# Can Transcranial Direct Current Stimulation Improve Cognitive Functioning in Adults with Schizophrenia?

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## Abstract

Cognitive impairment is nearly ubiquitous in schizophrenia. First-degree relatives of persons with schizophrenia often show similar but milder deficits. Current methods for the treatment of schizophrenia are often ineffective in cognitive remediation. Since transcranial direct current stimulation (tDCS) can enhance cognitive functioning in healthy adults, it might provide a viable option to enhance cognition in schizophrenia. We sought to explore whether tDCS can be tolerated by persons with schizophrenia and potentially improve their cognitive functioning. We examined the effects of anodal versus cathodal tDCS on working memory and other cognitive tasks in five outpatients with schizophrenia and six first-degree relatives of persons with schizophrenia. Each participant completed tasks thought to be mediated by the prefrontal cortex during two 30-minute sessions of tDCS to the left and right dorsolateral prefrontal cortex (DLPFC). Anodal stimulation over the left DLPFC improved performance relative to cathodal stimulation on measures of working memory and aspects of verbal fluency relevant to word retrieval. The patient group showed differential changes in novel design production without alteration of overall productivity, suggesting that tDCS might be capable of altering self-monitoring and executive control. All participants tolerated tDCS well. None withdrew from the study or experienced any adverse reaction. We conclude that adults with schizophrenia can tolerate tDCS while engaging in cognitive tasks and that tDCS can alter their performance.

**Key Words:** Schizophrenia, Transcranial Direct Current Stimulation (tDCS), Cognition, Memory-Short Term, Verbal Beh

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## Introduction

Persons with schizophrenia (SZ) suffer from widespread cognitive deficits (1), and their first-degree relatives (SZR) often show qualitatively similar but milder deficits (2). Cognitive dysfunction is a major cause of functional disability in SZ (3), independent of psychotic symptoms. Atypical antipsychotic medications can improve cognitive functioning in some patients, but the effects are small and inconsistent (4). Cognitive remediation shows more promise (5), but it is costly and time intensive, and it requires training and resources that are often unavailable. Clearly, new methods to treat cognitive dysfunction in SZ are needed.

## Clinical Implications

Despite the limitations described below, the results of this study suggest that some cognitive functions in schizophrenia can be altered by bifrontal stimulation of the dorsolateral prefrontal cortex. If these results can be replicated in sham-controlled randomized trials, tDCS might prove to be a safe, inexpensive, and portable means of treating cognitive dysfunction in schizophrenia. If these findings can be replicated in other first-degree relative samples, then tDCS might also improve cognitive functioning in persons with genetic susceptibility to schizophrenia.

Transcranial direct current stimulation (tDCS) is a noninvasive form of brain stimulation that can enhance cognitive functioning in healthy adults. It involves passing a weak electrical current, typically 0.5–2.0 mA, through the cranium via sponge-covered electrodes placed on the scalp. It appears to affect neural tissue in several ways to achieve neuromodulation. Anodal stimulation is thought to increase—and cathodal stimulation to decrease—cortical excitability, perhaps via alteration of neuronal resting potential and other mechanisms (6-8). Repeated stimulation sessions have been shown to instantiate longer lasting changes in cortical plasticity (9, 10). Hundreds of studies have shown that tDCS is safe and painless (11-13) in healthy adults. This suggests that, if tolerated, tDCS could be useful for the treatment of cognitive dysfunction in SZ.

In persons with schizophrenia, the dorsolateral prefrontal cortex (DLPFC) shows functional and structural abnormalities. These include abnormal temporal coherence of electrophysiological activity (14), as well as altered cerebral blood flow (15) and white matter connectivity (16), and reduced gray matter volume (17), all of which could contribute to cognitive dysfunction. Also, glutamatergic N-methyl-D-Aspartate (NMDA) receptor dysfunction and glutamate hypertransmission likely impede plasticity and cause neurotoxicity in SZ (18, 19). This is especially relevant as tDCS may modify NMDA receptor activity (20).

