The Effects of Anodal Transcranial Direct Current Stimulation on Working Memory

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Abstract The aim of this paper was to review the effects of anodal transcranial direct current stimulation (tdcs) on working memory in healthy population. Ten studies were identified involving 319 subjects. Working memory performance was measured using cognitive tasks such as the *n*-back task, digit span forward or digit span backwards test, Sternberg WM task, the Pacet Auditory Serial Addition Task (PASAT) and the Pacet Auditory Serial Subtraction Task (PASST), verbal and visuospatial tasks and the Operation Span (OSpan) task. All studies showed that anodal tdcs co-administered with cognitive tasks can significantly enhance working memory performance by inducing cortical excitability. Further research should be made towards older population as aging is accompanied with a decline in cognitive abilities and patients with memory deficits to demonstrate whether tdcs can be used as an interventional mean in clinical context as well.

Keywords Anodal transcranial direct current stimulation • Dorsolateral prefrontal cortex (DLPFC) • Working memory

1 Introduction

Normal ageing is accompanied by a decline in cognitive and motor abilities which result in the decrease of dexterity skills, speed and accuracy [1, 2]. Working memory (WM) is a cognitive system that is able to store, process and manipulate information for transient use [3]. According to Neuroimaging studies, during working memory tasks different areas of the prefrontal cortex are activating in young and older adults indicating that each group performs the tasks differently [1]. Older adults use compensatory mechanisms in order to perform the same as the younger adults in a motor task however they retain their ability to learn through practice [1, 2]. Recent

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studies have shown that non-invasive brain techniques such as the transcranial direct current stimulation (tdcs) can increase cortical excitability leading to the enhancement of working memory and motor learning in healthy subjects [4–6]. In most of the studies the dorsolateral prefrontal cortex (DLPFC), which includes Brodmann Areas 46 and 9, is stimulated because it has been shown to be highly involved in WM processing [7, 8].

2 Search Strategy and Selection Criteria

Pubmed, Science Direct, Springer and Sage databases were searched from June 2016 to August 2016 using the terms "working memory", "anodal transcranial direct current stimulation", "dorsolateral prefrontal cortex", "healthy population". The reference lists of systematic review articles and meta-analyses were scanned for any additional references missed from the above databases' search. The studies selected were examining only healthy population and were conducted the last decade. Only English literature was included for the current review.

3 Studies' Findings

Andrews et al. [7] investigated the relationship between cognitive activity and anodal tdcs on the left DLPFC (areas 9, 46) to enhance working memory in 10 participants aged 20–51 years old. All participants took part in the following three conditions at intervals of 1 week to prevent any carry-over effects from tdcs: Active or sham tdcs applied for 10 min during an *n*-back task or active tdcs applied for 10 min at rest. Before and after each condition a digit span forward & digit span backwards test was administered verbally by the experimenter. Their objective was to explore whether tdcs applied to the left DLPFC during the *n*-back task would improve performance on a digit span forward or digit span backwards test, to a greater extent than either tdcs or cognitive activity alone. Their results showed that active tdcs co-administered with the *n*-back task enhanced the performance on digit span forward, compared with the two other conditions. However, no significant result was found regarding the digit span backwards test. This study suggested that there may be potential benefit from the use of adjunctive cognitive activity to enhance the effects of tdcs.

Fregni et al. [8] examined the effect of anodal tdcs (active or sham) on working memory by stimulating the left DLPFC during a 3-back memory task in 15 subjects aged 19–22 years old. Seven participants also undertook a session of anodal tdcs on M1 and cathodal tdcs on the left DLPFC. Their study concluded that tdcs co-administered with a 3-back working memory task had significant results ($p = 0.0042$) comparing to sham stimulation, tdcs on primary motor cortex (M1) or cathodal tdcs.

Giglia et al. [9] compared anodal tdcs stimulation on right and left DLPFC to investigate any different effects on cognitive performance in ten right-handed participants. All participants undertook a sham condition as control. They concluded that only anodal tdcs on the right DLPFC ($p < 0.01$) was able to enhance performance on the memory guided visuospatial task compared to the other two conditions.

Hoy et al. [10] found that 1 mA of anodal tdcs produced the most significant effects ($p = 0.038$) compared to higher current of 2 mA or sham tdcs on the left DLPFC. Eighteen subjects were examined in all three conditions over a period of 3 weeks.

