# Noninvasive Brain Stimulation Improves Language Learning

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## Abstract

■ Anodal transcranial direct current stimulation (tDCS) is a reliable technique to improve motor learning. We here wanted to test its potential to enhance associative verbal learning, a skill crucial for both acquiring new languages in healthy individuals and for language reacquisition after stroke-induced aphasia. We applied tDCS (20 min, 1 mA) over the posterior part of the left peri-sylvian area of 19 young right-handed individuals while subjects acquired a miniature lexicon of 30 novel object names. Every subject participated in one session of anodal tDCS, one session of cathodal tDCS, and one sham session in a randomized and double-blinded design with three parallel versions of the miniature lexicon. Outcome measures were learning speed and learning success at the end of each session, and the transfer to the subjects' native language after the respective stimulation. With anodal stimulation, subjects showed faster and better associative learning as compared to sham stimulation. Mood ratings, reaction times, and response styles were comparable between stimulation conditions. Our results demonstrate that anodal tDCS is a promising technique to enhance language learning in healthy adults and may also have the potential to improve language reacquisition after stroke. ■

## INTRODUCTION

Transcranial direct current stimulation (tDCS) is a noninvasive, painless cortical stimulation technique (Nitsche & Paulus, 2000). Depending on the polarity of the current flow, brain excitability can either be increased (anodal tDCS) or decreased (cathodal tDCS). Anodal tDCS can increase corticomotoneuronal excitability (Nitsche & Paulus, 2001) and improve learning in implicit motor (Nitsche, Schauenburg, et al., 2003), visuomotor (Antal et al., 2004), and probabilistic classification (Kincses, Antal, Nitsche, Bartfai, & Paulus, 2004) tasks in healthy volunteers. Recent evidence also suggests that anodal tDCS may enhance motor function in chronic stroke patients (Hummel et al., 2005). Thus, the efficacy of anodal tDCS for improving motor functions has been conclusively demonstrated. However, studies on functions outside the motor domain are scarce to date. There are preliminary reports of improved verbal fluency (Iyer et al., 2005) and verbal working memory abilities (Fregni et al., 2005) in healthy subjects. One of the areas, for which a boost of function would be particularly desired, is language learning. In the clinical realm, persisting language deficits after a stroke contribute significantly to permanent disability and emotional suffering in patients (Bayley et al., 2007). Thus, it would be important if language learning could be enhanced by tDCS.

In the present study, we set out to probe if tDCS delivered to the language-dominant hemisphere can improve language learning in healthy volunteers. We applied tDCS over the left superior temporal cortex (Wernicke's area) because of its known critical involvement in language (word form) processing (Price, 2000). As a training task, we chose a previously developed paradigm of our group that mimics the acquisition of a novel lexicon with high ecological validity (Breitenstein et al., 2005; Breitenstein, Kamping, Jansen, Schomacher, & Knecht, 2004; Breitenstein & Knecht, 2002).

## METHODS

### Subjects

Nineteen healthy young subjects (age range: 22–32 years, mean ± *SD*: 25.6 ± 2.7; 9 women) gave written informed consent and participated in this double-blind, sham-controlled, and randomized crossover study. The study was approved by the Local Ethics Committee.

#### *Inclusion Criteria*

All subjects fulfilled the following inclusion criteria: (1) No current intake of medication that affects the central nervous system (e.g., antipsychotics or antidepressants); (2) normal routine medical and neurological examinations; (3) strong right-handedness (handedness score ≥70 in the Edinburgh Handedness Inventory; Oldfield,

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1971); (4) no signs of dementia (Mini-Mental State Examination of 29 or 30; Folstein & Luria, 1973); (5) no use of recreational drugs, as verified by questioning subjects and by a urine test for recreational drugs (Acon, Acon Laboratories, San Diego, CA 92121).

### *Cognitive Screening*

Subjects were screened with a comprehensive neuropsychological test battery prior to participation to ensure normal cognitive functioning. This battery comprised tests of general intellectual functioning, attention, verbal fluency, digit spans, and verbal and visuospatial memory (for details on neuropsychological tests, see Breitenstein et al., 2006; Breitenstein, Kamping, et al., 2004; Breitenstein, Wailke, et al., 2004). Scores were within the normal range for all subjects. Formal years of education ranged from 16 to 22 years (mean ± *SD* = 18.7 ± 0.4).

