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Effect of Transcranial Direct Current Stimulation on Executive Ability Among Individuals with Right Cerebral Hemisphere Dominance: A Double-Blinded Randomized Controlled Trial

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ABSTRACT

Background: The frontal lobe of the cerebrum controls executive functions such as cognitive abilities, including working memory, attention and focus, planning, processing, task sequencing, and problem-solving. Transcranial direct current stimulation (tDCS) is found to be an effective tool in improving calculative abilities. Therefore, the study aimed to determine the effect of tDCS on improving executive ability, focusing on calculation among individuals with dominant right cerebral hemispheres.

Methods: A two-group pre and post-test randomized controlled trial recruited forty volunteers, which were assigned into two groups, i.e., the experimental (tDCS with conventional treatment) and the control group (sham therapy with conventional treatment) three times a week for four weeks. Pre- and post-assessment were obtained using the Saint Louis University Mental Status Examination (SLUMS) and Montreal Cognitive Assessment (MoCA) as outcome measures.

Results: The mean differences between these groups' post-SLUM and pre-SLUM scores were 5.70 and 0.50, respectively. Meanwhile, the mean differences between post- and pre-MOCA scores in these groups were 5.20 and 1.85, respectively, which showed a significant difference. The z value of the experimental {-4.694 (0.001)} and the control group {-3.963 (0.001)} showed that the data was highly significant in both groups. The effect sizes and power of the study for SLUMS and MoCA are 1.34 and 2.60, and 98% and 100 %, respectively.

Conclusion: This study concluded that tDCS, along with exercise protocol, is an adjuvant tool to improve the calculation ability of individuals with dominant right hemispheres.

Keywords: Brain stimulation, cerebral dominance, executive function, numerical analysis, sham treatment.

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INTRODUCTION

The cerebrum comprises the right and left hemispheres, separated by fissures into the brain's frontal, parietal, temporal, and occipital lobes [1]. The corpus callosum connects these two hemispheres, each of which governs a distinct side of the body and contributes to communication between them [2]. The frontal lobe comprises over one-third of the cerebral hemisphere and affects cognitive abilities and behavior [3,4]. Various neurophysiological studies reveal evidence of parietal lobe function being co-linked with frontal lobe function, as it aids the frontal lobe in restoring and retrieving language knowledge [5,6]. Consequently, both hemispheres are activated while performing cognitive activities or executive functions in sequence order [7].

An executive function is a group of goal-directed, flexible, and purposeful processes [7]. Higher-order cognitive abilities include working memory, attention and focus, planning, processing, task sequencing, reasoning, problem-solving, and effortlessly thinking in novel settings [8,9]. Most studies revealed that three factors lead research to shift: Inhibition, suppression, an unwelcome diversion response, shifting (i.e., readily transition between two projects), and mental information manipulation [10]. Benavides-Varela S et al. study explains that despite decades of research, no proof had been generated that the right hemisphere plays a vital role in calculations or that the right hemisphere's potential in calculative abilities is overlooked [11]. However, Cragg L et al. were the authors who highlighted that the right hemisphere only contributes to calculations when the left hemisphere is severely damaged. Established that there was no evidence of negligence of the right hemisphere in calculations. [12]. Numerous studies available in the literature point out that the individual with the left-side dominant hemisphere, i.e., right-handed individuals, exhibits greater calculative abilities and abstract thinking as compared to the individual with the right-side dominant hemisphere, i.e., left-handed individuals, and tDCS is found to be an effective tool in improving calculative abilities [13]. Consequently, a study was needed to determine the effect of tDCS on the calculative abilities of individuals among left-handed individuals, to overcome obstacles in their cognitive abilities that may retard their academic growth, especially for those who want to pursue administrative jobs. The study aimed to determine the effect of tDCS on improving the calculative ability of individuals among left-handed individuals. The alternative hypothesis was that calculative ability significantly improves with tDCS among left-handed individuals.

