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The Methodology of Corpus Cavernosum Electromyography Revisited☆

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Abstract

Objective: The methodology of corpus cavernosum electromyography (CC-EMG) was revisited, in order to overcome current methodological difficulties that hinder its clinical application.
Materials and methods: Using an 8-channel device, CC-EMG was performed in 12 healthy volunteers. Surface electrodes were placed bilaterally on the penile shaft and the kneecap (reference electrode), the pubis region and the anterior superior iliac spine (ASIS). A band pass filter with cut-off frequencies of 0.1 and 20 Hz was used. At least 2 sessions of recordings were performed in each subject.
Results: Thirty-five of 46 recordings were interpretable. Significant time delays between potentials recorded from different sites of the CC were detected. Clear spatial voltage gradients related to CC-potentials were observed on the pubis region. No voltage changes related to CC-potentials, but electrical activity from other sources were recorded from the ASIS. In contrast to frequency, a clear correlation could be demonstrated between amplitude, duration and polyphasity of CC-potentials recorded in 2 different sessions in the same individual.
Conclusions: Multichannel monopolar recording of CC-EMG with surface electrodes is practical and has several advantages compared with bipolar recording. The results provide evidence that the recorded signals indeed reflect electrical activity of the CC and therefore offer a basis to pursue further clinical validation studies.

Keywords: Penis; Corpus cavernosum; Electromyography; CC-EMG; Monopolar

1. Introduction

In 1989 corpus cavernosum electromyography (CC-EMG) was introduced by Wagner and co-workers as a promising new method to evaluate the function of cavernous smooth muscle and its autonomic innervation [1]. Although several research groups have worked intensively on its clinical development [2–5], CC-EMG has failed to mature into a useful clinical tool. The most important reason for the lack of progress in this field is that doubts whether the signals indeed reflect electrical activity of the corpus cavernosum (CC) persist. Moreover, a lack of standardization of equipment, measurement and interpretation protocols made that the recordings of different centers could not be used for a quantitative comparison of patients with similar

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disease entities. Within the framework of the EU COST Action B18 program ‘‘corpus cavernosum EMG in erectile dysfunction’’ in which 22 scientists from 12 counties participate, we revisited the methodology of CC-EMG. In this study, the revised methodology is validated in a population of healthy volunteers.

2. Materials and methods

2.1. Equipment

An eight-channel Portilab Screener system (TMS International, Enschede, The Netherlands), connected to a portable computer (Toshiba Satellitepro6100), was used to record CC-potentials. The electrodes used were pre-gelled surface electrodes Medtronic 9021S0231 (1.5×2.0 cm in size, Medtronic, Copenhagen, Denmark).

2.2. Study population

Measurements were performed in 12 healthy volunteers with a mean age of 25.5 years (range 19–31). Body mass index (18–25 kg/m^2), blood pressure (systolic 90–150 mmHg, diastolic 60–90 mmHg) and pulse rate (50–120 beats/min) were in normal range. Within 12 hours prior to the measurements, alcohol, coffee, smoking and sexual activity was not allowed. Informed consent was obtained from each subject, and at least 2 recordings were performed with an interval of at least 24 hours.

2.3. Study protocol

Measurements were performed between 8 and 12 am, in a closed, semi-dark room with the examiner present. The room temperature was between 20 and 25 degree. The subject was placed in the supine or 45-degree sitting position on an examination table and was asked to relax as much as possible. The areas where the electrodes were to be placed were shaved without injury of the skin. Before application of the electrodes the skin was abraded lightly using a gauze and Nuprep gel (Weaver & Co., Nucla Way, USA) for about 10 strokes, and then was cleaned with alcohol to remove scales and to improve electrode adhesion. Depending on the size of the penis, four or six surface electrodes were placed on the shaft bilaterally (2 at the base of the penis, 2 close to the coronal sulcus, and 2 in between, if possible). After several pilot measurements (see discussion), it was decided to place the reference electrode over one of the kneecaps. The grounding electrode was placed on the thigh of the same side as the reference electrode. In 6 subjects, 4 additional electrodes were placed in the midline of the pubis and the anterior superior iliac spine (ASIS), aiming to observe electrical activity from these regions. Recording began after 10–20 minutes equilibration, lasting at least 20 minutes during flaccidity. Unfiltered as well as filtered signals were recorded simultaneously and stored digitally. The sampling frequency was 128 Hz. Filters with different cut-off frequencies were tested using the Matlab software (the MathWorks, Inc., Natick, MA, USA), and eventually a band pass filter with cut-off frequencies of 0.1 and 20 Hz was used.

