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A METHOD FOR THE ELECTROMYOGRAPHIC MAPPING OF THE DETRUSOR SMOOTH MUSCLE

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ABSTRACT

Various methods for detrusor EMG in the living mammal have been described in the literature. These methods do insufficiently take into account signal components that are caused by movement between the electrodes and the bladder wall. Reliable detrusor EMG has not been achieved yet.

This study investigates the feasibility of a new experimental set-up, in which the electrical activity of the detrusor smooth muscle can be examined. In six rabbits, after cervical dislocation, laparotomy and after excision of the heart, electrical signals of the detrusor muscle are measured with 240 electrodes. The electrodes are positioned on the serosal surface of the filled and isovolumetric bladder. During the recordings, no bladder contractions are deliberately evoked by any stimulus.

Consistent results in all six animals show a repetitive spike pattern on multiple electrodes with a repetition frequency of 1.2 Hz. Spikes are triphasic and have a mean duration of 0.47 s (STD = 0.15 s, n = 40) and a mean amplitude of 0.29 mV (STD = 0.07 mV, n = 40). On adjacent electrodes a time shift between the spikes is found, suggesting the propagation of electrical activity across the detrusor surface. The maximum conduction velocity of an arbitrary spike front in the direction of propagation is approximately 30 mm/s. In two animals slow waves are found on the edge of the highpass filter setting.

Extensive control experiments are executed to validate the set-up and to interpret the data obtained by the animal experiments. The bladder is still able to contract thirty minutes post mortem. The heart, as a distant signal source, generates a signal that is present on all electrodes and shows no detectable time shift from one electrode to any other. Motion imposed on the electrodes relative to the bladder wall does not reproduce the slow waves and spikes found in the animal experiments. The control experiments support that the results of the animal experiments show electrical activity originating from the detrusor muscle itself.

With the experimental set-up described in this paper, nearly artefact free detrusor EMG can be recorded. An electromyographic map of a considerable detrusor smooth muscle area can be obtained.

KEYWORDS: Bladder, EMG, lower urinary tract, methods, m. detrusor, smooth muscle.

INTRODUCTION

Efficient storage and expulsion of urine is highly dependent on the integrated functioning of the musculature of the lower urinary tract and the relevant neuronal control structures in the peripheral and central nervous system. Defects or dysbalances in any part of

the system may cause a loss of performance (Dijkema et al., 1993; Brindley, 1994; Bastiaanssen, 1996).

The diagnostic possibilities to check the integrity of neuronal pathways involved in micturition control are limited. The complexity of the neuronal control of the lower urinary tract was clearly shown in recent studies (Marani et al., 1993; Kinder et al., 1995; Bastiaanssen, 1996). The conventional technique used to evaluate bladder functioning consists of an intravesical and rectal pressure measurement (ICS, 1987, 1988). In absence of rectal activity the pressure difference is indi-

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cated as detrusor pressure and thought to be generated by the bladder muscle itself. The detrusor pressure is very useful to estimate the overall behaviour of the bladder, but it cannot be used to reveal underlying causes for dysfunction.

The need for more selective tools to evaluate the functioning of the lower urinary tract has become evident. The recording of an electromyogram of the detrusor smooth muscle could partly serve this need. Theoretically, there are several benefits of detrusor electromyography (detrusor EMG) over detrusor pressure determination. Firstly, the spatial resolution of detrusor EMG is higher: local electrical activity of the detrusor muscle can be evaluated, e.g., with multiple small electrodes. Detrusor pressure is the result of the mechanical behaviour of the whole detrusor muscle and its outlet: possible uncoordinated local contractions may not cause a pressure rise and will remain undetected. Secondly, the electrical activity of the detrusor muscle is more closely related to the activity of its neuronal innervation. Changes in neuronal activity will first result in changes of electrical activity, preceding any mechanical effects. Detrusor EMG gives information about the transfer from neuronal to mechanical activity at an early stage. With respect to a rise in detrusor pressure for example, the excitation-contraction coupling of the detrusor muscle fibers has to develop and endure. Thirdly, electrical recordings from the detrusor muscle are likely to comprise both a myogenic signal contribution from the detrusor muscle itself and a neurogenic signal contribution from the innervating nerve fibers. The differentiation between detrusor muscle deficits and disorders of its neuronal innervation might become possible. Based on pressure

measurements only, this differentiation can not be made.

Detrusor EMG might become useful in two areas: (1) the fundamental research both on micturition control and on bladder (patho-)physiology (Craggs & Stephenson, 1982, 1985); (2) the clinical evaluation of lower urinary tract function (Boyce, 1952; La Joie et al., 1975; Takaiwa & Shiraiwa, 1984). Unfortunately, detrusor EMG has been accompanied by many problems during the last 45 years, leading to contradictory reports in the literature (Corey et al., 1951; Boyce, 1952; Franksson & Petersen, 1953; Brunsting, 1958; Fredericks et al., 1969; Stanton et al., 1973, 1974; Cosgrove et al., 1974, 1977; Jones et al., 1974; Doyle et al., 1975; La Joie et al., 1975; Craggs & Stephenson, 1976, 1982, 1985; Kaplan et al., 1976; Kaplan & Nanninga, 1978; Nanninga & Kaplan, 1978; Abdel-Rahman et al., 1982; Takaiwa et al., 1983a, b, 1992; Takaiwa & Shiraiwa, 1984; Jünemann et al., 1994; Shafik, 1994). To review common problems of detrusor EMG to date, five exemplary cases will be discussed (Corey et al., 1951; Boyce, 1952; Brunsting, 1958; Stanton et al., 1973, 1974; Doyle et al., 1975; Craggs & Stephenson, 1976, 1982, 1985; Takaiwa et al., 1983a,b, 1992; Takaiwa & Shiraiwa, 1984).

In 1951, Corey et al. placed electrodes transurethraly into the human urinary bladder against the lateral surfaces of the vesical neck. A signal that varied as a "bladder wave" with an amplitude of about 0.6 mV and a frequency of 0.1 to 1.0 Hz was recorded during voiding (Fig. 1). It was stated that "When the fingers were rested lightly on the electrode-carrier near the urethral orifice, movements [of the electrode carrier] coinciding with the appearance of typical wave forms on

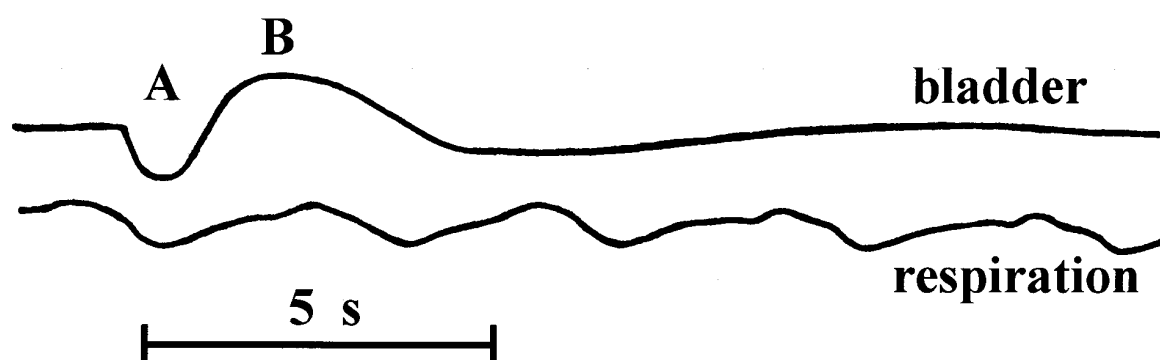


Fig. 1. NORMAL DIPHASIC "BLADDER WAVE" WITH 'A' AND 'B' DEFLECTIONS AS DESCRIBED BY COREY AND COLLEAGUES IN 1951. Note that no vertical scale is given. (Adapted from: COREY EL, BOYCE WH, VEST A, FRENCH CR (1951): Electro-potential changes in human urinary bladder: a method of measurement. *J Appl Physiol* 3: 631-636, fig. 2A, reprinted with permission.)

the tracing could frequently be detected" (Corey et al., 1951). This was seen as an indication that the signals found did represent contractions of the bladder musculature. Some years later, Brunsting (1958) tested several kinds of electrode materials (Ag, Ag/AgCl and stainless steel), electrode geometry's (needle shaped and ball-tipped electrodes) and recording sites (*in* the outer bladder wall and *against* the inner bladder wall) on an intact bladder in the anaesthetised cat. In control experiments he also conducted recordings with electrodes placed in or against a formalin-fixed bladder, a wet sponge, saline solution and a rubber bulb. Simple movement of the electrodes in a variety of situations consistently produced wave-like signals that were similar to the "bladder waves" reported earlier by Corey and Boyce (Fig. 2) (Corey et al., 1951; Boyce, 1952). Based on these observations, Brunsting suggested the "bladder wave" to be caused by bladder and electrode movement.

