

Volume 146

July 1991

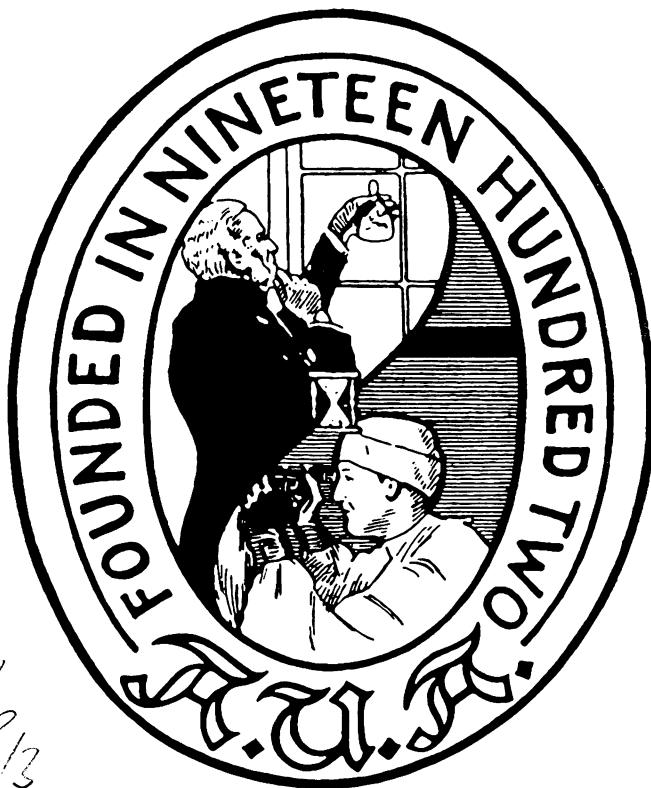
Number 1

742-410

166, 1-3

The Journal of UROLOGY®

Official Journal of the American Urological Association, Inc.
Founded In 1917 By Hugh Hampton Young



Annual Meeting, American Urological Association, Inc., Washington, D. C., May 10-14, 1992

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SINGLE POTENTIAL ANALYSIS OF CAVERNOUS ELECTRICAL ACTIVITY IN IMPOTENT PATIENTS: A POSSIBLE DIAGNOSTIC METHOD FOR AUTONOMIC CAVERNOUS DYSFUNCTION AND CAVERNOUS SMOOTH MUSCLE DEGENERATION

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ABSTRACT

Cavernous electrical activity was recorded in 214 patients with erectile dysfunction and in 39 normal patients. In 34 of the 39 normal patients potentials of a uniform shape were recorded during flaccidity. At cutoff frequencies of 0.5 to 500 Hz. the duration was 8 to 18 seconds (mean 12.8 ± 2.8 seconds, standard deviation), the amplitude was 250 to 750 μ V. (mean 444 ± 109 μ V.) and the polyphasicity was 8 to 22 (mean 13.8 ± 3.3). With increasing tumescence and rigidity during audiovisual sexual stimulation, high frequency potentials of low amplitude and short duration were found in the normal patients. In impotent patients with an upper motor neuron or peripheral lesion specific types of potentials were observed. In 11 of 14 impotent patients with insulin-dependent diabetes for more than 20 years and with clinical findings of cavernous myopathy the potentials showed low amplitude, irregular shape and slow depolarizations. Abnormal findings of cavernous electrical activity were recorded in 51.6% of the consecutive impotent patients. Our clinical study suggests that single potential analysis of cavernous electrical activity may be useful in the diagnosis of cavernous autonomic neuropathy and cavernous smooth muscle myopathy.

KEY WORDS: penis, impotence, evoked potentials

During the last decade the diagnosis of penile hemodynamic parameters was significantly improved by introduction of intracavernous injection of vasoactive drugs.¹⁻⁵ This intracavernous application of pharmacological agents induces cavernous hemodynamic changes similar to the physiological erection,^{6, 7} enabling a more accurate diagnosis of the functional cavernous organ.

To elucidate the neurogenic factor in impotence, the somatosensory penile innervation usually was examined due to the lack of tests for the cavernous autonomic nervous system. Measurement of the latency of the bulbocavernous reflex usually was done.^{8, 9} However, recent reports cast some doubts about the relevance of this procedure for autonomic neuropathy.¹⁰ Furthermore, tests for the sympathetic innervation¹¹ or the vibratory system were suggested but their clinical relevance is yet to be established. Gerstenberg et al first approached this major drawback in the diagnosis of erectile dysfunction when they suggested the registration of cavernous smooth muscle activity.¹² They recorded the cavernous electrical activity during flaccidity and during visual sexual stimulation.¹²⁻¹⁴ During flaccidity they observed periodic electrical activity that subsided in normal patients during visual sexual stimulation. When cavernous electrical activity did not change to an electrical zero line during visual sexual stimulation they assumed this to be a sign of autonomic cavernous dysfunction (dyscoordination).

