The Effect of tDCS on EEG-Based Functional Connectivity in Gait Motor Imagery

J. A. Gaxiola-Tirado[1](✉), M. Rodríguez-Ugarte[2], E. Iáñez[2], M. Ortiz[2], D. Gutiérrez[1], and J. M. Azorín[2]

[1] CINVESTAV, Monterrey's Unit, Vía del Conocimiento 201, PIIT, km 9.5 de la autopista nueva al aeropuerto, 66600 Apodaca, NL, Mexico
jgaxiola@cinvestav.mx, dgtz@ieee.org

[2] Brain-Machine Interface Systems Lab, Systems Engineering and Automation Department at Miguel Hernández University of Elche, Avda. de la Universidad s/n. Ed. Innova, 03202 Elche (Alicante), Spain
{maria.rodriguezu,eianez,mortiz,jm.azorin}@umh.es
http://www.monterrey.cinvestav.mx/, https://psblab.gutierrezruiz.com/, http://bmi.umh.es/

Abstract. Transcranial direct current stimulation (tDCS) is a non-invasive technique for brain stimulation capable of modulating brain excitability. Although beneficial effects of tDCS have been shown, the underlying brain mechanisms have not been described. In the present study, we aim to investigate the effects of tDCS on EEG-based functional connectivity, through a partial directed coherence (PDC) analysis, which is a frequency-domain metric that provides information about directionality in the interaction between signals recorded at different channels. The tDCS montage used in our study, was focused on the lower limbs and it was composed of two anodes and one cathode. A single-blind study was carried out, where eight healthy subjects were randomly separated into two groups: sham and active tDCS. Results showed that, for the active tDCS group, the central EEG electrodes Cz, C3 and C4 turned out to be highly connected within alpha and beta frequency bands. On the contrary, the sham group presented a tendency to be more random at its functional connections.

Keywords: PDC · Functional connectivity · Motor imagery · BCI · EEG · Gait · tDCS

1 Introduction

Transcranial direct current stimulation (tDCS) is a non-invasive technique for brain stimulation capable of modulating brain excitability [1]. It delivers low intensity, direct current (transferred between electrodes from anode to cathode) to cortical areas facilitating or inhibiting spontaneous neuronal activity. Specifically, anodal direct current stimulation has been shown to increase cortical

J. M. Ferrández Vicente et al. (Eds.): IWINAC 2019, LNCS 11486, pp. 3–10, 2019.
https://doi.org/10.1007/978-3-030-19591-5_1

excitability, whereas cathodal stimulation decreased it [2,3]. This technique has shown potential to improve motor performance and motor learning [4,5]. Thus, tDCS application is now explored as a promising tool applied in motor neurorehabilitation [6]. However, even though the beneficial effects of tDCS have been shown, its effects on functional connectivity and the underlying brain mechanisms have still not been described.

The majority of the studies have investigated the effects of tDCS as an augmentative technique to improve the performance of upper limbs [7–9]. Up to this date, only relative few studies have investigated how tDCS affects the lower limbs performance [10,11]. Hence, we are interested in to investigate the effects of tDCS in gait motor imagery (IM). From a cognitive perspective, brain activity during gait, involves the supplementary motor area (SMA), the primary motor cortex (M1), the primary somatosensory cortex (S1) and the premotor area (PM) [12]. Moreover, it has been shown that IM relies on neural processes also associated with these areas [13,14].

In the present study, we aim to investigate tDCS effects in functional connectivity, through a partial directed coherence (PDC) analysis, which is a frequency-domain metric that provides information about directionality in the interaction between electroencephalography (EEG) signals recorded at different channels. In this context, in [15] authors examinated time and frequency-based measures of EEG-based brain networks, connectivity analysis, and their applications on brain-computer interfaces (BCI). They also reported connections between the sensorimotor cortex and frontal areas during IM. Therefore, with better understanding of the mechanisms and dynamics of brain activity, it may be obtain useful and informative features for BCI applications as well as in motor neurorehabilitation.

2 Materials and Methods

In this section, we present the experimental procedure and the tDCS montage focused on lower limbs. Furthermore, we introduce the PDC, in order to evaluate the effects of tDCS in EEG-based functional connectivity.

2.1 EEG Acquisition

The brain activity was recorded using an EEG array of 30 electrodes (The StarStim R32 system) placed on the scalp according to the extended 10–20 placing system (P7, P4, CZ, PZ, P3, P8, O1, O2, C2, C4, F4, FP2, FZ, C3, F3, FP1, C1, OZ, PO4, FC6, FC2, AF4, CP6, CP2, CP1, CP5, FC1, FC5, AF3, PO3) at a sampling frequency of 500 Hz.