Starting in 1973, Stanton et al. (1973, 1974) inserted hook electrodes via the anterior vaginal wall into the inner bladder wall of conscious female patients. The investigators recorded low frequent

(0.1–5.0 Hz) signals with an amplitude of 0.1 to 2 mV and referred to similar recordings of Boyce (Corey et al., 1951; Boyce, 1952). The results of Brunsting (1958) were *not* discussed in their article. A second high frequency (spike) component of the detrusor EMG was identified, having a typical spike amplitude of 0.1 mV. In a later publication, Doyle et al. (1975) stated that it had not been possible to correlate changes in electrical activity with changes in bladder pressure and that movement artefacts were almost impossible to exclude with this technique.

Craggs and Stephenson (1976, 1982, 1985) attempted to record "the real bladder electromyogram". They stimulated the sacral ventral roots of 9 cats and one baboon. Platinum wire electrodes were inserted into the bladder wall from the exposed serosal surface (Craggs & Stephenson, 1976). They reported profuse random activity in the 0.07–1.0 Hz frequency band with an amplitude of 1 mV, which was also present in an isolated bladder kept in saline for 24 hours. Hence, this activity was interpreted as an artefact, probably resulting from fluid movement around the tip of the electrodes. Activity in the 40–200 Hz range showed no correlation with the

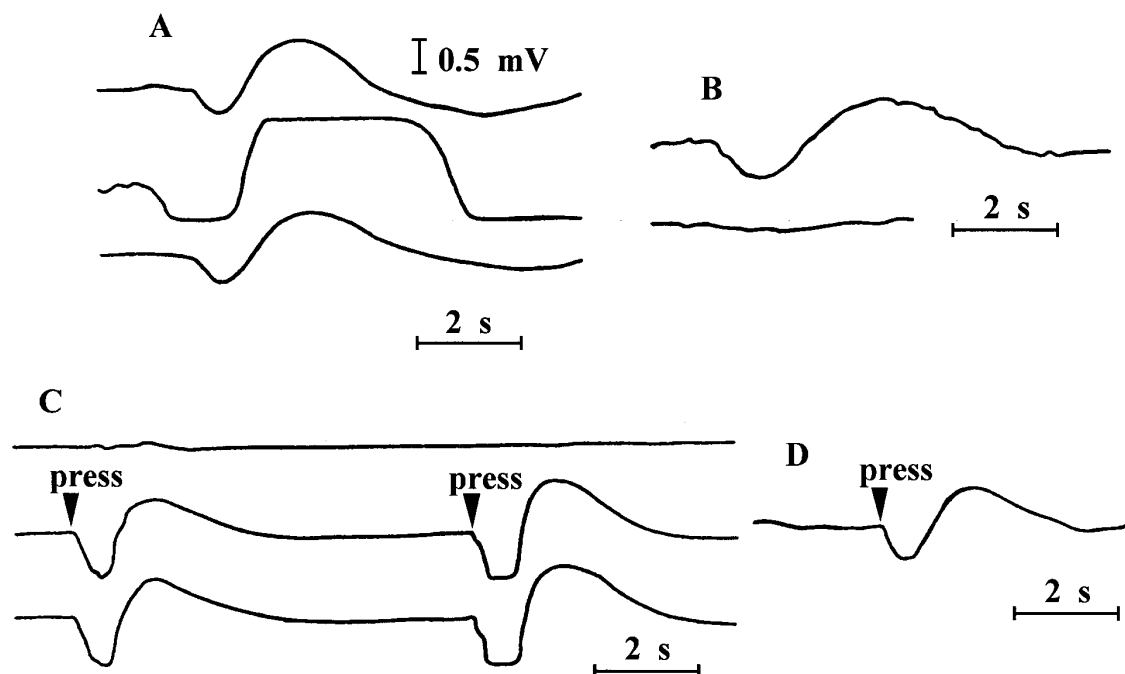


Fig. 2. EXAMPLES OF RECORDINGS FROM THE BLADDER OF A CAT USING EXTERNALLY IMPLANTED NEEDLE TYPE ELECTRODES. (A) typical "bladder waves" show initial downward phase followed by upward phase; (B) "bladder wave" of type occasionally seen during spontaneous activity. Note that it is not clear what the lower tracing stands for; (C) diphasic waves caused by pressing on one electrode in such a way as to push it deeper into the bladder. Note that it is not clear what the upper tracing stands for; (D) diphasic wave produced by pressing one of two electrode immersed in saline solution. (Adapted from: BRUNSTING CD (1958): An interpretation of the urinary bladder "electrocystogram" as artefact. *J Urol* 79: 165–170, fig. 2, reprinted with permission.)

recorded intravesical pressure and increased activity coincided with contractions of adjacent skeletal muscles. Only activity between 10 and 40 Hz seemed to correlate with contractions of the bladder. However, activity in the 10–40 Hz band was also present in the absence of voiding (Fig. 3), which was "...attributed to carry-over of the large amplitude activity in the adjacent 1–10 Hz band." (Craggs & Stephenson, 1976).

Taikawa and Shiraiwa (1984) investigated the electromyographic pattern of the detrusor muscle in 24 humans. They used carbon fiber surface electrodes that were fixed on the tip of a balloon catheter. The catheter was transurethraly inserted into the bladder and kept in position by inflating the balloon. The signals were highpass filtered at 5.3 Hz and lowpass filtered at 100 Hz. The 24 subjects with various manifestations of lower urinary tract disorders were grouped, based on the approximate amplitude (voltage) of the detrusor EMG signal: normal voltage group (normal, BPH; amplitude 0.05–0.1 mV); low voltage group (e.g., neurogenic bladder due to spina bifida; amplitude 0.01

mV); and a high voltage group (e.g., mild spinal cord injury; amplitude 0.3–2 mV). Earlier work showed a correlation between bladder volume and electromyographic activity (Fig. 4) (Takaiwa et al., 1983b). No statement was made about possible artefacts, while in 1992 (Takaiwa et al., 1992) they concluded that many problems accompanying this procedure still had to be solved. Movement of the bladder was mentioned as a major difficulty.

The results reported in the literature seem rather limited and the information about signal amplitudes and frequencies is contradictory. In our opinion, different causes have contributed to this unfavourable situation. Firstly, electrical activity of smooth musculature may involve signal components of less than one hertz in frequency. Hence, DC (direct current) recording might be considered. Phenomena near the electrode contact surface become more important when such low frequent signals are recorded (Cooper et al., 1969). A metal electrode immersed in a conducting fluid can generate a voltage between the electrode and the fluid. This volt-

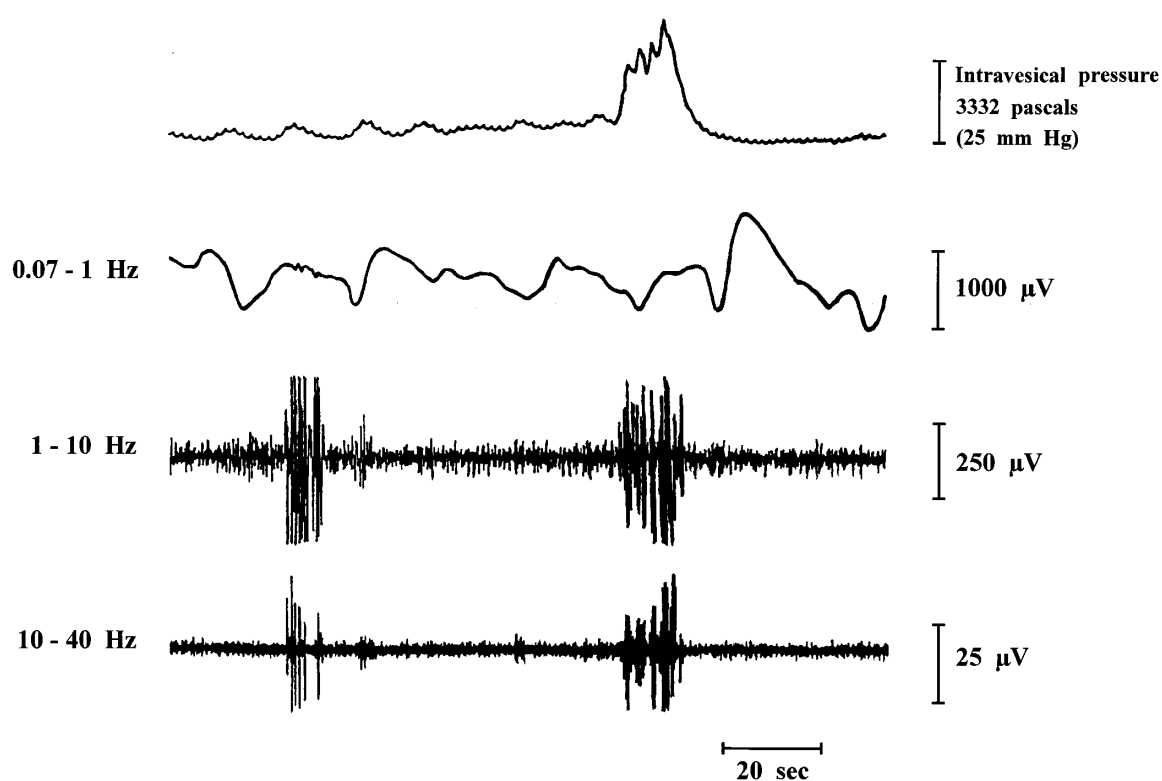


Fig. 3. INTRAVESICAL PRESSURE CHANGES AND BLADDER ELECTRICAL ACTIVITY DURING REFLEX VOIDING IN AN ANAESTHETISED CAT. An example of dissociation between activity in the 1–10 Hz band and reflex voiding. The small increase in activity in the 10–40 Hz band in the absence of voiding is attributed to carry-over of the large amplitude activity of the 1–10 Hz band. Note the different vertical scaling. (Adapted from: CRAGGS MD, STEPHENSON JD (1976): The real bladder electromyogram. *Br J Urol* 48: 443–451, fig. 4, reprinted with permission.)

