



Basic neuroscience

A novel approach to identify time-frequency oscillatory features in electrocortical signals

Huibin Jia¹, Weiwei Peng^{*,1}, Li Hu^{*}

Key Laboratory of Cognition and Personality (Ministry of Education) and Faculty of Psychology, Southwest University, Chongqing 400715, China

HIGHLIGHTS

- A novel approach was proposed to optimally identify oscillatory features.
- Time-frequency oscillatory features were identified based on their spatial distributions.
- The novel approach was validated using both simulated and real electrocortical datasets.
- The novel approach can help explore the precise functions of oscillatory activities.

ARTICLE INFO

Article history:

Received 18 February 2015

Received in revised form 27 April 2015

Accepted 26 May 2015

Available online 6 June 2015

Keywords:

Time-frequency analysis

Topographic segmentation analysis

Scalp topography

Event-related

synchronization/desynchronization

(ERS/ERD)

Time-frequency oscillatory features

ABSTRACT

Background: Sensory, motor, and cognitive events could not only evoke phase-locked event-related potentials in ongoing electrocortical signals, but also induce non-phase-locked changes of oscillatory activities. These oscillatory activities, whose functional significances differ greatly according to their temporal, spectral, and spatial characteristics, are commonly detected when single-trial signals are transformed into time-frequency distributions (TFDs). Parameters characterizing oscillatory activities are normally measured from multi-channel TFDs within a time-frequency region-of-interest (TF-ROI), pre-defined using a hypothesis-driven or data-driven approach. However, both approaches could ignore the possibility that the pre-defined TF-ROI contains several spatially/functionally distinct oscillatory activities.

New method: We proposed a novel approach based on topographic segmentation analysis to optimally and automatically identify detailed time-frequency features. This approach, which could effectively exploit the spatial information of oscillatory activities, has been validated in both simulation and real electrocortical studies.

Results: Simulation study showed that the proposed approach could successfully identify noise-contaminated time-frequency features if their signal-to-noise ratio was relatively high. Real electrocortical study demonstrated that several time-frequency features with distinct scalp distributions and evident neurophysiological functions were identified when the same analysis was applied on stimulus-elicited TFDs.

Comparison with existing methods: Unlike traditional approaches, the proposed approach could provide an optimal identification of detailed time-frequency features by making use of their distinct spatial distributions.

Conclusions: Our findings illustrated the validity and usefulness of the presented approach in isolating detailed time-frequency features, thus having wide applications in cognitive neuroscience to provide a precise assessment of the functional significance of oscillatory activities

© 2015 Elsevier B.V. All rights reserved.

Abbreviations: CWT, continuous wavelet transform; EEG, electroencephalography; ERPs, event-related potentials; ERD, event-related desynchronization; ERS, event-related synchronization; FDR, false discovery rate; LMM, linear mixed model; RT, reaction time; SNR, signal-to-noise ratio; TFDs, time-frequency distributions; TF-ROIs, time-frequency region-of-interests.

* Corresponding authors. Tel.: +86 18084053555; fax: +86 23 68252983.

E-mail addresses: wwpeng0923@gmail.com (W. Peng), huli@swu.edu.cn (L. Hu).

¹ Equal contribution.

<http://dx.doi.org/10.1016/j.jneumeth.2015.05.026>

0165-0270/© 2015 Elsevier B.V. All rights reserved.

1. Introduction

Brief sensory, motor, and cognitive events could elicit a number of transient changes in the ongoing electrocortical signals, including event-related potentials (ERPs), event-related synchronization and desynchronization (ERS and ERD) (Mouraux and Iannetti, 2008). While ERPs are time-locked and phase-locked to the presentation of stimuli, ERS/ERD reflects time-locked and non-phase-locked power modulations of ongoing electrocortical oscillations (Pfurtscheller and Aranibar, 1977; Pfurtscheller and Lopes da Silva, 1999). These modulations are characterized by either transient increase (ERS) or decrease (ERD) of oscillatory power, whose functional significance differs greatly according to their temporal, spectral, and spatial characteristics (Ohara et al., 2004). For example, ERD in the alpha band (8–12 Hz) has been hypothesized to reflect cortical activation (Mouraux et al., 2003; Yordanova et al., 2001), and ERS in the gamma band (30–100 Hz) has been suggested to play a crucial role in cortical integration and perception (Fries, 2009; Martinovic and Busch, 2011). Therefore, ERS/ERD is popularly used as an effective biological index to discriminate neurological disorders and monitor psychometric measures (Gross et al., 2007; Ploner et al., 2006b).

To estimate ERS/ERD, time-frequency decomposition algorithms (e.g., short-time Fourier transform and continuous wavelet transform [CWT]) are normally adopted to transform single-trial electrocortical responses to time-frequency distributions (TFDs) (Zhang et al., 2012). The obtained TFDs are suggested to express stimulus-elicited changes in oscillatory power (e.g., ERS/ERD), relative to a pre-stimulus reference interval (Grandchamp and Delorme, 2011). This time-frequency baseline correction has been demonstrated to be optimally achieved using the subtraction approach (i.e., subtracting the average of the pre-stimulus interval from each post-stimulus time-frequency point), which avoids the positive bias introduced by the percentage approach (i.e., dividing the post-stimulus values obtained at each frequency with the subtraction approach by the average of the pre-stimulus values at that frequency) (Hu et al., 2014b).

To investigate the functional significance of ERS/ERD by assessing their relationship with various experimental measures (e.g., reaction time and sensory perception), a region-of-interest in the time-frequency domain (TF-ROI) is normally required to be defined prior to measuring the ERS/ERD activities (Hu et al., 2013; Valentini et al., 2013). The TF-ROI was popularly defined using two different approaches: hypothesis-driven and data-driven approaches. The hypothesis-driven approach manually defined the time and frequency limits for each TF-ROI based on the findings of previous studies (Hu et al., 2014a; Peng et al., 2012). In contrast, the data-driven approach defined the boundary of TF-ROI by isolating the region that was modulated by some experimental manipulations, i.e., based on the output of statistical comparison (Tang et al., 2013; Zhang et al., 2012). However, both hypothesis-driven and data-driven approaches ignored two important facts. First, ERS/ERD of nearby time-frequency points may vary markedly in spatial distribution, which indicated that the adjacent ERS/ERD activities could be generated from distinct neural populations and capture different functional significance (Hu et al., 2013). Second, the TF-ROI, especially defined using data-driven approach, may be too large to represent one region containing single oscillatory response. In other words, the defined TF-ROI may contain several spatially/functionally distinct oscillatory responses. Therefore, the availability of a novel approach that could optimally and automatically define TF-ROIs based on the spatial and functional similarity of oscillatory responses is highly in demanding.

Recently, topographic segmentation analysis has gained its popularity to define brain microstates of electrocortical signals, each of which is characterized by a fixed spatial distribution and a distinct

functional state of the brain (Koenig et al., 2002; Van de Ville et al., 2010). In principle, brain microstates are isolated based on the similarity of scalp distributions of electrocortical responses (Murray et al., 2008a). Based on the same principle, the topographic segmentation analysis could be potentially advanced to define TF-ROIs by separating oscillatory responses in the time-frequency domain into spatially and functionally distinct features, which is the aim of the present study. The validity and usefulness of the proposed approach were demonstrated using both simulated and real electrocortical datasets.

2. Material and methods

2.1. Subjects

Resting electroencephalography (EEG) data were collected from 38 healthy right-handed volunteers (21 females) aged 21 ± 1.9 years (mean $\pm$ SD, range: 19–25 years), and event-related EEG data were collected from 18 healthy right-handed volunteers (9 females) aged 22 ± 2.5 years (mean $\pm$ SD, range: 19–29 years). All subjects gave their written informed consent and were paid for their participation. The local ethics committee approved the experimental procedures. Both datasets were already published in our previous studies (resting EEG: Peng et al., 2014; event-related EEG: Hu et al., 2013).