2.2 TDCS Supply

The StarStim R32 system was used to provide tDCS to the subject's brain. The tDCS montage was composed by one anode located over the right cerebrocerebellum (two centimeters right and one centimeter down of the inion), the other one over the motor cortex in Cz on M1, and the cathode over FC2 (using the International 10-10 system). The idea was to excite simultaneously the right cerebrocerebelum and the motor cortex considering that both areas are implicated in IM. The intensity was established to 0.2 mA and 0.3 mA for the cerebrocerebellum and Cz anodes respectively. The cathode current density was of 0.16 $\frac{mA}{cm^2}$. All the electrodes were 1 cm of radius (surface area of π cm^2), 3 mm of thickness and with 4 mm of space for the conductive gel.

2.3 Experimental Procedure

The experiment was based on visual cues in order to detect gait IM. Eight subjects were separated into two groups: *active tDCS* (labeled as S1t, S2t, S3t and S4t) and *sham* (labeled as S5s, S6s, S7s and S8s). After the initial stimulation, subjects stood in front of a screen that provided instructions while their EEG signals were being recorded. Two types of instructions were indicated: Imagine and +. During Imagine periods, they had to imagine a gait movement. Subjects were instructed to avoid blinking, head movements or any other artifact during the Imagine periods, postponing these actions to the + periods. The *sham* group received 15 min of fake stimulation to create a placebo effect, while the *active tDCS* group received 15 min of real stimulation. Participants performed one session each day for five consecutive days.

2.4 Partial Directed Coherence

The partial directed coherence (PDC) is a frequency domain measure of the relationships (information about directionality in the interaction) between pairs of signals in a multivariate data set for application in functional connectivity inference in neuroscience [16]. If one assumes a set $S = \{x_m, 1 \leq m \leq M\}$ of M EEG signals (simultaneously observed time series)

$$\boldsymbol{x}(n) = [x_1(n), x_2(n), \ldots, x_M(n)]^T \tag{1}$$

is adequately represented by a multivariate autoregressive (MVAR) model of order p, or simply MVAR(p):

$$\boldsymbol{x}(n) = \sum_{k=1}^{p} A_p \boldsymbol{x}(n-k) + \boldsymbol{e}(n), \tag{2}$$

where $\boldsymbol{A}_1, \boldsymbol{A}_2, \ldots, \boldsymbol{A}_p$ are the coefficient matrices (dimensions $M \times M$), containing the coefficients $a_{ij}(k)$ which represent the linear interaction effect of $x_j(n-k)$ onto $x_i(n)$ and where

$$\boldsymbol{e}(n) = [e_1(n), e_2(n), \ldots, e_M(n)]^T \tag{3}$$

is the noise vector (uncorrelated error process). A measure of the direct causal relations (directional connectivity) of x_j to x_i is given by the PDC defined by [16]

$$\pi_{i\leftarrow j}(f) = \frac{A_{ij}(f)}{\sqrt{\boldsymbol{a}_j(f)\boldsymbol{a}_j^T(f)}} \tag{4}$$

where $A_{ij}(f)$ and $\boldsymbol{a}_j$ are, respectively, the i, j element and the j-th column of

$$\boldsymbol{A}(f) = \boldsymbol{I} - \sum_{k=1}^{p} \boldsymbol{A}_k e^{-2\pi i f k}. \tag{5}$$

PDC values range between 0 and 1; $\pi_{i\leftarrow j}$ measures the outflow of information from channel x_j to x_i in relation to the total outflow of information from x_j to all of the channels.

2.5 EEG Processing and Analysis of Connectivities

The methods presented in this paper are implemented in the Matlab package ARfit [17]. For the purpose of this paper, we jointly analyze data from five experimental sessions. The first two seconds of each trial were discarded to assure the concentration of the subject in the task and to get rid of the visual cue artifacts on the EEG. A digital band-pass filter between 0.5 and 50 Hz, a notch filter with 50 Hz cut-off frequency and a laplacian filter as in [12], were applied to the data. Signals were processed in 2 s epochs (400 epochs for each subject). Each epoch undergoes independent component analysis (ICA) with EEGLAB toolbox [18] in order to detect visually the presence of blinking artifacts as in [4]. From now on, we will refer to EEG channel as an electrode.