The DLPFC is an attractive target for tDCS because some cognitive functions that are impaired in SZ can be enhanced in healthy adults with tDCS applied over this area. For example, anodal tDCS applied over the left DLPFC has been shown to enhance performance on n-back working memory and digit repetition in healthy adults (21-23). Likewise, tDCS was found to enhance working memory in Parkinson's disease (24) and stroke survivors (25). In addition, verbal fluency often is impoverished in SZ (1, 26), a deficit that fMRI studies have linked to hypoactivation of the left DLPFC (27). In healthy adults, tDCS has been shown to enhance prefrontal regional cerebral blood flow (28) and improve verbal fluency production (29). Other cognitive abilities that might respond to stimulation of the DLPFC include design fluency, processing speed, and manual speed/dexterity. We know of no studies of the effects of tDCS on design fluency, a nonverbal analogue of word fluency (30). Early lesion studies linked design fluency performance to right prefrontal brain function (31). Other studies suggest that some aspects of design fluency are distributed bilaterally (32, 33). Many tDCS studies have shown that anodal tDCS over the motor cortex improves motor functioning, while cathodal stimulation impedes that functioning (34). However, due to the more posterior location of primary motor cortex, tDCS applied to the DLPFC is not likely to affect simple motor functions. Thus, anodal tDCS over the left DLPFC had no effect on psychomotor speed in adults with depression (35).

While tDCS shows promise for treating hallucinations in SZ (36-38), its potential for remediating cognitive dysfunction is unknown. In one reported tolerability study, Mattai et al. (39) found that 12 patients with SZ tolerated 10 sessions (20 minutes each; 2.0 mA) of bilateral tDCS without adverse effects. Vercammen et al. (40) found that 2.0 mA of anodal tDCS applied at left DLPFC did not improve probabilistic association learning in 21 adults with schizophrenia. However, a subgroup of patients with relatively better probabilistic association learning prior to tDCS did benefit from tDCS. This intriguing finding suggests that pre-testing on a variable of interest might help identify potential tDCS responders. For example, it suggests that more cognitively intact individuals with schizophrenia might benefit most from tDCS. Thus, we conducted the present study as a proof-of-concept attempt to determine whether tDCS can alter cognitive processes associated with the DLPFC in adult outpatients with SZ or the first-degree relatives of persons with SZ, and to assess the tolerability of tDCS in these groups.

We hypothesized that anodal tDCS over the left DLPFC would alter performance on frontally-mediated cognitive tests relative to cathodal stimulation, especially working memory, ideational fluency and attention. We expected minimal or no effects of tDCS on processing speed or motor speed/dexterity based on our electrode montage.

## Methods

### *Participants*

Eleven adults (6 women) participated in this study. They included 5 outpatients with SZ (age M=32.4, SD=11.1; education M=12.8, SD=3.0) and 6 first-degree relatives (SZR) of a person with schizophrenia (age M=50, SD=7.7; education

M=13.3, SD=1.6). Ten participants were right-handed. Patients met *DSM-IV* (41) diagnostic criteria for SZ based on a clinical interview and review of available medical records by a board-certified psychiatrist. First-degree relatives were free of schizophrenia and other Axis I mental disorders. Other exclusion criteria for all study participants included current substance abuse, any significant sensory or motor impairment, any neurological disorder with cognitive morbidity, or native language other than English. This study was approved by the Johns Hopkins Institutional Review Board. All participants gave written informed consent to participate, and data were collected according to the approved protocol.

## Direct Current Stimulation

Direct current was delivered by a battery-driven constant current stimulator (Chattanooga Ionto™ Dual Channel Iontophoresis System) through a pair of electrodes covered with saline-soaked square sponges (36 $cm^2$). Electrodes were placed bilaterally over the DLPFC (F3 and F4 of the 10/20 International EEG system). In the terminology adopted here, the condition of stimulation is defined by the polarity of the electrode over the **left** DLPFC. Thus, for the anodal tDCS condition, we placed the anode over the left DLPFC and the cathode over the right DLPFC. For the cathodal tDCS condition, we placed the cathode over the left DLPFC and the anode over the right DLPFC. Participants received a constant current of 1.5 mA for 30 minutes. The current density at the stimulation electrodes was 0.043 $mA/cm^2$ for a total charge of 0.077 $C/cm^2$. Participants completed a side effects questionnaire before and after each session.