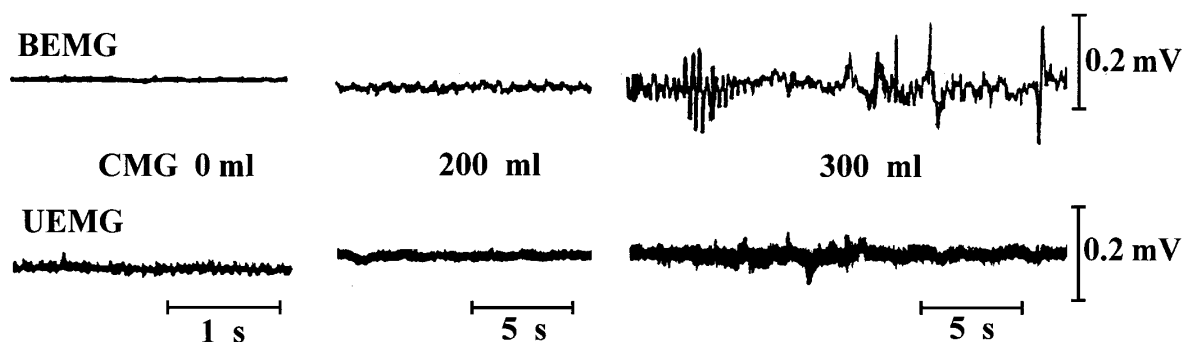


Fig. 4. CORRELATION BETWEEN INTRAVESICAL VOLUME (GAS INFUSION) AND ELECTRICAL ACTIVITY RECORDED FROM THE BLADDER. UEMG: Urethral electromyogram; BEMG: Bladder electromyogram; CMG: Cystometrogram. (Adapted from: TAKAIWA M, SHIRAIWA Y, KATAHIRA K, TSUKAHARA S (1983): A new urinary bladder electromyogram. *Urol Int* 38: 1-4, fig. 2A, reprinted with permission of S. Karger A.G.).

age depends on the electrode material and the temperature and is called electrode voltage. Applying more than one electrode, differences in electrode voltages give rise to an electrical current between the electrodes. Subsequent impedance changes between these electrodes, e.g., by movement, evoke slow potential changes that can easily result in erroneous interpretation of recordings. Urine is a salty solution (a good electrical conductor) and recordings with intravesical electrodes (Corey et al., 1951; Boyce, 1952) might therefore be bothered by these problems. Secondly, the detrusor muscle is stretched and rather thin when the bladder is full. The bladder is able to change its geometry drastically and has a high degree of freedom in movement. These aspects complicate the reliable fixation of wire or needle electrodes in the muscle. Thirdly, the lack of information given on the exact experimental set-up used and the wide variety of techniques applied complicate the objective comparison of the results obtained by the different research groups. Differences in electrode material, electrode geometry, registration site, filter and gain settings, sample frequency, data processing and species studied are known to have a considerable impact on the results. Finally, most studies focus on detrusor EMG in living mammals and the electrodes are in contact with the bladder wall (surface electrodes) or the detrusor muscle (needle or wire electrodes). This general set-up gives rise to various signal components that do not reflect electrical activity generated by detrusor smooth muscle cells. Electrical activity originating from the heart and striated musculature is sometimes picked up by the electrodes (Craggs & Stephenson, 1976). Comprising smooth muscles themselves, the bowels are likely to have electrical characteristics resembling those of the detrusor muscle (Weisbrodt, 1991a,b; Guyton & Hall, 1996) and their

electrical activity might be recorded as well. However, the most misleading signal components in the recordings are caused by movement between the electrodes and the bladder (Brunsting, 1958; Abdel-Rahman et al., 1982). Signal changes are unconditionally interpreted to be electrical detrusor activity and used as validation argument for the experimental set-up when they occur simultaneously with bladder contractions. This interpretation is based on the idea that the mechanical activity will be accompanied by (increased) electrical activity. Movement of the bladder to the recording electrodes as a possible signal source is neglected. Movement can for example be evoked by respiration, bowel activity or striated muscle activity (Abdel-Rahman et al., 1982). Stimulating the bladder by various means (e.g., peripheral nerve stimulation, chemical stimulation and filling cystometry), eventually resulting in bladder emptying, merely induces more movement between the electrode and the muscle. In some studies, the authors themselves (Doyle et al., 1975; Takaiwa et al., 1992) have *finally* concluded that movement is difficult to exclude, while other investigators (Brunsting, 1958; Abdel-Rahman et al., 1982) have suggested that movement is most likely to have caused the recorded signals. The problem is the separation of very small extracellular signals, reflecting actual membrane potential changes of detrusor muscle cells, from the large electromechanical artefact caused by electrode movement as the tissue contracts. However, in most studies no control experiments are done to determine to what extent relative movement of the bladder to the electrodes is responsible for the signals recorded.

In general, extensive control experiments to exclude or identify various signal components from sources other than the detrusor muscle are rare whenever a detrusor EMG technique is presented. Although the sig-

nals recorded in each of these studies might show a real detrusor electromyogram, its unequivocal identification is, in our opinion, impossible without relevant control experiments. As not much is known about the signal properties of the electrical detrusor activity either, the discrimination between true electrical activity from the detrusor muscle and these summated artefacts becomes difficult even when using appropriate recording equipment and sophisticated data-analysis techniques.

Reviewing the literature with the above mentioned problems in mind, it must be concluded that the amplitude, frequency and shape of the electrical detrusor activity measured with extracellular electrodes are still unknown. Reliable detrusor EMG has not been achieved yet.

This study aims therefore at the identification of electrical activity generated by the detrusor muscle with minimum disturbances in the recordings by any other signal source. The feasibility of an experimental set-up designed for this purpose is investigated.

New strategies are applied for the design and the validation of our experimental set-up and for the interpretation of the results: preliminary exclusion of several unwanted signal sources by working with a *post mortem* model; reduction of movement between the recording electrodes and the bladder wall by working with an isovolumetric bladder; application of multiple electrodes next to each other.

Animal experiments are conducted to test the performance of the complete experimental set-up and to determine the electrical signal properties of the detrusor muscle under isovolumetric conditions. No pharmacological or electrical bladder stimulation techniques are thought necessary for successful detrusor EMG as several *in vitro* studies reported that spontaneous electrical and mechanical detrusor activity can be found in various species, especially in rabbits (Creed et al., 1983; van Duyl et al., 1990; Bramich & Brading, 1996).

Although an experimental set-up with minimum disturbances is chosen, control experiments are necessary to exclude the presence of signal components other than electrical detrusor activity. Part of the control experiments have been described before (Brunsting, 1958) and are performed to demonstrate their effect on our specific set-up.

MATERIALS AND METHODS

Animal experiments

The animal experiments in this study were performed

on six rabbits (New Zealand White, male, mean weight: 2.9 kg).

A microtip pressure transducer catheter ($d = 2$ mm; Gaeltec Ltd, Dunvegan, Scotland) was applied to sense the intravesical pressure. The pressure signal was digitised at 3.4 Hz by a digital multimeter (M-3850; Metex, U.S.A.) and stored on a personal computer. A filling catheter ($d = 2$ mm) and a water bath (WB-7; Memmert GmbH, Schwabach, Germany) were used. The noise level of the pressure measurement was determined with the pressure transducer at a fixed height in the water bath at $T = 35^{\circ}\text{C}$. It was defined as plus and minus three times the standard deviation (STD) of the signal measured. This proved to be ± 0.05 kPa. The pressure transducer was zeroed just beneath the water surface at $T = 35^{\circ}\text{C}$ before each experiment started.

