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Contrasting single-trial ERPs between experimental manipulations: Improving differentiability by blind source separation

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Contrasting event-related potentials (ERPs) generated under different experimental conditions and inferring differential brain responses is widely practiced in cognitive neuroscience research. Traditionally, these contrasts and subsequent inferences have proceeded directly from ERPs measured at the scalp. For certain tasks, it is not unusual that ERPs from a subset of channels are given particular emphasis in data analysis, such as the channels displaying the maximum peak amplitude in regions of interest ("best sensors") or channels showing the largest averaged ERP waveform differences. With the aid of a blind source separation (BSS) algorithm, second-order blind identification (SOBI), which has been recently validated for its ability to recover correlated neuronal sources, we show that single-trial ERPs from previously validated neuronal sources were more distinguishable among different experimental manipulations than the single-trial ERPs measured at the comparable "best sensors". This suggests that by using validated SOBI-recovered neuronal sources, ERP researchers can improve the ability to detect differences in neuronal responses induced by experimental manipulations. Critically, our observations were made at the level of single trials, as opposed to the averaged ERP. Therefore, our conclusions are particularly relevant to phenomena involving trial-to-trial changes in brain activation, for example, rapid induction of brain plasticity and perceptual learning, as well as to the development of brain–computer interfaces. Similar advantages would also apply to analogous situations with magnetoencephalography (MEG).

Keywords: Blind source separation (BSS); Second-order blind identification (SOBI); Electroencephalography (EEG); Single-trial analysis; Event-related potential (ERP); Somatosensory evoked potential (SEP); Median nerve stimulation; Primary somatosensory cortex (SI); Neural networks; Back-propagation; Brain computer interface (BCI); Independent component analysis (ICA)

Introduction

In cognitive neuroscience, the event-related potential (ERP) is a frequently used tool for revealing different brain activation patterns associated with experimental manipulations. One is often interested in differences between ERP waveforms and their corresponding scalp distributions induced by different experimental conditions. As high-density EEG systems have become increasingly available, it is not immediately obvious how to best analyze such high dimensional data. One approach has been to focus on a subset of sensors where ERP differences have been observed under similar experimental conditions. This approach is often used for experimental situations where ERP waveform differences are expected to be relatively focal, i.e., present at a small subset of electrode sites. Under these circumstances, statistical tests of ERP differences have often been performed on waveforms at a small number of sensors. For example, to capture the differential activations of motor cortices prior to the generation of hand movements, motor readiness potentials have been indexed using two recording electrodes, one located over the left motor cortex (C3) and the other over the right (C4) (Coles, 1989). For a given task, the specific sensors chosen have often been shown to best differentiate between experimental conditions, in this case, left and right hand movement.

Implicit in this sensor-based ERP approach is the assumption that the EEG sensors displaying the maximal signal of interest (from here on referred to as the "best sensors") offer reasonable estimates of the underlying brain sources of interest and reasonable sensitivity to detect ERP differences between experimental conditions. One advantage of using the "best sensor" ERP approach is that the concept is intuitive and the method requires no special tools and is thus accessible to the majority of ERP researchers. Another advantage is that preselection of a few "best sensors" allows for more focused statistical tests as an alternative to the omnibus low-powered ANOVA test on data from all electrode locations. Similar to principal component analysis (PCA) or independent component analysis (ICA), which

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can be viewed as applying spatial filters to the EEG data, this "best sensor"-based approach can also be viewed as applying a specific kind of spatial filter. While in the case of PCA or ICA, the spatial filters are derived mathematically, in the case of the "best sensor" approach, the spatial filters are selected intuitively or heuristically. The effect of the "best sensor"-based filters is to retain signals from only the selected EEG sensors and exclude signals from all others. Because the scalp recorded EEG at each sensor contains a mixture of signals from both extra-cranial noise sources and intra-cranial neuronal sources from different brain locations, such filtering via the "best sensor" maintains the mixed nature of signals. Thus, in principle, the event-related activation from specific functional brain regions cannot be optimally indexed by scalp EEG sensor data, even when the signals are from the sensors with the largest ERP amplitude.

A variation on the "best sensor"-based analysis is taking an average surrounding and including the "best sensors". Although such averaging offers an opportunity to remove uncorrelated sensor noise, it does nothing to unmix or isolate signals from specific brain sources of interest from those originating within other brain regions. It is critical to note that this averaging process introduces a major source of subjectivity and uncertainty concerning how many surrounding sensors and which ones to include. These decisions can be difficult as the scalp voltage map may easily reveal activation at a large number of the sensors (e.g., Figs. 3C, D). Finally, averaging across the "best sensor" and its surrounding sensors would only serve to *reduce*, instead of increase, the resulting signal-to-noise ratio because, by definition, the maximum is always greater than the average. Therefore, the "best sensor" approach offers better signal-to-noise ratio than the "average sensor" approach.

Blind source separation (BSS) and ICA algorithms (Hyvarinen and Oja, 2000; Vigario et al., 2000; Stone, 2002; Makeig et al., 2004; Muller et al., 2004) are potential methods for separating the mixture of EEG signals into multiple components. Some of the components recovered from these algorithms correspond to noise sources, such as artifacts (Vigario, 1997; Jung et al., 1999; Tang et al., 2002b; Joyce et al., 2004), and others to neuronal sources of interest (Vigario et al., 2000; Tang et al., 2002b; Makeig et al., 2004; Muller et al., 2004; Tang et al., 2005a). Second-order blind identification (SOBI: Belouchrani et al., 1993; Cardoso and Souloumiac, 1996; Belouchrani et al., 1997) is one BSS algorithm that can isolate ocular artifacts and sensor noise from brain signals (Tang et al., 2000a, 2002b, 2005a; Joyce et al., 2004) and separate functionally distinct but sometimes correlated brain activity, for example, activity from left and right primary somatosensory (SI) cortices following median nerve stimulation (Tang et al., 2005a). Most importantly, it has been shown that the signal-to-noise ratio (SNR) of averaged somatosensory evoked potentials (SEPs) obtained from SOBI-recovered SI components is much higher than the SNR obtained from the "best sensors" over the SI hand region (Tang et al., 2005a). This suggests that patterns of neuronal activations associated with different sensory, motor, or cognitive activations – induced by experimental manipulation – should be rendered more distinguishable when using SOBI-recovered components than when using the EEG "best sensor" signals directly.