## Cognitive Assessment

In each session, after stimulation began, participants first practiced and then were tested on a brief battery of cognitive measures that included the Grooved Pegboard Test (GPT; 42), Finger Tapping Test (FTT; 43), Calibrated Ideational Fluency Assessment (CIFA; 30), Perceptual Comparison Test (PCT; 44), Wechsler Memory Scale, 3rd Ed. Spatial Span (WMS-III) and Wechsler Adult Intelligence Scale, 3rd Ed. (WAIS-III) Digit Span subtests (45). All tests were administered during stimulation. The primary dependent measures were: GPT: dominant and non-dominant hand completion times to assess manual dexterity; FTT: dominant and non-dominant hand to assess motor speed; PCT: total correct in 2 minutes to assess psychomotor speed; CIFA: Letter Word, Category Word, and Design Fluency totals correct to assess word and design fluency; totals correct for WAIS-III Digit Span and WMS-III Spatial Span forward (to assess attention) and backward (to assess working memory). We also coded word retrieval strategies, such as clustering and switching, for a secondary analysis of the verbal fluency data. Specifically, based on a modification (46) of the method developed by Troyer et al. (47), we tallied clusters of semantically related words, switches between clusters, and mean cluster size.

## Side Effects Questionnaire

An 18-item questionnaire was used to assess subjective responses to tDCS before and after stimulation at each session. The questionnaire includes 15 negative (headache, concentration, discomfort, fatigue, pain, tingling, nausea, anxiety, anger, sadness, tension, fear, visual changes, itching, and burning) and 3 positive (confidence, happiness, and alertness) possible responses.

## Experimental Protocol

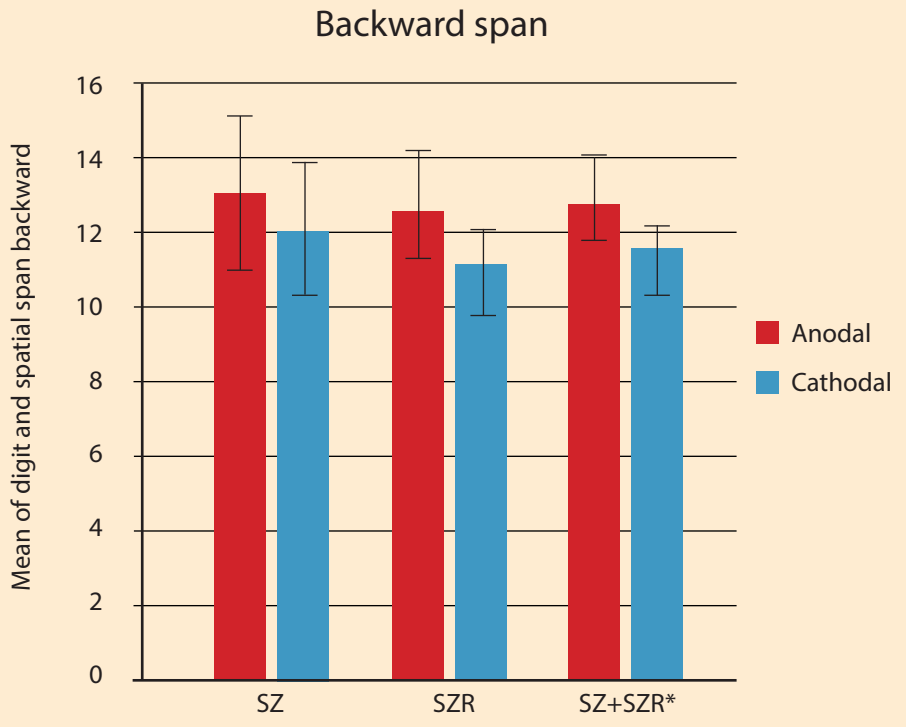
Each participant received both anodal and cathodal stimulation in counterbalanced order over two sessions with a washout period of 1 to 7 days (M=2.6) between sessions. The washout minimum of one day was based on reports that motor and cognitive after effects of a single tDCS session have not been shown to last more than 120 minutes (48, 49). Immediately after the start of stimulation, participants were given instructions for the tests and practiced them for 8–10 minutes. Thereafter, the tests were administered over 20–22 minutes to assess the cognitive effects of tDCS. Practice and testing were completed during the 30-minute stimulation session.

