論　文　内　容　要　旨

Transcranial direct current stimulation effects on hand sensibility as measured by an objective quantitative analysis device: A randomized single-blind sham-control crossover clinical trial

（経頭蓋直流電気刺激が手指感覚に及ぼす影響 ：定量的感覚測定装置を使用したクロスオーバー盲検無作為化臨床試験 ）

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Abstract

Background: Abnormal somatosensory perception is common in central and peripheral neurological disorders. The most prevalent and debilitating upper limb mononeuropathy, carpal tunnel syndrome (CTS), can lead to central sensitization and abnormal neuroplasticity, exacerbating treatment-resistance. Studies show that noninvasive neuromodulation techniques such as transcranial direct current stimulation (tDCS) can modulate somatosensory processing, but optimum parameters for tDCS effects on hand sensibility remain in question. To aid future CTS studies we wanted to better elucidate tDCS-induced neuroplasticity and best parameters to raise current perception threshold (CPT), quantitatively measured in a quick, noninvasive and reproducible way by PainVision PS-2100. **Objective:** We aimed to test the effects of anodal (atDCS) and cathodal tDCS (ctDCS) compared to sham tDCS (stDCS) of primary motor (M1) and somatosensory (S1) cortices on hand sensibility measured by an objective quantitative analysis device (PainVision) in healthy subjects. **Methods:** In this randomized, single-blind, sham-controlled crossover study, thirty-five healthy volunteers were assessed for eligibility. Three were screened out (2 were left-handed, 1 had skin lesions of both hands) and 2 dropped out prior to randomization for personal reasons. Thirty healthy, right-handed participants received six sessions of tDCS over six weeks: three sessions of tDCS over M1 with three different modes (anodal, cathodal and sham) and another three sessions over S1. Active electrode (anode or cathode) was centered over the left M1 or S1 depending on randomization order. Reference electrode was placed over the contralateral supraorbital area. M1 was marked 5cm below the vertex, roughly at C3 position (10–20 International EEG system); S1 was marked 2cm posterior to M1. Current perception threshold (CPT) was assessed using an objective quantitative analysis device. It raises the electric current at a steady rate until the participant first perceives sensation and presses a stop button with the thumb of non-dominant hand. STh here is measured by CPT, defined as the lowest electric current at which the sensation is perceived. CPT measured three times at each timepoint, and the results averaged offline to provide the final CPT value for each timepoint – before (baseline), immediately after (T0) and 30min after (T30) each tDCS session. The study followed Ethical Standards of Declaration of Helsinki and was approved by Research Ethics Committee of Biomedical and Health Sciences Institute, Hiroshima University. Informed consent was obtained from all participants after explaining study objectives, methods, and safety. **Analysis:** Intention-to-treat (ITT) approach was used for all analyses; last observation carried forward (LOCF) was implemented for missing data. We used the Shapiro-Wilk test to assess normality.

Quantitative continuous data was expressed as mean and standard deviation (SD). Dichotomous baseline data including gender was expressed as frequency and percentage (%). Analysis of variance (ANOVA) was used to detect confounding by carryover effect at baseline for each session. We used repeated-measures ANOVA for CPT comparisons across 3 timepoints (baseline, T0, T30) for each tDCS condition (a-, c- or stDCS) and each site (S1 or M1); post hoc tests were done with Bonferroni correction. We used ANOVA to compare CPT results at each time-point for each tDCS condition (anodal, cathodal or sham) for each site (S1 or M1). Mauchly's test assessed the sphericity assumption for repeated measures ANOVA. Greenhouse–Geisser corrected values were used when sphericity was violated. Z-score was calculated by: Z= [mean post CPT – mean baseline]/SD baseline. Effect size (ES) was determined by: Cohen's d = (mean post CPT – mean pre-CPT)／√ (((n1-1) SD12 + (n1-1) SD22)／(n1+n2-2)), where n=sample size. P-value <0.05 was considered significant. Analyses were done by IBM SPSS 23. **Results:** Thirty healthy, right-handed participants [16 females (53.3%), 14 males (46.7%)] (mean age: 26±4years, range: 21-33 years) were randomized. Our results showed that there were no significant baseline differences between a-, c- and stDCS, suggesting there was no carryover effect at baseline CPT assessments before each of M1 and S1 tDCS. Both atDCS and ctDCS of S1 and M1 significantly increased CPT. M1 ctDCS at T30 had the greatest effect of all M1 and S1 stimulation conditions (mean difference: 32.94%, Z: 3.12, ES: 1.82, p<0.0001). The largest effect at S1 was for atDCS at T30 (mean difference: 29.87%, Z: 2.53, ES: 1.72, p<0.0001). **Conclusions:** This study demonstrated CPT modulation in healthy subjects via atDCS, especially through S1, and ctDCS, especially through M1. Based on our results, ctDCS at M1 may be the optimum stimulation paradigm to modulate hand sensibility and this may be used to guide tDCS protocols for clinical studies in sensory disorders.

Keywords: *Current perception threshold; sensory threshold; neuromodulation; noninvasive brain stimulation.*