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Predictive role of subcomponents of the left arcuate fasciculus in prognosis of aphasia after stroke

A retrospective observational study

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Abstract

The relationship between the left arcuate fasciculus (AF) and stroke-related aphasia is unclear. In this retrospective study, we aimed to investigate the role of subcomponents of the left AF in predicting prognosis of aphasia after stroke. Twenty stroke patients with aphasia were recruited and received language assessment as well as diffusion tensor tractography scanning at admission. According to injury of the left AF, the participants were classified into four groups: group A (4 cases), the AF preserved intactly; group B (6 cases), the anterior segment injured; group C (4 cases), the posterior segment injured; and group D (6 cases), completely injured. After a consecutive speech therapy, language assessment was performed again. Changes of language functions among the groups were compared and the relation between these changes with segments injury of the AF was analyzed. After therapy, relatively high increase score percentage changes in terms of all the subcategories of language assessment were observed both in group A and C; by contrast, only naming in group B, and spontaneous speech in group D. Although no statistical difference was demonstrated among the four groups. In addition, there was no significant correlation between improvement of language function with segments injury of the AF. The predictive role of subcomponents of the left AF in prognosis of aphasia is obscure in our study. Nevertheless, it indicates the importance of integrity of the left AF for recovery of aphasia, namely that preservation of the left AF on diffusion tensor tractography could mean recovery potential of aphasia after stroke.

Abbreviations: ABC = Aphasia Battery of Chinese, AF = the arcuate fasciculus, BDAE = Boston Diagnostic Aphasia Examination, DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, FA = fractional anisotropy, MRI = magnetic resonance imaging, WAB = Western Aphasia Battery.

Keywords: aphasia, arcuate fasciculus, diffusion tensor imaging, diffusion tensor tractography, stroke

1. Introduction

Aphasia is one of the most common acquired language deficits in patients with left hemisphere stroke. It has been reported about 24%~48% of patients suffered aphasia in the acute stage of stroke and it remains 10%~18% developed chronic aphasia inspite of a certain percentage of spontaneous recovery which occurs mainly during the first three months after onset.[1,2] The clinical manifestations of patients with aphasia include difficulty in spontaneous speech, auditory comprehension, repetition, naming, reading, writing, calculation, and so on.[3,4] Due to communication barrier, aphasia frequently causes adverse impacts on the health-related daily life of patients.[5,6] Therefore, the prognosis of aphasia has been a remarkable clinical topic for decades.

Traditionally, several cerebral areas such as Broca's and Wernicke's areas, have been known to be responsible for language processing.[7] Constantly emerging literature has attempted to explore valid predictive factors of outcome of stroke-related aphasia by using brain computed tomography (CT), conventional brain magnetic resonance imaging (MRI), and functional neuroimaging. Some potential biomarkers were suggested, including lesion size and location of cerebral cortex function areas,[8–10] initial severity of aphasia,[11,12] the type of stroke and aphasia,[13] and some metabolic factors such as normal return of cerebral blood flow and glucose metabolism of infarcted tissue and perilesional regions, and the degree of successful reperfusion.[14–16] It seems that the most important factors are the lesion size and location, type and initial severity of

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The data used to support the findings of this study are available from the corresponding author upon request.

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aphasia while anagraphic factors (e.g., age, gender, handedness, education level, and intelligence) do not show significant influence on aphasia prognosis.[12,17] However, it remains difficult to accurately predict the prognosis of aphasia because the correlation between brain damage and type of language impairment has not yet been illuminated, and the boundaries among aphasia types are not clear-cut.[7,18]

Advances of in vivo neuroimaging and the emergence of diffusion tensor tractography (DTT) derived from diffusion tensor imaging (DTI) enable three dimensional reconstruction and accurate analysis of the neural fiber tracts at subcortical level in vivo.[19] With advantages,[20] DTI tractography has been used for exploring the relationship between neural tracts and the corresponding functions such as motor, cognition, and language of patients with brain damage and developmental disorder.[21–23]

It is broadly known that language processing in normal depends not only on cortical areas but also on the neural fiber tracts that connect them.[24] So, in recent decades, investigating the role of white matter fibers in aphasia has gradually became a hot study topic.[25,26] Among the white matter fiber bundles associated with language, the arcuate fasciculus (AF) which has been considered as the main neural pathway connecting Wernicke's (the comprehension center) and Broca's areas (the motor center of speech) is relatively known more. In addition, the AF in the dominant hemisphere (usually in the left) is one of the most studied neural tracts in brain and it has been regarded to support some language skills such as semantic comprehension, speech production, repetition, naming, and reading.[27,28]

Growing studies have reported that the AF has a complex anatomy structure. For example, Catani et al[29] reported a three-segment model of the AF: one direct long segment and two short indirect segments. Specially, the direct pathway connects Wernicke's and Broca's areas, and the anterior segment links Broca's with Geschwind's areas (i.e., inferior parietal lobule) while the posterior segment links Geschwind's with Wernicke's areas. Different segments could play different roles in language processing. (Fig. 1B). In the same year, Makris et al[30] proposed a four-segment model which is generally similar to those of Catani et al.[29] And subsequently, Glasser and Rilling[31] suggested a two-segment model which has a relatively low detection rates of the AF.[32] However, the three-segment model of the AF is widely recognized and used in language research because of a relatively higher detection rates of the AF.[33]