2.4. Evaluation and analysis of the recordings

Firstly, the recordings were evaluated globally. Attention was paid to the quality of the recording (e.g. the occurrence of noise and artefacts), the baseline characteristics, and the waveform of CC-potentials. The recordings with a stable baseline, and reproducible CC-potentials which were distinguishable from the baseline were regarded as good quality recordings. Upon this, whether the recordings were interpretable or not could be decided (Fig. 1(a) and (b) show examples of interpretable and ‘‘non-interpretable’’ recordings, respectively). Secondly, the temporal relationship of CC-potentials recorded from different sites of the CC, and the relationship of signals from the CC, the pubis and the ASIS were examined. Finally, the individual CC-potentials were analysed and the intra-individual reproducibility was determined, on basis of the first 2 interpretable recordings of each subject. Recordings from the 2 electrodes at the base of the penis were used and the parameters amplitude, polyphasity, duration and frequency (number of potentials per 10 minutes) were determined. For the first 3 parameters, the 10 most representative CC-potentials with definite beginnings and endings (5 from each side) were selected and analysed. Pearson correlation analysis was used, and a p-value <0.05 was considered statistical significant.

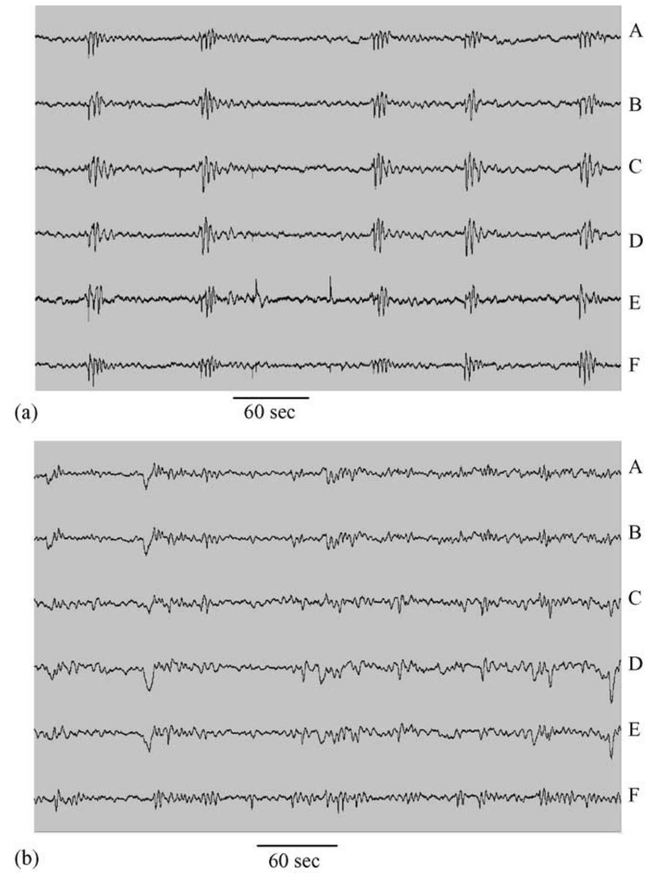

Fig. 1. (a) An interpretable recording from a 25 yr old healthy man. (b) A ‘‘non-interpretable’’ recording from a 24 yr old healthy man. A, B and C are from the left cavernous body, from the proximal to distal part in order; D, E and F are from the right side, from distal to proximal part in order.

3. Results

CC-potentials were strongly influenced by the cut-off frequencies of filters. Changing the lower cut-off frequency from 0.1 to 1 Hz resulted in a significant loss of the amplitude of CC-potentials. Changing the lower cut-off frequency from 0.1 to 0.05 Hz did not influence