2.2. Experimental procedures

To collect resting EEG data, each subject was required to seat on a comfortable chair in a silent, temperature-controlled room, and were instructed to keep relaxed and eyes open for at least 5 min.

To collect event-related EEG data, each subject was stimulated with nociceptive pulses using an oddball paradigm. Nociceptive stimuli were delivered to either the medial or the lateral side of subject's left hand dorsum. Nociceptive stimuli were constant-current square electrical pulses with 0.5 ms duration, delivered through a stainless steel concentric bipolar needle electrode consisting of a needle cathode (length: 0.1 mm; diameter: 0.2 mm) surrounded by a cylindrical anode (diameter: 1.4 mm) (Inui et al., 2002; Inui et al., 2006). The stimulus intensity was twice of individual perceptual threshold, which was previously proved to be able to preferentially activate the A δ nociceptive fibers without coactivation of the fast-conducting A β fibers (Mouraux et al., 2010).

Nociceptive stimuli were delivered in 2 blocks. In one block, target (rare stimuli: 20%) and non-target (frequent stimuli: 80%) stimuli were respectively delivered to the medial and lateral sides of subject's left hand dorsum. In the other block, the delivered sites of target and non-target stimuli were reversed. The order of blocks was counterbalanced across subjects. Each block consisted of 200 stimuli, including 40 target stimuli and 160 non-target stimuli, and inter-stimulus intervals were randomly varied between 2500 and 3000 ms. Subjects were required to respond as fast and accurately as possible to the predefined target stimuli by pressing the response button upon their detection of the targets using the right index finger, and the reaction times (RTs) were recorded.

2.3. EEG recording

Both resting and event-related EEG data were recorded using a 64-channel Brain Products system (pass band: 0.01–100 Hz; sampling rate: 1000 Hz for resting EEG and 500 Hz for event-related EEG; physical reference channel: nose for resting EEG and left mastoid for event-related EEG) with a standard EEG cap based on the extended 10–20 system. All channel impedances were kept lower than 10 k Ω . To monitor ocular movements and eye blinks,

electro-oculographic (EOG) signals were simultaneously recorded from four surface channels.

2.4. EEG data preprocessing

EEG data were preprocessed using EEGLAB, an open source toolbox running in the MATLAB environment (Delorme and Makeig, 2004). Resting EEG data (5 min) were band-pass filtered between 1 and 100 Hz, and segmented into 200 EEG epochs using a time window of 1500 ms. Event-related EEG data were low-pass filtered at 30 Hz. Epochs to target stimuli were extracted using a time window of 1500 ms (500 ms pre-stimulus and 1000 ms post-stimulus), and baseline-corrected by demeaning the EEG activity within the pre-stimulus interval. Epochs contaminated by eye-blinks and movements were corrected using an independent component analysis (ICA) algorithm (Delorme and Makeig, 2004). In all datasets, independent components with a large EOG channel contribution and a frontal scalp distribution were removed (Delorme and Makeig, 2004). Following, EEG epochs were re-referenced to a common average reference. Target trials without any reaction or with RTs < 200 ms or > 1000 ms, were discarded from the following analysis.

2.5. Time-frequency analysis

TFDs of single-trial EEG data were estimated using CWT (Mouraux and Iannetti, 2008). The central frequency and restriction of CWT were 5 and 0.15, respectively (Hu et al., 2013; Peng et al., 2012). CWT yielded an estimate of time-frequency spectra $P(t, f)$ at each time-frequency point (t, f) extending from –500 ms to 1000 ms in latency (in steps of 2 ms), and from 3 to 100 Hz (for resting EEG) or from 3 to 30 Hz (for event-related EEG) in frequency (in steps of 0.5 Hz). The magnitude of the spectrum was baseline-corrected by subtracting the average value within the pre-stimulus interval (–400 to –100 ms) for each estimated frequency (Hu et al., 2014b).

2.6. Simulation study

2.6.1. Generation of noise-free datasets

The noise-free datasets were generated by (1) defining four spatially-distinct time-frequency features and (2) multiplying these features with the power spectra of resting EEG data. The four spatially-distinct time-frequency features were defined within the following time-frequency regions (Fig. 1A): (1) 3–15 Hz, 101–200 ms; (2) 3–10 Hz, 201–300 ms; (3) 16–30 Hz, 101–200 ms; (4) 11–30 Hz, 201–300 ms. For these time-frequency features, the magnitudes of power spectra were maximal (10 μ V for each time-frequency point within the region) at Oz, Pz, Cz and Fz channels and minimal (2 μ V for each time-frequency point within the region) at Fpz, Fpz, Fpz/Oz/T7/T8, and Oz channels, respectively. The magnitudes of power spectra at other channels were computed through linear interpolation according to their spatial distances to the channels with maximal and minimal magnitudes. Considering that the magnitude of EEG spectra is higher in lower frequencies and lower in higher frequencies (Pfurtscheller and Lopes da Silva, 1999), the magnitudes of time-frequency features were multiplied with the power spectra of resting EEG data that were obtained by averaging TFDs across all time points within the interval from –400 ms to 900 ms and all channels for each subject (Fig. 1B). This procedure yielded a realistic and noise-free dataset for the simulation study (Fig. 1C).

2.6.2. Generation of noise-contaminated datasets

The noise-contaminated datasets with different levels of signal-to-noise ratio (SNR: range = –1–5 dB) were generated by adding the

TFDs of noise-free datasets with those of resting EEG, which were multiplied with different weights, for each subject (Fig. 1D). The SNR of the noise-contaminated datasets was estimated as follows (Delorme et al., 2007):

$$\text{SNR}_{\text{channel } i} = 10 \log_{10} \left(\frac{\overline{\text{signal}_{\text{channel } i}}}{\sigma^2(\text{Noise}_{\text{channel } i})} \right) \quad (1)$$

$$\text{SNR}_{\text{mean}} = \frac{\text{SNR}_{\text{channel } 1} + \text{SNR}_{\text{channel } 2} + \dots + \text{SNR}_{\text{channel } n}}{n} \quad (2)$$

where $\text{SNR}_{\text{channel } i}$ is the SNR of the i th channel, SNR_{mean} is the mean SNR across all channels, $\overline{\text{signal}_{\text{channel } i}}$ is the mean spectral power within the pre-defined TF-ROI of the i th channel in the noise-free datasets, $\sigma^2(\text{Noise}_{\text{channel } i})$ is the variance of the spectral power within the TF-ROI of the i th channel in noise-contaminated datasets, and n is the number of channels.

Noise-contaminated TFDs were baseline-corrected by subtracting the mean of power within the pre-stimulus interval (–400 to –100 ms) for each estimated frequency. Group-level TFDs were obtained by averaging baseline-corrected TFDs across all subjects (power: expressed in μ V; Fig. 1D). In addition, the resulted TFDs were normalized by subtracting the mean and dividing the standard deviation of all channels for each time-frequency point (expressed as Z score; Fig. 1E).

2.6.3. Topographic segmentation analysis

To test whether the spectral power within the post-stimulus interval (0–1000 ms) were significantly different from those within the pre-stimulus interval (–400 to –100 ms), we performed a bootstrapping approach on noise-contaminated TFDs for each channel (Durka et al., 2004). To control for multiple comparisons, the significance level (p value) was corrected using a false discovery rate (FDR) procedure (Nichols and Hayasaka, 2003). This analysis yielded TF-ROIs in the post-stimulus interval, within which the spectral power was significantly different from that within the pre-stimulus interval, for each channel and SNR level.

