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Factors Influencing Aphasia Outcome in Patients with Occlusive Stroke

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Abstract

Background: Aphasia related to ischemic stroke is a major health problem affecting the quality of life profoundly.

Aim of Study: Is to assess factors influencing aphasia outcome in patients with occlusive stroke and the role of functional magnetic resonance imaging in detection the patterns of post-stroke language recovery.

Patients and Methods: This was a prospective cohort study done at Neuropsychiatry Department and Center of Psychiatry, Neurology and Neurosurgery, Diagnostic Radiology, Tanta University, from January 2017 to January 2018. Aphasia Rapid Test (ART) at day 1 and follow-up at day 8 which is a bed side clinical test to assess aphasia severity, Diffusion Tensor Imaging (DTI) and fMRI were done at day 8 to assess aphasia severity. A total of 34 cases were finally included in this study after fulfilling the inclusion and exclusion criteria, 12 patients who had receptive or global aphasia, were not suitable for fMRI, their native language Arabic, age <80 years.

Results: The total number of the studied patients was 34 of them 18 patients (52.9%) were males and 16 patients were females (47.1%). The age of the studied patients ranged from 28-79 years. The older group of patients had severe language disability also those with global aphasia and perisylvian lesion, risk factors as HTN, DM, Cardiac Disease, Dyslipidemia had worse prognosis, those with no reconstruction of the Arcuate Fasiculus in DTI and fMRI data analysis showed negative effect of the site contralateral to lesion.

Conclusion: Age was a significant factor with the higher age group had the worst prognosis regarding aphasia. Large lesion sizes and those with damage to strategic language areas had a bad prognosis. fMRI and DTI were the cornerstone of our study and they were a highly reliable tools in the prognosis of language outcome, with those who had activity in the perilesional and bilateral activity (perilesional and contralateral homotopic) in fMRI to have better outcome than those with only contralateral activity, also DTI to delineate the AF and the degree of its integrity and reconstitution.

Key Words: *Aphasia outcome – Ischemic stroke – Prognosis – Prospective study.*

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Introduction

APHASIA is an acquired disorder of language processing which may affect speech comprehension, expression, writing or reading; leaving other cognitive capacity intact [1].

Aphasia in adults is most often secondary to stroke in the language-dominant cerebral hemisphere, present in 20% to 40% of acute stroke patients [2].

Functional Magnetic Resonance Imaging (fMRI) is promising tool in evaluation of patterns of aphasia recovery after stroke using different tasks of language [3]. fMRI shows different patterns of BOLD signal related to post-stroke language recovery seen in the hemispheres (dominant or non-dominant).

fMRI shows activation patterns in response to verb generation tasks [3].

Blood-Oxygenation-Level-Dependent (BOLD) fMRI considered now the most commonly used functional neuroimaging tool to study the cerebral representation of post-stroke language. It has an advantage to show the close link between local neuronal activity and its blood flow (neurovascular coupling) [4]. In acute infarction, local blood flow increases secondary to neuronal activity, leading to an increase the need of oxygenated blood which exceeds the need of oxygen for neuronal activity. As a result, there is an increase of the MR signal in those areas of the brain that are active due to deficiency of paramagnetic deoxygenate dhemoglobin [5].

The BOLD fMRI signal shows the function of dHb concentration, which occurs as result of turn adjustments in Cerebral Blood Flow (CBF), Cerebral Blood Volume (CBV) and Cerebral Metabolic

Rate of O_2 Consumption ($CMRO_2$); also shows the distribution of dHb in the infarcted tissue, as determined by the microvascular architecture [6].

This study designed to assess factors influencing aphasia outcome in patients with occlusive stroke and the role of fMRI in detection the patterns of post-stroke language recovery.

Patients and Methods

Inclusion criteria:

Age of patients <80 years who show aphasia after acute ischemic stroke, their native language were Arabic.

Exclusion criteria:

Inability to perform the language task due to (severity of aphasia, reduced general health status and hearing deficits), cognitive impairment other than aphasia like memory impairment, any contraindication to MRI like pacemaker or metallic foreign body.

Baseline and follow-up assessment: All included patients were subjected to the following:

1- History taking including the personal history and comorbid conditions.

2- Neurological and general clinical examination.

