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Physiological and pathological oscillatory networks in the human motor system

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Abstract

Human brain functions are heavily contingent on neural interactions both at the single neuron and the neural population or system level. Accumulating evidence from neurophysiological studies strongly suggests that coupling of oscillatory neural activity provides an important mechanism to establish neural interactions. With the availability of whole-head magnetoencephalography (MEG) macroscopic oscillatory activity can be measured non-invasively from the human brain with high temporal and spatial resolution.

To localise, quantify and map oscillatory activity and interactions onto individual brain anatomy we have developed the 'dynamic imaging of coherent sources' (DICS) method which allows to identify and analyse cerebral oscillatory networks from MEG recordings. Using this approach we have characterized physiological and pathological oscillatory networks in the human sensorimotor system.

Coherent 8 Hz oscillations emerge from a cerebello-thalamo-premotor-motor cortical network and exert an 8 Hz oscillatory drive on the spinal motor neurons which can be observed as a physiological tremulousness of the movement termed movement discontinuities. This network represents the neurophysiological substrate of a discrete mode of motor control. In parkinsonian resting tremor we have identified an extensive cerebral network consisting of primary motor and lateral premotor cortex, supplementary motor cortex, thalamus/basal ganglia, posterior parietal cortex and secondary somatosensory cortex, which are entrained in the tremor or twice the tremor rhythm. This low frequency entrapment of motor areas likely plays an important role in the pathophysiology of parkinsonian motor symptoms. Finally, studies on patients with postural tremor in hepatic encephalopathy revealed that this type of tremor results from a pathologically slow thalamocortical and cortico-muscular coupling during isometric hold tasks.

In conclusion, the analysis of oscillatory cerebral networks provides new insights into physiological mechanisms of motor control and pathophysiological mechanisms of tremor disorders.

Keywords: Coherence; Oscillations; Synchronisation; Tremor; Movement; MEG; DICS

1. Introduction

Functional neuroimaging has led to tremendous advances in our understanding of human brain function. So far, the main emphasis has been on localisation of distinct brain areas serving specific functions. An important aspect of brain function is the dynamic and temporally precise interaction between neural elements. Connectivity between brain areas may appear as correlated time behavior of neural activity. Coherence between magnetoencephalographic (MEG) or electroencephalographic signals of sensors or electrodes covering different scalp areas is commonly taken as a measure of functional coupling. However, this approach provides vague information on the actual areas involved. We have recently

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developed a new analysis technique, DICS (dynamic imaging of coherent sources), which allows the localisation of neural oscillatory activity and coherences between brain areas [1]. In the following the DICS method will be introduced and applications to the study of functional connectivity in the sensorimotor system during physiological movements as well as during parkinsonian and hepatic tremor will be presented.

2. Dynamic imaging of coherent sources

DICS uses a spatial filter in the frequency domain to estimate power or coherence in a specified frequency band. Coherence is a normalized measure of dependence between two signals in the frequency domain. It is computed from the fast Fourier transformation of the signals. The computation is performed for a large number of voxels covering the entire brain and the resulting tomographic map is overlaid on the anatomical MR images.

Typically an analysis starts with the computation of power spectra of EMG signals which represent the distribution of power over frequencies. Frequency bands of interest (e.g. corresponding to a tremor) can be identified. DICS is used to compute tomographic maps of cerebro-muscular coherence at the frequency band of interest. Local maxima in the functional map are identified and used as reference points for a computation of cerebro-cerebral coherence. Local maxima in the resulting maps represent areas which show the strongest coherence to the given reference region.

The regions of interest from the cerebro-muscular and cerebro-cerebral coherence analysis are used for the computation of coherence spectra. In general, spectra between all combinations of regions of interest are computed as well as spectra between each region and EMG signals. Statistical significance is assessed by calculating the 95% confidence level. For cerebro-muscular spectra the method described by Halliday et al. [2] is used. For cerebro-cerebral spectra the 95% confidence level is obtained from shuffled data. Both time series are randomly shuffled in the same way destroying coherence due to oscillatory coupling but preserving artificial coherence (e.g. due to volume conduction). The spectra provide the frequency ranges of significant coherence.

Once a significant interaction has been identified the direction of coupling is of interest. Unfortunately this information is difficult to obtain. For cerebro-muscular coupling the phase delay based on the Hilbert transform has been successfully applied [3]. A narrow band-pass filter is applied to both signals of interest. The Hilbert transform is used to compute the instantaneous phase and amplitude. The dominant phase difference at the times of strongest oscillations (resulting in the highest signal-to-noise ratio) is identified and expressed as time lag between both time series. Due to low conduction times these phase delays are often ambiguous when applied to cerebro-cerebral coupling. In this case the directionality index can be employed [4]. It has been introduced in the context of phase synchronisation and is a normalized measure of the asymmetry of information flow (1 and -1 representing an unidirectional flow from area A to area B (respectively B to A) and 0 representing bidirectional information flow).

3. Slow finger movements

Slow voluntary precision movements contain physiological oscillatory components which have been investigated in detail by Vallbo and Wessberg [5]. They demonstrated that the velocity of the finger during slow flexion and extension movements exhibits a rhythmic modulation at a frequency of about 8 Hz. These modulations originate from an alternating activation of agonist and antagonist muscles leading to alternating increases and decreases in the finger velocity. Further investigations revealed that these oscillations are not entirely due to peripheral feedback or the firing of individual motor units [6,7]. These modulations which are observed as well in EMG recordings seem to reflect a central modulation of the motor unit firing rate; i.e. the firing probability of individual motor units changes over time corresponding to central motor signals.

This hypothesis was recently confirmed by simultaneous recordings of EMG, finger velocity and neural activity with MEG in nine healthy subjects [8]. Significant cerebro-muscular coherence was demonstrated between EMG of the right extensor digitorum communis muscle (EDC) and the left sensorimotor cortex and the right cerebellum at the frequency of the movement discontinuities. The directionality index revealed an afferent coupling between EMG and postcentral somatosensory area and efferent coupling between EMG and precentral primary motor areas. These results provide the first evidence of a central origin of the rhythmic 8 Hz oscillations during voluntary slow movements. Since cerebro-muscular coherence together with the directionality index identified contralateral primary motor cortex as final output area for the central modulation of motor unit activity we used it as reference region for a cerebro-cerebral coherence analysis at the frequency of movement discontinuities. This analysis results in a tomographic functional map where the value at each volume element represents the coherence to the reference area. The most consistent areas were left premotor area, left thalamus and right cerebellum (Fig. 1). These areas constitute an oscillatory network with coupling at the frequency of the finger movement discontinuities.