MATERIALS AND METHODS

Study Design

A two-group experimental study with a pre-test and a post-test was conducted double-blinded with participants, and the assessor was kept blinded. This sample size was calculated using the statistical G Power 3.1.9.7 software, with alpha set at 0.05 as the level of significance and beta set at 0.95 as the study's power, with an effect size of 1.26,

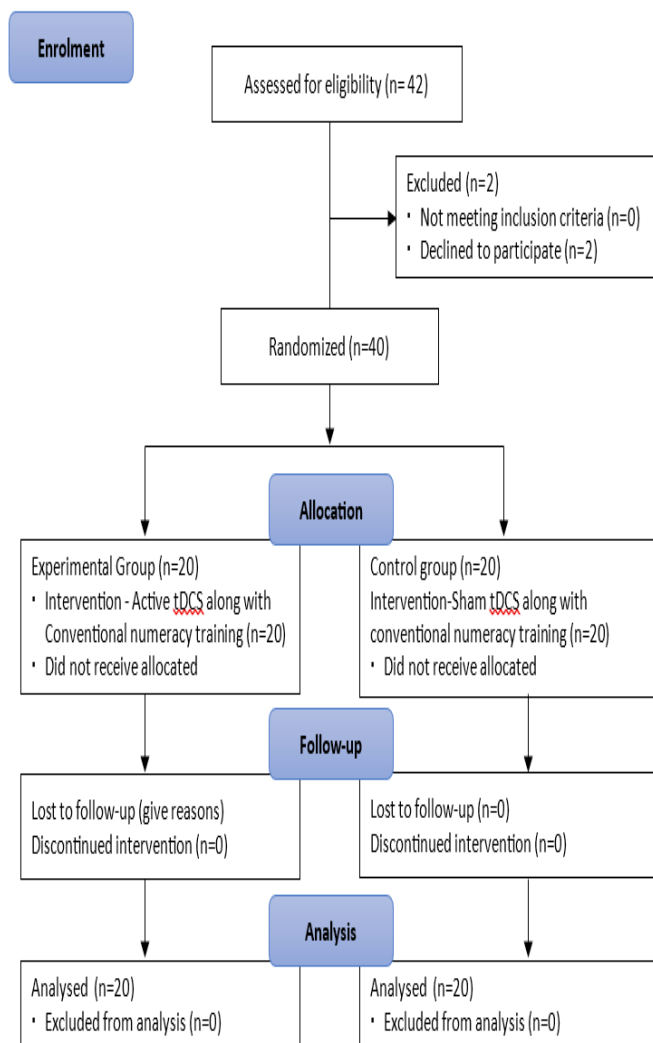
yielding 40 with a 30% dropout [14]. Before the study's commencement, all of the benefits and risks associated with the study were disclosed to the participants, who then provided written consent.

Selection and Description of Participants

This study recruited healthy volunteers (n=40) by using the "purposive sampling" (based on criteria) technique, and they were thoroughly examined through the selection criteria. This research study included male and female volunteers with left-hand dominance between 18 and 35 years who were engaged in engineering and business management courses and had a baseline score on MoCA and SLUMS between 15 and 26. However, this research study excluded volunteers with a history of drug abuse, neurological conditions (like seizures, cerebrovascular accidents, and infections of the central nervous system), traumatic conditions, surgical conditions, or a metal implant at the site where the electrodes would be placed.

After the volunteers were vetted using the selection criteria, they were randomly assigned to one of two groups using the block randomization method with the matrix design of 5x8: the experimental group (n=20) or the control group (n=20). Their allocation has been concealed using sequentially numbered opaque sealed envelopes. The trial has been reported per CONSORT guidelines (Figure 1).

