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Dynamic spatiotemporal brain analyses using high performance electrical neuroimaging: Theoretical framework and validation

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HIGHLIGHTS

- Microsegmentation suite that differentiates transition states from stable ERP microstates.
- Differentiation of event-related brain microstates from changes in global field power.
- Integrated within- and between-subject bootstrapping procedures to assess solution robustness.
- Microstate algorithm to promote mapping both which and when brain regions is activated by a task.

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ABSTRACT

Background: Since Berger's first EEG recordings in 1929, several techniques, initially developed for investigating *periodic* processes, have been applied to study *non-periodic* event-related brain state dynamics.
New method: We provide a theoretical comparison of the two approaches and present a new suite of data-driven analytic tools for the specific identification of the brain microstates in high-density event-related brain potentials (ERPs). This suite includes four different analytic methods. We validated this approach through a series of theoretical simulations and an empirical investigation of a basic visual paradigm, the reversal checkerboard task.
Results: Results indicate that the present suite of data-intensive analytic techniques, improves the spatiotemporal information one can garner about non-periodic brain microstates from high-density electrical neuroimaging data.
Comparison with existing method(s): Compared to the existing methods (such as those based on *k*-clustering methods), the current micro-segmentation approach offers several advantages, including the data-driven (automatic) detection of non-periodic quasi-stable brain states.
Conclusion: This suite of quantitative methods allows the automatic detection of event-related changes in the global pattern of brain activity, putatively reflecting changes in the underlying neural locus for information processing in the brain, and event-related changes in overall brain activation. In addition, within-subject and between-subject bootstrapping procedures provide a quantitative means of investigating how robust are the results of the micro-segmentation.

1. Introduction

The rapid growth of large-scale, high-spatial resolution neuroimaging technology has advanced our understanding of the neural underpinnings of various complex cognitive and social processes. For instance, work in cognitive and social neuroscience has identified the neural correlates of information processing operations, ranging from basic perceptual processing (e.g., checkerboard)

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to more complex cognitive (e.g., object or face recognition, decision making, action understanding, embodied cognition) and social processing (e.g., pair bonding, love, empathy, cooperation). However, high-spatial resolution neuroimaging techniques, such as functional magnetic resonance imaging (fMRI), have been limited in terms of the temporal information they provide in studies of brain function. In addition, the cost of fMRI has placed constraints on the statistical power of most studies, which in turn has compromised the replicability of research findings (cf. Button et al., 2013; Cacioppo et al., 2013a).

A key theoretical objective in neuroscience and medicine is not only to specify what brain areas are recruited during a behavioral task, but also to specify when and in what specific combinations they are activated (e.g., Cacioppo et al., 2013b; Crites et al., 1995; Decety and Cacioppo, 2012; Ito et al., 2004; Ortigue et al., 2004, 2005; Ortigue and Bianchi-Demicheli, 2008). By providing detailed information about the relationship between neuronal activity (i.e., post-synaptic dendritic potentials of a considerable number of neurons that are activated in pattern that yield a dipolar field) and the temporal resolution (millisecond by millisecond) of each component information processing operation required for behavioral performance, high-density electroencephalographic (EEG) recordings and averaged EEG (event-related potentials, ERPs) have provided a useful additional tool in investigations of brain function. Whereas fMRI analyses are performed in source space, EEG/ERP analyses are performed in sensor space, with high-density sensor recordings producing more detailed information about changes in brain activity measured across time and sensor space.

Since the first EEG study by German neurologist Hans Berger (1929), numerous techniques have been developed for investigating the brain state dynamics of *periodic* processes in the EEG, including standard waveform analyses, Fourier analysis, independent component analysis (ICA), principal component analysis (PCA), and *k*-means cluster analyses. Over the years, some have argued that measuring peaks and troughs was sufficient to the temporal processing of the brain, while others (e.g., Donchin and Heffley, 1978) argued, quite persuasively, that another approach, such as a statistical decomposition of the evoked brain states, was necessary. In the current work, we present a new method for identifying the underlying component structure of an ERP – specifically, we present a new method for identifying non-periodic brain state dynamics for the micro-segmentation and analysis of averaged high-density ERPs.

