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Transcranial direct current stimulation (tDCS) enhances reconsolidation of long-term memory

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ABSTRACT

A new and weak memory trace undergoes consolidation to gain resistance against interfering stimuli. When an encoded memory is recalled, it becomes labile and another round of consolidation, or reconsolidation, is required to restore its stability. Transcranial direct current stimulation (tDCS) is a non-invasive method of altering cortical excitability. The aim of this study was to examine the effects of tDCS on the reconsolidation of long-term verbal memory. Participants ($n = 15$) memorized words in the encoding session, then reactivated the memory of the words 3 h later using an old–new recognition task under anodal, cathodal and sham stimulation to the left dorsolateral prefrontal cortex (DLPFC). Finally, after another 5 h, they performed another round of the old–new recognition task and rated their confidence. Anodal tDCS during the second session resulted in significantly more words recognized in the third session as compared to cathodal and sham stimulation. Cathodal tDCS did not affect the recognition performance compared to sham stimulation. These results cannot be attributed to differences in response times and confidence ratings, as they were comparable in all conditions. In order to study whether the activation of a memory was crucial for the enhancing effects of anodal tDCS, a group of controls ($n = 15$) did not perform the recognition task in the second session but still underwent stimulation. Contrary to the main group, anodal stimulation did not enhance the memory performance for the control group. This result suggests that anodal tDCS over the left DLPFC can enhance the reconsolidation of long-term memory only when the memory has been reactivated.

Introduction

When people come across new information, the brain encodes it rapidly and forms a weak memory trace of it within seconds. Through a longer process of consolidation, the weak memory trace is strengthened and maintained for long-term memory [1]. Such a conversion from short to long-term memory allows the memory trace to remain resistant against competing memories for days and even years [2,3]. Consolidation may take hours to years to complete, and involves several other sub-processes like the stabilization and enhancement of the memory trace, and its integration with existing knowledge [4,5].

When an encoded memory is recalled or reactivated, it becomes labile and susceptible to interference again [6]. Nader [7] posits that another round of memory consolidation, or reconsolidation, is required to restore its stability. The destabilizing attribute of memory reactivation depends on the strength of the memory itself, with a longer period of reactivation required to destabilize a more intensively-trained memory [8,9]. It appears that the reconsolidation process typically takes 5 h to complete, with no significant memory impairments observed if reconsolidation inhibitors are introduced 5 h after memory reactivation [10,11]. However, researchers have looked less at reconsolidation than they have at consolidation, leading to a poor understanding of the biological underpinnings of reconsolidation [12]. This has led to disagreements on whether consolidation and reconsolidation are identical processes that occur at different times, or are inherently distinct mechanisms [13].

Sara [14]and Dudai [15] argued that both consolidation and reconsolidation are triggered by weak memory traces that require strengthening, and that both require protein synthesis to proceed. Researchers supporting the notion that both processes are analogous also point out that sleep-dependent developments are beneficial for both processes, indicating a shared dependence on specific sleep states and processes [12]. On the other hand, Taubenfeld, Milekic, Monti and Alberini [16] reported that other than engaging

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contrasting molecular systems, the consolidation of inhibitory learning depends heavily on the dorsal hippocampi but its reconsolidation does not. This dissociation in relevant brain areas required is supported in other studies, which found that the amygdala and nucleus accumbens are necessary for the consolidation but not reconsolidation of taste avoidance behavior and operant conditioning respectively [17,18]. Therefore, the evidence is divided between both groups of researchers and a deeper understanding of the biological bases of reconsolidation will help to reconcile their differences.

Several methods have been used to interfere with the reconsolidation process. The most straightforward technique involves introducing stimuli that are similar to the target memory just after it has been reactivated, resulting in competition for subsequent memory storage and retrieval [19]. Since protein synthesis and sleep-dependent stages are necessary for reconsolidation, other interferences include inhibiting protein synthesis [10,20] and blocking acetylcholine reuptake [21] and β-adrenoceptor activity [11], which imitate regular sleep-dependent processes. In addition, electroconvulsive shock [2,22] has also been used to disrupt the reconsolidation process. In this study, we aimed to examine the effects that transcranial direct current stimulation (tDCS) has on reconsolidation.

tDCS is a non-invasive method of brain stimulation that involves applying a weak electrical current on the scalp [23,24]. This temporarily modulates cortical excitability [25], with effects lasting beyond the duration of the stimulation [26,27]. The positions of the electrodes direct the flow of current, making the effects of tDCS site-dependent [28]. For example, stimulating the motor cortex affects limb movements [29,30], while stimulating the posterior parietal cortex influences attentional shifts between global and local feature-processing [31].