Mulquiney et al. [11] investigated whether transcranial random noise stimulation (tRNS) on left DLPFC can significantly enhance WM performance compared to anodal tdcs or sham stimulation. Ten subjects were examined in three conditions (tRNS or sham tdcs whilst performing the Sternberg WM task or anodal tdcs) at intervals of minimum 1 week. All participants performed the *n*-back task before and after each intervention to assess speed and accuracy. Results showed that only anodal tdcs significantly improved the speed of performance on 2-back memory task.

Pope et al. [12], following previous studies that showed improvement in cognitive performance due to anodal tdcs stimulation, aimed to determine whether anodal tdcs on the left DLPFC could similarly enhance WM performance when the cognitive task required is on higher demand. Sixty-three participants were separated in three equal groups receiving 20 min of anodal, cathodal or sham tdcs. Accuracy, latency and variability of correct verbal responses were assessed using the Pacet Auditory Serial Addition Task (PASAT) and the Pacet Auditory Serial Subtraction Task (PASST) before and after each intervention. Significant effects were found only on PASST after the anodal tdcs concluding that anodal tdcs can selectively improve difficult cognitive performance.

Stephens and Berryhill [13] examined cognitive performance in 90 older adults paired with 15 min of 1, 2 mA anodal tdcs or sham tdcs on the right prefrontal cortex (PFC). Their results found that 2 mA anodal tdcs induced significantly greater long-lasting results after 1 month without stimulation.

Zaehle et al. [14] investigated the effect of tdcs on WM performance and neural activity using a letter 2-back task after sham, anodal and cathodal stimulation on the left DLPFC. Their study showed that tdcs can change WM performance by modulating the underlying neural oscillation.

Jones et al. [15] tested 72 participants in 10 sessions of sham or anodal tdcs along with verbal and visuospatial tasks and the Operation Span (OSpan) task. All participants undertook a follow up testing after 1 month. Results showed that all subjects improved after WM tasks however only the participants who received anodal tdcs maintain significant effects after 1 month follow up.

Ohn et al. [16] investigated the effects of 1 mA anodal or sham tdcs on 15 young healthy participants. Their results showed that 1 mA of tdcs enhanced WM performance and the effects lasted for 30 min after the end of stimulation (Table 1).

Table 1 Studies of tdcs stimulation and working memory performance

Author	Type of study	Participants (N)	Anode electrode position	Duration	Amplitude/Electrode	Results
Andrews et al. [7]	Cross-over study	10 (mean age 28.1 ± 8.72)	F3 left DLPFC	10 min	1 mA: 35 cm^2	Active tdcs co-administered with the n-back task enhanced the performance on digit span forward, compared with the two other conditions
Fregni et al. [8]	Randomized controlled trial	15 (mean age 20.2)	F3 left DLPFC	10 min	1 mA: 35 cm^2	Tdcs on DLPFC co-administered with the 3-back task showed significant results comparing to sham and tdcs on MI or cathodal tdcs
Giglia et al. [9]	Quasi experimental study	10 (mean age 27 ± 2.3)	F3 left DLPFC or F4 right DLPFC	10 min	1 mA: 35 cm^2	Only anodal tdcs on the right DLPFC was able to enhance performance on the memory guided visuospatial task compared to the other two conditions
Hoy et al. [10]	Quasi experimental study	18 (mean age 24.71 ± 6.97)	F3 left DLPFC	20 min	1 or 2 mA: 35 cm^2	l mA of anodal tdcs produced the most significant effects compared to the other conditions
Mulquiney et al. [11]	Cross-over study	10 (mean age 29.5)	F3 left DLPFC	10 min	1 mA: 35 cm^2	Only anodal tdcs significantly improved the speed of performance on 2-back memory task
Pope et al. [12]	Randomized controlled trial	63 (mean age 22 ± 2.3)	F3 left DLPFC	20 min	2 mA: 25 cm^2	Significant effects were found only on PASST after the anodal tdcs concluding that anodal tdcs can selectively improve difficult cognitive performance
Stephens and Berryhill [13]	Randomized controlled trial	90 (mean age 69)	F4 right DLPFC	15 min	1 mA or 2 mA: 35 cm^2	2 mA anodal tdcs induced significantly greater long-lasting results after 1 month without stimulation
Zaehle et al. [14]	Randomized controlled trial	16 (mean age 25 ± 2)	F3 left DLPFC	15 min	1 mA: 35 cm^2	Tdcs can change WM performance by modulating the underlying neural oscillation
Jones et al. [15]	Randomized controlled trial	72 (mean age 64.38 ± 5.08)	F4 right DLPFC	10 min	1.5 mA: 35 cm^2	All subjects improved after WM tasks however only the participants who received anodal tdcs maintain significant effects after 1 month follow up
Ohn et al. [16]	Cross-over study	15 (mean age 27.7 ± 6.97)	F3 left DLPFC	30 min	1 mA: 25 cm^2	1 mA of anodal tdcs produced the most significant effects compared to sham tdcs and the effects lasted for 30 min after the end of stimulation