Figure 1: CONSORT



Technical Information

A Transcranial Direct Current Stimulator (tDCS- MIND ACQUITY, Walnut Medical™) has been used as the intervention tool for the participants. In both groups, tDCS electrodes were placed per the 10/20 EEG electrode placement system across regions F1/F2 and P3/P4. By measuring the head circumference difference between FP1 and FP2, anodal and cathodal electrodes were implanted over the frontal cortex at FP1 (left frontal region) and FP2 (right frontal region), respectively. The location of P3 on the right side and P4 on the left side and the measurements of the T5 and PZ markers were used to determine where to implant a second anodal and cathodal electrode over the parietal region (Figure 2).

Figure 2: Electrode placement at P3 & P4



The outcome measure used for the assessment is The Saint Louis University Mental Status Examination (SLUMS), an 11-item test with a scoring range of 0 to 30 that looks at orientation, problem-solving, thinking skills, and attention to measure cognitive decline [15]. Another outcome measure is Montreal Cognitive Assessment (MoCA) is a screening tool with a score range of 0 to 30 that demonstrates sensitivity to mild cognitive impairment by investigating executive function, immediate and delayed memory, abilities of visuospatial and attentional processing, working memory, language, and orientation to time and place [16]. Both outcome measures were used as primary outcome variables.

Intervention Procedure

The experimental group (n=20) was treated with active tDCS and the conventional intervention. In active tDCS, the volunteers receive active treatment in which the intensity is initially scaled up gently from zero to 2 mA and then progressively raised. It was then maintained at that level for 40 minutes until gradually ending. Each volunteer in the experimental group underwent this intervention in a ramped-up and ramped-down fashion for 3 days per week for 4 weeks.

The control group (n=20) was treated with sham tDCS along with the conventional intervention. In sham tDCS, the intensity is built up from zero to one mA initially for just one minute and then ramped down to zero intensity at a steady current for the remaining 19 minutes, giving the patient a placebo effect. Each volunteer in the control group received this treatment for 3 days per week for 4 weeks, with the frequency of treatment increasing and

decreasing over time.

The researcher designed the conventional intervention, consisting of a standard numeracy training regimen comprising forward and backward counting, breaking numeracy into 10 components, counting items, and two-digit problem-solving. Two physiotherapists were involved in the intervention method to provide the treatment to each group individually, and one blinded assessor was involved in evaluating the pre- and post-measures of the outcome variables. The intervention protocol's number registered with the copyright office of the government of India is 7470/2022-CO/L.

Statistical analysis

The statistical data was analyzed using the 20th version of the social software statistical package (SPSS). The distribution of the data was estimated using Kolmogorov-Smirnov test. The mean, standard deviation, and p-value (set at >0.05) were used for descriptive statistics [17]. The comparison between the groups via outcome variables was measured by a non-parametric test, i.e., the Mann-Whitney U test. In contrast, the within-group analysis via outcome variables was calculated by a non-parametric test, i.e., the Wilcoxon Signed Rank test. P-value < 0.05 was considered significant in both the between-group and within-group analyses [18]. Effect sizes were also determined with Cohen's d [(M1 - M2) / spooled], according to Cohen's criteria, proposed by Cohen (1992), effect sizes of > 0.8 were considered significant, 0.5–0.8 moderate, and 0.2–0.5 small. The post hoc analysis for each outcome variable was done using statistical G Power 3.1.9.7 software to calculate the power of the study.

RESULTS

Table 1 shows the descriptive statistics for the demographic characteristics of age, gender, height, weight, and BMI for the volunteers in this study. Data for two demographic characteristics, age (0.001) and gender (0.001), were found to be not normally distributed.

Table 1: Demographic characteristics of the participants (n=40)

S.no.	Demographic characteristics	(Mean ± SD)	p-value
1	Age (in years)	21.95±1.83	0.01
2	Height (in meters)	1.68±.085	0.154*
3	Weight (in Kg)	65.32±13.98	0.149*
4	BMI (in Kg/squared meters)	22.97±4.093	0.479*
5	SLUMS	22.10±3.24	0.56*
6	MoCA	23.37±2.45	0.23*

Abbreviations: (a) SD - Standard deviation; (b) BMI - Body Mass Index; (c) SLUMS - Saint Louis University Mental Status Examination; (d) MoCA - Montreal Cognitive Assessment.