The effects of tDCS are also polarity-dependent: an anodal stimulation enhances cortical excitability while cathodal tDCS dampens it [32]. Nitsche and Paulus [33] noted that stimulating the motor cortex with anodal tDCS increased its excitability compared to a baseline condition, as reflected by amplified motor-evoked potentials (MEPs) measured in the hand. Conversely, cathodal stimulation decreased the excitability of the motor cortex and led to reduced MEPs.

Ohn et al. [34] reported that a 20- or 30-min anodal stimulation boosted short-term memory performance significantly more than 10 min of stimulation did, demonstrating that the effects of tDCS intensify with a longer stimulation period. Additionally, Boggio et al.'s [35] study on patients with Parkinson's disease found that while a 1 mA anodal tDCS applied to the prefrontal cortex did not have an effect on their working memory, a 2 mA stimulation significantly improved subsequent memory performance. It therefore appears that stimulation duration and intensity are also critical parameters of tDCS [36].

Recent advancements in the field have centered on the effects of tDCS on working memory in patients and healthy participants [35,37]. In working with stroke patients with cognitive deficits, Jo et al. [38] reported that applying anodal stimulation to the left dorsolateral prefrontal cortex (DLPFC) for 25 min significantly improved patients' accuracies in a 2-back working memory task compared to sham stimulation. Employing a similar procedure, Fregni et al. [39] found that anodal tDCS administered to the left DLPFC of healthy participants similarly enhanced their performance on a 3-back memory test. In addition, tDCS has also been administered over the temporoparietal cortex to improve the recognition memory of patients suffering from Alzheimer's disease [40].

In contrast, little work has been done to examine the effects of tDCS on long-term memory. Javadi and Walsh [41] applied anodal tDCS to the left DLPFC of healthy participants when they were memorizing words and found that anodal tDCS improved their performance on a word recognition task carried out 60 min later. However, this was only true for words that were presented after the onset of anodal stimulation. On the other hand, cathodal stimulation impaired the subsequent recognition only for words that were presented during the stimulation. These findings suggest that anodal tDCS has an enhancing effect on the initial encoding of memory while cathodal tDCS hinders it. In another study, Javadi, Cheng and Walsh [42] applied a short duration of tDCS (1.6 s) on each trial over the same brain area to study, firstly, the effects of short-duration tDCS and secondly, whether the effects were affected by stimulation administered early or late in a trial. They showed that the application of anodal tDCS early in a trial significantly enhanced memory performance while cathodal stimulation impaired it.

However, the exact mechanism through which tDCS affects memory performance remains unclear. For example, Javadi et al. [41,42] proposed that the memory enhancement observed in their study could be attributed to either the stronger encoding of target words or the improved retention of encoded words. Furthermore, the activation of the planning [43,44] and decision-making [45,46] faculties during the left DLPFC stimulation could also have contributed to the memory modulation effects. The aim of this study was to extend on the current literature by exploring the effects of tDCS on the reconsolidation of long-term verbal memory. If the effects that tDCS has on long-term memory reconsolidation in this study match those for initial consolidation [41], it suggests that initial encoding and consolidation, and the reconsolidation of previously encoded memory are likely to engage similar mechanisms; or at least that tDCS modulates their respective mechanisms in the same way. This supports the notion that initial encoding and subsequent reconsolidation are largely equivalent processes.

Two groups of participants were tested: reconsolidation and control. In the reconsolidation group, stimulation was delivered while the participant was engaged with a recognition task. In the control group, stimulation was delivered without participants reactivating their memories to examine if the effects of tDCS could still be seen.

