Investigation of the Influence of Phonological Awareness Intervention and Transcranial Direct Current Stimulation on the Enhancement of Rapid Automatized Naming and Verbal Short Term Memory in Developmental Dyslexia: A Randomized Controlled Trial

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Abstract

Phonological deficits include phonological awareness (PA), rapid automatized naming (RAN) and verbal short term memory (VSTM). PA is defined as a conscious manipulation of the word subunits in word structure. Recently, transcranial direct current stimulation (tDCS) has been used as a complementary treatment with PA intervention in the dyslexia treatment. In this trial we had both a PA intervention group and a PA + tDCS group in which the tDCS is applied over the left parieto-temporal area. It was hypothesized that the PA + tDCS treatment can improve RAN and VSTM. A randomized, double-blind, sham-controlled clinical trial was conducted to evaluate the influence of PA + tDCS intervention in improving RAN and VSTM. Twenty-eight participants were randomly allocated to the active (PA + anodal tDCS) or sham (PA + sham tDCS) groups. Each dyslexic student participated in 15 intervention sessions. RAN and VSTM sub-tests were assessed at the baseline, at the end of the fifth, tenth, and final treatment sessions and finally 6 weeks after the treatment. In both groups, mean scores of RAN sub-tests significantly decreased and the mean scores of the VSTM sub-tests significantly increased during, immediately and also 6 weeks after intervention. There was no significant difference between the two groups in the mean scores of the outcome measures. PA intervention leads to improvement in RAN and VSTM abilities in dyslexic students for a longer period of time. Combined intervention (PA + tDCS) had no further effect on outcome measures than PA intervention alone.

Introduction

According to the phonological deficit hypothesis, phonological processing insufficiencies are the main cause of developmental dyslexia (DD) (1). These deficits are related to reading decoding, accuracy and speed in word recognition in DD (2, 3). Phonological processing deficits have three main dimensions; phonological awareness (PA), verbal short-term memory (VSTM) and rapid automatized naming (RAN) deficits(4, 5). PA is the ability to identifying, using and manipulating sub-lexical structures (6). RAN is defined as the time spend for a person to rapidly and correctly name a set of known visual stimuli such as; colors, letters, numbers and, objects(7, 8). And, VSTM is the ability to hold verbal information temporarily(5, 9). Each of these abilities affect one aspect of reading: RAN and PA predict reading speed and reading comprehension, respectively (10) ; VSTM also helps with the reading process by retaining phonemic information(11).

Several issues remain ambiguous about the association between PA, RAN and VSTM with reading(12). An important issue is the independence or integrity of PA, RAN and, VSTM in dyslexia. Some studies state that they should be speculated as an integrated phonological term(2, 4). Others argue that RAN and VSTM involve cognitive formulations that are separate from PA and are considered separate processes from phonological skills (12-14). It is stated that PA, RAN and VSTM share a common phonological base and are interconnected in DD(1). For phonological base of VSTM, it can be stated that one part of working memory (WM) ,called the phonological loop, that is involved in phonological store and articulatory formulation is associated with VSTM and leads to long-term phonological acquirements, such as new words learning (15). On the other hand, PA and RAN have similar patterns in the bidirectional relationship with reading and both are prerequisites for reading development (10). The bidirectional association between RAN and reading is mediated by PA (16). After PA, RAN deficits are considered the second source of reading disabilities (13).

Limited intervention studies have investigated the independence or integration of PA, RAN and VSTM. In one study, using presenting PA and RAN interventions to separate intervention groups, authors showed that PA and RAN training influenced different dimensions of reading ability. They concluded that PA and RAN training affect sub-

lexical spelling (decoding) and reading speed, respectively and are independent abilities(12). Evidence shows that although RAN, VSTM and PA are independent, phonological training enhances RAN (10, 16-18) and VSTM (19-21). In one study, children who received RAN intervention did not show improvement in RAN (22) and since PA tasks also involve VSTM, PA intervention results in VSTM enhancement (21). For the reasons above we chose PA intervention among the three of them.

