Technology and Health Care 28 (2020) S123–S130
DOI 10.3233/THC-209013
IOS Press

Development of a transcranial direct current stimulation device based on current limiter for simultaneous measurement of electroencephalography: A feasibility study

Young-Jin Jung[a,b], Yun-Sung Lee[c], Ga-Young Choi[c] and Han-Jeong Hwang[c,*]
[a]*Department of Radiological Science, Dongseo University, Busan, Korea*
[b]*Center for Radiological Environment and Health Science, Dongseo University, Busan, Korea*
[c]*Department of Electronics and Information Engineering, Korea University, Sejong, Korea*

Abstract.
BACKGROUND: Electroencephalography (EEG) measured during transcranial direct current stimulation (tDCS) can help understand the accurate impact of tDCS on the brain, but this has been hindered due to significant inflow of tDCS-induced electrical artifacts.
OBJECTIVE: In this study, we introduce a novel tDCS device developed based on current limiter, which can prevent the generation of significant electrical artifacts.
METHODS: To verify the feasibility of our developed tDCS device, we performed simultaneous measurement of EEG during tDCS application with five different current intensities (0, 500, 1,000, 1,500, and 2,000 μA). Changes in EEG power spectral density (PSD) and correlation between the PSD of non-stimulation and tDCS condition were investigated to see whether our tDCS device can be used for simultaneous EEG recording without significant inflow of tDCS-induced electrical artifacts.
RESUTLS: The mean EEG-PSD differences between non-stimulation and tDCS condition were not significant for all stimulation current intensities. Furthermore, EEG-PSDs estimated during non-stimulation and tDCS application showed statistically high correlation for all comparison cases.
CONCLUSION: Based on the results, we could demonstrate the feasibility of our tDCS device based on current limiter for simultaneous EEG measurement, which could potentially provide a way to investigate the impact of tDCS on the brain more accurately.

Keywords: Current limiter, transcranial direct current stimulation, simultaneous EEG recording, neuromodulation, precise brain stimulation

1. Introduction

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation method, which induces changes in cortical excitability [1]. In recent years, tDCS has received growing attention because it has been reported that tDCS is useful for the treatment of various psychiatric and neurological disorders [2–6].

*Corresponding author: Han-Jeong Hwang, Department of Electronics and Information Engineering, Korea University, Sejong 30019, Korea. Tel.: +82 44 860 1422; Fax: +82 44 860 1585; E-mail: hwanghj@korea.ac.kr

For example, one study found significant improvement in mood, attention, and working memory after applying tDCS to depressive patients [5], and another study showed that tDCS can significantly improve motor functions for stroke patients [6].

Even though good clinical outcomes have been continuously reported, the accurate effect of tDCS on the brain has been not well established and still controversial [8], and thus investigation on brain state measured during tDCS is required to clarify the exact impact of tDCS on the brain. There are a variety of neuroimaging modalities to measure brain activity during tDCS, such as electroencephalography (EEG), magnetoencephalography (MEG) [9], near-infrared spectroscopy (NIRS) [10], functional magnetic resonance imaging (fMRI) [11], and so on.

Among these, EEG has been most frequently used for simultaneous monitoring of brain state during tDCS [12–16] due to its high temporal resolution, good portability, and reasonable price. However, in the case of simultaneous EEG measurement during tDCS, EEG is significantly contaminated by a DC stimulator, and thereby original characteristics of EEG are distorted [12–16]; EEG amplitude dramatically increases during tDCS, leading to significant broadband increase in EEG spectral power [14–16]. A few of studies used an artifact rejection algorithm, such as independent component analysis (ICA), to remove tDCS-induced artifacts from simultaneously measured EEG during tDCS [12,14]. Even though the ICA-based method showed meaningful results in terms of removal of tDCS-induced artifacts, significantly contaminated EEG should be manually removed before using ICA, and ICA itself requires another manual selection procedure [14]. Therefore, it would be a more fundamental solution to minimize the generation of tDCS-induced electrical artifacts in order to see the exact impact of tDCS on the brain.

In this study, we introduce a novel tDCS device based on current limiter to minimize stimulation-derived artifacts, and thereby making it possible to simultaneously measure EEG without significant inflow of electrical artifacts during tDCS. To verify the feasibility of the developed tDCS device, we recorded resting-state EEG while subjects performed opening and closing the eyes, at which time tDCS was simultaneously applied around EEG electrodes. Power spectral densities (PSDs) of resting-state EEG was calculated to see their difference between non-stimulation and tDCS condition, and correlation analysis was also performed to see the similarity between the PSDs of non-stimulation and tDCS condition.