Previous studies have shown that applying anodal tDCS to the left DLPFC has a beneficial effect on the working [35,37–39] and long-term [41,42] memory while cathodal tDCS has an impairment effect [41,42]. Therefore, it was hypothesized that anodal tDCS would lead to higher performance in the final recognition session as compared to sham stimulation, while cathodal tDCS would result in poorer performance.

Method

Participants

A total of 30 university students (19 females, mean age 22.58 years, range 18–24 years) took part in this study. Participants were randomly split into two equal groups: reconsolidation and control. All participants were right-handed and had normal or corrected-to-normal vision. Participants were also fluent English speakers who were naïve to the purpose of the study. Informed consent in accordance with the Declaration of Helsinki and the guidelines approved by the ethical committee of University College London (UCL) was obtained from all participants. At the end of the study, participants were either reimbursed monetarily or given course credits.

Design

The study adopted a 3 × 2 mixed-factor design with stimulation condition (anodal/cathodal/sham) as the within-subject factor and group (reconsolidation/control) as the between-subject factor.

Participants attended three experimental days that were each separated by one week to minimize the carryover effects of stimulation [35]. The order of stimulation conditions was randomized.

Stimuli

A bank of 720 words was extracted from the MRC psycholinguistic database [47]. The words were controlled for number of letters (min = 3, max = 8, μ = 4.95, SD = 1.25), number of syllables (min = 1, max = 2, μ = 1.36, SD = 0.48), imagability (μ = 543.47, SD = 57.87), concreteness (μ = 519.47, SD = 89.72) and printed familiarity (μ = 546.49, SD = 38.19). The selected words were highly familiar and imaginable to ensure that participants knew all the words and were able to imagine them. Words were randomly selected for each session and different words were used each day.

Apparatus

The experiment was run on a PC computer with a 17-inch monitor, 75 Hz refresh rate and a resolution of 1024 × 768 pixels. Stimuli were presented in capital letters using white Arial font against a black background, subtending approximately 3–6 degrees of horizontal visual angle. Stimulus presentation and the recording of responses were attained using MATLAB (v7.5; MathWorks Company) and the Psychophysics Toolbox (v3; [48,49]). Data analyses were conducted with SPSS (v17.0; LEAD Technologies, Inc.).

Transcranial direct current stimulation

Direct electrical current was delivered with a NeuroConnDC Brain Stimulator Plus unit (Rogue Resolutions, Wales, UK). The left DLPFC was selected as the main stimulation site, while the contralateral supraorbital area was chosen as the position for the reference electrode [24,28]. For anodal and sham stimulation of the left DLPFC, the anode was placed over F3 according to the 10–20 international system for electrode placement [50] and the cathode was placed over the right supraorbital area. For cathodal stimulation, the electrode polarities were swapped.

Stimulation was administered via a pair of surface sponge electrodes soaked in saline solution. A direct current of 1.5 mA with a fade-in and fade-out time of 10 s was delivered for 20 min for the anodal and cathodal stimulation conditions and 30 s for sham stimulation [23]. Sponge electrodes of differing sizes were used: 35 × 35 mm^2 for the left DLPFC and 55 × 55 mm^2 for the reference electrode. Such an arrangement concentrated the stimulation at the main stimulation site by making the stimulation intensity at the DLPFC 2.5 times of that at the reference electrode, i.e. 1.22 $\mu A/mm^2$ for the left DLPFC and 0.49 $\mu A/mm^2$ for the reference electrode. This stimulation paradigm has been shown to be safe for use on humans [36,51].

Procedure

Each experimental day consisted of three separate sessions: encoding, stimulation and recognition (Fig. 1A). Before the start of the first session, participants were verbally informed that the design of the experiment included three experimental days, each consisting of three sessions. Participants were also told that during the first session of each day, 120 words would be presented to them singly and they should memorize the words for a recognition task later that day. Participants were explicitly reminded that during their free time between the sessions, they should not think about the words that they had seen. They were also introduced to the stimulation procedure and were told that they would be stimulated with different wave-forms in the second session of each experimental day.

In the first (encoding) session, participants were presented with 120 words and asked to imagine them to memorize them for subsequent memory tests. Each word was presented for 0.400 s, followed by a fixation cross that appeared for 2.1 s to represent the imagination period. Trials were separated by 0.750 s with a centrally-presented exclamation mark (Fig. 1B). The trials were split into 6 blocks of 20 words each, and participants were given 30 s rest time between each block.