3- National Institute of Health Stroke Score (NIHSS) is a tool used to quantify the impairment caused by a stroke. The NIHSS is composed of 11 items, each of which scores a specific ability between 0 and 4. For each item, a score of 0 typically indicates normal function in that specific ability, while a higher score is indicative of some level of impairment [7].

4- Routine laboratory investigations including arterial blood gases, complete blood picture, prothrombin time and activity, international normalized ratio, liver & renal functions, lipid profile and further lab investigations were ordered for each case individually (e.g. D-Dimer, LDH, CSF analysis, ... etc).

5- Radiological imaging:

- Non-enhanced CT brain was performed for all stroke patients to exclude intra cerebral hemorrhage.
- Magnetic resonance imaging.
- Technique is performed using standard 1.5 Tesla MRI scanner (GE, Sigma closed magnet) with head coil.
- DWI and FLAIR: To determine the size and the site of the lesion.

2- *fMRI BOLD technique:*

Patient entered the MRI machine and is instructed to relax for 30 seconds followed by the sentence reading paradigm and the patient is asked to complete the sentences vocally in a complete resting state to avoid any brain activity away from the targeted language areas. Brain activity is measured in the perilesional area (area around the lesion), contralateral homotopic area (language areas on the contralateral hemisphere) and is measured in both areas if present.

- Paradigm in the form of sentence reading was used to detect task in language areas, it composed of eight incomplete sentences in the form of four blocks. It should be finished using a single noun. Every sentence had 3-10 words presented into a single row. Each sentence was lasted for 5 seconds (s) then there was an Interstimulus Interval (ISI) of 3 second which represented by an empty space on the screen. The patients were asked to complete reading sentences in suitable nouns during the ISI. The duration of each block was 64 second [8].

Diffusion Tensor Imaging (DTI) helps in three-dimensional reconstruction and detection of the Arcuate Fasciculus (AF), the arcuate fasciculus is bundle of white matter that plays a key role in language processing, it present the left cerebral hemisphere.

DTI MR acquisition and directional mapping:

Diffusion Tensor MR images (DTI MRI) single shot echo planar sequence of (4500/71.8/4 [TR/TE/ excitations] was used, field of view was 240-mm with sections of 3-mm of and only 2 slabs, each slap contain 20 sections, matrix was 128 X 128 zero filled to 256 X 256, the size of voxel 1.87 X 1.873.0mm interpolated to 0.94.

Outcome assessment: Outcome of Aphasia: Outcome determined by Aphasia Handicap Scale (AHS): The outcome of aphasia assessed three months' post-stroke using the (AHS), a modified Rankin-score-like five-point scoring system for handicap in verbal communication [9].

Statiscal analysis: Data were fed to the computer and analyzed using IBM SPSS software package Version 20.0.

1- Mean value (X): The sum of all observations divided by the number of observation.

2- Standard Deviation [SD]: It measures the degree of scatter of individual varieties around their mean.

3- Student "*t*-test", was used to detect the significance of the difference between two means.
4- Chi-square test: For comparison between two groups as regards qualitative data.

Results

The total number of the studied patients was 34 of them 52.9% were males (18 patients) and 47.1% were females (16 patients). The age of the studied patients ranged from 28-79 years (Table 1).

Lesion size was a significant variable as those with complete (large) infarction had the worst prognosis and constituted the majority of severe language disability and mutism by 5/71.43% and 2/66.67% respectively followed by partial infarction, while those with lacunar infarction had the best outcome as its 5/83% of their patients fall in the normal, minor and mild language disability (Table 2).

Lesion site was vital regarding aphasia severity and prognosis as poorer prognosis found in peri-sylvian lesions affecting both Broca's and Wernicke's area, they constituted the majority of severe language disability 4/57.14% and mutism 2/66.67%, in contrary to extra-sylvian lesions that showed normal, minor and mild language disability in majority of their patients (5/71%), while 2/29% of their patients fall in the severe language disability and mutism. Also those with either Broca's or Wernicke's area lesion had worse outcome than those with extra-sylvian lesions yet better than those with peri-sylvian lesions (Table 4).

Patients who had activity in bilateral or perilesional area in fMRI showed better language outcome, in contrary patients with contralateral activity alone showed poorer outcome (Table 5).