2. Methods

2.1. Current limiter-based tDCS system

Figure 1a shows the control block diagram of our in-house tDCS device based on current limiter (only forward control). Because current limiter does not generate current/voltage ripples due to rejection of feed-forward control, our in-house tDCS device based on multiple current limiters also does not generate current/voltage ripples. To implement the current limiter, the REF200 (TI, USA) was used for precise current control, and the current limiter was utilized as a current source with an analogue switch (DG412, Maxim Integrated, Taiwan) to control the current flow. Figure 1b shows an actual tDCS device which comprises of a power module (voltage range: −5–35 V), MCU (MSP430-FR6989, TI, USA) and current source module based on current limiters with digital control. We conducted an experiment to validate the feasibility of our tDCS device based on multiple current limiters, where the ratio between input and measured current intensities were less than 0.3% for all cases, i.e., input current intensities: 0.6, 1.2, and 1.8 mA and measured current intensities: 0.59, 1.19, and 1.79 mA.

2.2. Experimental paradigm

To validate the feasibility of our tDCS system in terms of tDCS-induced artifacts on EEG, we conducted

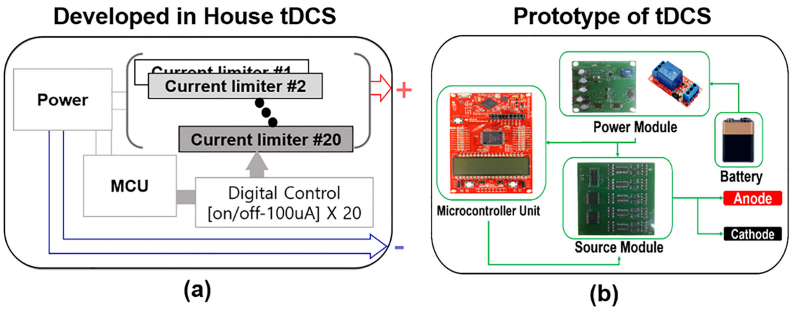

Fig. 1. (a) Block diagram of a developed in-house tDCS system, and (b) picture of a developed in-house tDCS system.

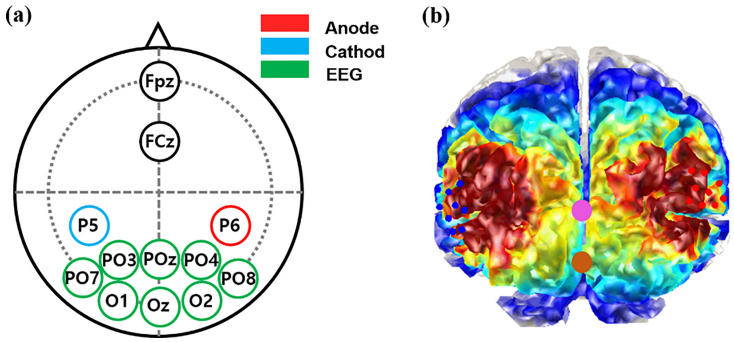

Fig. 2. (a) Locations of EEG (green), tDCS anode (red) and cathode (blue) electrodes. (b) Simulated electrical filed map generated by tDCS. The pink and brown circles represent POz and Oz used for data analysis.

simultaneous tDCS-EEG experiments with five healthy subjects. EEGs were measured with a sampling rate of 1 kHz (Brain Products, GmbH, Gilching, Germany) while each subject performed closing and opening the eyes each for 60 s. During EEG recording, tDCS was independently administered with five different current intensities (0, 500, 1,000, 1,500, and 2,000 μA) to see the effect of tDCS current intensity on EEG spectral characteristics. The order of the experiment was fully randomized in terms of stimulation intensities for counterbalancing. Also, we did not introduce sham condition that is generally needed in cognitive function tests, and instead non-stimulation condition without any current was introduced. Figure 2a shows the locations of EEG and tDCS electrodes, which were mainly attached on occipital areas according to the international 10–20 system because significant changes in brain activity are observed between eyes-closed (EC) and eyes-open (EO) condition around occipital areas. Figure 2b shows simulated electrical filed map generated by tDCS, where pink and orange circles represent POz and Oz used for data analysis.