Phonological processes are dispersed among several regions of the left hemisphere(23). The most commonly involved region during phonological tasks is the parieto-temporal region (24, 25). In dyslexic readers, the performance of these regions is decreased or disrupted compared to non-dyslexic readers while performing PA tasks (26). PA intervention enhances the performance disabled readers and leads to phonological improvement (23).

Various educational programs, even if intensive, rarely result in complete enhancement in reading abilities in DD (27). According to Frith, to overcome the limitations and to increase the efficacy of the intervention in DD, combined intervention should be used in dyslexia intervention(28). An adjunctive method that has been recently used in reading studies (29-33) is transcranial direct current stimulation (tDCS); a tolerable, cheap, portable and non-invasive brain stimulation tool that conveys a slight electrical current of 1–2 mA through two or more electrodes (a positively charged anode and a negatively charged cathode) positioned on the scalp (34). The first mechanism of action of tDCS-induced current is a polarization of neural membrane resting potential. Anodal stimulation increases cortical performance and stimulation ability (depolarization), while cathodal stimulation has adverse effects (hyperpolarization) (34-36). Neuroplasticity modulations linked to glutamatergic and GABAergic stimulatory and inhibitory function transformations appear minutes after stimulation (37). From another perspective, these plasticity modulations result in cortical activity, prolonging stimulation duration(38). Based on evidence, tDCS provides a basis for learning in the dyslexic population by stimulating neuronal plasticity (39).

Up to now, two studies have combined tDCS and PA as a means of treating auditory and visual WM in DD population (40, 41). In these studies, anodal stimulation has improved the auditory/verbal performance of the WM(40, 41).

We have two purposes in this study: First, we aimed to examine the efficacy of the PA intervention on RAN and VSTM. Second, we intend to consider the possibility of further improvement of RAN and VSTM with adjunctive PA+ tDCS treatment compared with PA intervention alone. For this purpose, we congregated two groups of DD participants: the active and the sham groups. In the active group, the students received PA+active (anodal) tDCS treatment whereas the sham group students received PA+sham tDCS as a behavioral intervention. We hypothesized that PA intervention leads to transfer effects on RAN and VSTM tasks in both active and sham groups and, the adjunctive intervention (PA+active tDCS) in which tDCS is over the left parieto-temporal region would be more effective than the PA only (PA+sham tDCS) in increasing RAN and, VSTM in DD.

Results

Recruitment:

one hundred and six suspected dyslexic students were referred to the study by elementary school teachers and learning disability centers. One hundred out of 106 students were assessed for eligibility; 6 were not available. Out of the 100 evaluated, 72 were excluded: 30 students did not score higher than the norm point on the Wechsler

Intelligence Scale for Children, 10 did not score lower than the norm point on the Nema reading test, 26 did not want to participate and 6 students were not available for contact. Twenty-eight phonological DD students (mean = 9.36 year, SD = 1.22), were included in the trial. No drop-outs occurred during the intervention process and all of the subjects took part in all intervention sessions. Supplementary Fig 1 demonstrates a flowchart of the study. Recruitment of the participants began in April 2020 and ended in December 2020.

Baseline Data

According Table 1, there were no differences between the two groups in terms of age and sex. Additionally, there was no significant difference between the two groups in terms of IQ. Descriptive statistics of the demographic and outcome measure characteristics of the students in the baseline stage are presented in Table 1. Demographic characteristics of participants of both groups were properly matched. The two intervention groups did not vary in terms of any of the outcome measures at the baseline (T0) (Table 1).

Table 1. Descriptive statistics of the demographic and baseline outcomes and their between-groups comparison.