We describe the registration of cavernous electrical activity with a different data processing method than that reported by Gerstenberg et al.¹² Whereas they interpreted their recordings according to the lack of electrical activity during erection, we have dispersed the electrical activity recordings on a wider time scale. This method permits a more specific interpretation of

the electrical potentials of the cavernous smooth muscles during flaccidity, thus, possibly allowing for a minimally invasive diagnosis of autonomic cavernous neuropathy and of cavernous smooth muscle degeneration.

PATIENTS AND METHODS

Since the introduction of single potential analysis of cavernous electrical activity into our routine diagnostic evaluation 182 consecutive patients with erectile dysfunction were evaluated multidisciplinarily at our impotence clinic. In all patients the minimum duration of impotence was 1 year. Our standard evaluation consisted of obtaining an over-all medical and sexual history, and performing physical examination, psychometry and laboratory blood tests, including testosterone and prolactin, as well as Doppler ultrasound of the penile arteries,¹⁵ standardized pharmacological testing,¹⁶ RigiScan real-time monitoring during visual sexual stimulation before and after intracavernous injection of 3 mg. papaverine and 0.1 mg. phenyltolamine, and single potential analysis of cavernous electrical activity. When indicated,¹⁶ pharmacocavernosometry and pharmacocavernosography or phalloarteriography were done. Furthermore, 39 patients from our urological ward (for example those with varicocele or other nononcological, nonpenile-related diseases) with normal erectile function underwent single potential analysis of cavernous electrical activity. Another 32 patients with erectile dysfunction were referred from other departments (especially the diabetes clinic) or centers especially for single potential analysis of cavernous electrical activity. The procedure as well as the indications for its application were approved by the university ethical committee. A total of 31 patients had insulin-dependent diabetes (14 for more than 20 years), while 12 had primary erectile dysfunction, 8 had chronic renal failure and 2 had multiple sclerosis. Five patients underwent cystoprostatectomy, 7 underwent radical prostatectomy and 3 underwent abdominoperineal extirpation of the rectum. Six patients had a complete traumatic lesion of the spinal cord above the T11 level, 1 had an incomplete T9 lesion

Accepted for publication January 29, 1991.

Read at annual meeting of American Urological Association, New Orleans, Louisiana, May 13-17, 1990.

Supported by a grant (Sti 96/2-1) from the Deutsche Forschungsgemeinschaft.

and 1 had an incomplete L5 to S1 lesion. Three patients had post-traumatic impotence, 12 had intervertebral disk prolapse and 2 had undergone hemipelvectomy. Three patients had undergone anterior extirpation of the rectum, 5 had a neurologically proved peripheral polyneuropathy, 1 had severe hypothyroidism and 1 had the cauda syndrome after meningoencephalitis. The age of the patients with erectile dysfunction was 22 to 69 years (mean age 49.6 years) and that of the normal patients was 20 to 68 years (mean age 44.0 years).

For the first 71 patients the cutoff frequencies were 2 to 2,000 Hz. and for the following patients they were 0.5 to 500 Hz. (as well as 2 to 500 Hz. for the following 32 patients). The last 37 patients were evaluated in a room with better electrical shielding. The patients were extensively informed about the procedure and possible risks (bleeding, infection and cavernous fibrosis) and they gave written consent.

With the patient in a sitting position a coaxial needle electrode (Dantec 9013 L, length 4 cm., surface of the tip 0.07 mm.²) was inserted laterally into the cavernous body without use of local anesthesia. The electrode was pushed forward into the proximal cavernous body until its tip was in the center of the cavernous body. The potentials were processed by an electrophysiological unit (modified Dantec Neuromatic 2000* and Wiest Space Recorder†). The signals were displayed continuously on a screen monitor as well as simultaneously recorded. The paper speed was 5 mm. per second. The cutoff frequencies were 2 to 2,000 Hz. for the first 71 patients, and then they were set at 0.5 to 500 Hz. The upper cutoff frequency of the Neuromatic thermewriter was 10 KHz., while for the Wiest thermewriter it was 100 Hz. Amplification was mostly at 50 μ v. per unit.

For an exact description of the potentials they were analyzed for initial depolarization (plus or minus), amplitude, length and polyphasicity (passages of the baseline). As in classical electromyography, negative depolarizations were defined as those in the upward direction and positive depolarizations were those in the downward direction in reference to the baseline.