Three hours later, in the second (stimulation) session, participants in the reconsolidation group underwent 20 min of tDCS while attempting an old–new recognition task. A total of 240 words were presented in 6 blocks. Each block contained 20 'old' words seen in

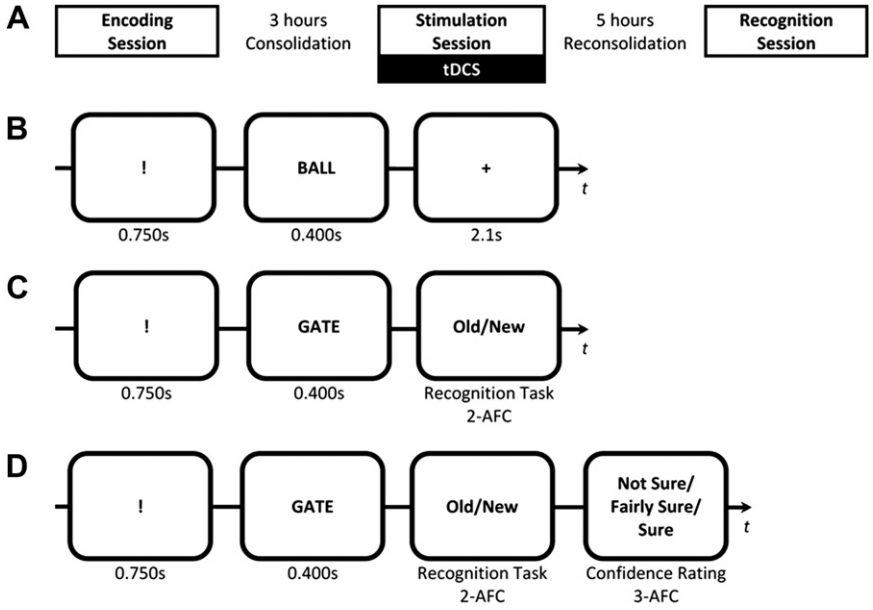

Figure 1. (A) Outline of an experimental day consisting of the encoding, stimulation and recognition sessions. (B) Procedure of a trial in the encoding session, where participants were required to imagine presented words in order to memorize them. (C) Outline of the recognition task in the stimulation session for the reconsolidation group. (D) Procedure of a trial in the recognition session, where participants had to rate their confidence after they performed the old-new recognition task again. AFC stands for 'alternative forced choice'.

the encoding session and 20 'new' words randomly drawn from the word bank. Participants were informed that they had seen half of the words before, and were asked to indicate using the keyboard whether they thought that the word presented was an old word or new one. Participants were reminded to respond as accurately and quickly as they could. Trials were again separated by an exclamation mark that was presented for 0.750 s (Fig. 1C). At the end of each block, the percentage accuracy for that block was shown on the screen for 3 s as feedback for participants. In contrast, participants in the control group were given 20 min of stimulation while they played simple computer games such as Tetris, Solitaire and Minesweeper.

The final (recognition) session was scheduled to occur 5 h after the stimulation session [10,11]. The old–new word recognition task was employed here as a measure of memory performance. The same set of old and new words shown in the stimulation session was used in this session. In addition to the old–new recognition task, participants were asked to rate how confident they were that their response was correct using a three-point scale: not sure, fairly sure and sure (Fig. 1D).

This entire procedure was repeated on 2 other experimental days but with different stimulation conditions (anodal/cathodal/sham).

Statistical analysis

Recognition session

The performance accuracies, response times and confidence ratings for old and new words in the recognition session of each participant in the reconsolidation and control groups were recorded as dependent variables for subsequent analysis. Confidence ratings were mapped onto a percentage scale so as to derive mean confidence ratings in percentage, with 50% representing 'not sure', 75% representing 'fairly sure' and 100% representing 'sure'. The dependent variables were split over old and new words and subjected to a 3 × 2 mixed-factor analysis of variance (ANOVA), with stimulation condition (anodal/cathodal/sham) as the within-subject factor and group (reconsolidation/control) as the between-subject factor. Moreover, to consider performance accuracies for old and new words under a single analysis, performance accuracies were converted into measures of *d'* [52]. Subsequently, a 3 × 2 mixed-factor ANOVA was run, with *d'* as the dependent factor and stimulation condition and group as independent factors.

