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TMS-induced EEG Artifacts Removal Methods based on Cross-Correlation Coefficients of ICA Components

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Abstract

In this study a noble TMS-induced artifact removal method is developed and discussed by estimating its parameters for various aspects of data, such as sampling rate, filtering order and ICA decomposition method, in both the EEG time series and in the independent components of the EEG by using the EEG data obtained from four healthy subjects who were receiving single pulse TMS-EEG and sham-EEG stimulus on the left Broca's area. A total of four healthy male subjects without any neurological disorder were selected in this study. ICA filters trained on the reduced version of 60 channel EEG data collected during single pulse TMS-EEG and sham-EEG recordings and identified the reduced number of statistically independent source channels. The decomposition algorithm of ICA considered in this study includes Jader , FastICA and cICA. The ICA components originating from the TMS-induced artifact are classified by comparing the cross-correlation coefficients between single pulse TMS-EEG and sham-EEG stimulus after ICA decomposition. Then, the estimation of parameters in the TMS-induced artifact removal for sampling rate 1.45kHz, filtering order 100 and ICA decomposition method FastICA was evaluated by the change of the ratio of the cross-correlation coefficients between single pulse TMS-EEG and sham-EEG stimulus before and after the ICA decomposition. The results showed the consistency in the assessment of the availability of the TMS-induced artifact removal suggesting the efficiency and the reliability of the method developed in this study.

Keywords: *TMS-EEG, Independent Component Analysis, TMS-induced artifacts*

1. Introduction

Transcranial magnetic stimulation (TMS) non-invasively activates cortical neurons by causing depolarization or hyperpolarization in them through the electromagnetic induction [1]. It can be used to activate or deactivate a specific part of the brain in order to study the activities depending on a stimulation parameter from which the functions of different brain areas and the connections between them can be assessed [2]. Specifically, it is widely used to measure the connectivity of the primary motor cortex and a muscle to evaluate brain damage and other disorders related to the motor cortex [3]. It is also used to study the effects of phosphenes by stimulating the primary visual cortex [4] and the speech processing by disrupting momentarily the Broca's area [5]. TMS, introduced by Barker et al. in 1985 [6],

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is divided into two types, single or paired pulse TMS and repetitive TMS (rTMS) depending on the stimulation mode. The stimulation is obtained by passing short current pulses through a coil, which induces a transient magnetic field and consequently an electrical current in the tissues of the head. Single pulse TMS causes neurons in the neocortex under the site of stimulation to depolarize and discharge an action potential. rTMS can increase or decrease the excitability of the corticospinal depending on the intensity of stimulation, coil orientation, and frequency, and therefore produce longer-lasting effects which are widely believed to reflect changes in synaptic efficacy.

In the study of cortical reactivity and connectivity, the applicability of TMS can be expanded by combining it with neuroimaging methods such as positron emission tomograpgy (PET), functional magnetic resonance imaging (fMRI) and Electroencephalory (EEG). Combined TMS-PET studies showed TMS-induced changes in the hemo-dynamics of the brain [7], covariations of the responses both at the stimulation site and remotely connected brain regions and cumulative changes in regional neuronal activity in the stimulated cortex and connected brain regions. The technique of combining TMS and fMRI, first demonstrated by Bohning and colleagues [4], has been utilized to investigate inter-regional interactions in the brain and the possible functional consequences as well as the brain response to TMS over motor system. Combining TMS and EEG offered insights into neural interaction during cognition which allows the investigation on the causal role of specific brain areas in behavior and the interactive connection between the brain areas [8]. In the last decade there has been rapid growth in the use of TMS-EEG to explore the dynamics of the brain at rest [9], the role of the frontal eye fields (FEFs) in attentional selection [10] and the role of medial frontal cortex in motor control [11].

EEG is a non-invasive technique to record spontaneous electrical activity of the brain by measuring the voltage fluctuations resulting from ionic current flows within the neurons of the brain [12]. That is, EEG signals represent the temporal profile of the change in the potential difference between two electrodes placed on the scalp. EEG recording systems amplify the small changes in voltage which are detectable through the skull and scalp. PET and fMRI rely upon the sluggish haemodynamic response occurring after increases in neural activity. Therefore, EEG has relatively worse spatial resolution but better temporal resolution than other methods such as fMRI and PET [4, 7]. EEG is used to clinically observe the type of neuronal oscillations. Epileptic activity, brain death, or sleep disorders can be diagnosed from their abnormal patterns of the EEG signals [8-11]. Furthermore, event-related potentials (ERPs), the EEG responses associated with certain actions or external stimuli, can give more information about the cortical areas involved in different cognitive tasks and processes. Therefore, functional connectivity between the areas can be analyzed from the spectral properties of EEG and the cohesion of the spontaneous oscillations in different brain area which is obtained by filtering and Fourier transformation.