Within the identified TF-ROI, the group-level TFDs (both power and Z score) were segmented into different time-frequency features, which were characterized uniquely by their distinct scalp distributions, using sLORETA software (Pascual-Marqui, 2002) for each SNR level. The proposed topographic segmentation analysis was achieved based on the application of a modified version of the classical k-means cluster algorithm to the group-average multi-channel TFDs, which would result in a certain number of clusters that best account for the whole data (Brunet et al., 2011; Murray et al., 2008). The k-means cluster algorithm, as a traditional pattern recognition method, is performed by an iterative procedure starting with an initial guess of scalp topographies and terminating when successive iterations differ negligibly (Ding and He, 2004; Jain, 2010; Pascual-Marqui et al., 1995). The topographic segmentation analysis was performed on multi-channel TFDs according to the following steps. (1) n (ranging from one to the total number of data points) time-frequency points within TF-ROIs were randomly selected to initially define n templates, each of which captured a different scalp topography. (2) The spatial correlation of scalp topographies between each template and each time-frequency point was assessed using Pearson cross-correlation analysis (Michel et al., 2004; Pascual-Marqui et al., 1995). (3) Global Explained Variance (GEV) was calculated to assess how well the templates described the whole data (Murray et al., 2008; Pascual-Marqui et al., 1995). (4) Each template was updated by averaging the topographies of the time-frequency points that showed the highest spatial correlation with the corresponding template as compared to other templates. Steps 2–4 were repeatedly performed until GEV remained stable. Finally, each time-frequency point within TF-ROIs was labeled as one of the templates according

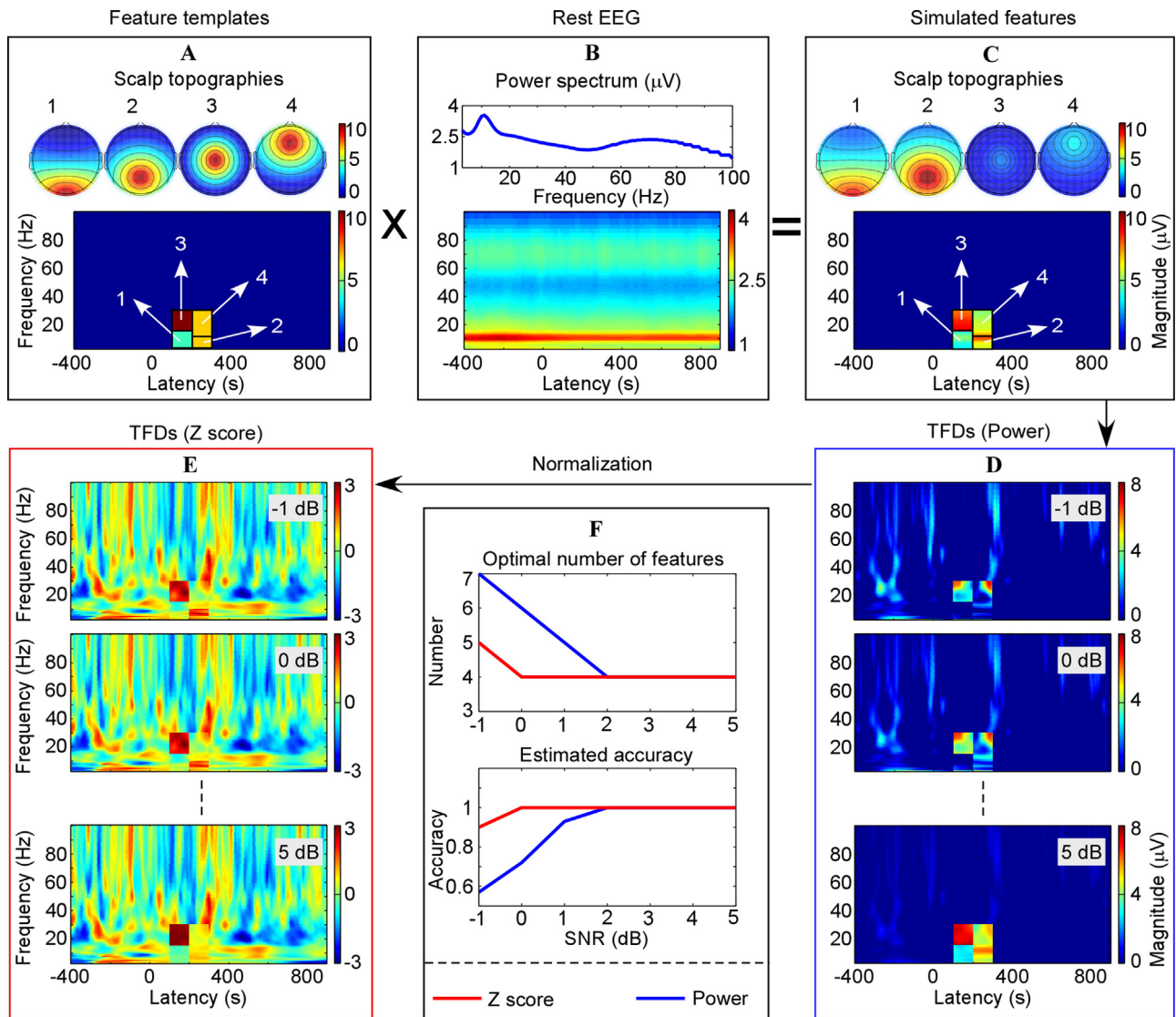


Fig. 1. Procedure and performance of simulation study. Template with four time-frequency features, each of which has a distinct scalp topography, was generated based on pre-defined time-frequency regions (panel A). The obtained time-frequency template was multiplied with the power spectra of resting EEG of 38 healthy subjects (panel B), to generate a more realistic and noise-free dataset (panel C). This noise-free dataset was subsequently added with TFDs of single-subject resting EEG to generate the noise-contaminated dataset (panel D). Note that TFDs of single-subject resting EEG was multiplied with different weights to ensure that the noise-contaminated dataset (expressed in power) has different SNR, ranging from -1 to 5 dB. For each level of SNR, the noise-contaminated dataset was normalized by subtracting the mean and dividing the standard deviation of all channels for each time-frequency point (expressed in Z score; panel E). Topographic segmentation analysis showed a better performance when the analysis was performed on TFDs of Z score than on TFDs of power (panel F).

to their spatial correlation. The optimal number of templates was defined by minimizing the cross-validation criterion (CV) value, which was calculated by dividing GEV by the degrees of freedom for a given set of templates (Brunet et al., 2011; Michel et al., 2004; Pascual-Marqui et al., 1995). To ensure a certain degree of continuity of labeling between neighboring time-frequency points, the obtained labels were adjusted according to the following two criteria: (1) the correlation coefficient of spatial topographies between each time-frequency point and its template should be higher than 0.9 (Brunet et al., 2011; Pascual-Marqui et al., 1995); and (2) the majority of the neighboring time-frequency points should be assigned into the same cluster. Finally the estimated accuracy was estimated through dividing the number of correctly-classified time-frequency points by the total number of time-frequency points within the identified TF-ROIs (expressed in percentage).

Note that the topographic segmentation analysis could also be performed using other methods (e.g., Atomize and Agglomerate

Hierarchical Clustering [AAHC] algorithm) (Brunet et al., 2011), and the performance between the k-means cluster and the AAHC algorithms was quantitatively compared using both simulation and real electrocortical studies (please refer to supplementary materials for details).