Outcomes	Active			Sham			P-value
	Mean(SD)	Minimum	Maximum	Mean(SD)	Minimum	Maximum	
1	9.18 (1.30)	7	11.08	9.54(1.15)	7.08	11.10	0.629
2	12 (85.71%)	-	-	10 (71.42%)	-	-	0.366
3	99.35 (3.38)	90	105	97.42(4.87)	87	102	0.378
4	78.30 (17.26)	50	105	78.14(22.58)	48	135	0.9
5	63.40 (14.57)	39	91	64.97(19.30)	37	95	0.810
6	53.13 (20.01)	28	91	45.72(11.32)	27	68	0.334
7	68.06 (18.56)	41	108	70.33(17.91)	40	107	0.745
8	49.67 (11.21)	29	66	49.56(14.61)	26	90	0.983
9	55.20 (17.35)	32	102	45.26(6.78)	35	57	0.056
10	80.59 (32.50)	36	155	70.36(23.96)	37	116	0.352
11	74.31 (24.62)	40	135	66.68(18.58)	39	96	0.363
12	522.70 (133.94)	321	816	491.03(115.93)	301	731	0.510
13	3.45 (1.50)	2	7	3.84(1.34)	2	6	0.396
14	3.00 (0.89)	2	4	3.15(0.80)	2	4	0.667
15	33.21 (4.59)	24	40	35.92(3.73)	24	39	0.098

1= Age, 2=Sex (Male), 3= IQ, 4= RAN_objects, 5= RAN_colors, 6= RAN_digit, 7= RAN_animals, 8= RAN_high-frequency capital letters, 9= RAN_ high-frequency lowercase letters, 10= RAN_ low-frequency capital letters, 11=

RAN_ low-frequency lowercase letters, 12= Total RAN score, 13= Forward digit span, 14= Backward digit span, 15= Non-word repetitio

Outcomes

Subtests of the RAN task and VSTM test during the five time points were analyzed using repeated measures analysis of variance, with time points as the within-subjects variable and grouping (anodal/sham treatments) as the between-subjects variable.

According to Mauchly's test, the assumption of sphericity, except for FDS, had been violated by the other outcome measures ($p < 0.005$). Therefore, the degrees of freedom were corrected using Greenhouse–Geisser estimates of sphericity ($\epsilon < 0.75$). Supplementary Table 1 shows the means, standard deviations, post hoc results for all variables at five time evaluation points. It is noteworthy that there was a significant difference in the mean scores of all outcome measures (except BDS) over time in both groups ($p < 0.001$) and the main effect of time in all outcome measures was statistically significant in both groups. However, the main effect of group and the interaction between time and group did not significantly differ in any of the outcomes (no significant difference was observed in any of the outcome measures between the two groups). Therefore, only the results of the main effect of time are presented in Supplementary Table 2.

Tingling (documented by 4 and 3 subjects in the anodal and sham groups, respectively) and itching (3 subjects in each group) were the most prevalent tDCS side effects. 2 subjects in the anodal group, reported a burning sensation due to having bulky hair. No sleepiness, headache, trouble concentrating or psychological problems- namely irritability and acute mood changes- were recorded. None of the subjects reported side effects during the follow-up stage.

Discusson

The current randomized controlled trial aimed to investigate the relationship between PA, RAN and, VSTM in reaching two study questions. First, we should state whether RAN and VSTM are separate from PA in treating PA and considering the influence on the two other componantes. Second, we intended to investigate the possibility of further improvement of RAN and VSTM with combined intervention (PA + tDCS) compared with PA training alone. Effects of both intervention groups were evaluated at two time points during intervention (T1 and T2) and, immediately after intervention (T3) and, 6 weeks after end of treatment (T4 = follow up) to eliminate only short-run influences of intervention on outcome measures.

The within group comparison results showed that PA intervention leads to transfer effects on RAN and VSTM tasks (except BDS) in both active and sham groups ($p < 0.001$). This finding supports the view of overlapping cognitive mechanisms between PA, RAN and, VSTM confirmed by studies reporting that the association between RAN and VSTM with reading were mediated by PA(42, 43). Based on the phonological representation hypothesis, phonological representation is impaired in DD and since PA, RAN and VSTM abilities are under the phonological umbrella, all of them are impaired in dyslexia(2). Additionally, The phonological processing limitation hypothesis shows that PA and VSTM depend on an unique phonological mechanism(44). It can be argued that the probable reason for the improvement of VSTM following the PA intervention is related to the phonological loop mechanism involved in VSTM. According to the phonological loop hypothesis, there are two detachable mechanisms; a temporary phoneme storage and a latent phonic rehearsal mechanisms for refreshing phonological components.

