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Recovering TMS-evoked EEG responses masked by muscle artifacts

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ABSTRACT

Combined transcranial magnetic stimulation (TMS) and electroencephalography (EEG) often suffers from large muscle artifacts. Muscle artifacts can be removed using signal-space projection (SSP), but this can make the visual interpretation of the remaining EEG data difficult. We suggest to use an additional step after SSP that we call source-informed reconstruction (SIR). SSP–SIR improves substantially the signal quality of artifactual TMS–EEG data, causing minimal distortion in the neuronal signal components.

In the SSP–SIR approach, we first project out the muscle artifact using SSP. Utilizing an anatomical model and the remaining signal, we estimate an equivalent source distribution in the brain. Finally, we map the obtained source estimate onto the original signal space, again using anatomical information. This approach restores the neuronal signals in the sensor space and interpolates EEG traces onto the completely rejected channels.

The introduced algorithm efficiently suppresses TMS-related muscle artifacts in EEG while retaining well the neuronal EEG topographies and signals. With the presented method, we can remove muscle artifacts from TMS–EEG data and recover the underlying brain responses without compromising the readability of the signals of interest.

Introduction

Transcranial magnetic stimulation (TMS) is a non-invasive method to artificially activate the cortex by applying brief and strong magnetic pulses to the brain (Barker et al., 1985). Navigation enables precise targeting of the stimulation to desired cortical areas (*e.g.*, Massimini et al., 2005; Julkunen et al., 2009). By combining navigated TMS with simultaneous electroencephalography (EEG) (Virtanen et al., 1999), we can measure directly how the TMS-evoked activity spreads in the brain. This makes TMS–EEG a useful method for studying effective connectivity (Ilmoniemi et al., 1997; Komssi et al., 2002; Massimini et al., 2005).

So far, TMS–EEG has mainly been used to study relatively medial cortical areas that do not lie directly under cranial muscles (Nikulin et al., 2003; Rosanova et al., 2009; Cona et al., 2011; Farzan et al., 2013). In principle, TMS–EEG could be used to study excitability and connectivity anywhere in the cortex, but this is often challenging because of the TMS-evoked muscle artifacts that are likely to occur when lateral areas are stimulated (Mutanen et al., 2013; Rogasch et al., 2013). Muscle artifacts often have 10 to 1000 times larger amplitudes than neuronal components and can last tens of milliseconds after the pulse (Mutanen et al., 2013). With some subjects, even the stimulation of more medial areas, such as primary motor cortex (M1), may result in severe muscle-artifact contamination (Mutanen et al., 2013). Therefore, effective artifact-removal methods are needed to improve the usability of TMS–EEG.

Independent component analysis (ICA) has been suggested to separate TMS–EEG data to brain and muscle-artifact signal components (Korhonen et al., 2011; Hernandez-Pavon et al., 2012; Rogasch et al., 2014). However, when using ICA, we have to make a strong assumption that the TMS-evoked muscle and brain responses are statistically independent. Another possible technique is the signal-space-projection (SSP) approach (Mäki and Ilmoniemi, 2011; Hernandez-Pavon et al., 2012; ter Braack et al., 2013). In SSP, we estimate the signal subspace containing the muscle artifacts and form a linear operator that removes most of the artifact from the measured signal. Mäki and Ilmoniemi (2011) showed that SSP is capable of suppressing muscle-artifact components in TMS–EEG signals. However, SSP tends to attenuate also other signals in the sensors close to the origin of the artifact. This makes the conventional interpretation of EEG waveforms and topographies difficult after applying SSP.

In this paper, we solve the SSP-related attenuation problem by using the suppressed data (and the suppressed lead fields) to compute source

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estimates that can be used to reconstruct artifact-free versions of the original neuronal EEG field patterns. We call this method *source-informed reconstruction* (SIR).

With simulations and analysis of measured EEG data, we show that the combined SSP–SIR is able to considerably suppress muscle artifacts while preserving the underlying neural responses of interest. We argue that the present algorithm provides a highly useful tool in analyzing artifactual TMS–EEG data.

Methods

In this section, we introduce the theoretical basis for the artifact suppression and source-informed data reconstruction. We also describe how we measured, simulated, and analyzed data to validate the approach.

Theory

We assume a linear data model for the measured EEG:

$$\mathbf{S} = \mathbf{LX} + \mathbf{A} + \mathbf{N}, \tag{1}$$

where $\mathbf{S}$ is the signal matrix whose entry $S_{i,t}$ contains the measured value of channel i at time t, $\mathbf{X}$ is the source matrix whose entry $X_{j,t}$ describes the activity level of a source j at a time t, and $\mathbf{L}$ is the lead-field matrix whose entry $L_{i,j}$ determines the sensitivity of channel i to source j. The elements $A_{i,t}$ and $N_{i,t}$ of matrices $\mathbf{A}$ and $\mathbf{N}$ describe muscle artifact and noise contamination in $S_{i,t}$, respectively.

