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TMS-evoked long-lasting artefacts: A new adaptive algorithm for EEG signal correction

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HIGHLIGHTS

- TMS-evoked decay artefact (DA) makes the analysis of TMS-evoked potentials (TEPs) difficult.
- We developed a new adaptive algorithm (ADA) to correct DA in a completely data-driven way.
- Our study showed that ADA is able to completely remove the DA without corrupting the TMS-evoked physiological response.

ABSTRACT

Objective: During EEG the discharge of TMS generates a long-lasting decay artefact (DA) that makes the analysis of TMS-evoked potentials (TEPs) difficult. Our aim was twofold: (1) to describe how the DA affects the recorded EEG and (2) to develop a new adaptive detrend algorithm (ADA) able to correct the DA.
Methods: We performed two experiments testing 50 healthy volunteers. In experiment 1, we tested the efficacy of ADA by comparing it with two commonly-used independent component analysis (ICA) algorithms. In experiment 2, we further investigated the efficiency of ADA and the impact of the DA evoked from TMS over frontal, motor and parietal areas.
Results: Our results demonstrated that (1) the DA affected the EEG signal in the spatiotemporal domain; (2) ADA was able to completely remove the DA without affecting the TEP waveforms; (3). ICA corrections produced significant changes in peak-to-peak TEP amplitude.
Conclusions: ADA is a reliable solution for the DA correction, especially considering that (1) it does not affect physiological responses; (2) it is completely data-driven and (3) its effectiveness does not depend on the characteristics of the artefact and on the number of recording electrodes.
Significance: We proposed a new reliable algorithm of correction for long-lasting TMS-EEG artifacts.

1. Introduction

In the last twenty years, the combination of transcranial magnetic stimulation (TMS) and electroencephalography (EEG) has provided new insights into the investigation of brain dynamics (Ilmoniemi and Kičić, 2010). However, besides the potential of combining these two techniques, their simultaneous use produces different EEG artefacts of electrical and physiological nature. Electrical artefacts result from the voltage induced in the electrodes by the TMS pulse, which is several orders of magnitude larger than the

Abbreviations: TMS, transcranial magnetic stimulation; EEG, electroencephalography; DA, decay artefact; ADA, adaptive detrend algorithm; MEP, motor-evoked potential; TEP, TMS-evoked potential; MFG, middle frontal gyrus; M1, primary motor cortex; IPS, inferior parietal sulcus; ICA, independent component analysis; RMT, resting motor threshold; FDI, first dorsal interosseous; GMFP, global mean field power; TRSP, TMS-related spectral perturbation; TOI, time window of interest.

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physiological responses (Virtanen et al., 1999). Indeed, the TMS pulse produces a high-frequency spike of several mV of electric nature lasting a few milliseconds (Veniero et al., 2009). In addition, TMS results in a number of physiological EEG artifacts. First, a large bipolar spike peaking at 4–10 and 8–20 ms is produced by the stimulation of scalp muscles and is particularly evident when stimulating lateral areas (Korhonen et al., 2011; Mutanen et al., 2013). Moreover, TMS stimulation results in both auditory and somatosensory artifacts produced by the coil click and tactile sensation (Nikouline et al., 1999; Tiitinen et al., 1999). Finally, a long-lasting artefact has been recently described by a few papers (e.g. Litvak et al., 2007; Rogasch et al., 2014) and termed decay artefact (DA). This artefact is characterized by a slow drift of the signal of a few electrodes (usually the ones underneath the stimulating coil) whose amplitude can vary from a few μV to tens of μV impeding the correct realignment to the baseline level for tens or hundreds of milliseconds after the TMS pulse (Rogasch et al., 2014; Hernandez-Pavon et al., 2012). The nature of the DA is still a matter of debate: some authors hypothesized that during the TMS pulse some currents can pass through the electrode-electrolyte interface causing a polarization and, consequently, an EEG baseline shift (Julkunen et al., 2008). Alternatively, it has been suggested that the artefact can be produced by the electromotive forces induced in the electrode wires (Sekiguchi et al., 2011) or from the scalp muscular activity evoked by the stimulation (Rogasch et al., 2014).

Throughout the years, several on-line and off-line strategies have been developed to deal with TMS-induced EEG artifacts of electrical and physiological nature. The progressive improvements in the amplifier technology have allowed the successful removal or reduction of the TMS pulse-induced artefact during the EEG recording (Ilmoniemi et al., 1997; Virtanen et al., 1999; Bonato et al., 2006). The on-line reduction of physiological artifacts is also possible. For instance, the use of an *ad-hoc* white noise masking the coil click minimizes the auditory artifacts (Massimini et al., 2005). Muscle artifacts can be reduced by varying the coil angle (Mutanen et al., 2013). Finally, somatosensory artifacts can be reduced by using a thick of a few millimeters to reduce the tactile sensation during the stimulation. Different off-line methods of correction have also been developed by using (1) a subtractive approach, in which a template artefact generated through a phantom (Bender et al., 2005) or a TMS control condition (Thut et al., 2003) is subtracted from the data; (2) independent component analysis (ICA) or principal component analysis (PCA) (e.g. Korhonen et al., 2011; Ter Braack et al., 2013; Metsomaa et al., 2014; Rogasch et al., 2014).