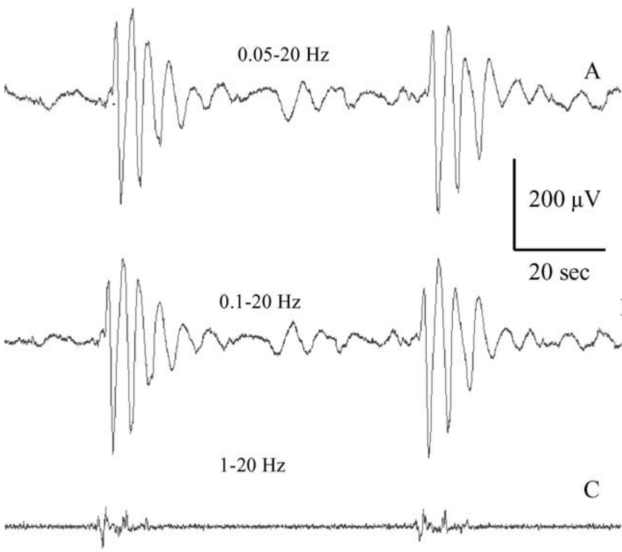

Fig. 2. A, B and C demonstrate the influence of changing lower cut-off frequency on CC-potentials. Most of the signal power seems to be between 0.1 and 1 Hz.

the amplitude of CC-potentials significantly, but the baseline became less stable (Fig. 2). Hence most of the signal power appeared to be between 0.1 and 1 Hz, and a band pass filter with cut-off frequencies of 0.1 and 20 Hz was considered to be the proper set-up.

Thirty-five of 46 recordings (76%) showed a stable baseline and interpretable CC-potentials, which could be easily analysed. Eleven recordings showed an unstable baseline, continuous oscillations, or CC-potentials interfered by disturbing signals or noise, making them impossible to analyse. The quality of the recordings seemed to be individual-dependent: all 4 recordings from a 24 years old subject and 4 out of 6 recordings from a 30 years old subject were ‘‘non-interpretable’’, while the other 10 subjects contributed 3 ‘‘non-interpretable’’ and 33 interpretable recordings. No clear physical, environmental, or psychological differences could be detected between those 2 and the other 10 subjects. See Fig. 1(a) and (b).

For the interpretable recordings, usually irregular signals were observed in the beginning, and gradually the recordings became stable, regular and interpretable. The time for stabilization differed among the subjects as well as intra-individually, varying from 0 to 20 minutes. The baseline was flat or showed slow wave-like activity, interrupted by the typical polyphasic CC-potentials. CC-potentials emerged non-periodically and the quality of the recordings and the frequency of CC-potentials seemed to be stress-dependent: the more relaxed the subject was, the better quality of the recordings, and the fewer CC-potentials. Sometimes, when a subject dozed off, ‘‘electrical silence’’ without any CC-potentials lasting for more than 10 minutes was observed. Often, after a period of ‘‘electrical silence’’, a group of CC-potentials or even a continuous long signal emerged.

CC-potentials recorded from different sites of the CC were not synchronous. Depending on the interelectrode distance, time delays were observed (around 0.5 second if the interelectrode distance was around 2.5 cm). In general, CC-potentials from proximal sites emerged earlier than those from distal sites. A few times, CC-potentials only existed at one of the cavernous bodies or even only from one electrode, while very weak oscillations were observed from other electrodes (Fig. 3).

The electrodes placed on the pubis region could also pick up electrical signals related to CC-potentials. However, their amplitude was lower, indicating a spatial voltage gradient: The further the electrodes were away from the CC, the lower the amplitudes of CC-potentials observed (Fig. 4). From the ASIS, no activity related to CC-potentials, but significant electrical activity from the heart and other sources (bowel, bladder?) could be picked up (Fig. 5).

Table 1 lists the parameters of CC-potentials and correlations between 2 recordings in 10 normal volunteers. The subject who contributed 4 ‘‘non-interpretable’’ recordings was not included. In the second measurement of another subject, the recording from the left side of the base of the penis showed much noise which severely disturbed CC-potentials, and therefore, this subject was also excluded from the correlation analysis. The amplitude, duration and polyphasity of CC-potentials in the 2 recordings showed a strong correlation, whereas the frequency of CC-potentials did not.

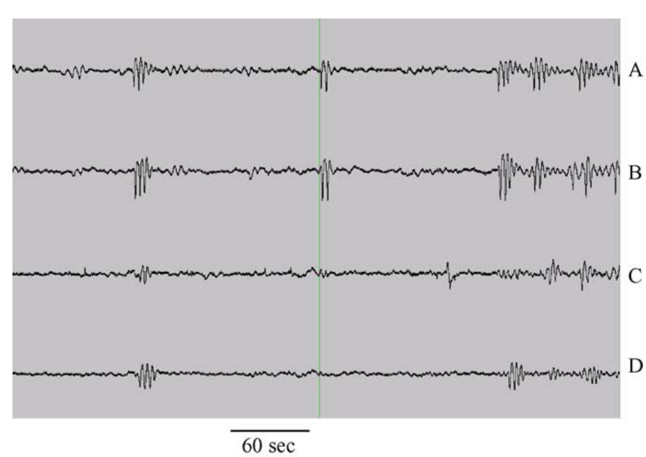

Fig. 3. The green line indicates that CC-potentials are only picked up from the left cavernous body (channel A and B), while weak oscillations are observed from the right side (channel C and D). A and D are from the base of the penis, B and C are from the distal part of the penis.