Patients who showed reconstruction of the AF using DTI had better recovery from aphasia than those who didn't.

Table (1): Age and sex of studied patients.

Age:		
Range	28-79	
Mean ± SD	54.8± 13.744	
	N	%
Sex:		
Male	18	52.94
Female	16	47.06

Table (2): Lesion size and its relation to aphasia outcome.

Lesion size	AHS											
	Normal		Minor		Mild		Moderate		Severe		Mutism	
	N	%	N	%	N	%	N	%	N	%	N	%
Partial (n.=21)	3	75	4	66.7	3	60	8	88.9	2	28.6	1	33.3
Complete (n.=7)	0	0	0	0	0	0	0	0	5	71.4	2	66.7
Lacunar (n.=6)	1	25	2	33.3	2	40	1	11.1	0	0	0	0

Table (3): Lesion site and its relation to aphasia outcome.

	Anatomical Site											
	N	%N		%	N	%	N	%	N	%	N	%
Broca's	2	50	4	66.7	2	40	5	55.6	1	14.3	0	0
Peri Sylvain	0	0	0	0	1	20	0	0	4	57.1	2	66.7
Extra Sylvain	2	50	2	33.3	1	20	1	11.1	1	14.3	1	33.3
Wernicke's	0	0	0	0.00	1	20	3	33.3	1	14.3	0	0

Table (4): fMRI (BOLD) and its relation to aphasia outcome.

fMRI BOLD	AHS												χ^2	*p*
	Normal		Minor		Mild		Moderate		Severe		Mutism			
	N	%	N	%	N	%	N	%	N	%	N	%		
Excluded (n.=12)	0	0	0	0.0	2	40	1	11.1	6	85.7	3	100	30.601	0.010*
Perilesional (n.=9)	2	50	3	50	0	0	4	44.4	0	0.00	0	0		
Contra. Homot. (n.=5)	0	0	0	2	0	0	2	22.2	1	14.3	0	0		
Bilateral (n.=10)	2	50	3	50	3	60.	2	22.2	0	0	0	0		

* : Significant.
AHS : Aphasia Handicap Scale.
fMRI : Functional MRI.
BOLD : Blood Oxygen Level Detection.

Table (5): DTI and its relation to aphasia outcome.

DTI	AHS												X^2	*p*
	Normal		Minor		Mild		Moderate		Severe		Mutism			
	N	%	N	%	N	%	N	%	N	%	N	%		
No reconstruction	0	0	0	0	0	40	8	88.9	7	100	3	100	25.4	<0.001
Recon. of Arc. Fasc.	4	100	6	100	3	60	1	11.1	0	0	0	0		

* : Significant. Recon. Arc. Fasc. : Reconstruction Arcuate fasiculus.
DTI : Diffusion Tensor Imaging. AHS : Aphasia Handicap Scale.

Patients:

Patient (1): Female patient, aged 45 years old, librarian, married with 2 offspring, she is not hypertensive (110/70), nor diabetic (RBS=130 mg/dl). She presented with acute onset of right side weakness associated with expressive aphasia.

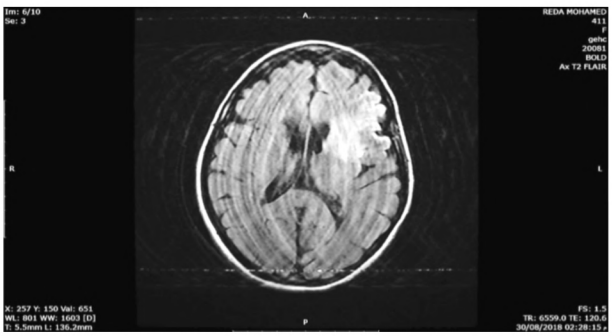

Fig. (1): FLAIR showing hyperintense signal in the Broca's area indicating infarction.

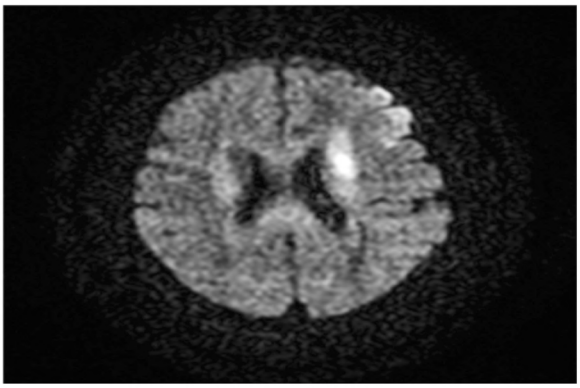

Fig. (2): DWI showing restricted diffusion in the basal ganglia.