Examination. Because all normal patients showed abnormal potentials up to 15 minutes after introduction of the needle electrode (that is these potentials were not recorded afterwards and reflect possibly potentials induced by the injury of the smooth muscle cells by the electrode), single potential analysis of cavernous electrical activity was begun 20 minutes after needle electrode introduction. After 25 minutes of registration of cavernous electrical activity during flaccidity, audiovisual sexual stimulation was applied for another 25 minutes with the examiner leaving the room (all normal patients consented to audiovisual sexual stimulation). At the end of audiovisual sexual stimulation the examiner evaluated the erectile response by inspection, palpation and interrogation. Then, recording was continued for another 10 minutes. After removal of the electrode tight penile compression was performed for approximately 60 seconds. Usually, the needle electrode was inserted into the left cavernous body. To evaluate whether the cavernous electrical activity is synchronous in different areas of the penis, 2 needles were inserted into each cavernous body or in 1 cavernous body proximally and distally in more than 50 patients.

RESULTS

We did not observe side effects, such as bleeding, infection or intracavernous fibrosis, after single potential analysis of cavernous electrical activity. Regarding the cavernous electrical activity, there was no significant difference between the younger (up to 40 years old) and the older (more than 40 years old) patients.

Electrical activity of the cavernous smooth muscles could not be registered in 1 impotent and 2 normal patients. When we

changed the lower cutoff frequency to 0.5 Hz. in the second normal patient with no recorded activity (patient 71 over-all) the potentials were easily recorded. Beginning with this patient we then chose 0.5 Hz. as the lower cutoff frequency. Lowering of the cutoff frequency from 2 to 0.5 Hz. resulted in an increase in amplitude of approximately 80 to 250% (fig. 1). In many patients low frequency depolarizations at the end of the potentials could be seen at 0.5 Hz. that were not visible at 2 Hz. In these patients potential duration and polyphasicity were also consecutively changed.

In 34 of 38 normal subjects with recorded activity the potentials were similar. The potentials began with a positive depolarization or a short-lasting negative followed by a positive depolarization. At cutoff frequencies of 2 to 2,000 Hz. the duration of the potentials was 3 to 12 seconds (mean 9.5 ± 0.3 seconds standard deviation), the amplitude was 60 to 250 μ v. (mean $153 \pm 31 \mu$ v.) and polyphasicity was 5 to 11 (mean 8.5 ± 0.3). At cutoff frequencies of 0.5 to 500 Hz. the duration was 8 to 18 seconds (mean 12.8 ± 2.8 seconds), the amplitude was 250 to 750 μ v. (mean $444 \pm 109 \mu$ v.) and the polyphasicity was 8 to 22 (mean 13.8 ± 3.3). The shape of the potentials was uniform for the same individual, although the frequency varied considerably depending on the degree of relaxation of the patient. Frequency was 0.6 to 2.6 potentials per minute.

Simultaneous recording of cavernous electrical activity in both cavernous bodies showed synchronization of the potentials (fig. 2). More superficial or deeper positioning of the electrode did not significantly alter the potentials.

To evaluate a possible influence of stress on the cavernous electrical activity single potential analysis of cavernous electrical activity was done approximately 1 hour preoperatively in 2 normal patients. In both patients a wave-like electrical activity with no specific potentials was recorded (fig. 3).

Of 39 normal subjects 23 had a full or almost full erection during audiovisual sexual stimulation, while 16 had only partial tumescence. Comparing the potentials during flaccidity and partial tumescence or erection, a uniform change could be observed. With increasing tumescence and rigidity an increase in frequency of the potentials with simultaneous decrease in amplitude and polyphasicity was noted (fig. 4). During full erection potentials were recorded in all patients. In contrast, no

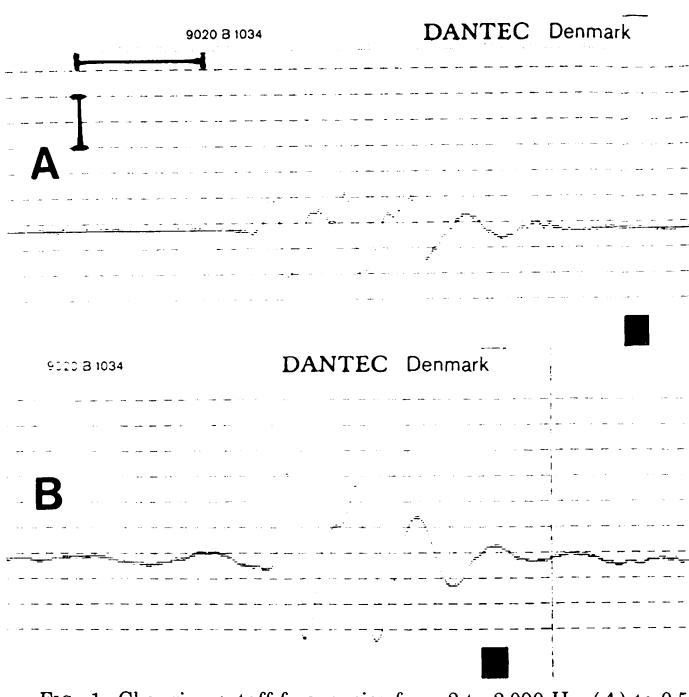


FIG. 1. Changing cutoff frequencies from 2 to 2,000 Hz. (A) to 0.5 to 500 Hz. (B) increased amplitude of potentials by 80 to 250%. Horizontal bar is 5 seconds and vertical bar is 100 μ v.