Despite these strategies have been successfully applied for the correction of most of the TMS-induced artefacts, their feasibility in removing the DA is problematic. Currently, an on-line correction for this artefact is still lacking. The most common off-line methods consist in (1) using a linear detrend function in order to realign the signal on the baseline level (e.g. Van Der Werf and Paus, 2006; Zanon et al., 2010) or (2) removing the DA-related components by means of ICA or PCA (e.g. Korhonen et al., 2011; Ter Braack et al., 2013; Metsomaa et al., 2014; Rogasch et al., 2014). However, none of these solutions may be considered optimal. The linear detrend fits and subtracts a linear model to the drift assuming that the DA follows a linear trend, which is not always true, especially for the first part of the drift (Litvak et al., 2007). Indeed, the DA can follow a non-linear trend, so that the correction with a standard linear detrend might cause an uncompleted removal of the artefact or a distortion of the signal. ICA is a computational method for decomposing multivariate signals into additive independent non-gaussian signals, which has been successfully applied to multi-channel EEG data (Onton et al., 2006). Although ICA has been used to correct muscle and blink artefacts produced by TMS (Hamidi et al., 2010; Korhonen et al., 2011; Hernandez-Pavon et al., 2012), it presents a number of limitations, discussed in the present manuscript.

In this study we propose an adaptive detrend algorithm (ADA) able to discriminate the different trends of the DA (i.e. linear or non-linear) and to adaptively compute and subtract a different model to the drift. Specifically, when the DA does not follow a linear trend, ADA computes a bi-exponential model to adequately describe the kinetics of the decay that generally shows to be the sum of two different patterns, i.e. a fast component in the initial phase and a slower component in the second part (Litvak et al., 2007). We performed two experiments: in experiment 1, we tested the efficacy of ADA in removing the DA evoked from TMS applied over M1 of a large sample of healthy volunteers (forty). We chose to stimulate M1 since the TMS-evoked potentials (TEPs) pattern over this area has been highly characterized by several studies. To test the efficacy of our algorithm, we compared the ADA-corrected signal with two common ICA algorithms, namely fastICA and INFOMAX. In experiment 2, we further tested the stability and reliability of ADA in removing the DA evoked from TMS of M1 and two other brain areas, namely the left middle frontal gyrus (MFG) and the left intraparietal sulcus (IPS).

2. Methods

2.1. Participants and procedure

Fifty right-handed healthy volunteers (27 females, mean age 24 ± 4 years) were enrolled for this study after giving written informed consent. All participants were tested for TMS exclusion criteria (Rossi et al., 2009). The experimental procedure was approved by the Local Institutional Review Board, and was in accordance with the Declaration of Helsinki (Sixth revision, 2008). In experiment 1, forty participant underwent a TMS block of stimulation consisting of 80 single-pulses delivered over the left M1 during multichannel EEG recordings. In experiment 2, ten participants received three TMS blocks over the left M1, MFG and IPS. Throughout the entire session participants were seated on a comfortable armchair in front of a monitor at 80 cm of distance. They were asked to fixate a white cross (6 × 6 cm) in the middle of a black screen, in order to avoid eye movements during the EEG recordings, and to maintain a relaxed position. During TMS participants wore in-ear plugs which continuously played a white noise that reproduced the specific time-varying frequencies of the TMS click, in order to mask the click and avoid possible auditory ERP responses (Massimini et al., 2005). The intensity of the white noise was adjusted for each participant by increasing the volume (always below 90 dB) until the participant was sure that s/he could no longer hear the click (Paus et al., 2001). To reduce the bone-conducted sound and the tactile sensation we used an EEG cap with a 4 mm plastic sheet that reduced the transmission of mechanical vibration produced by the coil (Nikouline et al., 1999).

2.2. Transcranial Magnetic Stimulation (TMS)

TMS was carried out using a biphasic Magstim R^2 stimulator (experiment 1) and a monophasic Magstim 200 stimulator (experiment 2) with a 70 mm figure-of-eight coil (Magstim Company Limited, Whitland, UK). For M1 stimulation, the position of the coil on the scalp was functionally defined as the site in which TMS evoked the largest MEPs in the relaxed first dorsal interosseous (FDI) muscle of the right hand. For MFG and IPS stimulation, we based on the 10–20 system, stimulating the F3 and P3 electrode, respectively. For M1 and MFG stimulation, the coil was oriented tangentially to the scalp at about 45° angle away from the midline. For IPS stimulation, the coil was oriented at about 15° angle toward