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# Transcranial electrical stimulation combined with interim testing promotes temporal memory in patients with schizophrenia

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## 1. Introduction

The human brain processes sequential information all the time, whether it is verbal communication, action implementation or situational memory, which essentially involves the representation of temporal information [1]. Temporal memory is an individual's memory of the order in which events occur, and is an important foundation for our correct understanding of the world and for memory and reasoning [2]. Research has shown that people with schizophrenia have impaired temporal memory, as evidenced by the patient's ability to re-recognize stimuli and their inability to recall information in sequence [3–5], which is consistent with pathological features such as thinking in schizophrenia[6].

Interim testing, a behavioral technique, produces forward testing effects by extracting non-target information, thus promoting the retention of target information (new information) [7,8]. tDCS is a neuromodulation technique involving non-invasive, low-intensity electrical stimulation of the cortical regions, modulating spontaneous neuronal activity in the stimulated area [9]. Previous studies have shown the benefits of using interim testing alone [7,8,10] and tDCS alone [11–13] in promoting memory retention in both healthy and clinical populations. However, there is limited research on the combined effects of these two techniques on spatial memory retention. Previous studies have found that combining cognitive training with anodal tDCS treatment of the L-DLPFC can improve visual-spatial memory and episodic memory retrieval [11,14], confirming the feasibility and efficacy of combining behavioral techniques

with neuromodulation techniques to enhance spatial memory retention. Therefore, the present study investigated the facilitation of temporal learning in patients with schizophrenia by a combined ad hoc test of two stimuli, tDCS and transcranial alternating current stimulation (tACS), respectively.

This study investigated the effects of an interim test combined with online tDCS and tACS on temporal memory in patients with schizophrenia. Using online tDCS to stimulate the left dorsolateral prefrontal lobe, during which patients learned static visual pictures for temporal memory. Compare the effects of intermediate tests on correct temporal memory in patients with schizophrenia during anodal and sham tDCS and tACS stimulation. It was hypothesized that the pre-test was significantly better than repeated learning for correctness, and that anodal stimuli were significantly more correct than tACS for correctness and false stimuli for correctness.

## 2. Methods

### 2.1 Participants

Seventy-five inpatients with schizophrenia were recruited from the Third People's Hospital of Lanzhou City (Lanzhou Mental Health Center-Psychiatric Medical Rehabilitation and Nursing Home) and grouped in parallel into 3 conditions, with the sample size depending on the effect size in the study of forward test effects in schizophrenia (Cohen's $d$ = 1.24), and to observe a significant level of forward test effects ( $\alpha = 0.05$; power = 0.80) a minimum of 11 individuals per group is required [15].

Diagnosis and assessment of patients with schizophrenia were conducted by two chief psychiatrists. Neuropsychological background tests included the Montreal Cognitive Assessment (MoCA) for general cognitive function and the Positive and Negative Syndrome

Scale (PANSS) for symptom assessment.

Inclusion criteria for patients with schizophrenia were: (1) meeting DSM-5 diagnostic criteria for schizophrenia; (2) age ≥ 18 years, any gender, education level of primary school or above; (3) all patients receiving stable antipsychotic medication treatment, in a stable phase of illness, able to understand testing requirements, and cooperate to complete all study tasks; (4) no history of neurological or other severe physical diseases, no mental retardation; (5) no color blindness, color weakness, normal vision or corrected vision.

Exclusion criteria were: (1) clear cognitive impairment caused by somatic or cerebral organic lesions, such as cerebrovascular disease, traumatic brain injury, etc.; (2) substance dependence or abuse, mental disorders caused by the use of psychoactive substances; (3) history of brain injury or other central nervous system-related organic diseases; (4) obvious risk of suicide or harm to others; (5) participation in similar experiments within the past 30 days.

2.2 Design

A between-groups experimental design with 2 (Learning condition: Interim testing, Relearning) × 3 (Stimulation type: tDCS stimulation, tACS stimulation, sham stimulation) was used. The dependent variables were the final recall accuracy and proactive interference.

2.3 Devices and Materials

2.3.1 Devices

We utilized the battery-driven direct current stimulation device from NE, Spain. All groups utilized the same electrode montage, with electrode placement following the 10-20

international electroencephalogram system. For tDCS and tACS intervention, 8cm$^2$ circular sponge electrodes were employed. The anode was positioned over F3 (i.e., L-DLPFC), and the cathode over Fp2 (i.e., right supraorbital area).

2.3.2 Materials

A chronological memory paradigm from previous research was used [16]. 128 pictures of common objects were selected from a library of standardized color photographs of objects [17] as temporal-sequence learning and testing materials, and a separate practice sequence was set up for subjects to familiarize themselves with the experimental manipulation. According to [18], the picture size was standardized to 350 × 350 (pixels). The 32 sets of sequence pictures were divided into 4 sequences, each of which was a block.