* Dantec, Copenhagen, Denmark.

† Wiest, Munich, Federal Republic of Germany.

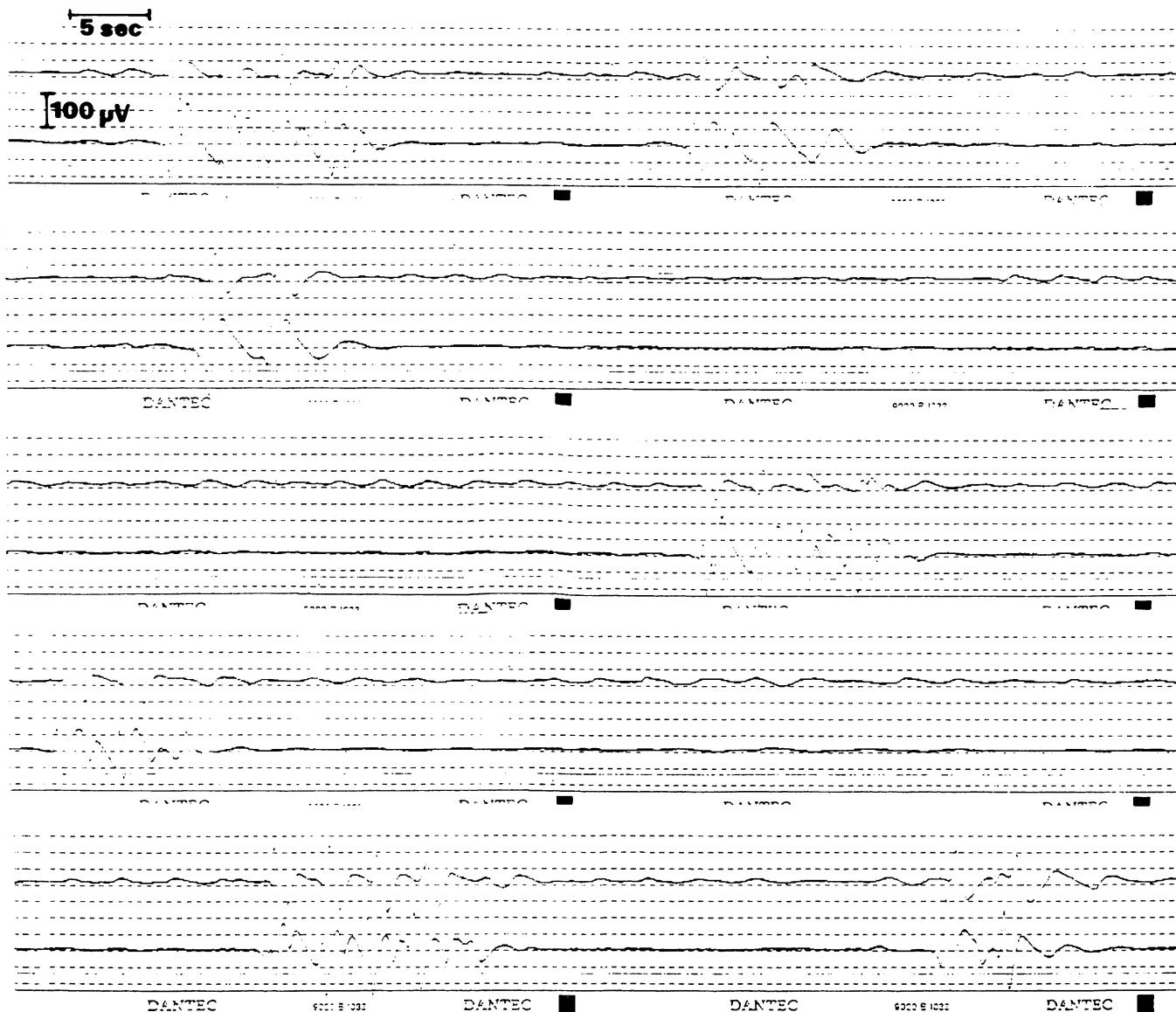


FIG. 2. Simultaneous continuous recording shows synchronization of cavernous electrical activity in both cavernous bodies in normal man