In 2011, Kim et al[34] reported that DTI tractography could provide useful information on evaluating the occurrence or severity of the AF injury in stroke patients with aphasia. Indeed, some other studies[35–37] have also used DTI tractography to investigate the relation between aphasia with the AF, and suggested that the left AF could play an important role in the presence, recovery, and predicting prognosis of aphasia. Nevertheless, no consensus has yet reached and the relationship between AF with aphasia is still unclear. Moreover, to our knowledge, few studies have reported the role of segments of the left AF in predicting prognosis of aphasia secondary to stroke and this field requires further elucidation.

Hence, in the current study, we aimed to furtherly investigate the relation between the prognosis of aphasia with the AF in the dominant hemisphere by using DTI tractography, and mainly focus on the predictive value of the subcomponents of the AF in prognosis of aphasia after stroke.

2. Methods

2.1. Participants

Twenty participants (17 males; mean age 53.55 ± 8.55 years, range 35~68 years; mean 100.35 ± 109.36 days from stroke onset; cerebral infarction, 15 patients; intracranial hemorrhage, 5 patients) were recruited according to the inclusive criteria: first, right-handedness and normal conscious; second, first ever left hemisphere stroke, either hemorrhagic, or ischemic, confirmed by MRI; third, presence of aphasia; fourth, no history of psychiatric disorder, head trauma, or other brain injury; and fifth, able to tolerate language assessment and MRI scanning session. The detailed characteristics of all patients are provided in Table 1. This study protocol was approved by the Ethics Committee of Jinan University First Affiliated Hospital, and the informed consent form was signed by one relative of each patient.

2.2. DTI tractography evaluation

The DTI sequence, as well as conventional brain axial T1-weighted images, T2-weighted images, and diffusion-weighted images (DWI) was acquired on a 3.0 Tesla Magnetic Resonance Imaging System (General Electric Medical Systems) by using a standard eight-channel phased-array head coil. A single-shot echo planar imaging sequence in 47 contiguous slices parallel to the anterior–posterior (AC–PC) plane was collected for each of the 25 noncollinear diffusion sensitizing gradients.[38,39] The DTI parameters were as follows: time of repetition (TR) = 5000 ms, time of echo (TE) = 68.0 ms, acquisition matrix = $96 \times 96\,mm^2$, reconstructed to matrix = 128×128 matrix, field of view (FOV) = $25.6 \times 25.6\,mm^2$, b = 1000 s/mm^2, number of excitations (NEX) = 1, slice thickness/slice spacing = 3 mm/0 mm. It took 135 seconds for DTI scanning.

Other MR sequence parameters were as follows: T1WI, TR = 360 ms, TE = 15.0 ms; T2WI, TR = 2200 ms, TE = 22.3 ms; DWI, TR = 3000 ms, TE = 71.0 ms; matrix = $128 \times 128\,mm^2$; FOV = $25.6 \times 25.6\,mm^2$; NEX = 1; and slice thickness = 4 mm with no inter-slice gap. In addition, a 3D brain volumes (BRAVO) T1-weighted sequence (TR = 8.2 ms, TE = 3.2 ms, FOV = $240 \times 240\,mm^2$, matrix = $25.6 \times 25.6\,mm^2$, slice thickness = 1.0 mm without gap) was scanned to acquire high resolution structural images for anatomical determinations.

The original DTI data were transferred into and processed in a dedicated workstation (Advantage Windows version 4.4) using Functool 9 (GE Medical Systems, Chicago, IL).[40,41] For reconstructing the bilateral AF, two regions of interest (ROIs) for use of a deterministic fiber-tracking approach[32,42] were selected: the seed ROI was manually placed on the posterior parietal area of the superior longitudinal fascicle, and the target ROI was located in the posterior temporal lobe.[43,44] Fiber tracking was initiated with a fractional anisotropy (FA) >0.18 and apparent diffusion coefficient (ADC) >0.01 at the center of a seed voxel. The maximum steps were 160.

Following the fiber tracking approach above, we collected and successfully reconstructed the bilateral AF of a normal adult male as a control (Fig. 1).

As shown, the AF connects Wernicke's and Broca's areas via Geschwind's area. This anatomy structure drawn in our study is consistent with the description of Catani et al.[29] Then, according to the left AF injury, the participants were classified into four groups: group A (patient number, 1–4), the AF was preserved intactly (i.e., no disconnection between Wernicke's and Broca's