2.7. Event-related EEG study

2.7.1. Definition of TF-ROIs

To test whether the spectral power within the post-stimulus interval (0 – 900 ms) was significantly different from that within the pre-stimulus interval (-400 to -100 ms) and to define the TF-ROI, the same bootstrapping approach was performed on average TFDs (without baseline correction) sampled at posterior parietal and occipital channels (P1 + Pz + P2 + PO3 + POz + PO4). The selection of these channels was based on the fact that oscillatory activities induced by target stimuli were dominantly observed at these

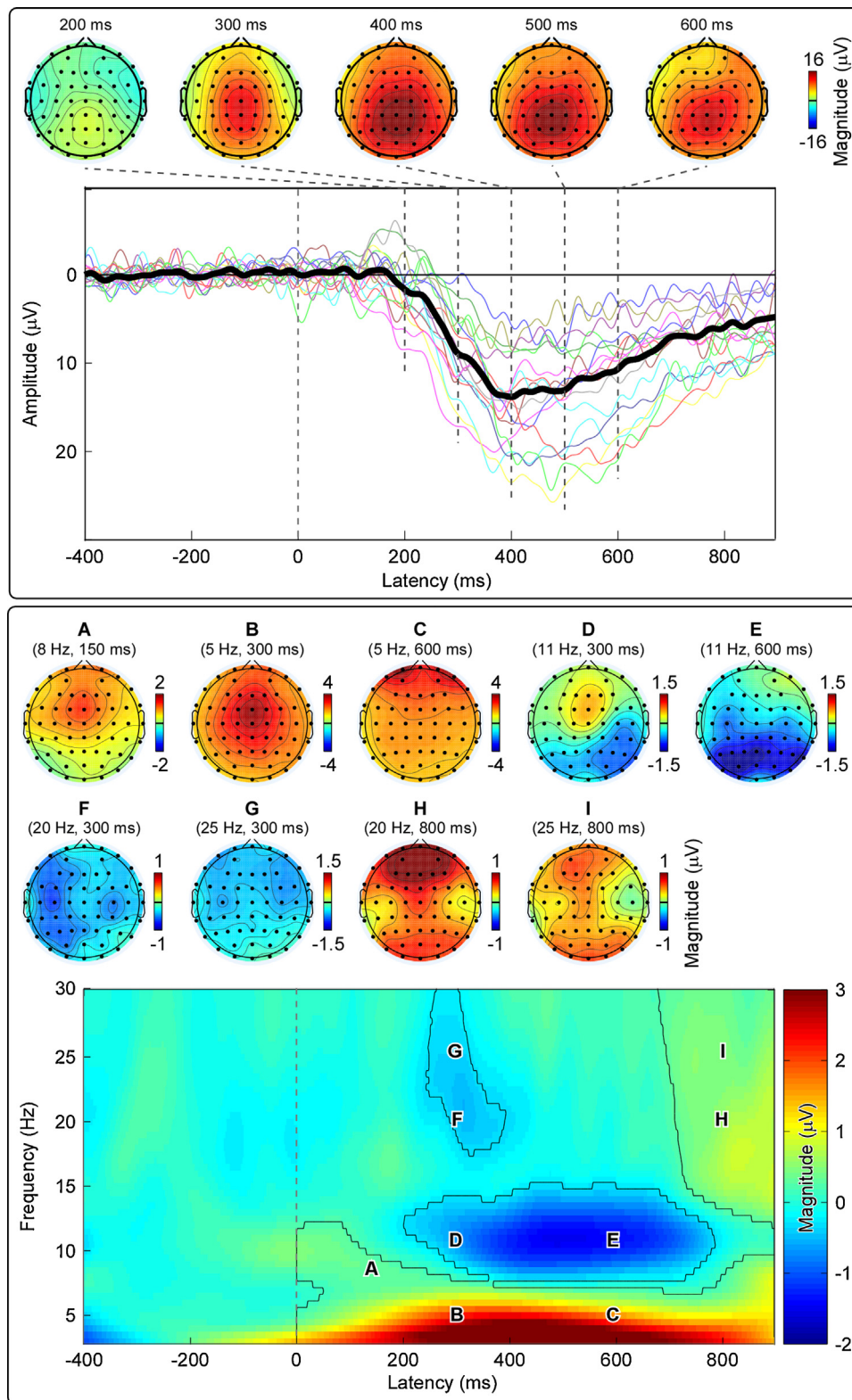


Fig. 2. Event-related potentials (ERPs) and event-related power modulations (ERS and ERD). *Top panel:* Group-average ERPs and scalp topographies elicited by target nociceptive stimuli of the left hand dorsum. Waveforms from different subjects are plotted in different colors and superimposed (their group average is highlighted in black bold line). Scalp topographies are displayed from 200 ms to 600 ms, in steps of 100 ms. *Bottom panel:* Group-average TFD and scalp topographies at several representative time-frequency points (A–I). Compared to the pre-stimulus interval, significant differences of time-frequency powers are outlined in black lines. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

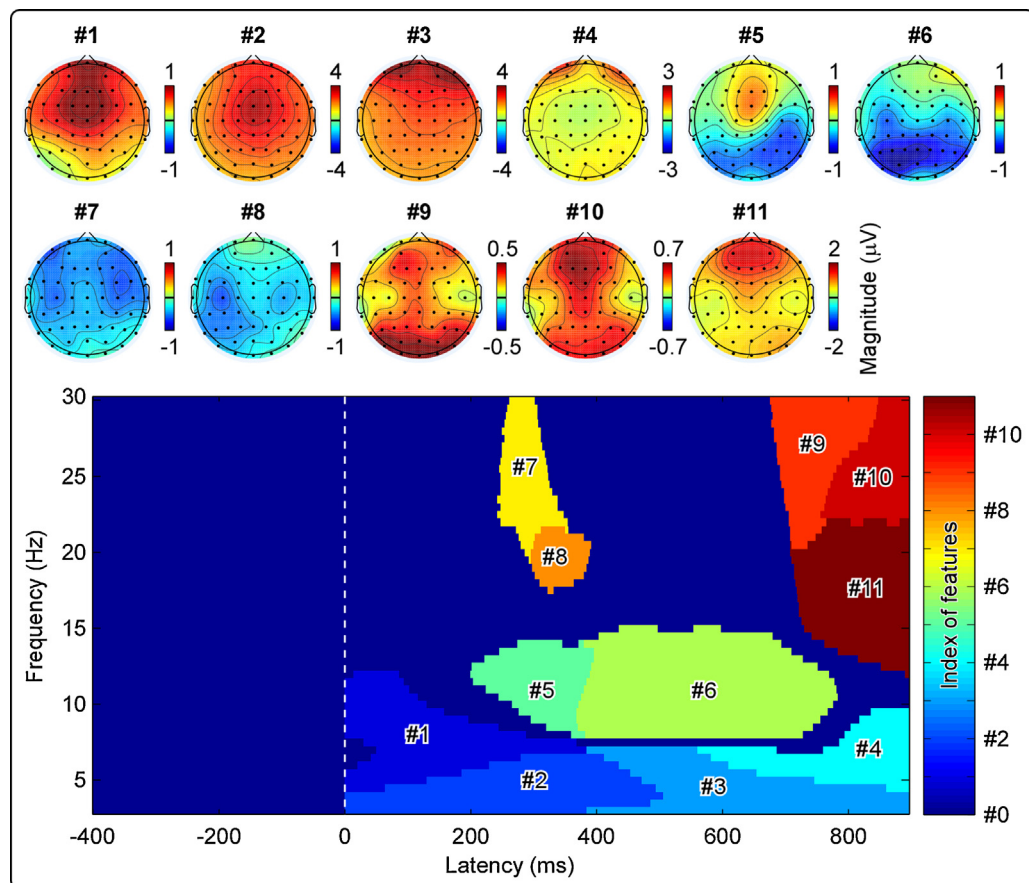


Fig. 3. Time-frequency features identified using topographic segmentation analysis. Eleven time-frequency features (#1–11), each of which captures a distinct scalp topography (top), are displayed in different colors (bottom).

channels (Peng et al., 2012). To control for multiple comparisons, the significance level (p value) was corrected using FDR procedure (Nichols and Hayasaka, 2003).

2.7.2. Topographic segmentation analysis

For each time-frequency point within the defined TF-ROI, spectral power was baseline-corrected and normalized across channels (expressed in Z score). Topographic segmentation analysis (the same procedure as in the simulation study) was applied on the normalized TFDs to identify time-frequency features with distinct scalp distributions. Note that such segmentation procedure was performed for ERS and ERD activities separately, considering their distinct functional significances. Small time-frequency regions consisting of less than 100 time-frequency points were merged into their neighboring features based on their topographic similarity.