## Experimental Procedures

### *General Outline*

Each subject was studied in three separate sessions to determine the effects of anodal tDCS, cathodal tDCS, or sham stimulation (see Figure 1) on associative language learning (see below, Language learning paradigm). Order of sessions (anodal, cathodal, sham) was randomized between subjects. Sessions were separated by at least 7 days to avoid carryover effects between conditions.

To assess cardiovascular arousal, blood pressure and heart rate were measured digitally every 30 min (Bose medicus memory; Bosch, Germany), starting with the subject's arrival on a given session. Furthermore, to assess tDCS effects on motivation and mood, subjects rated their subjective positive and negative feelings, using the Positive and Negative Affective Schedule every 30 min on a given session (PANAS: Watson et al., 1988). The PANAS consists of two 10-item mood scales, which measure the dimensions Positive Affect (high score: a state of high energy; low score: sadness and lethargy) and Negative Affect (high score: state of distress; low score: state of calmness).

Furthermore, participants evaluated their sense of discomfort/pain at the end of each session (scale from 1 to 10; 1 = no discomfort/pain at all, 10 = maximal discomfort/pain) on visual analog scales that have good internal consistency, reliability, and objectivity (Gracely, 1999). Additionally, after the completion of the study, subjects were asked to identify in which session they had received "real" cortical stimulation (tDCS). Instructions to the subjects were identical for all three sessions (tDCS and sham).

### *Transcranial Direct Current Stimulation*

tDCS was delivered by a battery-driven constant DC current stimulator (Schneider Electronic, Gleichen, Germany) using a pair of electrodes in a 5 × 7 cm saline-soaked synthetic sponge. Constant current flow (1 mA) was controlled by an amperemeter. The stimulating electrode (to which the terms anodal and cathodal stimulation refer) was centered over Wernicke's area (position Cp5 of the international 10–20 EEG system; see Figure 1). The second electrode (reference) was positioned on the skin overlying the contralateral supraorbital region.

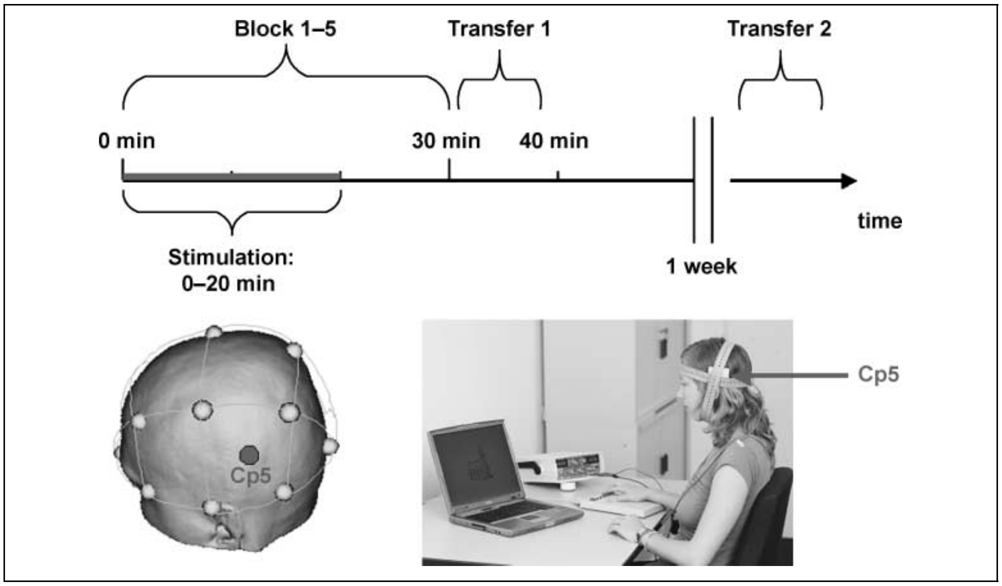

**Figure 1.** Overview of study design. Each subject participated in three separate sessions: anodal tDCS, cathodal tDCS, and sham stimulation. Order of sessions was randomized between subjects. At the start of each session, stimulation sites were identified. The brain area targeted with tDCS is indicated by a square and displayed on Colin's head on the left side of the brain (Cp5 = Wernicke's area); locations shown in circles refer to the standard 10–20 EEG system (see bottom left of the figure). Then, stimulation and associative learning task started simultaneously. Stimulation lasted for a total of 20 min, the language learning paradigm (block 1–5) for about 30 min. At the end of the 5 blocks, an immediate lexical knowledge test was administered ("transfer 1"). One week later, retention of the miniature lexicon was reassessed ("transfer 2"). On the bottom right of the figure, see photograph of a participant wearing the headgear with electrodes.

