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Improvement of visual scanning after DC brain polarization of parietal cortex in stroke patients with spatial neglect

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ABSTRACT

Previous studies have demonstrated that transcranial direct current (DC) brain polarization can modulate cortical excitability in the human brain. We investigated the effect of anodal DC brain polarization of right parietal cortex on visuospatial scanning in subacute stroke patients with spatial neglect. The patients underwent two neglect tests – figure cancellation and line bisection – before and immediately after anodal DC or sham in a double-blind protocol. Anodal DC was applied to the scalp over the right posterior parietal cortex (PPC) with an intensity of 2.0 mA for 20 min. Anodal DC brain polarization, but not sham, led to significant improvement in the both neglect tests. These results document a beneficial effect of DC brain polarization on neglect.

Many stroke patients with a nondominant parietal lobe lesion have visuospatial neglect of hemispace. This hemispatial neglect significantly contributes to disability after stroke because it has a negative impact on self-care, mobility, learning, and safety awareness in itself and has been found to be associated with poor functional recovery from stroke [25]. Although neglect as a major source of long-term disability after stroke, there are few effective therapeutic intervention for this complex and multifactorial syndrome. Noninvasive brain stimulation using magnetic or electrical instrument has been investigated as a mean of modulating cortical excitability. Transcranial direct current (DC) brain polarization, continuously applying a weak DC on the scalp is an effective method to manipulate human brain excitability [18,23]. The effect of DC brain polarization varies depending on the polarity of the electrode. It is known that anodal polarization increases cortical excitability, while cathodal polarization decreases it [18,19]. Recent human studies have demonstrated that anodal polarization increases the excitability of the motor, visual, and prefrontal cortices, and improve motor skill [3], working memory [8,20], and verbal fluency [11]. To our knowledge, there has been no report of the effects of DC brain polarization on neglect symptom in stroke patients.

In the present study, we applied 2.0 mA anodal DC brain polarization to the right posterior parietal cortex (PPC) for 20 min in stroke patients with visual neglect to investigate the effects of DC brain polarization on performance of neglect tasks.

Fifteen subacute stroke patients with neglect (10 men and 5 women; mean age 62.1 ± 8.8 years; postonet duration 29–99 days) were enrolled in the study (Table 1). All patients were right-handed and had a lesion in the right hemisphere. We excluded subjects who had metal in the cranial cavity or calvarium or skin lesions in the area of electrode. Patients who had uncontrolled medical problems and severe cognitive impairments were also excluded. The institutional review board of Chonbuk National University Hospital approved the study protocol, and written informed consent was obtained from all subjects before participation.

This study was designed as a double-blind, crossover, sham-controlled experiment. All of patients participated in both anodal and sham DC brain polarization with counterbalanced and randomized order and 48 h interval between two sessions. DC current delivered by a battery-powered device (Phoresor II Auto Model PM850, IOMED, USA), which is using a pair of saline-soaked surface sponge electrodes (5 cm × 5 cm). For anodal stimulation of the right PPC, the anode was placed over P4 in the international 10–20 EEG system for electrode placement and the cathode was placed over left supraorbital area. For active treatment, the current was

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Table 1
Demographic and clinical characteristics of 15 patients.

Patients	Sex	Age (year)	Etiology	Lesions	POD (days)	Baseline score		
						LB	LSC	SUC
1	F	67	Infarction	Pons	83	5.28	1	10
2	M	60	Infarction	F, T, P	48	56.00	37	44
3	M	73	Infarction	F, P	29	11.50	13	32
4	M	71	Hemorrhage	F	40	6.56	3	3
5	M	65	Infarction	F, T, P	46	9.76	4	6
6	F	69	Hemorrhage	F, BG	35	4.40	5	6
7	M	52	Infarction	F	38	16.20	8	37
8	M	58	Infarction	F, T, P	43	39.98	42	52
9	M	65	Infarction	F, P, O	38	31.95	17	37
10	F	59	Infarction	F, P	43	15.00	57	57
11	F	66	Hemorrhage	BG	50	20.11	17	23
12	M	62	Infarction	BG, Th	39	14.34	18	13
13	M	46	Hemorrhage	BG	31	9.47	9	6
14	M	44	Hemorrhage	BG	99	5.85	12	5
15	F	71	Infarction	BG	39	21.00	21	29

F, frontal lobe; T, temporal lobe; P, parietal lobe; BG, basal ganglia; O, occipital lobe; Th, thalamus; POD, postonset duration; LB, line-bisection test; LSC, letter-structured cancellation test; SUC, shape-unstructured cancellation test; LB was scored by percents deviation score; LSC and SUC were scored by the number of omission.

set at 2.0 mA and turned on for 20 min. For sham, the current was delivered for 10 s and then turned off.

Patients underwent three conventional neglect tests before and immediately after DC brain polarization. These were the line bisection test [26] and two different cancellation tests; the letter-structured cancellation test and the shape-unstructured cancellation test constructed by Mesulam [14]. The line bisection test consists of 20 lines of different sizes on an A4 size paper: six are centered to the left of the midline, six to the right of midline, six in the center, and a top and bottom line used for instruction. The examiner sat in front of the patients and asked the patients to draw a line through each line on the paper as close to its center as possible. To score the line bisection test, a percents deviation (PD) score was obtained by the formula: (measured left half − true half/true half) × 100. The letter-structured cancellation test was composed of 14 rows and 16 columns of Korean characters, randomly interspersed with a target letter. In the shape-unstructured cancellation test, 60 target shapes were scattered among 312 distractors symbols in a pseudo-random manner on the paper. Patients were asked to circle all the targets they saw with no time limit. The number of omissions and the completion time were recorded.