We can consider our EEG data lying in a multidimensional signal space where the dimension equals the number of EEG channels. When using SSP, we estimate two signal subspaces where the first is able to explain most of the artifact variance, the second being its orthogonal complement (Uusitalo and Ilmoniemi, 1997). We refer to the former as *artifact subspace* and the latter as *brain subspace*, although the artifact subspace is likely to contain a considerable amount of brain signal and *vice versa*. Once we have estimated the subspaces, we can construct a linear operator $\mathbf{P}$ that projects the data onto the brain subspace, discarding all information in the artifact subspace. Assuming an ideal operator, $\mathbf{PA} = 0$, we obtain from Eq. (1)

$$\mathbf{PS} = \mathbf{PLX} + \mathbf{PA} + \mathbf{PN} = \mathbf{PLX} + \mathbf{PN}. \tag{2}$$

Eq. (2) has the same form as an equation describing an artifact-free EEG measurement, where $\mathbf{PS}$ and $\mathbf{PL}$ are the new measurement and lead-field matrices, respectively. By using the l^2-minimum-norm estimate (MNE) (Hämäläinen and Ilmoniemi, 1994), we obtain an estimate $\hat{\mathbf{X}}$ for the source distribution:

$$\hat{\mathbf{X}} = (\mathbf{PL})^{\dagger}\mathbf{PS}, \tag{3}$$

where $(\mathbf{PL})^{\dagger}$ is the appropriately regularized pseudoinverse of $\mathbf{PL}$.

Next, we correct the SSP-caused distortions in the signals of interest with SIR; we calculate the signal matrix $\tilde{\mathbf{S}}$ in the original signal space generated by source estimate $\hat{\mathbf{X}}$:

$$\tilde{\mathbf{S}} = \mathbf{L}\hat{\mathbf{X}}. \tag{4}$$

A similar approach has been previously used in magnetocardiography (Numminen et al., 1995; Burghoff et al., 2000) and in magnetoencephalography (Uutela et al., 2001). Aside from being free from artifacts (exactly true if $\mathbf{PA} = 0$), $\tilde{\mathbf{S}}$ also contains less noise than $\mathbf{S}$. By regularizing Eq. (3) we do not map $\mathbf{S}$ onto the least significant lead-field directions that mainly explain noise $\mathbf{N}$. This reduces the effect of noise on the source estimate $\hat{\mathbf{X}}$, and thus, also on $\tilde{\mathbf{S}}$.

All in all, we can write the whole artifact (and noise) removal process with one equation:

$$\tilde{\mathbf{S}} = \mathbf{L}(\mathbf{PL})^{\dagger}\mathbf{PS}, \tag{5}$$

where $\tilde{\mathbf{S}}$ is the reconstructed, artifact-free data. We refer to the procedure described by Eq. (5) as SSP–SIR.

An essential question is of course how to find $\mathbf{P}$. In this paper, we use the approach suggested by Mäki and Ilmoniemi (2011), which is based on the difference in the frequency spectra between muscle artifacts and neuronal EEG signals. Fig. 1 shows a time–frequency plot of an EEG channel measuring both TMS-evoked neuronal activity and a muscle artifact. During the time when the artifact is present, the signal covers a much broader band than at other times, implying that the high-frequency parts are mostly due to the muscle activation and noise. This is also supported by the findings of Rosanova et al. (2009), who studied the frequency content of TMS-evoked EEG in various cortical locations. Furthermore, the general understanding is that EEG mainly reflects synchronous post-synaptic currents in neuronal populations (Nunez and Silberstein, 2000; Baillet et al., 2001) and that this activity is seen in EEG mainly below 100 Hz (Buzsáki and Draguhn, 2004). Thus, by taking the data corresponding to the time interval when the muscle artifact is present and filtering it with an appropriate high-pass filter H that satisfies $H(\mathbf{LX}) \approx 0$, we obtain from Eq. (1)

$$H(\mathbf{S}) \approx H(\mathbf{A}) + H(\mathbf{N}). \tag{6}$$

We assume that the low-frequency parts of the muscle artifact lie in the same signal subspace with the high-frequency parts. Then, we can estimate the artifact subspace by using the high-passed data. We first write the high-passed signals in terms of the singular value decomposition (SVD):

$$H(\mathbf{S}) = \mathbf{U}\boldsymbol{\Sigma}\mathbf{V}^{\mathrm{T}}, \tag{7}$$

where $\boldsymbol{\Sigma}$ has the singular values in a descending order on its diagonal and $\mathbf{U}$ and $\mathbf{V}$ have the left and right singular vectors as columns, respectively. The column vectors of $\mathbf{U}$ form an orthonormal basis for the signal space. Because the first singular directions (the leftmost column vectors of $\mathbf{U}$) explain most of the variance of the high-passed data and the power of the artifact is expected to dominate the noise during the first few tens of milliseconds, we obtain a good approximation for the

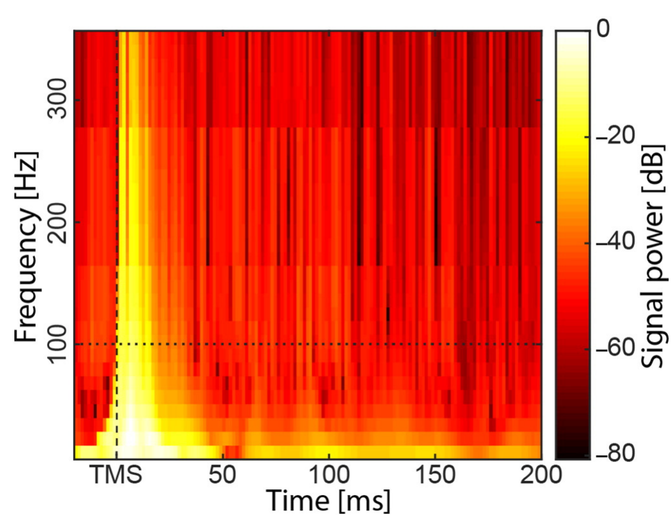

Fig. 1. A time–frequency plot of a typical TMS-evoked EEG response in an artifact-contaminated channel (subject 2, channel C1). We estimate the artifact subspace by high-pass filtering the data from 100 Hz. The plot was made using EEGLAB toolbox (Delorme and Makeig, 2004) with the Morlet-wavelet decomposition.