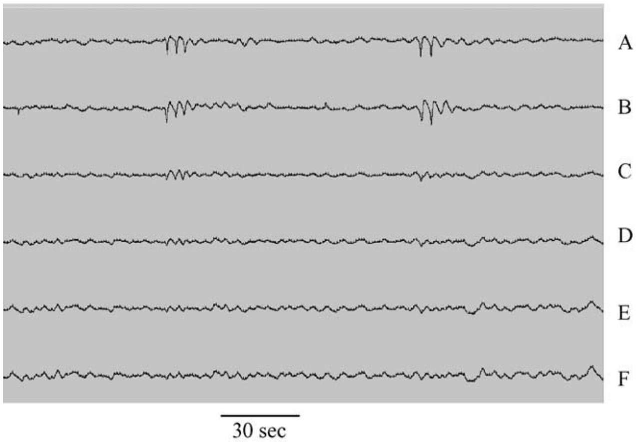

Fig. 4. A and B are from the base of the penis, C–F are from the mid line of the pubis region, 1.3; 3.1; 5; 6.4 cm (from the middle of the electrodes) to the base of the penis in order. The width of the electrodes is 1.5 cm. A clear spatial voltage gradient on the pubis region can be seen.

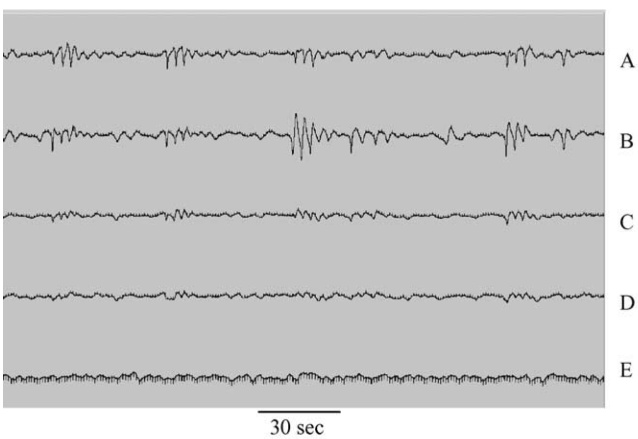

Fig. 5. A and B are from the base of the penis, C and D are from the mid line of the pubis region, 1.3; 3.1 cm to the base of the penis in order. E is from the right ASIS. A clear spatial voltage gradient on the pubis region can be seen. No voltage changes related to CC-potentials, but significant EA from the heart (ECG) is recorded from the ASIS (E).

Table 1
Parameters of CC-EMG potentials and correlation of 2 recordings in 10 healthy volunteers (data are presented as the mean ± S.D.)

	Recording 1	Recording 2	*R*	*p*-value
Amplitude (μV)	381.3 ± 79.1	365.6 ± 83.9	0.78	0.008*
Duration (s)	13.26 ± 3.61	13.76 ± 3.21	0.94	0.000*
Polyphasity	6.57 ± 2.07	6.91 ± 1.55	0.85	0.002*
Potentials/10 min	9.97 ± 6.01	9.28 ± 4.22	0.60	0.070

* Significance.

4. Discussion

So far, several systems have been used to record CC-potentials [6,7]. To our knowledge, only two studies reported multichannel (>2 channels) recordings [8,9]. The authors applied this method in a small group of patients, for a purpose of observing the relationship between signals from the CC and the limbs, and actually no multi-channel recordings from different sites of the CC were shown. In the literature, most studies used one or two channel devices, making the assessment of temporal relationship between potentials from different sites of the CC and investigation of spatial voltage gradients between adjacent regions impossible. However, both the assessment and the investigation are important for determining the origin of recorded signals. In this respect, the device used in this study had several advantages. Firstly, the availability of eight channels facilitated the study of the temporal relationship between CC-potentials and spatial voltage gradients. Secondly, monopolar as well as bipolar signals could be recorded, and the existing software made the post-hoc simulation of bipolar recordings out of two monopolar signals possible. Finally, the adjustability of the filter cut-off frequencies made the assessment of the optimal cut-off frequencies possible.