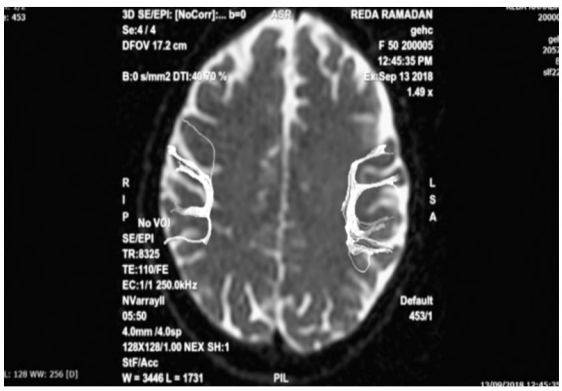

Fig. (3): DTI showing reconstruction of the arcuate fasiculus on the left hemisphere.

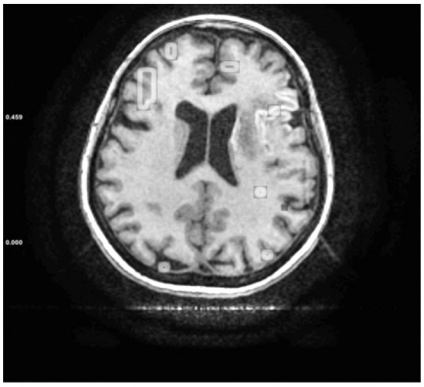

Fig. (4): FMRI BOLD shows Brocas area is involved in the infarcted area while Wernicke's area is displaced posteriorly.

Patient (2): Male patient aged 65 years, retired, known to be hypertensive, diabetic, his weight was 75kg, presented with Rt side weakness and global aphasia. fMRI BOLD caanot be obtained due un-copperation of patient.

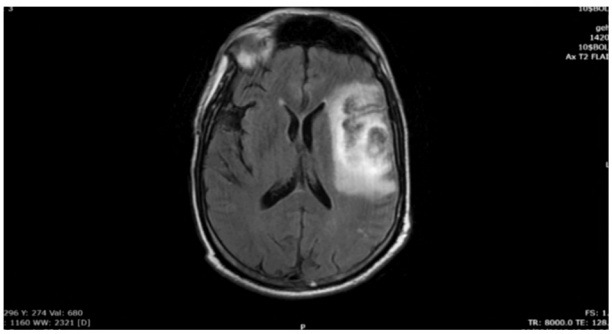

Fig. (5): FLAIR shows hyperintense signal in perisylvian area.

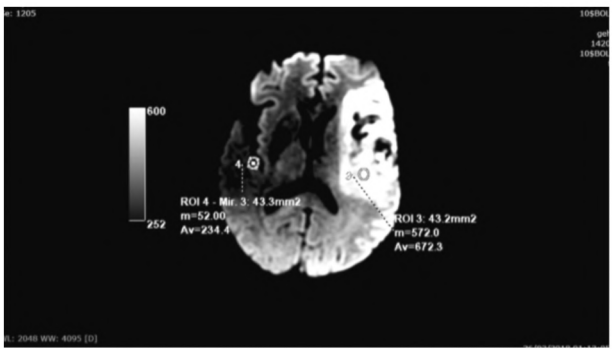

Fig. (6): DWI shows hyperintense signal in perisylvian area indicating restricted diffusion due to infarction.

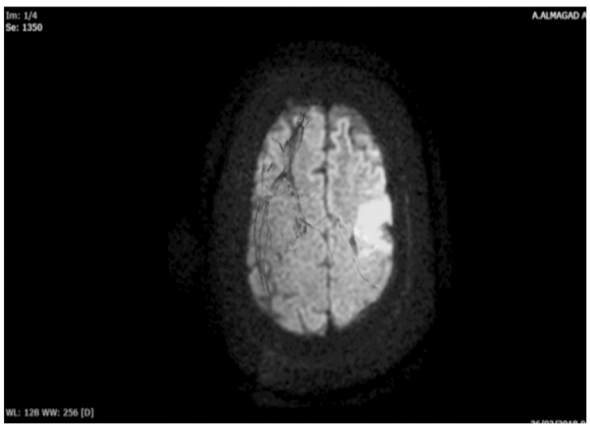

Fig. (7): DTI shows different size of both RT (thick) and LT (thin) of arcuate fasciculus.

