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General

A Comparison between the Effectiveness of computerized Cognitive Rehabilitation Training and transcranial Direct Current Stimulation on Dialysis Patients' Executive Functions

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Purpose

Executive function impairments are among the most common dialysis side effects. The present study aims to compare the efficiency of transcranial Direct Current Stimulation (tDCS) with computerized Cognitive Rehabilitation Training (cCRT) on dialysis patients' executive functions.

Research method

The present study, a quasi-experimental effort, adopted a pre-test/post-test method that included a control (sham) group.

Design

The study sample consisted of 30 participants, selected through the convenience sampling method, and categorized into three groups of cCRT, tDCS, and sham participants. The cCRT participants were asked to complete 8 tasks in Captain's Log MindPower Builder software. The tDCS participants were treated with a 0.06 mA/cm2 current with the anodal electrode on F3 and the cathodal electrode on Fp2. For the sham participants, the electrodes were put on the same regions but there was no current stimulation. The treatment lasted for 10 sessions carried out every other day.

Results

The results of MANCOVA showed no significant difference between the sham group and the cCRT group in any of the executive function items. . However, between the sham group and the tDCS group was detected a significant difference in spatial working memory ($p < 0.05$) and a marginally significant in cognitive flexibility ($p = 0.091$). No significant difference was reported between cCRT and tDCS groups in any item.

Conclusion

According to the findings of the study, given the efficacy of tDCS on spatial working memory and cognitive flexibility for dialysis patients, it can be used to improve these skills.

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INTRODUCTION

Chronic kidney disease (CKD) is a gradual, irreplaceable loss of function in a kidney.[1] The condition's acuteness is determined through Glomerular Filtration Rate (GFR). In the last stage of the condition, the patient cannot survive without kidney transplantation or dialysis.[2] 0.1 percent of the world's population is hemodialysis patients.[3] In Iran, the rate of hemodialysis patients has been reported as 288.9 in a million.[4]

On top of its somatic side effects, kidney deficiency entails cognitive problems as well.[5] These problems are an inherent part of kidney deficiency.[6] Brain blood circulation slump during the dialysis procedure,[7] urea's neurotoxicity, regular administration of angiotensin inhibitors, insomnia, and depression[8] are among cognitive-damaging elements in dialysis patients. In recent years, researchers have come to the conclusion that as CKD progresses, patients' cognitive functions deteriorate. Cognitive problems are much more prevalent among CKD patients compared to healthy individuals.[9] Researchers have identified navigation, attention, execution, and language as the most common serious problem areas in these patients.[10,11] Executive functions are among the most important capabilities impaired in CKD patients. Executive functions are high-level neurocognitive processes that control an individual's thinking and behavior.[12] Cognitive flexibility, planning, short-term memory, and response inhibition are among executive functions.[13] executive functions are vital for Mindfulness, mental control, and emotional control.[14] Researchers have demonstrated that as kidneys deteriorate, executive functions degrade.[15]

If impairments of executive functions remain untreated, they can have a detrimental impact on patients' follow-up medical treatment, endangering their mental and physical health.[16] CKD-induced cognitive problems can compromise a patient's ability to decide about measures necessary for their well-being.[11] Recent studies have demonstrated that as their cognitive impairments build up, patients need more help with their hemodialysis sessions.[8] Zuccalà et al.[17] have shown that cognitive impairments have a negative impact on hemodialysis patients' prognosis. Most important, as cognitive impairments build up, the mortality rate of CKD patients increases.[18] These studies confirm that dialysis patients' cognitive impairments, especially those related to executive functions, must be treated as soon as possible to prevent their damaging aftereffects.

Amending cognitive impairments and fixing executive functions is a lengthy process. Many methods have been employed to remedy cognitive impairments induced by chronic diseases, including medication,[19,20] psychotherapy,[21] and cognitive rehabilitation.[22] Using medications is not possible in many cases as their interaction with CKD drugs can pose a problem.[6] Psychotherapy is an expensive, time-consuming method whose impact on cognitive issues remains unclear (Cicerone et al., 2020). Other methods, such as cognitive rehabilitation and transcranial Direct Current Stimulation, however, have proven effective in many cases.