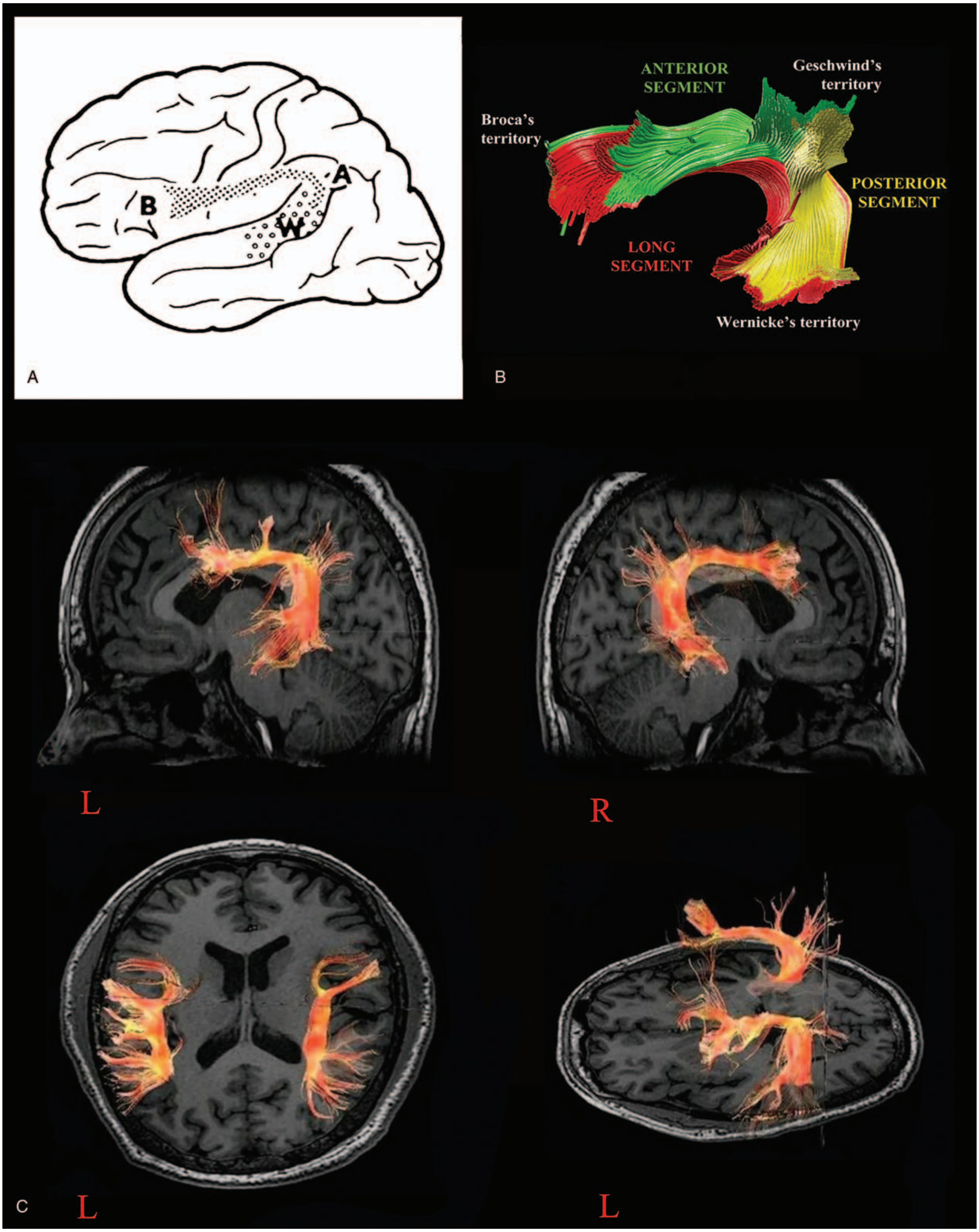

Figure 1. The outline of the AF. (A), Norman Geschwind's representation of the language network in 1970[45]; (B) the tractography reconstruction of the AF using two ROIs approach by Catani et al[29]; and (C) the bilateral AF of a 34 year-old normal man demonstrated on 3D BRAVO T1 images in this study.

areas, 4 cases, 2 males); group B (patient number, 5–10), the anterior segment injured (i.e., a disconnection between Broca's and Gerchwind's areas, 6 cases, 5 males); group C (patient number, 11–14), the posterior segment injured (i.e., a disconnection between Wernicke's and Gerchwind's areas, 4 cases, 4 males); and group D (patient number, 15–20), the AF was completely injured (i.e., the left AF couldn't be reconstructed, 6 cases, 6 males). Notably, disruption of the DTT

Table 1

Patient characteristics.