2.7.3. Relationship between time-frequency features and RTs

Linear mixed model (LMM) was adopted to assess the relationship between the magnitudes of each time-frequency feature (independent variable) and RTs (dependent variable) on the single-trial basis (Schulz et al., 2011). The fixed effect in the LMM approach captures the intra-individual relationship between independent and dependent variables, and the random effect models the inter-individual variability of both variables. Being performed on all channels, the LMM procedure yielded scalp topography of t values, representing the strength of the relationship between the magnitudes of each time-frequency feature and RTs. To control for multiple comparisons, the significance level (p value) was corrected using FDR procedure (Nichols and Hayasaka, 2003).

3. Results

3.1. Simulation study

The optimal number of time-frequency features and the estimated accuracy at each level of SNR, obtained by performing topographic segmentation analysis on TFDs of both spectral power and Z score, were displayed in Fig. 1F. A correct estimation of the number of time-frequency features ($n=4$) and a 100% estimation accuracy were obtained when the segmentation procedure was performed on TFDs of spectral power with a SNR higher than 2 dB, and on TFDs of Z score with a SNR higher than 0 dB. The stimulated results indicated that topographic segmentation analysis could achieve a better performance when the analysis was performed on TFDs of Z score than on TFDs of spectral power.

3.2. Event-related EEG study

Across subjects, RTs and error rates to target stimuli were 501 ± 19 ms and $5\% \pm 1\%$, respectively. As showed in the top panel of Fig. 2, nociceptive ERPs evoked by target stimuli were mainly characterized by a typical P300 wave (latency: 455 ± 81 ms; amplitude: 16.3 ± 5.6 μ V), which was maximal at posterior parietal and occipital channels (P1, Pz, P2, PO3, POz, and PO4). In addition, TFDs induced by nociceptive target stimuli at posterior parietal and occipital channels (P1, Pz, P2, PO3, POz, and PO4), showed several distinct time-frequency responses (Fig. 2, bottom panel). As revealed by bootstrapping test, event-related power modulations consisted of two prominent ERS activities (3–10 Hz, 0–900 ms; 13–30 Hz, 700–900 ms), and two distinct ERD activities (8–13 Hz,

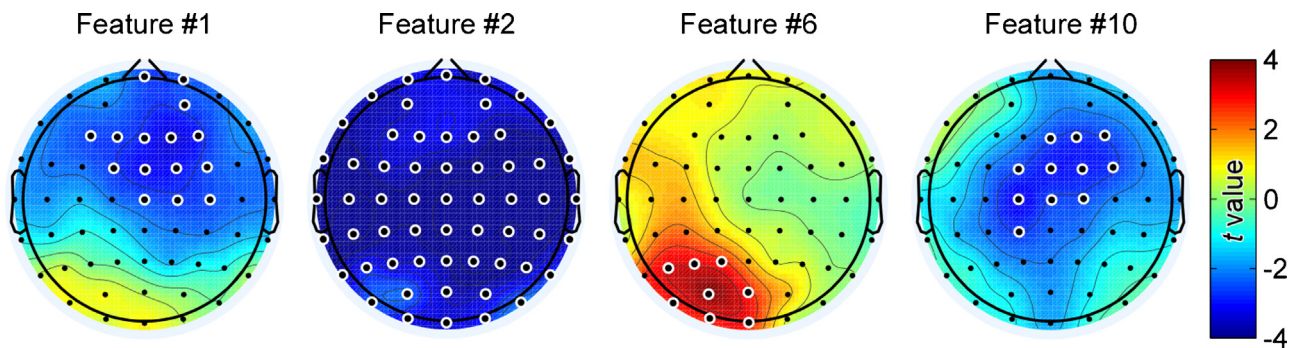


Fig. 4. Scalp topographies of the relationship between magnitudes of time-frequency features and RTs (expressed in statistical t value).

Scalp topographies of t values, estimated using LMM, showed that the magnitudes of features #1, #2, and #10 were negatively correlated with RTs at fronto-central, all, and central regions, respectively. In contrast, the magnitudes of feature #6 were positively correlated with RTs at occipital region. Channels with statistical significance ($p < 0.05$, FDR corrected) are highlighted with white circles. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

200–800 ms; 17–30 Hz, 250–400 ms). It should be noted that scalp topographies of time-frequency points within the same region (TF-ROI) were largely different (e.g., topographies A vs. C, and D vs. E). The results obtained by bootstrapping test indicated that each statistically-identified TF-ROI (e.g., the comparison of TFDs between post-stimulus and pre-stimulus intervals) should not be considered as a single entity, since it contained oscillatory activities with different scalp distributions and functional significances.

As summarized in Fig. 3, the topographic segmentation analysis, applied on TFDs of Z score, identified 11 spatially-distinct time-frequency features. The ERS activity in the delta and theta frequencies was segmented into four time-frequency features (#1: 4.5–12 Hz, 0–382 ms; #2: 3–6.5 Hz, 0–504 ms; #3: 3–7 Hz, 384–900 ms; #4: 4.5–9.5 Hz, 560–900 ms). Scalp topographies of features #1 and #2 showed a positive maxima at fronto-central channels (around FCz), and features #3 and #4 showed a positive maxima at bilateral anterior-frontal channels (Fp1 and Fp2). The ERD activity in the alpha frequencies was segmented into two time-frequency features (#5: 8–14 Hz, 200–394 ms; #6: 8–15 Hz, 380–782 ms). While feature #5 showed a negative maximum at contralateral-central channels (around C4 and C6), feature #6 was negatively maximal at parieto-occipital channels (around Pz and POz). The ERD activity in the beta frequencies was segmented into two time-frequency features (#7: 19.5–30 Hz, 242–354 ms; #8: 17.5–21.5 Hz, 296–388 ms), which showed negative maxima at bilateral fronto-central (around FC4 and FC5) and central (around C4 and C5) channels, respectively. The ERS activity in the beta frequencies was segmented into three time-frequency features (#9: 20.5–30 Hz, 678–846 ms; #10: 22–30 Hz, 756–900 ms; #11: 12–22 Hz, 708–900 ms), which also showed distinct scalp distributions, with positive maxima at bilateral occipital (around Oz), fronto-central (around FCz), and anterior-frontal (around AF3 and AF4) channels, respectively.

LMM analysis revealed that significant negative relationships between the magnitudes and RTs were maximal at fronto-central (around F2), contralateral central (around C4), and central (around Cz) channels for features #1, #2, and #10, respectively (Fig. 4). In contrast, a significant positive relationship between the magnitudes and RTs was observed maximally at left occipital channels (around PO3) for feature #6 (Fig. 4). It should be noted that a positive t value indicated that trials with higher magnitudes of ERS or lower magnitudes of ERD have longer RTs. The results obtained from event-related EEG study revealed that topographic segmentation analysis could be used to effectively isolate time-frequency oscillatory features, each of which captured distinct scalp distribution and functional significance.

4. Discussion

In the present study, we proposed to apply topographic segmentation analysis to effectively identify spatially-distinct oscillatory activities. The validity and usefulness of the presented approach were demonstrated in both simulation and event-related EEG studies. Simulation study showed that noise-contaminated time-frequency features could be successfully isolated using the topographic segmentation analysis, especially when this analysis was applied on TFDs of Z score. Event-related EEG study showed that several time-frequency features with distinct scalp distributions and evident neurophysiological functions were correctly identified when the same segmentation analysis was applied on stimulus-elicited TFDs.