2.3. EEG data analysis

For data analysis, two electrodes (POz and Oz) attached on the midline of the occipital lobe were only used because other electrodes were sometimes connected with the anode and cathode electrodes via saline solution used for attaching two tDCS electrodes, leading to significant inflow of tDCS-induced electrical artifacts to EEG. Also, because all EEG electrodes were connected with the tDCS electrodes via saline solution for one subject during the experiment, we excluded this subject for further data analysis. Note that brain areas related to the two electrodes selected for data analysis are influenced by tDCS even

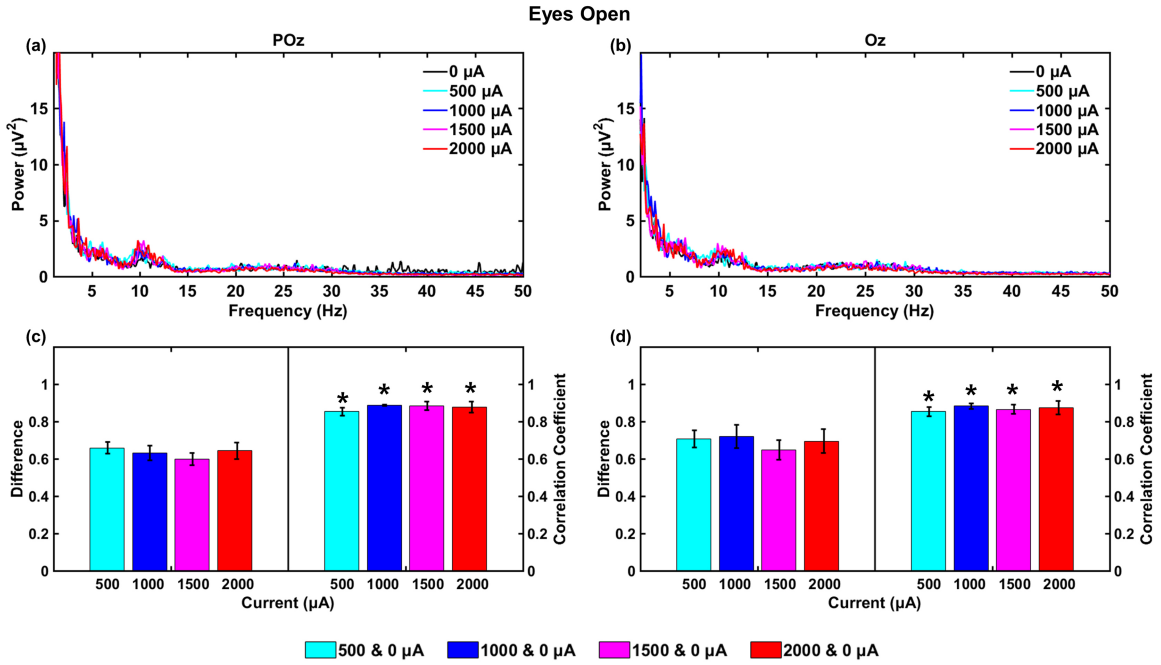

Fig. 3. Mean EEG-PSDs estimated during eyes open condition for (a) POz and (b) Oz in terms of current intensity, and PSD differences and correlation coefficients between non-stimulation (0 μA) and tDCS condition (500, 1000, 1500, and 2000 μA) for (c) POz and (d) Oz. No significant difference is found between PSD differences (RM-ANOVA: $p > 0.05$), and the PSD of non-stimulation condition is significantly correlated with those of tDCS conditions (Pearson correlation: $p < 0.05$). An asterisk represents statistical significance ($p < 0.05$). The vertical bars indicate the standard errors of estimated correlation coefficients for each subject.

