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The use of current source density as electrophysiological correlates in neuropsychiatric disorders: A review of human studies

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ABSTRACT

The use of current source density (CSD), the Laplacian of the scalp surface voltage, to map the electrical activity of the brain is a powerful method in studies of cognitive and affective phenomena. During the last few decades, mapping of CSD has been successfully applied to characterize several neuropsychiatric conditions such as alcoholism, schizophrenia, depression, anxiety disorders, childhood/developmental disorders, and neurological conditions (i.e., epilepsy and brain lesions) using electrophysiological data from resting state and during cognitive performance. The use of CSD and Laplacian measures has proven effective in elucidating topographic and activation differences between groups: i) patients with a specific diagnosis vs. healthy controls, ii) subjects at high risk for a specific diagnosis vs. low risk or normal controls, and iii) patients with specific symptom(s) vs. patients without these symptom(s). The present review outlines and summarizes the studies that have employed CSD measures in investigating several neuropsychiatric conditions. The advantages and potential of CSD-based methods in clinical and research applications along with some of the limitations inherent in the CSD-based methods are discussed in the review, as well as future directions to expand the implementation of CSD to other potential clinical applications. As CSD methods have proved to be more advantageous than using scalp potential data to understand topographic and source activations, its clinical applications offer promising potential, not only for a better understanding of a range of psychiatric conditions, but also for a variety of focal neurological disorders, including epilepsy and other conditions involving brain lesions and surgical interventions.

1. Introduction

Ever since Hans Berger reported his discovery of brain electrical activity in humans as measured by the electroencephalogram (EEG) (Berger, 1929), scientific and clinical applications of EEG has proliferated and achieved several milestones. One of the main advantages of EEG measures is its time resolution in milliseconds, a scale at which many of the key sensory, motor and cognitive phenomena take place at the neural level. The neuroelectric potentials as recorded from the scalp are measured and analyzed depending upon whether the recordings are made during task-related activity or in situations which are not characterized by the occurrence of a specific event. The ongoing (stimulus- and time independent) neuroelectric activity using scalp electrodes in a continuous fashion during a specific mental state (i.e., eyes-closed relaxed state, eyes-open steady state, meditation, hypnosis, sleep, coma, and other normal/altered states of consciousness) is the EEG (cf. Kamarajan and Porjesz, 2012) [see Fig. 1, top panel]. Common measures of EEG include, but not limited to, absolute and relative power as well as coherence in specific frequency bands, such as delta (1–4 Hz), theta (4–8 Hz), alpha (8–13), beta (13–30), and gamma (above 30 Hz). On the other hand, event-related potentials (ERPs) are voltage fluctuations (i.e., positive and negative components) that are associated in time (time-locked) in response to some physical or mental occurrence (i.e., sensory, motor, or cognitive event), and are extracted from the EEG data by means of filtering and signal/trial averaging (Picton et al., 2000). Generic ERP components include but are not limited to P1, N1, P2, N2, and P3 (with ‘P’ and ‘N’ referring to polarity) as they occur in temporal sequence (see Fig. 1, middle panel), and typically represent specific neural or neurocognitive event. For example, N1 represents physical stimulus characteristics (e.g., brightness or loudness) (Coles and Rugg, 1995; Johannes et al., 1995) as well as the selective attentional processing of the stimulus (e.g., attended/unattended) (Haider et al., 1964; Hansen and Hillyard, 1980; Naatanen and Picton, 1987; Rugg and Coles, 1996), while P3 (also called P300), the most robust and widely studied ERP component, represents context specific cognitive processing such as stimulus/feature/target identification or discrimination, response selection or inhibition, reward evaluation, etc., based on the task requirements and conditions (Sutton et al., 1965; Sutton and Ruchkin, 1984; Donchin and Coles, 1988; Verleger, 1988;

