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Aphasia outcome: the role of diffusion tensor tractography in patients with acute ischemic stroke

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Abstract

Backgrounds Recovery for poststroke aphasia has a decelerating trajectory, with the greatest improvement is within weeks and the slope of change decreasing over time. Therefore, it is essential to predict the prognosis of aphasia at an early stage as it could provide useful data in specific plans for management strategies. The aim of this work was to assess the arcuate fasciculus in stroke patients with aphasia and its impact on predicting the outcome. A prospective study was performed including 25 patients with acute ischemic stroke and aphasia and 10 healthy control subjects with no history of neurologic or psychiatric disease. All patients underwent language assessment using an Arabic version of the Comprehensive Aphasia Test (Arabic CAT), with the resultant mean T-score aphasia quotient (AQ). Early assessment of stroke and delayed assessment at three months. All patients had diffusion-weighted magnetic resonance imaging (DWI-MRI) of the brain to localize the lesion and 3D diffusion tensor imaging (DTI) of the arcuate fasciculus (AF) within 30 days of stroke.

Results Patients in whom the AF could not be reconstructed had a poor score in early and late AQ and a poor prognosis compared to those in whom the AF could be reconstructed. Preservation of the left AF on DTI could mean the potential recovery of aphasia after stroke.

Conclusion The prognosis of aphasia in patients whose left AF could be reconstructed was better than those whose left AF could not be reconstructed, irrespective of the AF's integrity. That is why, we can assume that evaluation of the DTI of the left AF at early stages of stroke can help in predicting outcome of aphasia.

Keywords Aphasia, Arabic Comprehensive Aphasia Test, Diffusion tensor imaging

Background

One of the most devastating effects of stroke is aphasia, with greater difficulties in resuming daily life activities [1]. Within days or months following a stroke, language functions start to improve to some extent [2], but the extent of recovery varies greatly [3]. As a result, it is crucial to predict the prognosis of aphasia in stroke patients at an early stage because doing so could help plan specific rehabilitation strategies and determine how long rehabilitation will take. The level of aphasia recovery has been correlated with demographic factors, age, lesion-related factors, the location and extent of the lesion, and clinical

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factors, including the subtype and severity of aphasia [4]. Furthermore, lesion-related parameters have been shown to have a strong correlation with long-term recovery [5]. On the other hand, clinical factors continue to be the most widely used measurements by clinicians to gain insight into a patient's clinical progression [6].

Regarding lesion-related factors, even though lesion size shows a good predictor of stroke and aphasia outcomes, the study of particularly damaged language structures shows a more accurate index for specific impairments [7]. The middle cerebral artery supplies the majority of these structures, including the superior temporal gyrus, the anterior insula, the inferior frontal gyrus, and the supramarginal gyrus [8, 9]. However, the white matter bundles are pathway structures linking areas responsible for language processing. Therefore, if white matter structures are crucial for language functions, they can be good predictors to support aphasia recovery [10].

The arcuate fasciculus (AF) is one of the brain's white matter structures, related to several language functions, from syntax processing to speech perception [11, 12], as it connects regions from the temporal, parietal, and frontal cortical areas through its three segments [8].

Neuroimaging modalities, including CT, MRI, and functional MRI, have been used in numerous studies to predict the outcome of stroke-related aphasia with limited results, as they cannot reconstruct and estimate neural tracts [13]. 3D diffusion tensor imaging (DTI), allows for 3D visualization of the architecture and integrity of neural tracts at the subcortical level, especially the arcuate fasciculus (AF) [14, 15].

The primary goal of current research is to assess the arcuate fasciculus in patients with dysphasia and its impact on predicting the outcome (clinical radiological correlation).

Methods

This was a prospective study carried out at two stroke units of our institutional hospitals after obtaining informed written consent. The study recruited 25 patients with acute ischemic stroke and 10 healthy control subjects.

