Short-Term Anomia Training and Electrical Brain Stimulation

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Background and Purpose—Language training success in chronic aphasia remains only moderate. Electric brain stimulation may be a viable way to enhance treatment efficacy.

Methods—In a randomized, double-blind, sham-controlled crossover trial, we assessed if anodal transcranial direct current stimulation compared to cathodal transcranial direct current stimulation and sham stimulation over the right temporo-parietal cortex would improve the success of short-term high-frequency anomia training. Twelve chronic poststroke aphasia patients were studied. Naming outcome was assessed after training and 2 weeks later.

Results—All training conditions led to a significant increase in naming ability, which was retained for at least 2 weeks after the end of the training. Application of anodal transcranial direct current stimulation significantly enhanced the overall training effect compared to sham stimulation. Baseline naming ability significantly predicted anodal transcranial direct current stimulation effects.

Conclusions—Anodal transcranial direct current stimulation applied over the nonlanguage dominant hemisphere can enhance language training outcome in chronic aphasia.

Clinical Trial Registration—URL: www.clinicaltrials.gov/. Unique identifier: NCT00822068.

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Key Words: anomia ■ neurorehabilitation ■ transcranial direct current stimulation

The most frequent symptom in poststroke aphasia is impaired word retrieval (anomia). Training at a sufficient intensity may significantly improve aphasic symptoms, but chronic anomia is relatively resistant to intervention and training adjuvant therapies need to be devised.[1]

Excitatory (anodal) transcranial direct current stimulation over left hemisphere areas has been shown to facilitate language learning in healthy subjects and aphasia patients.[1,2] However, the exact areas that contribute to language relearning success are still controversial,[3] and it remains unclear which brain areas should be facilitated. A recent study implicated right temporo-parietal areas with anomia treatment success.[4] Thus, we explored whether anodal transcranial direct current stimulation of this area can enhance the outcome of high-frequency short-term anomia training. In a randomized, double-blind crossover design, patients also participated in inhibitory (cathodal) transcranial direct current stimulation and placebo stimulation (sham) sessions. We hypothesized that anodal transcranial direct current stimulation would lead to more pronounced treatment gains compared to training under cathodal or sham stimulations.

Materials and Methods

Twelve patients with chronic anomia because of a first-time single left hemisphere ischemic stroke participated. All patients completed a baseline neurological examination and standardized language testing. Supplemental Table I (http://stroke.ahajournals.org) summarizes demographic and clinical sample characteristics. Supplemental Figure I (http://stroke.ahajournals.org) shows the lesion location of the patients. The local ethics committee approved the study and written informed consent was obtained from all patients.

For the anomia training, 45 pictures depicting common objects were individually selected for each patient ("trained objects"). These objects had been named incorrectly 3 times during 3 baseline runs comprising a standardized set of 344 object pictures. The 45 objects were divided into 3 sets of 15 objects matched for several linguistic variables. Patients took part in 3 consecutive training phases, each with a different stimulation condition (anodal or cathodal transcranial direct current stimulation and sham; sequence randomized across patients). During each phase, 1 of the sets was trained. Between stimulation conditions, an interval of 3 weeks was maintained (Figure 1A).

For each condition, patients received 2 hours of daily computer-assisted naming therapy across 3 consecutive days. Training involved a decreasing cueing hierarchy with 5 difficulty levels that have been shown to be highly effective to improve anomia.[4] Short-term and long-term treatment effects for the 3 conditions were