Cognitive training involves the remediation or compensation of cognitive deficits and associated outcomes through structured programs administered by therapists, aimed at restoring or enhancing cognitive functioning.[23] The trainability of cognitive functions has been described for a variety of processing including perception,[24] attention,[25-27] memory,[28,29] and social cognition.[30]

Computerized Cognitive Rehabilitation Training (cCRT) is a modern treatment method that is fast and free of unwanted side effects. Dardiotis et al.[31] believe cCRT can use computer software to train individuals through tasks that can expand their cognitive abilities, including executive functions,[32] and memory.[33] Several studies have demonstrated the method's efficacy in treating chronic patients.[34] Researchers have studied cognitive training, an approach close to cognitive rehabilitation, to show that it can improve the results of cognitive tests in patients suffering from renal diseases.[21] As far as the authors of the present study are aware, however, no study has been dedicated to analyzing the effects of cognitive rehabilitation on executive functions of dialysis patients.

transcranial Direct Current Stimulation (tDCS) is a non-invasive treatment during which a stable, low-voltage current is used to stimulate specific regions of the brain. During the process, the brain's neuroactivity is manipulated to induce the desired behavior.[35] As far as the authors of the present paper are aware, tDCS effectiveness on executive functions in dialysis patients has not been confirmed.

As demonstrated above, CKD patients, especially those under dialysis treatment, suffer from executive function impairments. It is not clear how effective cCRT and tDCS can be in amending executive function impairments in dialysis patients. Furthermore, a scientific comparison between these tools remains lacking. The present study is an attempt to determine how effective these interventions can be in amending executive function impairments of dialysis patients.

Two hypotheses and a question are examined in the present paper:

1. tDCS can improve executive functions in dialysis patients.
2. cCRT can improve executive functions in dialysis patients.
3. Which method is more effective in alleviating executive function impairments?

METHODOLOGY

Participants: The present study is a quasi-experimental research effort with a pre-test/post-test design that included a control (sham) group. The sample population consisted of all dialysis patients that were admitted to Labafinejad Hospital, Tehran in the Winter to Summer period of 2021 for the hemodialysis procedure. G*Power 3.1.9.2 software with an effect size of 0.55,[36] a significance level (α) of 0.05, and a sample size of 30 were used. The sample population consisted of 10 women and 20 men. A convenience-based, non-random sampling method was adopted for sampling. The participants were randomly categorized into three 10-patient groups: cCRT (2 women, 8 men), tDCS (3 women, 7 men), and sham (3 women, 7 men). The inclusion criteria were a) having a End-Stage CKD diagnosis; b) the patient's continuous admittance for dialysis three times a week; c) no vision, hearing, and upper body impairments; d) literacy; e) right-handedness; f) a minimum age of 20; g) familiarity with basic computer operations; and h) informed consent to be part of the study. The exclusion criteria were: a) an open head wound; b) severe mental disorders; c) mental retardation; d) cognitive disorders; e) Alzheimer's disease; f) epilepsy; g) using a pacemaker; and h) migraine.

Tools: The Cambridge Neuropsychological Test Automated Battery (CANTAB): One of the most trusted tools for research and clinical studies developed by the university of Cambridge in the 1980s. It consists of 25 tests covering the main five cognitive areas of attention, executive functions, visual memory, verbal memory, and decision making. The data are collected via a touchscreen so; a subject's language and culture have no bearing on the results. CANTAB provides the researcher with a quick profile of the subject's cognitive system.[37] For the present study, MOT and BLC were evaluated based on test-retest coefficients of 0.96 and 0.98, respectively. One of the attention subtests, RVP, was evaluated based on a test-retest coefficient of 0.67. IED, SWM, SOC, SSP, and AST executive function subtests were evaluated based on test-retest coefficients of 0.94, 0.78, 0.72, 0.55, and 0.86, respectively. In total, 8 subtests were evaluated in the present study.

