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Influence of Immediate and Long Term Effects of Repetitive Transcranial Magnetic Stimulation Combined with Speech Therapy on Post Stroke Non-fluent

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ABSTRACT

Background: *A high proportion of patients who have suffered a stroke also suffer from aphasia.*

The aim *of this work was to determine and investigate immediate and long term effects of repetitive transcranial magnetic stimulation combined with speech and language exercise therapy on non fluent motor aphasia (Broca's aphasia) in chronic cerebrovascular stroke.*

Methods*: Forty chronic cerebrovascular stroke patients represented the sample of the study. Their age ranged from 45 to 60 years. The patients were assigned randomly into two equal groups; study group (G1) and control group (G2). The patients in both groups received the same medical and physical care during treatment period to avoid any complications. The study group treated by selected speech exercises combined with rTMS. Different domains of speech function (repetition, reading, naming, writing, comprehension and spontaneous speech) were assessed by the Arabic translated form of the modified Chesher test and Token test of Aachen aphasia test (AAT). Power of stimulation intensity of rTMS (represents 90% of the resting motor threshold that recorded from contraction of the first dorsal interosseus of the unaffected hand) were measured pre, post and after three months of the end of the treatment to determine level of brain excitability.*

The results: *At the end of the treatment there was a significant improvement in all domains in (G1) of the Arabic translated form of the modified Chesher test. In the control group (G2) there was a change in total score of the Arabic translated form of the modified Chesher test in approximately all domains but not reach* *to significance level (P>0.05) except auditory comprehension and pantomime there was a significant increase (P<5). Comparison of mean values of all domains of (G1) and (G2) post treatment indicate significance improvement of all different domains measured by clinical tests or rTMS in (G1). A significant decrease in the mean value of power intensity of rTMS post treatment in (G1) was observed (P<0.05). There was a Strong negative correlation between improvements in total score of the Arabic translated form of the modified Chesher test and the decrease of the mean values of power intensity of rTMS in (G1).*

Conclusion: *Speech exercises combined with rTMS permit the mechanisms of transcortical disinhibition to enhance language function in chronic non- fluent aphasia post stroke patients. Low frequency rTMS delivered over Broca's area could improve language by enhancing long-term potentiation and synaptic plasticity within the stimulated areas involved in language network.*

Keywords: *Non-fluent motor aphasia modified Chesher test, rTMS, rehabilitation, stroke, language.*

INTRODUCTION

Speech is the neuromuscular process of articulation. It can be abnormal without any disturbance of Language. Language refers to the use of both perception (decoding), and production (encoding) of a special type of communication system (**Lewis** et al, 2009). The number of languages in the world varies between 6,000 and 7,000 (Bakas et al, 2006).

Aphasia was first described by Imhotep around 3.000 B.C. in what has come to be known as the Edwin Smith surgical papyrus. The early history of the study of aphasia inevitably focused upon the question of the localization of cortical function (EL Tamawy, 1980). Aphasia is an acquired disorder of previously intact language ability secondary to brain damage. This definition emphasizes two important aspects. First, it stresses the loss of previously acquired language. The second feature of the definition concerns the word Language which should be separated from both speech and thoughts (Barwood et al., 2011).

The most common cause of aphasia is cerebrovascular disease, particularly cerebral infarction. Aphasia complicates 15 to 38 percent of ischemic strokes. Infection, trauma, neoplasm and certain neurodegenerative diseases (primary progressive aphasia) can also cause aphasia (Grossman, 2010).

Broca area is often defined as Brodmann areas 44 and 45 areas of cytoarchitecture. It is commonly found in the left posterior inferior frontal cortex. Broca area implicated in a variety of language functions, including grammatical speech production, verb naming, comprehending syntactically complex sentences (e.g., passive voice), phonological working memory, and orchestrating speech articulation (Dronkers et al., 2007).

Evaluation of aphasic patients by clinical tests of aphasia and morphological imaging had value for accurately determining the extent and location of functional deficits. Investigators attempted to quantities the relationship of clinical manifestation of different types of aphasia of varying severity to regional cerebral blood flow and cerebral metabolism (Stowe et al., 2000).

No pharmacological treatments for aphasia have proven effective, although a number of drugs (dopaminergic, cholinergic, and neurotrophic) continue to be investigated. Various behavioral treatment approaches for aphasia exist. They are usually considered as restorative or compensatory recovery. Restorative approaches include practice of carefully selected syntactic structures, naming drills, or practice using self-selected communication needs such as using the telephone (Hamilton et al., 2010).

Compensatory approaches include training conversational partners to modify their own language and communication skills in ways that make it easier for the aphasic individual to communicate as writing or drawing to substitute for talking. Computerized approaches to both restorative and compensatory aphasia treatment are increasing. Many clinics offer both individual treatment and group treatment offering increased psychosocial support (Berthier et al., 2009).

Applications of repetitive transcranial magnetic stimulation (rTMS) to the motor cortex and measurement of the responses from contralateral muscles permits the evaluation of changes in motor cortex excitability and mapping of body part representations in the motor cortex. Repetitive transcranial magnetic stimulation is one of several techniques that have contributed to the study of plasticity in cortical circuits in health and disease. It can also be used to modulate plastic processes of possible relevance for neurorehabilitation. Integration of rTMS with other neurophysiological and neuroimaging techniques shed light on the mechanisms underlying cortical plasticity (Sanes and Donoghue, 2000).