We tested this hypothesis in a simple task domain where we attempted to differentiate single-trial ERPs induced by different stimulation conditions. We collected EEG data during an intermixed sequence of three different median nerve stimulations (left, right, and bilateral) and attempted to distinguish or classify, according to the single-trial SEPs, which of the three stimulations had been delivered during a given trial. If SOBI-recovered components isolate the neuronal responses from underlying sources better than the "best sensor" data, then one would expect that single-trial ERPs from the SOBI neuronal components should be classified with greater accuracy than those directly from the "best sensors". To quantify the differentiability of single-trial ERPs, we used back-propagation neural networks (BPNNs) to classify the EEG data from each trial according to the stimulus condition presented. BPNNs are commonly used for pattern classification and have been previously used to classify single-trial ERPs (e.g., Pfurtscheller et al., 1996, 1997). Here, we evaluated comparative performance between network classifiers trained with SOBI-recovered SI component data (SOBI component network) and those trained with the "best sensor" data ("best sensor" network). Specifically, we determined the percentage of single-trial SEPs that were correctly classified when the two different types of ERP representations were used.

It is important to point out that the goal of the present study was not to achieve optimal performance for classifying single-trial ERPs or to determine the best possible method for classification. The aim of the present study was to demonstrate the potential usefulness of SOBI preprocessing for ERP research relative to the use of the "best sensors" when contrasting the effects of experimental manipulations on brain activations at the level of single-trial. We tested a specific prediction that the SEPs of the SOBI-recovered components can serve as better indices for distinguishing among different patterns of brain activations associated with different sensory stimulations than the "best sensors" selected using information from all sensors. A variety of advanced signal processing methods, either alone or in combination, may result in further classification improvement.

Methods

The present study comprised the following steps: (1) collection of continuous non-averaged EEG data for single-trial classification; (2) application of SOBI to continuous non-averaged EEG data; (3) identification of components corresponding to left and right SI activations; (4) neural network classification of trial types using two kinds of input data: the SOBI component data derived in steps 2 and 3 and the "best sensor" data. It is important to point out that in the single-trial analysis literature, the phrase "single-trial analysis" does not imply that only data from a single-trial or epoch are used for the characterization or measurement of that trial or epoch. Instead, typically data from an entire experiment have been used by the algorithms to estimate parameters for a given trial/epoch type (Woody, 1967; Pham et al., 1987; Jaskowski and Verleger, 1999; Tang et al., 2002a). This is also the case for the single-trial classification study presented here.

Subjects

Four right-handed subjects (2 males), aged between 20 and 25 years, volunteered to participate in this experiment. No subjects reported a history of neurological or psychological disorder. Experimental procedures were conducted in accordance with the Human Research Review Committee at the University of New Mexico.

Experimental procedures

Three types of stimulation trials, unilateral (L: left, and R: right) and bilateral (B) median nerve stimulations, were delivered intermixed and pseudo-randomly at the wrist with no more than three consecutive identical stimulations. We chose this particular median nerve stimulation protocol to test the present hypothesis for the following reasons. First, median nerve stimulation is known to preferentially activate contralateral SI cortex (Allison et al., 1991) and thus displays selective response patterns to the different stimulation conditions. Second, the spatial location and time course of SI activations have been well characterized with converging imaging methods (Allison et al., 1989; Hari and Forss, 1999; Korvenoja et al., 1999; Arthurs and Boniface, 2003; Thees et al., 2003). Third, it has been demonstrated that SOBI can reliably recover SI activations from scalp recorded EEG (Tang et al., 2005a). Fourth, the inclusion of the bilateral stimulation condition creates spatially overlapping brain activation between different stimulation conditions, a basic feature of brain activation shared by more complex cognitive manipulations. Fifth, the mixed, in contrast to blocked, stimulus presentation is likely to generate greater trial-to-trial variability, thus offering a greater challenge for single-trial ERP classification.

Median nerve stimulations were generated using a pulse generator (S88) and a photoelectric stimulus isolation unit (SIU7) from Grass Instrument (Astro-Med, Inc. West Warwich, RI). Stimulus duration was 0.25 ms, and intensity ranged from 4.5 to 8.5 mA (M = 6.5 mA). Stimulation intensity was adjusted slightly below motor threshold to selectively activate somatosensory cortex while minimizing activation of motor cortex (Spiegel et al., 1999) as well as to minimize non-specific somatosensory activation associated with finger movement. The perceived intensities of left and right stimulations were reported to be perceptually similar by the subjects. The number of stimuli per condition was 400 for two subjects, 200 and 150 for the remaining two. Intertrial intervals (ITI) were uniformly distributed, ranging from 0.75 to 1.25 (for the two subjects with 400 trials), 1.25–1.75 (for the subject with 200 trials), and 1–2 s (for the subject with 150 trials) with increments of 0.05, 0.05, and 0.1 s respectively[1]. The total stimulation duration was less than 20 min. Subjects were instructed to keep their eyes closed throughout the experiment, and no behavioral responses were required.

EEG data

EEG signals were recorded using a 128-channel SynAmps EEG system (NeuroScan, El Paso, TX) with tin electrodes mounted in a custom-made cap (ElectroCap International, Eaton, OH) using a nose reference. Signals were continuously sampled at 1000 Hz and bandpass filtered between 0.1 and 200 Hz. In conventional data analysis, the continuous EEG data are typically epoched, baseline corrected, possibly filtered, and averaged. Data are typically reduced after rejecting or correcting epochs containing visually identifiable artifacts. Here, the SOBI BSS algorithm was applied directly to the continuous EEG data as it had been collected without epoching, artifact rejection, baseline correction, filtering, removal of bad channels, or signal averaging, as in previous applications of SOBI to EEG/MEG data (Tang et al., 2002b, 2005a).

