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·Original Article ·

Application of correlation techniques in the analysis of corpus cavernosum electromyographic signals

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Abstract

Aim: To establish an objective, easy-to-use and comprehensive method to analyze corpus cavernosum electromyographic signals (CC-potentials). **Methods:** CC-potentials were recorded during flaccidity in 23 young healthy volunteers, with surface electrodes placed on the penile shaft bilaterally. Based on the correlation function of Matlab software, an application program for the analysis of CC-potentials was developed. Individual CC-potentials and their autocorrelation function were evaluated, yielding parameters amplitude (*A*), duration (*D*), and dominant frequency (*DF*). The crosscorrelation function of both longitudinal and bilateral pairs of adjacent electrodes was calculated to assess the similarity and mutual delay of CC-potentials recorded simultaneously from different parts of the CC. The parameters derived were squared maximum cross-correlation coefficient (*Rmax*) and delay (τ). Based on the absolute value of τ and the corresponding inter-electrode distance, propagation velocity (*PV*) was calculated. **Results:** The values of the parameters were determined automatically. No significant difference related to the locations of the electrodes for parameters *A*, *D*, and *DF* was detected. The cross-correlation showed that both longitudinal and bilateral CC-potential pairs had highly similar waveforms (the absolute values of *Rmax* were 0.80 \pm 0.05 and 0.87 \pm 0.06, respectively). *PV* of longitudinal pairs was estimated as 6.15 \pm 3.98 cm/s. **Conclusion:** The application program for correlation analysis of CC-potentials is a comprehensive and versatile method to analyze corpus cavernosum electromyographic recordings. Its objectiveness makes multi-center application possible. (*Asian J Androl 2007 May; 9: 369–376*)

Keywords: corpus cavernosum; corpus cavernosum electromyography; electrophysiology; erectile dysfunction; smooth muscle

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1 Introduction

Corpus cavernosum electromyography (CC-EMG) has failed to mature into a useful clinical tool for diagnosing erectile dysfunction (ED), as a result of insuffi-

cient understanding of the electrophysiology of the corpus cavernosum (CC) and the recorded signals (CCpotentials), and a lack of standardization of the recording technique as well as signal processing and signal analysis methods [1]. Recently, significant progress has been made to overcome these shortcomings. The methodology of CC-EMG recording was revisited. Monopolar recording has been shown to be superior to the traditional bipolar recording [2]. With this setup, further evidence has been obtained to support the notion that CC-potentials reflect sympathetically mediated electrical activity of cavernous smooth muscle (CSM) [2, 3]. However, a valid, objective, and easy-to-use method to analyze CC-potentials has not been established yet. Most clinical investigators measured the values of parameters manually [4-6], which is time-consuming, imprecise and not objective. Stief et al. [7] and Kellner et al. [8] addressed this issue by introducing Fourier analysis and computerized classification of CC-potential components by fuzzy logic and neural networks. However, these methods have not been applied by other centers, probably because the required basic knowledge of linear systems analysis is generally beyond the expertise of clinical physicians. Later on the same group explored the application of cross-correlation function to estimate time delay of CC-potentials recorded at different sites of the penis, which has only been published in a monograph (in German) [9] and did not result in the introduction of this method for the evaluation of CC-EMG recordings.

This study was aimed at establishing an analysis method that is easy-to-use for physicians, comprehensive and objective. Because CC-potentials can be considered spindle-like wave complexes [2], correlation techniques were used in a CC-EMG application program. This program was applied to a set of recordings in a group of young volunteers.

2 Materials and methods

2.1 Data collection

The methodology to record CC-potentials has been described in detail in a previous study [2]. Briefly, with six or four surface electrodes (depending on the size of the penis) placed on the penile shaft bilaterally, CC-potentials were recorded simultaneously and monopolarly for 20–30 min during flaccidity. To allow monitoring the signals during the measurements, the recorded signals were digitized and filtered with a bandpass filter (cut-

Using Matlab software (MathWorks, Natick, MA, USA), the unfiltered signals of each channel were extracted separately and filtered with a digital second-order bandpass filter (cut-off frequencies 0.1 Hz and 5.0 Hz). The purpose of reducing the higher cut-off frequency to 5.0 Hz was to suppress high frequency, common signal components (in particular electrocardiographic signals) as much as possible without attenuating the CC-potential amplitude. It has been demonstrated that CC-potential power in normal subjects is actually below 5.0 Hz [2, 7].

