Archives of Psychiatry and Psychotherapy, 2020; 1: 56–62

DOI: 10.12740/APP/109146

The effects of transcranial Direct Current Stimulation on working memory in the elderly with normal cognitive impairments

Mahboubeh Firouzkouhi Moghadam, Mona Kamali Ardekani,
Alireza Shamsi

Summary

Objective: Reduced cognitive function is one of the problems caused by aging, which leads to reduced performance of the elderly. This is a study to evaluate the effects of transcranial Direct Current Stimulation (**t**DCS) on working memory in the elderly with normal cognitive impairments.

Methods: In this clinical trial, 45 elderlies participating in a self-care educational course in Zahedan, Iran, in 2016, were assigned into three groups of F3, F4, and sham stimulation. From all the participants, 2-back, forward and backward digit span, and Mini Mental State Examination (MMSE) tests were taken.

Results: The three groups showed no significant difference in the mean score of 2-back test at different time points.The three groups showed no significant difference in mean score of backward digit span test at different time points. The mean score of backward digit span test was significantly higher in the F3 group after the intervention.

Discussion: The results of this study indicate that the score changes in the 2-back and the forward digit span tests were significant only in the F3 group. Also, the F4 group showed a significant difference at all the time points after the intervention, compared to before the intervention, but this change was less than that in the F3 group.

Conclusion: This study shows that tDCS can improve working memory performance via F3method. The tDCS can cause working memory improvement and naming facilitation by stimulation.

cognitive function, elderly, transcranial Direct Current Stimulation (tDCS), working memory

INTRODUCTION

Aging (people aged over 60 years) has gained importance due to an increase in the world's elderly population [1]. According to the World Health Organization (WHO), the world's population is aging, and the global population of elderlies is expected to reach over two billions by the year 2050 [2]. However, the number of elderlies in southwest Asia (including Iran) in 2000 was about 7%, and it is predicted to constitute 15% of the total population by 2030 [3]. The elderly are at increased risk of chronic illnesses, loneliness, isolation, lack of social support, and physical and mental disabilities [4].

Mahboubeh Firouzkouhi Moghadam[1], **Mona Kamali Ardekani**[2], **Alireza Shamsi**[3]**:** [1]Department of Psychiatry, Research Center for Children and Adolescents Health (RCCAH), Zahedan University of Medical Sciences, Zahedan, Iran; [2]Department of Psychiatry, Zahedan University of Medical Sciences, Zahedan, Iran; [3]School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Correspondence address (wytłuszczone): ar.shamsi@sbmu.ac.ir

Natural cognitive status is dependent on the full functioning of various brain systems. Aging causes brain function impairment and cognitive problems in the individual, which may lead to a wide array of problems in the elderly [5]. Ageing has been related to cognitive decline and anatomical and functional neural changes [6].

Working memory (WM) denotes a brain system that includes the temporary storage and manipulation of the information essential for complex cognitive functions and supports higher cognitive functions such as reasoning, language comprehension, and learning [7]. This description has evolved from the theory of a unitary short-term memory system, where WM has been establish to need the simultaneous storage and processing of information [8]. WM relies on prefrontal and parietal cortical regions that are largely affected by small vessel disease (SVD) [9]. Administrative function of WM has received great consideration because it serves as a attention controller that assigns and coordinates attentional resources for cognitive tasks [10].

Transcranial Direct Current Stimulation (tDCS) is a non-invasive method, in which a short-wave direct current of 1 to 4 mA is introduced into the scalp, and by that, long-term changes are made in cortical polarization, following the depolarization and hyperpolarization of the neurons; in other words, this method impacts neurotransmitters. In this type of electrical stimulation, brain structures are targeted using weak electrical currents [11]. tDCS is a non-pharmacological intervention that can affect brain function through stimulating cortical irritability [12]. tDCS has been extensively tested in the past decade as a non-invasive, inexpensive, and safe alternative method to change cortical excitability by altering the cerebral cortical relaxation potential [13]. Today, tDCS therapy is a very useful treatment for attention deficit hyperactivity disorder (ADHD), learning disabilities, autism, mental retardation, major depressive disorder, and addiction to drugs such as amphetamines and alcohol [14].