The electrode device was made of polyester resin. It embedded an octagonal matrix of 256 electrodes (Ag, $d = 0.3$ mm; Maastricht University, Maastricht, The Netherlands) that were positioned 2.3 mm from each other (Fig. 5). Sixteen electrodes in the two outer left columns were not operational in the present study. The electrodes were made of silver pins, which were soldered to isolated and silvered copper wire. The resistance of the electrodes to the connector was 3Ω . The device had screened cables and could only measure electrical activity at the exposed electrode surfaces, as the rest was highly isolated. A large disk (Ag, $d = 24$ mm) was used both as a grounding and reference electrode. The recording equipment was validated for electrophysiological studies of the heart (Allessie et al., 1986; Hoeks et al., 1988). The signals picked up by the electrode device were amplified by an array of 240 amplifiers with an input impedance of $1 \text{ M}\Omega$ each. As the signal properties were not clear, the widest possible frequency range of the equipment was used. This frequency range was 0.7 to 500 Hz, which were the -3dB points of the first order hardware filters. All 240 signals were recorded unipolar, individually amplified (gain: 4000), filtered (bandwidth: 0.7 to 500 Hz), 8 bits AD converted (sample frequency: 1 KHz) and digitally stored on videotape. Signals with a maximum amplitude (top-top) of 0.5 mV could be recorded in this setting.

Each rabbit was anaesthetised with 0.5 ml/kg i.m. 'Hypnorm' (fentanyl (0.315 mg/ml) and fluanisone (10 mg/ml); Janssen Pharmaceutica, Beerssen, Belgium) and received heparin (1000 IU i.v.; Leo, Weesp, The Netherlands). After cervical dislocation a midsternal thoracotomy was performed to prepare the later excision of the heart. A laparotomy was carried out to expose the bladder. The filling and micro-tip pressure

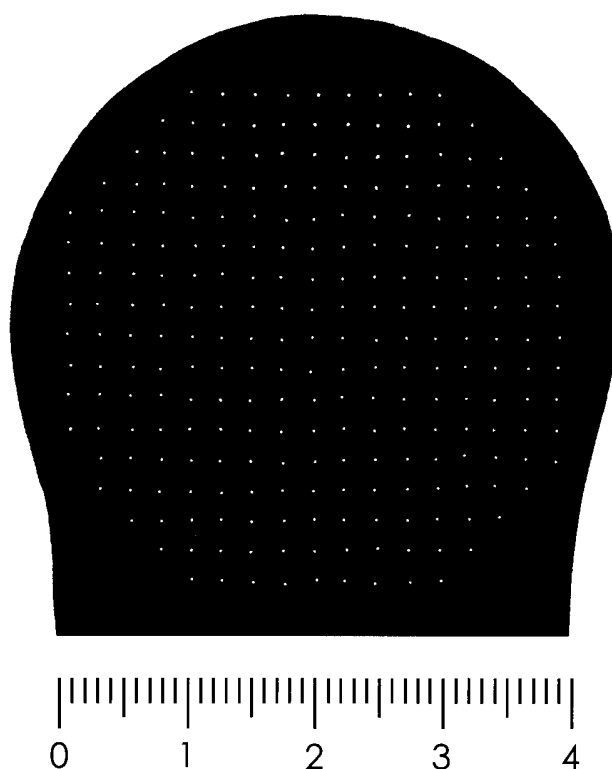


Fig. 5. THE CONFIGURATION OF THE 256 ELECTRODES, EMBEDDED IN THE ELECTRODE DEVICE. The scale below is in centimeters. Sixteen electrodes in the two outer left columns were not operational in the present study.

transducer catheter were introduced transurethrally into the bladder. The urethra was ligated to secure the two catheters and to prevent urine loss during the experiment. If necessary, saline solution ($T = 35^{\circ}\text{C}$) was infused through the filling catheter, until the bladder accommodated approximately 50 ml of fluid.

The electrode device was placed on the serosal surface of the exposed bladder and fixed against the ventral side of the bladder, above the trigone. The large disk, used both as a grounding and reference electrode, was placed in the thoracic region. The bowels were pushed away from the recording area. As soon as all preparations were finished, the heart was excised, followed immediately by the start of the recordings. The time which passed between the cervical dislocation and the removal of the heart was approximately six minutes (the maximum time was 8 min 30 s). The bladder volume was determined once the recordings were finished.

Final data analysis was carried out digitally. The power spectral density was calculated to determine the bandwidth of the measured signals. Digital filtering of the data was carried out in correspondence with the signal content using a fifth order Butterworth lowpass filter. Cross correlation ratios were calculated to compare the time relation between signals recorded on adjacent

electrodes. To calculate a cross correlation ratio, the offset of the signals was removed, the covariance was divided by the product of the two standard deviations of the signals and the degree of overlap was compensated for.

Control experiments

The control experiments consisted of two parts. The first part was performed on animals as well. Four rabbits (New Zealand White, male, mean weight: 3.1 kg) were used. A syringe filled with a mixture of saline solution and carbachol was prepared. For the second part a beaker filled with saline solution and a wet sponge on a dish were available. The remaining materials and the settings of the recording equipment were the same as described for the animal experiments.

The control experiments focused on three aspects. The first aim was to investigate for how long reliable detrusor EMG was possible in one single animal experiment. The second aim was to check the impact of one major disturbing signal with well known signal properties (ECG) on the recordings. The ECG served as a test signal to evaluate the proper functioning of the recording equipment. The third aspect of interest was whether the recordings obtained from the animal experiments

could be simulated by movement of the electrodes. The executed test procedure was tuned to the results of the animal experiments.

(1) *External mechano/chemical stimulation of the bladder combined with intravesical pressure measurements in three rabbits.*

The experimental set-up was as described for the animal experiments, with the exception that the electrode device was not positioned. The outer bladder surface was sprinkled with a mixture of saline solution and carbachol ($T = 35^{\circ}\text{C}$) from a 10 ml syringe. This first stimulus was given either five or ten minutes *post mortem*, depending on when the preparation of the experimental set-up was finished. The next stimuli followed each in five minutes time intervals until thirty minutes *post mortem*. In these thirty minutes the syringe was completely emptied. For rabbit no. 1, the concentration of carbachol was 25 $\mu\text{g/ml}$, for rabbit no. 2 and 3 the concentration of carbachol was reduced to 0.25 $\mu\text{g/ml}$.

(2) *Excision of the heart after the start of the recordings in one rabbit.*

The experimental set-up was as described for the animal experiments, with one exception: the heart was still in place when the recordings started. It was quickly removed after two minutes of recording with minimal disturbance of the experimental set-up in one male rabbit.

(3) a. *Movement of the electrode device immersed in a beaker filled with saline solution.*

Both the electrode device and the grounding electrode were inserted in a beaker filled with saline solution at room temperature. After an initial phase of rest, the electrode device was pushed gently by hand. A sinusoidal motion with a frequency of approximately 1 Hz was imposed. Two directions were tested: one direction perpendicular to the electrode surface, as to simulate pressure on the electrodes (normal); and one moving in the direction of the electrode surface, as to simulate slip (tangential). Two amplitudes of the imposed motion were tested: one amplitude (top-top) of approximately 0.4 cm and the other amplitude (top-top) of approximately 2 cm. The duration of the mechanical stimulus was 30 s continuously or 5 s on and 5 s off during a 30 s period (Table 1).

b. *Movement of the electrode device on a wet sponge that was placed in a dish filled with saline solution.*

The electrode device was positioned on top of the sponge and kept in place with an initial force. The

Table 1. Test procedure for the control experiments 3a–c. Frequency of all mechanical stimuli is 1 Hz.

Direction	Motion amplitude top-top (in cm)	Stimulation period of 30 s
normal	0.4	continuous
normal	0.4	5 s intervals
normal	2	continuous
normal	2	5 s intervals
tangential	0.4	continuous
tangential	0.4	5 s intervals
tangential	2	continuous
tangential	2	5 s intervals

grounding electrode was inserted in the sponge. After an initial phase of rest, the electrode device was pushed gently by hand. The test procedure as listed in Table 1 was executed.

c. *Movement of the electrode device underneath a bladder, which had been in situ for nine hours post mortem.*

The experimental set-up was as described for the animal experiments, with the exception that no catheters were inserted and the male rabbit was dead for nine hours at room temperature. The test procedure as listed in Table 1 was executed in one animal.

Final data analysis was performed digitally. No additional digital filtering was carried out; the frequency range of the signals shown in Figs. 10 and 11 is 0.7 to 500 Hz.

RESULTS

Animal experiments

In all six animals, consistent results were found. Frequency analysis of the recorded signals by means of power spectra showed that the significant signal frequencies were well below 25 Hz, except for the 50 Hz cycle interference (Fig. 6). The limit of 25 Hz was chosen as it provided a generous margin to the relevant signal frequencies below. Hence the signal to noise ratio could be improved. All signals were lowpass filtered (fifth order Butterworth filter) at 40 Hz to get rid of the 50 Hz cycle interference and to guarantee a high quality signal up to 25 Hz.