EEG signals are typically contaminated with biological and environmental artifacts. Biological artifacts include eye-induced artifacts, such as eye blinks, eye movements and extra-ocular muscle activities, cardiac artifacts, muscle activation-induced artifacts and glossokinetic artifacts [13]. Environmental artifacts include electrode spikes originating from a momentary change in the impedance of a given electrode due to body movement or settling of the electrodes, and 50 or 60 Hz line noise due to poor grounding of the EEG electrodes [14]. The TMS pulse in the TMS-EEG combining study introduces artifacts in the EEG electrodes which may mask the underlying neural activity lasting about 5 through even hundreds milliseconds after the pulse. Some of the

TMS artifacts are induced due to the polarization of the skin-electrode contact. The magnetic pulse of TMS affects the muscles and motor nerves underneath the coil causing the muscle activation and eye movement, which results in the induction of EEG artifacts. The magnetic pulse of TMS can also excite the somatosensory nerve endings and the coil click activates the auditory system of the subject, which can be seen in EEG as auditory or somatosensory evoked potentials [15]. The effect of artifacts can be attenuated by deleting data with amplitudes over a certain value. Independent component analysis (ICA) is known to be able to separate EEG data into neural activity and artifact [16]. Many artifact rejection methods are time consuming when applied to high-density EEG data. In this study a noble TMS-induced artifact removal method is developed and discussed by estimating its parameters for various aspects of data, such as sampling rate, filtering order and ICA decomposition method, in both the EEG time series and in the independent components of the EEG by using the EEG data obtained from four healthy subjects who were receiving single pulse TMS-EEG and sham-EEG stimulus on the left Broca's area.

2. Methods

2.1. Subjects

A total of 4 healthy male subjects (S, E, M and T) without any neurological disorder were selected in this study. Subjects were screened with the TMS Screening Questionnaire. Once informed consent was obtained, the inclusion and exclusion criteria were reviewed. Baseline measures included the modified Edinburgh Handedness Inventory and a baseline Minimental State Exam (MMSE).

2.2. TMS-EEG and sham-EEG

Subjects came in for the TMS-EEG study visit(s) 2 times separated by at least two days. One of the study visits were single pulse TMS-EEG, the other were sham-EEG. Subjects were included in either the sham-EEG first or the single pulse TMS-EEG first group by random assignment by using a random number generation method. 60 Channel EEG were recorded at rest, and pre and post first and second TMS intervention, a total of 16 TMS-EEG and 16 sham-EEG data. The single pulse TMS stimulus was treated on the left Broca's area. EEG data were sampled preliminary at 1.45kHz before applying ICA algorithms and then analyzing to estimate parameters for various aspects of data, such as sampling rate, filtering order and ICA decomposition method, in both the EEG time series and in the independent components of the EEG. Figure 1(a) and (b) show the schematic diagrams of the TMS-EEG and sham-EEG tasks, respectively. Trains of single TMS pulses were administrated at intervals of 300 ms for a 1 minute period at 80% of active motor threshold on left Broca's area (area 44) for the single pulse TMS-EEG group. Sham-EEG underwent the same procedure for identifying stimulus location used in subjects receiving single pulse TMS-EEG. Simulated TMS were administered using Magstim Placebo 70 mm figure-of-8 shaped coils producing discharge noise and vibration similar to a real 70 mm coil without stimulating the cerebral cortex. The electrical stimulation of the scalp, which is induced in the single pulse TMS-EEG experiment, was simulated by attaching surface electrodes underneath the sham coil and in contact with the scalp and using Nerve Conduction Study devices routinely to administer electrical shocks to the scalp simultaneous to each simulated TMS train.