The former holds phonemic information in memory, while PA intervention components (initial/final phonemes detection, segmentation, blending and as such) are performed; the latter is required to protect phonological components from reduction. Therefore, PA intervention leads to their improvement in the application of these mechanism(21). Regarding the transmission of the effect of PA treatment on RAN, it can be stated that several researchers believe that RAN is a subset of PA. According to Wenger and Torgesen, RAN is as the skill that "represents phonological codes from long-term memory" (4) or causes phonological recoding to lexical retrieval (45–47). Thus, PA and RAN may have common phonological features. Therefore, it is speculated that due to the common phonological base deficit between these abilities (PA, VSTM and RAN), intervention of one of them will transfer improvement to the others. The results of our trial are in line with other studies that have shown that with the PA intervention, improved RAN and VSTM (10, 17, 19, 20). The first study on the influence of PA training on improving verbal WM was conducted by Gillam and van Kleeck(9). However, our findings are opposed to the studies showing RAN and VSTM independent from PA. Cornwall (1992) and Stappen and Reybroek (2018) stated that each of these 3 abilities (PA, RAN and, VSTM) affects a different aspect of reading (reading accuracy, fluency and comprehension). They showed independence between these abilities (12, 48). This hypothesis was originally presented by Wolf and Bowers in the double deficit hypothesis. Proponents of this hypothesis advocated RAN as a separate element from the PA(13). Based on this hypothesis, Lovett et al showed that RAN did not improve with phonological treatments (49). Therefore, further studies are needed to determine whether these 3 skills are independent or all of them have a common and interconnected phonological base. PA training accelerates the inferior tempo-parietal and frontal regions and right hemisphere several areas activity that are involved in phonological processes (50). It is stated that there was a bilateral activity allocations in the anterior areas and an increased activity in the right hemisphere in the posterior areas before PA treatment. After treatment, brain neuronal activity in the right anterior and left posterior areas was increased (51).

Based on our results, PA intervention did not lead to improvement of BDS. This task is usually used to evaluate verbal WM rather than VSTM(19). Therefore, it can be stated that PA intervention does not affect WM.

In line with the second aim of the trial (comparing the effect of active and sham intervention on improving RAN and VSTM), results of this study showed no significant difference between the active and sham groups in improving RAN and VSTM (between-subject effect) (Supplementary Table 1). This loss of stimulation effect can initially be attributed to the lack of precise focal stimulation using two large electrodes that leads to the dissemination of current to external part of the accurate site of the stimulus. Specifically, the current might have diffused from the perito-temporal region to the broader parietal regions that are specifically involved in grapheme to phoneme correspondence in this trial. Therefore, it can be concluded that in the present study, phonological processing areas that are more involved in pure phonological tasks (such as, NW reading and decoding) rather than skills related to the whole word and semantic mechanisms such as RAN might have been stimulated. Second, since the site of dyslexic brain activity during RAN is related to the distributed networks in parietal and frontal regions (52) and VSTM is related to left intraparietal and the bilateral cingulate and the right dorsolateral prefrontal cortex (DLPFC) (53), stimulation of the parieto-temporal region has had no effect on improving the activity of these areas. Since the aim of the present study was PA training and stimulation of brain areas involved in phonological activities to investigate their effects on RAN and VSTM, parieto-temporal region was selected as the stimulation location in tDCs.

The first study on the effect of tDCS on DLPFC was performed by Fregni et al. The anodal stimulation of this region improved the sequential letter WM task(54). Meiron and Lavidor reached a similar conclusion. Stimulation

of the DLPFC facilitated performance in high demanding WM load state(55). But Marshall et al. had the opposite conclusion. In their study, the prefrontal region stimulation increased the reaction time in the WM task and disrupted the central neural processes associated with response selection and preparation (56). These studies were based on tDCS alone but, Bayat Mokhtari et al. used a combined intervention (PA + tDCS) to improve verbal WM and they showed that anodal stimulation increased performance on activities including auditory WM(41). Contrary to our study, Bayat Mokhtari et al. showed that tDCS improved verbal WM performance. The reason for this difference can be related to the current intensity provided and the stimulation location. In their study, the current of 1.5 mA was presented over the left DLPFC that is related to WM activity but, we transmitted current of 1 mA to the parieto-temporal region that is linked to phonological processing(24, 25). We aimed to investigate the transfer improving effect of the stimulation of the phonological processing areas on WM and RAN abilities, not direct stimulation of the brain areas associated with these abilities.