## Data Analysis

Test performances and side effect reporting were compared within subjects across stimulation conditions and between the SZ and SZR groups. Except as noted, raw scores for the cognitive measures served as dependent variables. Analyses were performed with IBM SPSS Statistics 22. Because our groups were small and most variables were not normally distributed, we used the nonparametric Wilcoxon signed ranks test to analyze within-subjects effects of stimulation (anodal vs. cathodal) on cognitive performances and changes in side effect reporting (pre- vs. post-stimulation). We used the Mann-Whitney U test to analyze between-group differences.

We examined performance on a range of tasks in order to assess the specificity of tDCS effects. We hypothesized that compared to cathodal stimulation, anodal stimulation over left DLPFC would improve performances on tests of working memory, ideational fluency, and attention, but not motor or psychomotor speed. Based on findings in healthy adults (50), we hypothesized that stimulation would alter word retrieval strategies (51) measured by clusters, switches and mean cluster size on CIFA word fluency tasks.

**Figure 1** **Performance on Working Memory Tasks by Stimulation Type for the Full Sample, Participants with Schizophrenia, and First-Degree Relatives of Persons with Schizophrenia**




Error bars indicate standard error of the mean. SZ=person with schizophrenia; SZR=first-degree relative of person with schizophrenia. *Denotes p<.05.

## Results

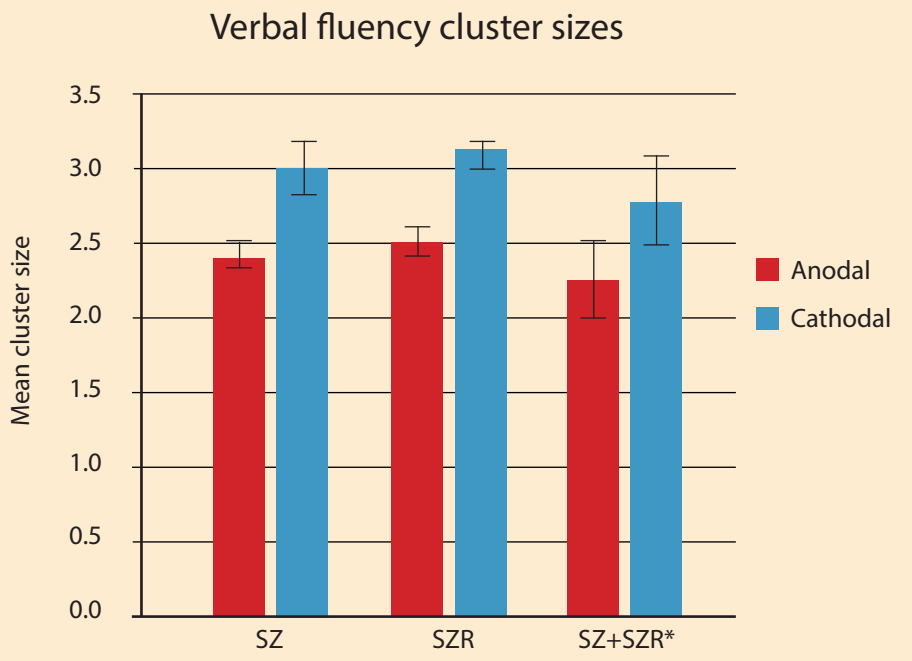
Because cognitive dysfunction may be an intermediate phenotype of SZ, and unaffected first-degree relatives of SZ probands often have mild cognitive deficits, in addition to examining the effects of stimulation on SZ and SZR groups separately, we also combined the two groups for analysis. As described below, nearly identical results emerged from the separate and combined groups analyses.

As expected, there were no significant effects of stimulation condition on tests of simple motor (Grooved Pegboard, Finger Tapping) and processing (Perceptual Comparison) speed in either subgroup or the combined sample (all p's>0.05). Contrary to our hypothesis, no effects of stimulation condition were observed on tests of attention (forward digit and spatial span) in either subgroup or the combined groups.