Once preprocessing was performed, we chose to analyze the directed interconnections in a set of $M = 9$ electrodes from the M1, SMA and PM regions: $S = \{$Cz, CP1, CP2, C1, C2, C3, C4, FC1, FC2$\}$. Under these conditions, the computation of the PDC was based on a method similar to the one used in [19], where a significance threshold for testing for nonzero PDC at a given frequency proposed in [20] was assessed.

In our case, in order to compute the PDC, the signals were fitted with a MVAR(9), where the model order was determined by the Akaike Information Criterion [21]. We analyzed the frequency range of 1 to 30 Hz, as they are within the range considered for the sensorimotor rhythm modulation. For the given set of frequencies, the PDC values from electrode j to electrode i ($i = 1, 2, \ldots, 9; j = 1, 2, \ldots, 9$) were obtained for each 2 s epoch (400 epochs for each subject) obtaining 9×9 matrixes. In all cases (epoch, frequency and direction), the threshold for the PDC to be significant was stored with a statistical significance for $\alpha = 0.05$ for all possible directions at a given frequency (for details see [19]). Then, those epochs for which the PDC value was higher than the significance threshold (i.e., the PDC whose confidence was enough to be regarded as indicative of directional connectivity) were retained in our calculations. For every directed interconnection at a given frequency, we found those more likely (in terms of the total number of epochs with significant interconnections) to be present.

3 Results

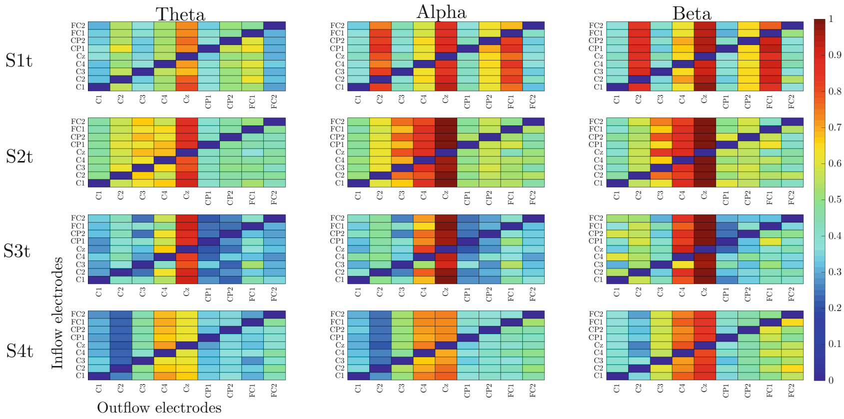
The preliminary results of the analysis proposed in Sect. 2.5 are shown in Figs. 1a and 1b for the cases of *active tDCS* and *Sham*, respectively. For each subject, we present the mean value of directed interconnections (in terms of the total number of epochs with significant interconnections) at the frequency bands theta (4–7 Hz), alpha (8–12 Hz) and beta (13–30 Hz). The color bar indicates the normalized number of epochs (out of 400) in which the corresponding directed interconnection was significant. Thus, red regions indicate high levels of connectivity (e.g., 1 indicates 100% of significative epochs) among the nine electrodes.

The results showed that brain connectivity of both groups increase mainly at the alpha and beta bands. Regarding the spatial distribution of the directed interconnections revealed by our analysis in these frequency bands, we note that for the *active tDCS* group (Fig. 1a), the central EEG electrodes Cz, C3 and C4 turned out to be highly connected. Specifically, we note the following cases:

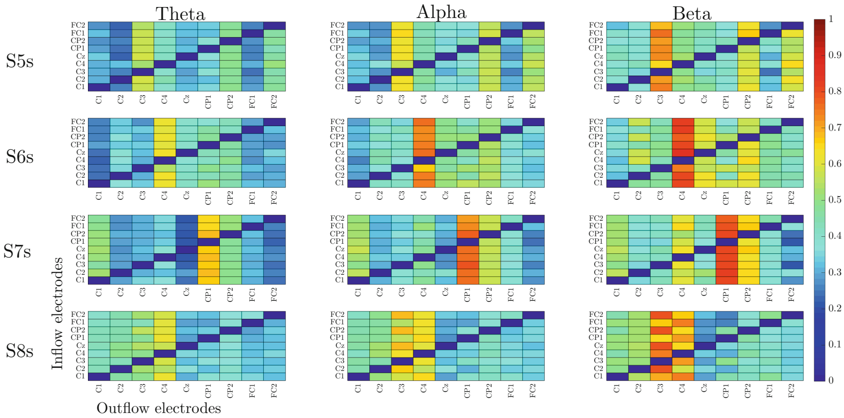
- An outflow greater than 90% (Subjects S1t, S2t and S3t) and 75% (Subject S4t) from Cz to all electrodes;
- An outflow greater than 80% (Subjects S2t, S3t and S4t) and 65% (Subject S1t) from C4, mainly in beta band;
- An outflow greater than 60% (Subjects S2t and S4) from C3;
- An outflow greater than 90% (Subject S1t) from C2 and 50% (Subjects S2t and S3t).