The diagnosis was made based on the clinical features in combination with brain imaging. The inclusion criteria were patients admitted with the diagnosis of acute ischemic stroke with dysphasia within 24 h of the onset of the symptoms. Exclusion criteria were patients admitted with acute ischemic stroke with a history of dementia or disturbed consciousness level, or those with cerebral hemorrhage.

A complete medical history was reviewed, including age, gender, smoking status, and vascular risk factors such as hyperlipidemia, hypertension, diabetes mellitus, and cardiac disease. Full general and neurological clinical assessments were performed initially at the acute stage and later on at a three-month follow-up visit. Language assessment using the Arabic version of the Comprehensive Aphasia Test (Arabic CAT) [16], with the resultant mean T-score aphasia quotient (AQ), was done on admission and after three months of follow-up. The modified CAT provides an outline of the linguistic abilities and impairments of an aphasic person through a quick but comprehensive and standardized profile of language performance. Additionally, the modified CAT battery was a valid and reliable test for determining the type of aphasia and the selection of therapy techniques. The following laboratory tests were done for all patients; complete blood count, fasting and glycosylated hemoglobin (HBA1c), serum lipid profile, serum uric acid, renal function tests, liver function tests, and serum electrolytes. All patients underwent magnetic resonance imaging of the brain and 3D diffusion tensor imaging (DTI) [1.5 Tesla, Philips Medical Systems, United States]. Fractionated anisotropy (FA) values were obtained in the region of interest, the AF. DTI images were performed approximately three or four weeks after onset. According to DTI fractionated anisotropy values, the patients were divided according to the reconstruction of the arcuate fasciculus into two groups: a reconstructed group in whom the arcuate fasciculus could be reconstructed and a non-reconstructed group in whom the arcuate fasciculus could not be reconstructed. Figures 1 and 2 show examples of our study.

Statistical analysis

The collected data was analyzed using Statistical Package for Social Science (SPSS 25, by IBM, Armonk, New York, USA). Descriptive statistics included the mean, standard deviation (± SD), and range for parametric numerical data, the median and interquartile range (IQR) for non-parametric numerical data, and the frequency and percentage of non-numerical data. Analytical statistics included the independent t-test used to assess the statistical significance between two study group means, the paired t-test used to analyze differences for the same study group at different times, and the Chi-Square test to examine the relationship between two qualitative variables. P-value < 0.05 was considered statistically significant.

Results

The aphasia group had 25 patients, while the control group had 10 healthy subjects. There was no statistically significant difference between both groups with regard to the demographic data and the risk factors, as shown in Table 1.

Fig. 1 Coronal (from the front) plane diffusion tensor imaging (DTI) with generation of color diffusion tractography of the AF showing disrupted left Broca's territory, and Wernicke's territory in comparison to the right side

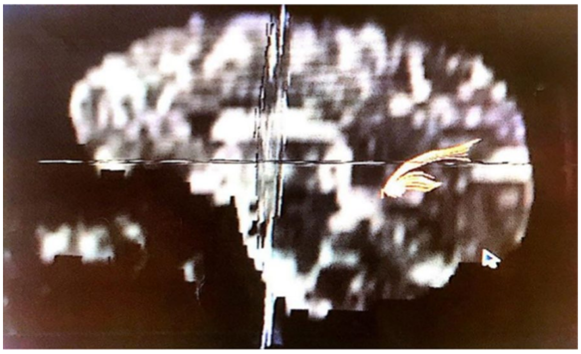

Fig. 2 MRI Sagittal view diffusion tensor imaging (DTI) with generation of color diffusion tractography of the AF (non-reconstructed AF)

Regarding the type of aphasia, five patients (20%) had Broca's aphasia, five patients (20%) had Wernicke's aphasia, six patients (24%) had global aphasia, four patients (16%) had transcortical motor aphasia, one patient (4%) had transcortical sensory aphasia, and four patients (16%) had conductive aphasia.

For the site of the lesion, four cases (16%) had left parietal infarction, and five cases (20%) had left fronto-temporal infarction, six cases (24%) had left fronto-tempro-parietal infarction, and 10 cases (40%) had left tempro-parietal infarction.