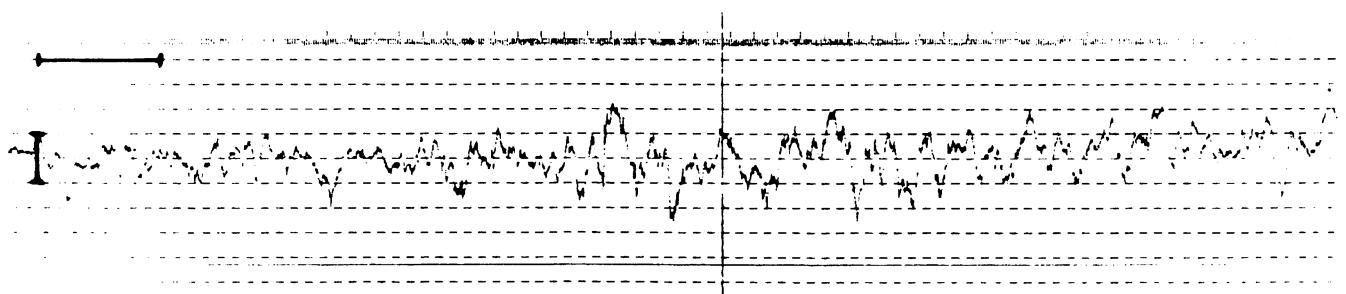


FIG. 3. Recording of 29-year-old patient with varicocele 1 hour preoperatively. Horizontal bar is 5 seconds and vertical bar is 100 μ V.

potentials (electrical silence) were recorded after intracavernous injection of papaverine and phentolamine or prostaglandin E1. In 1 normal subject normal as well as abnormal potentials were recorded. In another normal patient only a wave-like baseline activity without specific potentials was recorded.

In the patients with a presumable upper motor neuron lesion (complete traumatic T11 spinal cord injury) potentials with a duration of 28 seconds to more than 2 minutes were recorded (fig. 5). The amplitude of the potentials as well as the interval between the passages of the baseline was comparable to the potentials recorded in normal patients.

In the patients with a presumable peripheral autonomic nerve lesion (after cystoprostatectomy or abdominoperineal extirpation of the rectum) short potentials with a significantly decreased amplitude were recorded (fig. 6, A). In these patients short potentials with a fast convex phase of depolarization and a slower repolarization phase of concave shape (whip) were seen frequently. In 3 of the 5 patients after cystoprostatectomy and 1 of 3 after extirpation of the rectum normal potentials and pathological electrical activity were recorded (fig. 6, B). Furthermore, in some of these patients as well as in some with

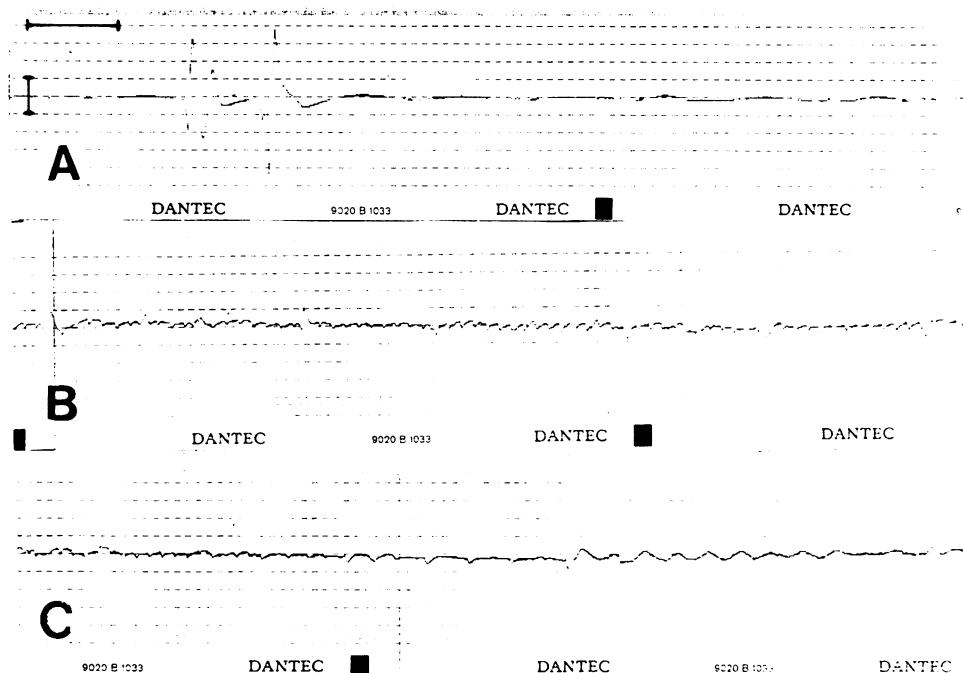


FIG. 4. A, recording during flaccidity in 22-year-old normal patient (1 large potential). B, electrical activity during tumescence with audiovisual sexual stimulation. C, electrical activity during almost full erection. Horizontal bar is 5 seconds and vertical bar is 100 μ V.