One of the problems in the elderly, who constitute a large portion of the population, is the decline in WM, which leads to lower performance. Therefore, studying WM in this population group is important. Herein, we evaluated the effects of tDCS on WM in the elderly with normal cognitive impairments.

METHODS

Study populations

Study populations were randomly selected among participants of a self-care educational course held by Zahedan university of medical sciences for elderlies (aged over 60 years old) in Zahedan, Iran, in 2016. In this clinical trial, we enrolled 45 elderlies aged over 60 years old.

The inclusion criteria comprised having informed consent to participate in the study, no history of mental and neurological diseases (such as depression, psychosis, Alzheimer's disease, multiple sclerosis, and cerebrovascular accident), and not having contraindications for

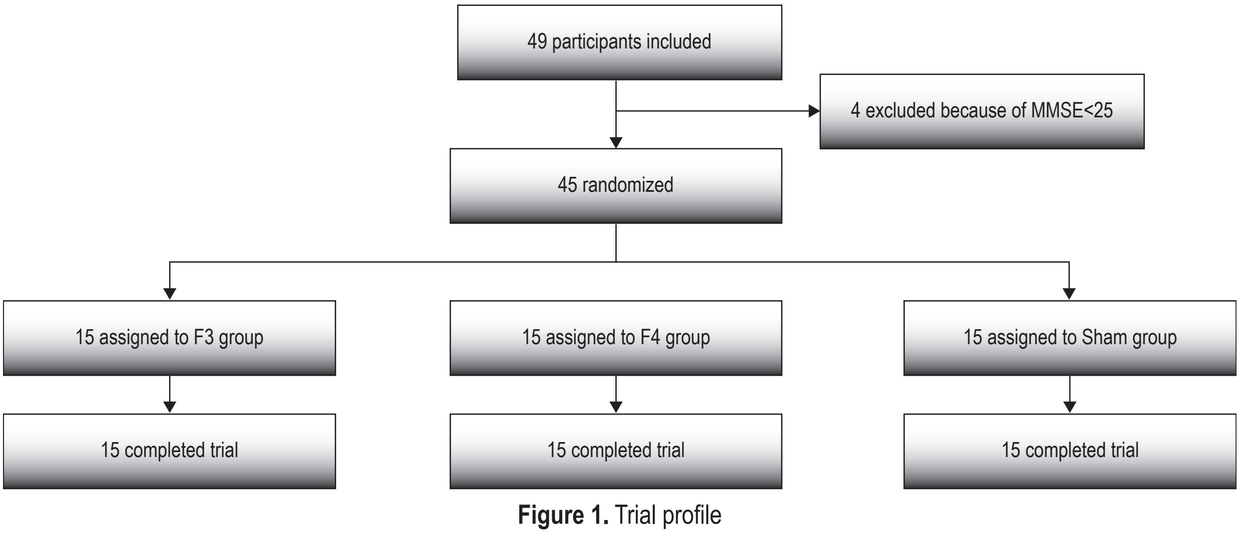

Figure 1. Trial profile

tDCS (history of brain surgery, history of seizure at any time, the presence of vascular clips in the brain, the presence of cardiac pacemakers, and history of schizophrenia or bipolar disorder).

The exclusion criteria were Mini-Mental State Examination (MMSE) score of less than 25, or experiencing complications of the intervention such as severe headache or aggravated skin inflammation. Trial profile is shown in figure 1.

tDCS

Brain stimulation was administered using a constant current stimulator that provided 2mA tDCS stimulation between two electrodes.

The participants were randomly divided into three groups of 15 (were matched according to age and educational level) as follows: F3 group: tDCS administered for participant's simulation with anode over F3 and cathode over the right supraorbital area; F4 group: tDCS administered for participant's simulation with F4 anode and cathode locations on the opposite side of the supraorbital area; and sham group: tDCS administer for participants with sham stimulation, that is, the participants were connected to a non-functioning device as the control group. Before the intervention, demographic information including age, educational level, sex, contact information, history of physical and mental illnesses, and occupational status were recorded. tDCS was executed five days in a week for each case. Participants and evaluators were unaware to the type of stimulation.