No.	Age / gender	Edu-level (years)	Poststroke (days)	Type of stroke	Lesion location	Hemiplegia	Type of aphasia	BDAE rank	Therapy time (days)
1	35/M	12	15	Infarction	Basal ganglia, temporal lobe, corona radiata	R	Broca's	1	81
2	58/F	16	15	Infarction	Basal ganglia, insula	N	Global	1	87
3	55/F	9	311	ICH	Basal ganglia	N	Conduction	3	61
4	48/M	12	9	Infarction	Basal ganglia, corona radiata	R	Broca's	1	90
5	60/M	12	46	Infarction	Frontotemporal parietal lobe	N	Conduction	2	95
6	42/M	16	52	Infarction	Frontotemporal lobe, insula	N	Anomic	3	125
7	63/M	12	310	Infarction	Temporal and parietal lobe	R	MTA	2	58
8	50/F	12	16	Infarction	Temporal and parietal lobe, corona radiata	N	Broca's	2	113
9	60/M	12	30	Infarction	Basal ganglia, corona radiata	R	Broca's	1	56
10	42/M	16	56	ICH	Frontotemporal lobe, insula	N	Anomic	1	62
11	68/M	12	69	Infarction	Basal ganglia, temporal and parietal lobe, corona radiata	N	TSA	2	65
12	49/M	16	10	Infarction	Temporo-occipital junction	N	Wernicke's	2	89
13	63/M	16	8	Infarction	Temporal and parietal lobe, corona radiata	R	Global	1	82
14	48/M	12	116	ICH	Temporal parietal lobe, insula	N	Broca's	1	64
15	60/M	9	58	ICH	Basal ganglia, frontotemporal lobe	R	Global	1	59
16	55/M	12	152	Infarction	Basal ganglia, frontoparietal lobe, insula	R	Broca's	1	58
17	50/M	16	123	Infarction	Basal ganglia, frontotemporal parietal lobe	R	Broca's	1	65
18	47/M	12	360	ICH	Frontotemporal lobe, insula	R	Wernicke's	1	75
19	63/M	12	75	Infarction	Frontotemporal parietal lobe	R	Global	1	78
20	55/M	12	176	Infarction	Basal ganglia, frontotemporal parietal lobe	R	Global	1	108

BDAE = Boston Diagnostic Aphasia Evaluation, score rank range 0~5, a low score rank means a high level severity of aphasia, Edu- = education, F = female, ICH = intracerebral hemorrhage, M = male, MTA = mixed transcortical aphasia, N = without hemiplegia, R = right hemiplegia, TSA = transcortical sensory aphasia.

integrity for neural tracts commonly indicates injury of the neural tract and the nonreconstruction of the AF could be ascribed to severe injury of the AF.[45] The representative cases of four types of the left AF injury are shown in Figure 2.

2.3. Language assessment and speech therapy

The standardized Aphasia Battery of Chinese (ABC) was used for language assessment and the Boston Diagnostic Aphasia Examination (BDAE) for evaluating the severity of aphasia[46] before and after a consecutive speech therapy. The standardized ABC, a revised version of Western Aphasia Battery (WAB) adapted to Chinese culture, is the most commonly used scale in China for aphasia assessment based on well-established reliability and validity.[47] It's composed of several subcategories of spontaneous speech, auditory comprehension, repetition, naming, writing, calculation, and summary of aphasia examination. In this study, we mainly focus on spontaneous speech, auditory comprehension, repetition (words and sentences repetition) and naming, as these four subcategories are considered to be probably related with the AF mentioned above.

After the first language assessment finished, all patients received speech therapy (mean 78.6 ± 20.2 days) including spontaneous speech, auditory comprehension, repetition, naming, writing, reading, and calculation training. The protocols of speech therapy were respectively designed based on the results of language evaluation of each patient. The therapy course was conducted for 1 hour per session, for twice a day and 5 days a week. At the ending of therapy, language assessment was performed again. Calculate and compare score percentage of the four subcategories according to a formula: the score percentage = (practical score/total score of each subcategory) × 100%.

2.4. Statistical analyses

The Statistical Package for the Social Sciences for Windows (SPSS, version 20.0) was used for all statistical analysis. All categorical variables (e.g., gender, type of stroke, type, and severity of aphasia among the four groups patients) were analyzed with Fisher's exact test. And all continuous variables (e.g., age, time from stroke onset, education level, and time of speech therapy) were analyzed with One-way ANOVA analysis. The paired t test was used for comparing the difference in the results of the twice language assessment. We also use one-way ANOVA analysis to determine significant differences in score percentage of language assessment among all of the 4 groups patients. Furthermore, the Spearman rank tests correlation analysis was performed to assess the correlation between score percentage changes after speech therapy and segments of the left AF injury. The statistical significance was accepted for P-values $< .05$.

3. Results

The demographic data are summarized in Table 2. No statistic differences are found among the four groups in age (A–B, $P = .510$; A–C, $P = .218$; A–D, $P = .307$; B–C, $P = .475$; B–D, $P = .676$; C–D, $P = .730$), level of education (A–B, $P = .482$; A–C, $P = .304$; A–D, $P = .957$; B–C, $P = .664$; B–D, $P = .399$; C–D, $P = .241$), time from stroke onset (A–B, $P = .973$; A–C, $P = .645$; A–D, $P = .343$; B–C, $P = .638$; B–D, $P = .274$; C–D, $P = .155$), and speech therapy time (A–B, $P = 1.000$; A–C, $P = .997$; A–D, $P = .994$; B–C, $P = .984$; B–D, $P = .978$; C–D, $P = 1.000$). As well, there is no significant difference in gender ($\chi 2 = 4.215$, $P = .211$), type of stroke ($\chi 2 = .901$, $P = 1.000$), type of aphasia ($\chi 2 = 16.748$, $P = .594$) and severity of aphasia ($\chi 2 = 8.672$, $P = .098$).