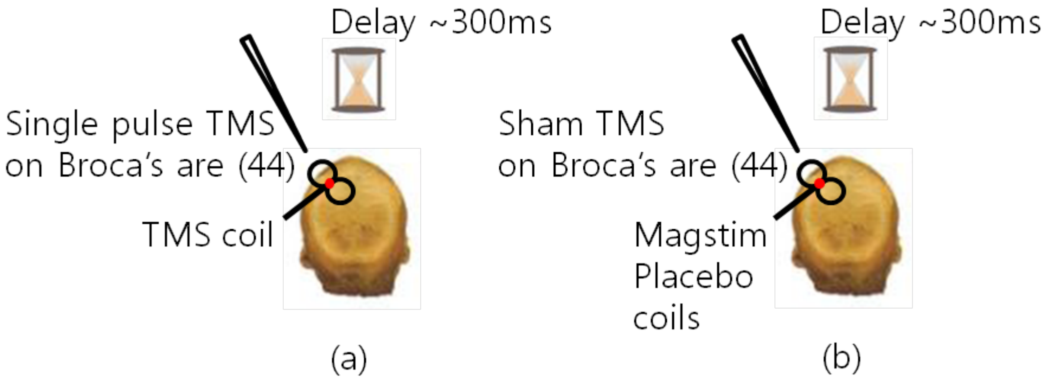

Figure 1. The Schematic Diagrams of (a) the TMS-EEG and (b) Sham-EEG Tasks

2.3. Sampling Rate

High-pass filter with cutoff frequency at 1Hz was applied to remove linear trends in the EEG data before artifact removal. 60Hz line noise was removed by notch filtering. The data were then sampled at various rates, 1.45, 0.7 and 0.35 kHz. The sampled data were re-referenced by using the average reference method which rests on the fact that the sum of the electric field values recorded at all scalp electrodes is always 0.

2.4. Filtering Order

Linear finite impulse response (FIR) filtering was constructed for low-pass filtering with cutoff frequencies at 100Hz using Matlab routine filtfilt(). The function filtfilt() applied the filter forward and then again backward to ensure that phase delays introduced by the filter are canceled. The filtering orders, 100, 200 and 400 were selected to estimate parameters in the TMS-induced artifact removal problem.

2.5. Independent Component Analysis

Independent component analysis can be used to separate the original source signals from their mixtures by estimating the weigh parameters based on the information of the independence of the sources. The mathematical model of ICA is described as the following equation, $\mathbf{x}=\mathbf{A}\mathbf{s}$ where $\mathbf{x}$ is the random vector whose elements are the mixtures $x_1, \ldots, x_n$, $\mathbf{s}$ is the random vector with elements $s_1, \ldots, s_n$ and $\mathbf{A}$ is the matrix with elements a_{ij} . The EEG data are recordings of electrical potentials in many different locations on the surface of the brain which are generated by mixing some sources of brain activity. ICA decomposes independent components from the mixture of sources. The components can be classified to signals from brain activities and artifacts induced by TMS stimulation as well as those by body movements or electrode mismatching. Principle component analysis (PCA) was processed initially to reduce the number of channels since the number of independent components is dependent on the number of channels and the required amount of data is generally proportional to the order of the number of channels. ICA filters trained on the reduced version of 60 channel EEG data collected during single pulse TMS-EEG and sham-EEG recordings and identified the reduced number of statistically independent source channels. The decomposition algorithm of ICA considered in this study includes Jader [22], FastICA [23] and cICA [24].

2.6. TMS-induced Artifacts Removal Method

Even though it is possible to classify the characteristics of the ICA components and separate artifactual components by visual inspection, it is very much time consuming and is not reliable. The ICA components originating from the TMS-induced artifact are classified by comparing the cross-correlation coefficients between single pulse TMS-EEG and sham-EEG stimulus after ICA decomposition, which is based on the fact that there are no TMS-induced artifacts in sham-EEG data. Then, the estimation of parameters in the TMS-induced artifact removal for various aspects of data, such as sampling rate, filtering order and ICA decomposition method, was evaluated by the change of the ratio of the cross-correlation coefficients between single pulse TMS-EEG and sham-EEG stimulus before and after the ICA decomposition.

