Journal of Neuroscience Methods 205 (2012) 148–158

Contents lists available at SciVerse ScienceDirect

Journal of Neuroscience Methods

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

Computational Neuroscience

Estimation of the spatiotemporal structure of event-related desynchronization and synchronization in magnetoencephalography

J. Żygierewicz[a,∗,1], C. Sielużycki[b], N. Zacharias[b], P. Suffczyński[a,2], P. Kordowski[a,2], H. Scheich[b], P.J. Durka[a,2], R. König[b]

[a] University of Warsaw, Faculty of Physics, Institute of Experimental Physics, Department of Biomedical Physics, ul. Hoża 69, 00-681 Warszawa, Poland[3]
[b] Leibniz Institute for Neurobiology, Special Lab Non-invasive Brain Imaging, Brenneckestraße 6, 39118 Magdeburg, Germany[4]

ARTICLE INFO

Article history:
Received 13 September 2011
Received in revised form 9 December 2011
Accepted 20 December 2011

Keywords:
Dynamic imaging of coherent sources
ERD – event-related desynchronization
ERS – event-related synchronization
MEG – magnetoencephalography
IS – inverse solutions
Multiple comparison problem

ABSTRACT

We present a comprehensive methodology for identifying cerebral areas involved in event-related changes of electromagnetic activity of the human brain, and also for tracing the temporal evolution of this activity. Information from pre- and peristimulus time intervals – in terms of event-related synchronization (ERS) and desynchronization (ERD) of the magnetoencephalographic (MEG) signal – was directly incorporated in the relevant test statistics. For the individual steps of the analysis, we used particular estimations of the time–frequency distribution of the energy along with particular error control methods, that is, short-time Fourier transform and false-discovery rate at the sensor level and multitapers and familywise error rate at the source level. This procedure was applied to two types of group-level tests, a within-condition test and a between-conditions test. The performance of the proposed methodology is assessed by (1) analyzing the event-related brain activity from two experimental conditions of an auditory MEG experiment—passive listening to a sequence of frequency-modulated sweeps and their active categorization with respect to the direction of frequency modulation, and (2) comparing the findings with those obtained with a widely used cluster-based analysis.

1. Introduction

Magnetoencephalography (MEG) and electroencephalography (EEG) are long-established methods to explore stimulus-evoked transient activity of the human brain, and the related estimation of sources from mean event-related magnetic fields (ERFs) or electric potentials (ERPs) constitutes a standard procedure in MEG and EEG research. The high temporal resolution of the two methods further allows relating the sources of event-related changes of oscillatory (rhythmic) electromagnetic activity, localized by solving the inverse problem, to behavioral data, an issue which has attracted considerable attention in recent years. The localization of sources of oscillatory activity has been performed by means of methods based on minimum norm estimates (Lin et al., 2004), minimum current estimates (Jensen and Vanni, 2002), or various beamforming techniques operating either in the time domain (e.g. Robinson and Vrba, 1997; Hillebrand and Barnes, 2005; Gaetz and Cheyne, 2006) or in the frequency domain (e.g. Laaksonen et al., 2008; Nieuwenhuis et al., 2008). This analysis is a complicated multi-stage process, and usually involves the following steps (e.g. Laaksonen et al., 2008; Nieuwenhuis et al., 2008):

I Analysis at the sensor level: Selection of time–frequency regions of interest (tf-ROIs) where the energy density of the signal differs between separate time windows within one condition or between corresponding time windows of two conditions.
II Analysis at the source level: Solution of the forward problem and the inverse problem in order to estimate, for each condition, the spatial distribution of power inside the brain, for the tf-ROIs selected in (I).
III Identification of brain areas with statistically significant differences in the power distribution within one condition or between conditions.

∗ Corresponding author at: University of Warsaw, Institute of Experimental Physics, Department of Biomedical Physics, ul. Hoża 69, 00-681 Warszawa, Poland. Tel.: +48 22 5532126; fax: +48 22 6226154.
E-mail addresses: jarekz@fuw.edu.pl (J. Żygierewicz), csieluzy@lin-magdeburg.de (C. Sielużycki), nzachari@lin-magdeburg.de (N. Zacharias), suffa@fuw.edu.pl (P. Suffczyński), pawel.kordowski@fuw.edu.pl (P. Kordowski), hscheich@lin-magdeburg.de (H. Scheich), durka@fuw.edu.pl (P.J. Durka), rkoenig@lin-magdeburg.de (R. König).
[1] Partially supported by the Polish Ministry of Science and Higher Education (Decision No. 119/N-COST/2008/0) and NEUROMATH Action.
[2] Supported from the Polish funds for science.
[3] http://brain.fuw.edu.pl.
[4] http://www.lin-magdeburg.de.

0165-0270/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.jneumeth.2011.12.013

In this work, we revise crucial points of the above procedure, and present an advanced and comprehensive approach which includes the following modifications:

(a) The test statistics for steps I and II were based on event-related desynchronization/synchronization (ERD/ERS) values, i.e. relative changes of the time–frequency energy density of each subject and experimental condition, rather than the raw energy density usually reported in literature.
(b) The energy distribution in the time–frequency domain was estimated by means of the short-time Fourier transform (STFT), whereas the estimation of the cross-spectral density (CSD) matrix at the source level was based on the multitaper method.
(c) The estimation of tf-ROIs of significant ERD/ERS effects at the sensor level was performed using a robust statistical procedure where contiguous time–frequency regions of significant energy changes emerged naturally as a result of an objective procedure based on the control of the rate of false detections (false discovery rate (FDR)).
(d) At the source level, we propose a non-parametric statistical procedure which controls the familywise error rate (FWER) in the strong sense, i.e. for any subset of the hypotheses tested. FWER is the probability of committing any error of type I (i.e. of declaring that the null hypothesis is false when it is true) in a family of comparisons.

