-loop neuroprosthetic control of bladder hyper-reflexia

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ABSTRACT

Individuals with spinal cord injury and other persons with neuropathic bladders develop bladder hyper-reflexia. We are developing an implantable neuroprosthesis to restore bladder function in these individuals using electrical recordings from, and stimulation of, nerves innervating the lower urinary tract. Six experiments were conducted on cats and hyper-reflexive-like bladder contractions were induced by isometric cystometry. Nerve cuff electrode recordings from the S1 spinal nerve root provided robust detection of bladder contractions. Electrical stimulation of the S1 dorsal root was able to terminate an ongoing reflex bladder contraction. S1 nerve signals were also recorded during the activation of the cutaneous and rectal receptors. A method for Wiener filter design to optimize S/N ratio was developed, and it was possible to improve the S/N ratio by 97%, and also to increase the modality selectivity of the recordings. Techniques to differentiate and classify different increases of sacral nerve root activity that arose by activation of different receptors were examined. Significant differences in the shape of the nerve signal autocorrelation functions were observed during activation of different receptors. A neural network was trained to classify nerve signals and recognize noise, and 87.5% correct classification among 4 classes was achieved. These results indicate that electrical recordings can be used to recover sensory information from the nerves innervating the lower urinary tract, and that signal processing and classification techniques enable greater recovery of information.

Keywords: bladder hyper-reflexia, natural sensors, nerve cuff recording, bladder control, signal processing

INTRODUCTION

Millions of individuals develop bladder hyper-reflexia (overactivity of the bladder), which causes serious medical problems including kidney damage, urinary infections, and bladder calculi, as well as creates psychological and social barriers 1,2). Several treatments exist to regain bladder control, but many times they are unpleasant and/or ineffective. An alternative to regain bladder control is an implantable, neuroprosthetic device 2). Brindley sacral anterior root stimulator 3) uses electrical stimulation to empty the bladder, and bladder overactivity is abolished by transection of sacral dorsal roots. The latter procedure has the drawbacks that it abolishes sensation and useful reflexes (e.g. reflex erection in man, reflex bowel emptying). To avoid transection of the sacral dorsal roots, we are developing a novel bladder neuroprosthetic device that would: 1) detect hyper-reflexive bladder contractions by recording sensory information arising from bladder afferents, 2) inhibit bladder contractions by electrical stimulation, and if necessary 3) determine bladder volume, and empty the bladder by electrical stimulation 4). Bladder afferent sensory information can, for example, be recorded by nerve cuff electrodes placed around the pelvic nerve or sacral roots 5). However, because these nerves are mixed, it is necessary to develop methods to increase selectivity of the neurographic recordings, and to classify nerve activity according to its origin. Further, because nerve signals are small in amplitude, there it is beneficial to increase the S/N ratio of the recordings. Signal processing methods (Wiener filtering, neural network classification, maximum likelihood detection) were developed and used to increase the S/N ratio and modality selectivity of neurographic recordings, to classify different nerve signals, and to detect hyper-reflexive bladder contractions. It was also shown that bladder contractions could be terminated by electrical stimulation of the S1 dorsal root.

METHODS

Animal experiments: The experiments were performed according to NIH guidelines and were approved by the CWRU Animal Care and Use Committee. Intact male cats (n=6, 3.5-4.3 kg) were anaesthetized (initial anaesthesia: ketamine-HCl, maintained with alpha-chloralose), intubated and respired. A transurethral catheter was inserted into the bladder and the urethra ligated. The catheter was connected to a pressure transducer or to an infusion pump. Another catheter with a balloon was inserted into the rectum. A lumbosacral laminectomy was performed to expose the sacral roots. Saline was infused into the bladder at 2.5 ml/min until supraspinal isovolumetric bladder contractions were induced. The infusion was then discontinued, but the quasiperiodic hyper-reflexive-like bladder contractions continued.