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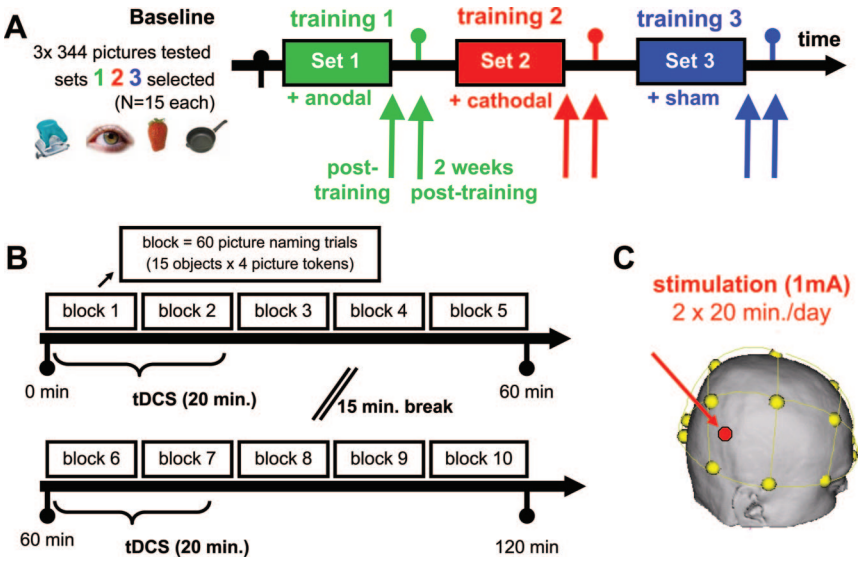

Figure 1. A, Subjects participated in 3 training and stimulation sessions. Post-testing was performed immediately after training and 2 weeks afterward. **B**, A training session. **C**, Transcranial direct current stimulation (tDCS) site is shown in red on head (yellow dots indicate standard 10- to 20-electroencephalogram system).

assessed during separate testing sessions in the afternoon of the third training day and 2 weeks after training. During these assessments, the 15 trained object names were probed 4 times in random order without cues. To increase the sensitivity of the score, each correct response was scored as 1 point.

Transcranial direct current stimulation was applied over right temporo-parietal cortex according to Menke et al[4] and centered on Talairach coordinates 57/−30/3 (Figure 1C). Anodal or cathodal transcranial direct current stimulations (1 mA) were administered during the first 20 minutes of each training hour (Figure 1B). During sham stimulation, the current was turned off slowly after 30 seconds. Systolic blood pressure, heart rate, and subjective ratings of fatigue, discomfort, or pain were also assessed and no differences between the conditions were found

Statistical Analysis

Main outcome parameter was naming ability for trained objects immediately after training and 2 weeks later (% correct naming). A repeated-measures ANOVA with the factors stimulation and time (immediately after training, 2 weeks later) was conducted to determine short-term and long-term training outcome. Pearson correlations of age, time since stroke, lesion size, and anomia severity (Aachen Aphasia Test naming subtest; baseline naming ability of 344 objects) with training success (anodal or cathodal better than sham) were calculated with Bonferroni corrected significance levels.

Results

Patients significantly improved after the training from 0% correct naming responses at the baseline assessment to a mean of 83%±22% (Supplemental Table II, http://stroke.ahajournals.org) correct responses after training (effect size pooled across stimulation conditions and short-term and long-term training outcome assessments, Cohen $d=3.77$).

A repeated-measures ANOVA with the repeated factors stimulation and time yielded a main effect of stimulation ($F(2,22)=4.23$; $P=0.05$). The effect remained significant after exclusion of patient 8, with the greatest improvement using anodal transcranial direct current stimulation ($F(2,20)=5.77$; $P=0.01$). Because there were no significant effects for time, data for short-term and long-term retentions were pooled for subsequent analyses. Post hoc tests revealed better overall improvement in the anodal condition compared to sham stimulation (paired t test, $t(11)=2.54$; $P=0.03$; Figure 2). There was no significant difference between cathodal and sham stimulations ($t(11)=1.14$; $P=0.28$). An exploratory analysis conducted separately for the 2 post-training assessments yielded an additional significant effect for cathodal transcranial direct current stimulation immediately after training (see Supplemental Materials, http://stroke.ahajournals.org). Anodal transcranial direct current stimulation tended to produce more pronounced effects than cathodal transcranial direct current stimulation (T1: $t(11)=1.4$, $P=0.1$; T2: $t(11)=1.8$, $P=0.05$; pooled data: $t(11)=1.7$, $P=0.05$).