2.2 CC-potential analysis

An application program for the analysis of CC-potentials was developed based on the correlation function of Matlab. Basically, the auto- and cross-correlation functions reduce the influence of noise, thus allowing the parameters of the CC-potential to be estimated more accurately than from the signal itself [10]. Because the onset and end of a CC-potential were not always definite, an objective method to decide them seemed necessary. With this application program the onset and end of a CCpotential could be set to correspond with oscillations exceeding a user-defined percentage of its maximum amplitude. After testing with different percentages, 20% turned out to be proper, because 20% of the maximum peak-to-peak amplitude was just above the baseline fluctuation (noise) level (approximately 75 μ V) [6].

Individual CC-potentials were characterized by analyzing the original signals and their autocorrelation functions, and the corresponding values of the parameters amplitude (A), duration (D), and dominant frequency (DF) were determined. In Figure 1A and Figure 1B a CC-potential and its autocorrelation function, respectively, are shown. A was defined as the voltage difference between the highest negative peak and the higher of the two adjacent positive peaks. This strategy was chosen because measuring the voltage difference between the highest negative peak and the highest positive peak not adjacent to the negative peak may be markedly affected by baseline fluctuations when the baseline is instable (Figure 2). D is the time window in seconds where the A of the CC-potential exceeds a user-defined percentage (20% in this study) of its maximum amplitude. DF (Hz), the frequency of a CC-potential where most signal power



Figure 1. (A): CC-potential. The two horizontal lines indicate the pre-selected percentage of its maximum amplitude (20% in the example shown), and the two vertical lines indicate its onset and end. All lines are determined automatically by the program. (B): Autocorrelation function of the CC-potential in Figure 1A. Lag is zero at highest positive peak (Rmax = 1).

is present, was calculated from the time intervals between zero crossings of the autocorrelation function.

To assess the similarity and mutual delay of CC-potentials recorded simultaneously from different sites of the corpora cavernosa, the cross-correlation function of both longitudinal and bilateral pairs of adjacent electrodes was calculated. Seven combinations were made for recordings with six electrodes (Figure 3), and four combinations in recordings with four electrodes. In Figure 4A and Figure 4B, respectively, two simultaneously recorded CC-potentials and their cross-correlation function are



Figure 2. The methods to determine amplitude. a: The voltage difference between the highest negative peak and the higher one of the two adjacent positive peaks, 491 μ V. b: The voltage difference between the highest negative peak and the highest positive peak (not adjacent to the negative peak), 531 μ V. b is possibly affected by the baseline fluctuations superimposed to the CC-potential.



Figure 3. Electrode combinations for cross-correlation analysis. The arrows indicate the seven combinations in recordings using six electrodes.

shown. The parameters derived from the cross-correlation function are the squared maximum cross-correlation coefficient (*Rmax*) and the delay (τ) between two CC-potentials. If the two signals are identical, then *Rmax* is 1; if they have no components in common, *Rmax* is 0; if they are identical but their phases are shifted by exactly 180° (i.e. mirrored), then *Rmax* is –1. All visually identified CC-potentials with a typical spindle-like polyphasic waveform and a definite start and end were included. However, in order to allow a comparison of recordings with different numbers of CC-potentials, only

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Figure 4. (A): Two CC-potentials simultaneously recorded from the proximal (solid line) and middle (dashed line) sites of the CC. The two horizontal lines indicate 20% of maximum amplitude of the smaller CC-potential; the two vertical lines indicate the start and end of the CC-potentials as determined automatically by the program. (B): Cross-correlation function of the CC-potential pair in Figure 4A. τ (+ or –) is determined from sample count corresponding to maximum closest to sample zero. *Rmax* = 0.81, τ = –0.73 s.