In all experiments, periods with spikes were seen. Looking at one of the 240 operational electrodes for forty seconds, a signal as shown in Fig. 7A could be recorded; the spikes exhibited a repetition frequency of 1.2 Hz. Reducing the time scale on the X axis to 0.7 seconds revealed more detailed information on the indi-

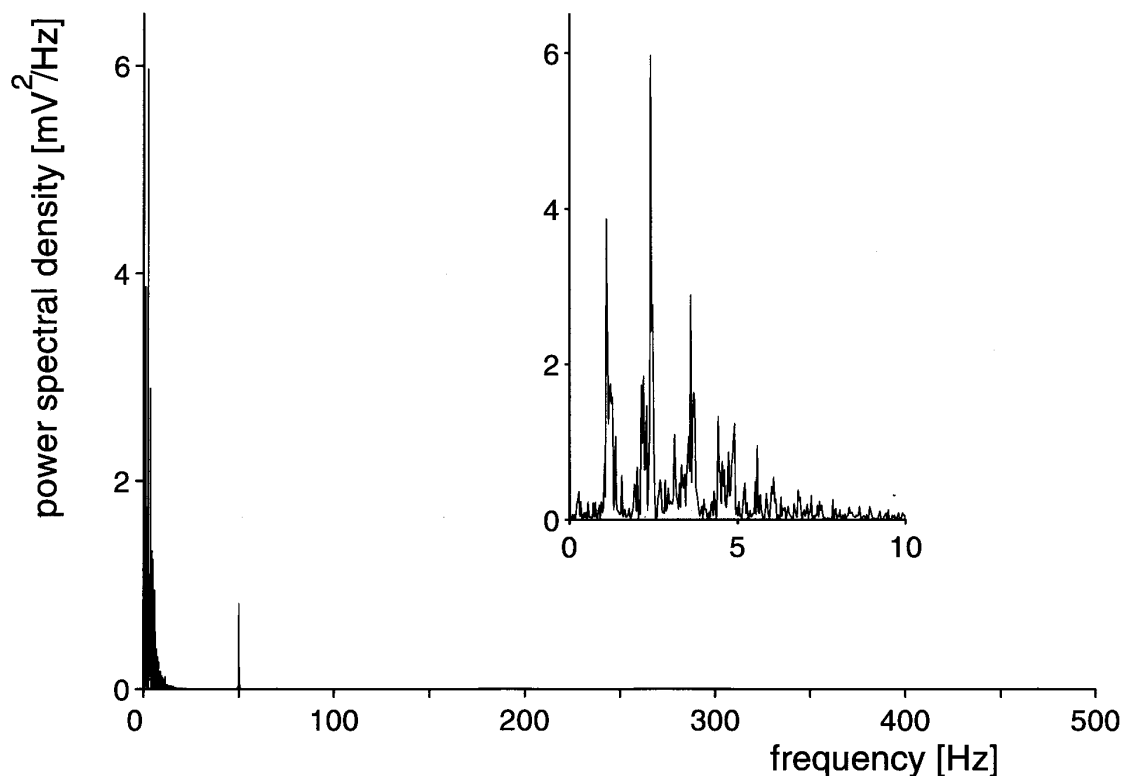


Fig. 6. THE POWER SPECTRAL DENSITY OF A RAW SIGNAL. The filtered version of the raw signal is shown in Fig. 7A.

vidual spikes (Fig. 7B). The two spikes, taken as a close-up from Fig. 7A, appeared to be triphasic and consisted of a modest first positive wave, followed by a fast, impressive negative deflection and a subsequent rise to conclude with a slow positive wave. The geometry of other recorded spikes varied between the two geometries shown in Fig. 7B. Quantitative analysis of forty individual triphasic spikes in Fig. 7A yielded a mean duration of 0.47 s (STD = 0.15 s); the mean amplitude (top-top) was 0.29 mV (STD = 0.07 mV).

Analysing an array of adjacent electrodes with a time scale of five seconds, the spikes appeared with a slight time shift (Fig. 8A). To investigate which spikes on two adjacent electrodes related best, the cross correlation ratio was calculated for the signals on two adjacent electrodes (Fig. 8B). The best correlation was found for the spikes with the minimum time shift going from one electrode to an adjacent one. This indicated that a unique spike on one electrode could be found on the next electrode as the time nearest spike.

The time shifts on multiple adjacent electrodes suggested a propagation of the electrical activity. To determine the direction and the speed of propagation, time shifts between the time nearest spikes on multiple adjacent electrodes were compared. These time shifts dif-

fered. The direction with the maximum time shift between the time nearest spikes on several adjacent electrodes is thought to indicate the direction of propagation. The corresponding conduction velocity, calculated by dividing the distance of the electrodes by this time shift, was up to 30 mm/s.

In two experiments slow waves were present (Fig. 9). The slow waves also showed a time shift between adjacent electrodes and were present on the edge of the highpass filter of 0.7 Hz.

The electrical activity in each animal was in general located on a limited and varying number of electrodes. The distribution across the 240 electrodes also varied in time. Taking an arbitrary moment in time and analysing a short period, there were regions in the recording area of intense electrical activity and regions of minor or no detectable electrical activity.

The spikes could be seen for at least thirty minutes *post mortem*; both the repetition frequency of the spikes and their amplitude decreased in time. The slow waves faded away maximally 15 minutes *post mortem*. After more than an hour all signals became flat and no electrical activity, no spikes or slow waves, could be measured.

The intravesical pressure measurement in one rabbit was excluded from further analysis, because the

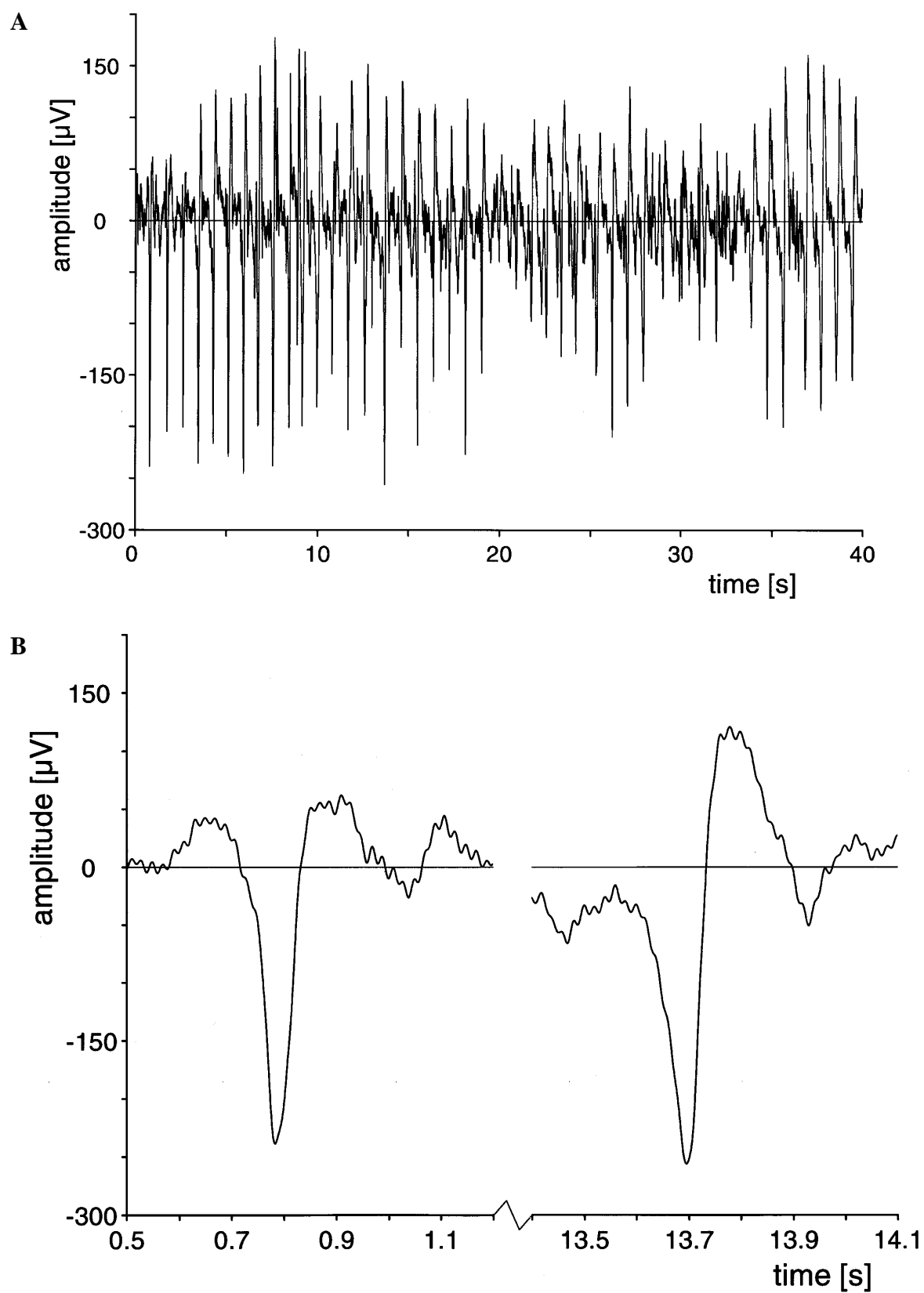


Fig. 7. (A) RECORDING FROM ELECTRODE 120. THE REPETITIVE SPIKE PATTERN IS CLEARLY SHOWN.