Nerve cuff recording: Bipolar silicone rubber cuff electrodes were placed around the extradural S1 sacral root, and in one experiment around the S1 dorsal and ventral roots. The cuffs were 6-15 mm in length, had inner diameters of 1.0-1.8 mm, and contained platinum ring contacts. Nerve cuff signals were recorded during excitation of bladder afferents (bladder contractions, rapid injections of saline into the bladder), rectal afferents (rectum was distended by inflating the rectal balloon), and cutaneous afferents (mechanical stimulation of the sacral dermatomes). The nerve signals were amplified and band-pass filtered 100-3000 Hz (raw ENG). Raw ENG was rectified and time-averaged=<|ENG|>, and further low-pass filtered off-line. The signals were digitized and stored on a VCR tape.

Electrical stimulation: Stimulation of the dorsal S1 root was performed in one cat to inhibit bladder contractions. The stimulation parameters were: 2-19 monophasic pulses at i=0.6 mA, f=1-2 Hz, PW=100 µs.

Signal processing: A maximum likelihood detection algorithm (cumulative sum=CUSUM algorithm) was used to detect increases in the <|ENG|> and thereby to detect the onsets of bladder contractions. This detection algorithm was compared to simple thresholding.

Wiener filters were designed for different receptor types using an artificially generated nerve cuff signal. The latter was constructed by random superposition of several action potentials recorded in another experiment on the porcine pelvic nerve following S3 root stimulation 6). The autocorrelation function of the artificial nerve cuff signal, properly scaled in time, and the autocorrelation function of the actual nerve cuff recordings were used to calculate Wiener FIR filter coefficients. S/N ratios of nerve cuff recordings before and after the filtering were compared. S/N ratio was defined as variance of the nerve signal divided by variance of the background noise.

We also calculated the autocorrelation functions of recordings made during the activation of cutaneous, bladder, and rectal mechanoreceptors, and the autocorrelation function when recording from a nerve that was transected proximally and distally to the cuff electrode. The latter autocorrelation function thus contained only noise and no true nerve signal. A multilayer perceptron with 2 hidden layers (hidden layers had 15 and 10 neurones) was trained with different autocorrelation functions described above, to classify nerve signal increases according to their origin (4 classes were used: cutaneous, bladder, rectal, and noise). A separate validation data set from all cats was used to evaluate the performance of the neural network after the training.

RESULTS

A. Detection of reflex bladder contractions

Reflex bladder contractions occurred in 5 of 6 cats. During bladder contractions bladder pressure increased by 30±17 cm H_2O, and the S1 root activity increased by 18±7% above baseline (n=30 contractions). The onset of reflex bladder contractions could be detected from increases in the S1 <|ENG|> using a simple thresholding of the estimated S1 <|ENG|> mean, μ_{est}. Use of the CUSUM algorithm enabled more reliable detection with fewer false positives and more correct detections. 29 of 30 contractions were detected within 6±8 s after the onset of the bladder contraction, when the pressure rose by 9±8 cm H_2O above the baseline. An example of simple thresholding and CUSUM detection is shown in Fig.1.

B. Inhibition of reflex bladder contractions

In one animal, the S1 dorsal root was electrically stimulated after the onset of a reflex bladder contraction. This resulted in termination of reflex bladder contraction. The terminated contractions were thus shorter (22±3 s, n=4) than the control contractions (81±17 s, n=9). One control and one terminated bladder contraction can be seen in Fig.2.

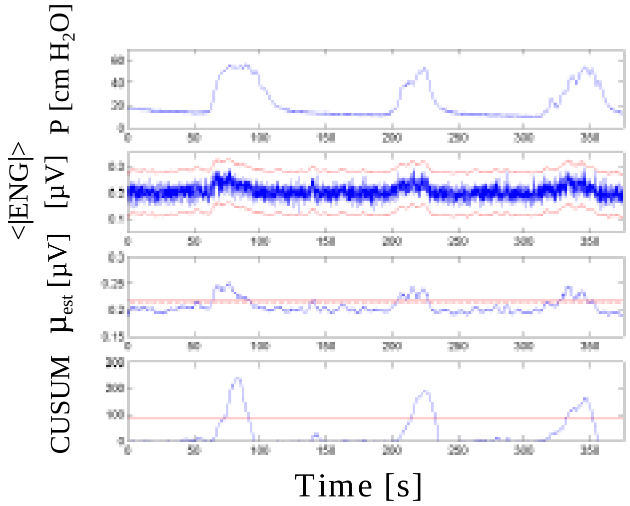

Fig.1: Bladder pressure, rectified and time-averaged nerve signal, estimated mean, and CUSUM detection during three reflex bladder contractions.