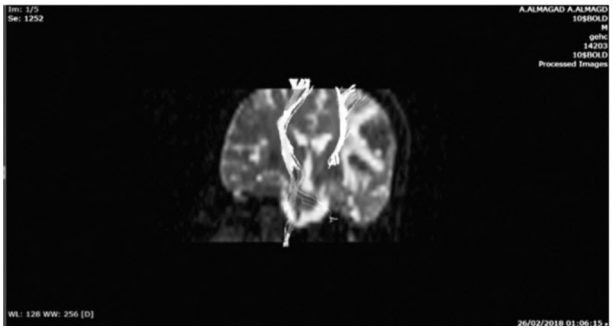

Fig. (8): DTI shows complete cutting of left arcuate fasciculus.

Discussion

The prognosis of aphasia requires consideration of a multiple inter related patient-specific and stroke-specific variables which are believed to influence functional outcomes for individuals with aphasia. Patient-related variables include: Age, handedness, gender, educational level, intelligence, motivation, depression, family support, beliefs and attitude regarding health care, and access to medical treatment. In contrast, stroke-related indices include site of lesion, size of lesion, aphasia type, pattern of recovery, and initial aphasia severity **[10]**.

The use of structural and functional neuroimaging applied to stroke patients has helped to better understand anatomical and metabolic factors associated with aphasia recovery. These can be distinguished into ipsilateral and contralateral factors **[11]**.

Regarding age, we found that the older age group 67.571 ±9.964 years, had severe language disability and mutism while the younger age group 35.750± 10.905 years had the best outcome which was concordant with Laska et al., 2001 who found that older age (66.55 ±8.65) is a negative predictor for improvement of aphasia and Watila et al., 2015 who found that younger patients (37.53 ±6.74) with aphasia improved better than older patient **[12,13]**. In contrary to, Holland et al., 2014 found that there was no influence of age on aphasia recovery **[14]**.

Regarding gender of studied patients, no statistically significant difference was found between both sexes which was going with Seniów et al., 2009 **[15]**.

Regarding lesion size in MR diffusion images, we found that 2/66.67% of those with mutism and 5/71% of those with severe language disability, have complete or large sized infarction which agreed with Maas et al., 2012 **[16]**. In contrary, small or lacunar infarction had better prognosis regarding outcome, as 5/83% of their patients had good outcome while 1/17% had poor outcome which agreed with Clarck et al., 2003 found that patients with small lesions exhibited significant improvement in auditory comprehension, verbal expression and written expression **[17]**.

Regarding lesion site, we found that patients with perisylvian region lesion constituted 2/66.6% of those with mutism and 4/57% of those with severe language deficit which agreed with Kang et al., 2010 **[18]**.

Regarding fMRI, we found that those with perilesional activation had better aphasia recovery, 2/50% of normal and 3/50% of mild aphasia deficits, also bilateral activation of both the perilesional and the contralateral homo-topic (on the right hemisphere) have better outcome as the majority of them fall in the category of normal, minor and mild AHS scores; while those with only activation of the contralateral site without the perilesional area have poor outcome; all their 3/100% patients had moderate and severe language disability, this could raise the suspicion of the inhibitory role of the non-dominant hemisphere when it is activated alone which agreed with Hamilton et al., 2011 **[19]**.

This is explained by Szaflarski et al., 2013 as he found that good recovery of language functions in aphasia patients is accompanied by greater perilesional than right hemisphere reorganization, while poorer recovery of language functions is accompanied by greater right-hemisphere than perilesional reorganization. Also, Jarso et al., 2014 explained that the nature of the contribution from the contralateral hemisphere is being debated while Rosen et al., 2000 suggested that activation of the right hemisphere is less efficient **[20,21]**.