Adult Self Report (ASR) form: The questionnaire was developed in the United States in 1997 as part of the Achenbach System of Empirically Based Assessment (ASEBA). It includes items that evaluate adjustment functions and disorders.[38] ASR consists of 8 criteria for 8 syndromes. Some of these criteria, including depression/anxiety (18 questions), isolation (9 questions), and bodily complaints (12 questions), measure an individual's introjective conduct. Others, including aggressive behaviors (15 questions), unruly behaviors (14 questions), and intruding behaviors (6 questions), measure an individual's projective conduct. Another group that includes attention problems (15 questions), thinking problems (10 questions), and other problems (21 questions) address specific cognitive issues. The questionnaire's Cronbach's Alpha is reported as 0.95. The tool's internal coherence is 0.91 and its external coherence is 0.84.[39]

Method: Following the approval of the Iran National Committee for Ethics in Biomedical Research (code: IR.SBU.REC.1400.011) in early 2021, access to Labafinejad Hospital's patients was possible. In face-to-face interviews, each patient was provided with a pamphlet comprising comprehensive information about the study. 30 regular hemodialysis patients were selected based on specific inclusion and exclusion criteria. Three groups, tDCS, cCRT, and sham, were formed based on random assignment. A pretest of executive functions, as well as an RVP subtest of attention capabilities, was conducted using CANTAB software installed on a tablet.

In the treatment phase, the tDCS group members were treated with a pre-determined electric current. The cCRT group members completed 8 cognitive tasks using a laptop. Each participant's progress was recorded to provide them with more challenging tasks in subsequent sessions. The sham group members' procedures were similar to the tDCS group, except that they received no electric current. After interventions, post-tests were conducted and the resulting data were analyzed through the multivariate analysis of covariance (MANCOVA) method carried out in SPSS 24 software.

Interventions: Captain's Log MindPower Builder (Experts version): This training software was developed by the US-based BrainTrain in 2000. It consists of 50 training modules and 2000 exercises to remedy cognitive impairments.[40] The participants of the present study trained with 8 specific subskills related to executive functions: CON-4 Domino Dynamite, Cat's Play, VMS-7 Concentration, VMS-3 Pop-N-Zap, ASD-5 Mouse Hunt, WMS-3 Puzzle Power, NUM-4 Counting critters, and VMS-6 Hide and Seek. Each session lasted for around 40 minutes. The treatment lasted for three weeks with a session every other day.

transcranial Direct Current Stimulation ActivaDose II: Bindman et al. developed tDCS in 1964. The method went through many changes before current devices came into circulation. The ActivaDose II device was developed by the US-based Caputron. It uses a weak current to prevent or encourage specific behaviors in the brain.[41] In the present study, a consistent 1.5 mA current at a density of 0.06 mA/cm^2 was used to stimulate the brain through 5cm in 5cm personal pads. The Activadose II device electrodes were placed on patients' heads using the 20-10 system, the anodal electrode on the F3 region and the cathodal electrode on the Fp2 region. The process was carried out in ten 30-minute sessions which were held every other day.

Sham: The control group underwent placebo treatment. The electrodes were placed on their heads similar to the tDCS group. They were provided with a full explanation of tDCS treatment. The ActivaDose II device was turned on, the current went up to 1.5 mA and then, the device was turned off using the sham mode. The process was carried out in ten 30-minute sessions which were held every other day for this group, too.

RESULTS

The three groups were compared based on age, education, and gender. The variance analysis test indicated no significant difference between these groups based on the mean age (α =0.05, F=1.719 , P=0.198). According to the chi-squared test, no significant difference was observed for education (α =0.05, χ^2 =4.66, p=0.79) and gender (α =0.05, χ^2 =0.37, p=0.83), either.

Descriptive measures of mean and standard deviation for each group—sham, cCRT, and tDCS—are represented in Table 1.

The pre-test/post-test data demonstrated in Table 1 were used to gauge the effectiveness of each intervention in improving various cognitive tasks.

