Clinical Neurophysiology 128 (2017) 622–634

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Intermittent bilateral coherence in physiological and essential hand tremor

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ARTICLE INFO

Article history:
Accepted 23 December 2016
Available online 14 January 2017

Keywords:
Physiological tremor
Essential tremor
Bilateral coupling
Coherence
Ballistocardiac impulse
Accelerometry
Wavelet analysis

HIGHLIGHTS

- The two hand oscillations are frequently mutually coherent in physiological and essential tremor.
- Epochs of strong coherence alternate with intervals of insignificant coherence.
- Transient entrainment of physiological tremor by ballistocardiac forcing is inferred.

ABSTRACT

Objective: To investigate the prevalence and the temporal structure of bilateral coherence in physiological (PT) and essential (ET) hand tremor.
Methods: Triaxial accelerometric recordings from both hands in 30 healthy subjects and 34 ET patients were analyzed using spectral coherence and wavelet coherence methods. In 12 additional healthy subjects, the relation between the hand tremor and the chest wall acceleration was evaluated using partial coherence analysis.
Results: The majority of both PT and ET subjects displayed significant bilateral coherence. While in PT, bilateral coherence was most frequently found in resting hand position (97% of subjects), in ET the prevalence was comparable for resting (54%) and postural (49%–57%) positions. In both PT and ET, epochs of strong coherence lasting several to a dozen seconds were separated by intervals of insignificant coherence. In PT, bilateral coherence at the main tremor frequency (8–12 Hz) was coupled with the ballistocardiac rhythm.
Conclusion: The oscillations of the two hands are intermittently synchronized in both PT and ET. We propose that in postural PT, bilateral coherence at the main tremor frequency arises from transient simultaneous entrainment of the left and right hand oscillations to ballistocardiac forcing.
Significance: Bilateral coherence of hand kinematics provides a sensitive measure of synchronizing influences on the left and right tremor oscillators.

1. Introduction

Physiological tremor and many of the pathological tremors typically occur in limbs on both the sides of the body, with similar fundamental frequency of the oscillation. This raises the possibility that the contralateral tremors may have a common source or are otherwise coupled. To confirm such coupling, however, it is necessary to systematically assess the dependence of the two tremor oscillations. This is commonly done by coherence analysis, which has been used in the previous literature to quantify kinematic

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http://dx.doi.org/10.1016/j.clinph.2016.12.027
1388-2457/

(Marsden et al., 1969a; Morrison and Newell, 1999) as well as inter-muscular (Lauk et al., 1999; Raethjen et al., 2000b) or cortico-muscular (Hellwig et al., 2001, 2003; Muthuraman et al., 2013) dependencies in various types of tremor. A finding of significant coherence between the tremors in opposite limbs points towards a common mechanism of tremor genesis. In addition, the understanding of bilateral tremor coherence is important in the context of bilateral entrainment tests for differential diagnosis of tremor diseases (McAuley and Rothwell, 2004).

Highly prevalent bilateral coherence was found in orthostatic tremor (Lauk et al., 1999) and psychogenic tremor (McAuley and Rothwell, 2004; Raethjen et al., 2004). For other tremor types, only limited evidence of bilateral coherence has been shown in the previous literature. In Parkinson disease tremor, (Moore et al., 2000) reported brief intervals of bilaterally coherent oscillation in hand kinematics, while studies assessing muscle activity (Lauk et al., 1999; Raethjen et al., 2000a) did not find any bilateral coherence. In essential tremor (ET), (Hellwig et al., 2003) found transiently occurring bilateral coherence of the wrist extensor muscle activities, while (McAuley and Rothwell, 2004) reported occasional kinematic bilateral coherence that was not accompanied by EMG coherence. In postural physiological tremor (PT), no bilateral coherence has been reported in either kinematic or EMG studies (Marsden et al., 1969a; Morrison and Newell, 2000; Timmer et al., 2000). However, highly prevalent bilateral coherence of finger motion was found in the resting tremor of healthy subjects (Marsden et al., 1969b), and was attributed to the mechanical effects of ballistocardiac forcing.

The occasional bilateral coherence of EMG activity observed in (Hellwig et al., 2003) correlated with simultaneous ipsilateral and contralateral EEG-EMG coherence, which was proposed to arise from a dynamic synchronization of the central ET generators in the left and right brain (Hellwig et al., 2003). Transient but recurring synchrony can in general result from weak coupling of nonlinear oscillators (Pikovsky et al., 2003). Indications of bilateral coupling have been obtained also for PT: (Morrison and Newell, 1999) showed that splinting the joints of the right arm altered the frequency profile and the intra-limb coupling of the tremors in both arms; other recent studies showed that bilateral correlation between tremulous muscle activities increased when muscle fatigue was induced on both (Boonstra et al., 2008) or either (Kavanagh et al., 2013) side of the body.

