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Physiological and harmonic components in neural and muscular coherence in Parkinsonian tremor

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Abstract

Objective: To differentiate physiological from harmonic components in coherence analysis of the tremor-related neural and muscular signals by comparing power, cross-power and coherence spectra.

Methods: Influences of waveform, burst-width and additional noise on generating harmonic peaks in the power, cross-power and coherence spectra were studied using simulated signals. The local field potentials (LFPs) of the subthalamic nucleus (STN) and the EMGs of the contralateral forearm muscles in PD patients with rest tremor were analysed.

Results: (1) Waveform had significant effect on generating harmonics; (2) noise significantly decreased the coherence values in a frequency-dependent fashion; and (3) cross-spectrum showed high resistance to harmonics. Among six examples of paired LFP–EMG signals, significant coherence appeared at the tremor frequency only, both the tremor and double tremor frequencies and the double-tremor frequency only.

Conclusions: In coherence analysis of neural and muscular signals, distortion in waveform generates significant harmonic peaks in the coherence spectra and the coherence values of both physiological and harmonic components are modulated by extra noise or non-tremor related activity.

Significance: The physiological or harmonic nature of a coherence peak at the double tremor frequency may be differentiated when the coherence spectra are compared with the power and in particular the cross-power spectra.

Keywords: Local field potential; Electromyograms; Spectral analysis; Coherence; Harmonics; Tremor

1. Introduction

The extensive networks in the central nervous system contributing to the generation of tremor have been a focus for neurophysiological study in both physiological and pathological tremor. One of the most common approaches is to physiologically detect the tremor related signals at different sites of the sensorimotor system, and the simultaneously recorded signals are subsequently analysed to reveal the functional interconnections among them so that a functionally linked network can be identified in spatial and temporal domains. There have been recent advances in physiological recording techniques such as magnetoencephalography (MEG) (Halliday et al., 2000; Marsden et al., 2001a; Timmermann et al., 2003; Volkmann et al., 1996) and depth local field potentials (LFPs) (Brown, 2003; Liu et al., 2002; Marsden et al., 2000, 2001b) that have taken the field beyond conventional electroencephalograhpy (EEG) and electromyography (EMG) (Mima and Hallett, 1999). Recently, there are rapid developments in signal processing techniques such as coherence (Halliday et al., 1995, 2000;

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Lenz et al., 1988), partial coherence (Liberati et al., 1997; Lopes-da-Silva et al., 1980a) directional measures (Cassidy and Brown, 2003; Kaminski and Blinowska, 1991; Sharott et al., 2005) or causality analysis (Brovelli et al., 2004; Kaminski et al., 2001; Liang et al., 2000).

However, despite the widespread deployment of these new techniques to tremor study, some technical improvements can still be made to the details of these methods. For instance, it is difficult to have confidence about whether or not a small peak in a coherence spectrum that is close to the upper 95% confidence limit based on the assumption of independence (Halliday et al., 1995) is statistically significant measure for correlation or not. Thus, we propose the computation of the exact confidence interval of the coherence estimates (Wang and Tang, 2004) for directly testing the dependence between a given pair of signals and to evaluate the efficiency of the coherence estimator (Wang et al., 2004).

Another extensively debated issue is how to determine the physiological or harmonic nature of the peaks apparent in a fast Fourier transform (FFT) based coherence spectrum between tremor related neural and muscular signals. For example, Marsden and colleagues (2000) found the peak in thalamic LFP–EMG coherence at tremor frequency (6 Hz) was accompanied by peaks at 12 and 21 Hz. They were not certain whether the peak at 12 Hz was related to physiological tremor and/or was a harmonic of the 6 Hz tremor. This phenomenon, namely that coherence peaks appear at tremor and double tremor frequencies was also demonstrated in another study (Timmermann et al., 2003) where strong MEG–EMG coherence was detected at tremor and also at the double tremor frequency, whereas the main frequency of cerebro–cerebral coupling corresponded to the double tremor frequency. In our previous studies on LFP–EMG coherence in Parkinsonian tremor (Wang et al., 2004) and dystonic tremor (Wang et al., 2003), peaks at the tremor and double tremor frequencies were also found. The functional significance of the component at double tremor frequency has been discussed by Pollok and colleagues (Pollok et al., 2004). On the one hand, a peak at double tremor frequency may represent the second harmonic of the fundamental tremor frequency, as the tremor signal in the EMG does not fit a pure sine wave. On the other hand, this frequency may also represent a real physiological feature of the motor system underlying the control of alternating activation of the agonist and antagonist forearm muscles (Pollok et al., 2004; Timmermann et al., 2003).

In the present study, we take a novel approach to differentiate physiological from harmonic components in coherence analysis of the neural and muscular signals in Parkinsonian tremor by comparing power, cross-power and coherence spectra. The objectives of the present study are (1) to identify the main factors influencing the generation of harmonics in coherence estimation using signals that simulate tremulous LFPs and EMGs with changes to the waveform and additional noise; and (2) to demonstrate that the physiological component in coherence spectra between the tremor-related LFPs of the subthalamic nucleus (STN) and EMGs may be differentiated from the harmonics by comparing power, cross-power and coherence spectra obtained from patients with Parkinson's disease.

2. Methods

2.1. Simulated signals

The envelope signal of the rectified EMGs related to Parkinsonian rest tremor is not sinusoidal and usually characterised as rhythmic bursts of an asymmetrical shape. In contrast, the LFPs related to Parkinsonian tremor are much closer to a sinusoidal waveform. Therefore, when artificial signals were simulated to investigate the influence of the waveform shape and noise on coherence estimation, rhythmic pulses varying in duration were formed to simulate the envelope of the rectified tremor EMGs, and sinusoidal waves varying in waveform, the noise level and frequency distribution simulated the LFPs. The envelope of rectified tremor EMGs was simulated by a repetitive half cycle sinusoidal waveform of 5 Hz with width of 0.16 and 0.08 s. Then extra random noise of 50 and 100% in amplitude of the simulated signal was added to investigate the influence of noise. The oscillatory LFPs were simulated by a sinusoidal waveform, half cycle sinusoidal waveform of 5 Hz with a fixed cycle width of 0.2 s. Then extra random noise of 100 and 200% in amplitude was added.

2.2. Signal recordings in patients

With the local research ethics committee approval and informed consent from each patient, LFPs were recorded with a bipolar configuration via the adjacent pair of contacts of the implanted macrostimulation electrode to the STN in 6 patients with Parkinsonian rest tremor. The patients were on medication and stimulator off on the day of recording. They were assessed by unified Parkinson's disease rating scale (UPDRS) and the tremor severity was assessed by its subscore of tremor at rest (Table 1). The bipolar configuration provides a powerful 'common mode rejection' to the far field activity and noise contamination. Surface EMGs were recorded using disposable adhesive Ag/AgCl electrodes (H27P, Kendall-LTP, MA, USA) over the selected flexor, extensor muscles of the forearm. Signals were amplified using isolated CED 1902 amplifiers ($\times$10,000 for LFPs and $\times$1000 for EMGs), filtered at 0–500 Hz and digitised using CED 1401mark II at rates of 2000 Hz, displayed on line and saved onto a hard disk using a custom written program in Spike2 (Cambridge Electronic Design, Cambridge, UK).