Results of this study showed that PA intervention could enhance RAN and VSTM abilities for a prolonged period of time after intervention (follow-up).

Our study had several potential limitations. First, because of prolonged intervention process and the availability of electrical current transition to brain, some parents were reluctant to permit their children to involve in the intervention process. Second, age and grade range in the current trial restrained our ability to adequately express the developmental variations in RAN and VSTM. Third, placement of the electrode in the left parieto-temporal region was determined according to previous studies in the current trial (25, 29). However, individual differences at the location of dyslexic's brain dysfunction were not investigated in determining the stimulation of the target region. Finally, there was no control group that did not receive a treatment. In fact, since that PA, VSTM and RAN are somewhat common in at least some phonological process components, it was not possible to compare the effect of PA intervention on RAN and VSTM between dyslexic and normal students.

Future studies are suggested to apply bilateral or right hemisphere anodal stimulation of the parieto-temporal area with higher current intensity (1.5–2 mA). Higher intensity currents may increase the influence of intervention results from increasing cortical excitability(57). The application of higher intensive current has also been investigated in depression (58). Therefore, higher current intensities, for example 1.5 or 2 mA, are recommended in future studies of DD. Furthermore, application of neuro-imaging techniques (such as, QEEG and fMRI) may be useful in determining the exact location of brain dysfunctions (left parieto-temporal region in the present trial). It helps with precise fixation of electrodes over the relevant regions. Finally, future trials may benefit from a larger sample size.

Conclusion

PA intervention has a transferred improvement effect on other phonological skills (RAN and VSTM). But, the providing of tDCS over the left parieto-temporal area has no further therapeutic effect on these skills.

Methods

Study design

The present study was a randomized, double-blind, sham-controlled research study. Participants were randomly assigned to the active and sham groups. PA training simultaneously with left anodal/right cathodal tDCS was

given to the active group participants, on the other hand participants in sham group had sham tDCS with PA intervention.

Participants

Study population consisted of 28 students with DD. There were 14 participants in the active group (12 males, 2 female) 7-11.08 years old (mean age 9.18, SD = 1.30 years). The sham group had 14 participants (10 males, 4 females) 7.08-11.10 years old (mean age 9.54, SD = 1.15 years). Dyslexia diagnosis was made based on the DSM-5 criteria for reading disorder (59); a speech-language pathologist assessed the type of dyslexia using a set of diagnostic tests, including word and non-word (NW) subtests from the Nema reading and dyslexia test (60) to include those with phonological dyslexia. Internal consistency for word and NW reading subtests was 0.098 and 0.095, respectively (61). Dyslexic students were collected from primary schools and learning disability centers and evaluations were performed in a private speech therapy clinic. Inclusion criteria included having correctness and/or speed of word and/or NW reading subtests at least 1.5 standard deviations under the population mean for the educational grade (60), a non-verbal IQ score >85 (62), not having associated disorders including seizure, attention deficit and hyperactivity disorders evaluated by clinical observation and by using Conners' Rating Scales –Revised (63), non-compensated hearing loss, native Persian speaking and being right-handed as evaluated by the Edinburgh inventory (64).

Exclusion criteria included history of a reading related intervention before treatment and use of prescribed medication associated with the cranial neural system disorders. An informed consent form, describing the aim of the study and processes involved was signed by the parents of all students after.