### *Working Memory*

Backward digit and spatial span tasks both assess working memory (45). As hypothesized, in the combined sample, anodal stimulation was associated with better overall backward span test performance (median=13, range=13) than cathodal stimulation (median=11, range=11). This difference was statistically significant (Wilcoxon Z=2.207, p=0.027, r=0.66). (Note: this effect size is calculated by taking the Z score from a nonparametric test and dividing by the square root of the N.) When SZ and SZR groups were analyzed separately, anodal stimulation also was associated with better overall backward span performance than cathodal stimulation in both groups (SZ medians=15 vs. 13; SZR medians=12.5 vs. 11). However, these differences failed to reach statistical significance (SZ: Wilcoxon Z=1.342, p=.180, r=0.60; SZR: Wilcoxon Z=1.826, p=0.068, r=0.75), likely due to lack of statistical power, as the effect sizes were similar in all three comparisons. These results are shown in Figure 1. Moreover, during anodal stimulation, every participant either equaled or exceeded his/her own backward span performance during cathodal stimulation. The SZ and SZR groups did not differ in total backward span during either anodal (Mann-Whitney U=0.18, p=.854) or cathodal (Mann-Whitney U=0.64, p=.518) stimulation.

**Figure 2** **Mean Cluster Size by Stimulation Type and Group. Letter-Cued Fluency is Shown on the Left, and Category-Cued Fluency is Shown on the Right**




SZ=person with schizophrenia; SZR=first-degree relative of person with schizophrenia.
*Denotes p<.05.

## Verbal Fluency

There were no significant differences between stimulation conditions in word fluency productivity in the SZ, SZR, or combined groups. However, anodal stimulation was associated with smaller word clusters (consecutive words grouped together based on their relatedness) than cathodal stimulation. Total cluster size (average of letter and category word clusters) was smaller during anodal (median=2.33, range=0.60) than cathodal (median=3.16, range=0.63) stimulation in patients with SZ (Wilcoxon Z=2.023, p=0.043, r=0.90). The same pattern emerged for anodal (median=2.41, range=0.88) and cathodal (median=3.16, range=0.63) stimulation in the SZR group (Wilcoxon Z=2.201, p=0.028, r=0.90), and in the pooled sample (anodal median=2.41, range=1.02; cathodal median=3.11, range=1.11; Wilcoxon Z=2.578, p=0.01, r=0.77). These results are shown in Figure 2. Again, the effect sizes were similar across analyses.