On the contrary, the *sham* (Fig. 1b) group presented a tendency to be more random at its functional connections. The characteristic patterns of this group presented relevant differences among subjects in the resulted interconnections. Expressly, the largest percent of outflows was presented in C3/CP2/FC2 (Subject S5s), C4 (Subject S6s), CP1/CP2 (Subject S7s) and C3/C4 (Subject S8s). It is important to note that the outflow number in this group, in the central electrodes Cz, C3 and C4 is always lower than the *active tDCS* group. It is important to note that the outflow number in this group, in the central electrodes Cz, C3 and C4 is always lower than the *active tDCS* group.

So far, based on preliminary findings more directional connectivity existed in the *active tDCS* group in comparison with the *sham* group. These results are in accordance with the tDCS montage used. As we mentioned above, the montage was composed by one anode located over the right cerebrocerebellum (two centimeters right and one centimeter down of the inion). The effects of the stimulation over the cerebellum are still nuclear [22]. However, recent studies have reported that anodal stimulation over the cerebellum, produces cortical excitability changes in a polarity-specific manner [23]. Furthermore, a second anode was placed over Cz on M1 with a slightly higher current, exciting the motor area, which can explain why the central EEG electrodes Cz, C3 and C4 turned out to be highly connected in the *active tDCS* group.



(a) *active tDCS*



(b) *sham*

Fig. 1. Functional brain connectivity during IM for the groups of (a) *active tDCS* and (b) *sham*. For each subject, the mean value of directed interconnections (in terms of the total number of epochs with significant interconnections) at the frequency bands theta (4–7 Hz), alpha (8–12 Hz) and beta (13–30 Hz) is presented. The color bar indicates the normalized number of epochs (out of 400) in which the corresponding directed interconnection was significant. Thus, blue regions indicate low and red regions indicate high levels of connectivity (e.g., 1 indicates 100% of significative epochs) among the 9 electrodes. In all cases the diagonal elements were set to zero. (Color figure online)

4 Conclusions

In conclusion, in this preliminary study we demonstrated that EEG-based PDC analysis is able to detect changes in functional connectivity mediated by the application of transcranial direct current stimulation (one anode located over the right cerebrocerebellum, the other one over the motor cortex in Cz on M1, and the cathode over FC2) in healthy subjects. Our future work will include a more rigorous assessment of our connectivity-based analysis in more complex sensor networks and extending our approach to the study of resting-state brain networks. Furthermore, in the context of BCI applications, we will study the effects of tDCS in the relationship between the brain connectivity (assessed through PDC) and the IM detection accuracy in operating a BCI, in order to development of brain plasticity over the course of training sessions. This information can be useful to help understanding the neuroplastic modifications induced by tDCS, and design therapies to motor neurorehabilitation.

Acknowledgments. This research has been carried out in the framework of the project Associate - Decoding and stimulation of motor and sensory brain activity to support long term potentiation through Hebbian and paired associative stimulation during rehabilitation of gait (DPI2014-58431-C4-2-R), funded by the Spanish Ministry of Economy and Competitiveness and by the European Union through the European Regional Development Fund (ERDF) "A way to build Europe". Also, the Mexican Council of Science and Technology (CONACyT) provided J. A. Gaxiola-Tirado his scholarship, under Grant 220145.

