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Single-trial time–frequency analysis of electrocortical signals: Baseline correction and beyond

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ABSTRACT

Event-related desynchronization (ERD) and synchronization (ERS) of electrocortical signals (e.g., electroencephalogram [EEG] and magnetoencephalogram [MEG]) reflect important aspects of sensory, motor, and cognitive cortical processing. The detection of ERD and ERS relies on time–frequency decomposition of single-trial electrocortical signals, such as to identify significant stimulus-induced changes in power within specific frequency bands. Typically, these changes are quantified by expressing post-stimulus EEG power as a percentage of change relative to the baseline pre-stimulus EEG power. However, expressing post-stimulus EEG power relative to pre-stimulus EEG power entails two important and surprisingly neglected issues. First, it can introduce a significant bias in the estimation of ERD/ERS magnitude. Second, it confuses the contribution of pre- and post-stimulus EEG power. Taking the human electrocortical responses elicited by transient nociceptive stimuli as an example, we demonstrate that expressing ERD/ERS as the average percentage of change calculated at the level of single trials introduces a positive bias, resulting in an overestimation of ERS and an underestimation of ERD. This bias can be avoided using a single-trial baseline *subtraction* approach. Furthermore, given that the variability in ERD/ERS is not only dependent on the variability in post-stimulus power but also on the variability in pre-stimulus power (e.g., variability in α-band EEG power), an estimation of the respective contribution of pre- and post-stimulus EEG variability is needed. This can be achieved using a multivariate linear regression (MVLR) model, which could be optimally estimated using partial least square (PLS) regression, to dissect and quantify the relationship between behavioral variables and pre- and post-stimulus EEG activities. In summary, combining single-trial baseline *subtraction* approach with PLS regression can be used to achieve a correct detection and quantification of ERD/ERS.

Introduction

Sensory, motor and cognitive events not only evoke time-locked and phase-locked changes of ongoing electrocortical signal (e.g., event-related potentials; ERPs and event-related fields; ERFs) (Luck, 2005), but also induce time-locked and non-phase-locked modulations of ongoing oscillatory activity (Neuper and Klimesch, 2006; Pfurtscheller and Lopes da Silva, 1999). These non-phase-locked modulations consist of decreases (event-related desynchronization, ERD) and increases (event-related synchronization, ERS) of oscillatory activity, usually confined to a specific frequency band (Pfurtscheller and Aranibar, 1977; Pfurtscheller and Lopes da Silva, 1999). The functional significance of ERD and ERS varies greatly according to their temporal, spectral, and spatial characteristics (Ohara et al., 2004). For example, ERD in the α band (8–12 Hz) has been hypothesized to reflect cortical activation, whereas ERS in the same frequency band has been interpreted as a reflection of cortical inhibition (Pfurtscheller and Lopes da Silva, 1999). ERD and ERS are extensively used to investigate sensorimotor processes and cognitive tasks, as well as to discriminate neurological disorders and psychometric variables (Fries, 2009; Gross et al., 2007; Neuper and Klimesch, 2006; Pfurtscheller, 1992; Pfurtscheller et al., 1998; Ploner et al., 2006; Schnitzler and Gross, 2005; Singer, 1993).

To measure ERD and ERS, single-trial electrocortical responses in the time domain are usually transformed in time–frequency distributions (TFDs) (Makeig, 1993), which represent signal power as a function of time and frequency, using various time–frequency decomposition methods, such as windowed Fourier transform and continuous wavelet transform (Mouraux and Iannetti, 2008; Zhang et al., 2012). The resulting single-trial TFDs are usually expressed relative to a pre-stimulus reference interval, to highlight stimulus-induced *changes* in oscillation magnitude (Grandchamp and Delorme, 2011). Such baseline-correction procedure is used because it allows identifying sometimes

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subtle stimulus-induced changes of ongoing oscillatory power. It is typically achieved using one of two alternative approaches: (1) *subtraction*, which assumes that ERD and ERS are added onto or subtracted from the existing pre-stimulus power at each frequency, and (2) *percentage* (i.e., subtraction and division), which assumes that ERD and ERS are proportionally decreased or increased with respect to the magnitude of existing pre-stimulus oscillatory power (Grandchamp and Delorme, 2011; Pfurtscheller and Aranibar, 1977). In both approaches the baseline correction can be performed on TFDs at single-trial, single-subject, or group level (Grandchamp and Delorme, 2011; Mouraux and Iannetti, 2008; Zhang et al., 2012). In any of those cases it is important to consider the effect of trial-to-trial (or subject-to-subject) fluctuations in the magnitude of pre-stimulus oscillatory activity on the ERD/ERS estimates. Particularly in the *percentage* approach, which consists in dividing the difference between post-stimulus and pre-stimulus amplitudes by the pre-stimulus amplitude, variations in pre-stimulus amplitude can have a very strong effect on the ERD/ERS estimates. Indeed, if the pre-stimulus amplitude is close to zero, even a very minor increase in amplitude will yield a spuriously high percentage increase. Considering that both pre- and post-stimulus amplitudes are always positive, the distribution of percentage estimates across trials (or subjects) will be highly asymmetrical, with a long tail of extremely high percentage values. Therefore, averaging such percentage values across trials (or subjects) will not provide a meaningful summary measure of ERD/ERS.

