Journal of Neuroscience Methods 235 (2014) 10–24

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

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

Computational Neuroscience

Detecting millisecond-range coupling delays between brainwaves in terms of power correlations by magnetoencephalography

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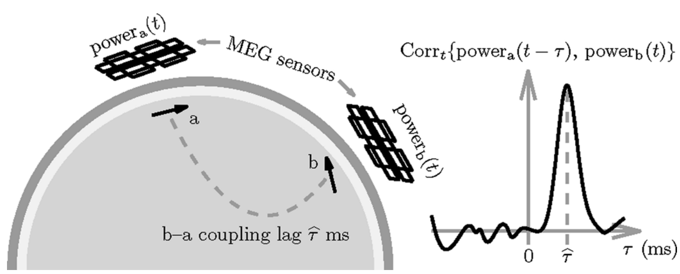
HIGHLIGHTS

- A new method to detect power correlations (PCs) between brainwaves is presented.
- The millisecond resolution of the PC method is demonstrated by simulations.
- The PC method is applied successfully to three healthy subjects measured by MEG.
- The PC method revealed diverse and meaningful delays in real MEG data.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 10 January 2014
Received in revised form 28 May 2014
Accepted 20 June 2014
Available online 28 June 2014

Keywords:
Brainwave
MEG
Coupling
Power correlation
Millisecond resolution

ABSTRACT

Background: The spatiotemporal coupling of brainwaves is commonly quantified using the amplitude or phase of signals measured by electro- or magnetoencephalography (EEG/MEG). To enhance the temporal resolution for coupling delays down to millisecond level, a new power correlation (PC) method is proposed and tested.
New method: The cross-correlations of any two brainwave powers at two locations are calculated sequentially through a measurement using the convolution theorem. For noise suppression, the cross-correlation series is moving-average filtered, preserving the millisecond resolution in the cross-correlations, but with reduced noise. The coupling delays are determined from the delays of the cross-correlation peaks.
Results: Simulations showed that the new method detects reliably power cross-correlations with millisecond accuracy. Moreover, in MEG measurements on three healthy volunteers, the method showed average alpha–alpha coupling delays of around 0–20 ms between the occipital areas of two hemispheres. Lower-frequency brainwaves *vs.* alpha waves tended to have a larger lag; higher-frequency waves *vs.* alpha waves showed delays with large deviations.

Abbreviations: EEG, electroencephalography; MEG, magnetoencephalography; PC, power correlation; RSN, resting-state network; ICM, intrinsic coupling mode; MSR, magnetically shielded room; PCA, principal component analysis; SSP, signal-space projection; SNR, signal-to-noise ratio; RO, LO, RF, LF, right (R), left (L), occipital (O), frontal (F); ECD, equivalent current dipole; s.d., standard deviation; LFP, local field potential; TMS, transcranial magnetic stimulation; HFO, high-frequency oscillation; ULF MRI, ultra-low-field magnetic resonance imaging; RMS, root mean square; ms, millisecond (10^{-3} s); fT, femtotesla (10^{-15} T); cm, centimetre (0.01 m).

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http://dx.doi.org/10.1016/j.jneumeth.2014.06.026

Comparison with existing methods: The use of signal power instead of its square root (amplitude) in the cross-correlations improves noise cancellation. Compared to signal phase, the signal power analysis time delays do not have periodic ambiguity. In addition, the novel method allows fast calculation of cross-correlations.

Conclusions: The PC method conveys novel information about brainwave dynamics. The method may be extended from sensor-space to source-space analysis, and can be applied also for electroencephalography (EEG) and local field potentials (LFP).

1. Introduction

Both electroencephalography (EEG) and magnetoencephalography (MEG, Hämäläinen et al., 1993; Näätänen et al., 1994; Hansen et al., 2010) are non-invasive and real-time, millisecond-resolution functional brain imaging methods, and sensitive to signals originating mainly from the cerebral cortex. Neuronal oscillations are generated at different frequency ranges which are named here δ, θ, α, β, γ, ϵ, $\epsilon_{>}$, $\epsilon_{\gg}$ and σ (see Table 1) irrespective of brain area. The alpha rhythm, discovered by Berger (1929), represents particularly strong oscillatory activity, which was the focus of many previous studies (see *e.g.* Lopes da Silva et al., 1974; Lopes da Silva, 1991; Chapman et al., 1984; Salmelin and Hari, 1994; Palva and Palva, 2007). It is known that many of the neuronal oscillations are coupled, such as β–α and γ–α in human MEG (Palva et al., 2005), and that brain functioning may depend on the phase of infraslow brainwaves (Monto et al., 2008) or *e.g.* α-range brainwaves (Busch et al., 2009). For a review on EEG/MEG α couplings, see Ref. Palva and Palva (2011). It has been shown that *e.g.* resting-state networks (RSNs) can be studied by both fMRI and MEG (Mantini et al., 2007; Brookes et al., 2011). Among different neuroimaging techniques, MEG is particularly attractive as it combines superior temporal resolution and relatively accurate spatial localization of neuronal activity (Hari and Salmelin, 2012). The aim of this work is to present a novel signal-power-based cross-correlation method (power correlation (PC) method) to study coupling delays between brainwaves, and to test the method on data obtained at rest.