SOBI preprocessing

SOBI decomposes n-channel continuous EEG data into n SOBI components, each of which corresponds to a recovered putative source that contributes to the scalp EEG signal. These putative sources may include sensor noise, ocular and other artifacts, and neuronal sources of interest. Each SOBI component, or SOBI-recovered putative source, has a time course of activation and an associated sensor space projection that specifies the effect of that putative source on each of the n electrodes. Let $\mathbf{x}(t)$ represent the n continuous time series from the n EEG channels and $\mathbf{x}_i(t)$ the readings from the ith EEG channel. Because various underlying sources are summed via volume conduction to give rise to the scalp EEG, each of the $\mathbf{x}_i(t)$ can be assumed to be an instantaneous linear mixture of n unknown sources $\mathbf{s}_i(t)$, via the unknown $n \times n$ mixing matrix $\mathbf{A}$,[2]

$$\mathbf{x}(t) = \mathbf{A}\,\mathbf{s}(t)$$

SOBI uses the EEG measurement $\mathbf{x}(t)$ and nothing else to generate an $n \times n$ unmixing matrix $\mathbf{W}$ that approximates $\mathbf{A}^{-1}$, and the putative sources $\hat{\mathbf{s}}(t)$, $\hat{\mathbf{s}}(t) = \mathbf{W}\mathbf{x}(t)$. The time course of the ith component is given by $\hat{\mathbf{s}}_i(t)$. SOBI exploits the time coherence of the source signals to decompose the mixture of sources. Specifically, SOBI finds $\mathbf{W}$ by minimizing the sum squared cross-correlations between one component at time t and another component at time $t + \tau$, across a set of time delays (τs) (for detailed description, see Cardoso and Souloumiac, 1996; Belouchrani et al., 1997; Tang et al., 2002b Appendix; Joyce et al., 2004). Because such cross-correlations are sensitive to the temporal characteristics within the time series, temporal information contained in the continuous EEG data affects the results of source separation. As such, detailed temporal characteristics of the ongoing activity of the underlying brain sources can provide useful information for source separation. This feature of SOBI contrasts with the insensitivity of InfoMax ICA (Bell and Sejnowski, 1995) and fICA (Hyvarinen and Oja, 1997) in that the latter two algorithms are insensitive to the shuffling of data points. The following set of time delays, τs (in ms), was used in the present study and chosen to cover a reasonably wide interval without extending beyond the support of the autocorrelation function:

$$\tau \in \{1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300\}.$$

Similar sets of τs have previously been used to effectively isolate task-related neuronal components as well as various artifacts from MEG and EEG data (Tang et al., 2002a,b, 2005a). By using multiple time delays, the SOBI algorithm has been shown to be

[1] These variations were for other purposes in the study from which the data were originally collected (Tang et al., 2005a).

[2] The general BSS problem requires $\mathbf{A}$ to be an $n \times m$ matrix, with $n \geq m$ (n: number of mixtures; m: number of sources). In most algorithmic derivations, an equal number of sources and sensors are assumed (Vigario and Oja, 2000).

more robust than when fewer time delays are used, particularly when SNR is relatively poor and when large spectral overlap between sources is present (Belouchrani et al., 1997). For an empirical study of how different combinations of temporal delays affect SOBI source separation quality of EEG data, see Tang et al. (2005b).

Identification of SOBI-recovered SI components

Following SOBI separation, spatial and temporal criteria were applied in multiple steps to identify the SOBI components that captured neuronal activity originating from left and right SI (Fig. 1). In step one, a subset of the 128 SOBI components (Subset 1) was selected based on both the presence of an evoked response in the stimulus-triggered averages, i.e., the averaged SEPs, and the presence of selective activation to contralateral stimulation. In step 2, another subset of the 128 SOBI components (Subset 2) was independently selected based on the components' sensor weights. The sensor weights of the ith component, $\hat{\mathbf{a}}^{(i)}$, are given by ith column of $\hat{\mathbf{A}}$, where $\hat{\mathbf{A}} = \mathbf{W}^{-1}$ and indicate how strongly each sensor would be affected by the component if it alone was activated. As components that correspond to neuronal sources all have distinct topographies and time courses of activation, candidate neuronal components are easily identified. Both steps 1 and 2 can be performed rather conservatively, excluding only components that unambiguously correspond to noise or known artifacts or show no evoked response to stimulation.

In step 3, a third subset (Subset 3) was formed, consisting of only components that belong to *both* Subsets 1 and 2. For these components, sensor space projections, $\hat{\mathbf{x}}^{(i)}(t)$, were computed as

$$\hat{\mathbf{x}}^{(i)}(t) = \hat{\mathbf{s}}_i(t)\hat{\mathbf{a}}^{(i)}.$$

Different from step 2, here, the component's sensor weights, $\hat{\mathbf{a}}^{(i)}$ are multiplied by a scalar $\hat{\mathbf{s}}_i(t)$, which indicates the component's time-varying signal strength, giving the component's SEP projected across all sensors. Because scalp current source density (CSD) maps (the second spatial derivative of the voltage distributions $\hat{\mathbf{x}}^{(i)}(t)$) are better at revealing visually the underlying generators than the voltage maps themselves (Lagerlund, 1999), they can be used to exclude components that correspond to ocular artifacts, noisy sensors, and non-SI neuronal sources from further consideration.

In step 4, equivalent current dipoles (ECD) were fitted to each of the remaining candidates' sensor space projections using BESA 5.0 (Brain Electrical Source Analysis; MEGIS Software, Munich, Germany) following procedures detailed in Tang et al. (2005a). Components were considered to correspond to SI activity if the components' sensor space projections could be adequately modeled by dipoles in the vicinity of the SI regions alone, accounting for at least 95% of the variance. By following this process, in all subjects, two components were identified, one corresponding to left and the other to right primary somatosensory cortex activation. Typical SEP projections for SI components as well as their corresponding dipole locations are shown at the bottom of Fig. 1.