*p-value was set at >0.05

The statistical within-group analysis for both the experimental and control groups, based on a p-value of 0.05, revealed that there was a significant difference between the pre-and post-values for both outcome variables, i.e., SLUMS and MoCA, in both groups, as shown in Figures 3 and 4.

Figure 3. Box and whisker representation of within-group comparison between pre-post intervention MoCA group 1, SLUM group 1

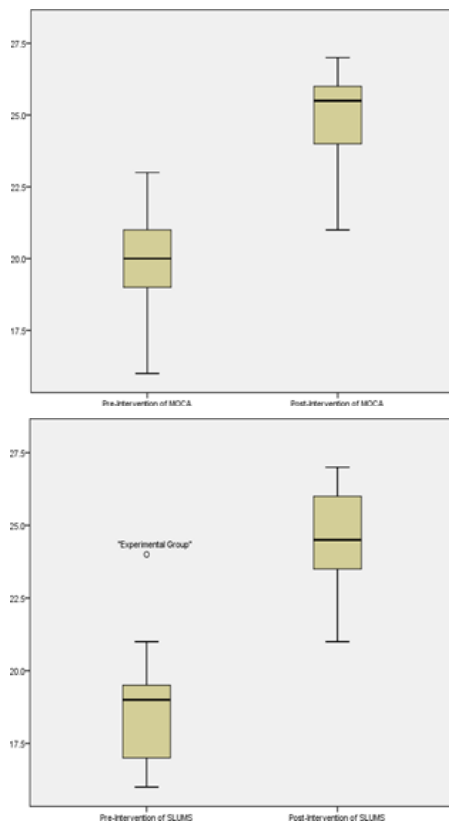


Figure 4. Box and whisker representation of within-group comparison between pre-post intervention MoCA group 2, SLUM group 2.

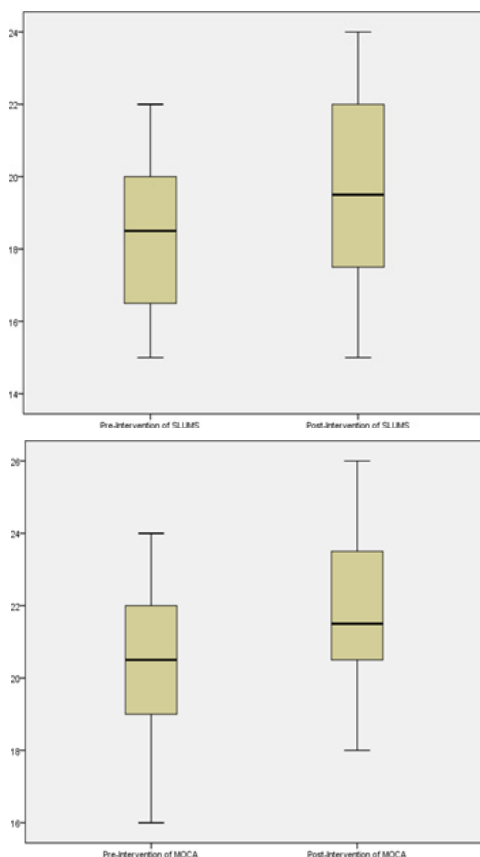


Table 2 reveals a statistical within-group analysis for the experimental and control groups based on a p-value of 0.05.