Across-trial variability in both pre- and post-stimulus amplitudes may reflect important factors such as changes in the sensory input and time-dependent habituation (Iannetti et al., 2008; Ohara et al., 2004; Stancak et al., 2003), as well as fluctuations in vigilance and expectation (Del Percio et al., 2006; Mu et al., 2008; Ploner et al., 2006). Thus, it is also crucial to dissect the contributions of pre- and post-stimulus power to the variability of ERD/ERS, especially when the trial-to-trial variability of pre-stimulus activity is significant and physiologically relevant (Addante et al., 2011; Salari et al., 2012; van Dijk et al., 2008; Wyart and Tallon-Baudry, 2009). Specifically, when investigating the trial-to-trial relationship between ERD/ERS and behavior variables (e.g., reaction times or intensity of perception), it is important to explore whether such relationship is determined by pre- or post-stimulus electrocortical activity, or both.

In summary, the correct interpretation of the functional significance of ERD/ERS relies on two important but often neglected conditions: (1) the baseline correction procedure should not introduce biases in the estimated ERD/ERS magnitude, and (2) the contribution of pre- and post-stimulus activity on the trial-to-trial ERD/ERS variability should be correctly dissected and quantified.

Here, we address these points using an electroencephalographic (EEG) dataset collected from a large population of healthy volunteers ($n = 96$). First, we quantitatively compared the two widely used baseline correction approaches (*subtraction* and *percentage*) at three different levels (single-trial, single-subject, and group), and show that the *percentage* procedure, especially when applied at single-trial level, can yield very misleading results, and largely overestimate ERS and underestimate ERD. Since baseline-corrected TFDs are influenced by the trial-to-trial fluctuations in the magnitude of pre-stimulus EEG activity, the *subtraction* approach, albeit unbiased, is not adequate to dissect the trial-to-trial relationships between electrocortical (pre- and post-stimulus EEG activity) and behavioral variables. Thus we characterized the trial-to-trial variability in pre-stimulus EEG power, and explored its influence on the post-stimulus EEG activity and baseline-corrected TFDs. Since ERD/ERS capture the mixed variability of pre- and post-stimulus EEG power, it is difficult to determine whether the trial-to-trial relationship between ERD/ERS and behavior variables is contributed by pre-stimulus activity, post-stimulus activity, or both. Therefore, we propose a multivariate linear regression (MVLR) model solved using partial least squares (PLS) method to dissect the trial-to-trial relationships between electrocortical (pre- and post-stimulus EEG activity) and behavioral variables (e.g., intensity of perception).

Materials and methods

Experimental design and EEG recording

Subjects

EEG data were collected from 96 healthy volunteers (51 females) aged 21.6 ± 1.7 years (mean ± SD, range = 17–25 years). All subjects gave their written informed consent and were paid for their participation. The local ethics committee approved the procedures.

Nociceptive stimulation

Radiant-heat stimuli were generated by an infrared neodymium yttrium aluminum perovskite (Nd:YAP) laser with a wavelength of 1.34 μm (Electronical Engineering, Italy). At this wavelength, laser pulses activate directly nociceptive terminals in the most superficial skin layers (Baumgartner et al., 2005; Iannetti et al., 2006). Laser pulses were directed on a square area (5 × 5 cm) centered on the dorsum of the left hand, and defined prior to the beginning of the experimental session. A He–Ne laser pointed to the area to be stimulated. The laser beam was transmitted via an optic fiber and its diameter was set at approximately 7 mm (~38 mm^2) by focusing lenses. The pulse duration was 4 ms, and four different energies (E1: 2.5 J; E2: 3 J; E3: 3.5 J; E4: 4 J) of stimulation were used. After each stimulus, the target of the laser beam was shifted by approximately 1 cm in a random direction, to avoid nociceptor fatigue or sensitization.

Experimental design

Prior to the EEG data collection, we delivered a small number of laser pulses with different stimulus energies to familiarize the subjects with the stimulation. During the EEG data collection we delivered ten laser pulses at each of the four stimulus energies (E1–E4), for a total of 40 pulses. The order of stimulus energies was pseudorandomized. The inter-stimulus interval (ISI) varied randomly between 10 and 15 s (rectangular distribution). An auditory tone delivered between 3 and 6 s after the laser stimulation (rectangular distribution) prompted the subjects to rate the intensity of the painful sensation elicited by the laser stimulus, using a visual analog scale ranging from 0 (corresponding to "no pain") to 100 (corresponding to "pain as bad as it could be").

EEG recording

Subjects were seated in a comfortable chair in a silent, temperature-controlled room. They wore protective goggles and were asked to relax their muscles and focus their attention towards the laser stimuli. EEG data were recorded using 64 channels positioned according to the extended 10–20 system (Brain Products GmbH, Munich, Germany; pass band: 0.01–100 Hz; sampling rate: 1000 Hz). The nose was used as the reference channel, and all channel impedances were kept lower than 10 kΩ. To monitor ocular movements and eye blinks, electro-oculographic (EOG) signals were simultaneously recorded from 4 surface electrodes: one pair placed over the upper and lower eyelids, the other pair placed 1 cm lateral to the outer corner of the left and right orbits.

EEG data analysis

EEG data preprocessing

EEG data were processed using EEGLAB (Delorme and Makeig, 2004), an open source toolbox running in the MATLAB environment, and in-house MATLAB functions. Continuous EEG data were band-pass filtered between 1 and 100 Hz. EEG epochs were extracted using a window analysis time of 1500 ms (500 ms pre-stimulus and 1000 ms post-stimulus) and baseline corrected in the time domain using the pre-stimulus interval (−500–0 ms). Trials contaminated by eye-blinks and movements were corrected using an infomax Independent Component Analysis algorithm (runica) (Delorme and Makeig, 2004; Jung et al., 2001; Makeig et al., 1997). In all datasets, these independent

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