Stimulation session

The performance accuracies and response times for old and new words in the stimulation session of each participant in the reconsolidation group were recorded as dependent variables for subsequent analysis. The dependent variables were split over old and new words and subjected to a one-way repeated measures of ANOVA, with stimulation condition (anodal/cathodal/sham) as the within-subject factor. Similar to the recognition session, performance accuracies were converted into measures of *d'* and subjected to a one-way ANOVA, with stimulation condition as the independent factor.

Post-hoc pairwise tests of three comparisons (anodal vs. cathodal, anodal vs. sham and cathodal vs. sham) were conducted, using a Bonferroni-adjusted alpha level of 0.016 (0.05/3). The dependent variables were checked for normal distribution using the Kolmogorov–Smirnov goodness-of-fit test.

Results

Recognition session

The mean performance accuracies for recognition of old words were subjected to a 3 × 2 mixed-factor ANOVA. The main effect of stimulation condition was significant, $F(2, 56) = 4.45$, $P = 0.016$. The main effect of group was highly significant, $F(1, 28) = 16.82$, $P < 0.001$. The interaction between the two factors was also significant, $F(2, 56) = 3.70$, $P = 0.031$. Fig. 2A shows the mean performance accuracy for old and new words for the reconsolidation and control groups.

Post-hoc paired-samples *t*-tests showed that a significantly higher proportion of old words was recalled under anodal stimulation compared to sham stimulation ($t(14) = 3.32$, $P = 0.005$) and cathodal stimulation ($t(14) = 3.34$, $P = 0.0048$) in the reconsolidation group. No other pairwise comparison in either of the groups showed a significant difference between the stimulation conditions ($P > 0.2$).

Similarly, the mean performance accuracies for recognition of new words were subjected to a 3 × 2 mixed-factor ANOVA. None of the comparisons were significant ($P > 0.1$).

Performance accuracies were converted into measures of *d'*, as reflected in Fig. 2B. A 3 × 2 mixed-factor ANOVA showed a significant main effect of stimulation condition, $F(2, 56) = 4.14$, $P = 0.021$, a significant main effect of group, $F(1, 28) = 10.56$, $P = 0.003$, and a significant effect of interaction of the two factors, $F(2, 56) = 3.81$, $P = 0.028$.

Post-hoc paired-samples *t*-tests on *d'* values showed a significant difference between anodal and cathodal stimulation conditions ($t(14) = 3.09$, $P = 0.008$) as well as a significant difference between anodal and sham stimulation conditions ($t(14) = 3.03$, $P = 0.009$) in the reconsolidation group. No other pairwise comparisons were significantly different ($P > 0.2$).

The response times of participants in the recognition session are presented in Fig. 2C. Two 3 × 2 mixed-factor ANOVAs were conducted on the data, split over old and new words. These analyses revealed non-significant effects on all the comparisons. These results point to a comparable response time under all conditions ($P > 0.6$).

The confidence ratings of participants in the recognition session (Fig. 2D) were also subjected to two 3 × 2 mixed-factor ANOVAs, split over old and new words. Again, no significant difference was found ($P > 0.5$).

Stimulation session

The performance accuracies and response times in the stimulation session (2nd session) for the participants in the reconsolidation group were also analyzed (Fig. 3A). Performance accuracies for old and new words were subjected to two one-way repeated measures ANOVAs, with stimulation condition as the independent factor. These analyses showed a non-significant main effect of stimulation condition for both old and new words ($P > 0.2$). Subsequently, performance accuracies were converted to measures of *d'* (Fig. 3B). These measures were subjected to a one-way ANOVA, with stimulation condition as the independent factor. This analysis showed a non-significant main effect of stimulation condition.

Similarly, response times for old and new words were subjected to two one-way repeated measures ANOVAs, with stimulation condition as the independent factor (Fig. 3C). These analyses showed a non-significant main effect of stimulation condition ($P > 0.5$).