In the early language assessment (Arabic CAT), the mean T-Score aphasia quotient (AQ) was 45.75 ± 6.37, while at the 3-month follow-up assessment, it was 46.69 ± 6.96. There was a statistically significant difference (P-value = 0.000), as shown in Table 2.

For the DTI findings, in 19 patients (76%), the AF could be reconstructed, and in 6 patients (24%), it could not be reconstructed. In the reconstructed group, according to the site of lesion in the AF, 9 patients (47.4%) were affected in the Broca's territory, 6 patients (31.6%) were affected in the Wernicke's territory, and 4 patients (21%) were affected in the central part, as in Table 3, and Figs. (1 and 2).

Regarding the FA values, there was a statistically significant difference in FA values between the aphasia and control groups in the left AF (P-value = 0.021), while in the right AF, there was no statistically significant difference in FA values between both groups (P-value = 0.649), as shown in Table 4.

There were no statistically significant differences between age, sex, handedness, education level, or risk factors in both reconstructed and non-reconstructed groups as shown in Table 5.

There was a highly statistically significant difference between both reconstructed and non-reconstructed groups, as global aphasia and large fronto-tempro-parietal infarction were detected only in the non-reconstructed group (P-value = 0.000), as shown in Table 6.

There was a statistically significant difference between both reconstructed and non-reconstructed groups in both early and late assessment for the AQ, with a significant increase in the AQ after 3 months (P-value = 0.001 and 0.000, respectively), as shown in Table 7.

In the reconstructed group, early and follow-up AQs in patients with Broca's territory affection were 46.77 ± 1.9 and 48.58 ± 2.38 respectively; patients with Wernick's territory affection were 43.09 ± 2.24 and 43.47 ± 2.0 respectively; and patients with central part affection were 57.55 ± 0.89 59.13 ± 0.56 respectively. Also, there was a statistically significant increase in the AQ if the Broca's or Wernicke's territories were affected (P-value = 0.007 and 0.002 respectively), with no significant difference if the central part was affected (P-value = 0.950), as shown in Table 8.

There was a highly statistically significant difference between both reconstructed and non-reconstructed groups as regards the FA of the left AF and the left/right FA ratio (p-value = 0.000), while there was no statistically significant difference between the FA of the right AF (P-value = 0.714). as shown in Table 9.

Table 1 Demographic data and risk factors of both groups

Demographic data and risk factors		Control group n = 10	Aphasia group n = 25	Test value	P-value
Age (years)	Mean ± SD	58.20 ± 3.33	56.88 ± 3.71	0.977•	0.336
	Range	54–64	50–64		
Sex	Females	3 (30.0%)	10 (40.0%)	0.306*	0.580
	Males	7 (70.0%)	15 (60.0%)		
Education level	Medium	3 (30.0%)	10 (40.0%)	0.306*	0.580
	High	7 (70.0%)	15 (60.0%)		
Smoking	No	3 (30.0%)	10 (40.0%)	0.306*	0.580
	Yes	7 (70.0%)	15 (60.0%)		
Diabetes	No	5 (50.0%)	10 (40.0%)	0.292*	0.589
	Yes	5 (50.0%)	15 (60.0%)		
Hypertension	No	6 (60.0%)	12 (48.0%)	0.412*	0.521
	Yes	4 (40.0%)	13 (52.0%)		
Atrial fibrillation	No	8 (80.0%)	17 (68.0%)	0.504*	0.478
	Yes	2 (20.0%)	8 (32.0%)		

Independent t-test, *Chi-square test

Table 2 Initial and 3-months follow up results of the aphasia test

Aphasia test	Early Aphasia test (Mean T score)	3 months Follow up aphasia test (Mean T score)	% change	Test value	P-value
Mean ± SD	45.62 ± 6.41	46.60 ± 7.05	2.02 ± 2.05	4.925	0.000*
Range	37.5 –58.4	37.5 –59.5	-0.26 –6.29		