3. Results and Discussions

Figure 2 (a) and (b) show the typical time series of the TMS-EEG and sham-EEG data of subject S with 1.45 kHz of sampling rate and before FIR filtering with 100 of order and notch filtering with 55-60 of cutoff frequency, respectively, where the x axis represents time (sec) and y axis, voltage (μV). Figure 3 (a) and (b) show the typical power spectra of the single pulse TMS-EEG data and sham-EEG data with 1.45 kHz of sampling rate after FIR filtering with 100 of order and notch filtering with 55-60 of cutoff frequency, respectively, where the channel maps for frequencies of 1.4, 5.7, 9.9, 19.8, 39.6 and 100.5Hz are shown for each power spectrum and the x and y axes represent the frequency (Hz) and the power intensity ($10\log_{10} \mu V^2/Hz$), respectively. The TMS-induced artifacts are noticeable at Figure 2 showing long lasting disruption in the EEG data. The linear trends and 60 Hz line noises are removed from EEG data as shown in Figure 2 (b) and 3 (b). Figure 4 (a) and (b) represents the time courses (top) and the 2-D scalp maps of each components (bottom) for single pulse TMS-EEG data and sham-EEG data, respectively with 1.45 kHz of sampling rate and FIR filtering with 100 of order. The cross-correlation coefficients were calculated for the components of single pulse TMS-EEG data and sham-EEG data with 1.45 kHz of sampling rate and FIR filtering with 100 of order. Component 1-5, 14, 15, 19, 35, 40, 45 and 58 of single pulse TMS-EEG data are the uncorrelated to those of sham-EEG data and can be considered as the TMS-induced artifacts. Figure 5 shows power spectrum along with channel maps for frequencies of 1.4, 5.7, 9.9, 19.8, 39.6 and 100.5Hz of the single pulse TMS-EEG data with 1.45 kHz of sampling rate and after rejecting component 1-5, 14, 15, 19, 35, 40, 45 and 58 for TMS-induced artifacts removal. The TMS-induced artifacts of TMS-EEG data are shown to be removed in the top of Figure 5. The estimation of parameters in the TMS-induced artifact removal for sampling rates 1.45, 0.7 and 0.35kHz, filtering orders 100, 200 and 400 and ICA decomposition methods, Jader, FastICA and cICA, where the estimation was done by evaluating the change of the ratio of the cross-correlation coefficients between single pulse TMS-EEG and sham-EEG stimulus before and after the ICA decomposition.

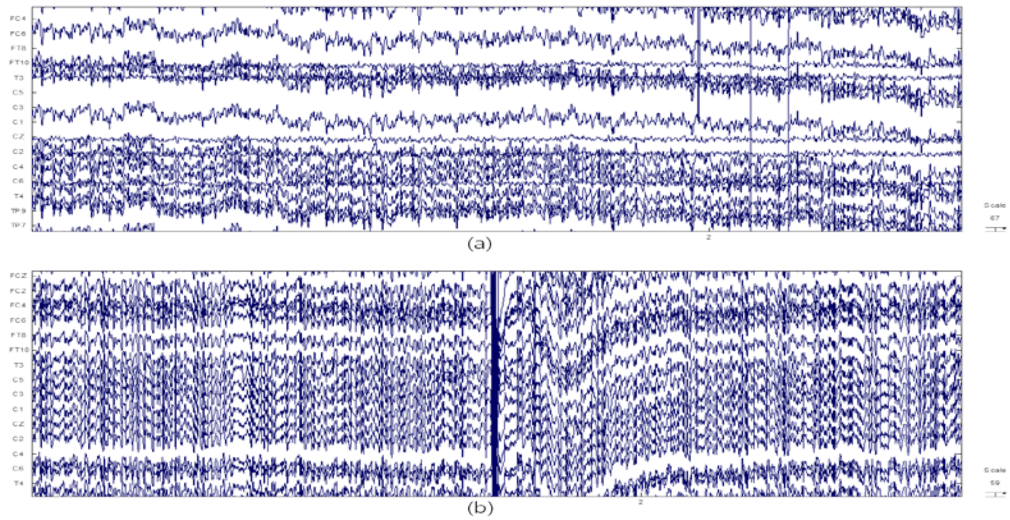

Figure 2. Typical Time Series of (a) the TMS-EEG and (b) sham-EEG data of Subject S with 1.45 kHz of Sampling Rate and before FIR Filtering with 100 of Order and Notch Filtering with 55-60 of Cutoff Frequency