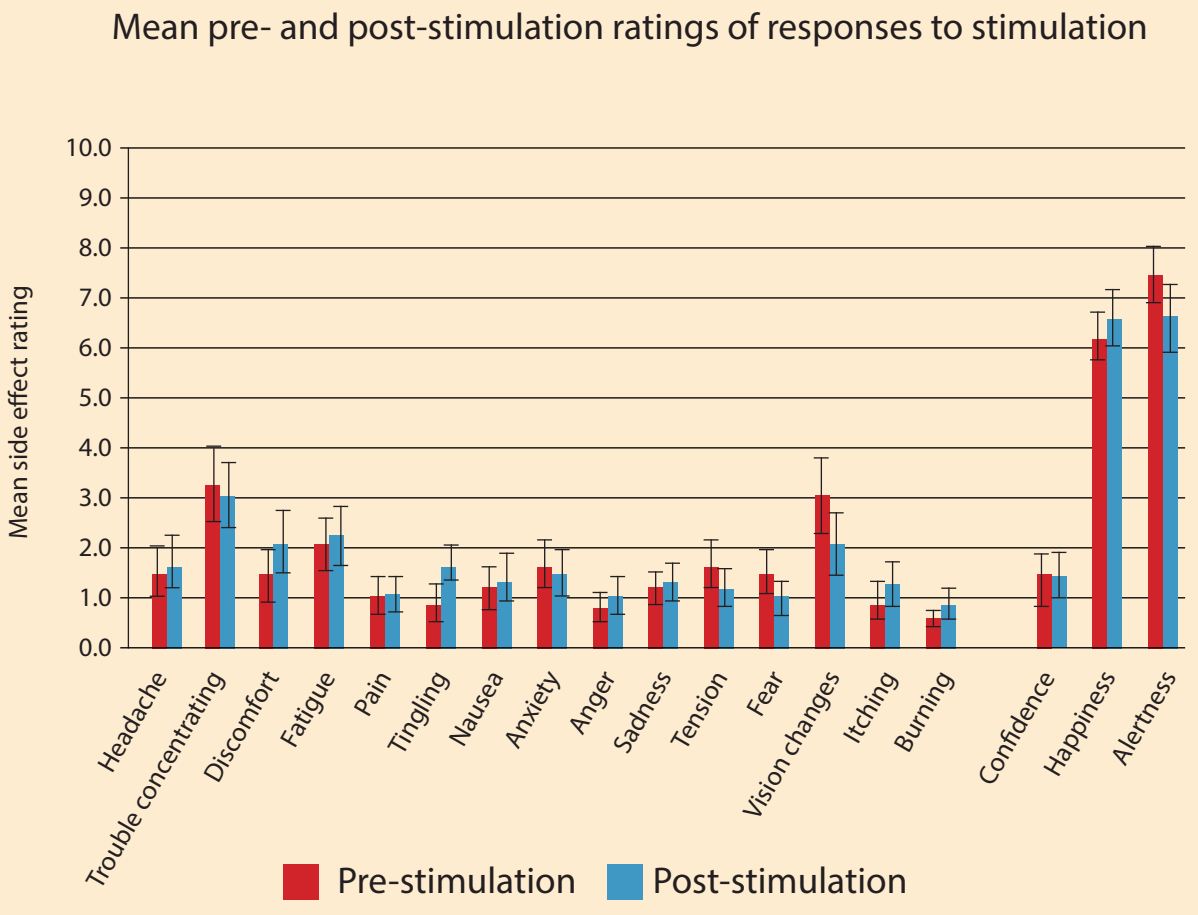
## Design Fluency

The SZ group produced more novel designs during anodal (median=11, range=14) than cathodal (median=9, range=10) stimulation (Wilcoxon Z=2.06, p=.039, r=.92). Although the SZR group also produced more novel designs during anodal stimulation (median=17.5, range=15) compared to cathodal stimulation (median=15, range=19), the difference was not significant (Wilcoxon Z=0.677, p=.498). In the combined sample, anodal stimulation was associated with greater productivity (median=17, range=15) than cathodal stimulation (median=15, range=19), but the effect fell just short of statistical significance (Wilcoxon Z=1.79, p=.073).

## Tolerability and Side Effects

No participant withdrew from the study or had any serious adverse reaction to stimulation. We compared perceived tDCS side effects before and after stimulation for the 15 "negative" and 3 "positive" possible effects described previously. Each putative side effect (e.g., tingling) was rated on a scale from 0 (e.g., no tingling) to 10 (e.g., the most extreme tingling imaginable). Based on a series of Wilcoxon signed ranks tests, no significant changes in self-ratings of the 18 potential side effects from pre- to post-stimulation were found in the combined sample (all p's>0.05), as shown in Figure 3.

**Figure 3** **Mean Pre- and Post-Stimulation Ratings (Averaged over Anodal and Cathodal Conditions) Reported by the Combined Sample**




Bars show standard error of the mean. Ratings can range from 0 (no experience of the effect) to 10 (most extreme experience imaginable).

Finally, we assessed whether simple learning effects might account for the obtained results by comparing changes in cognitive performance from the first to second session, averaged over stimulation polarity. Based on a series of Wilcoxon signed ranks tests, neither subgroup nor the combined sample performed significantly different during the second tDCS session than they did during the first session on any cognitive measure (all p's>0.05).

## Discussion

We hypothesized that anodal tDCS applied over the left DLPFC would improve working memory, ideational fluency, and attention relative to cathodal stimulation. The obtained results strongly support the hypothesis regarding working memory, weakly support the hypothesis regarding ideational fluency, and do not support the hypothesized effect on attention.

A basic aim of this study was to determine if tDCS could alter cognitive functions linked to the DLPFC in patients with SZ and in SZR, rather than to produce definitive data regarding the magnitude or direction of these effects. We chose not to use a sham condition in order to reduce the number of sessions, limit learning effects on dependent measures, encourage patient participation, and minimize the number of participants required for counterbalancing. However, not including a sham condition precludes a clear determination of whether anodal stimulation facilitated or cathodal stimulation impaired cognitive performance. The decision not to use a healthy control group also limits the interpretability of our data. It is possible that healthy adults

would be less responsive to tDCS because their cognitive functioning is closer to capacity. Alternatively, having more intact networks might enhance one's capacity to benefit from the neuromodulatory effects of tDCS, as suggested by the findings of Vercammen et al. (40). Consistent with this alternative, we found slightly stronger effects of tDCS in the SZR than SZ group. Others have found that tDCS not only enhances performance efficiency (52, 53), but with longer duration or repeated exposure, might actually raise the ceiling of cognitive performance (54, 55). Finally, spacing our sessions 1 to 7 days apart could raise concern about both learning effects and lingering effects of tDCS on cognitive performance from the first to second session. However, counterbalancing the current polarity across sessions enabled us to test and rule out learning effects on cognitive performance. Further, we know of no evidence that the neuromodulatory effects of a single session of tDCS lasts more than 2–3 hours, and the minimum washout period between sessions in this study was 24 hours.