Interventions

Intervention sessions (for both groups) were performed at the rehabilitation clinic in Tehran, Iran. Regardless of group allocation, each participant went through 15 60-minute intervention sessions [three times per week (T) for 5 weeks] (65). The study outcomes were measured at five steps: immediately before treatment (baseline) (T0) , at the end of the fifth intervention sessions (T1), at the end of the tenth intervention session (T2), immediately after the intervention (T3), and 6 weeks after the end of the intervention (T4) by a blinded investigator. To evaluate the stability of the treatment in both groups, 6-weeks follow-up was considered for each participant.

PA Intervention

PA treatment was performed in both the active and sham groups each session. The duration of each treatment session was 60 minutes (15 hours in total). We derived the PA intervention program from the "Gillon Phonological Awareness Training Program" (66). The Gillon PA treatment program covers nine skills(66):

- Rime abilities
- Phoneme analysis
- Phoneme recognition
- Phoneme segmentation
- Phoneme blending
- Tracing speech sounds
- Sound–symbol association

- Tracing speech sound with letters
- Reading and writing skills

According to the Gillon PA program, the time spent on each skill varied based on the participant's increasing skill level. For example, rhyme and phoneme analysis and recognition which are considered initial tasks were addressed in the first 4 to 6 sessions. Toward the end of the program (after 6 or 7 sessions), phoneme segmentation, blending and manipulation were performed and reading and writing skills were trained. Participant did not need to succeed completely with one before moving on to the next skill. Based on the progress of individuals in developing learning skills, other skills could be added in one session (66).

tDCS

Participants were randomly assigned to the sham and anodal tDCS. In order to determine the location of electrodes accurately, we used an EEG cap. The anode and the cathode electrodes were positioned over the left and the right parieto-temporal regions, respectively. An Activa Dose II Iontophoresis Delivery Unit tDCS was used to transit tDCS. In the active group, stimulation was performed by transiting the direct current between two conductive rubber electrodes. Each electrode was covered in a sponge pad. Two 5 cm x 7 cm electrodes were positioned on the scalp using an elastic rubber strip (Figure 1). Both sides of the sponge pads were moistened in dextrose 3.33% and sodium chloride 0.3% solution for better conductivity. Prior to placing the electrodes on the scalp, the therapist checked the head skin for any skin lesions. Electrodes position were similar in both the anodal and sham groups. Location of stimulation in the left and the right hemispheres coincided with the midway between T3 and P3 and midway between T4 and P4 according to the 10-20 international system (67). An anodal and a cathodal stimulation augmented the left parieto-temporal function and reduced the right parieto-temporal function, respectively. The bilateral stimulation motivates normalization of atypical brain function detected in dyslexic participants in the phonological tasks (50). In the active group, at the beginning of stimulation, the current was gradually increased over the first 30 seconds to 1 mA, the excitation threshold, as ramp-up and was declined gradually to 0 mA over the last 30 seconds as ramp-down at the termination of the stimulation. In the interval between the ramp-up and ramp-down, a steady direct current of 1 mA was transited for 20 minutes. In the sham group, the direct current was given to the brain only for 30 seconds and was turned off afterwards. This placebo-intervention induces tDCS-induced sensation (e.g. irritation and itching) indiscernible by the participants from an active intervention (68). Intensive combined intervention was applied three times a week for 5 weeks (15 sessions). tDCS was applied to the active group for 10 sessions with PA intervention, simultaneously (During the 60 minutes of the combined intervention, only 20 minutes of stimulation was provided to the active group participants).

Safety

Students filled in a questionnaire on adverse effects at the end of each treatment session. The items in the questionnaire were: "headache, neck pain, scalp pain, tingling, itching, burning sensation, skin redness, sleepiness, trouble concentrating and acute mood change". Participants gave each item a score from 1 to 4 (1, absent; 2, mild; 3, moderate; 4, severe). Students scored the intensity of their adverse effects (69). Turning off and resetting the device took place in case of moderate to high rated for adverse effects. If side effects remained, the stimulation intervention was postponed until the next session.

Outcome Measures

In the present study, RAN and VSTM abilities were evaluated using researcher-developed RAN task and VSTM related sub-tests from Wechsler Intelligence Scale for Children—Revised in Iran(62), respectively.