MATERIALS AND METHODS

Forty stroke chronic ischemic cerebrovascular stroke patients with non fluent motor aphasia represented the sample of the study. Their age ranged from 45 to 60 years. All the patients suffered from non fluent motor aphasia (Broca aphasia). The clinical diagnosis was confirmed by CT and/ or MRI. It was applied in the Neurophysiological Department, and the Inpatient Neurological Department of Kasr Al Aini Hospital, Cairo University. All the patients signed an informed consent before starting treatment. The protocol of this study was approved by the ethical committee of faculty of physical therapy.

Exclusion Criteria:

Patients with disturbed conscious level, uncooperative patient, presence of dementia, psychiatric disorders, patient with apraxia, patient with Implanted metallic devices: pacemaker, medication pump, vagal stimulator, deep brain stimulator, TENS unit or ventriculoperitoneal shunt, past history of seizure within one year, history of substance abuse within last six months were excluded from the study.

Instrumentations:

(a)For Assessment:

- Token test of Aachen aphasia test (AAT).

- The Arabic translated form of the modified Chesher test.
- Repetitive transcranial magnetic stimulation (rTMS).

- **Token test of Aachen aphasia test (AAT).**

This test was used to determine severity of aphasia. The test is originally German and has been translated into English, Dutch and Italian. It is valid and standardized according to well defined linguistic criteria. It consists of five parts (Nora et al, 2001).

- **The Arabic translated form of the modified Chesher test.**

It includes evaluations of communication means (e.g. repetition. Writing, reading, naming, comprehension, and spontaneous speech) (El- Tamawy, 1980; and Moustafa et al, 2004).

Each separate item of the modified Chesher test for aphasia has its specific graduation. The grading of repetition, naming, reading, comprehension, writing, and spontaneous speech were (0-12), (0-3), (0-5), (0-18), (0-12), and (0-40) respectively. The total score of the scale was 90 (El- Tamawy, 1980).

- **Repetitive Transcranial Magnetic Stimulation (rTMS):**

It applied to measure power intensity (represents 90% of the resting motor threshold that recorded from contraction of the first dorsal interosseus of the unaffected hand) pre , post and after three months of the end of the treatment. Magstim Rapid Magnetic Stimulator is used in conjunction with the System (1600-00), for the magnetic stimulation of neuromuscular tissue and the motor cortex. The system comprises: - Magstim Air-CooledDouble 70mm Stimulating Coil (1640-00), Coil Stand (1261-00), Vacuum Unit (1618-00).

(b) For treatment.

-The Magstim Rapid Magnetic nerve stimulator systems:

The Magstim Rapid magnetic nerve stimulator systems applied to stimulate human cortex. The device induce electrical currents in tissue using a non-invasive stimulating coil at frequencies of up to 100HZ

3-Procedures:

The patients were assigned randomly into two equal groups: study group (G1) and control group (G2).

G1: The study group received medical treatment, exercise therapy and repetitive transcranial magnetic stimulation.

G2: The control group received medical treatment only.

❖ **Assessment:**

1. Assessment of aphasia severity using token test of Aachen aphasia test (AAT).

It is used to determine severity of non fluent motor aphasia. The test includes five parts with 50 items. In each part patient is asked to follow the therapist order. For example each patient was asked to:

- Touch a circle.
- Touch a square.
- Touch a flower.
- Touch a house.
- Touch the yellow square.
- Touch the black circle.
- Tough the green circle.
- Touch the white square.
- Touch the red circle and green Square.
- Touch the yellow Square and black square.
- Put the red circle or green square.
- In addition to touching the yellow square touch the white circle square.
- Instead of the green flowers touch white house.

At the end of the test scores were recorded for all items and then the total score was calculated. Aphasia severity was graded as

(0-3)-----Very severe.

(3-6)-----Severe.

(6-9)-----Moderate.

(9-12)----Mild

2. Assessment of speech function using the Arabic translated form of the modified Chesher test.

- The Arabic translated form of the modified Chesher test was conducted for each patient from a comfortable sitting position on a chair.
- Reading items were written in clear and suitable font.
- Items of copying were drawn with clear size.
- The following aspects were assessed:
- Repetition (12 points): this domain contained repetition of single words and phrases. The patient was asked to repeat different words and sentences.
- Comprehension (18 points): consisted of auditory comprehension, written words, token test and pantomime. In this domain the patient was asked to point to a certain picture and written words.

- Spontaneous speech (40 points): this domain consists of eight sub domains. Communicative speech, articulation and prosody, automated language, semantic structure, syntactic structure, verbal output, initiation and effort and phrase length. The patient was asked to discuss specific situation.
- Naming (0-3): in this domain the patient was asked to name different objects (for example pen, key, flowers).
- Writing (0-12): this domain consists of four sub domains composition, dictation, copying, and spelling. The patient was asked to write different words, to write the name of object drawn in card and to copy different words and sentences.
- Reading (0-5) : patient was asked to read different words and sentence
- The scores of each item were recorded and then the total score was calculated

❖ **Treatment:**

The designed program of physiotherapy consists of selected therapeutic exercises combined to repetitive transcranial magnetic stimulation adapted from Breier et al, 2009; Friedemann et al, 2001 and Taub et al, 1999 consist selected exercises will be applied for 12 weeks. The session started by applying rTMS followed by therapeutic exercises. Home routine program started from the beginning of treatment and continued for 24 weeks. Each patient was asked to repeat the selected exercises program five times per day under supervision of relative.