Anodal and cathodal tDCS (current of 1 mA) were delivered for 20 min in the respective sessions and with an ultra-short (<30 sec) stimulation at the start of the sham session. At the onset of all three sessions (anodal tDCS, cathodal tDCS, sham), the current was increased in a ramp-like fashion (Nitsche, Liebetanz, et al., 2003), eliciting a transient tingling sensation on the scalp that faded over seconds, consistent with previous reports (Nitsche, Schauenburg, et al., 2003). In all three sessions, currents were turned off slowly over a few seconds, a procedure that does not elicit perceptions (Hummel et al., 2005; Nitsche, Schauenburg, et al., 2003), out of the field of view of the subjects.

Language learning started at the beginning of the stimulation in each session and continued after the end of tDCS or sham stimulation (20 min) for another 10 min (see Figure 1).

### *Language Learning Paradigm*

The detailed structure of the vocabulary learning task has been described elsewhere (Breitenstein et al., 2005; Breitenstein & Knecht, 2002). The learning principle consists of associative learning: The "correct" pairings of a visually presented daily object and a novel (pseudo)-word (e.g., car and /glump/) co-occur over the course of the five training blocks 10 times more often as "incorrect" pairings (e.g., bike and /glump/), which are shown only once. For each subject and each condition, there were a total of 600 training trials (5 blocks × 120 trials), in which subjects were trained in 30 novel object names. Each trial consisted of a visually presented object picture, presented 200 msec after the onset of the auditory presentation of a novel word (pseudoword, all normalized to a duration of 600 msec). During picture presentation, which lasted for 1 sec, subjects had to press one of two keys with their right hand on a response pad to indicate whether the pairing was correct. To prevent subjects from reflecting on their responses, the intertrial interval was limited to 1 sec. The instruction was to "intuitively decide if objects and novel words match or not." Subjects were told that only responses occurring in the 1-sec interval of picture presentation were accepted for data analysis. They were not informed about the underlying frequency principle, ensuring incidental learning conditions for all subjects.

Subjects' ability to explicitly translate the novel words into German was tested in a transfer test immediately after each training session. During this transfer test (1 block with 120 trials), German object names were acoustically presented in pairs with one of the spoken pseudowords. Subjects had to decide whether the pairing was correct. The transfer test was administered again 1 week after the last training day to assess retention of the vocabulary.

A different version of the novel vocabulary was used for every condition. The three training sets were matched for word frequency and number of syllables of the German objects names, for familiarity of the (visual) objects, and for number of syllables, associations with existing words, and acoustic valence of the pseudowords.

Dependent variables were learning speed (increase of correct responses from block 1 to block 5) and overall learning success (performance on block 5 and on the transfer task) immediately after the training and at the retention sessions 1 week post. In addition to accuracy, response times and response styles (hits, correct rejections, misses, false alarms) during the vocabulary training were analyzed to determine unspecific arousal effects.

## Statistical Analysis

Data analysis was performed by an investigator blind to the intervention type. No significant deviations from a normal distribution could be assessed for any of the dependent measures using the Kolmogorov–Smirnov test of normality (set to $p < .05$) prior to data analysis.

### *Language Learning*

Main outcome parameter was accuracy on the vocabulary learning task (Breitenstein et al., 2006; Breitenstein, Kamping, et al., 2004; Breitenstein, Wailke, et al., 2004; Knecht et al., 2004). Reaction times were analyzed as dependent variables to assess unspecific arousal effects of tDCS.

*Accuracy data.* Repeated measures analysis of variance (ANOVA) with a polynomial contrast analysis on the factor time was used to test the influence of the repeated factors block$_{1,2,3,4,5}$ and stimulation$_{\text{anodal, cathodal, sham}}$ on learning success (% of correct trials). To assess learning success and lexical knowledge, repeated measures ANOVA was used to test the influence of stimulation$_{\text{anodal, cathodal, sham}}$ on learning success (% of correct trials) in the final block of learning (Block 5) and the immediate and the delayed transfer sessions.