RAN task: In this study, a RAN task was designed based on Denckla (8). The sub-tasks of the RAN task are as follows:

1. RAN_ objects: objects selection was based on the frequency of occurrence in Persian, more familiar semantic concepts for the student, mono-syllabic structure and simple production structure. For this purpose, Persian core vocabulary study was used(70) which has extracted all perceptual and productive words of students from first to fifth grade. Therefore, all the vocabulary produced by primary school students were examined and a list of words that met the above criteria was constructed (ball, table, bed, dish and hand).
2. RAN_ colors: colors were selected based on the frequency of occurrence (high-frequent) and simple syllabic structure from Persian colors category(71). These words were examined and 5 colors that had the highest frequency in elementary school textbooks (blue, green, black, red and yellow) were selected.
3. RAN_ digits: mono-syllabic digits were selected based on their frequency of occurrence in elementary school math textbooks (1, 2, 3, 6, 9).
4. RAN_ animals: The most frequent and well-familiar animals in Persian, in accordance with the words of the textbook of primary schools were selected(70). The animal names ranged from mono-syllabic to tri-syllabic (cow, dog, mouse, horse, pigeon).
5. RAN_ high-frequency capital letters: These letters were selected based on Mansouri high-frequency capital letters performed in Persian (آ ا ب پ ت ث ج د ذ ر ز س ش ص ط ظ ف ق ک گ چ پ ژ) (72).
6. RAN_ high-frequency lowercase letters: These letters were selected based on Mansouri high-frequency lowercase letters performed in Persian (آ ا ب پ ت ث ج د ذ ر ز س ش ص ط ظ ف ق ک گ چ پ ژ) (72).
7. RAN_ low-frequency capital letters: These letters were selected based on Mansouri low-frequency capital letters performed in Persian (ا ب پ ت ث ج د ذ ر ز س ش ص ط ظ ف ق ک گ چ پ ژ) (72).
8. RAN_ low-frequency lowercase letters: These letters were selected based on Mansouri low-frequency lowercase letters performed in Persian (ا ب پ ت ث ج د ذ ر ز س ش ص ط ظ ف ق ک گ چ پ ژ) (72).

Photographs were extracted from the Stanford-Binet IQ test_ Persian version in pictured sub-tasks (RAN_ animals and, RAN_ objects)(73).

Each of the five items in RAN sub-tasks was illustrated by color photographs organized randomly in 10 columns × 5 rows on a white A3 sheet. The letters and digits typed with B Nazanin size 36. Each sheet was placed on the table in front of the child, orderly. Initially, task instructions were then explained to the participant and the task items were preceded by examples items which involved a collection of addition items to prevent pre-activation of the task real items. Participants had to name all the items from right to left rapidly and correctly. It is noteworthy that if needed the meaning of the words were explained in case the child wasn't aware of it. Timing started with the participant's first naming after "Go" using turning on a stopwatch. After naming all the items in each sub-task, the stopwatch was turned off. Total naming time for each sheet/sub- task and number of errors was noted on a separate sheet. Self-corrections were not considered as an error but time was consumed. RAN time was calculated in seconds. There was a 1 minute break between each sub-task naming.

VSTM Test: In the present study, to evaluate VSTM were used from forward digit span (FDS) and backward digit span (BDS) and non-word repetition test (NWRT). These subtests are as follows:

1. *FDS and BDS*: to evaluate these abilities, the FDS and BDS subtests from Wechsler Intelligence Scale for Children - Persian version- were used(62); each span (FDS and BDS) including 2 sets; each of them with 7 series of digit (total digits=14) for repetition in forward and backward order. Digits in each series increase gradually (3-9 digits in FDS and, 2-8 digits in BDS). For correct repetition of each series, a score is awarded to the participant. If a participant fails to repeat each digits series, no score will be awarded. The maximum score for each span is 14. The test re-test reliability of the sub-tests of this test were 0.44 to 0.94.
2. *The NWRT*: in this study NWRT was used to evaluate NWR ability (74). This test consists of 40 non-words (NWs) (1-3 syllables) that were created by changing one or two phonemes of the real word phonemes. NWs do not convey meaning and are not available in the Persian vocabulary but are in accordance with the rules of Persian phonology. In the process, items were presented with a live voice and a covered mouth. The time interval between the presentation of each NW was 3 seconds. All participants were given directions that they would have to repeat a non-sense item that with no concept. Participants were asked to express it as accurately as possible. Before the start of the test, 4 training items were presented to each participant. Participants were given the main target NWs to repeat. In case of completely correct repetition of each NW, a score of 1 and otherwise a score of zero was given to the participant. The maximum test score was 40 at this test. The content validity of the test was 95.5. Correlation coefficient between results of the NWRT, the FDS and BDS were 0.76 and 0.75, respectively (concurrent validity).