Repetitive TMS:

Repetitive TMS applied (inhibitory 1-Hz rTMS) over the right triangular part of the inferior frontal gyrus (IFG; TMS group) using a Magstim Rapid stimulator with a double 70-mm coil. The distance measurements to localize the IFG applied with a marker. The target structure was stimulated only in the intervention group (Naeser et al., 2011).

- Repetitive TMS was performed with a Magstim Rapid stimulator (Magstim Company, Whitland, UK) equipped with an air-cooled figure-of-eight coil (each loop 70 mm in diameter).
- The patients were seated in a reclining chair that allowed them to keep their arms and hands relaxed with the head leaning on the head-rest to be sure that it was immobile during rTMS procedure.
- The coil was placed tangentially to the scalp over the right IFG (RIFG).
- Resting motor threshold (RMT) was determined in each patient before starting treatment, post treatment and after three months of the end of the treatment. It was defined as the "minimum stimulus intensity able to elicit a motor evoked potential (MEP) of at least 50 mV in 5 or more of 10 consecutive stimulations" (Barwood et al., 2011).

- The resting motor threshold that recorded from contraction of the first dorsal interosseus of the unaffected hand.
- Intensity of magnetic stimulation (power intensity) was applied at 90% of the resting motor threshold (RMT) at 1Hz frequency.
- In order to maximize the inhibitory rTMS after-effect over the whole RIFG area, we stimulated two parts of Broca's area homologues: the anterior part (pars triangularis—PTr) and posterior part (pars opercularis—POp) (fig.1)
- To target the regions of interest precisely, the coil was placed on the scalp according to the coordinates.
- The anterior stimulation site was 2.5cm posterior to the canthus along the canther-tragus line and 3cm superior to this line; the posterior stimulation site was 4.5cm posterior and 6cm superior to the canther-tragus line.
- On each day of treatment, rTMS was applied for 20min. (10 minutes over the PTr and 10 minutes over the Pop respectively.).
- The stimulation parameters were chosen according to current safety guidelines for rTMS (Caroline et al., 2011).

According to Naeser et al, 2002 treatment stimulation sessions were conducted five days per week for a two week period, yielding eight to ten sessions for each patient. During every session, the patients were stimulated for 20 minutes with a frequency of 1Hz and a stimulation intensity of 90% of the defined individual motor threshold.

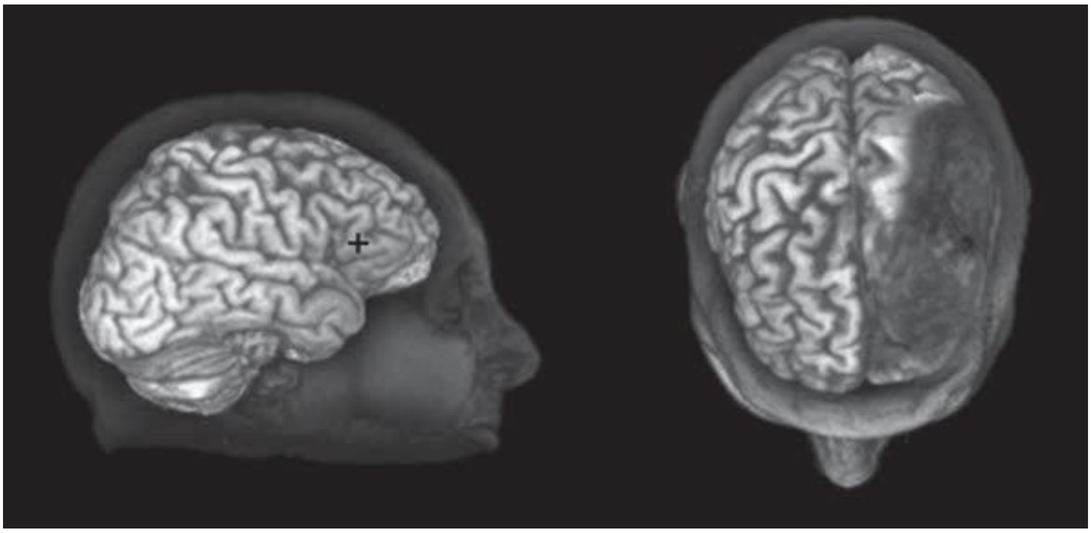

Fig.(1): The stimulation target, homologue to Broca's area 44 &45marked on a 3D reconstruction of a patient's brain. (Naeser et al., 2011)

DATA ANALYSIS AND STATISTICAL DESIGN

- The arithmetic mean as an average (Sum divided on 20) description of central tendency of the results.

- The standard deviation as a mean of dispersion of the results.
- Paired t-test for comparison of means pre and post treatment within each group (study and control group).
- Un-Paired t-test for comparison of means between pre and post treatment of two independent groups.
- Analysis of variance (ANOVA) to compare power intensity of rTMS among pre, post and after three months of treatments in both groups.
- Pearson rank correlation test to correlate between variables post treatment in study group. Values of (r) ranged from 0 (no correlation), 0-0.6 (very low and probably meaningless) and 0.6 -1.00 (very high correlation) (Betty and Jonathan, 2003).

RESULTS

1-The repetitive transcranial magnetic stimulation evaluation (rTMS) in (G1& G2):

a-The mean values of the power intensity of rTMS in both groups:

Comparison of the mean values of the power intensity that elicited pre treatment in both groups (G1& G2) revealed no significant difference in both groups (P=0.816).Comparison of the mean values of the same variable that elicited post treatment in both groups revealed significant improvement. There is significance decrease in the mean values of the power intensity post treatment in (G1) (P= 0.0001).