data of five CC-potential pairs with the highest absolute values of *Rmax* were included. Based on the absolute value of τ and the corresponding inter-electrode distance, propagation velocity (*PV*) was estimated. To improve the accuracy, *PV* was calculated only from pairs of recordings with all five, or four out of five selected CCpotential pairs having either a positive or a negative t and thus the same "propagation" direction. When four out of five selected CC-potential pairs had the same sign of τ , only these values were included and the CC-potential pair with opposite sign of τ was omitted. As a pilot study, electrode combinations not adjacent to each other were analyzed in several subjects. The results showed that the sum of τ between, for example, distal-middle electrodes and middle-proximal electrodes were approximately equal to τ between distal and proximal electrodes (data not shown). Therefore, it seems that including more combinations may not provide extra information, while it would be much more time-consuming.

In practice, the cross-correlation analysis was performed first, in order to select five longitudinal CC-potential pairs with the highest absolute *Rmax* for the autocorrelation analysis.

2.3 Study population and recording equipment

Twenty-three healthy Caucasian men with a mean age of 24.7 years (range 19–32 years) were included in this study. The volunteers were asked to refrain from alcohol, coffee, smoking and sexual activity within a period of 12-h prior to the measurements. Informed consent was obtained from each subject.

Screener or a Porti system (TMS International, Enschede, the Netherlands) connected to a portable computer (Satellitepro 6100, Toshiba, Tokyo, Japan) was used to record CC-potentials. The amplifier parts of the two systems were identical. The two systems had a slightly different, fixed sampling rate (128 Hz and 100 Hz, respectively). This difference does not affect the digitized CC-potentials, since the same filter was used to process the signals recorded with the two devices, and the low-pass cutoff frequency was only approximately 4–5% of the sampling rates. The electrodes were pregelled surface electrodes (type 9021S0231; Medtronic, Copenhagen, Denmark).

2.4 Statistical analysis

SPSS software (SPSS Inc., Chicago, USA) was used for the statistical analysis. One-Sample K-S Test was applied to test the normality of distribution of parameter values. Two Factorial Analysis of Variance was used to test the effect of electrode location (left and right side, proximal, middle and distal site) on the values of the parameters.

3 Results

Among all 23 subjects, 10 had six electrodes and the

Table 1. Effects of electrode locations on CC-potential parameters (tested with Two Factorial Analysis of Variance). [#]Sides represent left and right sides. ^{\$}Positions represent proximal, middle and distal sites.

		P value		
	Effect	Α	D	DF
Six electrodes	Sides [#]	0.484	0.834	0.279
	Positions ^{\$}	0.089	0.823	0.102
	Sides + positions	0.848	0.827	0.954
Four electrodes	Sides	0.451	0.739	0.543
	Positions	0.185	0.699	0.086
	Sides + positions	0.444	0.741	0.904

tials recorded with these electrodes were excluded.

3.1 Single CC-potential analysis

The values of the parameters A, D, and DF were determined automatically by the program. Normal distribution was found in the values of all the three parameters. The three parameters of CC-potentials recorded at the same level (proximal-middle-distal) but on opposite sides of the penis did not differ significantly (Table 1). Therefore, the values on both sides were taken together. The values of these parameters are shown in Table 2. No significant difference related to the loca-

Table 2. Value of parameters A, D, and DF. Data are given as mean \pm SD. *The recording from one subject with six electrodes was excluded because electrode pairs from both side of the penis showed nearly identical baseline fluctuations and CC-potentials, indicating a short circuit between them.

		n	<i>Α</i> (μV)	<i>D</i> (s)	DF (Hz)
	Proximal	9*	378 ± 104	12.34 ± 2.32	0.28 ± 0.06
Six electrodes	Middle	9	415 ± 99	12.44 ± 3.14	0.27 ± 0.06
	Distal	9	333 ± 115	12.97 ± 3.88	0.24 ± 0.05
Four electrodes	Proximal	13	342 ± 81	13.04 ± 3.35	0.24 ± 0.03
	Distal	13	306 ± 92	12.72 ± 2.63	0.23 ± 0.03

Table 3. "Propagation" direction of longitudinal CC-potential pairs. The "propagation" direction was determined based on the sign of delay (τ) between two CC-potentials, e.g., if τ between two CC-potentials recorded at left-proximal and left-distal sites (proximal-distal), respectively, is positive (in other words, the CC-potential from left-proximal site appear earlier than that from left-distal site), the "propagation" direction is assumed as "from proximal to distal". *Two or more out of the five CC-potential pairs had a "propagation" direction different from the others.