2. Non-periodic brain microstates

Over the past three decades, efforts have been made to complement the traditional analyses of ERP peaks and troughs at specific electrode positions with more comprehensive analyses of time-varying activity across the entire scalp. For instance, introduced in the 1980s by Dietrich Lehmann, the brain microstate approach (Lehmann and Skrandies, 1980) is a method to identify stable configurations of global electric brain activity (rather than signals collected from one electrode). Because this approach is extensively used and has been detailed previously in several review articles and scientific reports (Brunet et al., 2011; Decety and Cacioppo, 2012; Michel et al., 1999, 2001; Murray et al., 2008; Pascual-Marqui et al., 1995; Ortigue et al., 2004, 2005, 2009, 2010), here we provide only the essential details. With respect to ERP analyses, the brain microstate approach considers data in the spatial domain first, and then in the temporal domain, providing a display of the constantly changing spatial distribution of the brain activity. The goal of the brain microstate approach is to provide information about the brain activity associated with the sequence of discrete (and putatively non-periodic) information processing operations evoked by the presentation of a stimulus within the context or a particular experimental task, with exogenous ERP components sensitive to the characteristics of the stimulus and endogenous ERP components sensitive to the stimulus in the context of the task. This sequence of information processing is composed of a series of stable brain activities, called brain microstates, each of which is characterized by the performance of specific cognitive computations and a relatively stable spatial distribution of brain activity. For instance, after a visual presentation of a face, the sequence (also called syntax) of various evoked brain microstates is thought to reflect the different steps of face processing (cf. Pizzagalli et al., 2000, 2002; Lehmann et al., 2005).

The successive occurrence of brain microstates does not imply that their brain networks occur in a sequential way (Pascual-Marqui et al., 1995). The underlying mechanism by which the brain enters a microstate with a given brain network may be composed of any number of sequential or parallel physiological sub-processes. Investigators can address this issue in several ways. For instance, lesion studies permit tests of the role of and relationship (e.g., dependence) between temporally activated neural regions; fMRI can be used to investigate functional connectivity between regions of activation; and experimental studies in which microstate segmentation is applied to high-density EEG/ERP data can be used to test contrasting hypotheses (brain models) to explain the chrono-architecture of the observed microstates.

Common brain areas may sustain different microstates, and the same microstate may be observed in two different conditions (e.g., fear faces and sad faces). In the latter case, the intensity of the activation and/or the onset or the duration of this microstate, but not its configuration, may significantly vary between conditions. For instance, one microstate may occur earlier in one condition compared with another condition, which may provide valuable information regarding the temporal dynamic of these two conditions.

The notion underlying the brain microstate approach is that each microstate refers to a time-limited information processing operation. Consistent with this notion, a growing body of studies shows that the presence of different brain microstates is associated with distinct cognitive operations (Lehmann and Skrandies, 1980). As such, the global pattern of brain electrical activity identified as a microstate is characterized by its electrical maxima (positive and negative), the orientation of its maxima (anterior, posterior), the location of its maxima (left hemisphere, right hemisphere), and the onset and duration of the configuration (Lehmann and Skrandies, 1980, 1984). Each brain microstate may remain significantly stable for a certain amount of time (e.g., for tens to hundreds of milliseconds), and then changes into another brain microstate that remains stable again (e.g., Cacioppo et al., 2013a,b; Decety and Cacioppo, 2012; Ortigue et al., 2009, 2010). This approach suggests that the global pattern of brain electrical activity is modeled as being composed of a time sequence of decomposable brain microstates (Lehmann and Skrandies, 1980; Pascual-Marqui et al., 1995).

In the previous literature, these brain microstates have typically been identified using data clustering techniques (e.g., *k*-means cluster analysis) on the group-averaged ERPs of each experimental condition to identify the start, end, and nature of each brain microstate. Given the group averaged ERP data set consists of N discrete samples over n (e.g. 128 or 256) electrodes, the activity across the n electrodes at each discrete sample can be expressed as a topographic scalp potential map. In the classic approach to microstate segmentation, the N topographic maps are segmented by the *k*-means algorithm. The value of k defines the number of discrete microstates that will be identified; k can range from 1 to N, but in practice is usually limited to 1–20 for a time period of 500 ms post-stimulus onset. First, k timeframes (where timeframe refers to the electric potentials from all electrodes within a discrete range of time in the ERP) are selected at random. These k selected