Results of the first and follow-up ABC demonstrate significant improvements in all of subcategories (spontaneous speech, before

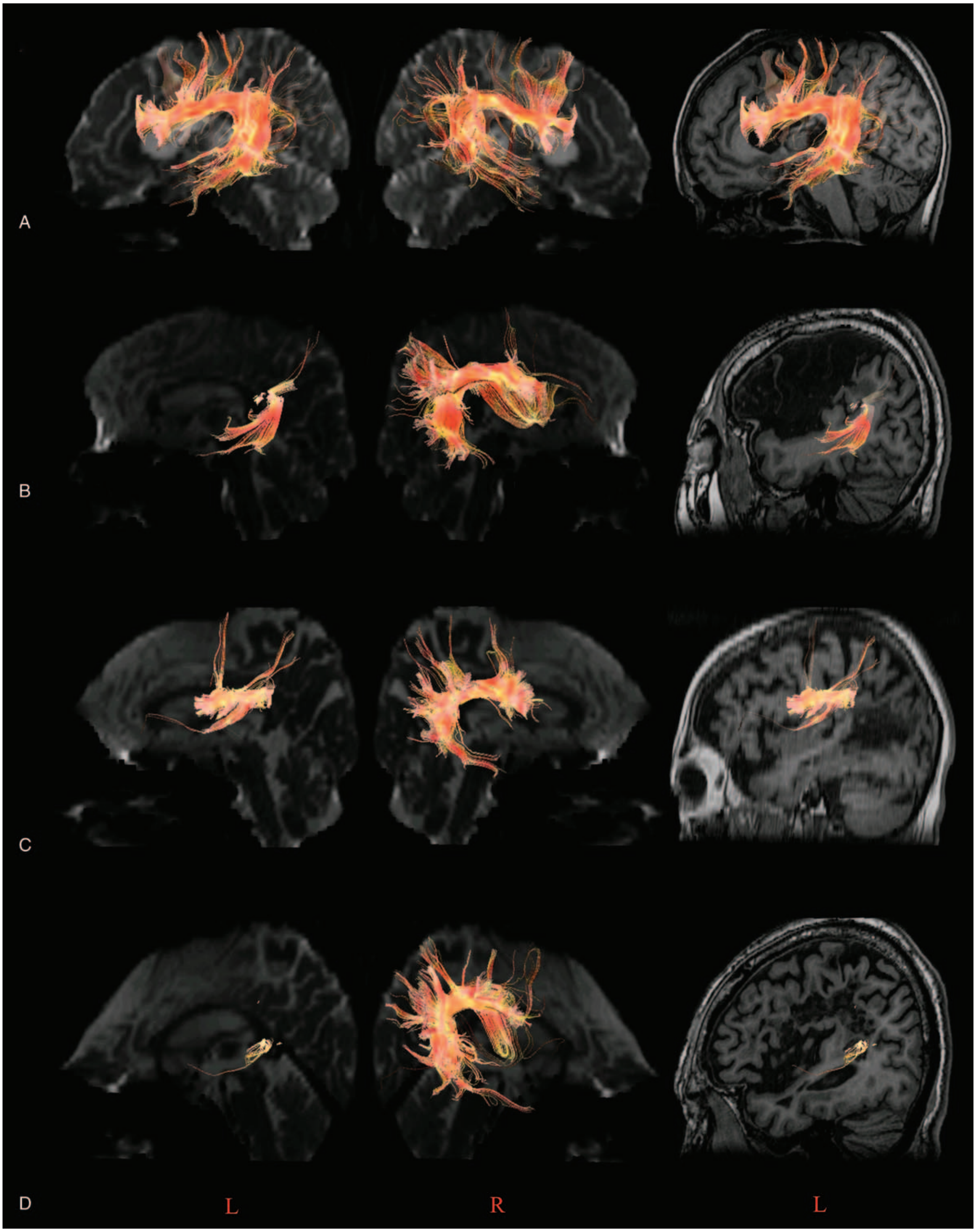

Figure 2. The representative cases in the four types of the left AF injury.

55.00% ± 22.18, after 75.94% ± 12.72, P = .002; auditory comprehension, before 39.53% ± 22.52, after 59.31% ± 24.58, P = .001; repetition, before 31.75% ± 24.57, after 55.90% ± 25.54, P < .001; and naming, before 16.83% ± 15.70, after 40.37% ± 24.67, P = .001) after speech therapy.

Concretely, before speech therapy, the score percentage of the four subcategories of language assessment in group A and B is higher than in group C and D. Notably, group A has the lightest severity of aphasia in relative while group D has the heaviest. After speech therapy, all of the four groups patients have some extent improvement of language function.

Furtherly, the score percentage changes in terms of the four subcategories in group A and C are higher than in group B and D. By contrast, it has relatively high increase of score percentage

Table 2

Demographic data of four groups patients*.