Regarding DTI, we found that the majority of patients with reconstruction of the Arcuate Fasic-

ulus (AF) have better prognosis, while those who have not, had the worst prognosis (severe language deficits and mutism) which agreed with Kim and Jang 2013 found that patients with stroke in whom the left AF could not be reconstructed due to its severe injury had worse prognosis **[22]**.

Conclusion:

Age was a significant factor with the higher age group had the worst prognosis regarding aphasia. Large lesion sizes and those with damage to strategic language areas had a bad prognosis. fMRI and DTI were the cornerstone of our study and they were a highly reliable tools in the prognosis of language outcome, with those who had activity in the perilesional and bilateral activity (perilesional and contralateral homotopic) in fMRI to have better outcome than those with only contralateral activity, also DTI to delineate the AF and the degree of its integrity and reconstitution.

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Conflicts of interest:

No conflicts of interest declared.

Authors' contributions:

All authors had equal role in design, work, statistical analysis and manuscript writing. All authors have approved the final article work.

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العوامل المؤثرة على مآل الحبسة الكلامية فى مرضى السكتة الدماغية

الحبسة الكلامية هو إضطراب مكتسب فى معالجة اللغة التى قد تؤثر على الكلام والفهم والتعبير والكتابة والقراءة دون التآثير على القدرة المعرفية، وتعتبر نسبة حدوث الحبسة الكلامية بين مرضى السكتة المخية الإنسدادية تقدر ب ٢٠-٤٠٪ من الحالات. بعض العوامل لها علاقة مباشرة بإستعادة القدرة على الكلام مثل مكان وحجم الإصابة وقدرة الجزء المصاب والفص المقابل من المخ (الغير مسيطر)، وعوامل آخرى ليس لها علاقة مباشرة مثل نوع الجنس والعوامل البيئية المحيطة، ويعد التنبؤ بالشفاء من الحبسة الكلامية آمر صعب حتى بين الآشخاص الذين يعانون من نفس الإصابة، لذلك يتم إستخدام عدة فحوصات قد تساعد على التنبؤ مثل الرنين المغناطيسى الوظيفى على المخ.

الهدف من الدراسة: هدف هذه الدراسة هو التنبؤ بحدوث الشفاء فى مرضى الحبسة الكلامية نتيجة الجلطة الدماغية إعتماداً على الحالات المرضية المصاحبة والفحص الإكلينيكى والأشعة التشخيصية.

المرضى وطرق البحث: تم إجراء هذه الدراسة على ٣٤ مريض مصابين بالحبسة الكلامية الناتجة عن سكتة دماغية بقسم الأمراض العصبية والنفسية ومركز الطب النفسى التابعين لمستشفيات جامعة طنطا فى الفترة من يناير ٢٠١٧ حتى يناير ٢٠١٨. تم دراسة كل من التاريخ المرضى والفحوصات المعملية كاملة والفحص الطبى الشامل متضمناً مقياس جلاسكو للغيبوبة ومقياس السكتة الدماغية للمعهد الوطنى للصحة ومقاييس لتقييم مدى تآثر اللغة. تم إجراء آشعة الرنين مغناطيسى وظيفى للمرضى لتوضيح نشاط المناطق المسئولة عن اللغة، وكما تم رسم المسارات الآساسية بواسطة الرنين المغناطيسى المعالج. كما تم إعادة تقييم المرضى بعد ثلاثة شهور لمعرفة مآل الحبسة الكلامية.

الخلاصة: تعتبر الحبسة الكلامية من آكثر المضاعفات الناتجة عن الجلطة الدماغية تآثيراً على جودة الحياه، لذا تم دراسة العوامل المؤثرة عليها، يعتبر علاج آسباب الخطورة كآمراض الضغط والسكر والقلب وإرتفاع الدهون تؤثر إيجاباً على مآلها كما آنه كلما زاد حجم الجلطة وكلما كانت فى موقع حيوى كالمناطق المسئولة عن اللغة فى الفص المسيطر كلما كانت آسوآ، ويعتبر الرنين المغناطيسى الوظيفى والآشعة المحددة لمسارات اللغة حجر الزاوية فى هذه الدراسة، حيث آن النشاط فى الناحية المسيطرة والمقابلة لها معاً فى نفس الوقت وسلامة مسارات اللغة من آهم المؤثرات الإيجابية على تحسن الحبسة الكلامية.