4 Discussion

Working memory is associated with complex cognitive tasks such as learning and reasoning that tend to decline while ageing [1, 17]. The aim of this review was to investigate whether tdcs stimulation whilst administered with a cognitive task can induce cortical excitability in the DLPFC and enhance WM performance in healthy subjects.

All studies showed that anodal tdcs co-administered with cognitive tasks can significantly enhance working memory performance. Six studies [7, 8, 10, 11, 13, 14] used the *n*-back task which has been found to activate the DLPFC [14]. The rest of the studies [9, 12, 15] used other verbal and visuospatial tasks such as the PASAT, the PASST and the OSpan task. Their results demonstrated that only anodal tdcs, compared to the other conditions tested, produced significant results.

The findings suggested that anodal tdcs combined with a cognitive task can modulate working memory performance implicating that tdcs can be used as a therapeutic mean in clinical context. Two studies [18, 19] have investigated the effect of tdcs stimulation on patients. Ulam et al. [19] demonstrated significantly positive effects of tdcs on WM of patients with Traumatic Brain Injury (TBI). Boggio et al. [18] examined tdcs stimulation on patients with Parkinson's disease (PD) and their results highlighted the important effects of 2 mA anodal tdcs on WM performance as indexed by task accuracy. Boggio and colleagues concluded that tdcs can induce positive effects on WM of PD patients but it depends on the intensity and site of stimulation.

There is also evidence of some non significant effects of tdcs on WM in three studies [3, 11, 12]. Berryhill and Jones tested 25 older subjects (mean age 63.7) in WM performance according to their educational background. The less educated group presented no benefit from tdcs stimulation on cognitive tasks contrary to the educated group that was uniformly affected. Berryhill and Jones hypothesized that possibly the educated group employed different strategy on WM tasks by recruiting better structures of PFC. Their results are supported from previous studies [20, 21] that demonstrated that expert participants showed greater activation of the PFC and performed better on cognitive tasks compared to novice participants. Mulquiney et al. [11] and Pope et al. [12] concluded that tdcs does provide evidence of cortical excitability but only in some aspects of DLPFC and can selectively enhance cognitive performance in difficult cognitive tasks.

Eight studies [7–12, 14, 16] examined only young healthy participants. Six of these studies set the tdcs current at 1 mA except from Pope and colleagues (2 mA) and Hoy and colleagues (1 and 2 mA). Hoy and colleagues, found the most significant effects after 1 mA of tdcs which contradicts their hypothesis that higher current would have greater improvement on WM performance. Stephens and Berryhill [13] and Jones et al. [15] included older participants and the current was set at 2 and 1.5 mA respectively showing that possibly older adults need higher intensity for long lasting effects. Although the results of the studies reviewed were promising, further research should be made towards older population as aging is accompanied with a decline in cognitive abilities. Future studies, may also compare young and old participants on their performance in a WM task, to demonstrate whether tdcs will boost the performance of older participants compared to the young group.

5 Conclusion

There are several evidence that tdcs can induce cortical excitability leading to better cognitive performance. This indicates the importance for further research to demonstrate whether tdcs can be used as an interventional mean in patients with memory deficits. Future studies should focus on including larger sample size and exploring possible differences between young and old participants, to demonstrate whether it is tdcs that boosts cognitive performance or practice of a cognitive task itself. Also, more studies are needed to investigate the variations of current density, the duration of stimulation and the number of sessions for long-lasting effects.

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