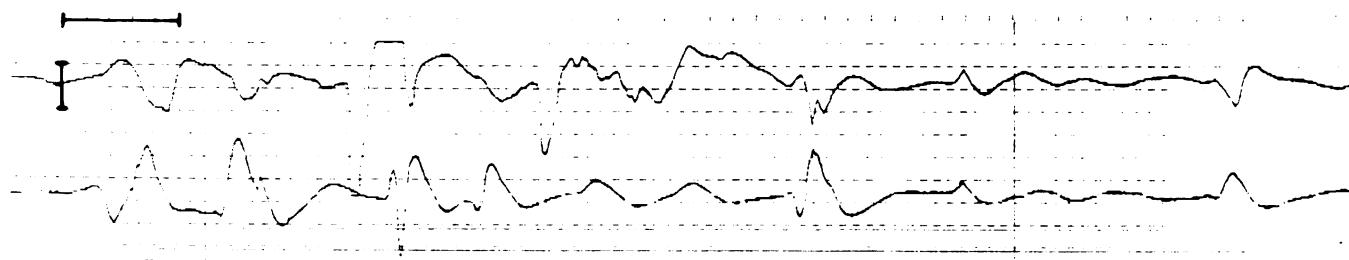


FIG. 5. Potentials of long duration are found in upper motor neuron lesions in 44-year-old patient with C6 complete traumatic spinal cord lesion. Upper (right cavernous body) and lower (left cavernous body) lines are simultaneous recordings and show synchronization of electrical activity of both cavernous bodies. Horizontal bar is 5 seconds and vertical bar is 100 μ V.

a presumable upper motor neuron lesion groups of extremely short depolarizations (bursts) were recorded (fig. 6, C).

Three of 7 patients after radical prostatectomy showed normal electrical activity of the cavernous smooth muscles, whereas 4 showed normal as well as abnormal potentials. No patient showed completely abnormal electrical activity (as did 2 of 5 patients after cystoprostatectomy) in this group. In 11 of 14 patients with insulin-dependent diabetes mellitus (duration more than 20 years) multidisciplinary examination showed signs highly suspicious for cavernous smooth muscle degeneration.¹⁷ On palpation the penis in these patients was much smaller compared to other patients. All patients had only a poor response to the intracavernous injection of vasoactive drugs and showed extensive venous leakage on cavernosometry and cavernosography. During single potential analysis of cavernous electrical activity these patients showed potentials of low amplitude, irregular shape and slow depolarization (fig. 7). In 2 patients with erectile dysfunction the recordings could not be interpreted due to wave-like baseline activity.

DISCUSSION

Our findings show that the electrical potentials of cavernous smooth muscle activity can be recorded. The reproducible recordings and the similarity of the potentials in normal patients, as well as the different recordings during full erection to audiovisual sexual stimulation on one hand and to intracavernous injection of vasoactive drugs on the other hand strongly suggest

that the recordings are not artifacts. The potentials recorded in normal patients are similar to smooth muscle potentials recorded in other smooth muscle organs in other species.¹⁶ Different types of autonomic lesions may be differentiated by single potential analysis of cavernous electrical activity.

Whereas the etiology of the potentials seems to be well correlated to the neurological status, the etiology of bursts remains unclear. Further studies must prove if these recordings are artifacts (for example by instruments close to the examination room) or physiological events. The etiology of single extremely short-lasting depolarizations (spikes) is most likely of noncavernous origin, since recording of spikes disappeared almost completely with better electrical shielding.

The patients in the groups with defined neurological lesions were mostly of younger age and, therefore, had presumably a good cavernous smooth muscle. All but 1 of these patients achieved full erection with the intracavernous injection of 0.5 ml. papaverine (15 mg./ml.) and phentolamine (0.5 mg./ml.) or less. This full erectile response to a minimal dose of vasoactive drugs¹⁷ strongly suggests intact penile hemodynamics with subsequent intact cavernous smooth muscles in these patients. Therefore, the alteration in the recording of the cavernous electrical activity in this case is most probably due to the neurological lesion of the patient and not to smooth muscle degeneration. Nevertheless, further electron microscopic studies must elucidate the influence of smooth muscle degeneration on single potential analysis of cavernous electrical activity.