*: Paired t-test

Table 3 Diffusion tensor imaging findings

	Number	%
Non-reconstructed AF	6	24
Reconstructed AF	19	76
Lesion site in reconstructed AF		
Broca's territory affected	9	47.4
Wernicke's territory affected	6	31.6
Central part affected	4	21

Discussion

The field of the neurobiology of language is changed from the Broca-Wernicke-Geschwind language model to new pathways and concepts, such as the Language Connectome, as language is not one functional process or region, but many. The left arcuate fasciculus (AF) is one of the critical language pathways in the human language connectome [17]. DTI represents an effective technique for the demonstration of white-matter fibers in the living

Table 4 Fractionated anisotropy (FA) findings of the study cases

		Control group n = 10	aphasia group n = 25	Test value	P-value
Left/Right AF Ratio	Mean ± SD	1.02 ± 0.03	0.72 ± 0.41	2.318	0.027*
	Range	0.99 – 1.09	0 – 1.02		
Left FA to AF	Mean ± SD	0.46 ± 0.02	0.32 ± 0.18	2.425	0.021*
	Range	0.44 – 0.49	0 – 0.47		
Right FA to AF	Mean ± SD	0.46 ± 0.02	0.45 ± 0.02	0.459	0.649*
	Range	0.43 – 0.49	0.4 – 0.5		

AF Arcuate Fasciculus, *FA* Fractional Anisotropy, *: Independent t-test

Table 5 Comparison of demographic data and risk factors between reconstructed and non-reconstructed groups

		Non-Reconstructed group	**Reconstructed group**	**Test value**	**P-value**
		n = 6	**n = 19**		
Age	Mean ± SD	54.50 ± 3.62	57.63 ± 3.50	− 1.897•	0.071
	Range	50 – 60	50 – 64		
Sex	Females	2 (33.3%)	8 (42.1%)	0.146*	0.702
	Males	4 (66.7%)	11 (57.9%)		
Education level	Medium	2 (33.3%)	8 (42.1%)	0.146*	0.702
	High	4 (66.7%)	11 (57.9%)		
Smoking	No	2 (33.3%)	8 (42.1%)	0.146*	0.702
	Yes	4 (66.7%)	11 (57.9%)		
Diabetes	No	2 (33.3%)	8 (42.1%)	0.146*	0.702
	Yes	4 (66.7%)	11 (57.9%)		
Hypertension	No	2 (33.3%)	10 (52.6%)	0.680*	0.409
	Yes	4 (66.7%)	9 (47.4%)		
Atrial fibrillation	No	3 (50.0%)	14 (73.7%)	1.176*	0.278
	Yes	3 (50.0%)	5 (26.3%)		

• Independent t-test, *Chi-square test

Table 6 Type of aphasia in reconstructed and non-reconstructed groups

	Non-reconstructed group		**Reconstructed group**		**Test value***	**P-value**
	n	**%**	**n**	**%**		
Type of aphasia • Broca's aphasia	0	0.0%	5	26.3%	25.000	0.000
• Conductive aphasia	0	0.0%	4	21.1%		
• Global aphasia	6	100.0%	0	0.0%		
• Trans cortical motor aphasia	0	0.0%	4	21.1%		
• Trans cortical Sensory aphasia	0	0.0%	1	5.3%		
• Wernicke's aphasia	0	0.0%	5	26.3%		
Site of the Lesion • Left deep- parietal	0	0.0%	4	21.1%		
• Left Fronto- temporal	0	0.0%	5	26.3%	25.000	0.000
• Left Fronto- tempro- parietal	6	100.0%	0	0.0%		
• Left tempro- parietal	0	0.0%	10	52.6%		

*:Chi-square test

Table 7 Comparison of early and late AQ test between reconstructed and non-reconstructed groups