Table 1. Research variables' descriptive measures for sham, cCRT, and tDCS groups

		Sham		cCRT		tDCS	
		Mean	SD	Mean	SD	Mean	SD
Problem-solving (SWM)	Pre-test	38.200	4.131	37.300	3.529	39.900	3.446
	Post-test	36.500	4.240	35.000	3.091	37.700	3.164
Spatial working memory (SWM)	Pre-test	54.100	26.648	57.200	13.863	60.300	15.246
	Post-test	45.300	22.877	33.600	17.614	45.200	19.887
Short-term memory capacity (SSP)	Pre-test	4.800	1.317	5.500	0.850	4.100	0.876
	Post-test	5.100	1.370	6.100	1.197	5.000	1.333
Planning (SOC)	Pre-test	6.400	1.647	5.600	1.776	5.600	2.547
	Post-test	6.900	1.912	7.900	1.197	7.100	1.912
Rapid visual information processing (RVP)	Pre-test	410.204	40.068	408.163	117.205	533.872	140.092
	Post-test	383.688	33.588	312.155	44.387	400.841	82.693
Sequencing (RVP)	Pre-test	0.948	0.049	0.0934	0045	0.916	0.058
	Post-test	0.960	0.048	0.969	0.023	0.967	0.025
Cognitive flexibility (IED)	Pre-test	52.800	18.414	64.200	49.416	67.000	33.029
	Post-test	52.800	18.036	52.400	28.060	60.100	26.660
Attention altering (AST)	Pre-test	344.018	160.930	351.374	119.986	203.362	188.653
	Post-test	252.239	167.668	206.449	90.249	240.487	143.968

To test the hypothesis of normality, the Kolmogorov–Smirnov test was used. The significance of most of the study's variables was above 0.05, confirming the normality which means the final analysis could be carried out. According to Levene's test, all of the study's variables were insignificant, pointing to equality of variances. The variance analysis test indicated the insignificance of interactions between pre-test variables, which confirms the equality of variances.

According to the study's first hypothesis, executive function impairments should be reduced following a cCRT intervention. To confirm the hypothesis, eight dependent variables (problem-solving, spatial working memory, short-term memory capacity, planning, rapid visual information processing, sequencing, cognitive flexibility, attention altering), one two-layer, independent variable (the cognitive rehabilitation group and the sham group), and covariate variables (pre-test scores) were used to run a multivariate analysis of covariance (MANCOVA). According to the Table 2, the cCRT's effect on the set of eight dependent variables was not significant (⟐^{24} = 0.306, $p > 0.05$, F = 0.073). Furthermore, according to the chi-squared test results, there was no significant difference between the cognitive rehabilitation group and the sham group in any of the study's variables. While no statistically significant difference was observed between the two groups, according to the eta-squared effect size measure, cognitive rehabilitation was most clinically and practically influential on rapid visual information processing and sequencing (⟐^{24} = 0.308 and ⟐^{24} = 0.261, respectively.

According to the study's second hypothesis, executive function impairments in dialysis alleviate following a tDCS treatment period. multivariate analysis of covariance (MANCOVA) method was used to test this hypothesis. According to the results, tDCS had no significant effect on the 8 dependent variables (⟐^{24} = 0.817, $p > 0.05$, F = 0.710). The test to determine within-group effect differences between the tDCS and sham groups pointed to a significant difference in the spatial working memory variable (⟐^{24} = 0.581, $p < 0.05$, F = 8.331). As demonstrated in Table 3, there was a marginally significant difference between the tDCS group and the sham group in the cognitive flexibility variable (⟐^{24} = 0.403, p = 0.091, F = 4.048). According to the eta-squared effect size measure, tDCS is clinically and practically most effective on spatial working memory and cognitive flexibility variables, with eta-squared values of 0.581 and 0.403, respectively.

To answer the study's question ("Which method is more effective in alleviating executive function impairments?"), the multivariate analysis of covariance(MANCOVA) method was adopted. According to the Table 4, no significant effect on the 8 dependent valuables was observed (⟐^{24} = 0.971, $p > 0.05$, F = 5.568). However, the within group effect test pointed to a marginally significant difference between cCRT and tDCS in sequencing (⟐^{24} = 0.448, p = 0.069, F = 4.877). According to the eta-squared effect size measure, from clinical and practical points of view, the cCRT and tDCS were most divergent in sequencing, rapid visual information processing, and cognitive flexibility variables with eta-square values of 0.448, 0.328, and 0.287, respectively.