4.1. The demanding of isolating time-frequency features

Various events could elicit transient changes of oscillatory activities (e.g., ERS/ERD) in ongoing electrocortical signals (Hu et al., 2013; Mouraux et al., 2003; Peng et al., 2012; Pfurtscheller and Lopes da Silva, 1999; Zhang et al., 2012). These oscillatory activities are normally characterized by distinct distributions in the temporal, spectral, and spatial domains (Hu et al., 2013; Pfurtscheller and Lopes da Silva, 1999; Ploner et al., 2006a). As documented in previous studies (Mouraux et al., 2003; Mouraux and Iannetti, 2008; Peng et al., 2012; Ploner et al., 2006b; Schulz et al., 2011), these oscillatory activities could be optimally explored using time-frequency analysis, which transforms single-trial electrocortical signals into multi-channel TFDs. Even multi-channel TFDs are characterized by the abundance of the recorded signal in temporal, spectral, spatial domains (Durka et al., 2004; Koenig et al., 2001), the mapping between multi-channel TFDs and oscillatory features is not straightforward. In other words, the isolation of time-frequency oscillatory features from multi-channel TFDs is technically difficult. Currently, researchers normally define TF-ROIs prior to measuring the oscillatory activities using either a hypothesis-driven or data-driven approach (Durka et al., 2004; Hu et al., 2013; Peng et al., 2012; Ploner et al., 2006a; Schulz et al., 2011). However, these approaches ignore the possibility that the defined TF-ROI may contain several spatially/functionally distinct oscillatory activities (Fig. 2). Therefore, the development of novel approaches that could isolate time-frequency oscillatory features from multi-channel TFDs based on their complex topographic information is highly in demanding. The availability of these approaches could help extract the detailed characteristics (e.g., latency, frequency, magnitude, and scalp distribution) of time-frequency features, thus providing a more straightforward way to assess their relationship with various sensory, motor, and cognitive processes.

4.2. The rationale of using topographic segmentation analysis

To fulfill the practical need, we proposed the use of topographic segmentation analysis to effectively define TF-ROIs of spatially-distinct oscillatory features. The topographic segmentation analysis could parse adjacent scalp topographies with distinct landscape in the time-frequency plane into a small number of features characterized by different temporal-spectral-spatial patterns (Fig. 3). It is derived from a k-means spatial cluster method (Koenig et al., 2002; Lehmann et al., 2005; Pascual-Marqui et al., 1994), and can be used to identify the most dominant features (each feature captures a distinct scalp distribution) embedded in multi-channel TFDs. The optimal number of time-frequency oscillatory features in the multi-channel TFDs is determined objectively by a cross validation procedure (Pascual-Marqui et al., 1995). Note that this approach has been repeatedly and successfully used in the time domain to identify functional microstates (Brandeis and Lehmann, 1989; Koenig and Lehmann, 1996; Pourtois et al., 2008; Zhao et al., 2015), each of which showed quasi-stable scalp topography for several tens of milliseconds and was believed to represent a functional “atom” of information processing in the brain (Michel and Murray, 2012; Michel et al., 2004). Adapting such topographic segmentation analysis in the time-frequency domain, each extracted time-frequency feature would capture a distinct and quasi-stable scalp distribution. Considering that different scalp topographies may reflect activations of different neural sources/networks (Michel and Murray, 2012), the identified time-frequency features may be generated by distinct neural sources/networks, thus having disparate functional significances.

4.3. The validity and usefulness of the proposed approach

The validity and usefulness of topographic segmentation analysis in isolating time-frequency oscillatory features from multi-channel TFDs were demonstrated in both stimulation and real electrocortical studies.

Simulation study showed that noise-contaminated time-frequency features could be successfully identified when the topographic segmentation analysis was performed on TFDs of spectral power with a SNR higher than 2 dB, and on TFDs of Z score with a SNR higher than 0 dB (Fig. 1F). Note that the across-channel normalization procedure that transformed TFDs of spectral power into TFDs of Z score could diminish the variations of the signal in the time-frequency domain, thus contributing to a better performance of feature identification (e.g., more robust to the noise). Considering that the topographic segmentation analysis was performed on group-average multi-channel TFDs, the SNR of the responses could be simply improved by increasing the number of trials and subjects (Hu et al., 2014b; Quian Quiroga and Garcia, 2003). Therefore, the simulation study demonstrated that, given a sufficient number of trials and subjects to increase the SNR of TFDs, the topographic segmentation analysis would provide an accurate identification of time-frequency oscillatory features.

Event-related EEG study demonstrated that topographic segmentation analysis, applied on stimulus-elicited TFDs, identified 11 time-frequency features, each of which captured distinct scalp distribution and functional significance (Figs. 3 and 4). The validation of this segmentation analysis could be justified by the following physiological/psychological relevance of the identified time-frequency features.

First, the identified ERS features #1 (4.5–12 Hz, 0–382 ms) and #2 (3–6.5 Hz, 0–504 ms) were maximal at fronto-central channels (Fig. 3), and their magnitudes were negatively correlated with RTs (Fig. 4). In line with previous studies (Chien et al., 2014; GarciaLarrea et al., 1997; Iannetti et al., 2008; Schulz et al., 2011), both features are the time-frequency representations of the

typical phase-locked vertex potentials. The vertex potentials can be elicited by stimuli of various sensory modalities (e.g., auditory, visual, and somatosensory) (Baseler et al., 1994; Goff et al., 1977), and regardless of the sensory modality of the applied stimuli, the vertex potentials captured similar shape, scalp topography, and sensitivity to experimental manipulations (Mouraux et al., 2011). In addition, plentiful of studies revealed that the vertex potentials were mainly generated from bilateral insula and anterior cingulate cortex (Mouraux et al., 2011), and involved in bottom-up cognitive mechanisms of saliency-detection, arousal, or attentional reorientation (Iannetti et al., 2008; Iannetti and Mouraux, 2010; Legrain et al., 2011; Mouraux et al., 2011). For these reasons, it's not surprising that the magnitudes of both features were negatively correlated with RTs (i.e., the larger the magnitudes, the shorter the RTs; Fig. 4). In contrast, the ERS features #3 (3–7 Hz, 384–900 ms) and #4 (4.5–9.5 Hz, 560–900 ms), which were maximal at bilateral anterior-frontal channels (Fig. 3) and were not correlated with RTs, are likely to reflect part of the non-cortical artifacts of eye blinks or movements that were not detected using ICA (Delorme and Makeig, 2004).

Second, alpha ERD was segmented into two temporally and spatially segregated subcomponents, i.e., feature #5 (8–14 Hz, 200–394 ms) and #6 (8–15 Hz, 380–782 ms) (Fig. 3). This observation confirmed the dissociation between a sensory-related alpha ERD that is maximal at contralateral central channels and a task-related alpha ERD that is maximal at posterior parietal and occipital channels (Hu et al., 2013; Mouraux et al., 2003; Ploner et al., 2006b). Importantly, the magnitudes of task-related alpha ERD (feature #6) were positively correlated with RTs at left occipital region (i.e., the larger the alpha ERD, the shorter the RTs; Fig. 4), which would indicate the functional role of occipital alpha ERD in allocating attentional resources associated with task requirements (Hu et al., 2013; Ohara et al., 2004). In other words, once a target is detected by the system, attentional resources would be intensively allocated to the rare target so as to prepare and execute the required action according to the pre-defined task (Peng et al., 2012; Polich, 2007), and this attentional allocation process could be indexed by the occipital alpha ERD (Hu et al., 2013).

Third, beta ERD, which was observed before the execution of the movement, was segmented into two time-frequency features (#7: 19.5–30 Hz, 242–354 ms; #8: 17.5–21.5 Hz, 296–388 ms), showing a negative maximum at bilateral central channels (Fig. 3). This result is consistent with previous studies, which showed that beta ERD could not only be induced by nociceptive stimuli over contralateral somatosensory cortex (i.e., right side) (Hu et al., 2013; Ploner et al., 2006a), but also by movement initiation over contralateral sensorimotor cortex (i.e., left side) (Kühn et al., 2004; Pfurtscheller and Lopes da Silva, 1999). The extracted bilateral central beta ERD is likely to reflect the summarized effects of sensory processing of nociceptive stimuli and the executive control of finger movements. The two beta ERD (features #7 and #8) may reflect, in different strength for different features, both sensory-related and movement-related cortical processes.