Monopolar recording facilitates the assessment of a potential difference between the electrode placed directly over/in the bioelectric source of interest and the reference electrode at a distant site at which there is no signal from this source present. Bipolar recording means that the potential difference is recorded between two electrodes (or two poles of a bipolar electrode) placed over/in the bioelectric source [7,10]. Until now, most CC-EMG studies are based on bipolar recordings [1–5]. Since a bipolar signal is a deduction of potentials between 2 monopolar electrodes, a substantial part of information may be lost. Furthermore, taking the significance of time delays of CC-potentials from different sites of the CC into account, one can imagine that the signals recorded bipolarly are dependent on the exact location of the electrodes. Placing the electrodes bilaterally or unilaterally, 2 cm or 5 cm away will make a significant difference. Moreover, because the dimensions of the penis vary widely depending on penile tumescence, it is difficult to fix the interelectrode distance exactly. Therefore, it would be problematic to make an intra-individual, inter-individual or inter-institutional comparison of bipolar recordings. These problems do not exist in monopolar recording. Although bipolar recording has the advantage that it may reduce unwanted signal components [10], all the information contained in bipolar recording is present in monopolar recording, since a post-hoc bipolar montage scheme can be derived from monopolar raw data, but not vice versa [10]. Therefore, we used monopolar recording instead of the traditional bipolar recording to revalidate the methodology of CC-EMG and to make the methodology suitable for multicenter application.

In monopolar recording, the ideal position of the reference electrode is at the site where the electrical field induced by the bioelectrical source has declined to zero; Furthermore, at this position, no specific electrical activity should be generated by itself (i.e. electrically inactive region) [10,11]. At first the pubis was under consideration, however, clear voltage changes related to CC-potentials were recorded at this location. The ASIS was then chosen. However, electrical activity of the heart and other sources (bowel, bladder?) were picked up from the ASIS, and significantly affected CC-potentials. Due to the following characteristics, the kneecap turned out to be the optimal reference position: (1) It is far away from the CC and other organs containing smooth muscle. (2) There are no major muscles or nerves underlying the skin. With this placement, most of the recordings showed a stable baseline and interpretable CC-potentials.

Despite efforts to rule out confounding factors (a strict study protocol was used, involving only young healthy volunteers who were prohibited to drink alcohol and coffee, smoke or have sexual activity 12 hours prior to the measurements, the room temperature was kept constant and all the measurements were performed by the same investigator [X.G.J.]), one in four recordings was "non-interpretable". In the literature, "non-interpretable" recordings are reported in about one in three subjects [6]. This may be partly due to improper skin preparation, electrodes placement or faulty connections, stress in the subject or movement artefacts. Additionally, tumescence changes due to skin preparation and electrode placement may play a role in inducing sympathetic activity and thus inducing irregular signals. Also, the electrode gel needs time to penetrate the skin to build a stable gel-skin interface [12]. However, the fact that the quality of the recordings in the present study was individual-dependent cannot be explained by these factors. We speculate that the reproducible "non-interpretable" recordings are caused by an intrinsic high basic sympathetic tone of the subject. The consistent finding in the literature and the present study of irregular signals in the beginning of the measurements which is explained by a high sympathetic tone due to "stress" or anxiety supports our speculation [2,4]. Further studies in more subjects are needed to verify this hypothesis and to clarify the underlying mechanism.

As described earlier [7], the optimal filter cut-off frequencies are still to be decided. Stief et al. demonstrated that the signals are in a frequency range below 5 Hz [4,13,14]. In accordance with their observation, our results clearly show that most of the signal power is between 0.1 and 1 Hz: Decreasing the lower cut-off frequency below 0.1 (to 0.05 Hz) does not influence the amplitude of the CC-potential significantly, whereas the included low frequency baseline fluctuations may impair the interpretation of CC-potentials. Therefore, 0.1 Hz is recommended as the lower cut-off frequency. The higher cut-off frequency should be at least above 5 Hz, but below 50 Hz to avoid the 50 Hz mains noise. Hence, we recommend 20 Hz as the higher cut-off frequency.