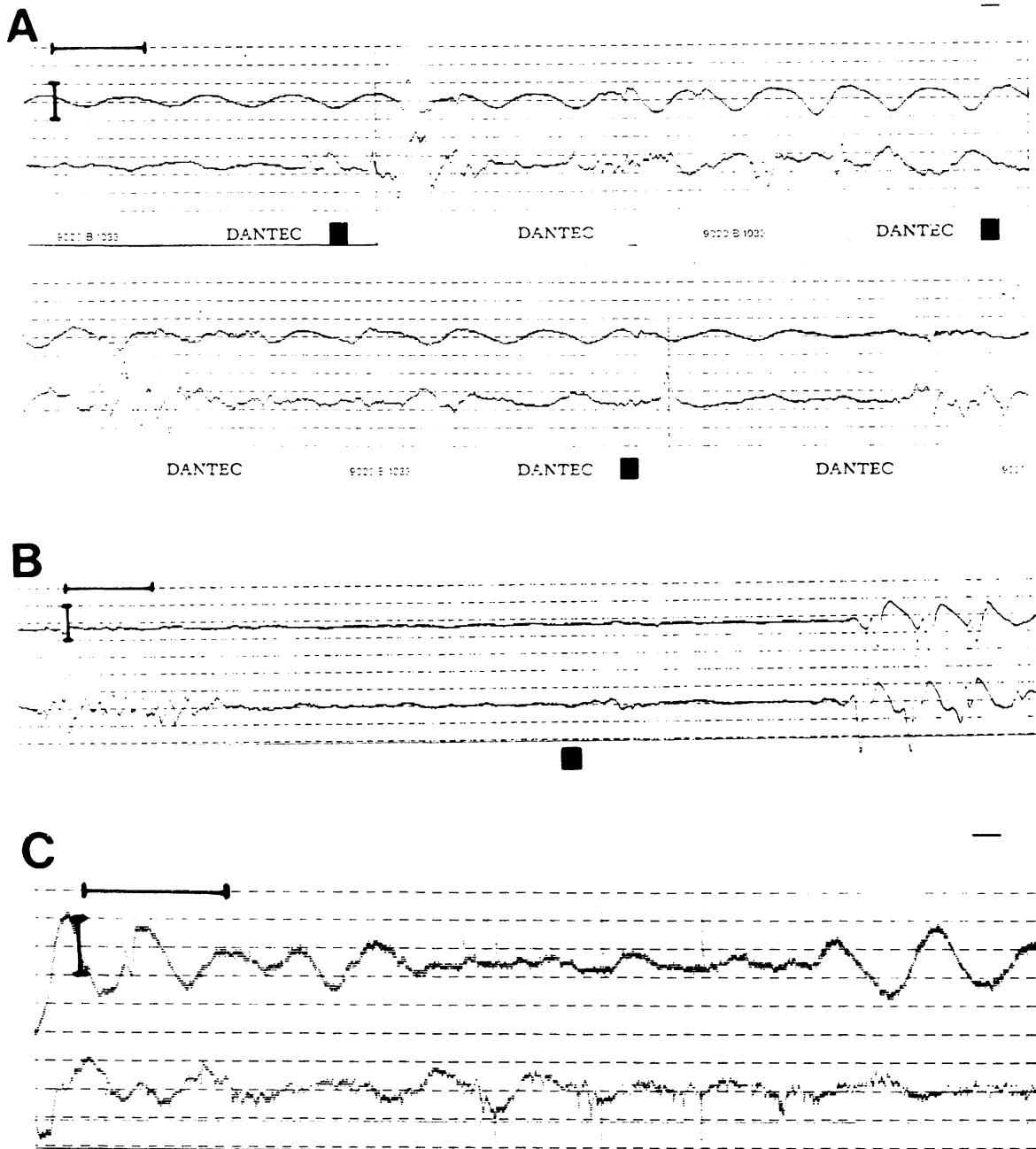


FIG. 6. *A*, simultaneous recording in both cavernous bodies of 55-year-old patient who underwent abdominoperineal extirpation of rectum 2 years previously shows desynchronization of electrical activity. *B*, 1 year after radical prostatectomy single potential analysis of cavernous electrical activity shows abnormal (only in lower recording, that is left cavernous body) as well as normal (synchronous in both cavernous bodies) potentials in 65-year-old impotent man. *C*, in 41-year-old impotent patient with prolapse of intervertebral nucleus (level L4 to L5), extremely short depolarizations (spikes) were recorded. Horizontal bar is 5 seconds and vertical bar is 100 μ V.

