別記様式第 6 号（第 16 条第 3 項，第 25 条第 3 項関係）

論 文 審 査 の 結 果 の 要 旨

博士の専攻分野の名称	博士（　保健学　　）	氏名	Hanan Ibrahim Zehry Abdelrahman
学 位 授 与 の 条 件	学位規則第 4 条第 1・2 項該当		

論　文　題　目

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）

論文審査担当者

主　　査　　教　授　　桐本　光　　印

審査委員　　教　授　　浦川　将

審査委員　　教　授　　中西　一義

〔論文審査の結果の要旨〕

Peripheral nerve disorders such as entrapment neuropathy or nerve injury in the hand can lead to central sensitization and abnormal neuroplasticity, exacerbating treatment-resistance. One of the ways to solve this central nervous disorder is using the neuromodulation technique. Studies show that transcranial direct current stimulation (tDCS) as one of noninvasive neuromodulation techniques can modulate somatosensory processing, but optimum parameters for tDCS effects on hand sensibility remain in question. The purpose of this study is to elucidate the suitable parameters of tDCS-induced neuroplasticity quantitatively. Specifically, applicants hypothesized that anodal or cathodal tDCS on the primary motor (M1) or somatosensory (S1) would modulate current perception threshold (CPT) more than sham tDCS.

In this randomized, single-blind, sham-controlled crossover study, Applicants assessed the modulatory effects of a single session of tDCS over left S1/M1 cortical regions as measured by CPT. The study followed Ethical Standards of Declaration of Helsinki and was approved by Research Ethics Committee of Hiroshima University Hospital. Thirty healthy, right-handed participants [16 females (53.3%), 14 males (46.7%)] (mean age: 26±4years, range: 21-33 years) received six sessions of tDCS over six weeks: three sessions of tDCS over M1 with three different modes (anodal(a), cathodal(c) and sham(s)) 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. All tDCS sessions lasted 20 min, including 10 s of ramping up and down at the beginning and end to maintain participant blinding. The current was maintained at 2 mA throughout atDCS and ctDCS, and at 0 mA between ramping periods during stDCS. All subjects were crossed over to six tDCS conditions on a weekly basis. CPT was assessed in a quick, noninvasive, and reproducible way using an objective quantitative analysis device (Pain Vision PS-2100). 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. It can measure the sensory and pain perception threshold quantitatively, and sensory perception threshold 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. I 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). Analyses were done by IBM SPSS 23, and p-value <0.05 was considered significant.

There were no significant baseline differences among atDCS, ctDCS and stDCS, suggesting that 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, $p<0.0001$).

This study found that S1 a- and ctDCS significantly increased CPT compared to baseline immediately and 30min after stimulation. For M1, CPT rose immediately after ctDCS and continued to rise for 30min, but atDCS increased CPT only 30min later. These findings suggest that one session of S1 atDCS and M1 ctDCS significantly increased CPT and thus modulated hand sensibility. Any tDCS parameter alterations may change neural networks modulated. It is important to recognize that the sensorimotor cortex is considered morphologically and functionally distinct and hand movements activate overlapping areas within M1 and S1. This implies overlap between M1 and S1 modulation by tDCS and may explain why CPT modulation was in the same direction (increased) after M1 and S1 tDCS. Also, though maximum current would be under the active electrode, S1 tDCS likely modulates M1 (which lies in the direction of current flow between S1 and right supraorbital reference) to a greater degree than S1 (which is posterior to M1) would be modulated by M1 tDCS. This potentially greater involvement of somatosensory cortex may explain why our results showed atDCS modulation earlier at S1 than M1.

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.

Based on these results, this study provides the effective protocol of tDCS application for hand sensibility modulation, and in the field of rehabilitation, its use has a potential of future treatment method for peripheral nerve disorders, especially in the hand. Therefore, all the committee members admitted that this dissertation is of sufficient value to confer the Doctor of Philosophy in Health Sciences to Hanan Ibrahim Zehry Abdelrahman.