Comparison of the mean values of the power intensity that elicited pre and post treatment in (G1) revealed that there is significant improvement post treatment. There is significance decrease in the mean values of the power intensity (P=0.0001). Comparison of the mean values of the power intensity that elicited pre and post treatment in (G2) revealed that there is no significant difference post treatment (P=0.366) (table 1)

Table (1): The mean values of the power intensity of rTMS pre and post treatments in both groups (G1&G2):

Items	Power intensity (%)			
	G1	G2	t-value	P-value
	Mean ±SD	Mean ±SD		
Pre-treatment	77.05±5.38	76.60±6.71	0.234	0.816
Post-treatment	65.45±5.49 ↓	77.80±6.45 ↑	6.518	0.0001
t-value	13.84	0.927		
P-value	0.0001*	0.366		

P> 0.05= not significant; p< 0.05= significant.

b-The mean values of the power intensity of rTMS pre, post and after three months of the end of the treatment using ANOVA in both groups:

Multivariate analysis of variance was used to compare the mean values of the power intensity of rTMS *(represents 90% of the resting motor threshold that recorded from contraction of the first dorsal interosseus of the unaffected hand)* pre, post and after three months of the end of the treatment in both groups (G1) and (G2). This was used to reveal the association between the levels of brain excitability at different time of evaluation (table, 2).

Comparison of the mean values of the power intensity of rTMS using ANOVA revealed significant decrease in the mean values at different time of evaluation. Where the F-value was (56.18) and P- value was (0.0001).

Comparison of the mean values of the power intensity of rTMS using ANOVA revealed no significant difference in the mean value at different time of evaluation. Where the F-value was (0.260) and P- value was (0.774).

Table (2): The mean values of the power intensity pre, post and after three months of the end of the treatment using ANOVA in both groups (G1&G2).

Items	Power intensity					
	G1			G2		
	Pre	Post	After 3 months	Pre	Post	After 3 months
Mean ±SD	77.50±5.39	65.45±5.49	55.35±8.17	76.60±6.72	77.80±6.45	76.50±5.92
F-value	56.18			0.260		
P-value	0.0001*			0.774		

P> 0.05= not significant; p< 0.05= significant.

2-The Arabic translated form of the modified Chesher test examination:

a- The mean values of the Arabic translated form of the modified Chesher test pre-treatment in both groups:

Comparison of the mean value of each domain in (G1) with the corresponding mean value in (G2) revealed no significant difference of all domains (p>0.05).

b-The mean values of the Arabic translated form of the modified Chesher test post-treatment in both groups:

The mean values of total score of Arabic translated form of the modified Chesher test post treatment in (G1) was 55.35±2.12and in (G2) was 36.45±1.76. Comparision of the mean values of the total score of Arabic translated form of the modified Chesher test post treatment in (G1) and (G2) reveled significant increase in (G1) by percentage of improvement (52.35%) (p= 0.0001).

Comparison of the mean value of each domain in (G1) with the corresponding mean value in (G2) revealed significant increase of all domains ($p<0.05$). The percent of improvement of the sub test domains repetition, naming ,reading, comprehension, writing, spontaneous speech post treatment were 33.33%, 50.00%, 38.24%, 56.25%, 59.80%, and 55.46% respectively (table 3)

Table (3) : The mean values of total score of the Arabic translated form of the modified Chesher test and sub test domain post treatment in both groups (G1 & G2):

Variable	Post treatment				
	Mean±SD in (G1)	Mean±SD in (G2)	t-value	P-value	Improvement (%)
Repetition	7.40±1.45	5.55±1.74	3.71	0.039*	33.33%
Naming	2.70±0.47	1.80±0.33	8.46	0.033*	50.00%
Reading	2.35±0.67	1.70±0.49	10.72	0.031*	38.24%
Comprehension	16.25±2.45	10.40±2.32	14.31	0.0001*	56.25%
Writing	8.15±0.60	5.10±0.84	7.65	0.031*	59.80%
Spontaneous speech	18.5±1.03	11.90±0.74	8.47	0.021*	55.46%
Total score	55.35±2.12	36.45±1.76	20.13	0.0001*	52.35%

P> 0.05= not significant; p< 0.05= significant.

3-Correlation of mean value of changes in total score of the Arabic translated form of the modified Chesher test with mean power intensity in G1and G2:

Pearson rank correlations (r) between the post treatment changes in total score of the Arabic translated form of the modified Chesher test and mean power intensity in G1 and G2 was -0.82, -0.48 respectively. The results indicated that there was a strong significant negative correlation between improvement in total score of the Arabic translated form of the modified Chesher test and decrease in mean power intensity of rTMS in (G1) (P=0.0001). There was no significant correlation changes in total score of the Arabic translated form of the modified Chesher test and changes in mean power intensity of rTMS in G2 (p=0.086) (table 4)

Table (4): Correlation of mean value of changes in total score of the Arabic translated form of the modified Chesher test with mean power intensity of rTMS in G1:

Variables	Total score of Arabic translated form of the modified Chesher post treatment in G1	Mean power intensity
Mean±SD	55.35±2.12	65.45±5.49
R	-0.82	
P	0.0001*	

DISCUSSION

The present study was conducted to determine the immediate and long term effects of designed program of physical therapy exercises combined with repetitive transcranial magnetic stimulation (rTMS) on the management of moderate to severe motor aphasia in chronic cerebrovascular stroke patients. Token test of Achen aphasia test was used to determine the severity of motor aphasia. Forty chronic ischemic cerebrovascular stroke patients suffering from moderate to severe motor aphasia participated in this study. The patients were assigned into two equal groups. The control group was under medical treatment only. The study group treated by the same medical treatment in addition to the designed program of physical therapy combined with rTMS.

