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Source-based artifact-rejection techniques available in TESA, an open-source TMS–EEG toolbox

Dear Editor,

Two recently published artifact-rejection techniques [1,2]; designed for analyzing electroencephalography (EEG) data following transcranial magnetic stimulation (TMS), are now included in an open-source data-analysis toolbox TESA [3]. The new implementations of signal-space-projection–source-informed-reconstruction (SSP–SIR) [1] and source-utilized noise-discarding algorithm (SOUND) [2] (see Fig. 1) are computationally efficient and easy to use, allowing the TMS–EEG researchers to suppress unwanted signal components, such as the TMS-evoked muscle artifact and TMS-pulse-elicited auditory or somatosensory responses [1,2,4].

TMS–EEG is a powerful, non-invasive technique to study, *e.g.*, effective connectivity, reactivity, or inhibitory and excitatory mechanisms *in vivo* in the human cortex (for review see, *e.g.* Ref. [5]). Unfortunately, the fully flexible use of TMS–EEG is still hindered by the TMS-evoked muscle artifacts, which are particularly prominent when lateral brain regions are targeted [6]. Moreover, auditory and somatosensory responses to TMS may mask the genuine TMS-evoked EEG activity, causing a risk of misinterpretation of the data [7,8]. Additionally, TMS–EEG suffers from other noise sources, including electrode-polarization-decay artifacts, line noise, DC drifts, and constant muscle tension [3].

The standard approach to tackle these disturbances is to reject the contaminated data segments or bad channels, based on heuristic visual inspection [3]. The popularity of visual rejection methods and independent component analysis (ICA) [6] might be partially explained by their prevalence in several open source analysis toolboxes (*e.g.*, Ref. [9]). However, both using heuristics to reject data and applying ICA to TMS-evoked EEG have their shortcomings [10], suggesting that more objective data-cleaning methods are needed. Recently, SSP–SIR was developed to suppress TMS-evoked muscle artifacts, while controlling the level of distortions in the neuronal signals of interest [1]. In short, SSP rejects topographies (signal-space directions) that are estimated to best capture the artifact. Because SSP also distorts the brain-signal topographies, an additional SIR step is needed; SIR uses inverse and forward calculations to reconstruct the original artifact-free EEG signals.

After SSP–SIR, a closely related method SOUND was developed to automatically detect and remove noise or artifacts from TMS–EEG signals [2]. SOUND uses an iterative minimum-norm-estimate-based cross-validation across the channels to find a spatial Wiener filter that provides optimal[1] estimates for the neuronal EEG signals. SOUND filters out those signal components that are not likely to originate from intracranial post-synaptic currents, *e.g.*, electrode-polarization, line-noise, and electrode-movement artifacts.

SSP–SIR and SOUND provide complementary tools and flexibility to conventional TMS–EEG preprocessing. For instance, unlike with ICA, the assumption for statistical independence between the artifacts and brain signal is not needed. As semiautomatic methods, SSP–SIR and SOUND can substantially enhance data analysis. Both methods are now available in TESA, a TMS–EEG data analysis plugin, which works inside the well-established EEG-analysis toolbox EEGLAB [9]. The EEGLAB platform enables a flexible use of completely graphical user interface (GUI) and/or MATLAB (The Mathworks Inc., Natick, MA, USA) scripting with the researcher's own custom code. Furthermore, because of EEGLAB's extensive input–output functionality, TESA and its SSP–SIR and SOUND functions can now be used with a wide range of EEG systems.

SSP–SIR and SOUND utilize inverse and forward modelling of the neuronal EEG signals (see Refs. [1,2] for details). For this, a lead-field matrix, which describes the sensitivity of the EEG channels to all possible cortical sources, is needed. If the lead field is not available, the SSP–SIR and SOUND functions (`tesa_sspsir` and `tesa_sound`) automatize this process by computing a lead field based on a spherical three-layer model and the theoretical channel locations on the standard 10–20 layout. Both `tesa_sspsir` and `tesa_sound` functions are very efficient, requiring only seconds of processing time for a standard TMS–EEG dataset (e.g., consisting of 140 x 2-s epochs, measured with 62 channels and 1000-Hz sampling rate) on a standard desktop computer. For SOUND, this means over a fivefold decrease in the computation time compared to the original implementation [2].

In addition to muscle-artifact rejection, SSP–SIR appears to be able to recover genuine TMS-evoked EEG signals under the TMS-related sensory responses [4]. Using control data consisting of only somatic and auditory responses to TMS, the most significant sensory-response topographies were estimated and suppressed from the actual TMS–EEG data. We provide the implementation of this process in the new `tesa_sspsir` function. The process can be easily generalized to suppress other artifacts, provided the artifacts can be captured in additional control data and the topographies are uncorrelated from the TMS-evoked neural sources.

To conclude, TESA now includes new source-based spatial filtering methods, SSP–SIR and SOUND, allowing a more flexible removal of some of the most-challenging, unwanted TMS-evoked

[1] Optimal in the sense that the expectation value of the root-mean-square differences between the estimated and the true noiseless neuronal signals are minimized.