Correlations of neuropsychological parameters with training success were examined using Pearson correlation coefficients with Bonferroni-corrected significance levels.

*Response times.* Repeated measures ANOVA with a polynomial contrast analysis on the factor time was used to test the influence of the repeated factors block$_{1,2,3,4,5}$ and stimulation$_{\text{anodal, cathodal, sham}}$ on response times (msec).

### *Blood Pressure, Heart Rate, Mood Ratings, Discomfort*

Repeated measures ANOVA with a polynomial contrast analysis on the factor time was used to test the influence of the repeated factors time$_{\text{base, 30 min, 60 min, 90 min}}$ and stimulation$_{\text{anodal, cathodal, sham}}$ on systolic blood pressure, diastolic blood pressure, heart rate, and mood ratings

(PANAS) over the course of the study. Repeated measures ANOVA was used to evaluate the effect of stimulation$_{\text{anodal, cathodal, sham}}$ on discomfort.

Stimulation differences were analyzed post hoc using paired $t$ tests, as appropriate.

Data were considered significant at a level of $p < .05$. All data are expressed as mean ± *SEM*, unless stated otherwise.

## RESULTS

### Language Learning: Accuracy Data

As shown by the Stimulation × Block interaction, learning speed was significantly accelerated in the anodal condition compared to the cathodal and sham conditions [linear trend; $F(1, 18) = 6.6, p < .05$; see Figure 2]. With respect to overall learning success, a significant difference emerged for performance on Block 5 between the three stimulations [main effect of stimulation: $F(2, 36) = 4.8$, $p < .05$, Greenhouse–Geisser corrected]. Post hoc analysis revealed a significantly higher percentage of correct responses in the anodal condition compared to the cathodal and sham [paired $t$ tests: $t(18) = 3.5$, $p < .05$ for anodal vs. cathodal, Block 5; $t(18) = 2.84$, $p < .05$ for anodal vs. sham, Block 5; see Figure 2]. Baseline differences between the three sessions were excluded by a repeated measures ANOVA on accuracy (%) in the first block, which did not yield significance [$F(2, 36) = 1.0$, $p = .35$, Greenhouse–Geisser corrected; see also Figure 2].

For the immediate lexical knowledge test (transfer test; see Figure 3), there was also a significant difference between the stimulations [$F(2, 36) = 5.0$, $p < .05$, Greenhouse–Geisser corrected], due to better lexical knowledge in the anodal condition compared to cathodal and sham [paired $t$ tests: $t(18) = 4.0$, $p < .05$ for anodal vs. cathodal; $t(18) = 3.5$, $p < .05$ for anodal vs. sham]. No significant difference between the conditions was found for the delayed lexical knowledge test after 1 week ($p = .6$).

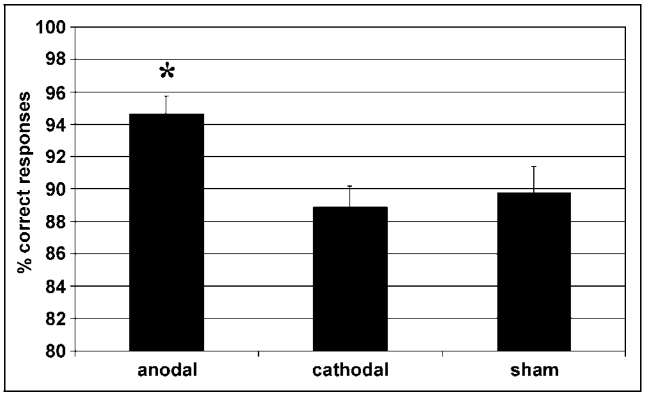

**Figure 3.** Transfer of the vocabulary into subjects' native language. Immediately after the training session, subjects' ability to explicitly translate the novel words into German was tested with a transfer test. Here, German object names were acoustically presented in pairs with one of the spoken pseudowords. Transfer (means ± *SEM*) was better with anodal stimulation compared to cathodal and sham stimulations. * denotes significance ($p < .05$).

Training success under anodal tDCS was not significantly correlated with any of the neuropsychological parameters.