Back-propagation neural networks (BPNNs)

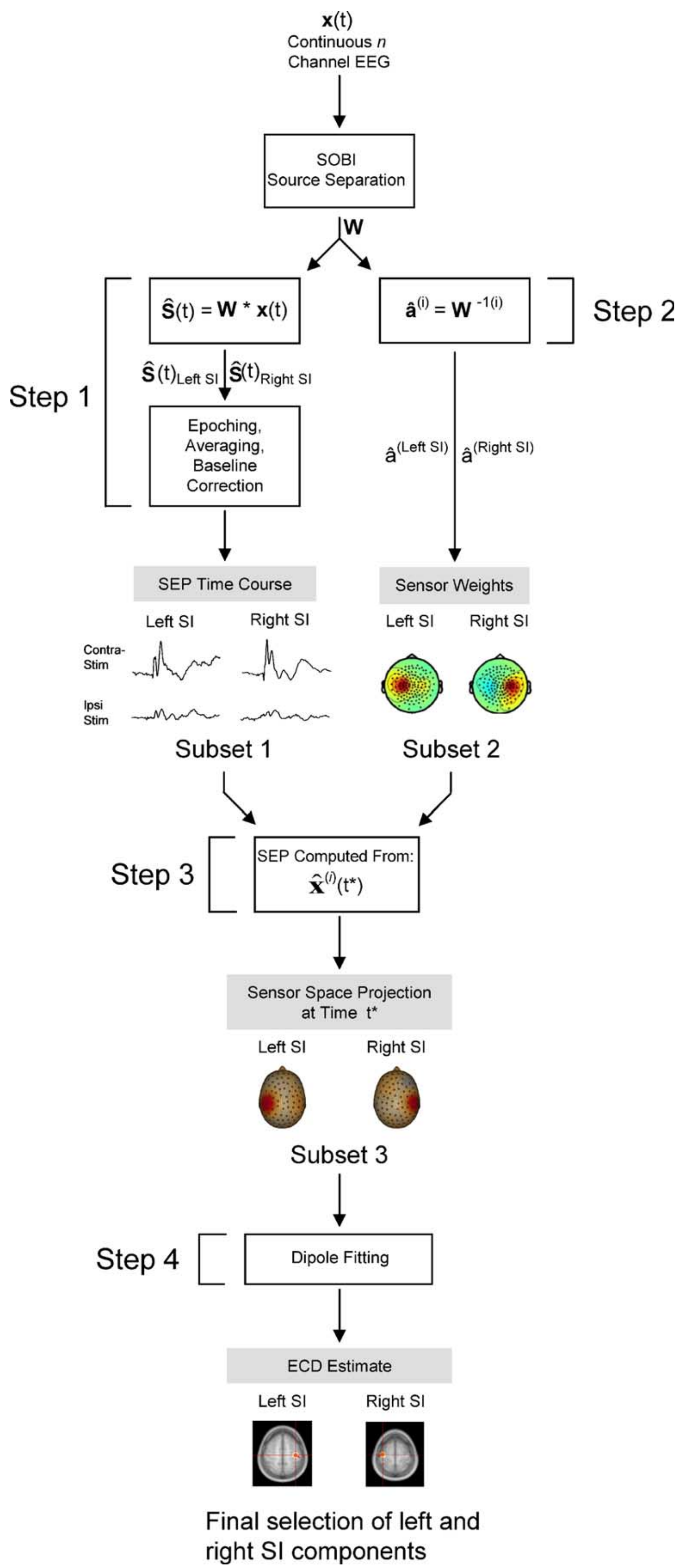
Two types of input were provided to the networks: (1) single epochs from the SOBI-recovered left and right SI components and (2) single epochs from the "best sensors". The "best sensors" were operationally defined as the EEG sensors with the maximum response amplitude to contralateral stimulation, one over left and the other over right SI. Note that this "best sensor" selection process itself entails the use of information from all sensors because one must examine all sensors to identify which one is the best. Second, to insure comparability, the SEPs from the SOBI-recovered components were projected and measured at the same electrode locations as the two "best sensors". The difference between the "best sensor" and SOBI component networks, therefore, was not in the amount of information (number of EEG channels) used but in how the same information from the EEG sensor data was utilized. In the case of the "best sensors", the information was used in a simple and intuitive manner by visually inspecting the averaged ERPs to select the appropriate channels to supply as inputs to the networks. In the case of SOBI, a more complex mathematical transformation resulted in the extraction of neuronal component information.

ERP researchers typically perform their analysis after rejecting data from trials that are contaminated by various artifacts. Rejection rates can be as high as 1/3 of the total number of trials and vary depending upon the type of experiment, the subjects studied, and the specific recording session (Picton et al., 2000). Rejected trials are those trials that are not classified when using the EEG sensor data. Thus, the rejected trials should be considered classification failures. In contrast, when using SOBI, artifactual signals are isolated and separated into distinct components without the need to discard trials containing such artifacts. Therefore, in our opinion, a good performance measure should consider this difference in potential failure rates, which can be achieved by having the two BPNNs classify all trials, instead of classifying only preselected subsets of the trials.

The very idea of including only "clean" trials in the testing data set implies that if a current method does not handle artifact-contaminated trials well, any alternative method should only be evaluated on artifact free data. This would have missed the whole point of introducing the alternative method. Similarly, the idea of including only "clean" trials in the training data also implies that one should throw away data that could have been used by the SOBI component networks to achieve better classification. To allow the component networks to take advantage of all trials collected, one might propose to build the training data set from artifact free trials for *only* the "best sensor" networks and to include all trials for the component networks. However, this approach would lead to results that are difficult to interpret when comparing the performance of the "best sensor" and component networks. For instance, if the two types of training data are associated with different classification accuracy, one would not know whether it is caused by data type (sensor versus component) or by the amount of data available (all trials or a subset of trials) or data quality (with or without artifacts).

Given these considerations, for both the SOBI component and the "best sensor" networks, no artifact rejection was performed on the input data. To prepare the training and testing data, first, baseline correction was performed using the 200-ms window prior to

Fig. 1. A step by step procedure for identifying SOBI components corresponding to left and right SI activation following median nerve stimulation. Step 1: obtain a candidate set using temporal information (Subset 1). Step 2: obtain a candidate set using spatial information (Subset 2). Step 3: for the overlapping set between Subsets 1 and 2, compute SEP topography (Subset 3). Step 4: identify left and right SI by the location of the equivalent current dipole.


x(t)
Continuous n
Channel EEG
SOBI
Source Separation
W
Step 1
Step 2
ŝ(t) = W * x(t)
â(i) = W -1(i)
ŝ(t)Left SI
ŝ(t)Right SI
Epoching,
Averaging,
Baseline
Correction
â(Left SI)
â(Right SI)
SEP Time Course
Sensor Weights
Left SI
Right SI
Contra-
Stim
Ipsi
Stim
Subset 1
Subset 2
Step 3
SEP Computed From:
x̂(i)(t*)
Sensor Space Projection
at Time t*
Subset 3
Step 4
Dipole Fitting
ECD Estimate
Final selection of left and
right SI components

stimulus onset as the baseline interval for both the component trials and the "best sensor" trials. Second, for the left and right components/sensors, 10 averages consisting of 10 ms of consecutive data points were computed for a specific time window (20 to 120 ms after stimulus onset). Thus, a total of 20 values were used as inputs to the 20 input units to describe each stimulation trial, 10 each from the left and right side. Re-referencing to the common average was not performed because classifying the L, R, and B stimulation types relies on the differences between the left and right component/sensor activations and adding or subtracting a common component to all input units should not affect such classification.