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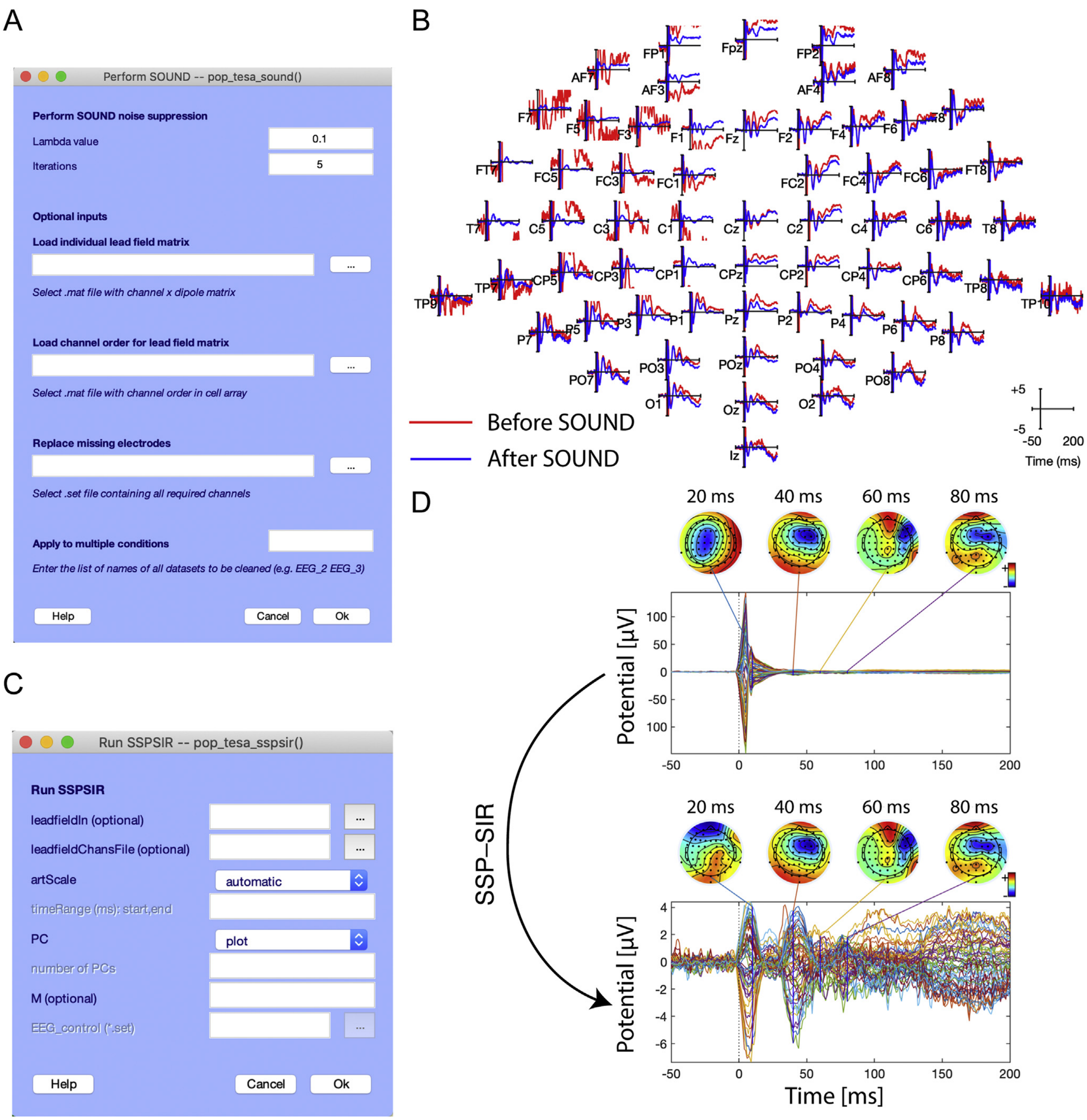

Fig. 1. An example of the application of the new TESA functions `tesa_sound` and `tesa_sspsir`. A: GUI for the `tesa_sound` function. B: TESA example data before (red curves) and after (blue curves) applying the `tesa_sound` function with the default settings. The noisy channels, e.g., on the left lateral side, are cleaned while the good-quality channels are preserved, e.g., Cz. C: GUI for the `tesa_sspsir` function. D: The EEGLAB visualizations of TESA example data before (top panel) and after (bottom panel) applying the `tesa_sspsir` function with the default settings. After rejecting the muscle-artifact topographies, an early deflection at 20 ms is uncovered. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

signals (*e.g.,* muscle and multisensory responses), as well as other common recording artifacts. Additional upgrades with the latest TESA version include improvements to the ICA visualization tool, extended filtering options, and capacity to remove TMS-pulse artifacts from continuous data. Alongside with this publication, we provide comprehensive documentation for the new methods and an example script, showing how the functions can be incorporated in practice inside a TMS–EEG preprocessing pipeline. In the future, the TESA developers aim to keep publishing TMS–EEG-analysis tools from voluntary contributors, to make novel methods more accessible to a wide range of TMS–EEG researchers. Further information on TESA, including code and training manual, is available from: https://nigelrogasch.github.io/TESA/

Declaration of competing interest

Risto Ilmoniemi is an advisor and a minority shareholder of Nexstim Plc. He has received funding from Business Finland to prepare commercialization of TMS technologies.

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