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NIRS-EEG joint imaging during transcranial direct current stimulation: Online parameter estimation with an autoregressive model

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HIGHLIGHTS

- Transient coupling between EEG 0.5 Hz–11.25 Hz band-power and NIRS oxy-hemoglobin signal in the low frequency (≤0.1 Hz) regime is proposed during tDCS.
- Time varying autoregressive (ARX) model is presented to track this transient coupling relationship during tDCS.
- Online parameter estimation of the ARX model is presented with a Kalman filter.
- Time varying poles associated with the ARX model were comparable across the healthy subjects during tDCS.
- Time varying zeros associated with the ARX model varied across the healthy subjects during tDCS.

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ABSTRACT

Background: Transcranial direct current stimulation (tDCS) has been shown to perturb both cortical neural activity and hemodynamics during (online) and after the stimulation, however mechanisms of these tDCS-induced online and after-effects are not known. Here, online resting-state spontaneous brain activation may be relevant to monitor tDCS neuromodulatory effects that can be measured using electroencephalography (EEG) in conjunction with near-infrared spectroscopy (NIRS).
Method: We present a Kalman Filter based online parameter estimation of an autoregressive (ARX) model to track the transient coupling relation between the changes in EEG power spectrum and NIRS signals during anodal tDCS (2 mA, 10 min) using a 4×1 ring high-definition montage.
Results: Our online ARX parameter estimation technique using the cross-correlation between log (base-10) transformed EEG band-power (0.5–11.25 Hz) and NIRS oxy-hemoglobin signal in the low frequency (≤0.1 Hz) range was shown in 5 healthy subjects to be sensitive to detect transient EEG-NIRS coupling changes in resting-state spontaneous brain activation during anodal tDCS. Conventional sliding window cross-correlation calculations suffer a fundamental problem in computing the phase relationship as the signal in the window is considered time-invariant and the choice of the window length and step size are subjective. Here, Kalman Filter based method allowed online ARX parameter estimation using time-varying signals that could capture transients in the coupling relationship between EEG and NIRS signals.
Conclusion: Our new online ARX model based tracking method allows continuous assessment of the transient coupling between the electrophysiological (EEG) and the hemodynamic (NIRS) signals representing resting-state spontaneous brain activation during anodal tDCS.

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1. Introduction

Transcranial Direct Current Stimulation (tDCS) is a non-invasive way of modulating cortical excitability (Nitsche and Paulus, 2000) and spontaneous brain activity (Spitoni et al., 2013). It is a form of non-invasive brain stimulation (NIBS) which uses low direct electrical currents delivered directly to the brain area of interest through electrodes placed on the scalp. Anodal

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tDCS generally increases cortical neuronal excitability and activity (Nitsche and Paulus, 2000), however the mechanisms are not known. Here, online resting-state spontaneous brain activation may be relevant to monitor tDCS neuromodulatory effects, specifically the relationship between cortical neural activity and regional hemodynamics, which can be respectively monitored using electroencephalography (EEG) in conjunction with functional near-infrared spectroscopy (NIRS).

During cortical activation, the electric currents from the excitable membranes superimpose at a given location in the extracellular medium and generate a potential which can be recorded as electroencephalogram (EEG) signals from scalp with excellent temporal resolution (milliseconds) and reasonable spatial resolution (usually around 6–9 cm but can be improved to 2–3 cm with Current Source Density estimates) (Burle et al., 2015). Anodal tDCS after-effects have been shown to be limited to the alpha frequency (8–12 Hz) band of EEG signals (Spitoni et al., 2013). The respective neural activity due to changes in cortical excitability requires a supply of oxygen and glucose that is delivered via the process of neurovascular coupling (NVC). NVC closely relates, spatially and temporally, to the regional hemodynamic response (Girouard and Iadecola, 2006), which can be captured by functional magnetic resonance imaging (fMRI) (Amadi et al., 2014; Peña-Gómez et al., 2012) and functional NIRS neuroimaging (Dutta et al., 2015; McKendrick et al., 2015). Functional NIRS allows us to monitor the regional hemodynamic response non-invasively with reasonable spatial (~1 cm, 0.5–2 cm depth penetration (Fukui et al., 2003)) and good temporal resolution (Devor et al., 2012). Fast NIRS sampling at 250 Hz is possible technically and relevant for fast and localized event-related optical signals (Gratton et al., 1997). However the time course of the regional hemodynamic response via NVC is much slower (in order of seconds) that limits the overall temporal resolution of the conventional NIRS method (Gratton and Fabiani, 2010).