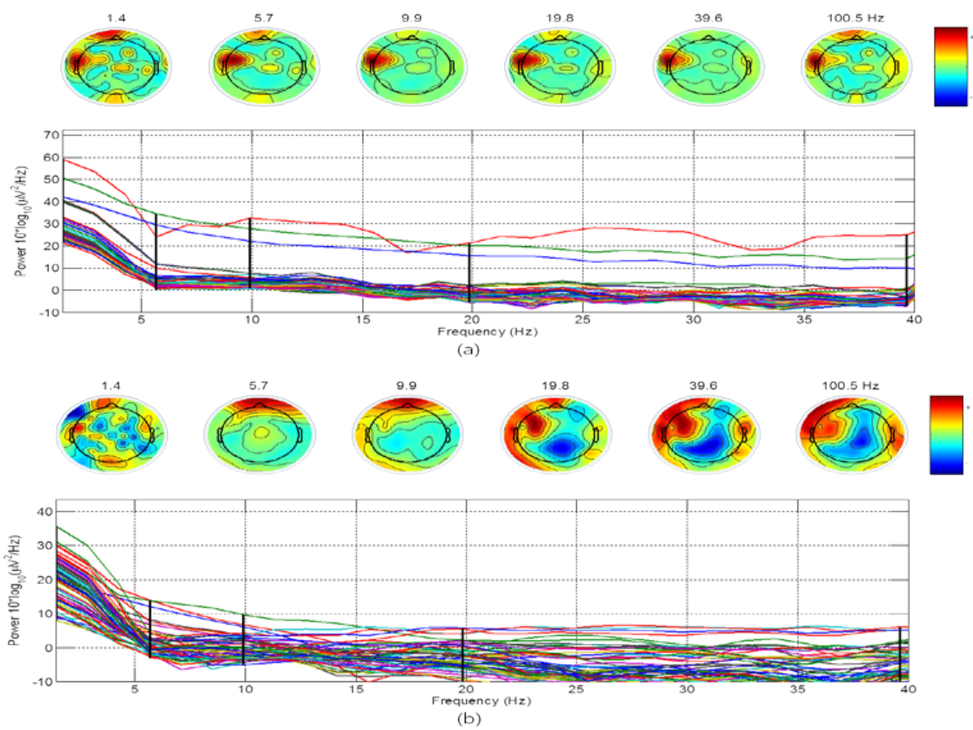

Figure 3. Typical Power Spectra of the Single Pulse TMS-EEG Data (top) and Sham-EEG Data (bottom) with 1.45 kHz of Sampling Rate and Before and After, Respectively FIR Filtering with 100 of Order and Notch Filtering with 55-60 of Cutoff Frequency

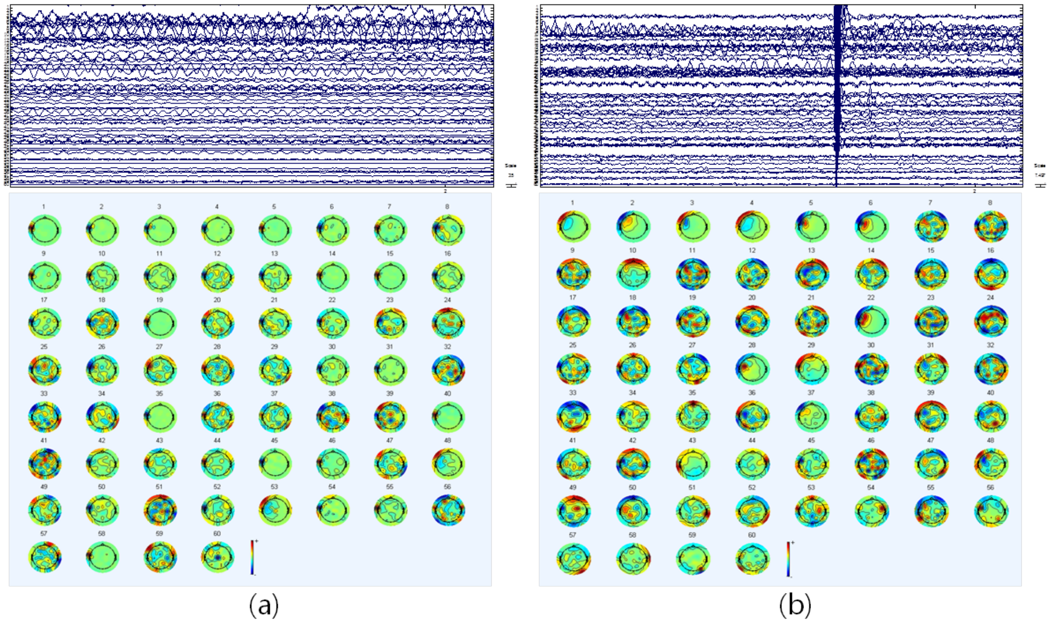

Figure 4. The Time Courses (top) and the 2-D Scalp Maps of each Components (bottom) for (a) Single Pulse TMS-EEG Data and (b0 Sham-EEG Data, Respectively with 1.45 kHz of Sampling Rate and FIR Filtering with 100 of Order