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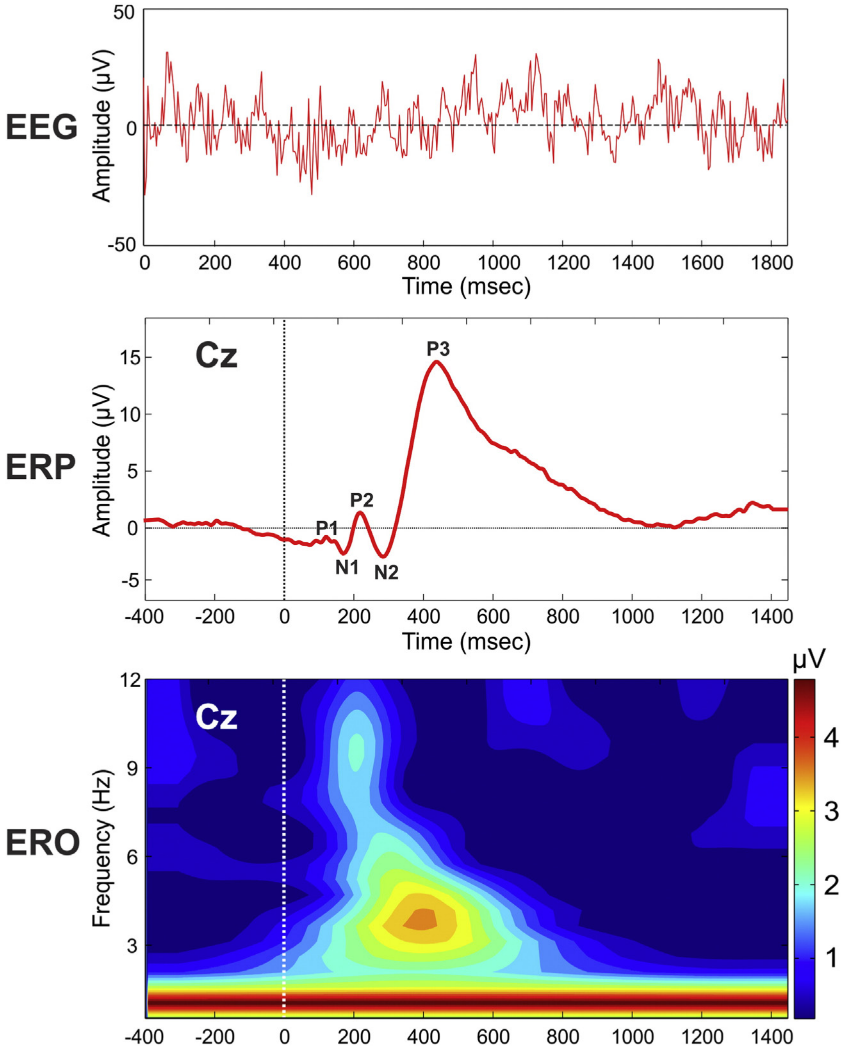

Fig. 1. Illustration of typical EEG trace (top panel), ERP waveform (middle panel), and ERO time–frequency map at Cz electrode in a visual oddball paradigm, recorded with nose tip as reference and forehead as ground electrode placements. EROs were computed using the S-transform algorithm as described in Jones et al. (2006). The horizontal axis in all panels represents time in milliseconds, and the color scale in bottom panel indicates amplitude in μV. In the middle and bottom panels, zero (0) millisecond represents the stimulus onset during a task.

Salisbury et al., 2004; Kamarajan et al., 2009). Finally, event-related oscillations (EROs), obtained by time–frequency analysis of the ERP recordings, represent both time and frequency information for a specific sensory, motor or cognitive event, and brain oscillations of different frequency bands are related to various cognitive functions (Basar, 1999a, 1999b; Basar et al., 1999, 2000, 2001). ERO measures often include power and coherence/synchrony for specific time and frequency ranges, and are considered to be involved in the generation of ERPs (see Sauseng et al., 2007 for a critical discussion).

Despite the fact that EEG has excellent temporal resolution, its spatial resolution (i.e., the information about the specific location or source of the recorded neuroelectric activity) is poor, due to the “blurring effects” of volume conduction, as the head acts like a low-pass spatial filter, transmitting to the scalp broad, as opposed to focal, spatial patterns of activity (Srinivasan et al., 1998b). The EEG activity recorded from each scalp electrode does not represent the specific activity of local brain sources (i.e. directly underneath the electrode), but the “volume-conducted” activity from multiple spatially dispersed sources. While this problem of removing or reducing the volume conduction effects has been a huge challenge for EEG technology, several methods have been devised to spatially represent the local effects of the brain sources responsible for the recorded scalp potentials. One such method is to calculate the current source density (CSD) or the Laplacian (second spatial derivative) of the scalp voltage using one of a number of specific algorithms.

Mapping of the CSD is often used to identify the neuronal generator patterns contributing to scalp-recorded EEG by providing a global empirical and biophysical context for generator localization (Tenke and Kayser, 2012). CSD transformations are implemented by algorithms that compute estimates of the current projected radially towards the skull and scalp from the underlying neuronal tissue at a given surface location, from a spatially weighted sum of the potential gradients directed at this site from some or all recording sites (cf. Kayser and Tenke, 2006a). In essence, the CSD maps represent the magnitude of the radial (transcranial) current flow from the brain to the scalp (source) and to the brain from the scalp (sink) (Perrin et al., 1989a; Kayser et al., 2012). In the CSD-converted scalp potentials, source and sink may correspond to the positive and negative (going) activity respectively. For instance, positive-going CSD activity related to a P3 potential is termed as P3 source while the negative-going CSD activity to an N1 component is described as N1 sink (Kayser et al., 2006). In effect, the CSD transformation functions as a high-pass spatial filter that minimizes the electrical distortions produced by the mediums between cortical surface and sensor (electrode) such as skull and scalp, thus facilitating spatial separation of temporally overlapping components (Turetsky et al., 2000). Therefore, the benefits of a CSD transform are a reference-free, spatially enhanced representation of the direction, location, and intensity of current generators that underlie the recorded scalp potentials (cf. Kayser and Tenke, 2006b), and provides topographies with more sharply

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