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Effects of Transcranial Direct Current Stimulation on Working Memory in Patients with non Fluent Aphasia Disorder

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Abstract: Researchers aimed to investigate the effect of high intensity transdirect stimulation in (2 mA-20 min) as a helper technique in improvement of working memory and aphasia quotient in patients with non-fluent aphasia disorder. To achieve this goal, researchers evaluate the efficacy of transcranial direct current stimulation over dorsolateral prefrontal cortex of the brain upon non-fluent aphasia recovery, included 20 chronic and stroke-induced aphasia patients who each underwent 10 sessions of anodal transcranial direct current stimulation (2 mA-20 min) and 10 sessions of sham transcranial direct current stimulation (20 min) treatment. It was revealed that after transcranial direct current stimulation with 2 mA intensity and 10 sessions working memory and aphasia quotient (according to lesion location but not genders) improves significantly in non-fluent aphasia patients as compared to sham transcranial direct current stimulation. So, treatment with more sessions of anodal transcranial direct current stimulation with high intensity (2 mA-20 min) enhance working memory and functional recovery in non-fluent aphasia patients after stroke. Here, the lesion location but not gender factor plays a main role in its outcomes.

Key words: Anodal, transcranial direct current stimulation, non-fluent aphasia, Left Dorsolateral Prefrontal Cortex (LDPC), enhance working memory, Iran

INRODUCTION

One of the main language disabilities is aphasia or speechlessness disorders. It usually caused by head injury (left hemisphere or stroke) but it can develop slowly from a brain tumor, dementia, infection and dysnomia (learning disability) (Baker *et al*., 2010; Postman-Caucheteux *et al*., 2009; Crosson *et al*., 2007; Crinion and Leff, 2007). According to Naeser *et al*. (2010) and Pedersen *et al*. (2010) literatures, the main reason of the aphasia is stroke, approximately 80,000 cases of adult aphasia is due to stroke and >50-60% of them have chronic communicative impairment.

The aphasia disorders can be divided into global, Broca's, trans-cortical motor, mixed trans-cortical, Wernicke's, trans-cortical sensory, conduction and anomic types. This kind of classification is according to the assessing profiles of language for repetition, fluency, comprehension and naming (Baker *et al*., 2010). The ranges of language disorder in regard to lesion location and intensity of it is different and vary from unable in naming pictures, speaking, writing and reading to deficits in Working Memory (WM).

Here, the global type of aphasia are more prevalence form and consist approximately 20-40% of aphasias whereas the classic aphasia are found only in a 25% of patients and 10-15% of patients are unclassifiable (Kang *et al*., 2010).

The main reason of those kind disorders is due to impairment in Left Hemisphere (LH) or in Left Dorsolateral Part of Prefrontal Cortex (DLPFC) (Baker *et al*., 2010; Kang *et al*., 2010).

The critical function of left Dorsolateral part of Prefrontal Cortex (DLPFC) in verbal working memory has been approved by Didit-Span test in pathological studies by Baker *et al*. (2010) and the study including effects of Trans Magnetic Stimulation (TMS) on left dorsolateral prefrontal cortex (Beauchamp *et al*., 2003; Dockery *et al*., 2009). Those studies showed that local damage and destruction of left dorsolateral part of prefrontal cortex

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region not right dorsolateral part of prefrontal cortex region cause degradation in verbal Working Memory (WM).

Understanding of theoretical basis of working memory for the assessment and treatment of their disorders is important. It was reported that working memory has a main role in linguistic processing (comprehension and production of language), attention and executive function. It as a system holds actively multiple pieces of transitory information in the mind when needed for verbal and non-verbal tasks such as reasoning and comprehension and to make them available for further information processing. Working memory tasks are tasks which require monitoring or manipulation of information or behaviors as part of directed action to a goal in the face of interfering processes and distractions.

Rehabilitation therapies such as speech therapy have been somewhat able to remedy this kind of stroke disorders but it does not seem enough. Today's, stimulation by transcranial Direct Current (tDCS) as a safe and non-invasive brain stimulation techniques and painless form of neuron stimulation methods have become increasingly important for the diagnosis and treatment of neuropsychiatric diseases (Baker *et al.*, 2010). These techniques are used to stimulate cortical neuronal assemblies and thereby it leading to increase or decrease of cortical excitability (Arul-Anandam *et al.*, 2009).