Variables	A	B	C	D	P
Age (years)	49.0±10.2	52.8±9.5	57.0±10.0	55.0±6.0	.608
Range	35~58	42~63	48~68	47~63	
Gender (F/M)	2/2	1/5	0/4	0/6	.211
Education level (years)	12.3±2.9	13.3±2.1	14.0±2.3	12.2±2.2	.584
Range	9~16	12~16	12~16	9~16	
Time from stroke onset (days)	87.5±149.0	85.0±111.2	50.8±51.9	157.3±108.9	.484
Rang	9~311	16~310	8~116	58~360	
Type of stroke					1.000
Type of aphasia					.594
Severity of aphasia					.098
Time of therapy (days)	79.8±13.0	84.8±30.3	75.0±12.5	73.8±18.6	.817
Range	61~90	56~125	64~89	58~108	

* Values are given in Mean±SD.

changes only in terms of naming for group B as well as only in terms of spontaneous speech for group D. Although no significant difference in the score percentage changes is observed among groups (spontaneous speech: A–B, $P=.146$; A–C, $P=.727$; A–D, $P=.865$; B–C, $P=.271$; B–D, $P=.149$; C–D, $P=.831$; auditory comprehension: A–B, $P=.813$; A–C, $P=1.000$; A–D, $P=.729$; B–C, $P=.775$; B–D, $P=.942$; C–D, $P=.693$; repetition: A–B, $P=.649$; A–C, $P=1.000$; A–D, $P=.771$; B–C, $P=.811$; B–D, $P=.987$; C–D, $P=.873$; and naming: A–B, $P=.631$; A–C, $P=.764$; A–D, $P=.053$; B–C, $P=.422$; B–D, $P=.093$) except significant difference in terms of naming between group C and D (C–D, $P=.028$). (Tables 3 and 4; Fig. 3)

In addition, the score percentage changes is not significantly correlated with segments of the left AF injury (spontaneous speech, $r=0.352$, $P=.128$; auditory comprehension, $r=0.136$, $P=.566$; repetition, $r=0.331$, $P=.154$ and naming, $r=-0.078$, $P=.744$).

4. Discussion

In the current study, we preliminarily explored the role of different subcomponents of the left AF in predicting prognosis of aphasia after stroke. The results show no clear correlation between segments injury of the left AF and the prognosis of aphasia. This seems to run counter to our expectation that different segments of the AF could play different roles in predicting prognosis of aphasia, just as in physiological language processing. Nevertheless, observing the different changes of language functions among the groups, it still implies the importance of integrity of the AF in the dominant hemisphere for recovery of aphasia after stroke. We hence suggest the tendency that relatively strong recovery potential could occur along with preserved architecture of the left AF; conversely, when lesion location involves the AF, especially in the case of discontinuation or non-reconstruction on DTI tractography, it could present weak recovery potential.

Table 3

The score percentage of the subcategories among the 4 groups before and after speech therapy*.

Score (%)	A	B	C	D	P
Before					
Spontaneous-speech	53.77±31.29	68.24±15.35	55.67±29.61	42.14±10.52	.253
Auditory-comprehension	50.86±26.77	56.18±13.79	22.41±10.03	26.72±19.47	.020
Repetition	32.25±22.46	50.83±24.79	31.00±26.62	12.83±9.22	.050
Naming	21.49±18.96	29.78±14.07	10.21±11.62	5.18±5.11	.022
After					
Spontaneous-speech	81.13±8.71	78.93±12.48	78.77±14.23	67.61±13.04	.303
Auditory-comprehension	82.33±11.20	68.82±9.52	56.03±29.86	36.64±20.92	.009
Repetition	64.75±21.09	66.00±22.95	69.50±28.97	30.83±9.77	.006
Naming	52.44±20.61	55.59±16.63	44.66±28.06	14.23±8.96	

* Values are given in Mean±SD.

Table 4

The score percentage changes of the subcategories among the 4 groups before and after therapy*.

ΔScores (%)	A	B	C	D	P
Spontaneous-speech	27.36±22.88	10.69±10.24	23.11±18.83	25.47±16.74	.379
Auditory-comprehension	31.47±25.98	12.64±6.46	33.62±27.13	9.91±2.91	.087
Repetition	32.50±18.65	15.17±9.24	38.50±32.05	18.00±4.15	.142
Naming	30.95±11.11	25.81±18.42	34.45±24.99	9.04±7.53	.096

* Values are given in Mean ±SD.

