

## MONITORING NERVE SIGNALS FROM SACRAL ROOTS IN PIGS USING CHRONICALLY IMPLANTED ELECTRODES

### Aims of Study

Neurogenic detrusor overactivity (NDO) is conventionally managed by medication or surgical intervention, such as bladder augmentation or bladder deafferentation. NDO can also be managed using electrical stimulation. This relies on activating existing spinal reflexes, which are capable of interrupting a detrusor contraction. It has for example been shown that electrical stimulation of afferent branches of the pudendal nerves inhibits bladder contractions. Stimulation does not need to be continuously but preferably only when a contraction occurs. This implies that a sensor is needed to detect the onset of bladder contractions. Implantable sensors with sufficient long biocompatibility and reliability are difficult to build, but with the advent of methods for long term electrical interfacing with nerves, recording from the natural sensors in the human body have become a realistic alternative. Recent acute studies have shown that afferent nerve signals related to mechanical bladder activity can be recorded by using cuff electrodes placed on the pelvic nerves or (dorsal) sacral roots in pigs, cats and human.

The aim of this study was to monitor bladder activity using chronically implanted electrodes around the sacral nerve roots in pigs.

### Methods

Göttingen mini-pigs (n=6) have been implanted with a tripolar cuff electrode connected to a subcutaneous telemetric device. The cuff electrode was placed on the extradural sacral nerve root which resulted in the largest increase in bladder pressure to electrical stimulation with a hook electrode. The telemeter was placed in the subcutaneous fatty tissue layer, about 15 cm cranial and lateral to the processus transversus of the lumbal vertebrae. The telemeter transmitted the recorded and amplified nerve signals to an external receiver. Follow-up experiments were initially performed under general anesthesia. To test the neural interface, sensory compound action potentials (CAPs) were elicited by electrical stimulation of the clitoral nerve using a bipolar surface electrode. After this test, signals were recorded from perturbations of the sacral dermatomes and the rectum. To distend the rectum, a balloon consisting of a latex glove mounted on a standard catheter, was filled with two 100 ml bolus injections of saline. After the anesthesia was turned off, the empty bladder was filled with 300-400 ml saline. Bladder and rectal pressure, as well as the nerve signal, were recorded during the process of waking up. Additionally a cystometry was performed in one awake pig, placed in a restriction cage.

### Results

Cuff electrodes were implanted on the S1 (n=1), S2 (n=3), and S3 (n=2) sacral nerve roots. In all 6 pigs nerve signals could be recorded at right after implantation, and in 4 pigs two weeks postimplant. In the remaining 2 pigs, no follow-up recordings could be made due to technical problems. The most successful implant lasted 54 weeks. Among the reasons for terminating a chronic experiment were puncture of the skin, infection around the telemeter and suspected brain damage after anesthesia.

The maximum peak-to-peak amplitude of the elicited CAPs is an indication for the quality of the neural interface over time. The course of the CAP amplitudes resembled findings from other long-term implant studies and was, after an initial decrease, nearly constant over time, indicating that the nerve-cuff interface did not deteriorate.

In 3 out of 6 anesthetized pigs, an increase in afferent ENG could be measured during rectal distentions 2 weeks after implant. Applying rectal distention in the awake pig was more difficult because manipulations of the rectal balloon often triggered a defecation reflex, causing the balloon to be expelled. A rectal afferent response in the awake pig was difficult to detect because of the amount of other neural signals, mostly from cutaneous receptors and efferent origin.

Bladder fillings during wake-up state resulted in micturition, but no correlation between nerve signal and bladder pressure was observed. During cystometries in the awake state, a nerve signal correlating with bladder activity was seen. A small increase in baseline caused by bladder and urethra afferents could be seen during voiding. However, strong movement artefacts were seen prior and following voidings. Phasic urethral and perineal contractions, reflected in bladder pressure, were also present in the nerve signal.

## **Conclusions**

The results show that it is possible to measure sacral root nerve signals related to different pelvic organs using implanted electrodes. Reflex detrusor and rectal activity, usually suppressed by anesthesia in acute experiments, could be induced while the chronic implant allowed realtime monitoring of the neural activity involved. The awake recordings show that further improvement of signal processing methods is necessary in order to detect bladder contractions. Recording and processing of bladder related neurographic signals, combined with electrical stimulation into an implantable closed-loop system, would offer an alternative option to treat NDO without the necessity of dorsal rhizotomy.