The stimulating effects and the continuity of this kind of changes depend on several factors such as:

- Types of stimulation (anodal, cathodal and sham stimulation). The anodal stimulation is positive (V+) stimulation that increases the neuronal excitability of the area being stimulated. Cathodal (V-) stimulation decreases the neuronal excitability of the area being stimulated
- The length and intensity of stimulation (The effects of stimulation increase as the duration of stimulation increases or the strength of the current increases)
- The session durations and location of the brain lesion (Fregni *et al.*, 2005, 2006; Boggio *et al.*, 2006, 2008)

As noted, the intensity of stimulation, the session durations and lesion location have main factors that effects on cortical excitability and recovery of working memory. Along, to those many treatments were designed to reveal the role of stimulation intensity of tDCS and number of sessions in aphasia recovery. Therefore, researchers decided to investigate the effect of ten 20-min anodal tDCS (2 mA) sessions on working memory according to the role of lesion location in the aphasia recovery in the patient with non-fluent aphasia disorder.

MATERIALS AND METHODS

Subjects: About 20 right hand Persian patients with chronic-non-fluent aphasia disorders (range 47-61 years mean age, 55.937±2.4 years at ≈60 month post-stroke) participated in the present study. All of the subjects gave their written informed consent before participation. In this study, the patients were excluded if had been any speech therapy or had been used medication or psychotropic drugs during the 4 weeks prior to the study. And also, they were informed to avoid alcohol, cigarettes and drink of caffeinated things on the day of the test and none reported fatigue due to inadequate sleep.

The Persian Aphasia test: This test includes the tests of continuous speech (content and fluency of speech), auditory perception and continuous orders, naming and repeating. Each test had 10 scores that were in totally 60 scores. At the end of the test, the obtained number multiplied by 10 and then divided by 6. The obtained number is aphasia quotient (Nilipour, 2011, 2012) (Table 1).

The 2-Back test: The 2-Back task has been used to evaluate the working memory ability in neurologically intact individuals as well as multiple clinical populations. It includes 100 number (1-9) that are randomly repeated. The 2-Back needs contributors to process a stream of incoming data and respond when the current stimulus is the same as the stimulus 2 items ago. In this study, the number of correct answers has been considered as a test score (Owen *et al.*, 2005).

Electrodes and stimulation of the brain: In this study, direct current was induced by a pair of electrodes in a 5×5 cm saline-soaked synthetic sponge and delivered by a battery steered constant current stimulator using (included of 20 min of 2 mA). According to Nitsche *et al.* (2003), the device used is particularly trustful for double-blind studies, a switch can be enabled to interrupt the electrical current while retaining the (ON) display and showing the stimulation parameters throughout the procedure to the participant. In these conditions, the interaction between the two hemispheres during task execution is also under control. So, in present study, for left dorsolateral part of prefrontal cortex stimulation, the anodal electrode was located over the left dorsolateral part of prefrontal cortex and the cathodal

Table 1: Base line patient characteristics

			Local lesion	
Sex	Mean age	N	Anteroposterior	Anterior
Male	55.500	12	5	7
Female	56.375	8	4	4
Total	55.937	20	9	11

electrode over the right dorsolateral part of prefrontal cortex. For the stimulation of sham group, the electrodes were located at the same positions as for stimulation in active manner but the stimulator was turned on only for 30 sec. Thus, these participants felt the primary itching sensation associated with transcranial Direct Current Stimulating (tDCS) but received no active current for the remainder of the stimulation period (Knoch *et al*., 2008).

Experimental design: About 20 participants (8 women and 12 man) were randomly assigned to receive cathodal electrode over the right predestinated dorsolateral part of prefrontal cortex area (by using of the 10/20 EEG system) and anodal electrode as an active stimulation over the left predestinated dorsolateral part of prefrontal cortex area (n = 20) and sham stimulation or no stimulation group (n = 20). After selecting the participants, reasearchers consisted three ordered phases separated by at least 3 days interval. In the first phase, the written informed consent was given to the participants prior to their inclusion in the study. Then, the technique of MMSE test for Dementia and test for identify the type of aphasia was done in the same session. In the second phase (3 days after the first session), working memory and aphasia quotient were evaluated by 2-Back and Persian Aphasia test, respectively and results were recorded in the patient questionnaire as a before tDCS treatment results.