With these limitations in mind, we found that the polarity of tDCS applied over the left DLPFC differentially altered performance on tasks requiring verbal and spatial working memory, design fluency, and selected aspects of lexical retrieval, both in patients with schizophrenia and unaffected first-degree relatives of schizophrenic probands. We also found that tDCS was well tolerated. These findings suggest that tDCS merits further study as a potential treatment for cognitive dysfunction in persons with schizophrenia.

Working memory dysfunction is characteristic of schizophrenia. After 20 minutes of 1.5 mA anodal stimulation over the left DLPFC, we found better online performance on backward span tasks relative to 20 minutes of cathodal stimulation over the same region. This is consistent with previous reports that anodal stimulation of the left DLPFC enhanced verbal working memory performance in healthy adults (21-23) and patients with depression (35). This is the first report of left DLPFC stimulation differentially altering spatial working memory. Absent the use of sham condition stimulation, we cannot conclude with certainty whether anodal stimulation facilitated working memory, cathodal stimulation inhibited it, or both effects occurred. However, clinical "norms" for the WMS-III backward span tasks among similarly aged SZ patients (56) sum to a mean backward span of 11.4. This is nearly identical to the mean backward span (11.8) shown by our SZ group during cathodal stimulation over the left DLPFC, and significantly lower than the mean backward span (13.0) of the SZ group during anodal stimulation. This suggests that anodal tDCS enhanced working memory while cathodal stimulation had little effect.

The apparently minimal effect of cathodal stimulation also is consistent with a recent meta-analysis, which found that cathodal stimulation has small to negligible effects on cognitive processes (57). However, there is enough heterogeneity in working memory performance among patients with SZ (58) that further research with sham stimulation as a control is essential to quantify the effects of stimulation on working memory. Notably, in our study, stimulation had similar effects on working memory in the SZ and SZR groups. While the study was underpowered to directly compare the groups (nonparametric analyses showed no significant differences), the direction of the effect was the same for both: anodal stimulation of left DLPFC was associated with better working memory performance than cathodal stimulation over the same region.

In this study tDCS altered *how* participants retrieved words on verbal fluency tasks. When asked to name supermarket items, respondents typically retrieve words quickly from one subcategory such as fruits (i.e., clustering). Then they apply top-down control to switch to another subcategory (i.e., switching). Persons with SZ typically generate fewer words than healthy adults on word fluency tasks primarily because they make fewer switches (59) and take longer to switch (60). The left DLPFC is thought to subserve top-down control of lexical retrieval (switching), while the posterior temporal cortex is most closely linked to the more automatic (clustering) aspects of retrieval (61). Here, tDCS did not affect overall word production, but anodal stimulation of the left DLPFC decreased the size of word clusters. Thus, instead of naming four vegetables when asked to report supermarket items, participants receiving anodal stimulation might name only three before switching to a new category. Although the increased tendency to switch categories more often with anodal stimulation did not increase productivity, it may have led to the production of fewer unusual words, which has possible implications for reducing the bizarreness of speech in schizophrenia.