"Propagation" direction	Number of	Percentage	
	electrode pairs	(%)	
5 distally	34	56.7	
4 distally	9	15.0	
5 proximally	3	5.0	
4 proximally	2	3.3	
Other*	12	20.0	
Total	60	100.0	

Table 4. "Propagation" direction of bilateral CC-potential pairs. *Two or more out of the five CC-potential pairs had a "propagation" direction different from the others.

Number of Percentage (9		
lectrode pairs	Tercentage (70)	
10	21.3	
3	6.4	
8	17.0	
6	12.8	
20	42.6	
47	100.0	
	Number of lectrode pairs 10 3 8 6 20 47	

tions of the electrodes was found for any parameter (Tables 1 and 2).

other 13 had four electrodes. Five electrode pairs showed nearly identical baseline fluctuations and CC-potentials ($Rmax \approx 1$ and $\tau \approx 0$), indicating a short circuit between the corresponding adjacent electrodes. The CC-poten-

3.2 Analysis of CC-potential pairs

Data of 60 longitudinal and 47 bilateral electrode pairs were analyzed. The values of *Rmax* and *PV* showed normal distribution. The mean \pm SD of *Rmax* of longitudinal and bilateral pairs were 0.80 ± 0.05 and 0.87 ± 0.06 ,

respectively. In Tables 3 and 4 the "propagation" direction of longitudinal and bilateral CC-potential pairs are shown. In 71.7% of longitudinal pairs all five or four out of five CC-potential pairs propagated distally, and in 8.3% of them all five or four out of five CC-potential pairs propagated proximally. *PV* of longitudinal pairs of CC-potentials was estimated at 6.15 ± 3.98 cm/s (mean \pm SD). The bilateral pairs had similar counts for a delay from left to right (27.7%) and in the opposite direction (29.8%).

4 Discussion

In this study the correlation techniques are introduced as an easy-to-use, comprehensive, and objective method to analyze CC-potentials. In neurophysiology, correlation analysis is a well-established methodology to quantify the properties of striated muscle EMG and other bioelectrical signals [10–12]. By analyzing original signals and their autocorrelation functions, individual bioelectric signals, such as CC-potentials, can be characterized accurately. The cross-correlation function allows quantifying the similarity of simultaneously recorded signals (quantified as *Rmax*) and estimating their mutual time delay (τ). If a signal, such as a CC-potential, is propagating between two electrodes, *PV* can be simply calculated [10, 11].

CC-potential amplitude (A) is the most commonly used parameter [4-6]. In this study the value of A in healthy men (Table 2) was in the same range as those in the published literature [6]. Because CC-potentials recorded with surface electrodes are supposed to reflect the superimposed oscillatory membrane currents of a group of adjoining CSM cells [1], presumably, a decrease of A is expected when: (i) the CSM content is decreased (CSM degeneration), (ii) the thickness of the tissue enveloping CSM is increased, (iii) the intercellular communication via gap-junctions is impaired, (iiii) the sympathetic input is affected. The latter two situations may result in a diminished synchronization of the depolarization and repolarization of the CSM cell membranes. This presumption has been supported by the observation that the CC-potential A was decreased in patients with CSM degeneration [13], penile edema [14], diabetes mellitus [4], and in patients undergoing radical pelvic surgery, and so on [5, 15].

Correlation analysis and spectral (Fourier) analysis of CC-potentials provide the same information in the time domain and the frequency domain, respectively. Accordingly, *DF* calculated from the autocorrelation function corresponds with the frequency with the highest power in the power density spectrum [7]. As CCpotentials are supposed to reflect the superimposed membrane currents caused by Ca^{2+} influx through L-type voltage gated Ca^{2+} channels of *CSM* cells [1], the value of *DF* as calculated in this study (approximately 0.25 Hz) is likely to correspond with the kinetics of these Ca^{2+} channels [16]. Theoretically, myogenic pathologies changing the membrane properties of CSM cells may alter the value of *DF*.