We trained three-layer networks to classify the single-trial SEPs into three stimulus classes: L, R, or B stimulation. The three classes were coded by 3 output units, one representing each of the three types of stimulation. The hidden layer consisted of 20 units. To train the network, the traingdx learning algorithm (Matlab Neural Network Toolbox, MathWorks, Inc., Natick, MA) was employed, which uses gradient descend with momentum and variable learning rate in batch learning mode (Hagan et al., 1996). While gradient descend with momentum can avoid a shallow local minimum, a variable learning rate can make the learning as fast as possible while maintaining stability. The batch learning mode was used to update the network weights after all training data were presented.

We assessed classification performance by comparing the ability of a trained network classifier to generalize from one subset of data (training set) to another (test set) when two types of input data were used respectively: the SOBI component and the "best sensor" data. After a network was trained with 50% of the data (training set, randomly selected) to a 90% classification accuracy, the generalization performance of the trained network was then evaluated using the remaining 50% of the data (test data). To properly estimate classification accuracy, this training–testing process was repeated 100 times, each time using a different randomly selected pair of training–testing datasets along with a different set of random starting weights at the beginning of training (i.e., 100 × cross-validation).

Results

SOBI-recovered left and right SI components

The spatial and temporal aspects of previously validated SI components (see, Tang et al., 2005a) from a typical subject are shown in Fig. 2. The CSD maps and the corresponding equivalent current dipole models (Fig. 2, top) revealed the spatial origin of the two identified components, one corresponding to the left and the other to the right SI. The differential SEPs to contra- and ipsilateral stimulations–selective response to contralateral stimulation (Fig. 2, bottom)–further confirmed the components' spatial origins. Most

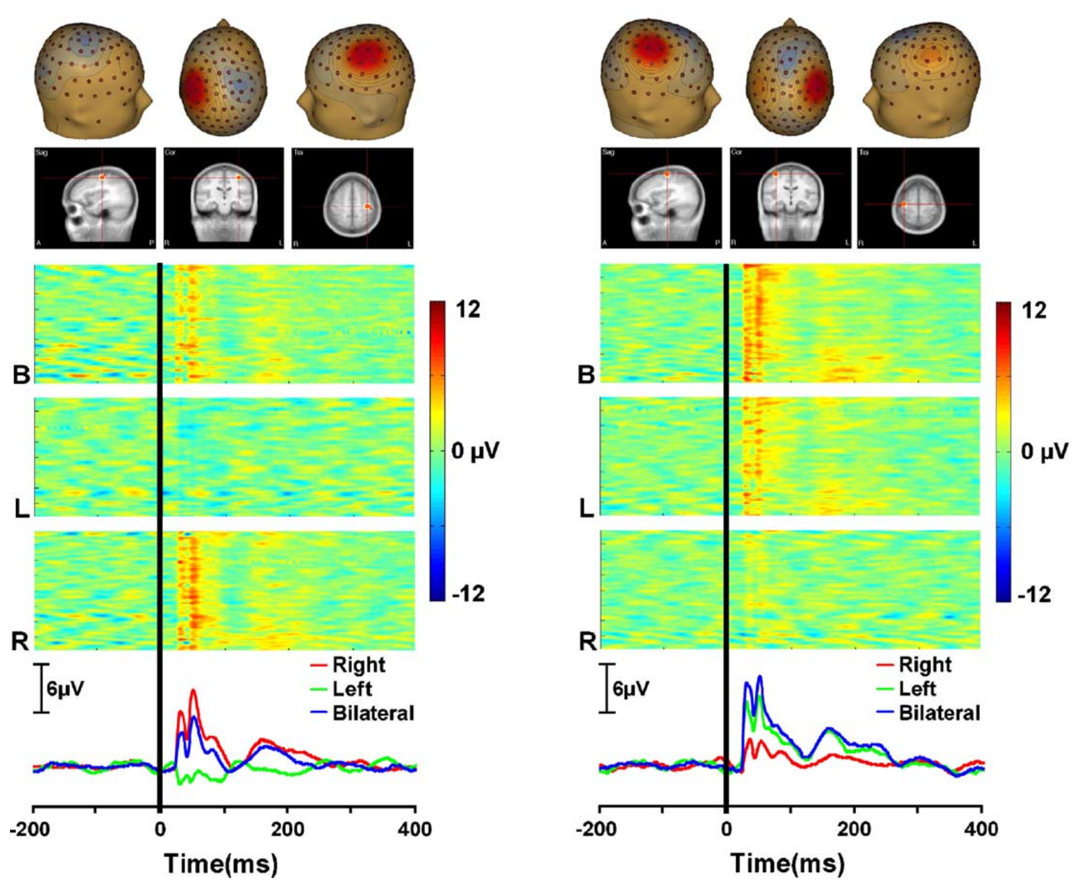


Fig. 2. SOBI-recovered left and right SI components from one subject. *Top*: current source density (CSD) maps and equivalent current dipole (ECD) locations for the SOBI components (goodness of fit >95%) recovered from a typical subject. *Middle*: differentiability of single-trial SEPs among three stimulation conditions. Color single-trial images following left (L), right (R), and bilateral (B) stimulations. Each row of pixels corresponds to a trial. Trials are arranged in chronological order within each stimulation type from bottom to top. *Bottom*: averaged SEPs for each of the stimulation types.