Preliminary studies have shown that anodal tDCS increases regional cerebral blood flow (Zheng et al., 2011) and evokes neuronal and hemodynamic responses in the brain tissue (Dutta et al., 2015), where widespread effects of tDCS on human NVC, vasomotor reactivity (VMR), and cerebral autoregulation have been found (List et al., 2015; Vernieri et al., 2010; Terborg et al., 2000). Some of these tDCS effects may be montage specific, such that a decrease in VMR after anodal tDCS (Vernieri et al., 2010) may be related to an extra cephalic montage (e.g., cathode placed on shoulder) affecting the brainstem (List et al., 2015). Therefore, in the present study, we used a 4×1 ring high-definition tDCS (HD-tDCS) montage, where HD-tDCS constrains the electric field between the active anode electrode at the center and the four surrounding return electrodes (~4 cm apart) in a ring montage (Datta et al., 2009), to study local online resting-state spontaneous brain activation using the coupling between electrophysiological (EEG band power) and hemodynamic (NIRS oxy-hemoglobin: oxy-Hb) signals.

Prior EEG work has shown that spontaneous fluctuations in the alpha band (8–14 Hz) activity captures the momentary state of visual cortex excitability (Romei et al., 2008), which is the same frequency band that captured tDCS after-effects (Spitoni et al., 2013). Furthermore, during awake resting-state joint EEG-NIRS measurements, slow (0.07–0.13 Hz) hemodynamic (oxy-Hb) oscillations have been shown to temporarily (duration ~100 s) couple with slow EEG (alpha and/or beta power) power fluctuations in the sensorimotor cortex (SMC) areas (Pfurtscheller et al., 2012). The driving mechanisms responsible for these slow (0.07–0.13 Hz) hemodynamic oscillations is unclear; however, Nikulin et al. (Nikulin et al., 2014) recently showed that monochromatic ultra-slow oscillations (MUSO) around 0.1 Hz in the EEG signals were related to the NIRS oxy-Hb signals, and the authors hypothesized that EEG MUSO represents an electric counterpart of the hemodynamic responses. Such fluctuations in the local cerebral oxygenation levels measured by oxygen polarography has been postulated to be driven by local cerebral autoregulation mechanisms (Cooper et al., 1966), which plays an important role in oxygen delivery where impaired cerebral oxygenation oscillations may indicate a neurologic pathology (Schytz et al., 2010). Indeed, spontaneous dynamic cerebral autoregulation primarily reflected in the NIRS oxy-Hb (and total Hb) signal (Schytz et al., 2010) can be a powerful tool to assess tDCS-induced cerebral vasodilation and autoregulation (Obrig et al., 2000).

In principal accordance, we developed in our prior work (Dutta et al., 2013) a phenomological model to capture the capacity of cerebral blood vessels to dilate during anodal tDCS due to neuronal (primarily synaptic) activity. Here, the coupling between the oxy-Hb time-series and log-10 (base-10) transformed ($\log_{10}$) mean-power (in 0.5–11.25 Hz) time-course of EEG during anodal tDCS was shown (Dutta et al., 2015), and the corticospinal excitability changes could be elucidated with NIRS-EEG joint-imaging (Jindal et al., 2015). Specifically, our prior work on four chronic (>6 months) ischemic stroke case series showed non-stationary effects of anodal tDCS on $\log_{10}$ mean-power of EEG within 0.5–11.25 Hz frequency band that correlated with the NIRS oxy-Hb response (Dutta et al., 2015). An important aspect of the temporal profile of the NIRS oxy-Hb response was an initial dip at the beginning of anodal tDCS that corresponded with an increase in the $\log_{10}$ mean-power of EEG within 0.5–11.25 Hz frequency band (Dutta et al., 2015), which was explained by the 'metabolic hypothesis' of NVC (Girouard and Iadecola, 2006). However, an objective method for online tracking of the transient coupling relation between EEG and NIRS during tDCS could provide information on the momentary state of cortical excitability (Romei et al., 2008) and bidirectional interactions within the neurovascular unit (Dutta, 2015) that would be important for determining the dose of tDCS neuromodulation. Limitations of existing sliding window cross-correlation calculations (Dutta et al., 2015; Nikulin et al., 2014; Pfurtscheller et al., 2012) and conventional autoregressive-moving average models (Salinet et al., 2015) that are sensitive to the subjective choice of the window length and step size for continous monitoring of such non-stationary coupling relationship, have prevented development of such an online tracking model. Such window based cross-correlation calculations also have a fundamental problem in computing the phase relationship between NIRS and EEG, as the signal in the window is considered as time-invariant.

For the precise continous online monitoring of the EEG and NIRS phase changes, it is required to use the framework of online tracking with an iterative update function which can assume the EEG and NIRS signals as time-varying. Therefore, in this methods paper, we developed and experimentally tested on 5 healthy subjects a computational autoregressive (ARX) model for online parameter estimation with a Kalman filter to track resting-state transient coupling relations between $\log_{10}$ mean-power EEG band (0.5–11.25 Hz) and NIRS oxy-Hb signals ($\leq$0.1 Hz) acquired simultaneously from the left SMC during anodal HD-tDCS.

2. Materials and methods

2.1. Subjects

Five healthy male subjects (age 36.6 ± 13.13, all right-handed) volunteered to participate in this study after informed consent, and all experiments were conducted in accordance with the Declaration of Helsinki. The subjects had no known neurological or psychiatric history, nor any contraindications to tDCS. During the experiment, the subjects were comfortably seated with eyes-open in an armchair with adjustable height.