In examining effects of tDCS on design fluency, we found that anodal stimulation of the left DLPFC was associated with a trend toward increased production of novel designs relative to cathodal stimulation. Although differences in error rates associated with anodal and cathodal stimulation were not significantly different in either the SZ or SZR group, both groups made more errors during cathodal stimulation. There were no differences in overall productivity between conditions. This suggests that the two types of stimulation may have differentially altered executive control and accuracy, rather than productivity. Such an effect might seem counterintuitive for excitatory stimulation of the left DLPFC given that design fluency is a nonverbal analogue of word fluency and once was thought to depend on right hemisphere functioning. However, functional brain imag-

ing studies suggest that design fluency production invoked bilateral brain activation (32, 33). Results from developmental studies suggest that fluency in generating exemplars of both verbal and visual categories may be represented by a single latent factor (62). This latent factor can be conceptualized as ideational fluency or generativity (63), as it appears to be material-independent. Given these considerations, we speculate that our stimulation montage altered both word and design fluency, but with slightly different effects. If the switching processes are mediated by left DLPFC activity, excitatory stimulation of this region could boost design fluency production because it requires switching after every response. But the same stimulation might be insufficient to boost word fluency production because switching contributes less than clustering to overall productivity on word fluency tasks, which require switching only after subcategories are exhausted (30).

Our tDCS montage involved the simultaneous bilateral stimulation of DLPFC. In both conditions, the cathodal electrode was active rather than inert (as when an extracephalic site is used). Our bifrontal montage might produce stronger effects due to contralateral disinhibition. Other studies suggest that cortical stimulation can alter inter-hemispheric inhibition between brain structures and their contralateral homologues in motor cortex (64, 65) and other frontal and temporal regions (66, 67). In this study, cathodal neuromodulation of right DLPFC might have amplified the excitatory effect of anodal stimulation over left DLPFC by reducing contralateral inhibition. Other tDCS studies have used a bilateral stimulation montage (68-71) to achieve more robust effects, perhaps by capitalizing on contralateral disinhibition. Unfortunately, this arrangement also complicates interpretation of the results because one cannot disentangle whether tDCS effects are due to modulation at one or both target sites.

An important secondary aim of our study was to determine whether patients with SZ could be recruited for tDCS research and whether they would tolerate stimulation while performing cognitive tasks. Many people with SZ have delusions about being influenced by machines (72). We wondered if their delusions or suspiciousness would lead patients with SZ to refuse to participate in or withdraw from the study. One patient did refuse to participate in any study involving electricity, but the rest agreed after reviewing the experimental procedures. Patients with SZ asked more questions about the tDCS device and required more reassurance about its safety than the first-degree relatives. Several asked questions about the experimenter's activities during the experiment, but all 11 participants returned for the second tDCS session, and none withdrew from the study. Our 18-item side effects questionnaire showed a modest but statistically significant increase in discomfort in the SZ group that was not observed in the SZR or combined groups. No other unpleasant sensations were rated as increasing significantly during stimulation by either group or the combined sample. These results were consistent with our observations during the study, wherein all participants seemed comfortable. Nonetheless, it must be noted that our analyses lacked sufficient statistical power to detect small effects. The ability of participants to maintain task focus while receiving stimulation is particularly important to establish, and it may be a prerequisite for enhancement of cognition with tDCS.

When using tDCS to alter plasticity, it has been suggested that the relevant networks must be active during stimulation to capitalize on "functional resolution" (54, 73). Most investigators using tDCS in schizophrenia have sought to diminish psychotic symptoms, typically by stimulating passive participants. Passive reception of stimulation might be less taxing and anxiety provoking than performing cognitively demanding tasks. Our stimulation session, at 30 minutes, was longer than the 20 minutes used by most others (10, 39, 40). It also entailed a substantial cognitive demand in order to promote functional resolution. Thus, our findings suggest that persons with schizophrenia may tolerate relatively long periods of stimulation while engaged in cognitive training tasks.

We included an SZR group for two reasons. One was that if relatives found tDCS safe and painless, family members with SZ might feel reassured about joining the study. However, recruitment was less difficult than expected. The other reason for testing tDCS in an SZR group is that the latter has mild cognitive deficits that are similar to those seen in SZ (2). We predicted any tDCS-related cognitive enhancement found for SZ would generalize to SZR, although possibly to a lesser extent. We found that the effects were at least as large in the SZR group, if not larger, which is consistent with the findings of one other study (40).

Despite the limitations described above, the results of this study suggest that some cognitive functions in SZ can be altered by bifrontal stimulation of the DLPFC. If these results can be replicated in sham-controlled randomized trials, tDCS might prove to be a safe, inexpensive, and portable means of treating cognitive dysfunction in schizophrenia. If these findings can be replicated in other SZR samples, then tDCS might also improve cognitive functioning in persons with genetic susceptibility to schizophrenia.

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