Since the introduction of CC-EMG, doubts whether the recorded signals reflect electrical activity of the CC have persisted. Other possibilities suggested in the literature include distant electrical events [8], retractile movements of the penis [15], changes in volume of the penis caused by blood flow [16], and sympathetic skin response (SSR) [8]. The results of this study provide strong evidence that the recorded signals indeed reflect electrical activity of the CC: Firstly, the non-synchronicity of potentials recorded at different sites of the penile shaft proves that they are generated from the penis. It is a common knowledge that signals from a distant source would be synchronous [17]. Furthermore, the existence of spatial voltage gradients related to CC-potentials measured on the pubis region indicates that the penis, rather than other organs, is the source of the recorded signals. Moreover, the existence of signals on the pubis region accompanying CC-potentials rules out that CC-potentials are caused by the retractile movements or changes in volume of the penis, since it is unlikely that the retractile movements or changes in volume also occurs there. Finally, the facts that the signals recorded at the pubis were not identical to signals recorded at the penis but appeared to be spatial voltage gradients, and their absence at a more distant region (the ASIS) indicates that they are not SSR, because SSR is a widespread and not a local phenomenon.

Besides so-called representative CC-potentials, a substantial number of "non-representative" CC-potentials were encountered, for example CC-potentials disturbed by movement artifacts or noise, potentials with low amplitude and short duration (i.e. signals from a distant source), or continuous long signals. If all these potentials were included for quantitative analysis, the value of the parameters would have been variable and unreliable. Therefore, in line with the literature [6] only representative CC-potentials were included for the assessment of reproducibility. The results show that amplitude, duration and polyphasity of CC-potentials are reproducible, whereas frequency, i.e. number of CC-potentials per time unit is not. In the literature, only one study reported reproducibility analysis of 2 independent recordings [5]. Although the authors concluded that the parameters of CC-potentials are poorly reproducible, on closer examination of their data, parameters such as amplitude and duration of CC-potentials appeared to be reproducible, whereas polyphasity was not analyzed. The most irreproducible parameter was number of potentials per time unit. The fact that the latter is not reproducible does not come as a surprise, since the number of CC-potentials per time unit is highly dependent on the sympathetic tone of the subject, which can vary significantly.

5. Conclusion

The objective of this study was to revalidate the methodology of CC-EMG, using state-of-the-art equipment and strict protocols, within the framework of a European collaboration. We could demonstrate that multichannel monopolar recording of CC-potentials has several advantages as compared to the traditional bipolar recording. Therefore, a multichannel equipment allowing to perform monopolar recording should be used. The filtering setting of the equipment should be adjustable, and a band pass filter with cut-off frequencies of 0.1 and 20 Hz is recommended. The parameters: amplitude, duration and polyphasity of CC-potentials appear to be reproducible, while frequency does not. By using this methodology time delays between CC-potentials recorded from different sites of the CC and spatial voltage gradients at the level of the pubis region could be demonstrated. These results provide strong evidence that the recorded signals indeed reflect electrical activity of the CC and therefore offer a basis to pursue further clinical validation studies.

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Editorial Comment

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CC-EMG has been considered, for many years, a test of great potential for direct assessment of penile neurogenic function. Yet, despite 15 years of experience, this test has not emerged from the research lab into the clinic. This attests to some basic difficulties still unresolved, regarding basic features of the CC-EMG wave. We are not sure what is the origin of the wave, how reproducible it is in the intra- and inter-individual level, how sensitive it is to pathological conditions, and therapeutic interventions. Further, even the technical details of the recording of this waveform are still under debate. We think that there is a clear need for basic animal research, that could elucidate the open basic mechanistic questions. For example, severing various nerves, and pharmacological interventions could be used to deduct, by elimination, what is the source of the potential. Secondly, elaborate work on the technical aspects of the recording should be conducted.

The present paper represents a small step in this direction, trying to evaluate some of the technical aspects of the CC-EMG recordings in normal controls. The strategy of spatial voltage gradient is an elegant one, and convincingly shows that the potential probably originates at penile tissue. Still, several questions come to mind when reading this article. First, what is the mechanism underlying the periodic electrical activity recorded from the penis—is it sympathetic? parasympathetic? somato-ensory potentials? Second, why are a quarter of the recordings 'un-interpretable'? Is it technical only? Could a clinical test be useful if it does not apply to a quarter of patients? Thirdly, reproducibility reported in this paper relates to simple parameters of the potential, and does not try to auto-correlate the waveforms from the two sessions between themselves, in an attempt to verify whether it is the same source of potentials in the two recording sessions.

While this paper represents a certain step forward, the questions mentioned above are still open, and CC-EMG will not move to light before a serious research effort is carried out to sort these issues out.