Fourth, beta ERS, which was observed after the execution of the movement, was segmented into three time-frequency features (#9: 20.5–30 Hz, 678–846 ms; #10: 22–30 Hz, 756–900 ms; #11: 12–22 Hz, 708–900 ms), showing positive maxima at bilateral occipital, fronto-central, and anterior-frontal regions, respectively (Fig. 3). These beta ERS activities, representing post-movement beta rebound (Pfurtscheller and Solis-Escalante, 2009), normally begin shortly after the termination of movement and last for up to 1 s (Cassim et al., 2001; Jurkiewicz et al., 2006; Pfurtscheller et al., 1996). It should be noted that the beta ERS is affected by changes in many different parameters related to both motor and sensory aspects of cognitive control (Cassim et al., 2001; Feige et al., 1996). In other words, several beta ERS, each of which has distinct

functional significance, should exist in the cortical responses. As confirmed by combined EEG-fMRI studies, post-movement prefrontal beta ERS was thought to be generated from anterior-central sulcus and reflected the inhibition of motor cortex (Jurkiewicz et al., 2006), whereas post-movement parietal-occipital beta ERS was believed to be generated from posterior-central sulcus and reflected the sensory reafference (Parkes et al., 2006).

For all these reasons, we believe that the use of topographic segmentation analysis to isolate time-frequency oscillatory features from multi-channel TFDs is methodologically valid and physiologically/psychologically useful.

5. Conclusion

We presented a novel approach to precisely identify oscillatory features based on topographic segmentation analysis. The validity and usefulness of the proposed approach to decompose multi-channel TFDs were demonstrated in both stimulation and event-related EEG studies. Therefore, the topographic segmentation analysis could efficiently extract a limited number of important time-frequency features, each of which captured a distinct scalp distribution, from multi-channel TFDs. This approach would have wide applications in both basic neuroscience and clinical neurophysiology, since it allows identifying time-frequency oscillatory features that coded specific sensory, cognitive, or emotional processes in the human brain (Murray et al., 2004; Pegna et al., 1997; Rigoulot et al., 2008). In the meantime, the functional significance of the identified time-frequency oscillatory features could be better understood by assessing their relationship with various experimental measures (e.g., reaction time and sensory perception) and exploiting their neural generators (Buzsaki and Draguhn, 2004; Ducommun et al., 2002; Pegna et al., 2002; Pourtois et al., 2008; Schnider, 2003). With the increased understanding of time-frequency oscillatory features (Birbaumer, 2006; Wolpaw, 2004), some brain computer interface (BCI) systems that relied on the use of ERD/ERS have gained increasing success. This kind of BCI systems would also benefit from the application of the presented topographic segmentation analysis by detecting important oscillatory features (Pfurtscheller et al., 2006; Pfurtscheller and Neuper, 2006). The detection of the important oscillatory features would increase the specificity in capturing the cortical information about the subjects' intention for controlling external devices, thus improving the performance of the BCI systems potentially.

Conflict of interest statement

The authors declare no competing financial interests.

Acknowledgements

LH is supported by the National Natural Science Foundation of China (31200856, 31471082).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jneumeth.2015.05.026>

References

Baseler HA, Sutter EE, Klein SA, Carney T. The topography of visual evoked response properties across the visual field. *Electroencephalogr Clin Neurophysiol* 1994;90:65–81.

Birbaumer N. Breaking the silence: brain-computer interfaces (BCI) for communication and motor control. *Psychophysiology* 2006;43:517–32.

Brandes D, Lehmann D. Segments of event-related potential map series reveal landscape changes with visual-attention and subjective contours. *Electroen Clin Neuro* 1989;73:507–19.

Brunet D, Murray MM, Michel CM. Spatiotemporal analysis of multichannel EEG: CARTOOL. *Comput Intell Neurosci* 2011;2011:813870.

Buzsaki G, Draguhn A. Neuronal oscillations in cortical networks. *Science* 2004;304:1926–9.

Cassim F, Monaca C, Szurhaj W, Bourriez J-L, Defebvre L, Derambure P, et al. Does post-movement beta synchronization reflect an idling motor cortex? *NeuroReport* 2001;12:3859–63.

Chien J, Liu C, Kim J, Markman TM, Lenz FA. Painful cutaneous laser stimuli induce event-related oscillatory EEG activities that are different from those induced by nonpainful electrical stimuli. *J Neurophysiol* 2014;112:824–33.

Delorme A, Makeig S. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Methods* 2004;134:9–21.

Delorme A, Sejnowski T, Makeig S. Enhanced detection of artifacts in EEG data using higher-order statistics and independent component analysis. *NeuroImage* 2007;34:1443–9.

Ding C, He XF. Cluster structure of K-means clustering via principal component analysis. *Lect Notes Artif Int* 2004;3056:414–8.

Ducommun CY, Murray MM, Thut G, Bellmann A, Viad-Delmon I, Clarke S, et al. Segregated processing of auditory motion and auditory location: an ERP mapping study. *NeuroImage* 2002;16:76–88.

Durka PJ, Zygierevicz J, Klekowicz H, Ginter J, Blinowska KJ. On the statistical significance of event-related EEG desynchronization and synchronization in the time-frequency plane. *IEEE T Bio-Med Eng* 2004;51:1167–75.

Feige B, Kristeva-Feige R, Rossi S, Pizzella V, Rossini P-M. Neuromagnetic study of movement-related changes in rhythmic brain activity. *Brain Res* 1996;734:252–60.

Fries P. Neuronal gamma-band synchronization as a fundamental process in cortical computation. *Annu Rev Neurosci* 2009;32:209–24.

GarciaLarrea L, Peyron R, Laurent B, Mauguier F. Association and dissociation between laser-evoked potentials and pain perception. *NeuroReport* 1997;8:3785–9.

Goff GD, Matsumiya Y, Allison T, Goff WR. The scalp topography of human somatosensory and auditory evoked potentials. *Electroencephalogr Clin Neurophysiol* 1977;42:57–76.

Grandchamp R, Delorme A. Single-trial normalization for event-related spectral decomposition reduces sensitivity to noisy trials. *Front Psychol* 2011;2:1–14.

Gross J, Schnitzler A, Timmermann L, Ploner M. Gamma oscillations in human primary somatosensory cortex reflect pain perception. *PLoS Biol* 2007;5:e133.

Hu L, Cai MM, Xiao P, Luo F, Iannetti GD. Human brain responses to concomitant stimulation of Aδ and C nociceptor. *J Neurosci* 2014a;34:11439–51.

Hu L, Peng WW, Valentini E, Zhang ZG, Hu Y. Functional features of nociceptive-induced suppression of alpha band electroencephalographic oscillations. *J Pain* 2013;14:89–99.

Hu L, Xiao P, Zhang ZG, Mouraux A, Iannetti GD. Single-trial time-frequency analysis of electrocortical signals: baseline correction and beyond. *NeuroImage* 2014b;84:876–87.

Iannetti GD, Hughes NP, Lee MC, Mouraux A. Determinants of laser-evoked EEG responses: pain perception or stimulus saliency. *J Neurophysiol* 2008;100:815–28.

Iannetti GD, Mouraux A. From the neuromatrix to the pain matrix (and back). *Exp Brain Res* 2010;205:1–12.

Inui K, Tran TD, Hoshiyama M, Kakigi R. Preferential stimulation of Aδ fibers by intra-epidermal needle electrode in humans. *Pain* 2002;96:247–52.

Inui K, Tsuji T, Kakigi R. Temporal analysis of cortical mechanisms for pain relief by tactile stimuli in humans. *Cereb Cortex* 2006;16:355–65.

Jain AK. Data clustering: 50 years beyond K-means. *Pattern Recognit Lett* 2010;31:651–66.

Jurkiewicz MT, Gaetz WC, Bostan AC, Cheyne D. Post-movement beta rebound is generated in motor cortex: evidence from neuromagnetic recordings. *NeuroImage* 2006;32:1281–9.

Kühn AA, Williams D, Kupsch A, Limousin P, Hariz M, Schneider GH, et al. Event-related beta desynchronization in human subthalamic nucleus correlates with motor performance. *Brain* 2004;127:735–46.

Koenig T, Lehmann D. Microstates in language-related brain potential maps show noun-verb differences. *Brain Lang* 1996;53:169–82.

Koenig T, Marti-Lopez F, Valdes-Sosa P. Topographic time-frequency decomposition of the EEG. *NeuroImage* 2001;14:383–90.