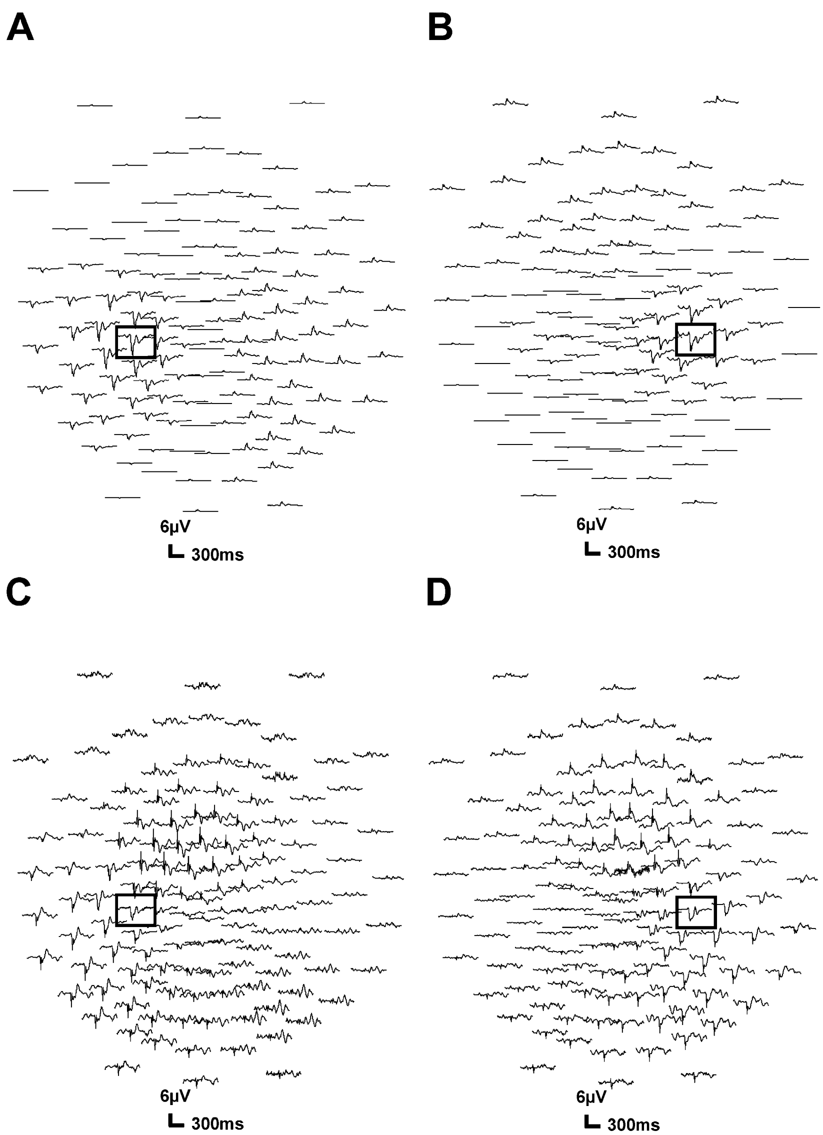


Fig. 3. Topographies of SEP projections and determination of "best sensor" locations. (A, B) SEP projections of the SOBI-recovered left and right SI components in response to contralateral stimulation. (C, D) SEP projections without SOBI preprocessing in response to contralateral stimulation (conventionally generated). Some of the hang-down electrodes have been excluded for aesthetic purposes. *Solid boxes*: best sensor locations. Note that in order to determine which sensors are "best sensors", information from all other EEG sensors are needed.

importantly, the single-trial SEPs displayed distinct patterns of activation to the three temporally intermixed stimulation conditions (L, R, and B) which produced spatially overlapping activation at the scalp (Fig. 2, middle). During right stimulation (R: bottom panels), the left component displayed clear evoked responses, whereas the right component showed little activation. In contrast, during left stimulation (L: middle panels), an opposite pattern was observed. During bilateral stimulation (B: top panels), both components showed clear responses but the amplitude of the right SI component was greater than that of the left component[3]. These contrasting patterns of activation between the left and right SI components are the basis of the following classification.

[3] This is an interesting observation, which will be investigated in a separate paper.

Topographies of average SEPs and selection of the "best sensor" locations

SEPs from the above SOBI-recovered left and right SI components, projected at all channels, are displayed in Figs. 3A, B. The pattern of the projections revealed that even focal neuronal sources, as indicated by the fact that these components were fitted with dipoles whose goodness-of-fit value were greater than 95%, can affect a large number of EEG sensors. The sensors with the greatest SEP amplitudes (solid boxes) appeared to be the most sensitive to the corresponding SI source activations given this subject's brain and scalp structure. Thus, they were chosen as the "best sensors" for this subject. In comparison to the topography of the SOBI components (Figs. 3A, B), the conventionally generated SEP topographies (Figs. 3C, D) displayed a wider area of activation at the scalp, presumably reflecting, at least partially, neuronal sources of activations beyond primary somatosensory cortex.

SOBI Improved single-trial SEP classification and reduced cross-subject variation

Segments of single-trial SEPs measured between 20 and 120 ms after stimulus onset at the "best sensor" locations (Fig. 2, solid boxes) are shown for the SOBI-recovered left and right SI components (Fig. 4A, left) and for the left and right "best sensor" data (Fig. 4A, right). These segmented and down-sampled (averaged over 10 ms) data were used as input to the neural networks. Although the "best sensor" single-trial data appeared to be significantly noisier than that of the SOBI components, some noise, such as that shared between the left and right sensors did not affect BPNN classification. Network classification accuracies from the test data sets are shown in Fig. 4B. The networks which used SOBI component data achieved accuracies of 83.31% ± 2.27% (Mean ± SEM), while networks that used the "best sensor" data only reached accuracies of 64.12% ± 5.64%. The classification performance using SOBI component data was significantly higher than that using the "best sensor" data by nearly 20% (Wilcoxon test, $N = 4$, $P < 0.05$, one tailed, Fig. 4B). In addition to the above difference in average classification performance, cross-subject variations also differed between the networks trained with SOBI components and "best sensor" data (Fig. 4B). Specifically, classification accuracy ranged from 51.69% to 78.72% (~27%) for the networks trained using "best sensor" data and from 79.22% to 88.89% (<10%) for networks trained using SOBI component data. A variance test (Snedecor and Cochran, 1967; Howell, 1987) showed that this between-subject variability was significantly lower for networks trained with SOBI component data than those trained with "best sensor" data ($t(2) = 4.72$, $P < 0.05$; Fig. 4B).