### Language Learning: Response Times

Response times were comparable between stimulations and blocks for correct trials (no significant interaction or main effects of block$_{1,2,3,4,5}$ and stimulation$_{\text{anodal, cathodal, sham}}$, $p = .7$), indicating that anodal tDCS did not lead to an unspecific increase in arousal.

### General Drug Arousal: Response Styles

To determine whether the accelerated learning speed of the anodal tDCS group could be explained with a more

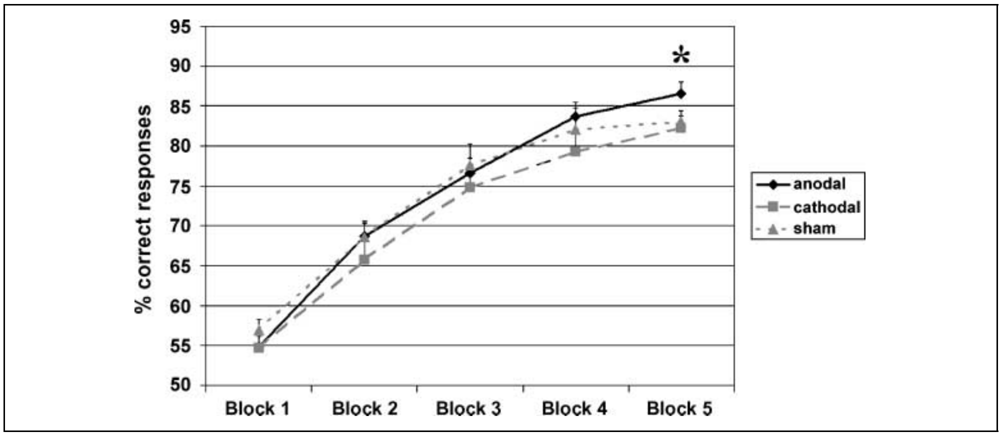

**Figure 2.** Learning curve over the 5 blocks, for all three stimulations (anodal, cathodal, and sham). Note that in all three conditions, learning success (percent correct responses) was similar in Block 1. With anodal stimulation, subjects showed a stronger increase in correct responses and reached a significantly higher percentage of correct responses at the end of the learning session (Block 5), compared to cathodal and sham stimulations. * denotes significance ($p < .05$); vertical bars depict standard errors of the mean.

risky response style as part of a general tDCS arousal effect (e. g., more ''yes'' responses' leading to more errors of the ''false alarm'' type), subjects' responses were classified into hits, correct rejections, false alarms, and misses.

A repeated measures ANOVA with a polynominal contrast analysis on the factors stimulation$_{\text{anodal, cathodal, sham}}$, response style$_{\text{hits, correct rejections, false alarms, misses}}$, and block$_{1\text{–}5}$ did not reveal a significant three-way interaction or significant two-way interactions involving the factor stimulation.

### Blood Pressure, Heart Rate

Blood pressure (systolic/diastolic) and heart rate were similar in all three conditions (at the beginning, 127/77 mm Hg and 82 bpm, 131/77 mm Hg and 83 bpm, 124/75 mm Hg and 74 bpm in anodal, cathodal, and sham sessions, respectively; at the end, 124/73 mm Hg and 73 bpm, 122/72 mm Hg and 76 bpm, 121/74 mm Hg and 78 bpm). No significant interaction of Time × Stimulation, or a main effect of stimulation emerged for either systolic blood pressure, diastolic blood pressure, or heart rate.

### Mood Ratings (Positive and Negative Affective Schedule)

There was no significant interaction of Time × Stimulation, or a main effect of stimulation, for positive or negative feelings.

### Discomfort

The experienced discomfort, mostly due to the headband, was negligible in all subjects and stimulation conditions, ranging between 1 and 2 out of 10, and was comparable in the three stimulation conditions. All participants were unable to distinguish between anodal tDCS, cathodal tDCS, and sham sessions.

## DISCUSSION

In this study, we show for the first time that anodal tDCS, delivered over the left hemisphere, significantly improves the acquisition of a novel vocabulary (faster learning and higher overall success) in healthy subjects. This finding suggests that noninvasive brain stimulation, combined with intense training, can enhance language acquisition in healthy individuals and maybe even in patients with chronic aphasia after brain lesion.