(B) FOCUS ON TWO SPIKES OF FIG. 7A. THEY ARE TRIPHASIC, WITH SOME VARIABILITY IN THEIR APPEARANCE.

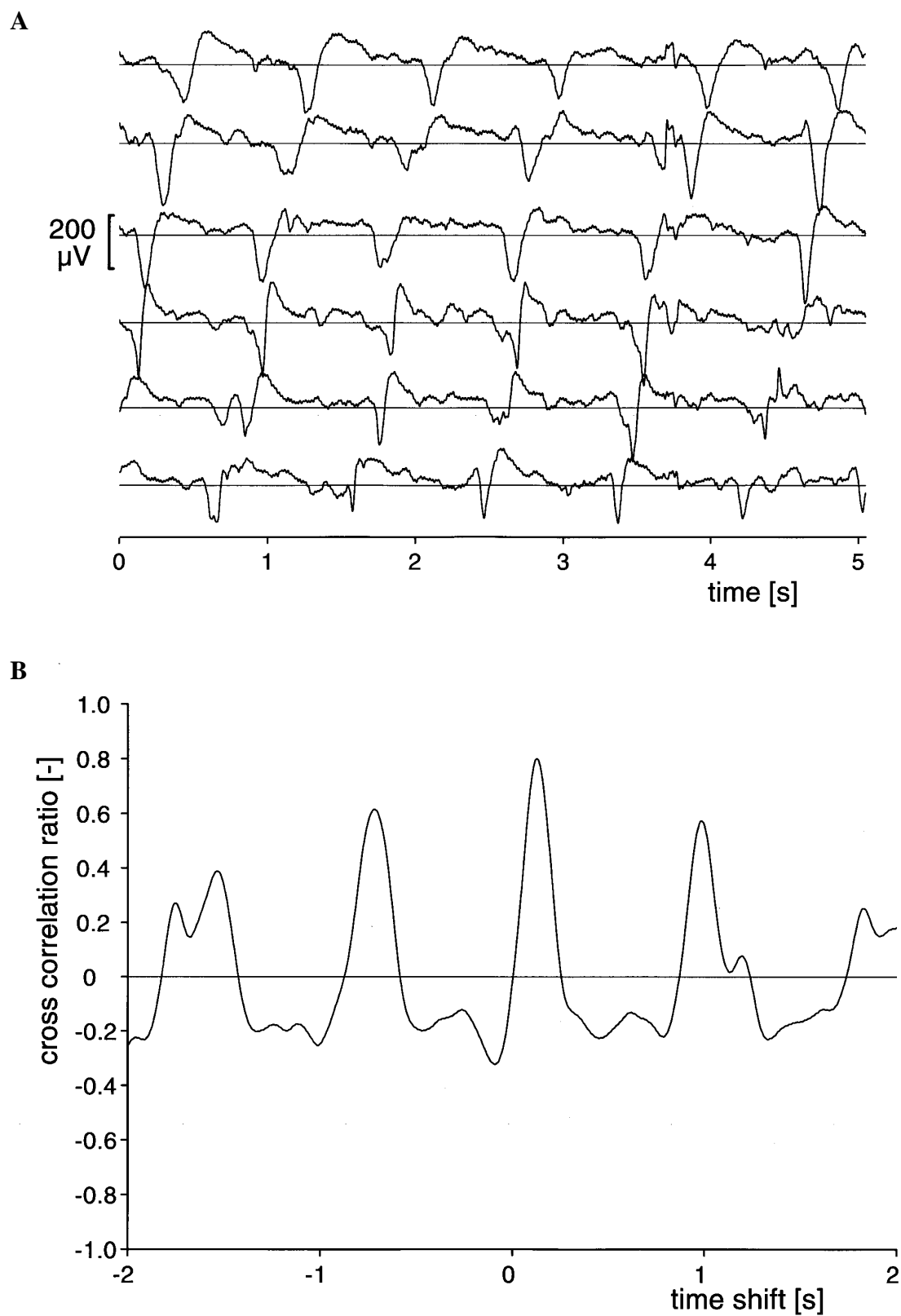


Fig. 8. (A) THE PROPAGATION OF SPIKES ACROSS THE VERTICAL ELECTRODE ARRAY 99–104, WHICH IS LOCATED NEAR THE CENTRE OF THE ELECTRODE DEVICE.

(B) TYPICAL CROSS CORRELATION RATIO, HERE SHOWN FOR THE TWO UPPER TRACINGS OF FIG. 8A. THE HIGHEST CROSS CORRELATION RATIO OF 0.8 OCCURS AT A TIME SHIFT OF 0.13 s MEANING THAT THE TIME-NEAREST SPIKES ON THESE TWO ADJACENT ELECTRODES CORRELATE BEST.

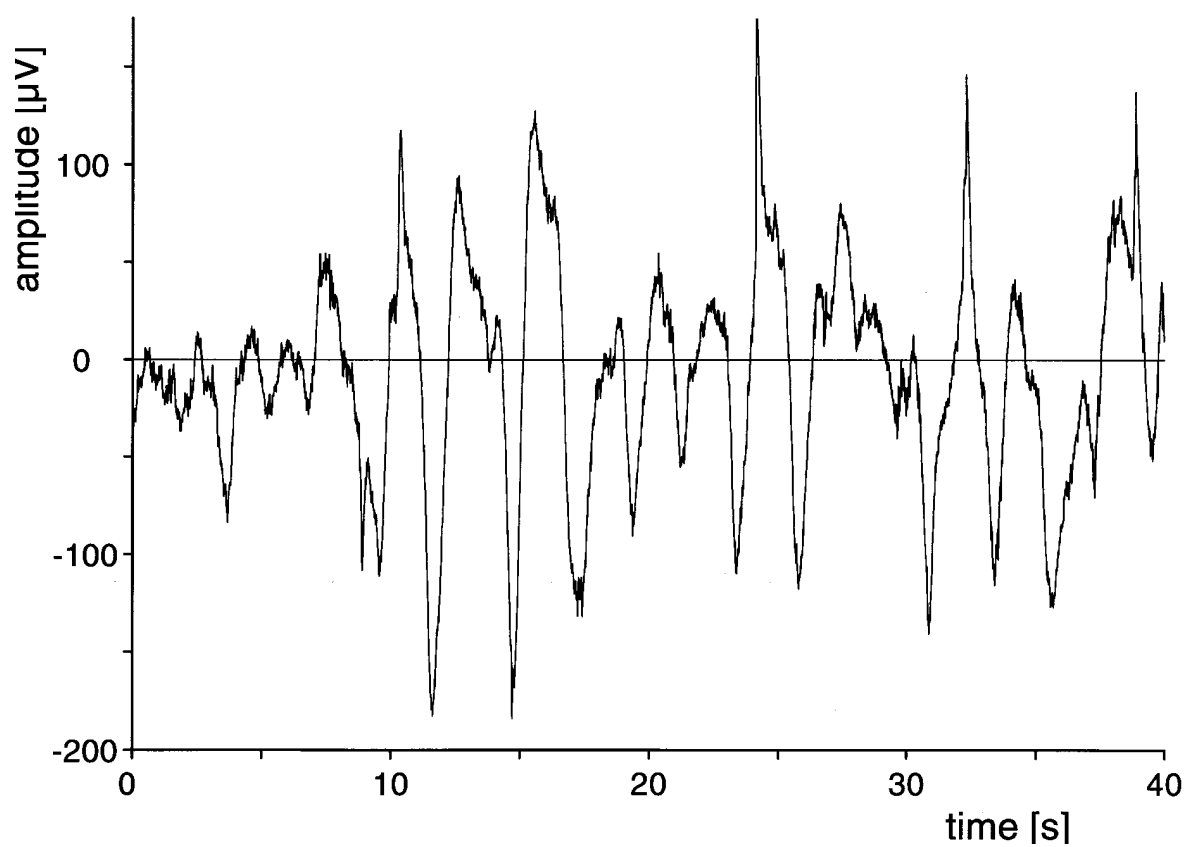


Fig. 9. A SLOW WAVE ON ELECTRODE 91.