Table 2: Comparison of pre and post-measures of outcome variables within the experimental group and control group

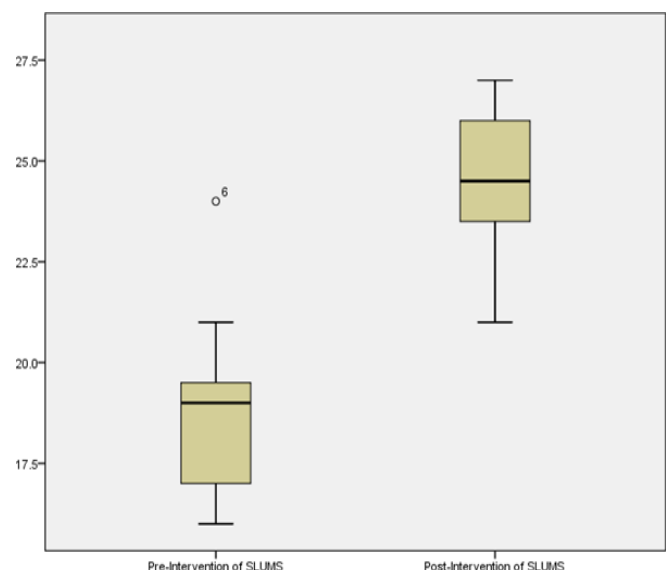
Participants	Outcome Variables	Timeline	Mean (95% CI)	p-value
Experimental group (n=20)	SLUMS	Pre	18.75(17.87 ± 19.62)	0.001*
		Post	24.45(23.66 ± 25.23)	
	MoCA	Pre	19.70(18.81 ± 20.56)	0.001*
		Post	24.90 (24.12 ± 25.67)	
Control group (n=20)	SLUMS	Pre	18.25(17.25 ± 19.24)	0.001*
		Post	19.75(18.49 ± 21.00)	
	MoCA	Pre	20.15(19.18 ± 21.11)	0.001*
		Post	21.85(20.82 ± 22.87)	

Abbreviations:- (a) SLUMS - Saint Louis University Mental Status Examination; **(b) MoCA** - Montreal Cognitive Assessment.

*p-value was set at < 0.05

Additionally, the statistical analysis between the experimental and control groups revealed significant results for the post values of both outcome variables (i.e., SLUMS and MoCA), depicting that the experimental group improved the participants' calculative ability better than the control group shown in Figure 5.

Figure 5: Box and whisker representation of Comparison of pre and post-measures of outcome variables (SLUMS & MoCA) between the experimental and control groups.



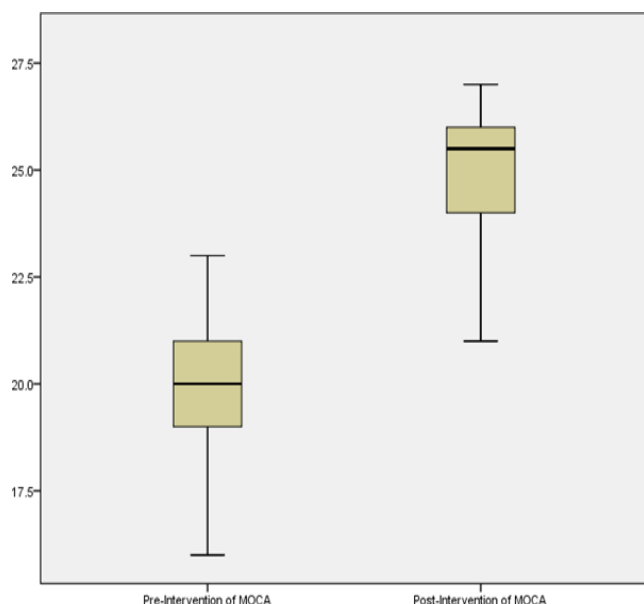


Table 3: Comparison of pre and post-intervention measures of outcome variables between the experimental group and control group.

Outcome variables	Time-line	Experimental Group (n=20)		Control Group (n=20)		p-value
		Mean (95% CI)	Range	Mean (95% CI)	Range	
SLUMS	Pre	18.75 (17.87-19.62)	16-21	18.25 (17.25-19.24)	15-22	0.591
	Post	24.45 (23.66-25.23)	21-27	19.75 (18.49-21.00)	15-24	0.001*
MoCA	Pre	19.70 (18.81-20.58)	16-23	20.05 (19.12-20.97)	16-24	0.527
	Post	24.90 (24.12-25.67)	21-27	21.85 (20.82-22.87)	18-26	0.001*

Abbreviations: (a) SLUMS- Saint Louis University Mental Status Examination; (b) MoCA - Montreal Cognitive Assessment.