In the last phase (including treatment session) for stimulation of the left dorsolateral prefrontal cortex and right dorsolateral prefrontal cortex the anodal electrode and cathodal electrode were located over the left and right chosen sites, respectively for 10 days.

In this study for active stimulation, the subjects received a safe and steady current of 2 mA intensity for 20 min. At the end of treatment, working memory and aphasia quotient were evaluated by the 2-Back and Persian Aphasia test, respectively and results were recorded in the patient questionnaire. For statistical analysis, data was analyzed by SPSS 19 and Manova test and used Pearson correlation coefficient. It also describes the test score (before and after treatment) (DaSilva *et al*., 2011; Fregni *et al*., 2005, 2006, 2008).

RESULTS AND DISCUSSION

All subjects without any complications ended the tree treatment phases. The ratings of subject's self-reported of attention perceived pain and fatigue were not statically significant during the treatment sessions, ($F(2, 13) < 1$, $p > 0.26$). All of the measures completed within 20 min of the tDCS cessation.

The 2-Back test: The results of statistical analysis of the 2-Back test are shown in Table 2-5 and Fig. 1. In Table 2 and Fig. 1a, it was shown that the results of statistical analysis the 2-Back test before and following A-tDCS treatment was significant ($p = 0.000$; $F = 164.395$). And also, the result of the 2-Back test was significant among patients with different lesion location (anterior and posterior-anterior) (Table 3, Fig. 1b) ($p = 0.010$; $F = 5.539$) but not sex (Table 4 and Fig. 1c) ($p = 0.982$; $F = 0.056$).

Table 2: The results of the 2-Back and Aphasia Quotient test according to treatment time

Fact 2	2-Back test	Aphasia quotient
Before		
Mean	7.45000	28.00000
Variance	3.62900	7.68400
SD	1.90498	2.77204
SE of kurtosis	0.99200	0.99200
Sham		
Mean	7.40000	27.90000
Variance	2.88400	6.93700
SD	1.69830	2.63379
SE of kurtosis	0.99200	0.99200
Treatment		
Mean	9.05000	30.25000
Variance	3.20800	9.14500
SD	1.79106	3.02403
SE of kurtosis	0.99200	0.99200
Total		
Mean	7.96670	28.71670
Variance	3.72800	8.85100
SD	1.93072	2.97499
SE of kurtosis	0.60800	0.60800

Table 3: The results of the 2-Back and Aphasia Quotient test according to lesion location

Lesion location	2-Back test	Aphasia quotient
Anterior		
Mean	8.96970	30.72730
Variance	3.28000	4.76700
SD	1.81116	2.18336
SE of kurtosis	0.79800	0.79800
Posterior-anterior		
Mean	6.74070	26.25930
Variance	1.58400	2.81500
SD	1.25859	1.67774
SE of kurtosis	0.87200	0.87200
Total		
Mean	7.96670	28.71670
Variance	3.72800	8.85100
SD	1.93072	2.97499
SE of kurtosis	0.60800	0.60800

Table 4: The results of the 2-Back and Aphasia Quotient test according to sex

Sex	2-Back test	Aphasia quotient
Male		
Mean	8.02780	28.58330
Variance	4.88500	8.87900
SD	2.21019	2.97969
SE of kurtosis	0.76800	0.76800
Female		
Mean	7.87500	28.91670
Variance	2.11400	9.12300
SD	1.45400	3.02046
SE of kurtosis	0.91800	0.91800
Total		
Mean	7.96670	28.71670
Variance	3.72800	8.85100
SD	1.93072	2.97499
SE of kurtosis	0.60800	0.60800