Aphasia test		**Non-reconstructed group**	**Reconstructed group**	**Test value•**	**P-value**
		n = 6	**n = 19**		
Early	Mean ± SD	38.47 ± 0.64	47.88 ± 5.68	− 3.990	0.001
	Range	37.5–39.4	40.73–58.4		
Follow up (3 month later)	Mean ± SD	38.43 ± 0.64	49.18 ± 6.07	− 4.270	0.000
	Range	37.5–39.4	41.3–59.5		
% change	Mean ± SD	− 0.09 ± 0.13	2.69 ± 1.90	− 3.518	0.002
	Range	− 0.26–0	0.21–6.29		

•: Independent t-test

Table 8 AQ test change according to lesion site in reconstructed group

	Aphasia test (% change)		Test value	P-value
	Mean ± SD	Range		
Broca's territory affected	3.86 ± 1.95	0.41 – 6.29	-3.094	0.007
Wernicke's territory affected	0.89 ± 0.38	0.21 – 1.4	3.607	0.002
Central part affected	2.75 ± 0.85	1.54 – 3.55	0.064	0.950

AQ Aphasia Quotient, •: Independent t-test

brain, and it can be used to evaluate the integrity of AF in the speech dominant hemisphere [18].

Aphasia is present in about 21–38% of acute stroke patients and is associated with short- and long-term morbidity and mortality [19]. Even in the most severe cases of post-stroke aphasia, recovery is possible. The greatest degree of language recovery in post-stroke aphasia takes place within the first few weeks [1, 20]. Age, lesion characteristics, education, and possibly sex are clinically recognized predictors of language recovery [21]. These elements, when combined, only account for 40% of the variance; therefore, more elements may be involved in recovery. Earlier research has revealed that the AF in the speech dominant hemisphere supports many language functions [15, 22, 23].

The current study revealed that poststroke aphasia patients with favorable outcomes were those with localized infarction, less severe aphasia at onset, a good early AQ score, and the ability to reconstructed AF using DTI, while patients with poor outcomes were those with large infarct size, more severe aphasia at onset, global aphasia, a poor early AQ score, and non-reconstruction of the left AF by DTI. Nakagawa and colleagues reported a similar finding [24], describing that age, initial aphasia severity, aphasia subtype, lesion location, lesion volume, and stroke severity are potential prognostic factors for post-stroke aphasia.

In this study, there was a statistically significant decrease in the FA value of the left AF of the patients compared with those of the control group but not in the right AF. Several studies have concluded that the AF may be more complex and transmit signals and information in bidirectional manner between the two critical language processing areas [25]. Based on this bidirectional transfer of signals and information, the AF could also play a role in more domain-specific language functions [26, 27], and injury to the AF could cause various types of language dysfunction, including deficits in speech production, comprehension and speech repetition [14, 28].

The current study showed that patients in whom the AF could not be reconstructed had a poorer score in early and late AQ and worse prognosis compared to those in whom the AF could be reconstructed, irrespective of the integrity of the left AF. Kim and colleagues [29] studied 25 patients using DTI and found similar results as our study. Similarly, Tak and colleagues [30] found the same results. Non-reconstruction of the left AF could be due to direct injury and/or Wallerian degeneration following severe neurological insults [8]. Primaßin and colleagues [31] concluded that preservation of the AF was an important predictor for good language recovery. They found that even cases with large insults of the AF were surprisingly capable to recover their language functions with intensive therapy. All these reports emphasize the importance of the AF for the recovery of aphasia after stroke [25, 28, 29]. Lee and colleagues also concluded that DTI-based language-related analysis (the arcuate, superior longitudinal, and inferior frontal occipital fasciculi) may help predict the severity of language impairment in 64 patients with aphasia following stroke [32].