2.4 Procedure

Before the start of the experiment, the experimenter explained the task and experimental procedure of this experiment, and after the participants understood and agreed to it, they entered the practice phase and started the formal experiment after completion. During this period, participants were informed that after learning each sequence, the computer would randomly decide whether the item order would be tested or not. In fact, whether or not they would be tested was a pseudo-randomized setting, and the test group was tested after learning each sequence. The repeat learning group, on the other hand, was required to learn again. The experimental material was presented on a 14-inch laptop display (resolution 1920 × 1080), with subjects facing the monitor at a distance of about 60 cm, and the screen brightness and contrast were such as to avoid causing discomfort to the subjects.

The classical paradigm incorporating the forward testing effect. Participants first learned the item pictures of the first sequence, displaying the picture items individually in the center of the screen, with each item presented for 2 s. The learning phase required participants to memorize the order of the items that appeared in each sequence, and to press the key to select the order in which the probe items were presented. After the first sequence was learned both groups of subjects solved as many simple math problems as possible within 30s (e.g., 22 + 9 = ?) . Next, subjects in the temporary test condition were presented with the probe item from Sequence 1, presented for 3 s, followed by the presentation of a combinatorial figure consisting of an array of three objects, and participants were asked to select the object that was presented immediately after it (the target item) from the array of three objects. The setup was the same as in Experiment 1. At the end of the test, learning and testing proceeded with Sequences 2 through 4, with the same process as in Sequence 1.

The learning process of the repeated learning group was the same as that of the temporary test group, with the difference that the repeated learning group did not have test items in Sequences 1-3, and followed the process of the learning phase to learn the pictures of the items in Sequences 1-3 again, i.e., the order in which the items were presented. The difference is that after learning once in sequence 4, it is no longer necessary to repeat the learning, but to enter the testing phase, which is the same as the setup of sequence 4 in the temporary testing group. The experimental flow is shown in Figure1.

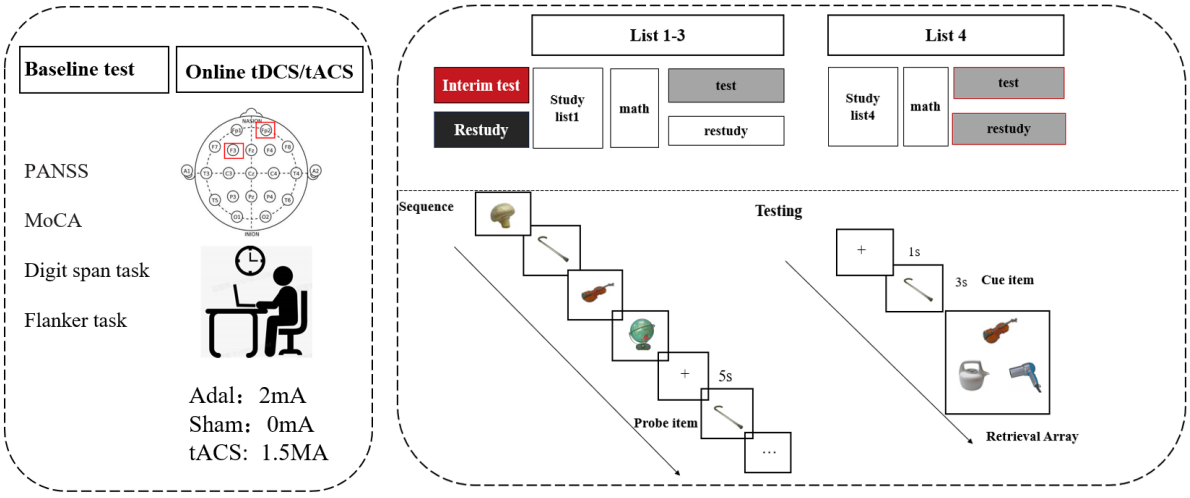


**Figure 1.** Experiment procedure.

2.5 Date scoring & analysis

The results of the experiment were processed using SPSS 26.0. Experimental assistants calculated correct recall and proactive interference rates for each participant's temporal memory.

A mixed-design analysis of variance (ANOVA) was conducted to compare the correct recall rates and proactive interference scores between the two learning strategies under two stimulation conditions. All statistical tests were performed at a significance level of 0.05, and post-hoc comparisons were adjusted using Bonferroni correction. Effect sizes were reported using partial eta-squared ($\eta_p^2$; ANOVAs).

## Study Status

**Record Verification: August 2024**

**Overall Status: Not yet recruiting**

**Study Start: August 20, 2024 [Anticipated]**

**Primary Completion: September 30, 2024 [Anticipated]**

**Study Completion: September 30, 2024 [Anticipated]**

## List of abbreviations

**tDCS** transcranial electrical stimulation

**L-DLPFC** left dorsolateral prefrontal cortex

**tDCS** transcranial alternating current stimulation

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