though they are less influenced as compared to those around the anode and cathode electrodes, as shown in Fig. 2b. Raw EEG data were first bandpass filtered with a Butterworth filter (0.5–50.5 Hz). After that, PSD was calculated using short-time Fourier transform (window size: 10 s with 90% overlap), and PSDs estimated along the time were averaged for each frequency. This analysis was separately applied to the EEG data measured for the five conditions with different current intensities (0, 500, 1000, 1500, and 2000 μA). To see the impact of tDCS application on EEG in terms of tDCS-induced electrical artifacts, PSD difference was calculated for each frequency by subtracting PSDs estimated during non-stimulation (0 μA) from those measured during tDCS (500, 1000, 1500, and 2000 μA). As only difference between non-stimulation and tDCS condition was of interest, absolute values of PSD differences were taken for each frequency. To check whether PSD differences between non-stimulation and tDCS conditions (500, 1000, 1500, and 2000 μA) are statistically different, repeated measures (RM) analysis of variance (ANOVA) was performed. Because there was no significant difference between four conditions (500 vs. 1000 vs. 1500 vs. 2000 μA), no multiple comparison was performed (Figs 3 and 4). Also, we estimated correlation coefficients between the PSDs of non-stimulation and tDCS condition to investigate how much PSDs estimated during non-stimulation are retained or changed during tDCS.

3. Results

Figure 3a and b present the mean PSDs of two EEG electrodes ((a) POz and (b) Oz) of all subjects during EO with respect to current intensity (0, 500, 1000, 1500, and 2000 μA). As is well documented,

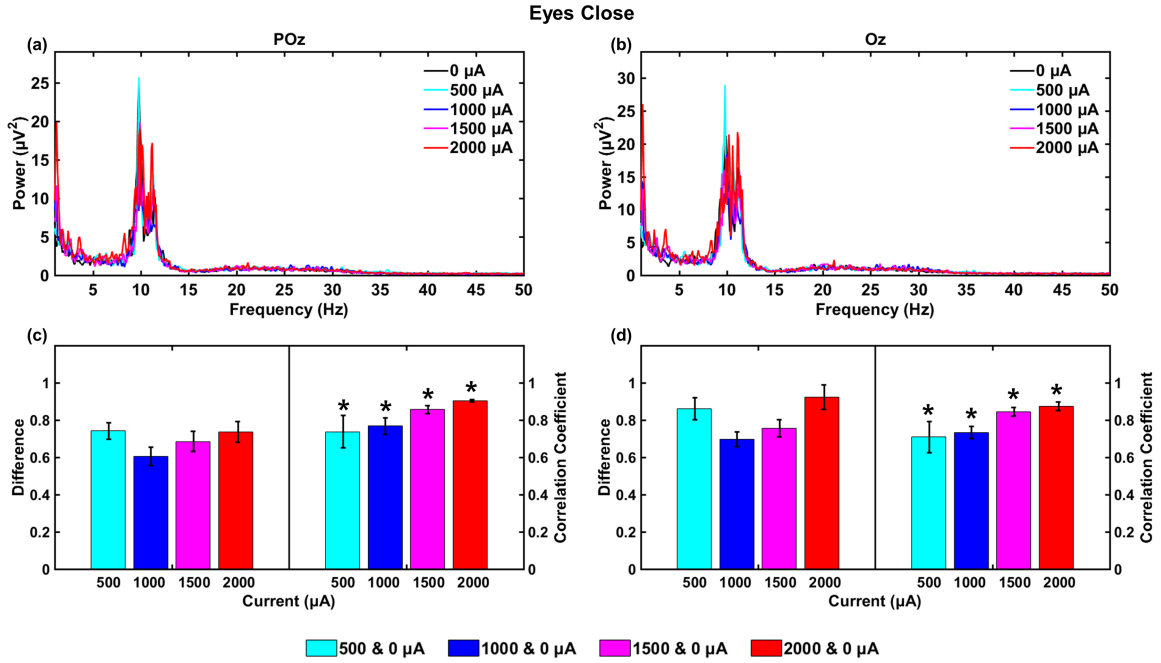

Fig. 4. Mean EEG-PSDs estimated during eyes closed condition for (a) POz and (b) Oz in terms of current intensity, and PSD differences and correlation coefficients between non-stimulation (0 μA) and tDCS condition (500, 1000, 1500, and 2000 μA) for (c) POz and (d) Oz. No significant difference is found between PSD differences (RM-ANOVA: $p > 0.05$), and the PSD of non-stimulation condition is significantly correlated with those of tDCS conditions (Pearson correlation: $p < 0.05$). An asterisk represents statistical significance ($p < 0.05$). The vertical bars indicate the standard errors of estimated correlation coefficients for each subject.

higher PSDs are observed in low frequencies (e.g., δ-band), and PSD significantly and continuously decreases with a small peak in α-band (8–13 Hz), regardless of current intensity, for both POz and Oz. PSD differences and their correlation coefficients for both electrodes are presented in Fig. 3c and d, respectively. The degree of PSD differences between non-stimulation and tDCS condition is almost consistent across all conditions; no increasing PSD difference is observed as current intensity increases. A statistical test result also confirmed this trend that there is no statistically significant difference between all conditions in terms of PSD difference (RM-ANOVA: $p > 0.05$). Most importantly, the PSD of non-stimulation condition is highly correlated with those of all tDCS conditions (Pearson correlation: $p < 0.05$), meaning that EEG were not significantly affected by tDCS.