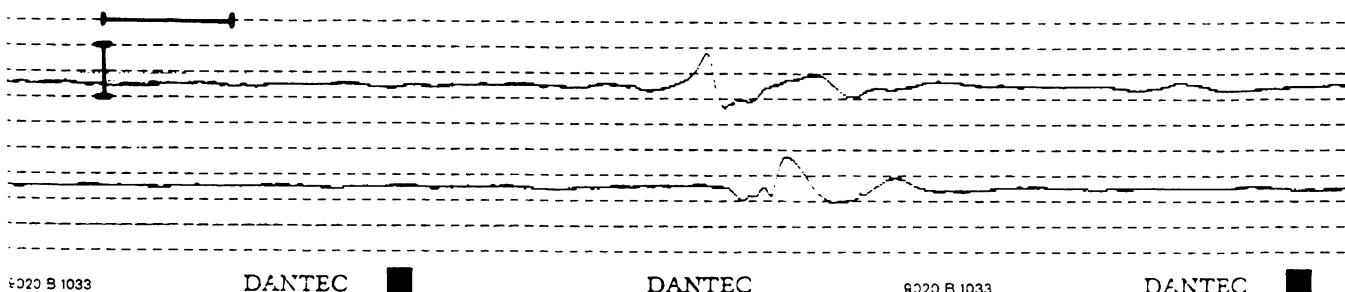


FIG. 7. Recordings in 32-year-old patient with insulin-dependent diabetes 21 years in duration show potentials of low amplitude and slow depolarizations (electrodes in both cavernous bodies). Horizontal bar is 5 seconds and vertical bar is 100 μ V.

The coexistence of normal potentials and pathological electrical activity in 7 of 12 patients after radical cystoprostatectomy or after abdominoperineal extirpation of the rectum represents possibly a partial destruction of the autonomic cavernous supply. This partial disruption of the autonomic nerve supply results in a focal denervation, represented by normal and abnormal potential on single potential analysis of cavernous electrical activity.

In the patients with an onset of insulin-dependent diabetes more than 20 years in duration and signs of extensive cavernous smooth muscle degeneration in the clinical evaluation significant changes of cavernous electrical activity were found. Desynchronization of cavernous electrical activity seems to indicate peripheral autonomic dysfunction, whereas the low amplitude and the slow depolarization of the potentials are suggestive of cavernous smooth muscle degeneration. This assumption correlates well with the electron microscopic findings in patients with venous leakage.¹⁸

Our findings in normal patients suggest that during flaccidity the contractions of the cavernous smooth muscle cells are synchronized by the sympathetic tone. This event results in a potential of high amplitude and long duration that can be simultaneously recorded in different areas of both cavernous bodies. During sexual arousal, and with increasing tumescence and rigidity the sympathetic tone is dramatically decreased, resulting in nonsynchronization of the contractions of the smooth muscle cells. This event results in potentials of decreased amplitude and duration but an increase in frequency. In contrast to this physiological erection, erection induced by vasoactive drugs is accompanied by electrical silence at the amplification used. Further examinations with higher signal amplification must show if this electrical silence at 50 μ V. per unit is not electrical activity at higher amplification.

Our study showed abnormal findings on single potential analysis of cavernous electrical activity in 51.6% of 182 consecutive patients with erectile dysfunction. Although we have a relatively high rate of patients with presumably neurological lesions in this series, this rate seems to be surprisingly high compared to approximately a 10% rate of neurogenic factors in the etiology of impotence in the literature. Nevertheless, it must be considered that this rate was mostly based on the measurement of the bulbocavernosus reflex latency. Comparing the possibility of damage to the autonomic (possibly diagnosed by single potential analysis of cavernous electrical activity) or somatosensory (diagnosed by bulbocavernous reflex latency) systems, it is well known that damage to the autonomic system may occur much earlier in time.¹⁹ Furthermore, electron microscopic findings showed pathological findings of the cavernous innervation in 40% of the patients.²⁰ These studies showed degeneration of the Schwann cells as well as of the nerve axons themselves. In all patients the diagnosis of abnormal autonomic innervation could be made by single potential analysis of cavernous electrical activity without audiovisual sexual stimulation, whereas synchronous recording with 2 needles in each cavernous body facilitated the diagnosis. In our opinion the individual response to audiovisual sexual stimulation cannot be standardized due to possible patient disapproval of such methods in general or of specific portions of the videotape. Therefore, many normal patients achieved only partial tumescence to audiovisual sexual stimulation and showed desynchronization of cavernous electrical activity. In disagreement with Gerstenberg et al.,¹² we believe that dyscoordination of cavernous electrical activity is more likely of psychogenic than of

organogenic origin, suggestive of a high sympathetic cavernous tone during audiovisual sexual stimulation.

We believe that single potential analysis of cavernous electrical activity may be a minimally invasive and reproducible diagnostic method to evaluate autonomic cavernous innervation. A diagnosis of cavernous smooth muscle degeneration by single potential analysis seems to be possible. Further comparative studies with electron microscopic controls must evaluate the correlation of our interpretation of single potential analysis of cavernous electrical activity with the morphological findings.

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