In the present study repetitive transcranial magnetic stimulation (rTMS) was used. It is objective assessment method and non-invasive brain stimulation techniques. It proved to be beneficial neuromodulatory techniques for the rehabilitation of communication disorders. Repetitive transcranial magnetic stimulation is regarded as a safe neural stimulation capable of directly manipulating cortical brain activity. These results are in agreement with Ridding et al., 2007, who found that rTMS has garnered momentum as a method of establishing causative links between specific brain regions and measurable behavioural responses, across a myriad of cognitive domains in neuroscience. The author added that the innovative neuromodulatory technique has therapeutic merit via the direct modulation of specific pathways in the brain, which may influence longer -term communication outcomes.

Barwood et al., 2011; also added that rTMS generates a rapidly fluctuating magnetic field that penetrates the scalp and skull unimpeded. It induces a changing electrical field in the cerebral cortex below the coil. The current flow causes physiologic response in the cortical tissue, which leads to neuronal depolarization

In the present study low frequency rTMS at (1Hz) applied to the motor cortex in right hemisphere (RH) language homologues. It was stated that low frequency stimulation decrease corticospinal excitability. Application of rTMS to Broca's area in the undamaged hemisphere suppresses activity in that region of interest (ROI). These results may be attributed to cortical neuroplastic changes which are not restricted only to the cortex contralateral to the deafferentation, but result in bilateral reorganization affects sensorimotor areas of both hemispheres. This permits reactivation of some areas within the damaged hemisphere, promoting some functional recovery. These results are in consistence with Lefaucheur, 2006 and Mylius et al., 2012).

Cotelli et al., 2012; found that the frequency of stimulation is critical determinant in the modification of the cortical response. The author studied both high (>5 Hz) and low frequency (≤1 Hz) rTMS on the modification of the cortical response. The Low frequency (≤1 Hz) rTMS reported to have inhibitory effect and the high frequency stimulation has an excitatory.

In contrast to the result of the present study Finocchiaro et al., 2006 observed a significant and lasting improvement in action production following the application of high-frequency rTMS over the left frontal cortex versus the right one. The author attributed this improvement to the reduction of vocal reaction times (vRTs) when administration of rTMS at appropriate time intervals. This discrepancy between Finocchiaro et al., 2006 study and the result of the present study may be due to the difference in the sample size and subjects characteristics. The author applied this technique on a single healthy subject.

Houdayer et al., 2008; added that both HF and LF rTMS may have mixed excitatory and inhibitory effects. For example doubling the duration of stimulation can reverse the outcome from inhibition to excitation and vice versa. Gamboa et al., 2010; reported that the underlying mechanisms of "excitatory" versus "inhibitory" aspects of rTMS paradigms should also be taken as relative. Motor evoked potential (MEP) increase after "excitatory" HF rTMS might be the result of a decrease of gamma-amminobutyric acid (GABA)-mediated intracortical inhibition (hence inhibition of inhibition), rather than a direct enhancement of motor cortex excitability. Conversely, LF rTMS can enhance the net inhibitory corticospinal control, via GABA-B transmission.

The results of the present study proved that rTMS influences the activity of the brain centers close to and distant from the stimulated site. It may be due to strengthening of the synaptic activity of the surviving neurons in the stimulated network. The modification of cortical activity through the use of rhythmic stimulation may readjust pathological patterns of brain activity, thus providing an opportunity to induce new, healthier activity patterns within the affected functional networks (Crosson et al., 2007).

The current study proved that repetitive transcranial magnetic stimulation (rTMS) combined with therapeutic exercises produces a modulation and a rearrangement of synaptic efficiency within a given network, which in turn lead to more effective processing. Cortical neuroplastic changes are not restricted only to the cortex contralateral to the deafferentation, but result in bilateral reorganization that affects sensorimotor areas of both hemispheres. Repetitive transcranial magnetic stimulation has long-term improvement in the modulation and facilitation of language performance in motor aphasic patients (Murdoch and Barwood, 2013).

The designed program of physical therapy of the current study combined with rTMS proved that this program induces long-term language improvement in chronic stroke patients with motor aphasia. After three months of the treatment improvement was observed in the power of stimulation intensity (represents 90% of the resting motor threshold that recorded from contraction of the first dorsal interosseus of the unaffected hand). Greater improvement measured after six months of the end of the treatment. This long term effect may be attributed to engage mechanisms of neural plasticity. These results are in agreement with that reported by Martin et al., 2009; Naeser et al., 2010; Hamilton et al., 2010.

The results of the present study reported severe impairment in syntactic and semantic variant in cases of non fluent Broca's aphasia pre treatment in the study group (G1) and control group (G2). These variants reflect prominent pathological involvement of the anterior language areas. The result of the present study are in consistent with that reported by Hillis et al., 2004, who investigate action naming in a large sample of patients with Broca's aphasia. The authors showed that Broca's aphasia is severe in the oral modality specifically lexical representations. The authors added that there is selective atrophy of left prefrontal cortex that occurs in Broca's aphasia.

In the present study significant improvement was observed post treatment in number of words per longest phrase length and propositional speech in (G1) comparing to (G2). A moderate non fluent patient increased from one-word phrase length to three-word phrase length. The results of the present study are consistent with results of Hamilton et al., 2010. The authors found significant improvement on the number of narrative words, nouns, mean sentence length over time, and use of closed class words compared to baseline performance post treatment by rTMS and exercise therapy.