The difference between anodal tDCS and the two other conditions cannot be explained by unspecific arousal differences. Subjects' blood pressure, heart rate, as well as their mood ratings, were comparable across sessions, a finding consistent with previous tDCS reports (Hummel et al., 2005; Nitsche, Schauenburg, et al., 2003). Likewise, response styles were similar under the different stimulation conditions. The positive effects of tDCS on learning were thus selectively due to an improved sensitivity to recognize correct pairings and to reject incorrect pairings. Reaction times did not differ between anodal, cathodal, or sham stimulations, indicating that the beneficial effect of anodal tDCS on learning did not stem from increased neuronal sensitivity within a sensory pathway (Zohary et al., 1994).

### Previous Studies on Noninvasive Cortical Stimulation and Language

So far, noninvasive cortical stimulation during language-related tasks has been conducted predominantly with transcranial magnetic stimulation (TMS). Here, two strategies have been used. The first tried to facilitate language processing directly by stimulating language-relevant structures in healthy individuals (Mottaghy et al., 1999). However, the effects were small, short-lived, and highly variable between subjects. The method has never been translated into the clinical realm. The second approach is based on the concept of hemispheric competition (Hilgetag, Theoret, & Pascual-Leone, 2001) and tried to indirectly enhance language processing by inhibiting the nondominant hemisphere in healthy individuals and in aphasic patients (Martin et al., 2004; Knecht et al., 2002). Although first promising results have been reported in patients with chronic aphasia after TMS to the right-sided Broca homolog (Naeser et al., 2005; Martin et al., 2004), larger, controlled, and randomized studies are needed before any definite conclusions can be drawn.

With tDCS, only two pioneering studies to date reported improved verbal fluency (Iyer et al., 2005) and verbal working memory functions (Fregni et al., 2005) in healthy subjects. A recent report, originally designed to test the effect of tDCS on motor symptoms in stroke patients, found an unexpected improvement in a language test in four out of five patients that also suffered from aphasia (Hesse et al., 2007). The study included neither a control group nor a control stimulation, and examined stroke patients in the subacute stage (4–8 weeks post onset). The crucial question if brain stimulation can enhance language learning has therefore neither been addressed with TMS nor with tDCS.

### Left Temporo-parietal Cortex and Vocabulary Acquisition

The temporo-parietal region receives polymodal information, pointing to its role in the integration of visual, somatosensory, and auditory projections (Calvert, Campbell, & Brammer, 2000; Seltzer & Pandya, 1994). The formation of the mental lexicon is based on thousands of (mostly) arbitrary sound–meaning associations, which are frequently repeated throughout life without conscious awareness for the learning process. We tried to simulate this natural language learning process in our vocabulary learning task: Subjects had to associate existing semantic knowledge (as indexed by the object pictures) with novel phoneme sequences.

Our tDCS results support our preceding functional magnetic resonance imaging results (Breitenstein et al., 2005), which demonstrated that activity modulations in a neural network comprising the left temporo-parietal region mediates the acquisition of novel word–object contingencies in healthy subjects. Prior studies in the field had likewise shown that the (left) posterior language areas are functionally relevant for the processing of an already acquired mental lexicon (one's native language; Andoh et al., 2006; Drager, Breitenstein, Helmke, Kamping, & Knecht, 2004; Knecht et al., 2002; Sparing et al., 2001; Mottaghy et al., 1999; Topper, Mottaghy, Brugmann, Noth, & Huber, 1998).

However, the exact left-hemispheric location of our learning enhancing effect cannot be determined in the present study due to the large area covered by the electrode over Cp5. We did not stimulate left-hemispheric control sites because three learning sessions were considered the maximum for each volunteer (within-subject design). Therefore, we cannot rule out that stimulation of a different (left hemisphere) location would have yielded similar effects on language learning. Future studies should therefore investigate additional control sites, for instance, left inferior frontal areas (Broca's area) to clarify this issue.

Additionally, effects on different linguistic tasks, for example, grammar learning (Newman-Norlund, Frey, Petitto, & Grafton, 2006), should be assessed with tDCS over left-hemispheric language areas.