DISCUSSION

In examining the first hypothesis ("cCRT can improve the executive functions of dialysis patients"), the results indicated that in comparison to the control (sham) group, cCRT had not improved any of the executive functions of

Table 2. Within group effect tests (cCRT)

Dependent variable	Sum of squares	DF	Mean of squares	F	P	�[24]
Problem-solving (SWM)	0.558	1	0.558	0.077	0.790	0.013
Spatial Working Memory (SWM)	114.061	1	114.061	0.508	0.503	0.078
Short-term memory capacity (SSP)	0.275	1	0.275	0.863	0.389	0.126
Planning (SOC)	1.593	1	1.593	0.381	0.560	0.060
Rapid visual information processing (RVP)	3360.446	1	3360.446	2.675	0.153	0.308
Sequencing (RVP)	0.001	1	0.001	2.119	0.196	0.261
Cognitive flexibility (IED)	18.926	1	18.926	0.359	0.571	0.057
Attention altering (AST)	1140.503	1	1140.503	0.095	0.768	0.016

Table 3. Within group effect tests (tDCS)

Dependent variable	Sum of squares	DF	Mean of squares	F	P	�[24]
Problem-solving (SWM)	0.065	1	0.065	0.013	0.914	0.002
Spatial Working Memory (SWM)	604.150	1	604.150	8.331	0.028	0.581
Short-term memory capacity (SSP)	0.108	1	0.108	0.079	0.788	0.013
Planning (SOC)	1.204	1	1.204	0.493	0.509	0.076
Rapid visual information processing (RVP)	402.501	1	402.501	0.086	0.779	0.014
Sequencing (RVP)	0.001	1	0.001	0.282	0.615	0.045
Cognitive flexibility (IED)	125.601	1	125.601	4.048	0.091	0.403
Attention altering (AST)	521.335	1	521.335	0.036	0.855	0.006

Table 4. Test of within group effects on dependent variables' scores (cCRT and tDCS)

Dependent variable	Sum of squares	DF	Mean of squares	F	P	�[24]
Problem-solving (SWM)	0.001	1	0.001	0.001	0.990	0.001
Spatial Working Memory (SWM)	65.033	1	65.033	0.588	0.472	0.089
Short-term memory capacity (SSP)	3.475	1	3.475	2.394	0.173	0.285
Planning (SOC)	1.792	1	1.792	0.796	0.407	0.117
Rapid visual information processing (RVP)	13568.320	1	13568.320	2.925	0.138	0.328
Sequencing (RVP)	0.001	1	0.001	4.877	0.069	0.448
Cognitive flexibility (IED)	76.785	1	76.785	2.418	0.171	0.287
Attention altering (AST)	4770.192	1	4770.192	0.498	0.507	0.077

the dialysis patients. It should be noted that cCRT had didimprove variables such as rapid visual information processing and sequencing, but only marginally. These results mirror Chung et al.'s[42] metanalysis results but reject the findings of Amato et al.,[32] Chen et al.,[43] and Bogdanova et al.[22] The statistical insignificance can be attributed to the limited number of sessions, which had to be restricted to 10 to create homogenous conditions for both treatment approaches (cCRT and tDCS). Two variables, rapid visual information processing and sequencing, were affected by these approaches, albeit, marginally, a fact that points to the possibility of an increase in effectiveness as the number of sessions increases. Furthermore, Captain's Log Mind-Power software is a relatively new tool that was introduced less than two decades ago to improve cognitive capabilities. It has been used to boost attention capabilities in ADHD cases. As such, the fact that attention-related tasks, especially those related to visual capabilities, were most improved seems understandable.

In examining the second hypothesis ("cCRT can improve executive functions in dialysis patients"), no significant treatment-induced executive function changes were observed in the participants, except in spatial working memory. There were marginally significant changes in cognitive flexibility. These results mirror Imburgio & Orr's[44] met-analysis results.