Figure 4 shows the same results as Fig. 3, but for mean EEG-PSDs during EC. Significant PSD increase is observed in α-band for both electrodes (Fig. 4a and b), which is a well-known neurophysiological phenomenon observed during EC as compared with EO [17]. Except the significant increase in α-power, a similar trend is observed as compared to those shown in Fig. 3 in terms of PSD differences and correlation coefficients between non-stimulation and tDCS condition. The degree of PSD differences between non-stimulation and tDCS condition is not significantly different across current intensities (RM-ANOVA: $p > 0.05$), but correlation coefficients between non-stimulation and tDCS condition are significantly high (Pearson correlation: $p < 0.05$), as shown in Fig. 4c and d, respectively.

Tables 1 and 2 summarize all individual results presented in Fig. 3c and d and Fig. 4c and d for POz and Oz, respectively. The mean PSD differences of EO and EC condition mostly ranges from about 0.6 to 0.7, and mean correlation coefficients are more than 0.7 for all comparison cases.

Table 1
Individual EEG-PSD differences and correlation coefficients between non-stimulation and tDCS conditions for eyes open and eyes closed condition at Oz. The values in parentheses indicate the standard errors

Subject	Current intensity (μA)	Eyes open		Eyes closed	
		PSD difference	Correlation coefficient	PSD difference	Correlation coefficient
S1	500	0.62 (0.08)	0.79	0.63 (0.05)	0.53
	1000	0.87 (0.16)	0.92	0.67 (0.06)	0.69
	1500	0.60 (0.06)	0.94	0.84 (0.09)	0.80
	2000	0.71 (0.11)	0.89	0.81 (0.09)	0.84
S2	500	0.88 (0.12)	0.91	1.02 (0.17)	0.92
	1000	0.71 (0.11)	0.89	0.78 (0.11)	0.84
	1500	0.86 (0.16)	0.80	0.77 (0.10)	0.90
	2000	0.73 (0.14)	0.76	1.07 (0.17)	0.94
S3	500	0.60 (0.10)	0.88	0.76 (0.07)	0.57
	1000	0.47 (0.05)	0.88	0.51 (0.05)	0.68
	1500	0.53 (0.07)	0.87	0.46 (0.05)	0.81
	2000	0.60 (0.11)	0.90	0.60 (0.06)	0.84
S4	500	0.71 (0.09)	0.84	1.04 (0.16)	0.81
	1000	0.83 (0.15)	0.84	0.83 (0.10)	0.72
	1500	0.50 (0.11)	0.85	0.97 (0.13)	0.87
	2000	1.74 (0.16)	0.95	1.21 (0.18)	0.88
Mean	500	0.71 (0.05)	0.85	0.86 (0.06)	0.71
	1000	0.72 (0.06)	0.88	0.70 (0.04)	0.73
	1500	0.65 (0.05)	0.86	0.76 (0.05)	0.84
	2000	0.79 (0.06)	0.87	0.92 (0.07)	0.90

Table 2
Individual EEG-PSD differences and correlation coefficients between non-stimulation and tDCS conditions for eyes open and eyes closed condition at POz. The values in parentheses indicate the standard errors

