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SELECTIVE ACTIVATION OF PUDENDAL NERVE BY SKIN SURFACE ELECTRODES TO INHIBIT BLADDER ACTIVITY

Hypothesis / aims of study

Our previous study has shown in normal cats under anesthesia that transcutaneous electrical stimulation with a novel stimulation waveform could inhibit bladder activity when it was applied to the skin area between the base of the tail and the sciatic notch. At this stimulation site it is possible to activate either pudendal nerve or tibial nerve (a branch of sciatic nerve). Previous clinical studies reported that both pudendal and tibial nerve stimulation could significantly inhibit bladder activity. The goal of this study was to further investigate the selectivity of this non-invasive transcutaneous stimulation method in order to identify whether the stimulation activated pudendal or tibial nerve when bladder inhibition was induced. This preclinical study is aimed at developing a selective transcutaneous stimulation method to treat overactive bladder and prevent incontinence.

Study design, materials and methods

The Selective Nerve Stimulation (SNS, known as “Project SyNapSe”) device provides non-invasive neurostimulation through a controlled, amplitude-modulated waveform. This carrier waveform is designed to be of sufficient frequency to overcome skin and tissue impedance. The pulse envelope contains selective frequency, pulse width, amplitude, and shape waveform that designed to stimulate specific nerves. In the present study, the SNS method was used to activate the pudendal-to-bladder inhibitory reflex non-invasively in 12 normal female cats under α-chloralose anesthesia. A pair of self-adhesive surface pad electrodes was attached to the skin area between the base of the tail and the sciatic notch after removal of the fur. A high-frequency sinusoidal waveform, modulated by a low-frequency (5 Hz) electrical pulse, was delivered to the skin via the pad electrodes at different intensities. The stimulation intensity threshold (T) is defined as the minimal voltage that could produce observable twitching of anal sphincter. A double lumen catheter was inserted through the urethra into the bladder to monitor the bladder pressure and infuse (1.0 - 2.0 ml/min) saline. The ureters were cut and drained externally. A pair of needle electrodes was inserted through the skin into the anal sphincter muscle on the left and right sides. The tibial nerve was isolated from the medial side of left hindlimb at a site above the ankle. A small pool was formed around the tibial nerve by retracting skin flaps and the pool was filled with warm mineral oil. A pair of stainless steel hook electrodes was placed on the tibial nerve for recording the evoked potentials. The study was conducted under an IACUC approved protocol.

Results

Under isovolumetric bladder condition, starting from 1.5 T the inhibitory effect of the transcutaneous stimulation gradually increased until the stimulation completely suppressed the rhythmic bladder contractions at an intensity above 2.0 T. Hindlimb movement was induced only when the stimulation intensity was increased above 3.0 T. The transcutaneous stimulation also significantly increased bladder capacity to 145.8±10.7% of the control capacity during CMG at intensities between 2.0 - 3.0 T.

Electromyography (EMG) was recorded from anal sphincter during rhythmic isovolumetric bladder contractions. Maximal EMG was evoked by the transcutaneous stimulation at an intensity between 2.0 - 2.5 T when the bladder activity was completely inhibited. Meanwhile, evoke potential was not recorded from the tibial nerve at the same stimulation intensity, which was in agreement with the lack of hindlimb movement at an intensity below 3.0 T.

Interpretation of results

This study indicated that the 5 Hz transcutaneous stimulation modulated by a novel high-frequency carrier waveform could selectively activate the pudendal nerve without activation of the tibial nerve at an intensity between 2.0 – 3.0 T when it was applied to the skin area between the tail and the sciatic notch in the cats. The pudendal-to-bladder inhibitory reflex was maximally activated at this intensity range resulting in about 50% increase of the bladder capacity. The adverse effect of hindlimb movement could be prevented by maintaining the stimulation intensity below 3.0 T. The maximal activation of anal sphincter EMG at the intensity range between 2.0 -2.5 T without recording evoked potentials from the tibial nerve further indicated the ability for the transcutaneous stimulation to selectively activate pudendal nerve without activating the tibial nerve. These results also indicated that the inhibitory effect on bladder activity induced by the transcutaneous stimulation in our previous study was highly likely due to the activation of pudendal nerve rather than the activation of tibial nerve.

Concluding message

This study demonstrates a potential clinical application to treat overactive bladder and prevent incontinence by a non-invasive approach using skin surface electrodes on the lower back to selectively stimulate the pudendal nerve. Our study shows that a

stimulation intensity window exists for the transcutaneous stimulation method to be used clinically to induce maximal inhibitory effect on bladder with less discomfort or adverse movement of the legs. Development of a selective stimulation method targeting the pudendal nerve will further promote the application of the non-invasive neuromodulation method to treat bladder overactivity and prevent incontinence.

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