Treatment success for both transcranial direct current stimulation conditions was not associated with age, education, time since stroke, and lesion size. Poorer naming performance before treatment was associated with more pronounced improvement selectively during anodal transcranial direct current stimulation (Aachen Aphasia Test naming subtest; $r=-0.73$, $P=0.0067$; 344 objects: $r=-0.91$, $P<0.0001$).

Discussion

Our results demonstrate that short-term high-frequency anomia training has a large effect on naming ability in chronic aphasia that was maintained for at least 2 weeks. Anodal transcranial direct current stimulation, applied over the non-language dominant hemisphere, further improved language training outcome at both assessment points. Consistent with previous reports,[5] the beneficial effect of anodal transcranial direct current stimulation cannot be explained by unspecific arousal differences, because autonomic responses and mood ratings were comparable across stimulation conditions. Cathodal transcranial direct current stimulation, which reduces intracortical excitability in neurophysiological studies, resulted in a weaker and less consistent effect that was not maintained.

Only 1 group study so far addressed transcranial direct current stimulation effects on treatment-induced recovery and found improved naming ability after anodal transcranial direct current stimulation applied over perilesional areas in relatively well-recovered anomia patients.[1] However, in line

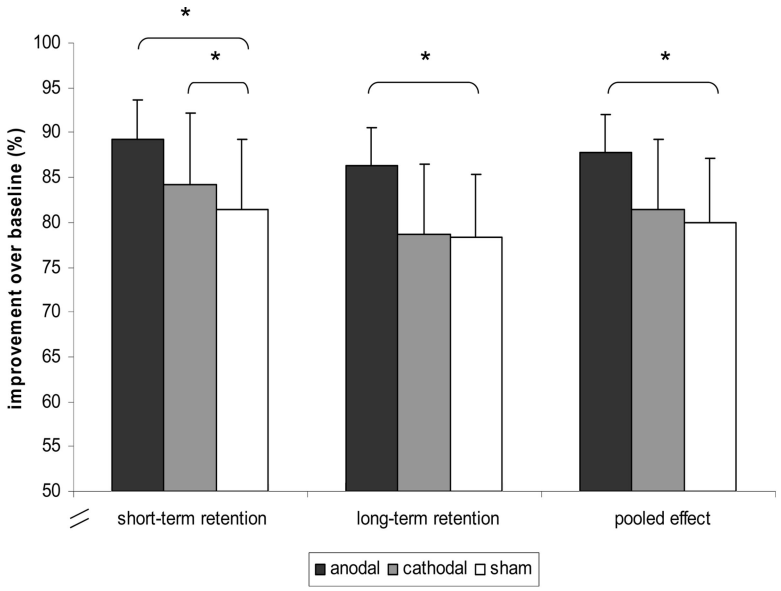

Figure 2. Effects of the 3 stimulation conditions (immediately after training, 2 weeks later, and pooled effects; means/standard error of the mean). *Significant differences between conditions at $P<0.05$.

with our own previous functional MRI study, upregulation of right hemispheric homologues of "classical" language regions might be crucial in aphasia patients with only partial recovery.[4] This hypothesis was supported by the fact that patients with more severe anomia showed more pronounced gains after anodal transcranial direct current stimulation, and at least 1 of the 2 more severely affected patients in the study by Baker et al[1] did not show improvement after left frontal stimulation. However, this does not preclude the possibility that patients with less severe aphasia in our study may have benefited from left-side stimulation as well. The question of whether left perilesional areas, or homologous areas of the right hemisphere, are more crucial for recovery can be addressed only in a study that directly compares anodal transcranial direct current stimulation effects of these areas.

Conclusions

In summary, transcranial direct current stimulation represents a promising new tool to enhance treatment effects, can easily be administered during behavioral treatment, and is less expensive and aversive than repetitive transcranial magnetic stimulation.[5] Based on these promising results, implications for clinical practice should be ascertained in larger multicenter trials. Moreover, the current study suggests that baseline naming ability, but not overall lesion size, significantly predicted anodal transcranial direct current stimulation effect. However, predictors for a favorable response to this type of stimulation remain to be more thoroughly delineated (see Supplemental Materials for additional Methods, Results, and Discussion, http://stroke.ahajournals.org).

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Disclosures

None.

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