Subject	Current intensity (μA)	Eyes open		Eyes closed	
		PSD difference	Correlation coefficient	PSD difference	Correlation coefficient
S1	500	0.52 (0.07)	0.79	0.50 (0.04)	0.51
	1000	0.69 (0.12)	0.89	0.58 (0.05)	0.71
	1500	0.53 (0.06)	0.91	0.67 (0.07)	0.81
	2000	0.89 (0.10)	0.88	0.71 (0.09)	0.89
S2	500	0.69 (0.07)	0.90	0.66 (0.09)	0.91
	1000	0.44 (0.07)	0.89	0.45 (0.05)	0.88
	1500	0.53 (0.08)	0.82	0.57 (0.07)	0.89
	2000	0.54 (0.09)	0.79	0.76 (0.13)	0.90
S3	500	0.53 (0.08)	0.88	0.64 (0.04)	0.64
	1000	0.43 (0.04)	0.87	0.27 (0.03)	0.66
	1500	0.34 (0.06)	0.88	0.29 (0.03)	0.82
	2000	0.41 (0.09)	0.89	0.39 (0.04)	0.91
S4	500	0.89 (0.06)	0.84	1.16 (0.14)	0.89
	1000	0.96 (0.09)	0.90	1.11 (0.19)	0.82
	1500	1.00 (0.08)	0.92	1.21 (0.19)	0.90
	2000	1.02 (0.08)	0.95	1.08 (0.16)	0.92
Mean	500	0.66 (0.03)	0.85	0.74 (0.04)	0.74
	1000	0.63 (0.04)	0.89	0.61 (0.05)	0.77
	1500	0.60 (0.03)	0.88	0.68 (0.05)	0.86
	2000	0.64 (0.04)	0.88	0.73 (0.06)	0.90

4. Discussion

Simultaneous measurement of brain activity is necessary during tDCS in order to investigate the accurate impact of tDCS on the brain, but which has been generally hindered when using EEG as a neuroimaging modality due to the inflow of significant tDCS-induced electrical artifacts. Most previous studies conducted based on a simultaneous EEG-tDCS paradigm reported that significant PSD increase is observed for all frequency bands during tDCS as compared to non-stimulation condition [12–16]. In this study, we introduced a current-limiter-based tDCS device to mitigate the impact of tDCS-induced artifacts on EEG. To demonstrate the feasibility of the developed current-limiter-based tDCS device, we performed simultaneous EEG-tDCS experiments, where resting-state EEG was measured during tDCS with different current intensities (0, 500, 1000, 1500, and 2000 μA).

Eight electrodes were attached to measure EEGs during tDCS, but as aforementioned only two electrodes, POz and Oz, were used for data analysis due to the connection issue between tDCS and EEG electrodes via saline solution. It would be better to use all EEG electrodes for data analysis to more strongly demonstrate the feasibility of our tDCS device based on current limiters in terms of tDCS-induced electrical artifacts. Thus, using only two electrodes is one limitation of this study. However, because the brain areas related to the selected two electrodes were also affected by tDCS, as shown in Fig. 2b, our results derived from the selected two electrodes would be still valid. On the other hand, we did not introduce a specific ramped-up time, but about 5–7 s was automatically introduced for ramped-up due to the nature of scalp conduction. To provide more stable current for tDCS, we will revise our tDCS device by introducing a particular ramped-up time in the near future.

The mean PSD differences between non-stimulation and tDCS condition were between 0.6 and 0.7 for most cases, regardless of current intensity. Considering that PSD values were observed with up to more than 25 (Fig. 4a and b), it can be thought that the PSD differences between 0.6 and 0.7 is not significantly high. In particular, even though a current intensity increases, no significant changes in PSD were observed (Figs 3a and b and 4a and b), meaning that our developed tDCS device can provide stable current for different intensities due to current limiters. Also, all correlation tests presented statistically high relationship between the PSDs of non-stimulation and tDCS conditions ($p < 0.05$), showing that the characteristics of PSDs do not significantly change even during tDCS. The mentioned results could demonstrate the feasibility of using our developed tDCS device based on current limiter when investigating the impact of tDCS based on electrical brain activity (EEG) because little tDCS-induced electrical artifacts are introduced.

In most previous tDCS studies that investigated the impact of tDCS on EEG, after-effects of tDCS were generally investigated by comparing EEG measured before and after tDCS [12–16]. Because considerable tDCS-induced electrical artifacts are generally introduced to ongoing EEG during tDCS, tDCS impact could not be accurately explored during tDCS. As demonstrated in this study, because our tDCS device based on current limiter does not introduce significant artifact inflow, the impact of tDCS on EEGs can be investigated more accurately than previous studies that only investigated after-effects of tDCS [12–16]. For example, resting-state EEGs can be measured before, during, and after tDCS, and thereby the impact of tDCS can be more precisely investigated using our developed tDCS device.