Discussion

The post-hoc *t*-tests conducted on the performance accuracies revealed a significantly higher accuracy under anodal stimulation, compared to the cathodal and sham stimulation conditions for the reconsolidation group. This advantage that anodal tDCS brings to the word recognition task cannot be explained by slower reaction times on anodal trials, as response times on all trials were not

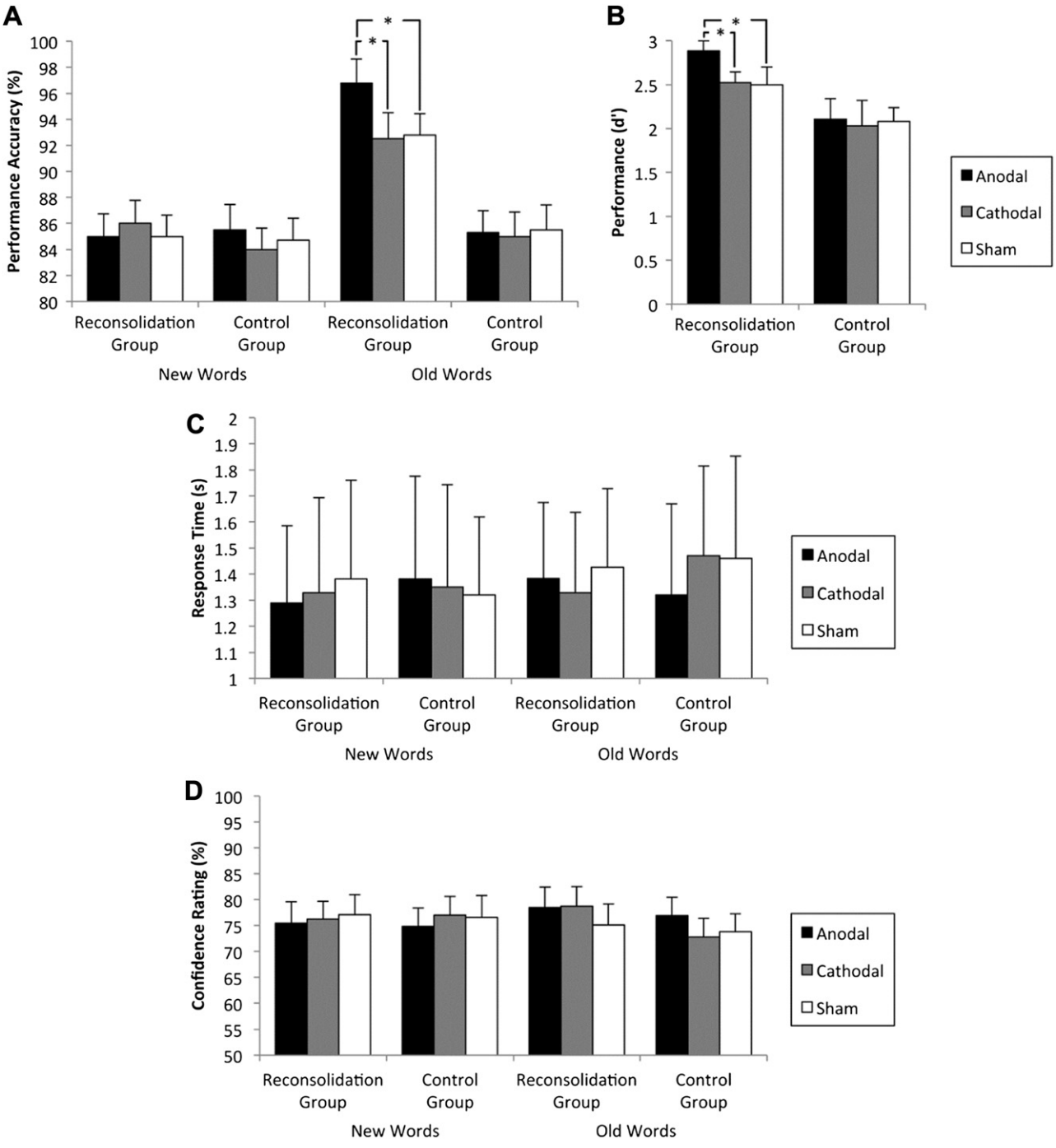

Figure 2. Performance of the participants in the word recognition task during the recognition session (3rd session), split over old and new words and the reconsolidation and control groups. (A) The mean percentage performance accuracies, (B) performance measure in *d'*, (C) response times and (D) confidence ratings. Error bars represent one standard deviation of the mean; * indicates a $P < 0.016$ Bonferroni-corrected paired-samples *t*-test.