The high *Rmax* of longitudinal pairs (0.80 ± 0.05) indicates that the waveforms of CC-potentials recorded simultaneously at different sites along the penile shaft are highly similar, although not identical. Therefore, *Rmax*, a parameter quantifying the similarity of CC-potentials recorded simultaneously in different parts of the CC, may be useful to reflect coordination of electrical activity in different parts of the CC. According to the existing knowledge, the sympathetic input and communication via gap junctions between CSM cells are responsible for the initiation, propagation and coordination of electrical activity within the CC [17, 18]. Based on this notion, sympathetic neuropathy or conditions affecting the communication between CSM cells may result in a decreased *Rmax* of CC-potential pairs by, for example, having irregular waveforms, different DF and D, or even a failure of propagating electrical activity from one site to another.

The majority of CC-potentials propagated in a distal direction, towards the tip of the CC (Table 3) indicating that CC-potentials are mostly initiated in the proximal part of the CC. However, in 38.3% of the longitudinal pairs the CC-potentials propagated both distally and proximally, suggesting that CC-potentials may be initiated at more than one site in the CC. In 5% of the pairs all five CC-potentials propagated in a proximal direction, suggesting that the initiation sites can be present in the distal part of the CC.

Although bilateral CC-potential pairs had highly similar waveforms (high *Rmax*), the fact that bilateral pairs had no preferential direction of τ (Table 4), together with the existing knowledge that the left and right corpora cavernosa are innervated separately [17], indicate that the coordination of electrical activity in the two cavernous bodies possibly occurs in the pre-CC level (e.g. spinal cord), rather than by a mechanism in which electrical activity propagates among CSM cells via gap junctions as happens within one CC.

In this study, PV was estimated as 6.15 ± 3.98 cm/s, whereas Gorek et al. [9] calculated a similar mean value of 5 cm/s. This value indicates that CC-potentials travel via gap junctions among CSM cells rather than via nerve fibers. In the latter case, PV would have been much higher (approximately 100 cm/s) [19]. Although a change in PV is an important indicator of muscle disease in striated muscle EMG [20], the value of PV to detect myogenic pathology in CC-EMG is questionable. Because the inter-electrode distance cannot be kept constant during a 20-30 min recording session (the penile length changes depending on a subject's sympathetic tone, room temperature, etc.), PV is only useful if its change caused by pathology is larger than the variation caused by the variable inter-electrode distance. Furthermore, PV can only be estimated correctly when the electrodes are aligned with the propagation direction. Because CSM is a three-dimensional structure, CC-potentials may propagate in various directions, even though the overall direction is longitudinal.

No difference for any parameters in relation with the electrodes locations was detected, indicating that only using one or two electrodes would be enough to obtain representative CC-potentials. In fact, in our later study we only included CC-potentials from left and right proximal sites for calculating the values of A, D and DF, although four electrodes were used. The reason we included CC-potentials from both sides of the penis is that, under certain circumstances (e.g. unilateral cavernous nerve damage following pelvic surgery), the change in CC-potential patterns may be only unilateral and, therefore, recording CC-potentials only from one CC may result in a false-negative finding. In order to assess the coordination of the electrical activity in different parts of the penis (by calculating Rmax), four electrodes were still used, although the CC-potentials from the distal electrodes were not included for calculating other parameters.

In conclusion, the application program for correlation analysis of CC-potentials introduced in this study is a comprehensive and easily applicable method to analyze CC-EMG recordings. Its objectiveness makes multi-center application possible. By calculating the parameters *A*, *D*, *DF*, *Rmax*, and *PV*, CC-potentials can be characterized adequately. The next steps of our study are to test the reproducibility (stability) of the parameters, and to investigate their sensitivity and specificity to detect myo- and neurogenic pathology of the CC.

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