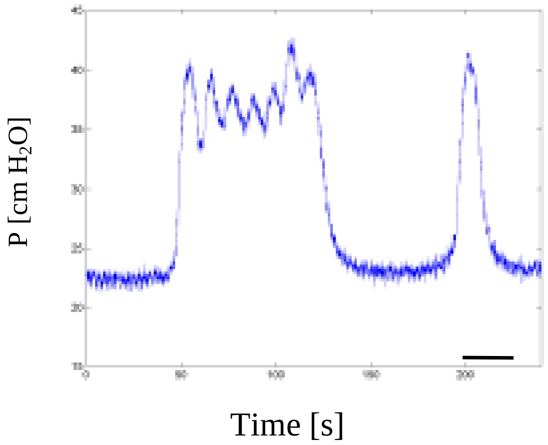

Fig.2: Bladder pressure during control reflex bladder contraction, and during bladder contraction terminated by electrical stimulation of the dorsal S1 root (bar).

C. Wiener filtering of nerve cuff recordings

16 different nerve signals from 4 cats recorded during activation of different receptors were filtered with corresponding Wiener filters designed for cutaneous, bladder, and rectal afferents. Wiener filtering improved the S/N ratios of the nerve signals by 33±21%, 144±101%, and 41±16% for the different receptor types respectively. The average improvement across all animals was 97±93%. The modality selectivity of the recordings was also increased: Wiener filters designed for rectal afferents increased the signal during the activation of the rectal receptors, but decreased it during the activation of cutaneous receptors, and also decreased the noise spike artifacts. Nerve signal recorded during rapid injection of saline into the bladder that excited bladder afferents is plotted together with the Wiener filtered signal in Fig.3.

D. Classification of nerve signals

Significant differences in the shapes of the nerve signal autocorrelation functions were observed during activation of different receptors. The mean times of the first zero-crossing of the autocorrelation function after the first minimum was reached were 1.39±0.35 ms (n=26, 3 animals), 1.86±0.42 ms (n=66, 4 animals), and 2.96±0.55 ms (n=18, 2 animals) for cutaneous, bladder, and rectal receptors respectively. Nine examples of autocorrelation functions calculated during activation of different receptors are plotted in Fig.4 (cat 6 recordings). A multilayer perceptron with 20 input neurones and 2 output neurones was trained with first 2.375 ms of different autocorrelation functions. Data originating from cutaneous, bladder, rectal receptors, and noise was split for training and validation as follows: 22/12, 44/25, 13/7, and 24/12 autocorrelation functions respectively. The classification results were: 87.5%, 88%, 71.4%, and 100% correct classification for cutaneous, bladder, rectal receptors, and noise.

Fig.3: Wiener filtering increased the S/N ratio of the nerve cuff recording (T_s=0.125 ms).

Fig.4: Autocorrelation functions R_{xx} recorded during activation of cutaneous, bladder, and rectal receptors.

DISCUSSION AND CONCLUSION

It was demonstrated that S1 nerve root recordings made by cuff electrodes can be used to detect bladder contractions after only a small increase in the bladder pressure. The CUSUM algorithm enabled a reliable detection of changes in the rectified and time-averaged nerve signal. It was possible to terminate an ongoing bladder contraction by electrical stimulation of the S1 dorsal root. Methods were developed to classify nerve activity according to its origin and thus to detect increases originating from bladder afferents only. Autocorrelation functions had different shapes when the nerve activity originated from different receptor types. This allowed classification of nerve signals, and also of noise, using a neural network. A method was also developed to design Wiener filters for neurographic recordings, which resulted in improved modality selectivity of the recordings, and increased the S/N ratios of the nerve signals to better detect signal changes.

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