significantly different. Moreover, this effect was observed only in the reconsolidation group, indicating that the reactivation of the memory was necessary for tDCS applied over the left DLPFC to modulate memory.

Previous studies have reported that anodal tDCS enhances cortical excitability for up to an hour after stimulation [33,53]. Therefore, participants would have resumed normal cortical functioning when attempting the word recognition task in the recognition session, which took place 5 h after stimulation was administered. As a result, the improvement observed in memory performance under anodal tDCS here also cannot be attributed to an enhanced cortical excitability produced by tDCS. A plausible explanation for the results described here is that anodal tDCS applied in the stimulation session had a reinforcing effect on the reconsolidation of reactivated memories, thereby leading to stronger reconsolidation of the words that could easily be recognized in the recognition session.

In Javadi and Walsh's [41] and Javadi et al. [42] studies, anodal tDCS that was applied during initial encoding enhanced performance on a subsequent word memory task. This raises the possibility that anodal tDCS used during initial encoding can be combined with anodal tDCS administered during subsequent

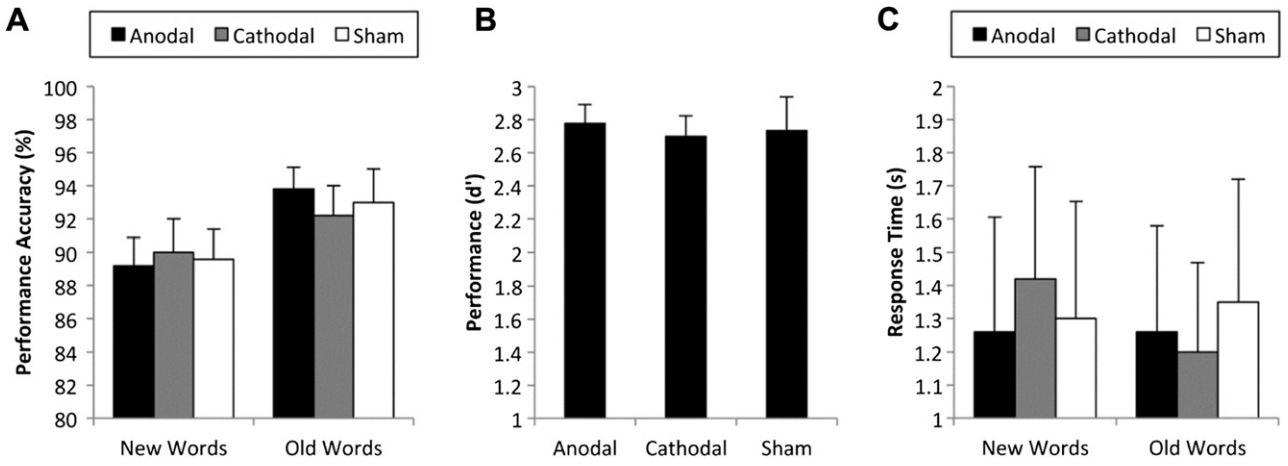

Figure 3. Performance of the participants in the word recognition task during the stimulation session (2nd session), split over old and new words for the reconsolidation group. (A) The mean percentage performance accuracies, (B) performance measure in *d'* and (C) response times. Error bars represent one standard deviation of the mean.

reconsolidation in order to bring larger memory improvements to people. However, more research needs to be conducted to examine if the beneficial effects of tDCS during encoding and reactivation are additive, or if there is a limit on the extent to which tDCS can enhance memory performance. Studies involving patients with Alzheimer's and Parkinson's diseases have shown that anodal tDCS improves various forms of working memory in patients [38,40]. It will therefore be useful to investigate if the improvements that anodal tDCS confers on long-term memory in this study can be extended to patients with memory deficits.