Koenig T, Prichep L, Lehmann D, Sosa PV, Braeker E, Kleinlogel H, et al. Millisecond by millisecond, year by year: normative EEG microstates and developmental stages. *NeuroImage* 2002;16:41–8.

Legrain V, Iannetti GD, Plaghki L, Mouraux A. The pain matrix reloaded: a salience detection system for the body. *Prog Neurobiol* 2011;93:111–24.

Lehmann D, Faber PL, Galderisi S, Herrmann WM, Kinoshita T, Koukkou M, et al. EEG microstate duration and syntax in acute, medication-naïve, first-episode schizophrenia: a multi-center study. *Psychiatry Res: Neuroimaging* 2005;138:141–56.

Martinovic J, Busch NA. High frequency oscillations as a correlate of visual perception. *Int J Psychophysiol* 2011;79:32–8.

Michel CM, Murray MM. Towards the utilization of EEG as a brain imaging tool. *NeuroImage* 2012;61:371–85.

Michel CM, Murray MM, Lantz G, Gonzalez S, Spinelli L, Grave de Peralta R. EEG source imaging. *Clin Neurophysiol* 2004;115:2195–222.

- Mouraux A, Diukova A, Lee MC, Wise RG, Iannetti GD. A multisensory investigation of the functional significance of the pain matrix. *NeuroImage* 2011;54:2237–49.
- Mouraux A, Guerit J-M, Plaghki L. Non-phase locked electroencephalogram (EEG) responses to CO₂ laser skin stimulations may reflect central interactions between A δ - and C-fibre afferent volleys. *Clin Neurophysiol* 2003;114:710–22.
- Mouraux A, Iannetti GD. Across-trial averaging of event-related EEG responses and beyond. *Magn Reson Imaging* 2008;26:1041–54.
- Mouraux A, Iannetti GD, Plaghki L. Low intensity intra-epidermal electrical stimulation can activate A δ - nociceptors selectively. *Pain* 2010;150:199–207.
- Murray MM, Brunet D, Michel CM. Topographic ERP analyses: a step-by-step tutorial review. *Brain Topogr* 2008;20:249–64.
- Murray MM, Michel CM, Grave de Peralta R, Ortigue S, Brunet D, Gonzalez Andino S, et al. Rapid discrimination of visual and multisensory memories revealed by electrical neuroimaging. *NeuroImage* 2004;21:125–35.
- Nichols T, Hayasaka S. Controlling the familywise error rate in functional neuroimaging: a comparative review. *Stat Methods Med Res* 2003;12:419–46.
- Ohara S, Crone NE, Weiss N, Lenz FA. Attention to a painful cutaneous laser stimulus modulates electrocorticographic event-related desynchronization in humans. *Clin Neurophysiol* 2004;115:1641–52.
- Parkes LM, Bastiaansen MCM, Norris DG. Combining EEG and fMRI to investigate the post-movement beta rebound. *NeuroImage* 2006;29:685–96.
- Pascual-Marqui RD. Standardized low-resolution brain electromagnetic tomography (sLORETA): technical details. *Methods Find Exp Clin Pharmacol* 2002;24:5–12.
- Pascual-Marqui RD, Michel CM, Lehmann D. Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. *Int J Psychophysiol* 1994;18:49–65.
- Pascual-Marqui RD, Michel CM, Lehmann D. Segmentation of brain electrical activity into microstates: model estimation and validation. *IEEE Trans Biomed Eng* 1995;42:658–65.
- Pegna AJ, Khateb A, Murray MM, Landis T, Michel CM. Neural processing of illusory and real contours revealed by high-density ERP mapping. *NeuroReport* 2002;13:965–8.
- Pegna AJ, Khateb A, Spinelli L, Seeck M, Landis T, Michel CM. Unraveling the cerebral dynamics of mental imagery. *Hum Brain Mapp* 1997;5:410–21.
- Peng WW, Hu L, Zhang ZG, Hu Y. Causality in the association between P300 and alpha event-related desynchronization. *PLoS ONE* 2012;7:e34163.
- Peng WW, Hu L, Zhang ZG, Hu Y. Changes of spontaneous oscillatory activity to tonic heat pain. *PLoS ONE* 2014;9:e91052.
- Pfurtscheller G, Aranibar A. Event-related cortical desynchronization detected by power measurements of scalp EEG. *Electroencephalogr Clin Neurophysiol* 1977;42:817–26.
- Pfurtscheller G, Brunner C, Schlogl A, da Silva FHL. Mu rhythm (de)synchronization and EEG single-trial classification of different motor imagery tasks. *NeuroImage* 2006;31:153–9.
- Pfurtscheller G, Lopes da Silva FH. Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clin Neurophysiol* 1999;110:1842–57.
- Pfurtscheller G, Neuper C. Future prospects of ERD/ERS in the context of brain–computer interface (BCI) developments. *Prog Brain Res* 2006;159:433–7.
- Pfurtscheller G, Solis-Escalante T. Could the beta rebound in the EEG be suitable to realize a brain switch? *Clin Neurophysiol* 2009;120:24–9.
- Pfurtscheller G, Stancak A Jr, Neuper C. Post-movement beta synchronization. A correlate of an idling motor area? *Electroencephalogr Clin Neurophysiol* 1996;98:281–93.
- Ploner M, Gross J, Timmermann L, Pollok B, Schnitzler A. Oscillatory activity reflects the excitability of the human somatosensory system. *NeuroImage* 2006a;32:1231–6.
- Ploner M, Gross J, Timmermann L, Pollok B, Schnitzler A. Pain suppresses spontaneous brain rhythms. *Cereb Cortex* 2006b;16:537–40.
- Polich J. Updating p300: an integrative theory of P3a and P3b. *Clin Neurophysiol* 2007;118:2128–48.
- Pourtois G, Delplanque S, Michel C, Vuilleumier P. Beyond conventional event-related brain potential (ERP): exploring the time-course of visual emotion processing using topographic and principal component analyses. *Brain Topogr* 2008;20:265–77.
- Quian Quiroga R, Garcia H. Single-trial event-related potentials with wavelet denoising. *Clin Neurophysiol* 2003;114:376–90.
- Rigoulot S, Delplanque S, Desprez P, Defoort-Dhellemmes S, Honore J, Sequeira H. Peripherally presented emotional scenes: a spatiotemporal analysis of early ERP responses. *Brain Topogr* 2008;20:216–23.
- Schnider A. Spontaneous confabulation and the adaptation of thought to ongoing reality. *Nat Rev Neurosci* 2003;4:662–71.
- Schulz E, Tiemann L, Schuster T, Gross J, Ploner M. Neurophysiological coding of traits and states in the perception of pain. *Cereb Cortex* 2011;21:2408–14.
- Tang DD, Hu L, Chen AT. The neural oscillations of conflict adaptation in the human frontal region. *Biol Psychol* 2013;93:364–72.
- Valentini E, Betti V, Hu L, Aglioti SM. Hypnotic modulation of pain perception and of brain activity triggered by nociceptive laser stimuli. *Cortex* 2013;49:446–62.
- Van de Ville D, Britz J, Michel CM. EEG microstate sequences in healthy humans at rest reveal scale-free dynamics. *Proc Natl Acad Sci USA* 2010;107:18179–84.
- Wolpaw JR. Brain–computer interfaces (BCIs) for communication and control: a mini-review. *Suppl Clin Neurophysiol* 2004;57:607–13.
- Yordanova J, Kolev V, Polich J. P300 and alpha event-related desynchronization (ERD). *Psychophysiology* 2001;38:143–52.
- Zhang ZG, Hu L, Hung YS, Mouraux A, Iannetti GD. Gamma-band oscillations in the primary somatosensory cortex—a direct and obligatory correlate of subjective pain intensity. *J Neurosci* 2012;32:7429–38.
- Zhao C, Valentini E, Hu L. Functional features of crossmodal mismatch responses. *Exp Brain Res* 2015;233:617–29.