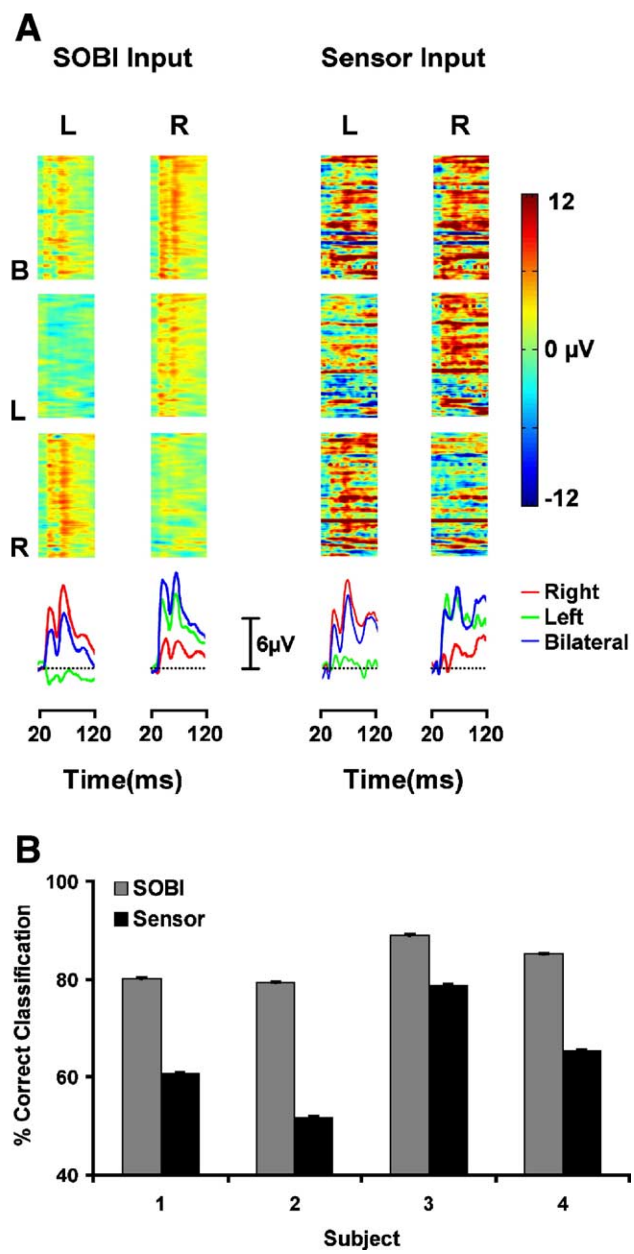


Fig. 4. Back-propagation neural network (BPNN) classification of single-trial SEPs. (A) An example of the input data sets to the BPNNs from one subject. Single-trial images and their corresponding averages for the 100-ms time windows used for classification. (B) Classification performance with the testing data set (i.e., generalization performance). A total of 100 networks per subject per condition were trained with different random samples of trials selected as training and testing data sets and with different initial weights. Data are expressed as mean ± SEM. Chance level performance is 33.3%.

Discussion

The goal of the present study was to evaluate whether single-trial ERPs from previously validated SOBI neuronal components were more distinguishable among different experimental manipulations than the single-trial ERPs from the comparable "best sensors". Using the performance of back-propagation neural networks as a quantitative measure of the differentiability of single-trials, we showed that single-trial ERPs from appropriately selected SOBI-recovered components were more distinguishable than those ERPs from the "best sensors". Specifically, we found that when the neural networks were trained with half of the data and tested with the remaining half, the performance of the SOBI component networks was ~20% better than the performance of the "best sensor" networks. This finding was consistent with our prediction that SOBI-recovered neuronal sources offer an improved ability to detect single-trial ERP differences associated with differential brain activations induced by different experimental manipulations.

SOBI neuronal components as spatial filter

The importance of classifying mental processes or states given single-trial ERP data has long been recognized by those interested in understanding mental processes associated with various psychological functions (Squires and Donchin, 1976; Horst and Donchin, 1980) and by those who wish to improve communication between locked-in patients and their environment, through a brain computer interface (BCI: Donchin et al., 2000; Wolpaw et al., 2000, 2002; Sajda et al., 2003; Sellers et al., 2004). A critical step for successful classification of mental processes using single-trial ERPs is the derivation of spatial filters that allow for the description of mental processes associated with distinct functions and anatomical locations (Muller-Gerking et al., 1999; Ramoser et al., 2000).

In ERP research, the selection of spatial filters has been implied by the choice of performing and reporting statistical analysis on a subset of EEG sensors or the "best sensors". Such a selection process has not been formalized but is, rather, dictated by convention. Because the EEG sensor signals contain a mixture of intra-cranial signals originating from different brain locations, the "best sensor" filters do not serve to "unmix" the signals of one specific brain region from others. The mixed nature of the signals leads to lower SNRs in the "best sensor" ERPs when compared to the SNRs of validated SOBI-recovered neuronal component ERPs (Tang et al., 2005a). This relatively low SNR in sensor EPRs can in turn lead to low differentiability of single-trial ERPs among different experimental manipulations. Therefore, SOBI's ability to improve single-trial classification lies in its ability to generate spatial filters that isolate the classification-relevant neuronal sources.

SOBI reduces cross-subject variability in single-trial ERP classification

Large between subject variability in the performance of BCI systems, which require single-trial ERP classification, is not uncommon (e.g., Pfurtscheller et al., 1996; Anderson et al., 1998). One source of this variability is the sensitivity of performance to the varying presence of artifacts in the EEG. In some cases, artifact-free EEG data are required, as the presence of artifact in a single-trial could alter the derived filters and degrade classification performance (Ramoser et al., 2000). In the present study, we found rather large between subject variability in the classification accuracies of single-trial SEPs when using the "best sensor" data. In contrast, between-subject variability was significantly reduced when the SOBI component SEPs were used for classification. This reduction in cross-subject variability was expected because of SOBI's ability to simultaneously separate a variety of noise sources with varying temporal characteristics (Tang et al., 2000a,b, 2002a,b, 2005a; Joyce et al., 2004; Muller et al., 2004) and multiple neuronal sources from signals arising from functional distinct brain regions (Tang et al., 2002a,b, 2005a).