We performed repeated measures ANOVA with intervention (real and sham) and time (pre and post) and assessed whether the interaction term intervention vs. time was significant. When appropriate, post hoc comparisons were carried out using Tukey test. Then correlation test was performed to evaluate whether there was a correlation between test performance changes after real DC and individual baseline performance using Pearson's correlations. Finally, we performed paired *t*-test to assess the learning effect—we compared the baseline (pre) scores of the first session and the second session for each test. The patients and examiner performing neglect tests were blind to the type of intervention (real or sham DC), which was operated by a separate investigator who did not participate in neglect test or data analysis.

Repeated measures ANOVA revealed that the interaction term intervention vs. time was significant on both PD scores of the line bisection test ($F = 6.91$, $P = 0.014$) and the number of omissions in the shape-unstructured cancellation test ($F = 5.89$, $P = 0.022$) (Fig. 1). Post hoc analysis showed a significant improvement of PD score (from 18.55 ± 10.95% at pre to 15.03 ± 10.40% post-DC polarization, $P < 0.05$) and the number of omissions (from 23.40 ± 19.20 to 19.93 ± 18.33, $P < 0.05$) after real DC polarization only. In the letter-structured cancellation test, the interaction term intervention vs. time was not significant. There was no significant correlation between test performance changes after real DC and baseline performance ($r = -0.366$, $P = 0.18$ in the line bisection test; $r = -0.346$, $P = 0.206$ in the shape-unstructured cancellation test; Fig. 2). In the analysis of learning effect, there was no significant difference across the first and second baseline conditions in three tests (17.82 ± 14.56 at the first session and 17.74 ± 10.99 at the second session in the line bisection test; 24.00 ± 18.50 at the first session and 23.73 ± 17.43 at the second session in the shape-unstructured cancellation test; 17.60 ± 16.01 at the first session and 14.60 ± 14.80 at the second session in the letter-structured cancellation test).

Our results show that visual neglect is improved by 20 min of anodal DC polarization over the right PPC in stroke patients. The percent of leftward deviation and the number of omission were decreased in neglect tests immediately after DC brain polarization compared to baseline. To our knowledge, this is the first study to demonstrate the effects of DC brain polarization on visuospatial perception. It is well known that DC brain polarization can induce a polarity-dependent excitability shift of stimulated brain areas, which has a modulatory effect on behavioral outcomes [18,19]. In particular, DC polarization with anode is known to increase excitability of underlying local cortex. Therefore, improvement of visuospatial attention is likely due to enhanced local excitability in the right PPC cortex in our study. In previous studies, therapeutic effects of anodal DC polarization have been demonstrated for a variety of conditions in stroke patients. Clinical trials of DC polarization, however, so far have been conducted regarding motor deficits, memory impairments or language disturbances [4,10,15,27].

Heilman et al. have defined hemispatial neglect as a failure to report, response, or orient to novel or meaningful stimuli presented to the side opposite a brain lesion [9]. Although neglect

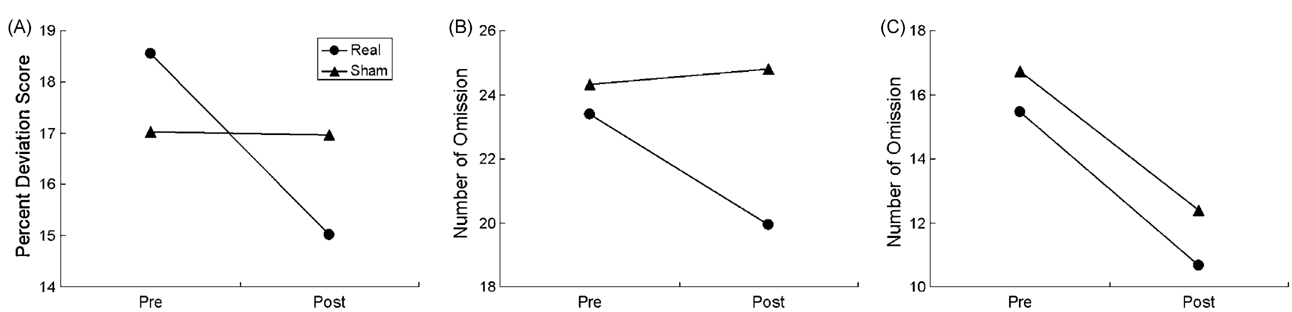

Fig. 1. Effects of DC brain polarization on the line-bisection test (A), the shape-unstructured cancellation test (B), and the letter-structured cancellation test (C). Repeated measures ANOVA showed a significant interaction term intervention (real and sham) × time (pre and post) was significant in the line bisection test and the shape-unstructured cancellation test and post hoc analysis revealed a significant improvement after real DC polarization only in these two test.