In this study, in the reconstructed group, there was a statistically significant increase in the AQ if the Broca's or Wernicke's territories were affected, with no significant difference if the central part (both parts) was affected. A similar study on the AF's functional role in language in aphasics found that the group with damaged both AF

Table 9 Comparison of FA between reconstructed and non-reconstructed groups

		Non-reconstructed group	Reconstructed group	Test value•	P-value
		n = 6	n = 19		
Left/Right FA Ratio	Mean ± SD	0.00 ± 0.00	0.94 ± 0.04	− 58.139	0.000
	Range	0–0	0.86–1.02		
Left FA to AF	Mean ± SD	0.00 ± 0.00	0.42 ± 0.02	− 53.495	0.000
	Range	0–0	0.38–0.47		
Right FA	Mean ± SD	0.46 ± 0.02	0.45 ± 0.02	0.371	0.714
	Range	0.43–0.5	0.4–0.48		

FA Fractional anisotropy, *AF* arcuate fasciculus, •: Independent t-test segments had the lowest language scores [23]. Bae and colleagues investigated the relationship between the change of aphasia and the changes of both AFs in 35 patients with stroke [33]. The DTI for the AF were performed twice (first time averagely 29.40 days after onset, and second time averagely 181.77 days after onset). They found that the FA values of both AFs decreased, and the diffusivity increased at the chronic stage than those at the subacute stage of stroke. However, a positive correlation was detected between the change of the AQ and the change of the FA value of the left AF, whereas no correlation was observed in the right AF. Ramsey and colleagues [34] also reported that damage to various parts of AF was also associated poorer recovery of various aspects of language. Due to AF's involvement in the auditory feedback circuit, which integrates sensorimotor data for online monitoring of speech production, AF could mediate speech fluency; spontaneous speech, repetition and naming [35]. In their study, Yu and colleagues [23] highlight the significance of the left AF's integrity for the recovery of aphasia, highlighting the possibility of aphasia recovery following stroke if the left AF or its subcomponents are preserved on DTI. A review article aims to analyze the DTI-based studies that have reported the mechanisms of aphasia recovery in stroke patients by demonstrating the changes in the language-related neural tracts, Jang and colleagues observed that although there are various neural tracts for language processing, eight of the ten studies focused only on the role of the AF in the recovery process. Moreover, it appears from the different studies that only one recovery mechanism of aphasia via the restoration of the integrity of the injured AF in the dominant hemisphere was clearly demonstrated. However, because various neural tracts are involved in language processing, there could be other mechanisms that have not yet been elucidated [36]. That is why further studies with different lesion sites and severity levels of injuries to the language-related neural tracts are necessary; as the recovery mechanisms of aphasia in stroke could be dependent on various factors.

This study has some limitations. First, a small number of the patients Second, we did not conduct a follow-up DTI tractography examination to allow estimation of changes in an injured AF. Third, there is a lack of correlation between the DTI of AF and different language domains (word finding, grammatical construction, repetition, reading, word comprehension, and sentence comprehension). So, further studies with larger samples and follow-up DTIT scanning of the AF will allow estimation of changes in an injured AF as regeneration, degeneration, or resolution of surrounding edema. Finally, correlation of patterns of recovery in different language domains with DTI of different AF subcomponents.

Conclusion

In this study, we can conclude that the preservation of AF in the speech dominant hemisphere is important for aphasia recovery. The prognosis of aphasia in patients whose left AF could be reconstructed was better than those whose left AF could not be reconstructed, irrespective of the AF's integrity. That is why, we can assume that evaluation of the DTI of the left AF at early stages of stroke can help in predicting outcome of aphasia.

Abbreviations

AF	Arcuate fasciculus
AQ	Aphasia quotient
DTI	Diffusion tensor imaging
DW-MRI	Diffusion Weighted Magnetic Resonance Imaging
FA	Fractional anisotropy

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Author contributions

All authors have participated in designing the study, acquisition of data, data interpretation and revising. All authors recruited the patients and carried out clinical evaluation, participated in interpretation of the study results and editing the manuscript. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to institutional limitations, yet they are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Research Ethics Committees, Faculty of Medicine, Ain Shams University, Egypt, in December 2019. Participation was voluntary and all contributors received detailed information about the aims of this research work and an informed written consent was obtained prior to the commencement of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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