Mini-Mental State Examination (MMSE)

The mini-mental state examination (MMSE) is a brief screening tool evaluating cognitive impairment. This instrument contains items on language, recall, attention, and orientation. The original test was developed by Folstein et al. (1975) for screening patients with dementia [15]. Scores lower than 25 may be due to a number of conditions including delirium, dementia, and depression. Cognitive impairment is unreliably identified by interaction with the patient; thus, a routine screening tool such as MMSE should be considered, specifically in higher-risk groups such as elderly patients. In this study, the MMSE was completed by our participants before and two weeks after the intervention.

2-back test

The 2-back test is a simple test for the evaluation of working memory [16]. This test is based on succession, where a figure is shown to a person, and the person must press a button if the presented figure is repetitive. In this study, this test was performed before the intervention, before the third section, after the intervention, and two weeks post-intervention.

Forward and backward digit span test

Forward and backward digit span is a test for the assessment of short-term memory and working memory; this test is used in many cognitive and neuroscience research labs [17]. This tool is a comprehensive pursuit scale used for the assessment of brain function, disorders of attention, planning, problem solving, and executive functions.8 The forward digit span test contains random number sequences (range 0-9) presented to the subject. The subject must repeat the numbers in the exact sequence, and for backward digit span test, the orally presented numbers must be stated backwards.18 In this study, this test was performed before the intervention, before the third section, after the intervention, and two weeks after the intervention.

Statistical analysis

Descriptive data are summarized as mean, standard deviation, and percentages. To analyze the data, one-way analysis of variance (ANOVA), Chi-square test, and t-test were run in SPSS version [18].

Ethics statement

The study protocol was reviewed and approved by the Ethics Committees of Zahedan University of Medical Sciences (code: IR.ZAUMS.REC.1394.273), and the study was registered at the Iranian Registry for Clinical Trials (https://www.irct.ir, code: IRCT201605299014N101).

RESULTS

In this study, 45 elderlies (48.8% female) were enrolled in two intervention groups (F3 and F4) and a control group (sham). The mean age of the subjects was 61.9±2.2 years old, and the mean year of education was 10.6±2.6 years. There was no significant difference between the three groups regarding age, sex, and education years (P>0.05; Table 1).

Table 1. Comparison of the mean age and education years in the three groups using one-way ANOVA

Variable	F3 Group	F4 Group	Sham Group	P-value
Age (Mean±Sd)	62.1±2.2	61.1±2.1	61.7±2.4	0.924
Education years (Mean±Sd)	10.8±2.5	11.0±3.1	10.0±2.3	0.680
Variable	F3 Group	F4 Group	Sham Group	P-value
Age (Mean±Sd)	62.1±2.2	61.1±2.1	61.7±2.4	0.924
Education years (Mean±Sd)	10.8±2.5	11.0±3.1	10.0±2.3	0.680

The average scores of MMSE were 27.2±1.4, 27.1±1.0, and 26.2±1.1 in the F3, F4, and sham groups, respectively, before the intervention (P=0.136). After the intervention, the mean scores of MMSE were 27.2±1.4, 27.2±1.3, and 26.9±1.1 in the F3, F4, and sham groups, respectively (P=0.833). The three groups showed no significant difference in mean scores of MMSE (P>0.05).

The mean scores of 2-back and forward and backward digit span tests are compared in Table 2 at four time points using paired t-test and one-way ANOVA.

Table 2. The mean scores of 2-back and forward and backward digit span tests in the three groups

Section	Groups	Before the intervention	Before the third section	After the intervention	Two weeks after the intervention
2-back	F3	572±86	551±80	519±77	527±80
	F4	515±86	513±90	511±92	521±82
	Sham	489±64	486±53	472±44	486±61
	P-value	0.084	0.204	0.367	0.453
Forward digit span	F3	9.6±1.1	10.4±1.0	11.0±0.8	11.0±0.8
	F4	8.0±1.1	8.4±1.2	8.3±0.9	7.8±1.0
	Sham	8.2±0.8	8.4±0.7	8.3±0.5	8.3±0.7
	P-value	0.002	0.001	0.001	0.001
Backward digit span	F3	6.7±1.5	8.0±1.6	8.6±1.9	8.6±1.5
	F4	6.1±1.2	7.1±1.4	7.0±1.4	6.9±1.6
	Sham	6.1±1.2	6.7±1.1	6.9±0.9	6.7±0.9
	P-value	0.503	0.115	0.024	0.008