The finding that SOBI leads to a reduction in cross-subject variability in single-trial ERP classification performance may have important implications for both basic cognitive neuroscience research and for the development of improved BCI systems. When evaluating the effects of an experimental manipulation, between-subject variations are typically considered as noise against which an experimental treatment effect is evaluated. Larger between-subject variance makes it more difficult to detect an effect of a given size, but this can be compensated for by using a relatively large sample. However, when performance on a single-trial for a given individual is particularly important, cross-subject variability itself can be a critical measure with significant practical implications. For example, one may not take a medicine if it is known to significantly alleviate symptoms in half of the patients tested but worsens symptoms among the other half. One is more likely to prefer a treatment that produces benefits of lesser magnitude but does so consistently. Similarly, we believe that if BCI technology is to continue to evolve as a viable aid for locked-in patients, minimization of between-subject performance variability will be critical. Our finding that SOBI preprocessing reduced between-subject variability in single-trial classification offers a potential solution for this critical problem in BCI systems.

Data and model-driven approaches to single-trial ERP classification

In the BCI literature, the derivation of spatial filters has been mainly accomplished by selecting a subset of EEG sensors a posteriori according to their importance in the classifier (Muller-Gerking et al., 1999; Parra et al., 2002). For example, one can experiment with different combinations of sensors as inputs to the classifier. Regardless of its physiological or anatomical interpretation, the combination of sensors that gives the best ERP classification performance is then used as the optimal filter. This could also be viewed as combining feature selection and discrimination into a single step. Similar approaches (Hastie et al., 1994, 1995) have been taken in the analysis of other types of brain imaging data as well, such as in the case of positron emission tomography (PET) (Kustra and Strother, 2001). A possible drawback of such a data-driven approach is that the classification results are strongly influenced by artifacts (Ramoser et al., 2000). In contrast, the SOBI approach presented here is robust against such noise because these artifacts can be simultaneously isolated into separate components distinct from the neuronal components of interest (Tang et al., 2000a, 2002b, 2005a).

This data-driven approach contrasts with the SOBI-based approach to classification in that the latter can be viewed as a combination of data and model-driven approaches. On one hand, SOBI decomposition is data driven because SOBI is a blind source separation method. On the other, the identification of SOBI neuronal sources that are effective for classification is model driven. In the context of the present study, we assumed that the neuronal sources of the left and right SI are, in principle, the optimal inputs for the specific classification task at hand—that is to distinguish single-trial ERPs evoked by left, right or bilateral stimulations. This assumption is based on the prior knowledge that median nerve stimulation results in preferential activation of the contralateral SI cortex, and that higher processing areas, such as the secondary somatosensory (SII) cortex and other multi-modal processing areas, tend to receive neural inputs from both contra- and ipsilateral pathways, thus affording less differentiability between left and right stimulation conditions.

SOBI and hybrid approaches to single-trial EEG/ERP classification

Because the present study was designed to investigate comparative performance between single-trial ERP classification using two different types of input data, we did not attempt to optimize the absolute level of performance. In fact, we suspect that absolute performance may be further improved by using alternative methods or combining SOBI preprocessing with additional methods for classification. For example, absolute performance for both SOBI and "best sensor"-based approaches may be further improved by employing standard preprocessing steps (e.g., manual artifact rejection and filtering), by extracting temporal features using wavelet analysis (Bostanov, 2004; Loring et al., 2004), by further optimizing specific network training parameters (e.g., number of hidden units, distributed output representations, etc.), by using time-dependent neural networks (Haselsteiner and Pfurtscheller, 2000), or possibly, by using other classification techniques, such as support vector machines (Pfurtscheller et al., 2000; Garrett et al., 2003).

Nevertheless, the differential performance observed in this study suggests that SOBI may serve as an effective preprocessing tool to provide inputs to other feature extraction and classification methods, consequently leading to enhanced overall performance using a hybrid of methods. This possibility has been explored recently when classifying whether a subject had made a correct or incorrect response on a given trial using single-trial EEG data. We found that when SOBI components were used as inputs to a hybrid method, in comparison to using EEG sensor data, classification performance increased from approximately 75% to 90% (Tang et al., 2004).

PCA as an alternative method

Principal component analysis (PCA) is among the earliest methods used in ERP research for extracting components with distinct functional features (Donchin, 1966; Picton et al., 2000). To our knowledge, the correspondence between PCA components and neuronal sources at distinct brain locations has not been empirically established. Theoretically, because PCA components are constrained to be orthogonal to each other and neuronal activities at certain functionally distinct brain regions can have correlated activations due to either common inputs or reciprocal connections, PCA components are unlikely to correspond to neuronal sources with distinct neuroanatomical locations and neurophysiological functions. Therefore, in principle, they are not the best candidates for revealing distinct patterns of brain activations associated with different experimental manipulations. Empirically, studies have shown that PCA does not perform as well as SOBI (Tang et al., 2005a) or InfoMax ICA (Jung et al., 2000) at isolating known noise sources.

Limitation of the SOBI approach to single-trial ERP classification

The current results were obtained using high-density EEG data from 128 channels. Independent from SOBI, the accuracy of source localization has been shown to deteriorate as the number of EEG sensors decreases (Ferree et al., 2001; Luu et al., 2001). Similarly, localization of the neuronal sources from SOBI components deteriorates as data from fewer sensors are provided for SOBI decomposition (unpublished data). Therefore, the ability to differentiate single-trial ERPs using SOBI-recovered neuronal sources may depend on the availability of a high-density EEG system. We expect that SOBI would offer clear advantage in single-trial ERP classification with a 64-channel system (Tang et al., 2003) but perhaps not with a 32-channel system. Most critical is that a turn-key system that provides an interface between SOBI and ERP researchers is not currently available to allow the mathematics and programming requirements to become transparent. Efforts have been initiated in creating such a system.

Summary

We demonstrated that SEPs from SOBI-recovered components can serve as better inputs to neural network classifiers to achieve improved single-trial ERP classification over the "best sensor" ERPs. This finding is consistent with our hypothesis that patterns of neuronal activations associated with different sensory, motor, or cognitive activations – i.e., the experimental manipulations – can be made more distinguishable when represented as SOBI component ERPs than as the "best sensor" ERPs over the same regions of interest. This finding may have significant implications for basic cognitive neuroscience research and BCI technology.

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