The result of the present study showed that there is an improvement in the spontaneous speech and naming ability in the evaluation of clinical aphasia in (G1). These finding may be attributed to the manipulation of the intact contralesional cortex in patients with non fluent aphasia result in language benefits that generalize beyond naming and language production. These results are greatly consistent with that obtained by Hamilton et al., 2010. The authors reported significant improvement on the Western Aphasia Battery subscale for spontaneous speech with improvements on both the information content and fluency.

The present study proved also improvement in repetition ability in (G1) comparing to (G2). These results may be attributed to suppress right Broca's area and shift in activation from (RH) frontal areas to new activation in left (LH) perilesional, perisylvian areas and left supplementary Motor Cortex (SMA). These results are in agreement with Martin et al., 2009, who continued to show this activation pattern at three months and up to 16 months post treatment of motor aphasia by rTMS combined with exercise therapy.

The results of the present study showed significant improvement post treatment in writing and reading ability in (G1) comparing to (G2). These improvements may be attributed to increase activation of the left SMA post-rTMS and language therapy. These results are compatible with Breier etal., 2009, who used fMRI studies to examine the left cerebral hemisphere. The author observed new left (SMA) activation present in aphasia patients with better outcome. This improved LH activation is also compatible with Richter et al., 2008, who observed better outcome following language therapy combined with rTMS to be associated with new, LH activation.

In the present study combination of treatment modalities in treatment of chronic aphasia patients (pharmacological intervention, speech therapy, physical therapy and rTMS) proved to be effective. These combination permits neural network reinforcement immediately post treatment. These also optimize the plastic changes resulting in increased clinical gains, even in chronic stroke patients. These results are consistent with that found by Talelli and Rothwell, 2006.

Cotelli et al., 2012 also reported a significant improvement in language production after a combination of treatment by speech therapy, physical therapy and series of rTMS. These improvements may be attributed to the modulation of abnormal inter hemispheric inhibition in chronic stroke where imbalanced excitability of the healthy hemisphere is present, due to release of inhibition from the damaged hemisphere. Slow 1Hz rTMS used to suppress the disinhibition (hyperexcitability) of the undamaged hemisphere in these stroke patients.

Maher et al., 2003, also reported significant improvement in language production in chronic motor aphasic patients following (CVA) after a series of treatments by constraint-induced language therapy (CILT). This improvement may be attributed to gradual successive approximation of behavior in small steps toward the desired goal. The patients' response after training is gradually increased from single words, up to phrases and even sentences. Mustafa et al., 2004; added that the initial language recovery within the first year post-stroke aphasia linked primarily to functional recovery in the dominant hemisphere. Long-term recovery in aphasia is related to slow and gradual compensatory functions in the contralateral hemisphere.

In the current study there was improving in approximately all domains of the control group by clinical evaluation but didn't reach to a significance level. Auditory comprehension and pantomime sub domains reported significance improvement in G2). These improvements may be attributed to the effect of pharmacological intervention. These results are in consistence with Hasanin et al., (1995); who found significant improvement in aphasic patients with and without repetitive disorders by using Bromocriptine in a dose of 7.5 mg/ day for 6 months (starting by 1.25 mg/day then gradually increasing the dose).

At the end of the treatment a significant negative correlation between changes in total scores of the Arabic translated form of the modified Chesher test and changes in mean values of power of intensity was observed in (G1); while there was no significant negative correlation between changes in total score of the Arabic translated form of the modified Chesher test and changes in mean values of power of intensity intensity in (G2). These findings can be explained from the physiological point of view as the results of the current study proved that there is a crucial role in supporting linguistic performance after left hemispheric damage has been traditionally assigned to the right hemisphere. Functional reorganization of the language system has been described. The physiological finding of this study explained the results of the clinical evaluation by The Arabic translated form of the modified Chesher test. These results are greatly consistent with that obtained by Saur and Hartwigsen, 2012, who found that the modulation of abnormal inter hemispheric inhibition in chronic stroke to improve language production. Sonty et al., 2007, added that examination of patients with motor non fluent aphasia revealed changes in language network connectivity rather than hypoactivity.

CONCLUSIONS AND RECOMMENDATIONS

- On the basis of the present data, it is possible to conclude that the effect of a designed physical therapy program speech therapy combined with repetitive transcranial magnetic stimulation) on non fluent motor aphasia in chronic cerebrovascular stroke patients is significant. Repetitive transcranial magnetic stimulation is proved to be beneficial neuromodulatory techniques for the rehabilitation of communication. Repetitive transcranial magnetic stimulation is thought to induce long-lasting changes in cortical excitability, depending on the frequency of stimulation. This long term effect may be attributed to engage mechanisms of neural plasticity.

- A similar study should be conducted on a large number of patients to provide wide representation of the data. A similar study should be conducted to compare the effect of rTMS and physical therapy exercises on different types of aphasia. Further studies are needed to demonstrate the therapeutic potential of the induction of long-term neuromodulatory effects using rTMS. Indeed, in Alzheimer disease.