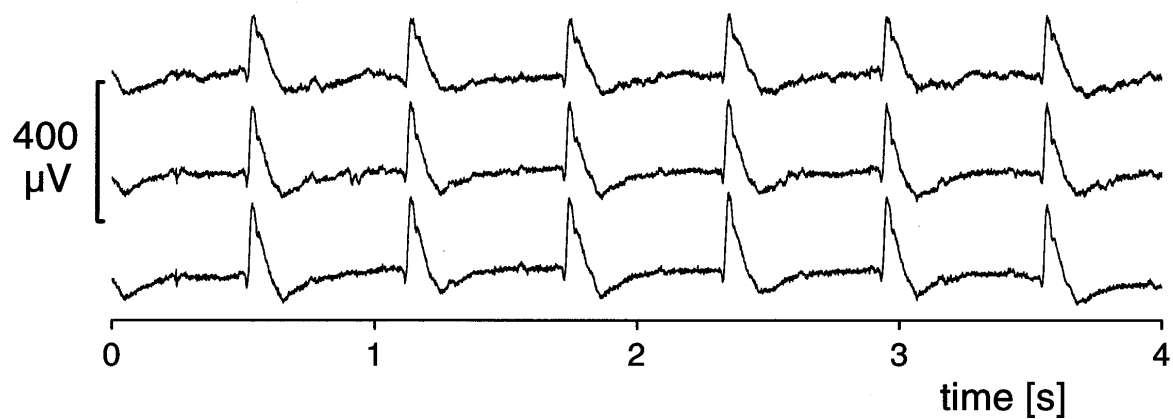


Fig. 10. THE EFFECT OF ECG ON THE RECORDINGS OF ELECTRODES 20, 130 AND 240. The distance between electrode 20–130 and 130–240 is 16 mm, between 20–240 it is 32 mm. The ECG was present at all electrodes and showed no detectable time shift from one electrode to any other.

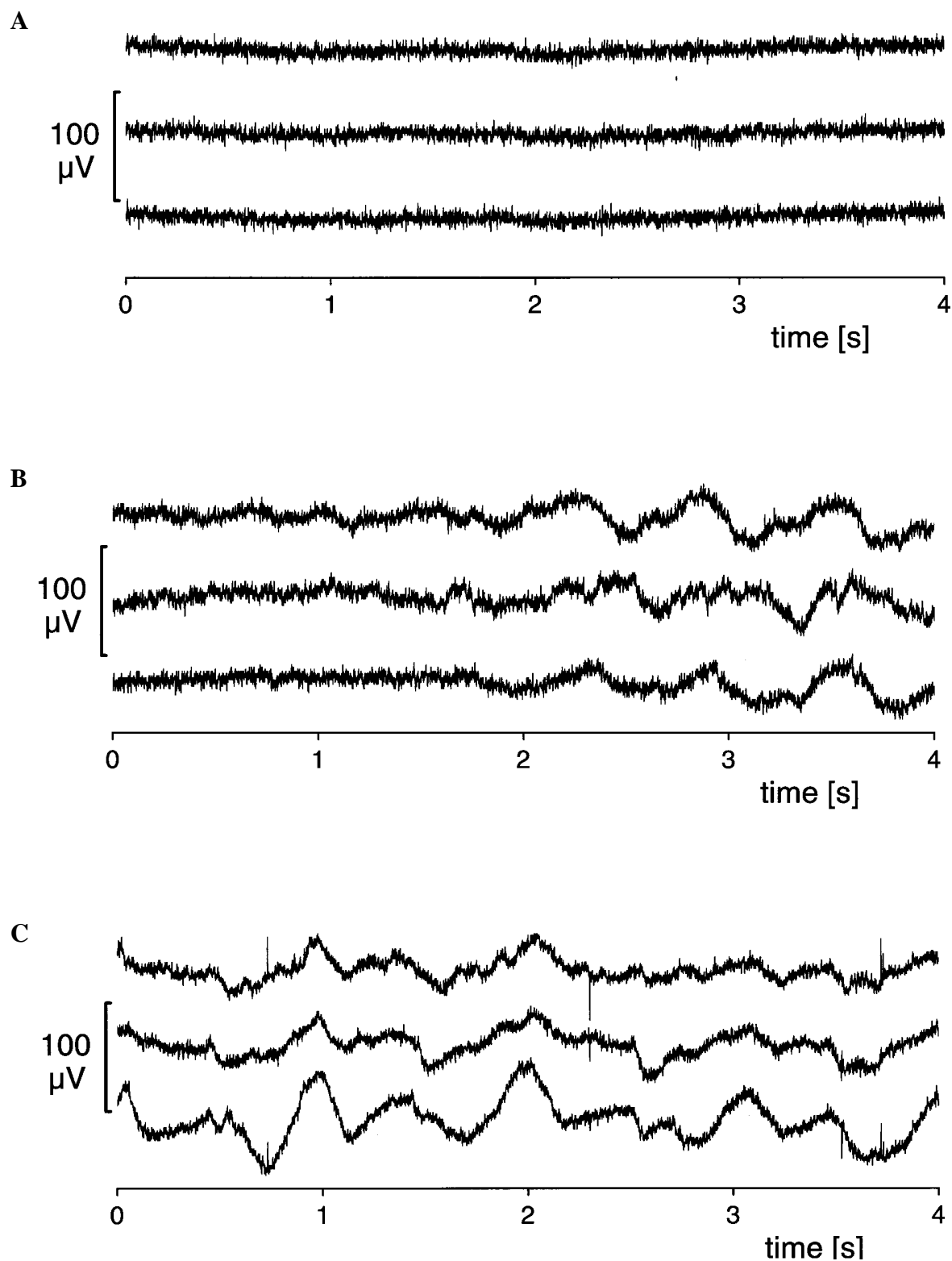


Fig. 11. (A) THE ELECTRODE DEVICE WAS PLACED UNDERNEATH A FILLED BLADDER OF A RABBIT (NINE HOURS *POST MORTEM*). Here it was not moving and the recordings on three adjacent electrodes showed noise only. No spikes or slow waves were present nine hours *post mortem*. (B) THE SAME SET-UP AS FIG. 11A. A period of rest (no imposed motion) was followed at second 2 by moving the electrode device with an amplitude of 0.4 cm in tangential direction. The signals recorded on three adjacent electrodes are shown. The signal amplitudes were about 0.06 mV. (C) THE SAME SET-UP AS FIG. 11A. The imposed motion now had an amplitude of 2 cm in the normal direction and was applied continuously. Recordings from three adjacent electrodes are shown. The signal amplitudes were about 0.1 mV.

microtip pressure transducer catheter was placed in the urethra rather than in the bladder. The pressures recorded in the remaining five bladders were rather low, e.g., ten minutes *post mortem* the mean pressure was 0.51 kPa (STD = 0.15 kPa; $n = 5$) with a mean bladder volume of 51 ml (STD = 10 ml; $n = 5$). The bladder pressures showed no spontaneous contraction-like changes exceeding the noise level (± 0.05 kPa) of the pressure measurement throughout the electrical recordings.

Control experiments

(1) A massive, clearly visible contraction of the bladder muscle was seen when the outer surface of the bladder in rabbit no. 1 was sprinkled with the high dose of carbachol (25 $\mu\text{g}/\text{ml}$, $T = 35^\circ\text{C}$) ten minutes *post mortem*. The pressure rise was 0.42 kPa. The bladder wall changed its colour to white and got very stiff upon subjective touch. Once these visible changes had taken place, it was no longer possible to elicit a visible or detectable bladder contraction by sprinkling concentrated carbachol solution at five minutes time intervals. For rabbit no. 2 and 3, the concentration of carbachol was decreased to 0.25 $\mu\text{g}/\text{ml}$. Bladder contractions, verified by intravesical pressure measurements, occurred at every stimulus (applied at five minutes time intervals) and could be evoked at least thirty minutes *post mortem*. Table 2 lists the relative pressure, i.e. the pressure just prior to the stimulus (P_{prior}) subtracted from the maximum pressure after the stimulus was given (P_{max}).

(2) Start of the recordings with the heart left *in situ* resulted in a clear contribution of an ECG in the recordings (Fig. 10). The ECG could be identified as a periodic signal with an amplitude of 0.3 mV and a decreasing frequency in time (start frequency was 1.7 Hz). It was present on all electrodes and showed no detectable time shift from one electrode to any other. The ECG disappeared immediately in the recordings after the final excision of the heart.

(3) General observations could be made once the electrode device was positioned in the saline solution, on the wet sponge or underneath the bladder nine hours *post mortem*. No signal components other than background

noise were recorded as long as the electrode device was not moving (Fig. 11A). This indicates that signal components possibly caused by spontaneous variation in ion concentrations at the silver electrodes or impedance changes between them are attenuated by the highpass filter settings at 0.7 Hz. Moving the electrode device with a frequency of 1 Hz resulted in a recorded signal with a frequency of around 1 Hz as well; a repetitive pattern of disturbances could be generated by imposing a repetitive pattern of motion on the device. The two repetition frequencies were related on a one to one basis. A higher imposed motion amplitude of the electrode device resulted in a higher amplitude of the recorded signals.

a) Moving the electrode device, which was immersed in a beaker of saline solution, with the motion amplitude of 0.4 cm had no clearly visible effect on the recordings in either direction of movement. Moving the electrode with the motion amplitude of 2 cm in either direction resulted in distorted sinusoidal-like signals with a maximum amplitude (top-top) of 0.15 mV on some electrodes and minor, less coordinated smooth disturbances on the other electrodes with an amplitude of about 0.05 mV.

b) Moving the electrode device with the motion amplitude of 0.4 cm on a wet sponge, as to simulate pressure on the electrodes, resulted in sinusoidal-like signals with a frequency of 1 Hz on almost all electrodes. Very few recorded signals had an amplitude of around 0.25 mV; most signals showed an amplitude in the range of 0.07 mV. Applying the higher motion amplitude in the same direction resulted in periodic wave-like signals of around 1 Hz and a signal amplitude of maximally 0.3 mV.