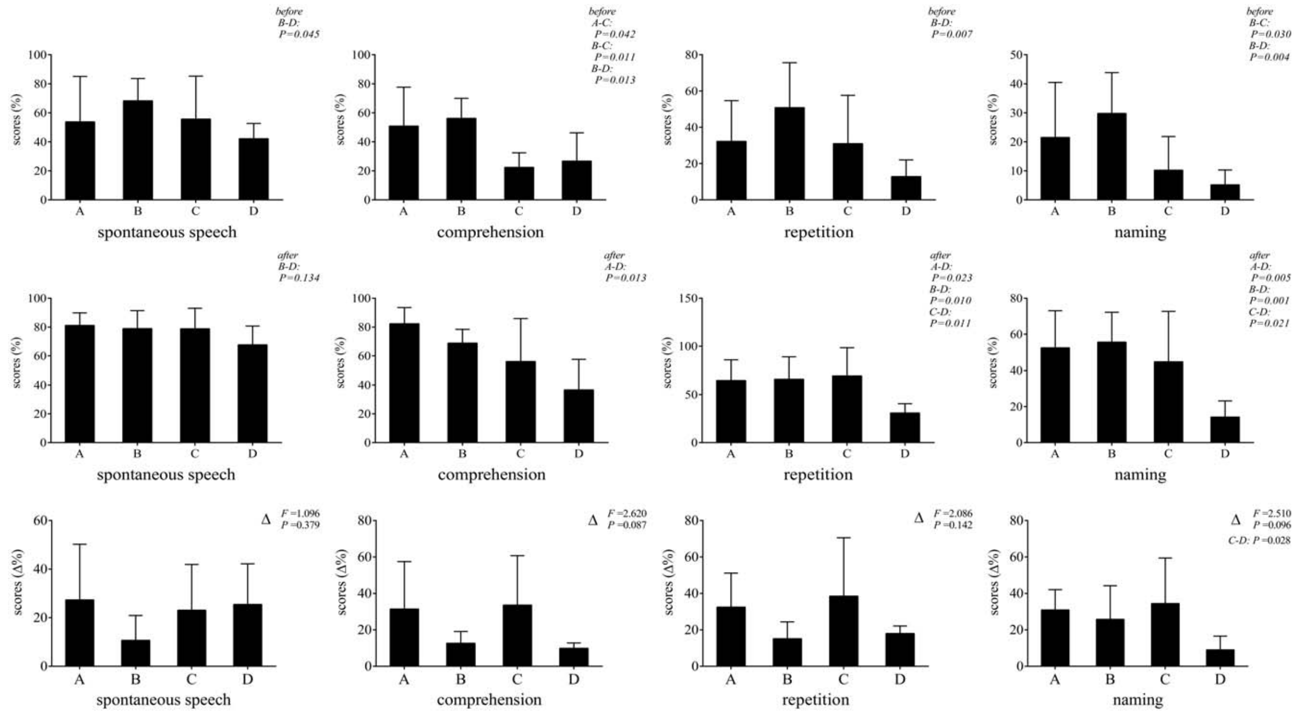

Figure 3. The score percentage of subcategories among the four groups before and after speech therapy. (Δ: the score percentage changes).

Since identified by Catani and Mesulam,[45] because of the special tract that connects Wernicke's and Broca's areas, the AF had been considered to play an important role in transmitting information from Wernicke's area to Broca's areas, and thus, it was mainly responsible for speech repeating for a long time. Damage to the AF would cause a special type of aphasia: conduction aphasia defined as a language deficit characterized by poor repetition with a relative preservation of fluent spontaneous speech and good comprehension.[41] In fact, accumulating studies have suggested that the AF may be more complex and transmit information in bidirection between the two critical language processing centers.[48] Based on this bidirectional transfer of information, the AF could also play a role in more domain language functions[26,49] and injury of the AF could cause various types of language dysfunction (e.g., deficits of comprehension or speech production) more than just difficulty of speech repetition.[34,50]

As for recovery of aphasia, some properties of the AF may be important factors in predicting prognosis of aphasia. Hosomi et al[51] recruited 13 stroke patients with aphasia to examine the clinical value of DTI tractography in assessing aphasia, and suggested that loss of leftward asymmetry of fiber number of the AF on DTI tractography could predict prognosis of aphasia in acute stage of stroke. Schlaug et al[52] observed increases in the number and volume of the AF fibers that were accompanied by improvements in verbal expression. Marchina et al[50] collected thirty chronic stroke patients and estimated the volume of the left AF, uncinate fasciculus and extreme capsule. They found that lesion location and size of the left AF were significant variable for predicting language function in terms of rate, informativeness, efficiency of speech, and naming ability. In the same year, Forkel et al[53] found that the language function of patients with aphasia at 6 months after stroke onset was strongly related to the degree of lateralization of the AF. Wang et al[54] found that lesion load (lesion site and size) of the AF could be a critical factor of determining poor fluency and naming outcomes of aphasia poststroke. Recently, Hillis et al[55] reported that the lesion load in the left AF was associated with poorer naming outcome, indicating that recovery of naming could be negatively influenced by lesion load of the left AF in acute poststroke aphasia.

Specially, Kim et al[56] recruited 25 patients and used DTT for investigating whether the integrity of the AF in the left hemisphere could be a factor in predicting of prognosis of aphasia after stroke. They found that patients whose left AF could be reconstructed on DTT had better outcome of aphasia than the patients whose left AF could not be reconstructed, irrespective of integrity of the AF. This study suggested that it could be helpful in predicting prognosis of aphasia in the early stage of stroke by using DTT to evaluate of the left AF. Coincidentally, Tak et al[37] found that patients with discontinuation of integrity or nonconstruction of the left AF displayed on DTT had poorer language assessment scores than the patients who didn't show those findings. They proposed that discontinuation or nonconstruction of the left AF was a critical factor for language function of the stroke patients with aphasia. Similarly, Primaßin et al[57] reported that preservation of the AF was an important predictor for good language recovery. Even though, they also pointed out that even patients with large lesions in the AF were able to recover their language functions during intensive therapy. Obviously, all of these rare reports highlight the importance of the preservation or residual structure of the AF for recovery of aphasia after stroke. In the current study, we observe that the level of language function at baseline in group D which the left AF could not be reconstructed due to severe injury is lower compared with other groups; meanwhile poorer improvement presented after speech therapy. These results indicate that the preservation of AF in the dominant hemisphere is important for aphasia recovery, and the findings of our study are coincided with the opinions of the previous studies described above.