## Mechanisms for tDCS-enhanced Learning

The formation of new memories or the acquisition of new skills is accompanied by changes in neuronal activity and excitability (Muellbacher, Ziemann, et al., 2002; Karni et al., 1995). They might reflect changes in synaptic strength, for example, *N*-methyl-D-aspartate (NMDA) receptor-dependent long-term potentiation (LTP) (Rioult-Pedotti, Friedman, Hess, & Donoghue, 1998; Hess & Donoghue, 1996). Successful manipulation of cortical excitability to improve learning processes has been demonstrated in humans in neuropharmacological investigations (Breitenstein, Kamping, et al., 2004; Breitenstein, Wailke, et al., 2004; Butefisch et al., 2002), with TMS (Butefisch, Khurana, Kopylev, & Cohen, 2004), and with deafferentation of adjacent or *contralateral* body parts (Floel et al., 2004; Muellbacher, Richards, et al., 2002). tDCS presents an interesting alternative to these approaches because it is noninvasive, painless (compared to TMS and deafferentation), and without serious side effects (compared to pharmacological agents). Neurophysiologically, Nitsche and Paulus (2000, 2001) showed that anodal tDCS of the human motor cortex elicits prolonged cortical excitability increases, probably by subthreshold neuronal membrane depolarization (Purpura & McMurtry, 1965). Moreover, it has been shown that the evoked after-effects are NMDA receptor dependent (Liebetanz, Nitsche, Tergau, & Paulus, 2002), and thus, share some similarity with the LTP and LTD presumed to underlie learning processes (Rioult-Pedotti et al., 1998). In summary, anodal tDCS has the potential to improve learning by increasing cortical excitability and modulating NMDA receptor-dependent plasticity. For the present study, both mechanisms may have facilitated the language learning process. The effect could have been driven by a direct modulation over a classical language region (Wernicke's area) or indirectly (trans-synaptically; Chouinard, Van Der Werf, Leonard, & Paus, 2003; Paus, 1999) via connected structures. One such connected structure could be the left hippocampus, which is functionally involved in the acquisition of a novel lexicon (Breitenstein et al., 2005). The hippocampus is directly connected to the cortical area stimulated in the present study, with the role of binding information processed in the temporo-parietal cortex to form lasting memory traces (Rugg, Otten, & Henson, 2002; Squire & Zola, 1996). Increased hippocampal activity during language learning, shown to correlate with learning success (Breitenstein et al., 2005), could have been enhanced by anodal tDCS. This hypothesis should be tested in future studies combining tDCS and functional magnetic resonance imaging.

Cathodal tDCS, which reduces intracortical excitability (Nitsche, Liebetanz, et al., 2004; Nitsche & Paulus, 2000), did not lead to a significant modulation of verbal associative learning in the current study. This result is in line with previous studies on the effect of cathodal tDCS on motor learning (Nitsche, Schauenburg, et al., 2003). In future studies, it will be important to study if cathodal tDCS, which reduces intracortical excitability in neurophysiological studies (Nitsche & Paulus, 2000), has the potential to enhance verbal learning when applied over the non-language-dominant hemisphere.

## Limitations

In the present study, unspecific effects of tDCS were controlled by both sham and cathodal tDCS conditions. Therefore, we feel confident that our results were indeed mediated by the well-described effects of anodal tDCS on cellular learning systems. In future studies, more elaborate attentional tasks, as well as right-hemispheric control sites, should be included to determine to which degree the tDCS effect on language learning may be based on improved attentional processes.

Improved learning success after anodal tDCS was no longer significant after 1 week. In previous studies, the effects of anodal stimulation on motor cortical excitability only lasted minutes to hours, and additional pharmacological enhancement was needed to prolong the effects to the following day (Nitsche, Grundey, et al., 2004). It is conceivable that longer tDCS, or tDCS combined with pharmacological enhancement, may lead to a more sustained tDCS after-effect on learning. This hypothesis is supported by a recent report which demonstrated a 1-month lasting positive effect of repetitive anodal tDCS (10 sessions over a 2-week period) on clinical symptoms in depressed patients (Boggio et al., 2007).

## Conclusions

In summary, this study demonstrates that anodal tDCS over the left (posterior) hemisphere significantly improves the acquisition of a novel vocabulary in healthy subjects. Furthermore, our findings lay the foundation for clinical trials probing the effects of tDCS on language reacquisition in the neurorehabilitation of aphasic patients.

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