In Section 2, we describe all these steps in detail and thus present a comprehensive framework for ERD/ERS source localization in MEG and its statistical analysis across subjects and conditions. In Section 3, we apply the proposed methodology to analyze and contrast two simple, exemplary MEG data sets, viz recordings from an auditory experiment with frequency-modulated (FM) sweeps as stimulus. FM sweeps play a fundamental role in human speech as well as in animal vocalizations, and can be easily separated into two natural categories with respect to the underlying direction of frequency modulation, upward vs. downward (Ohl et al., 2001; Poeppel et al., 2004; Brechmann and Scheich, 2005; König et al., 2008). This paradigm allows contrasting ERD/ERS source-localization results from two different experimental conditions – a *passive* condition, in which the subjects were only listening to the sweeps, with an *active* condition, in which the sweeps had to be categorized with regard to the FM direction – and thus serves as a suitable test case for the assessment of the performance of our methodology, in particular of the statistical analyses. Moreover, since the paradigm evokes a sequence of cortical processing steps like stimulus anticipation and processing, decision making, motor preparation and movement execution, it also allows studying the spatiotemporal capabilities of the proposed methodology. In Section 4, we assess our methodology and compare it with other approaches, in particular with the cluster-based method proposed by Maris and Oostenveld (2007) and implemented in the widely used FieldTrip toolbox.[5]

2. Materials and methods

2.1. Analysis at the sensor level

2.1.1. Measure of the modulation of event-related activity

Recently, we showed that it is advantageous for the ERD/ERS analysis of MEG data to use a planar gradient representation of the signal (Żygierewicz et al., 2008). Such a representation can be obtained either directly by using an MEG system equipped with planar gradiometers, or, in case the MEG signals were acquired with a system based on magnetometers, by approximating the signal using an appropriate transformation (Żygierewicz et al., 2008). The results presented in this work were computed using the latter approach.

The time–frequency distribution of the energy $E(t,f)$ of the signal $x(t)$ was estimated by means of STFT, but other methods, like the wavelet transform or adaptive signal approximations, yield consistent and similar results (Żygierewicz et al., 2005). For condition c, subject s, channel ch, and trial tr, $E(t,f)$ is given by

$$E_{c,s,ch,tr}(t,f) = |\mathrm{STFT}(x_{c,s,ch,tr}(t))|^2. \quad (1)$$

For any frequency f, the mean energy during the pre-stimulus baseline period T_b is given by

$$B_{c,s,ch}(f) = \langle E_{c,s,ch,tr}(t,f)\rangle_{tr,t\in T_b}, \quad (2)$$

where $\langle . \rangle$ is the operator of taking the average across the variables indicated by the subscript—in the case of Eq. (2), it is the average across all trials and across the pre-stimulus baseline time interval. Taking $B_{c,s,ch}(f)$ as a reference for the frequency f, ERD and ERS (denoted as *ERDS* in all equations from here) can be expressed in time–frequency coordinates (t,f) as

$$ERDS_{c,s,ch}(t,f) = \frac{\langle E_{c,s,ch,tr}(t,f)\rangle_{tr} - B_{c,s,ch}(f)}{B_{c,s,ch}(f)}. \quad (3)$$

In other words, ERD is the relative decrease and ERS the relative increase of the energy of a given time–frequency window with respect to the baseline period (Pfurtscheller, 1999a,b; Pfurtscheller and Lopez da Silva, 1999b).

2.1.2. Statistical analysis at the sensor level

The identification of regions in which ERD/ERS changes are above the level of fluctuations requires statistical tests to be applied in the time–frequency domain, discretized into *resels* (*res*olution *el*ements) in compliance with the time–frequency uncertainty principle. The size of these resels was chosen such that $\Delta t \times \Delta f = 1/2$ (for a discussion, see Durka et al., 2004).

Two fundamental tests can be performed at the sensor level, one with regard to ERD/ERS effects within an individual condition, and one with regard to ERD/ERS differences between two conditions. We adopted a massive univariate approach in which we tested the null hypotheses H_0 for each resel, followed by the correction for multiple comparisons. This approach has the advantage that it allows baseline- and peristimulus-interval to have different durations. Moreover, since, at the sensor level, meaningful time–frequency maps can be obtained even for single trials, the permutation test was performed at the trial level.

2.1.2.1. Within-condition statistic. For the within-condition test, we propose to use the following statistic for each channel:

$$T_{c,ch}(t,f) = \frac{\langle ERDS_{c,s,ch}(t,f)\rangle_s}{\sigma_{c,ch}}, \quad (4)$$

where $\sigma_{c,ch}$ is the standard deviation of $ERDS_{c,s,ch}(t,f)$ across subjects. The null hypothesis for this test is that there is no difference in energy between the pre-stimulus baseline and peristimulus resels. Thus, under H_0, resels belonging to the baseline period and to the peristimulus period are exchangeable and can be randomly swapped for each trial.

2.1.2.2. Between-conditions statistic. For the between-conditions test, we propose to evaluate the ERD/ERS contrast common to all subjects in terms of the mean difference between the two

[5] Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, The Netherlands, http://fieldtrip.fcdonders.nl.