Earlier research has concentrated on using signal phase and amplitude to study brainwave couplings (Nikouline et al., 2001; Le Van Quyen and Bragin, 2007; Tort et al., 2010; Onslow et al., 2011; Palva and Palva, 2012), although power couplings have also been investigated (Hipp et al., 2012). The signal power cross-correlations were typically calculated without delay. However, neuronal interactions are not instantaneous but rather occur with delays, which should be properly taken into account. The traditional use of power correlations has not been optimal in the study of “stereotyped spatiotemporal patterns of activity (transients)” (Friston, 1997), but the new approach may help to ameliorate this. It should be mentioned that although delayed neural correlations have been studied with a coarse timescale earlier (see *e.g.* Nir et al., 2008; Honey et al., 2012), millisecond-range power interactions have not yet been widely acknowledged. It should be noted that the PC method is also applicable to amplitude as well as power cross-correlations. Here, the use of power is preferred over amplitude (square root of power), because the square root makes the combination of signal power and noise power nonlinear (see Section 2.2.1). While earlier methods detected amplitude couplings at around 0.1 Hz, coupling dynamics at almost 1 kHz should be discoverable with the PC method, which has earlier been possible only with phase cross-correlations. This may lead to a better understanding of “intrinsic coupling modes” (ICMs) (Engel et al., 2013).

2. Methods

The methods applied in the PC analysis are explained starting from measurement details, followed by signal analysis procedures and the cross-correlation method itself.

2.1. Measurements and signal processing

The study was approved by the Ethics Committee of the Helsinki University Central Hospital and was performed in compliance with the Declaration of Helsinki. The measurements of three healthy adults were made with a 306-channel (superconducting quantum interference device (SQUID) sensors at 102 locations with one magnetometer and a pair of orthogonal planar gradiometers) MEG device (Vectorview™, Elekta Oy, Helsinki, Finland) at BioMag Laboratory (Helsinki University Central Hospital, Finland) with a sampling frequency of 3 kHz (measurements m1, m2a and m2b) or 600 Hz (measurement m3), and a low-pass-filtering cutoff frequency at 1 kHz or 200 Hz, respectively (the arabic numeral after the m stands for the subject 1, 2 or 3 and the trailing letters for different recordings). A 5-min empty-room measurement was performed just before measurements m1, m2a and m2b; the empty-room data of m2b were used in the analysis of the m3 data which were measured on the previous day. The subject was in supine position in the dimmed and silent magnetically shielded room (MSR) for 30 min (m1, m2a and m2b) or 10 min (m3). From m1, 22 min of data were used, when the subject was awake with eyes closed. In both measurements m2a and m2b, the subject was at rest with sequentially 2 min eyes open, 12 min eyes closed, 2 min eyes open, 12 min eyes closed and 2 min eyes open.

2.1.1. Noise suppression

Before the cross-correlation analysis, the empty-room measurements associated with each brain measurement were used to project out artefacts from the brain measurement. In brief, the 5-min 204 gradiometer signals were used to build a covariance matrix that was used in principal component analysis (PCA) to build an orthogonal matrix whose 5 eigenvectors with largest eigenvalues were used in signal-space projection (SSP) (Uusitalo and Ilmoniemi, 1997) to project out artefacts in the gradiometer brain measurements (Parkkonen et al., 1999). The selection of 5 eigenvectors was justified by noting that only their corresponding noise components had notably higher energies than the rest of them.

2.1.2. Signal extraction

Signal epochs of 12 s were filtered (Butterworth, bidirectionally to avoid signal deformation and phase delays) to obtain the oscillations in a specific frequency range (see Table 1; filter order 2 for δ, 3 for θ and α and 4 for the rest of the waves; the lower filter orders for low-frequency waves with narrow passbands ensured numerical stability in filtering) in the cross-correlation analysis. The locations of the sensors were chosen in order to cover cortical areas with pronounced alpha oscillations, although for the demonstration