The three groups showed no significant difference in terms of mean score of 2-back test at different time points (P>0.05). The mean score of forward digit span test was significantly higher in the F3 group than the other groups before the intervention (P=0.002). The three groups showed no significant difference in the mean score of backward digit span test at different time points (P=0.503). The mean score of backward digit span test was significantly higher in the F3 group than the other groups after the intervention (P=0.008).

The comparison of score changes showed that the score of 2-back test significantly changed only in the F3 group (from 572±86 to 527±80 two weeks after intervention; P=0.003; Table 3). The changes in forward digit span scores were significant in group F3, which was 9.6±1.1 before the intervention and increased to 11.0±0.8 two weeks post-intervention (P=0.001; Table 3). The greatest score alterations in backward digit span test scores are noted in the F3 group (from 6.7±1.5 before the intervention to 8.6±1.5 two weeks after the intervention; P=0.001; Table 3). In this regard, a significant difference in score can be observed in the F4 group at all times after the intervention, while in the control group, a significant difference was seen only at the time before the third section and after the end of the section (P<0.05; Table 3).

Table 3. The comparison of score changes in the three groups usingpaired t-test

Section	Groups	Before the intervention with before the third section (P-value)	Before the intervention with after the intervention (P-value)	Before the intervention with two weeks after the intervention (P-value)
2-back	F3	0.083	0.001	0.003
	F4	0.808	0.566	0.297
	Sham	0.850	0.088	0.601
Forward digit span	F3	0.011	0.001	0.001
	F4	0.168	0.343	0.443
	Sham	0.509	0.678	0.591
Backward digit span	F3	0.001	0.001	0.001
	F4	0.001	0.019	0.037
	Sham	0.005	0.011	0.081

DISCUSSION

The results of this study indicate that the score changes in the 2-back and the forward digit span tests were significant only in the F3 group. The greatest score changes in the backward digit span test were observed in the F3 group. Also, the F4 group showed a significant difference at all the time points after the intervention, compared to before the intervention, but this change was less than that in the F3 group. This result shows that the effect of F3-right supraorbital method with F3 anode is more significant.

According to previous studies, visual working memory is related to the lateral prefrontal cortex of the right hemisphere, and the right parietal cortex is vital to visuospatial perception [19]. Jeon et al. reported the right tDCS over the prefrontal cortex as an anodal stimulation target. The tests performed with the electrode on the left side of the prefrontal line showed a more significant effect. These changes were steady after two weeks and showed that tDCS in the left frontal lobe was effective in improving working memory [18] Based on the mentioned findings, it can be established that the visuospatial attention test exhibited significant enhancement in the right prefrontal cortex functioning. Lally et al. showed that electrode positioning is a main potential confounder when comparing tDCS effects on both brain activity and behavior [20]. However, they reported the effectiveness of stimulation in the initial stages of learning via the placement of negative electrode on the left dorsolateral frontal cortex (F3) and the positive electrode on the opposite side.20 More stimulation on the right parietal lobe and direct stimulation of the right prefrontal cortex could lead to the stimulation of a small area of the cortex [21]. However, further studies addressing the biological and behavioral consequences of different electrode placements are required.

Cheng et al. [22] and Saunders et al [23] reported the positive effects of tDCS on the elderly with cognitive decline. They also proved the cognitive benefits of tDCS for active memory exercises and as dual stimuli in these individuals. Saunders et al. demonstrated that tDCS can improve neuro-psychological and behavioral symptoms in people with weak active memory functioning [23]. Meinzer et al. ascribed that the elderly had more errors than younger subjects at the beginning of the stimulation, but the mistakes of the elderly reduced after the administration of tDCS [24]. Cognitive function in the intervention group receiving tDCS was clearly better than the sham group, which was the same as our results.