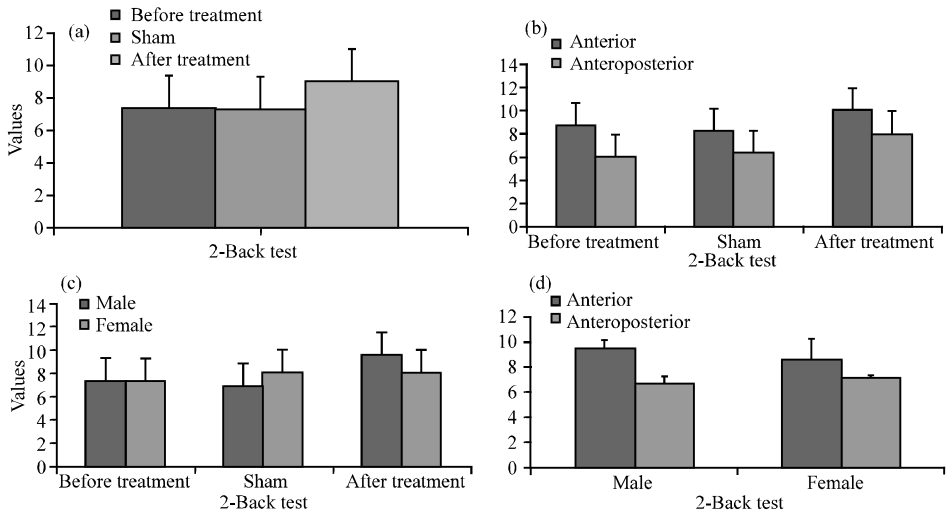

Fig. 1: The results of 2-Back test: a) Before and after stimulation; b) Lesion location; c) Sex; d) Lesion location and sex; Error bar indicate fixed value

Table 5: Descriptive statistics of the 2-Back test before and after treatment according to lesion location and sex

Tests	Lesion location	Mean±SD	N
2-Back test-before			
Male	Anterior	8.5714±1.98806	7
	Posterior-anterior	6.0000±1.00000	5
	Total	7.5000±2.06706	12
Female	Anterior	8.7500±1.25831	4
	Posterior-anterior	6.0000±0.81650	4
	Total	7.3750±1.76777	8
Total	Anterior	8.6364±1.68954	11
	Posterior-anterior	6.0000±0.86603	9
	Total	7.4500±1.90498	20
2-Back test-treatment			
Male	Anterior	9.5714±2.29907	7
	posterior-anterior	7.2000±1.78885	5
	Total	8.5833±2.35327	12
Female	Anterior	8.7500±1.70783	4
	Posterior-anterior	7.7500±0.50000	4
	Total	8.2500±1.28174	8
Total	Anterior	9.2727±2.05382	11
	Posterior-anterior	7.4444±1.33333	9
	Total	8.4500±1.95946	20
2-Back test-sham			
Male	Anterior	8.8571±1.95180	7
	Posterior-anterior	6.8000±0.83666	5
	Total	8.0000±1.85864	12
Female	Anterior	9.2500±1.70783	4
	Posterior-anterior	6.7500±1.70783	4
	Total	8.0000±2.07020	8
Total	Anterior	9.0000±1.78885	11
	Posterior-anterior	6.7778±1.20185	9
	Total	8.0000±1.89181	20

Here, when the variables, gender and location of the lesion, considered together, no significant ($p = 0.585$; $F = 0.669$) relationships were revealed between the results of the 2-Back test among patients before and following A-tDCS treatment (Table 5 and Fig. 1d).

Aphasia Quotient test: The results of statistical analysis of the aphasia quotient test are shown in (Table 2, 3, 4, 6, 7 and Fig. 2). From Table 2 and Fig. 2a, it was concluded

Table 6: Descriptive statistics of the Aphasia Quotient test, before and after treatment, according to lesion location and sex