None of the effects in the 3×2 mixed-factor ANOVA conducted on the performance accuracy of new words were significant, indicating comparable performance accuracies for new words across different stimulation conditions and across the reconsolidation and control groups. This shows that the rate of false alarm (new words being falsely judged as old) was not affected by stimulation condition, nor by whether participants were from the reconsolidation or control groups.

This study also found that the confidence ratings of participants were not significantly altered when they responded under different stimulation conditions. This suggests that participants were not subjectively aware that they were performing better under the anodal tDCS condition. However, participants' confidence ratings across all conditions and groups were on average 75%, which translates to the "Fairly Confident" option. This suggests that participants may not have put in effort to rate their confidence accurately. Therefore, confidence rating might not be a good measure of self-rated competence of memorization in our study.

Cathodal stimulation administered during the stimulation session in this study did not impair later memory performance during the recognition session. Taken together with the enhancing effects of anodal stimulation, this result suggests that while it is easy to restore the stability of a reactivated memory by anodal stimulation, it is comparatively more difficult to disrupt a formed memory using cathodal tDCS. However, these findings do not corroborate with those reported in the Javadi and Walsh [41] study that looked at the effects of tDCS on initial encoding. These disparities may have arisen because cathodal stimulation was only able to demolish the relatively weak memory traces during initial encoding but was not strong enough to alter the relatively stable memory traces that had undergone a 3-h consolidation period. This means that the consolidation process in this study may have been sufficient to prevent the impairing effects of cathodal stimulation from becoming effective. An alternative account for the different findings is that reactivating memories does not destabilize them to a form as unstable as they were when first acquired, and that reactivated memory is stronger than newly-acquired memory as a result of rehearsal or practise effects. This implies that reconsolidated memory is stronger than consolidated memory, which explains why cathodal tDCS can only impair consolidated memory but not reconsolidated memory. Such an explanation would also claim that consolidation and reconsolidation are different processes because the latter produces stronger memories. However, a conclusive verdict on the debate of whether initial encoding of a memory and restoration of a reactivated memory are the same processes remains elusive if the neural mechanisms of tDCS are not clearly understood.

Contrary to what Javadi and Walsh [41] reported, performance in the stimulation session (2nd session) was not significantly modulated by the stimulation in different conditions. Based on their results, one might expect to observe a higher performance accuracy for anodal stimulation of the left DLPFC and a slightly lower performance accuracy for cathodal stimulation of the same brain area. This deviation in findings could be due to the duration of the retention interval. In the current study, the duration between the encoding and stimulation session, in which participants in the reconsolidation group were asked to do an old/new recognition task, was much longer than the retention interval in Javadi and Walsh's study [41]. We argue that the time interval in between encoding and retrieval of the stimuli plays a critical role in the effectiveness of tDCS over the left DLPFC: with an increase of this time interval, the effects of tDCS become weaker.

Meanwhile, the mechanisms underlying the effects of tDCS continue to be poorly researched. While tDCS has been shown to modulate cortical excitability [32], it is not clear how this translates to a memory enhancement or impairment subsequently. Therefore, it remains uncertain if the same neural correlates are responsible for the improvements that anodal tDCS brings to reactivation here and to encoding in Javadi and Walsh's [41] or Javadi et al.'s [42] study. The need to address the exact functional role that tDCS plays in memory studies is especially pressing given that other systems may have also been engaged with DLPFC stimulation. These include planning skills [44], learning ability [46] and verbal fluency [43], which may have individually contributed to the memory improvement observed under anodal stimulation. Developing theoretical models that describe how tDCS achieves its effects will help advance the research in this field and promote the use of tDCS to a wider audience.

In conclusion, anodal tDCS over the left DLPFC significantly improved the performance of participants in a long-term verbal memory task. However, this was only true when the memory for those words was reactivated. The results cannot be attributed to differences in response times, as they were the same in all conditions. Cathodal stimulation, contrary to findings in previous studies, did not impair subsequent memory, possibly because consolidated memory is too strong. Together with tDCS administered during encoding, tDCS applied to reactivated memories has a potentially meaningful role to play in the rehabilitation of patients with memory deficits.

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