Outcome measures were evaluated at all five time points: T0, T1, T2, T3, and T4.

Randomization

To prevent collection bias and imbalanced confounding between the project groups, a computer-based randomization approach was used (www.sealedenvelope.com). To create a random archive, we included 28 participants and 4 blocks of the same size. To conceal the randomization process, a unique code, generated by the software, was given to participants. These unique codes were used on the cubes that represented the type of empirical groups and thus participants were randomly assigned into one of these groups.

Blinding

None of the participants, main therapist and evaluators were informed of group allocations. A sealed opaque envelope approach was used to conceal groupings. Assistant therapist received randomly created intervention assignments within sealed opaque envelopes. After a participant entered the study, the envelope was unsealed. Both the subjects and the main therapist who performed the intervention in both groups were blinded to the stimulation situation. Only the assistant therapist who set up the tDCS device was informed of the intervention allocation (active or sham). Additionally, the investigator involved in measuring outcomes and analysis was also blinded to group allocation.

Sample Size and Statistical Analysis

Sample size was calculated based on Cohen's scale (75) and using the G*Power software to compare the means for 5 measurements (76). Effect size was determined as $f = 0.45$, and the α and β errors were considered to be 0.05 and 0.20, respectively. A sample size of 14 participants in each group (28 participants in total) was determined.

Characteristics of the study population were presented as mean (SD, range) for continuous variables and frequency (%) for categorized variables (Table 1). Kolmogorov–Smirnov test was used to investigate the

distribution of the data. Comparison of the two groups was performed using Student t-test or Mann Whitney U test for continuous variables and Chi square test or Fisher's exact test for categorized variables. Data of the two groups over time was analyzed using the repeated-measures analysis of variance (ANOVA) with the between-subjects factor group and within-subjects factor time. In all analyses, $p < 0.05$ was considered statistically significant. If the results of the ANOVA test showed significant time $\times$ group interactions, exploratory post-hoc Student's t -tests were used to examine significant differences at each time point between the two groups. To calculate the effect size, partial eta squared (η_p^2) was determined. A Bonferroni correction was considered for all the performed tests. All statistical analyses were performed using the SPSS software version 23.

Declarations

Ethics approval and consent to participate

The present study was performed according to the ethics principles and the standards for performing medical research in Iran. The approval ID of IR.IUMS.REC.1399.1377 of the Iran National Committee for Ethics in Biomedical Research was obtained.

Consent for publication

Although the researchers are able to use the trial data for academic and scientific aims, prior to manuscript submission, written consent was attained from the trial funder. All information of the participants is kept confidential and not accessible for public access. Additionally, any document and data, are coded by a subject identification digit, and the participants names are kept confidential.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author contributions

RM and SSM: conception and study design

SSM and BA: studying the literature.

JA and SSM: analysis and interpretation

SSM: cardinal operator in designing the trial, manuscript writing, providing treatment and data collection.

BA: native text editing.

SSM, RM and BA: review and approval of the final manuscript

Competing Interest

The authors declare that they have no competing interests.

Additional information: Supplementary information is available in Supplementary information file.

Trial registration

This trial was registered in <https://en.irct.ir/>. The registration reference is IRCT20201211049676N1 (<https://en.irct.ir/trial/52926>). Data of registration: 20.4.2021.

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Figures

Figure 1

Electrodes Location

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