*p-value was set at <0.05

The effect sizes obtained from the present study showed the large effect sizes of the SLUMS and MoCA. The study's value and power showed that it was very effective, and these results are shown in Table 4.

Table 4: Effect size index and power of the study.

S. No	Outcome Variables	Effect size	Power of the study
1.	SLUMS	-1.34	98%
2.	MoCA	2.60	100%

Abbreviations: (a) SLUMS - Saint Louis University Mental Status Examination; (b) MoCA - Montreal Cognitive Assessment.

DISCUSSION

In this era of intense competition, acquiring the knowledge required to fix numerical issues, analyze them accurately, and tackle more difficult arithmetic problems such as addition and subtraction is essential. If there is an impairment in performing these functions, it will be a great challenge for an individual to solve these problems, such as in a child

with developmental dyscalculia. Therefore, it creates more challenges in their academics to achieve good grades during school and at the start of their professional careers. The literature we have analyzed thus far has compared the effects of left and right brain dominance on high school students' mathematical abilities [19]. A personality exam and a test of mathematical performance were utilized as end measures, and the researchers concluded that each person is either right- or left-brain dominant [20]. They also established the influence of right-brain and left-brain dominance on mathematical learning achievement [20]. Learning mathematics requires the use of both hemispheres of the brain, yet those whose dominant hemisphere is the right exhibit only 28% of their brain's involvement, while those whose dominant hemisphere is the left show 46.7% involvement, and This finding demonstrates the distinct impact of mathematics on brain dominance [21].

The tDCS had previously been used in the literature on right-handed individuals; to the best of my knowledge, this is the first study to use the tDCS for left-handed individuals [22]. The tDCS has shown promise as an approach for improving cognitive performance in previous research [22]. This study evaluates how left-handed dominant individuals benefit from tDCS to enhance their intellectual capabilities. So, our study aims to improve the academic performance of these students by enhancing their calculative ability through the stimulation of the right hemisphere. Our study included 40 volunteers, two physiotherapists who administered the treatment regimen, and one blinded evaluator who measured pre- and post-treatment outcome factors. Most students with developmental dyscalculia persist throughout childhood and have poor numerical skills [23]. Approximately 3 to 7 percent of the child population is affected and struggles with various areas of numeracy abilities. Due to impairments in brain activity and structure, specific tasks requiring numeracy skills, such as bill payments, remembering phone numbers, grocery calculations, etc., might be challenging. It has also been noticed that students with dyscalculia remain unemployed even at the age of 30. Grabner RH et al. 2015 measured dyscalculia for performance enhancement among students by stimulating their posterior parietal cortex parts and found that in the experimental group where left anodal and right cathodal electrodes were placed, significant changes were observed with $f = 9.61$ and a $p\text{-value} > 0.26$. This research also revealed that each participant's brain lateralization and polarity differed [23].

A study by Hauser TU et al. 2013, showed the beneficial effect of tDCS on learning math and subtraction problems [20]. Non-invasive brain stimulation of the posterior parietal cortex improves arithmetic performance and mathematics learning [25]. Learning improves to 19% in subtraction solution rates after anodal stimulation over the posterior parietal cortex, whereas sham stimulation improves to 6%. However, these results only show subtraction improvement but not multiplication [25]. Task dependency was consistent with the findings of two previous studies that used tDCS of the posterior parietal cortex to improve arithmetic learning performance, where