Acknowledgments

This research was supported by the Original Technology Research for Brain Science through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science & Technology

(2015M3C7A1031969 and 2019M3C7A1031278), by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI) funded by the Ministry of Health & Welfare (HI17C1501), and by the BB21 + Project in 2019. This research was also supported the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2019R1I1A3A01060732), the Ministry of Trade Industry & Energy (MOTIE, Korea), the Ministry of Science & ICT (MSIT, Korea), and the Ministry of Health & Welfare (MOHW, Korea), the Technology Development Program for AI-Bio-Robot-Medicine Convergence (20001650).

Conflict of interest

None to report.

References

[1] Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J Physiol. 2000; 527(3): 633-9.
[2] Schlaug G, Vijay R, Dinesh N. Transcranial direct current stimulation in stroke recovery. Arch Neurol. 2008; 65(12): 1571-6.
[3] Donde C, Nicholas HN, Pierre AG. The Impact of Transcranial Direct Current Stimulation (tDCS) on Bipolar Depression, Mania, and Euthymia: a Systematic Review of Preliminary Data. Psychiatr Q. 2018; 89(4): 855-67.
[4] Benninger DH, Lomarev M, Lopez, G, Wassermann EM, Li X, Considine E, Hallett M. Transcranial direct current stimulation for the treatment of Parkinson's disease. J Neurol Neurosurg Psychiatry. 2010; 81(10): 1105-11.
[5] Loo CK, Alonzo A, Martin D, Mitchell PB, Galvez V, Sachdev P. Transcranial direct current stimulation for depression: 3-week, randomized, sham-controlled trial. Br J Psychiatry. 2012; 200(1): 52-9.
[6] Fregni F, Boggio PS, Mansur CG, Wagner T, Ferreira MJL, Lima MC. Transcranial direct current stimulation of the unaffected hemisphere in stroke patients. Neuroreport. 2005; 16(14): 1551-5.
[7] San-juan D, Morales-Quezada L, Garduño AJO, Alonso-Vanegas M, González-Aragón MF, Espinoza López DAE. Transcranial direct current stimulation in epilepsy. Brain Stimul. 2015; 8(3): 455-64.
[8] Woods AJ, Antal A, Bikson M, Boggio PS, Brunoni AR, Celnik P. A technical guide to tDCS, and related non-invasive brain stimulation tools. Clin Neurophysiol. 2016; 127(2): 1031-48.
[9] Esterer S, Abbott L, Magazzini L, McGonigle D. Concurrent tDCS-NIRS-MEG: Insights from a technical pilot. Brain Stimul. 2019; 12(2): 497.
[10] Han CH, Song H, Kang YG, Kim BM, Im CH. Hemodynamic responses in rat brain during transcranial direct current stimulation: a functional near-infrared spectroscopy study. Biomed Opt Express. 2014; 5(6): 1812-21.
[11] Meinzer M, Lindenberg R, Darkow R, Ulm L, Copland D, Flöel A. Transcranial direct current stimulation and simultaneous functional magnetic resonance imaging. J Vis Exp. 2014; 86: e51730.
[12] Faria P, Fregni F, Sebastião F, Dias AI, Leal A. Feasibility of focal transcranial DC polarization with simultaneous EEG recording: preliminary assessment in healthy subjects and human epilepsy. Epilepsy Behav. 2012; 25(3): 417-25.
[13] Schestatsky P, Morales-Quezada L, Fregni F. Simultaneous EEG monitoring during transcranial direct current stimulation. J Vis Exp. 2013; 76: 50426.
[14] Roy A, Baxter B, He B. High-definition transcranial direct current stimulation induces both acute and persistent changes in broadband cortical synchronization: a simultaneous tDCS-EEG Study. IEEE Trans Biomed Eng. 2014; 61(7): 1967-78.
[15] Soekadar SR, Witkowski M, Cossio EG, Birbaumer N, Cohen L. Learned EEG-based brain self-regulation of motor-related oscillations during application of transcranial electric brain stimulation: feasibility and limitations. Front. Behav. Neurosci. 2014; 8: 93.
[16] Boonstra TW, Nikolin S, Meisener AC, Martin DM, Loo CK. Change in mean frequency of resting-state electroencephalography after transcranial direct current stimulation. Front Hum Neurosci. 2016; 10: 270.
[17] Barry RJ, Clarke AR, Johnstone SJ, Magee CA, Rushby JA. EEG differences between eyes-closed and eyes-open resting conditions. Clin Neurophysiol. 2007; 118(12): 2765-73.