Lally et al. demonstrated the results of 2-back test after excitatory tDCS, which did not support improvement across multiple days [20]. This result is in line with our findings and those of other studies; in comparison with sham stimulation, Zaehle et al [25] and Ohn et al. [26] did not report significant performance enhancements in the 2-back task immediately following tDCS.

Nonetheless, in a number of studies, the results were different from our and the abovementioned findings. For example, Horvath et al. reported that using tDCS did not affect cognitive status and or active memory [27]. Keshvari et al. demonstrated that difference in electrode placement can impact the results [27]. The results of the 2-back test in the stimulation of the anode on the left lateral dorsal side [28] differed with those obtained by the stimulation of the left anode. However, the insertion of the cathode on the right and anode on the left negatively affected the results [20]. Hoy et al. [29] and Nikolin et al. [30] showed a stimulation of 2 mA did not lead to a higher degree of cognitive enhancement, but most positive effects on cognition can be observed at the stimulation of 1 mA. This suggests that the position of electrode and amplitude of stimulation can change performance and the results of tDCS on cognitive function and working memory.

In spite of methodological differences, the information published to date support the use of tDCS as a treatment strategy for psychiatric disorders and working memory. Reduction of executive function, such as working memory, has been employed in many neurological and psychiatric conditions and can be used for schizophrenia, depression and similar diseases. However, it should be further investigated before becoming a routine clinical treatment.

The present study showed that tDCS significantly increases the performance of active memory, and improvement in the F3 group was significantly higher than the other groups. tDCS can cause working memory improvement and naming facilitation by stimulation. It can also affect early learning stages in the elderly. According to our results, tDCS can be used to enhance cognitive function and working memory in the elderly.

REFERENCES

1. Courtin E, Knapp M. Social isolation, loneliness and health in old age: a scoping review. Health & social care in the community. 2017;25(3):799-812.
2. Prince MJ, Wu F, Guo Y, Robledo LMG, O'Donnell M, Sullivan R, et al. The burden of disease in older people and implications for health policy and practice. The Lancet. 2015;385(9967):549-62.
3. Adib-Hajbaghery M, Aghahoseini S. The evaluation of disability and its related factors among the elderly population in Kashan, Iran. BMC public Health. 2007;7(1):261.
4. Olson A, Reiland S, Davies S, Koehler AR. Learning about the experience of living with chronic conditions: A framework analysis of nursing students' reflections on their conversations with older adults. Gerontology & geriatrics education. 2018;39(3):295-315.
5. Farajzadeh M, Gheshlagh RG, Sayehmiri K. Health related quality of life in Iranian elderly citizens: a systematic review and meta-analysis. International journal of community based nursing and midwifery. 2017;5(2):100.
6. Archer JA, Lee A, Qiu A, Chen SA. Working memory, age and education: A lifespan fMRI study. PloS one. 2018;13(3):e0194878.
7. Reid SN, Ryu J-k, Kim Y, Jeon BH. The Effects of Fermented Laminaria japonica on Short-Term Working Memory and Physical Fitness in the Elderly. Evidence-Based Complementary and Alternative Medicine. 2018.
8. Jaroslawska AJ, Rhodes S. Adult age differences in the effects of processing on storage in working memory: A meta-analysis. PsyArXiv September. 2018;28.
9. Otsuka Y, Osaka N, Morishita M, Kondo H, Osaka M. Decreased activation of anterior cingulate cortex in the working memory of the elderly. Neuroreport. 2006;17(14):1479-82.
10. Alain C, Khatamian Y, He Y, Lee Y, Moreno S, Leung AW, et al. Different neural activities support auditory working memory in musicians and bilinguals. Annals of the New York Academy of Sciences. 2018.
11. Fregni F. Transcranial direct current stimulation (tDCS). The International Journal of Neuropsychopharmacology. 2008;11:60.