The cCRT method's inefficacy can be due to various factors. First, tDCS, as a new treatment approach, has not been completely tested yet. Researchers have been looking for years for an answer to this question: Can tDCS alter the prefrontal cortex in a meaningful way leading to observable improvements in executive functions? Previous studies have yielded inconsistent results. The tDCS method has been shown to be ineffective in some studies,[44] while in others, the method was effective only in some items.[45] There have been studies where significant improvements in executive functions have been observed as well.[32] Similar to the first category of these studies, the present study confirmed that tDCS is not significantly effective in improving executive functions, at least in a sample made of dialysis patients.

Second, homogenous samples have been lacking in many studies. Executive functions can be influenced by factors such as age and patients' underlying diseases and these diseases' acuteness. In the present study, researchers had access to a limited number of patients and the sample was inevitably selected on a volunteer/convenience basis. Patients with a wide age range were included in the study, which might have compromised their cognitive flexibility, inluencing its statistical significance. Future studies should try to employ more homogenous samples.

In comparing tDCS and cCRT groups with the control group, it came to light that cCRT had not improved any of the executive function items, while tDCS had notably improved spatial working memory. The study's results indicated that, not taking the control group into account, none of the interventions was preferable to the other as an intervention to improve executive functions in dialysis patients. Sequencing, rapid visual information processing, and cognitive flexibility were improved in tDCS patients, but the improvement remained statistically insignificant. These results confirm the conclusions Sacco et al.[46] reached, but reject Park & Yoon's[47] findings. This inconsistency might be due to the nature of these two interventions. The tDCS approach is a short-term intervention whose effects, the results of stimulation of specific regions of the brain, manifest quickly. The cCRT approach, however, is a patient-dependent intervention whose results rely on the intensity of a patient's efforts.

To homogenize the study's sample, the treatment was limited to ten sessions for both of these approaches. The cCRT approach, however, might lead to better results, similar to those achieved by the tDCS approach, if the number of sessions increases. It is important to reiterate, however, that none of these approaches is preferable to the other. Based on the results of the present study, none of these interventions can be recommended for dialysis patients, except for tDCS in a limited capacity to improve spatial working memory.

CONCLUSION

As demonstrated above, cCRT failed to improve any of the executive functions in dialysis patients. The tDCS intervention, however, did improve spatial working memory notably. According to these results, it seems cognitive rehabilitation cannot be recommended as a treatment to improve dialysis patients' executive functions unless future studies can demonstrate more sessions or different tasks may be more effective.

However, given the tDCS treatment's success in improving spatial working memory, researchers can remain optimistic about its potential for future studies, where stronger currents, more sessions, and fewer study limitations may yield better results in treating dialysis patients. Hopefully, as a fast, safe, and inexpensive approach, tDCS can become a part of dialysis patients' treatment regimens to improve their executive functions, especially spatial working memory.

RECOMMENDATIONS FOR FUTURE STUDIES

The number of sessions and sample sizes should be increased and study groups should be more homogenized to form a better picture of tDCS' and cCRT's effectiveness. A higher current density in the tDCS group might yield different results. Also, different cognitive rehabilitation software solutions, featuring more tasks designed for executive function improvement, can be used in future studies. In future studies, a fourth group can be introduced to examine the effects of a treatment regimen which employs the tDCS and cCRT approach simultaneously to improve executive functions in dialysis patients. Furthermore, other executive functions, such as response inhibition and organization should be examined in future studies. The effectiveness of tDCS, as a transcutaneous electrical stimulation (tES), can be compared with transcranial Static Magnetic Stimulation (tSMS) in dialysis patients.

STUDY LIMITATIONS

The participant's wide age range and difference in the number of years they had been undergoing dialysis were variables that, due to the sample's limited size, could not be controlled.

AUTHOR'S CONTRIBUTION

Fatemeh Firouzan: collected the data, performed the analysis, wrote the paper.

Vahid Sadeghi-Firoozabadi: Conceived and designed the analysis, proposed research on this topic, introduced facilities and other professors and made them available.

Vahid Nejati: advised how to use the therapeutic tools and provided them.

Jalil Fathabadi: Contributed the data and analysis tools.

Ahmad Firouzan: Introduced dialysis patients and gave orders and recommendations regarding medical procedures. helped in the field of medical information.

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