they discovered an encouraging effect of the tDCS only in the case of subtraction problem solving [19,26]. Hauser TU et al. 2013 established neurophysiological evidence that investigated the neurocognitive bases of subtraction and multiplication dissociation [20]. They recruited more participants with difficulty assuming numerical problems, which was solved by anodal stimulation of the posterior parietal cortex (PPC) [20, 23]. Tobias U. Hauser et al., tDCS combined with electrophysiological activity improved arithmetic learning, and Grabner RH et al. aim was to find the effect of tDCS over the left parietal and frontal region [22,23]. To gain a more skilled analysis, they have also investigated EEG analysis and tDCS for behavior and neuropsychological levels, which are done at the beginning, during, and after the stimulation [22-24]. Their result indicates significant gains in numerical processing in participants who received stimulation in the frontal region, whereas participants receiving sham stimulation showed no difference [22-23]. Traditional numeracy training improved numeracy skills in children with numeracy difficulties. It includes forward and backward counting, object identification, and counting, counting verbally, problem estimation, and breaking down numeracy into ten elements. The study aids in the improvement of the calculative ability to perform numerical skills in middle-aged students with developmental dyscalculia [19, 27].

The previous research findings were inconsistent with those of the present study. There was a visible, significant improvement in calculative ability among the experimental group as compared to the control group when assessed with the Saint Louis University Mental State Examination (SLUMS) as well as the Montreal Cognitive Assessment Tool (MoCA). The results of the experimental group showed that there was an improvement in volunteers with a right-side dominant hemisphere after applying the stimulation to the frontal and parietal cortex, where the anode at FP1 and cathode at FP2, along with posterior parietal cortex, where the cathode at P3 and anode at P4 were placed. The mean differences between the post-SLUM and pre-SLUM scores in the experimental and control groups were 5.70 and 0.50, respectively. The mean differences between post- and pre-MOCA scores in the experimental and control groups were 5.20 and 1.85, respectively, which showed that there was a significant difference between the scores of these outcome variables as well as that the SLUM score showed a better improvement as compared to the MoCA score. The z value of the experimental group was -4.694 (0.001). The control group was -3.963 (0.001), which shows that the data was highly significant in both groups but that the experimental group showed better improvement. Considering the findings of previous and current studies, the alternative hypothesis, i.e., tDCS can improve mathematical ability in participants with left-handed dominance, was proposed. As well, the results of the post-intervention measures of SLUMS (p-value = 0.001) and MoCA (p-value = 0.001) with less than significant p-values (i.e., 0.05) contributed further to the acceptance of the alternate hypothesis. The study's effect size and power measures obscured the study's findings. The MCID values for the outcome variables, i.e., SLUMS and MoCA, were calculated at 1.16 and 7.24,

respectively. The current study provides strong evidence that bi-frontal anodal tDCS improves working memory used during mathematics, which will be helpful for future perspectives on better performance in academics and job sectors. In this study, we calculated the effect sizes of the variables used in the study; they came out to be 1.34 for SLUMS and 2.60 for MoCA, and the power of the study established that this was 98% for SLUMS and 100% for MoCA. In the current study, we also determined the MCID value, which was 1.16 for SLUMS and 7.24 for the MoCA. These results were relatable to the previous research. Still, as we have mentioned above, this was the first study, according to our best knowledge, that involved healthy volunteers with a right-side dominant hemisphere, so there was a lack of exact and consistent results for comparison with the previous research.

CONCLUSION

The present study concluded that tDCS is an adjuvant that can be used along with a proper exercise protocol consisting of conventional numeracy training to improve the calculation ability among individuals with left-hand dominance.

Limitations and Future recommendations of the study

In addition to providing favorable outcomes, like improving the mental ability and capability to improve the activities of daily living and requiring only minimal space to perform the intervention, this study also had some limitations. Because of the high cost of the necessary equipment and the length of time required for the procedure, tDCS is not readily available or affordable to all people. Additionally, this research focuses solely on quantitative ability. Moreover, because the tDCS was used on a hairy part of the scalp, it was impossible to determine whether the hair removal would impact the outcomes. Therefore, it can be advised that future studies, along with other treatment protocols, be done with an emphasis on qualitative abilities, employing hair removal together with functional MRI and EEG to determine the area affected and changes in brain activity.

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