Tests	Lesion location	Mean±SD	N
Aphasia quotient-before			
Male	Anterior	29.4286±1.71825	7
	Posterior-anterior	25.8000±1.30384	5
	Total	27.9167±2.39159	12
Female	Anterior	31.0000±2.16025	4
	Posterior-anterior	25.2500±0.95743	4
	Total	28.1250±3.44083	8
Total	Anterior	30.0000±1.94936	11
	Posterior-anterior	25.5556±1.13039	9
	Total	28.0000±2.77204	20
Aphasia quotient-treatment			
Male	Anterior	30.7143±2.81154	7
	Posterior-anterior	27.0000±2.34521	5
	Total	29.1667±3.15748	12
Female	Anterior	31.0000±2.58199	4
	Posterior-anterior	27.0000±0.00000	4
	Total	29.0000±2.72554	8
Total	Anterior	30.8182±2.60070	11
	Posterior-anterior	27.0000±1.65831	9
	Total	29.1000±2.91818	20
Aphasia quotient-sham			
Male	Anterior	30.5714±1.71825	7
	Posterior-anterior	26.8000±2.16795	5
	Total	29.0000±2.66288	12
Female	Anterior	32.7500±1.50000	4
	Posterior-anterior	25.5000±1.73205	4
	Total	29.1250±4.15546	8
Total	Anterior	31.3636±1.91169	11
	Posterior-anterior	26.2222±1.98606	9
	Total	29.0500±3.23590	20

Table 7: The results of the correlation rate of 2-Back and Aphasia Quotient test

Tests	2-Back test	Aphasia quotient
2-Back test		
Pearson correlation	1.000	0.801**
Sig. (2-tailed)	-	0.000
N	60.000	60.000
Aphasia quotient		
Pearson correlation	0.801**	1.000
Sig. (2-tailed)	0.000	
N	60.000	60.000

**Correlation is significant at the 0.01 level (2-tailed)

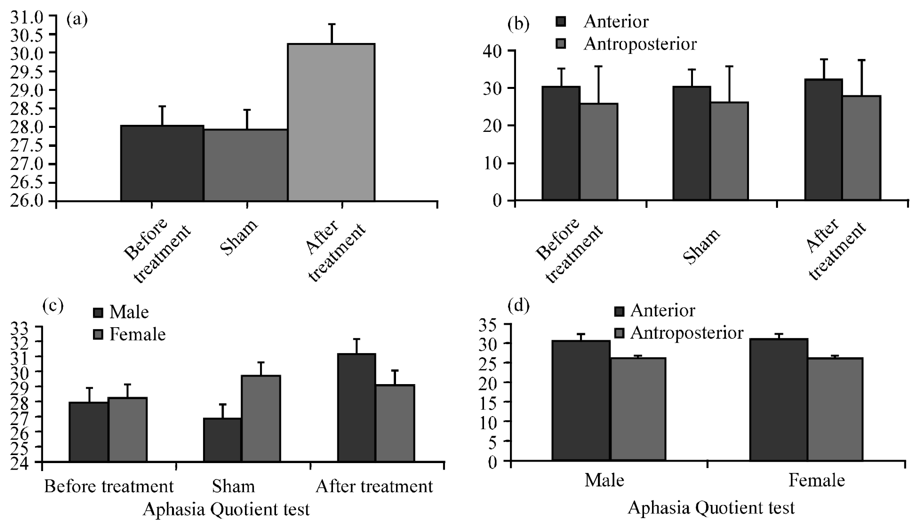

Fig. 2: The results of Aphasia Quotient test: a) Before and after stimulation; b) Lesion location; c) Sex; d) Lesion location and sex; Error bar indicate fixed value

that there are a significant difference between the results of the Aphasia Quotient test among the patients before and following A-tDCS treatment ($p = 0.000$; $F = 659.266$).

And also, the result of Aphasia Quotient test was significant difference among patients with different lesion locations (anterior and posterior-anterior) (Table 3, Fig. 2b) ($p = 0.000$; $F = 15.312$). But there are no significant relationships between patients with different sex (Table 4, Fig. 2c) ($p = 0.806$; $F = 0.327$).

Like other tests, the variables such as gender and location of the lesion when considered together, there no significant ($p = 0.234$; $F = 1.601$) relationships were revealed between the results of Aphasia Quotient test among patients before and following A-tDCS treatment (Table 6 and Fig. 2d). The correlation rate of 2-Back test and Aphasia Quotient: As shown in Table 8, the correlation between 2-Back test and Aphasia Quotient is significant ($p = 0.000$; $r = 0.801$) (Table 7).