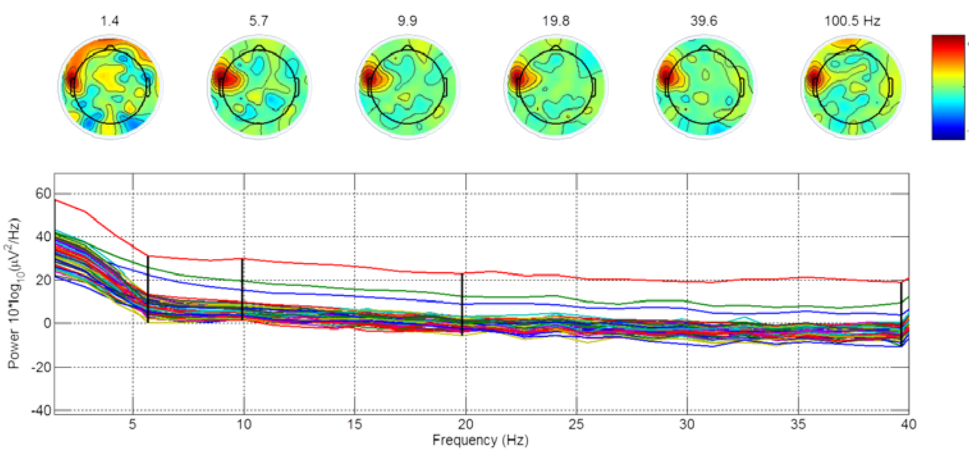

Figure 5. Power Spectrum along with Channel Maps for Frequencies of 1.4, 5.7, 9.9, 19.8, 39.6 and 100.5Hz of the Single Pulse TMS-EEG Data with 1.45 kHz of Sampling Rate and after Rejecting Component 1-5, 14, 15, 19, 35, 40, 45 and 58 for TMS-induced Artifacts Removal

4. Conclusions

TMS activates non-invasively cortical neurons by causing depolarization or hyperpolarization in them through the electromagnetic induction. It can be used to activate or deactivate a specific part of the brain in order to study the activities depending on a stimulation parameter from which the functions of different brain areas and the connections between them can be assessed. In the study of cortical reactivity and connectivity, the applicability of TMS can be expanded by combining it with neuroimaging methods such as positron PET, fMRI and EEG. There has been rapid growth in the use of TMS-EEG to explore the dynamics of the brain at rest, the role of the frontal eye fields in attentional selection and the role of medial frontal cortex in motor control. However, EEG signals are typically contaminated with biological and environmental artifacts. The TMS pulse in the TMS-EEG combining study introduces artifacts in the EEG electrodes which may mask the underlying neural activity lasting about 5 through even hundreds milliseconds after the pulse. Independent component analysis (ICA) is known to be able to separate EEG data into neural activity and artifact. Even though it is possible to classify the characteristics of the ICA components and separate artifactual components by visual inspection, it is very much time consuming and is not reliable. In this study a noble TMS-induced artifact removal method is developed and discussed by estimating its parameters for various aspects of data, such as sampling rate, filtering order and ICA decomposition method, in both the EEG time series and in the independent components of the EEG by using the EEG data obtained from four healthy subjects who were receiving single pulse TMS-EEG and sham-EEG stimulus on the left Broca's area. The ICA components originating from the TMS-induced artifact are classified by comparing the cross-correlation coefficients between single pulse TMS-EEG and sham-EEG stimulus after ICA decomposition, which is based on the fact that there are no TMS-induced artifacts in sham-EEG data. Then, the estimation of parameters in the TMS-induced artifact removal for various aspects of data, such as sampling rate, filtering order and ICA decomposition method, was evaluated by the change of the ratio of the cross-correlation coefficients between single pulse TMS-EEG and sham-EEG stimulus before and after the ICA decomposition. The estimation of parameters in the TMS-induced artifact removal for sampling rate 1.45 kHz, filtering order 100 and ICA decomposition methods FastICA, was evaluated by the change of the ratio of the cross-correlation coefficients between single pulse TMS-EEG and sham-EEG stimulus before and after the ICA decomposition. The results showed the consistency in the assessment of the availability of the TMS-induced artifact removal suggesting the efficiency and the reliability of the method developed in this study.

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