12. Manor B, Zhou J, Lo A, Harrison R, Granger T, Zhu H, et al. Transcranial direct current stimulation (tDCS) improves cognitive-motor performance in older adults with cerebral microvascular disease. Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation. 2017;10(2):469.
13. Kuo M-F, Mosayebi M, Jamil A, Nitsche MA. S181. Optimizing the neuroplastic effects of cathodal transcranial direct current stimulation (tDCS) over the primary motor cortex. Clinical Neurophysiology. 2018;129:e209.
14. Bahr Hosseini M, Hou J, Bikson M, Iacoboni M, Saver JL. Abstract TP72: Transcranial Direct Current Stimulation (tDCS) for Neuroprotection in Acute Cerebral Ischemia: Meta-analysis of Preclinical Studies and Implications for Human Clinical Trials. Stroke. 2018;49(Suppl_1):ATP72-ATP.
15. Galea M, Woodward M. Mini-mental state examination (MMSE). Australian Journal of Physiotherapy. 2005;51(3):198.
16. Dagenbach D. Insights into cognition from network science analyses of human brain functional connectivity: Working memory as a test case. Connectomics: Elsevier; 2019. p. 27-41.
17. Little J, Mcneill KT, Poole C, Hall EE, Ramos T, Evans ES. The Effect of Acute Aerobic Exercise on Attention and Affect in Middle-aged Women: 387 Board# 228 May 30 11. Medicine & Science in Sports & Exercise. 2018;50(5S):86.
18. Jeon SY, Han SJ. Improvement of the working memory and naming by transcranial direct current stimulation. Annals of rehabilitation medicine. 2012;36(5):585-95.
19. Indahlastari A, Chauhan M, Schwartz B, Sadleir RJ. Changing head model extent affects finite element predictions of transcranial direct current stimulation distributions. Journal of neural engineering. 2016;13(6):066006.
20. Lally N, Nord CL, Walsh V, Roiser JP. Does excitatory fronto-extracerebral tDCS lead to improved working memory performance? F1000Research. 2013;2.
21. Tseng P, Wang M-C, Lo Y-H, Juan C-H. Anodal and cathodal tDCS over the right frontal eye fields impacts spatial probability processing differently in pro-and antisaccades. Frontiers in neuroscience. 2018;12:421.
22. Cheng CP, Chan SS, Mak AD, Chan WC, Cheng ST, Shi L, et al. Would transcranial direct current stimulation (tDCS) enhance the effects of working memory training in older adults with mild neurocognitive disorder due to Alzheimer's disease: study protocol for a randomized controlled trial. Trials. 2015;16(1):479.
23. Saunders N, Downham R, Turman B, Kropotov J, Clark R, Yumash R, et al. Working memory training with tDCS improves behavioral and neurophysiological symptoms in pilot group with post-traumatic stress disorder (PTSD) and with poor working memory. Neurocase. 2015;21(3):271-8.
24. Meinzer M, Lindenberg R, Antonenko D, Flaisch T, Flöel A. Anodal transcranial direct current stimulation temporarily reverses age-associated cognitive decline and functional brain activity changes. Journal of Neuroscience. 2013;33(30):12470-8.
25. Zaehle T, Sandmann P, Thorne JD, Jäncke L, Herrmann CS. Transcranial direct current stimulation of the prefrontal cortex modulates working memory performance: combined behavioural and electrophysiological evidence. BMC neuroscience. 2011;12(1):2.
26. Ohn SH, Park C-I, Yoo W-K, Ko M-H, Choi KP, Kim G-M, et al. Time-dependent effect of transcranial direct current stimulation on the enhancement of working memory. Neuroreport. 2008;19(1):43-7.
27. Horvath JC, Forte JD, Carter O. Quantitative review finds no evidence of cognitive effects in healthy populations from single-session transcranial direct current stimulation (tDCS). Brain stimulation. 2015;8(3):535-50.
28. Kadish N, Brunke M, Spychalski P, Müller F, Berghaeuser J, Pedersen A, et al. PB19. tDCS in the left DLPFC: When to stimulate and which cognitive domains it affects. Clinical Neurophysiology. 2018;129(8):e63-e4.
29. Hoy KE, Emonson MR, Arnold SL, Thomson RH, Daskalakis ZJ, Fitzgerald PB. Testing the limits: investigating the effect of tDCS dose on working memory enhancement in healthy controls. Neuropsychologia. 2013;51(9):1777-84.
30. Nikolin S, Martin D, Loo CK, Boonstra TW. Effects of TDCS dosage on working memory in healthy participants. Brain stimulation. 2018;11(3):518-27.