REFERENCES

1. Bakas T, Kroenke K, Plue LD. Outcomes among family caregivers of aphasic versus non aphasic stroke survivors. Rehabil Nurs 2006; 31:33.
2. Barwood CH, Bruce E. Murdocha, Whelana B, Lloyda D, Riekb S, O'Sullivanc J, Coulthardd A, Wongc A, Aitken P,Hallf G. The effects of low frequency Repetitive Transcranial Magnetic Stimulation (rTMS) and sham condition rTMS on behavioral language in chronic non fluent aphasia: Short term outcomes 2011; 28: 113-128.
3. Betty R, Jonathan A. Essential medical statistics. 2nd edition, Blackwell Publishing 2003; Pp102-117.
4. Breier J I, Juranek J, Maher LM, Schmadeke S, Men D, Papanicolaou AC. Behavioral and neurophysiologic response to therapy for chronic aphasia. Arch Phys Med Rehabil.2009; 90(12), 2026-2033.
5. Cotelli M, Manenti A, Alberici M, Brambilla M, Cosseddu O, Zanetti A, Miozzo A, Padovani C, Miniussi C, Borroni. Prefrontal cortex rTMS enhances action naming in progressive non-fluent aphasia. European Journal of Neurology 2012; 19: 1404-1412.
6. Crosson B, McGregor K, Gopinath KS, Conway TW, Benjamin M, Chang YL. Functional MRI of language in aphasia: a review of the literature and the methodological challenges. Neuropsychol Rev 2007; 17:157-177.
7. Dronkers NF, Plaisant O, Iba-Zizen MT, Cabanis EA. Paul Broca historic cases: High resolution MR imaging of the brains of leborgne and lelong. Brain. 2007; 130: 1432-1441.
8. El-Tamawy MS. Cerebrovascular aphasia. Msc. Thesis, Cairo University; 1980.
9. Finocchiaro C, Maimone M, Brighina F, Piccoli T, GigliaG, Fierro B. A case study of primary progressive aphasia: improvement on verbs after rTMS treatment. Neurocase 2006; 12: 317–321.
10. Friedemann P., Bettina N., Thomas E., Bettina M., Brigitte R.,Peter K., Edward T. Constraint-Induced Therapy of Chronic Aphasia After Stroke. Stroke 2001; 32: 1621-1626.

11. Gamboa OL, Antal A, Moliadze V, Paulus W. Simply longer is not better: reversal of theta burst aftereffect with prolonged stimulation. Exp Brain Res 2010; 204:181-7.
12. Grossman M. Primary progressive aphasia: Clinical pathological correlations. Nat Rev Neurol. 2010, 6: 88-97.
13. Hamilton RH, Sanders L,Benson J, Faseyitan O, Norise C, Naeser M. Stimulating conversation: Enhancement of elicited propositional speech in a patient with chronic non fluent aphasia following transcranial magnetic stimulation. Brain and Language. 2010; 45-50.
14. Hasanin A, Helmy AA, Moustafa M, Kora F. Correlation of neuroimaging techniques, EEG and clinical diagnosis in cerebrovascular aphasia. MD Thesis. Cairo University; 1995.
15. Hillis AE, Oh S, Ken L. Deterioration of naming nouns versus verbs in primary progressive aphasia. Ann Neurol 2004; 55: 268–275.
16. Houdayer E, Degardin A, Cassim F, Bocquillon P, Derambure P, Devanne H. The effects of low- and high-frequency repetitive TMS on the input/output properties of the human corticospinal pathway. Exp Brain Res 2008; 187:207-17.
17. Lefaucheur JP. Stroke recovery can be enhanced by using repetitive transcranial magnetic stimulation (rTMS). NeurophysiolClin 2006; 36(3):105-115.
18. Maher LM, Kendall D, Swearengin JA, Pingle K, Holland A, Rothi LJ. Constraint induced language therapy for chronic aphasia: Preliminary findings. Journal of the International Neuropsychological Society2003; 9:192-199.
19. Martin PI, Naeser MA, Ho M, Doron K W, Kurland J, Kaplan J, Wang Y, Nicholas M, Baker EH, Fregni F, Pascual L A. Overt naming fMRI pre- and post-TMS: Two nonfluent aphasia patients, with and without improved naming post-TMS. Brain Lang. 2009; 111(1), 20-35.
20. **Moustafa M, Hosna M, Ibtesam F, Manal EK, Amany M, Nervana EF, Hala EG, Noha AK**. Cerebral blood flow changes in vascular aphasia: A clinical and SPECT study. Egypt J. Neurol. Psychiat. Neurosurg. 2004; 41(1): 251-261.
21. Murdoch BE, Barwood CH. Non-invasive brain stimulation: A new frontier in the treatment of neurogenic speech-language disorders. Int J Speech Lang Pathol 2013; 15:234-244.
22. Mylius V, Ayache SS, Zouari HG, Aoun-Sebaïti M, Farhat WH, Lefaucheur JP. Stroke rehabilitation using noninvasive cortical stimulation: hemispatial neglect. Expert Rev Neurother 2012; 12:983-91.
23. Naeser M., Theoret H., Kobayashi M., Martin P., Nicholas M. Modulation of cortical areas with repetitive transcranial magnetic stimulation to improve naming in nonfluent aphasia. 8th International Conference on Functional Mapping of the Human Brain. Sendai, Japan.Neuroimage. 2002; 332:340.