Motivated by these findings, we hypothesized that a weak coupling between the left and right oscillators in ET and in PT may lead to bilateral coherence that is transient or intermittent, and could sensitively depend on the posture and the evaluated kinematic parameters. We therefore systematically assessed, using both stationary and nonstationary (wavelet-based) analysis methods, the bilateral coherence of hand tremor in healthy subjects and in ET patients. Tri-axial accelerometer recordings allowed us to examine a more complete set of kinematic variables than in most previous studies. To probe the nature of the coupling of the left and right tremors, we examined the temporal structure of kinematic bilateral coherence, its dependence on ballistocardiac forcing in healthy subjects, and the relations between bilateral coherence and tremor amplitude.

2. Methods

2.1. Experimental methods

2.1.1. Subjects

The tremor kinematics analyzed in this study was recorded from three groups of subjects. The first group consisted of 34 patients diagnosed with ET according to the criterion stated in (Deuschl et al., 1998), age 56.7 ± 17.4 yr, age range: 19–81 yr, disease duration: 24.3 ± 16.0 yr. The tremor was evaluated on the Fahn-Tolosa-Marín rating scale (Jankovic and Tolosa, 2007), total score in items 1–9 (magnitude of tremor in different body parts): 11.8 ± 5.6, range 5–29. The demographic data and tremor scores of individual patients are provided as supplementary material (Supplementary Table S1). The second group consisted of 30 healthy subjects, age 53.8 ± 17.4 yr (range 19–81 yr). These two groups are the same as analyzed in (Šprdlík et al., 2011), with 5 added ET patients (bilateral coherence was not assessed in that study). To perform control experiments and to study the effect of balistocardiac forcing on bilateral coherence, an additional group of 12 healthy subjects (age 34 ± 8 yr, range 26–51 yr, 8 females and 4 males) was measured in the present study. Healthy subjects in both the second and the third groups did not have any previous record or family history of movement disorders. Subjects with a history or clinical signs of enhanced physiological tremor were excluded from the study. The study was approved by the research ethics committee at First Faculty of Medicine, Charles University in Prague, and all participants provided signed, informed consent before entering the study.

2.1.2. Experimental setup and data acquisition

The measurement procedure was as described in (Šprdlík et al., 2011). In brief, hand tremor was recorded in three positions (see Fig. 1). The first, in which the hands hung freely from the wrist, was used to measure the rest tremor. The other two positions – with hands extended, and with the arms extended towards a horizontal target – were used to study postural tremor (Šprdlík et al., 2011, or Fig. 1). In all the positions the subjects were seated comfortably in a sturdy armchair, and were instructed to lean their back into the backrest. No loads or stress exercises were used in any of the reported experiments. For at least 15 min prior to the measurements, each patient or healthy subject was seated and not engaged in physical activity. The patients were instructed to avoid any stimulant (including caffeine) or any sedative drugs (including sleep pills) during 12 h preceding the measurement.

Integrated inertial measurement units MTx by Xsens Technologies (Netherlands) were placed on subjects' hand dorsa over third and fourth metacarpal bones using neoprene bands with hook-and-loop fasteners. The units measure linear acceleration in all three spatial axes. In addition, one unit was firmly attached to the chest (5 cm to the left of the sternum) and used to record the chest wall acceleration. Two sets of 20 s measurements were performed in each hand position, separated by a 10 s interval of rest to avoid muscle fatigue. In the data taken from (Šprdlík et al., 2011), the hand acceleration measurements were transmitted by

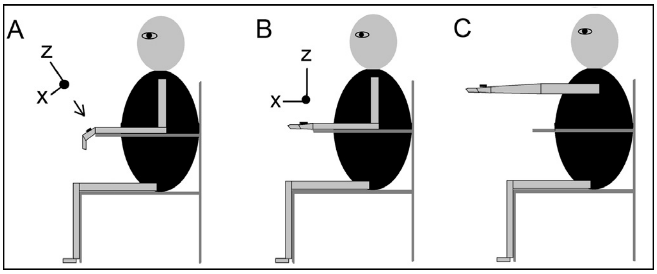

Fig. 1. Cartoons of positions in which the hand acceleration was measured. (A) Position 1. forearms leaned on the armrests and hands hanging freely down. (B) Position 2. forearms leaned on the armrests and hands extended forward horizontally. (C) Position 3. arms held forward horizontally towards a horizontal target placed in front of the subject at the height of shoulders, hands pronated. *X*, *Y* and *Z* indicate the orientation of the acceleration components measured by the triaxial accelerometers placed on the hand dorsa.