Imposing tangential movement with the motion amplitude of 0.4 cm, the limits of the recording equipment were already reached as some signals exceeded 0.5 mV. These signals were either periodic and sinusoidal shaped (frequency = 1 Hz) or had more random, irregular shapes. Other electrode signals stayed well beneath 0.5 mV and were sinusoidal. The imposed motion amplitude of 2 cm showed periodic signals with an amplitude of more than 0.5 mV on all electrodes. The sinusoidal-shape was heavily distorted.

Table 2. Relative intravesical pressure rise after stimulation with carbachol solution. The number of stimulations with carbachol is denoted by n . The maximum and minimum pressure value in rabbit no. 2 occurs at the third and fourth stimulus respectively. In rabbit no. 3 this is found at the first and third stimulus respectively.

Rabbit	Mean $P_{\text{max}} - P_{\text{prior}}$ (in kPa)	STD $P_{\text{max}} - P_{\text{prior}}$ (in kPa)	Max. $P_{\text{max}} - P_{\text{prior}}$ (in kPa)	Min. $P_{\text{max}} - P_{\text{prior}}$ (in kPa)
No. 2 ($n = 6$)	0.18	0.06	0.26	0.13
No. 3 ($n = 5$)	0.25	0.04	0.28	0.20

c) Moving the electrode device nine hours *post mortem* underneath the bladder gave several results. Imposing the motion amplitude of 0.4 cm in either direction, small sinusoidal-like signals with a frequency of slightly more than 1 Hz and an amplitude of 0.06 mV were recorded (Fig. 11B). The maximum signal amplitude found on one electrode was 0.1 mV. With the 2 cm motion amplitude applied, the signal amplitudes were a rather stable 0.1 mV, regardless of the direction of movement (Fig. 11C).

DISCUSSION

We want to investigate whether the presented spikes and slow waves are electrical detrusor activity indeed or merely the result of some other phenomena. The impact of signal sources other than electrical detrusor activity will be evaluated and some results of the control experiments will be discussed. Observations made on the spikes and slow waves will be used for their interpretation, but detailed physiological implications of the present findings are beyond the scope of this paper.

One observation is that the recorded signals fade away in time. This indicates a physiological origin somewhere in the *post mortem* animal rather than a signal source outside the animal. Possible electrical signal sources inside the animal might be the bowels, the nerve fibers running on the detrusor surface, the striated musculature and the detrusor muscle itself.

Electrical gastrointestinal activity is known to be too slow to measure with the present set-up as it is attenuated by the highpass filter settings at 0.7 Hz (Weisbrodt, 1991a,b; Guyton & Hall, 1996). Moreover, picking up electrical bowel activity is unlikely, because the electrodes are in direct contact with the bladder wall, the bowels are pushed at a considerable distance from the recording site and the electrode device itself has a good isolation except for the contact surfaces of the electrodes.

Signals might be recorded from nerve fibers, which are present on the bladder surface, when the electrode device is placed on top of them. The signal components are expected to resemble recordings with wire hook electrodes around nerve fibers meaning that they would contain frequencies clearly exceeding 25 Hz (Andresen & Yang, 1989; Le Feber et al., 1997). The electrical activity of striated muscles is known to exceed 25 Hz as well (Abdel-Rahman et al., 1982; Stöhr & Bluthardt, 1983). Since the power spectral density of a raw signal

shows no relevant signal components above 25 Hz (except for the 50 Hz cycle interference) it can be concluded that: either the nerve fibers on the bladder surface were not active or their activity could not be demonstrated with the equipment used; the contribution of striated muscle activity to the present recordings must have been insignificant.

Contractions of the bowels or striated muscles may induce movement of the electrodes or the bladder and result in unwanted signal components. However, the recorded spikes and slow waves show a time shift on adjacent electrodes and a varying distribution in time on the electrodes. This observation indicates that neither a distant (electrical) signal source nor contractions of the bowels or striated muscles cause the recorded signals. Any event that affects the recordings but originates from outside the recording area is expected to result in a similar disturbance on all electrodes at virtually the same moment in time. This is illustrated by the control experiments, especially by the ECG signal. The ECG signal is present on all electrodes and shows no detectable time shift from one electrode to any other. Besides, the ECG signal shows that neither the 240 amplifiers nor other hardware introduce a relevant time shift of the spikes and slow waves on adjacent electrodes.

These considerations point out the detrusor muscle as being the origin of the spikes and slow waves recorded. Since detrusor smooth muscle electrical activity is invariably accompanied by muscle contractions (Creed et al., 1983; Bramich & Brading, 1996), we wonder to what extent the signals found are caused by each of them. Firstly, contractions of detrusor muscle fibers in our animal experiments do not result in detectable overall intravesical pressure changes. This observation suggests the contractions to be small and/or uncoordinated, which is supported by the local and chaotic appearance of electrical activity in time across the 240 electrodes. Secondly, the control experiments with the bladder nine hours *post mortem* provide test conditions which are closest to the situation in which the spikes and slow waves were recorded. For contractions of detrusor smooth muscle fibers would predominantly generate motion relative to the fixed electrode device in tangential direction, it seems reasonable to assume that these contractions would produce movement artefacts similar to those generated in the control experiments by moving the electrode device in tangential direction underneath the bladder nine hours *post mortem*. The signals generated nine hours *post mortem* do not exceed 0.1 mV, regardless of the

parameters chosen from the test procedure. In contrast, both the spikes and slow waves show amplitudes of up to 0.3 mV, while movement of the electrode device or the isovolumetric bladder is not observed by visual inspection. Thirdly, the triphasic waveform of the spikes corresponds to what is expected with unipolar recording on a muscle by surface electrodes and the grounding and reference electrode on a distant place in the body (Waring, 1974). The typical geometry of the spikes could not be reproduced in the control experiments.

This leads us to the conclusion that signal components in the recordings due to moving muscle fibers of the isovolumetric bladder must be minimal: the recorded spikes and slow waves represent changes in the transmembrane potential of detrusor smooth muscle cells.

The results of our control experiments, in which motion was imposed on the electrodes, confirm earlier reports (Brunsting, 1958), keeping in mind the materials and methods used here. It is clear that the slow waves can not be further investigated and validated with the present system settings employed. The slow waves appear on the edge of the present highpass filter setting and their representation may already be attenuated by this first order filter. For more detailed investigation, equipment is needed with highpass filters at a lower cut-off frequency.

Methodological implications

The electrical activity of the detrusor smooth muscle, as recorded in our *post mortem* model, contains components actually resembling several artefacts that can occur in a living mammal. The sources of these artefacts were however excluded in our study. This might indicate a major problem for detrusor smooth muscle electromyography in living mammals. The aim of EMG is the study of muscle (patho-)physiology, i.e. the (patho)physiologic basis of (ab)normal mechanical activity. Therefore the relationship between electrical and mechanical activity has to be known. However, the normal functioning of the bladder (collection of urine and bladder emptying) introduces movement of the bladder to the electrodes and hence unwanted signal components which possibly mask the electrical detrusor activity in the recordings completely. Under these circumstances EMG simply would not be a suitable tool to study smooth muscle (patho-)physiology; electromyography would rather produce a detrusor "mechanogram" (Brunsting, 1958). One might argue

that a detrusor "mechanogram" is still useful for the study of mechanical muscle activity but then it should not be presented as being detrusor EMG. Instead, one could further explore methods for the study of detrusor smooth muscle physiology which provide more reliable information on mechanical activity (e.g., the application of strain- and force transducers or fluorescent markers (Van Bavel et al., 1996)). The present results on the electrical detrusor activity underline that it will be difficult to obtain reliable information on the functional electromechanical relationship using traditional concepts.

However, the knowledge obtained on signal shape, amplitude and frequency can be used to develop alternative approaches for detrusor EMG in living mammals. For this purpose the experimental set-up and recording equipment described here might be optimized and incorporated or completely different approaches might be chosen. One example of the latter is bladder EMG in humans measured with surface electrodes placed on the abdominal skin as suggested earlier (Kinder et al., 1996). Innovations in data-acquisition techniques can be used to exploit the feasibility of such a new set-up. The advantages of a non-invasive bladder EMG technique, where bladder contractions now indeed seem suitable for validation since the electrodes no longer contact the bladder, are clear.

CONCLUSION

A method for detrusor EMG was introduced, in which unwanted signal sources are eliminated or their effect is reduced. The feasibility of the set-up to identify nearly artefact free electrical detrusor activity on a considerable area of the bladder was shown. For detrusor EMG neither the experimental set-up has, to our knowledge, been described before, nor have the propagating spikes and slow waves as presented in this paper. The relationships between mechanical, neuronal and electrical detrusor activity have not been investigated in this study. This remains to be done within the limitations set by detrusor EMG in general.

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