24. Naeser MA, Martin PI, Lundgren K, Klein R, Kaplan J, Treglia E. Improved Language in a Chronic Non fluent Aphasia Patient After Treatment With CPAP and TMS. Cogn Behav Neurol. 2010; 23(1), 29-38.
25. Naeser MA, Martin PI, Theoret H, Kobayashi M, Fregni F, Nicholas M, Pascual-Leone A. TMS suppression of right pars triangularis, but not pars opercularis, improves naming in aphasia. Brain and Language 2011; 119(3): 206-213.
26. Nora W.,Alexander T.,Ilona R., Alexander H., Josef K., Lutz K., Thomas K., Wolf D. Effects of Repetitive Transcranial Magnetic Stimulation in Aphasic Stroke. Stroke 2001; 42: 409-415.
27. Richter M, Miltner WH, Straube T. Association between therapy outcome and right-hemispheric activation in chronic aphasia. Brain 2008; 131(Pt 5):1391-1401.
28. Ridding MC, Rothwell JC. Is there a future for therapeutic use of transcranial magnetic stimulation? Nat Rev Neurosci. 2007; 8: 559-567.
29. Sanes JN, Donoghue JP. Plasticity and primary motor cortex. Annu Rev Neurosci. 2000; 23:393-415.
30. Saur D, Hartwigsen G. Neurobiology of language recovery after stroke: lessons from neuroimaging studies. Arch Phys Med Rehabil 2012; 93(1 Suppl):S15-S25.
31. Sonty SP, Mesulam MM, Weintraub S, Johnson NA, Parrish TB, Gitelman DR. Altered effective connectivity within the language network in primary progressive aphasia. J Neurosci 2007; 27: 1334–1345.
32. Stowe LA. Sentence comprehension and the left inferior frontal gyrus: Storage, not computation. Behavioral Brain Sci. 2000; 23: 51.
33. Talelli P, Rothwell J. Does brain stimulation after stroke have a future? Curr Opin Neurol 2006; 19(6), 543-550.
34. Taub E., Uswatte G., Pidikiti R. Constraint-induced movement therapy: a new family of techniques with broad application to physical rehabilitation: a clinical review. *J Rehabil Res Dev*. 1999; 36:237–251.

تأثيرالتمرينات العلاجية مع التحفيز المغناطيسى عبر الجمجمة على فقد القدرة على الكلام بعد السكتة الدماغية المزمنة

المستخلص

مرجعية: نسبة عالية من المرضى الذين يعانون من السكتة الدماغية يعانون ايضا من الحبسة الكلامية. تهدف هذه الدراسة الى بحث و دراسة التاثير الاكلينيكي والفسيولوجى للتحفيز التكرارى المغناطيسى عبرالجمجمة مع التمرينات العلاجية على الحبسة الكلامية الحركية غير المسترسلة(حبسة بروكا الكلامية) فى مرضى السكتة الدماغية المزمنة. **طرق البحث:** أربعون مريضا من السكتة الدماغية يعانون من الحبسة الكلامية المزمنة مثلوا عينة هذة الدراسة. تراوحت اعمارهم بين 45-60 عاما وقسموا الى مجموعتين متساويتين مجموعه دراسه " ج 1 " ومجموعه ضابطه " ج 2" . المرضى فى المجموعتين خضعوا الى نفس العلاج الدوائى فى فترة العلاج لتفادى حدوث اى مشاكل. وقد خضع المرضى فى المجموعة الدراسة للعلاج بتمرينات علاجية للكلام مختارة مع تحفيز مغناطيسى تكرارى عبر الجمجمة. تم تقيم وظائف الكلام (التكرار-القراءة- تسمية الاشياء- الكتابة- القدرة على الفهم- الكلام التلقائى) بواسطة اختبار تشيشير المعدل المترجم للغة العربية و اختبار الكلام المأخوذ من اختبار إشين . و قياس حدة قوة التنبية باستخدام جهاز التحفيز المغناطيسى عبر الجمجمة قبل و بعد العلاج و بعد ثلاثة اشهر من إنتهاء المداخلة العلاجية لتحديد مستوى استثارة المخ. **النتائج:** بعد الأنتهاء من العلاج ظهر تحسن ذو دلالة احصائية فى كل النقاط المدروسة فى المجموعة الدارسة بواسطة اختبار تشيشير المعدل المترجم للغة العربية .فى المجموعة الضابطة ظهر اختلاف فى المجموع الكلى بواسطة اختبار تشيشير المعدل المترجم للغة العربية فى جيع النقاط المدروسة تقريبا ولكن لم يصل إلى تحسن تحسن ذو دلالة احصائية إلا فى القدرة على فهم اللغة المسموعة و التمثيل الإيمائى حيث ظهر لهم تحسن ملحوظ ذو دلالة إحصائية. بمقارنة النتائج فى جميع النقاط المدروسة فى المجموعتين بعد الانتهاء من العلاج ظهر تحسن ملحوظ ذو دلالة احصائية فى كل النقاط المدروسة بين كلا المجموعتين (الضابطة و الدارسة) واظهرت النتائج ايضا وجود ارتباط سلبى ذو دلالة احصائية بين النتائج العمليه للاختبار الاكلينيكى و النتائج الفسيولوجيه للتحفيز المغناطيسى عبر الجمجمة فى المجموعة الدارسة **الخاتمة:** ومن هنا يتضح ان برنامج العلاج الطبيعى المختار مع التحفيز المغناطيسى التكرارى عبر الجمجمة كان ناجحا فى تثبيط النشاط عبر قشرة الدماغ ليحفز وظائف اللغة فى مرضى الحبسة الكلامية الحركية غير المسترسلة. وهذا التحسن يرجع إلى تشابك آليات المطاوعة العصبية.

الكلمات الدالة: الحبسة الكلامية الحركية الغير مسترسلة, اختبار تشيشر المعدل , التحفيز المغناطيسى التكرارى عبر الجمجة, التاهيل, السكته الدماغيه, اللغة.