Deficits in working memory, speaking writing and reading are the main symptom of the aphasia disorders. Today, there have been proposed various methods for the treatment of aphasia disorders however, it seems insufficient. One of the main and effective treatments is treatment by a safe, painless and relatively noninvasive technique, tanscranial Direct Current Stimulation (tDCS). The factors such as stimulation types intensity, session and lesion location have main role in treatment outcomes. In the present study, researchers evaluated the effectiveness of transcranial direct current stimulation on dorsolateral prefrontal cortex in aphasia disorders patients, it was shown that this part of brain specially the left dorsolateral prefrontal cortex has a main role in working memory (Zaehle *et al*., 2011).

The brain has two hemispheres, right and left hemispheres. Every part of the hemispheres has different functions and damage to them can lead to diseases. Working memory disorders related to aphasia (non-fluent aphasia) is a disease that occurs by lesion to the left hemisphere (left dorsolateral prefrontal cortex). The study by Baker *et al*. (2010) revealed a positive and linear relationship between severity of activation of the left hemisphere, especially the left frontal cortex and non-fluent aphasia recovery. They concluded that this region (left dorsolateral prefrontal cortex) is exceedingly important for working memory related to aphasia recovery. Other studies showed that transcranial direct current stimulation over a region of the left cortex of frontal lob implicated in aphasia recovery and improved aphasia related disorders (non-fluent aphasia) (Fridriksson, 2010; Sarno and Levita, 1979).

The study by Zaehlel *et al*. (2011) and Beeli *et al*. (2008) revealed that stimulation of the DLPFC by trans Direct Current (tDCS) can affect in the working memory, risk-taking behavior, making of a decision and in response to visual material emotions in healthy people. In addition, the study by Valle *et al*. (2009) and Zaehle *et al*. (2011) was revealed that the stimulation of the frontopolar cortex by tDCS affect in performance of a probabilistic classification learning task. Here, the results revealed that ten 20 min anodal tDCS (2 mA) sessions, significantly improves working memory, aphasia quotient or severity and the correlation rate in non-fluent aphasia patients as compared to sham-tDCS. Additionally, the study demonstrated there was a significant difference in the results of our test before and following A-tDCS treatment between patients with different lesion locations (anterior and posterior-anterior) but not different genders.

In the present study, the difference in treatment outcome between A-tDCS and S-tDCS was not related to the patients blood pressure and heart rate because they recorded from pre to post-tDCS administrations were found to be comparable across both tDCS conditions. In the studies by Fregni *et al*. (2006) and Boggio *et al.* (2008, 2006), it was revealed that after five 20 min anodal tDCS (1 mA) sessions it has beneficial effect on aphasia recovery and enhanced Working Memory (WM) in healthy persons as measured by 3-back working memory method and in patients with Parkinson's disease. Therefore, it has been convincingly shown that tDCS can affect in functions of prefrontal cortex (working memory). In the similar study by others it was revealed that tDCS modulated efficiency of working memory by hanging the brain activity in a polarity-specific way. They observed a growth in working memory performance and amplified oscillatory power in the anodal tDCS treatment not sham tDCS treatment as shown in current study.

Sandrini *et al*. (2012) investigated the effects of transcranial Direct Current Stimulation (tDCS) on working memory load performance and they concluded that, verbal working memory (tested by n-back task (2-back) and ANOVA before and after the application of bilateral tDCS over posterior parietal cortex (left anodal-right cathodal, left cathodal-right anodal or sham) was a significant interaction between tDCS and task. These findings are in agreement with the results demonstrating that Anodal-tDCS over the left cortex improves language processing and working memory.

It seems that A-tDCS increases cortical excitability, it presumably improved the patients' working memory by focally stimulating function of the left frontal cortex similar to the present research. Other studies have implicated the specific cortical location of left hemisphere in aphasia recovery it is probable that improved speech and language functioning following aphasia treatment relies at least partly on spared left hemisphere regions (Sarno and Levita, 1979; Arul-Anandam *et al*., 2009; Nilipour, 2011).

CONCLUSION

Researchers concluded that the high intensity and more sessions (Ten 20 min anodal tDCS (2 mA) sessions) has a positive effects on the working memory deficiency in the patient with non-fluent aphasia disorders and also the lesion location has a main role in working memory deficiency related aphasia recovery.

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