Moreover, it's also worth noting that, several literatures ever argued that the AF might not be as important as thought, or even not necessary for recovery of speech repetition of stroke patients with aphasia.[34,48,58] This viewpoint is obviously unsuitable for the current study.

Since the three-segment model was proposed by Catani et al,[29] which subsequently was validated by using intracortical stimulation, postmortem dissections and functional MRI,[59,60] the role of subcomponents of the AF has been investigated. Catani et al[29] suggested that the functions of these different segments would differ in language: the direct long segment could be related with phonological functions (e.g., speech repetition) while the anterior indirect pathway could be involved in vocalization of semantic information and the posterior indirect pathway could be involved in auditory comprehension.

Some other studies have also explored the relation between segments of the AF with language function successively, and support for the viewpoint of Catani et al[29]. For example, Dick and Tremblay[61] reported that the long segment of the AF plays a crucial role in language function. Catani et al[62] reported that different subcomponents of the AF have different developmental sequences: the anterior segment matures within the first year of life while the direct and posterior segments mature later during development. The anterior segment was proposed to be responsible for informative actions and the direct and posterior segments were respectively devoted to pragmatic integration and syntactic processing. However, Tak et al[63] found that the posterior segment of the AF tract developed firstly and the direct long segment matured last in identical hemispheres. They also pointed out that these sequential developmental patterns seemly supported the opinion that acquisition of comprehensive ability of language precedes expressive ability. Specially, they suggested that last maturation order of the direct segment could be related to higher cognitive functional processes of language, because of connecting the comprehension center of Wernicke's area with the expression center of Broca's area. This viewpoint indicates that a poor outcome of language would occur along with severe injury of the AF, and this may be one of the mechanisms that the patients in group D did not show a good recovery of aphasia.

Several reports on stroke also pointed out the relation between segments of the AF and prediction outcome of aphasia. Fridriksson et al[64] suggested that the primary structural damage in the posterior segment of the left AF was most closely associated with impaired speech repetition. In a later study, Fridriksson et al[65] furtherly found that the anterior segment of the left AF was a strong factor of predicting impaired speech fluency in patients with aphasia, namely that damage to the anterior segment had a particularly negative impact on speech fluency of aphasia. Sequently, Basilakos et al[36] found damage to the aslant area and anterior segment of the AF was associated with speech fluency. They hence suggested a synergistic association of these regions with speech fluency in stroke-induced aphasia based on a hypothesis that the AF could mediate speech fluency depending on playing a role in auditory feedback circuit for integrating sensorimotor information for online monitoring of complex speech production.[66]

However, contrary to these findings, Forkel et al[33] reported that the volume of the other segments in the right and left hemisphere did not show correlation with recovery except that the volume of the long direct segment of the right AF in the acute stage of stroke was an important factor for predicting recovery of aphasia at 6 months after onset. And, Ivanova et al[26] conducted a study included thirty seven stroke patients with aphasia. They also found no significant relation between the anterior segment of the AF with language processing while the temporal portion (i.e., posterior segment) of the AF was significantly associated with both comprehension and speech production equally at the word and sentence level. In our study, the results showed no significant relationship between improvement of language function with segments of the left AF injury in stroke patients with aphasia. For example, a relatively high improvement in terms of all the four subcategories of language function presented in group C which the posterior segment of the left AF injured, while less increase took place in group B which the anterior segment injured. We think this difference could be due to the contribution of ceiling effects that a comparatively high level of language ability at the baseline leaves small possibilities for significant improvements at the post test, as described in a four single-case study of Primaßin et al.[57]

5. Conclusions

In the current study, we found no significant relation between the prognosis of aphasia with segments injury of the left AF. Nevertheless, the findings of this study indicate the importance of integrity of the left AF for recovery of aphasia, namely that preservation of the left AF on DTT could mean recovery potential of aphasia after stroke. This will provide useful information for clinicians on prognostic judgment and designing rehabilitation strategies.

In addition, several limitations of this study should be mentioned. First, a small sample is the major limitation. However, it's difficult to recruit the cases with typical injury of different segments of the AF in clinical trials. Second, the parameter of DTI (i.e., 25 noncollinear diffusion sensitizing gradients) and the fiber-tracking approach (i.e., a deterministic approach). Although some studies also adopted a parameter of 25 diffusion sensitizing gradients and it's reported that the deterministic method could adequately detect the AF, the probabilistic tracking algorithm as well as much more diffusion sensitizing gradient parameter (i.e., 32 or more) seems more popular. Third, we did not assess the impact of the lesions involved cerebral areas and other neural tracts associated with language function (e.g., superior longitudinal fasciculus, uncinate fasciculus and inferior longitudinal fasciculus). We also did not conduct a follow-up DTI tractography examination, the role of the AF and the possible mechanisms of recovery of aphasia remain unclear in this study. So, further studies with larger samples and optimized parameters as well as studies combinated functional neuroimaging techniques and DTI tractography are warranted to explore the role of white matter fiber in aphasia.

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Author contributions

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