References

1. Gandiga, P.C., Hummel, F.C., Cohen, L.G.: Transcranial DC stimulation (tDCS): a tool for double-blind sham-controlled clinical studies in brain stimulation. Clin. Neurophysiol. **117**(4), 845–850 (2006)
2. Brunoni, A.R., et al.: Clinical research with transcranial direct current stimulation (tDCS): challenges and future directions. Brain Stimul. **5**(3), 175–195 (2012)
3. Nitsche, M.A., Paulus, W.: Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J. Physiol. **527**(3), 633–639 (2000)
4. Angulo-Sherman, I.N., Rodríguez-Ugarte, M., Sciacca, N., Iáñez, E., Azorín, J.M.: Effect of tDCS stimulation of motor cortex and cerebellum on EEG classification of motor imagery and sensorimotor band power. J. Neuroeng. Rehabil. **14**(1), 31 (2017)
5. Matsumoto, J., Fujiwara, T., Takahashi, O., Liu, M., Kimura, A., Ushiba, J.: Modulation of mu rhythm desynchronization during motor imagery by transcranial direct current stimulation. J. Neuroeng. Rehabil. **7**(1), 27 (2010)
6. Reis, J., Fritsch, B.: Modulation of motor performance and motor learning by transcranial direct current stimulation. Curr. Opin. Neurol. **24**(6), 590–596 (2011)
7. Lee, S.J., Chun, M.H.: Combination transcranial direct current stimulation and virtual reality therapy for upper extremity training in patients with subacute stroke. Arch. Phys. Med. Rehabil. **95**(3), 431–438 (2014)
8. Butler, A.J., Shuster, M., O'hara, E., Hurley, K., Middlebrooks, D., Guilkey, K.: A meta-analysis of the efficacy of anodal transcranial direct current stimulation for upper limb motor recovery in stroke survivors. JJ. Hand Ther. **26**(2), 162–171 (2013)
9. Kim, D.Y., et al.: Effect of transcranial direct current stimulation on motor recovery in patients with subacute stroke. Am. J. Phys. Med. Rehabil. **89**(11), 879–886 (2010)

10. Foerster, Á., Dutta, A., Kuo, M.F., Paulus, W., Nitsche, M.A.: Effects of anodal transcranial direct current stimulation over lower limb primary motor cortex on motor learning in healthy individuals. Eur. J. Neurosci. **47**(7), 779–789 (2018)
11. Fernandez, L., et al.: Cathodal transcranial direct current stimulation (tDCS) to the right cerebellar hemisphere affects motor adaptation during gait. Cerebellum **16**(1), 168–177 (2017)
12. Rodriguez-Ugarte, M., Iáñez, E., Ortiz-Garcia, M., Azorín, J.M.: Effects of tDCS on real-time BCI detection of pedaling motor imagery. Sensors **18**(4), 1136 (2018)
13. Bakker, M., De Lange, F., Stevens, J., Toni, I., Bloem, B.: Motor imagery of gait: a quantitative approach. Exp. Brain Res. **179**(3), 497–504 (2007)
14. Parsons, L.M., et al.: Use of implicit motor imagery for visual shape discrimination as revealed by PET. Nature **375**(6526), 54 (1995)
15. Hamedi, M., Salleh, S.H., Noor, A.M.: Electroencephalographic motor imagery brain connectivity analysis for BCI: a review. Neural Comput. **28**(6), 999–1041 (2016)
16. Baccalá, L.A., Sameshima, K.: Partial directed coherence: a new concept in neural structure determination. Biol. Cybern. **84**(6), 463–474 (2001)
17. Neumaier, A., Schneider, T.: Estimation of parameters and eigenmodes of multivariate autoregressive models. ACM Trans. Math. Softw. (TOMS) **27**(1), 27–57 (2001)
18. Delorme, A., Makeig, S.: EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J. Neurosci. Methods **134**(1), 9–21 (2004)
19. Gaxiola-Tirado, J.A., Salazar-Varas, R., Gutiérrez, D.: Using the partial directed coherence to assess functional connectivity in electroencephalography data for brain-computer interfaces. IEEE Trans. Cogn. Dev. Syst. **10**(3), 776–783 (2018)
20. Schelter, B., et al.: Testing for directed influences among neural signals using partial directed coherence. J. Neurosci. Methods **152**(1–2), 210–219 (2006)
21. Akaike, H.: A new look at the statistical model identification. IEEE Trans. Autom. Control. **19**(6), 716–723 (1974)
22. van Dun, K., Bodranghien, F.C., Mariën, P., Manto, M.U.: tDCS of the cerebellum: where do we stand in 2016? Technical issues and critical review of the literature. Front. Hum. Neurosci. **10**, 199 (2016)
23. Galea, J.M., Jayaram, G., Ajagbe, L., Celnik, P.: Modulation of cerebellar excitability by polarity-specific noninvasive direct current stimulation. J. Neurosci. **29**(28), 9115–9122 (2009)