

Correlation between focal lesion sites and language deficits in the acute phase of post-stroke aphasia

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Abstract

Introduction: Focal lesion sites can predict the language function of patients with aphasia during the subacute or chronic phases. However, the relationship between focal lesion sites and language deficits in the acute phase remains unclear. Therefore, our study aimed to investigate the relationship between focal lesion sites and fluency, auditory comprehension, repetition and naming deficits in patients with acute aphasia to further understand the pathophysiological mechanism of aphasia.

Material and methods: We included a total of 52 patients with acute aphasia who had their first-ever stroke between June 2018 and June 2021 to investigate the association between focal lesion sites and fluency, auditory comprehension, repetition and naming deficits. Language function was assessed by the Western Aphasia Battery scale within one month of onset. The lesion sites were independently assessed by three professional speech and language pathologists according to the main sulcus of the brain within 1-2 days after stroke.

Results: Lesions involving the superior temporal gyrus, middle frontal gyrus, inferior frontal gyrus, precentral gyrus, postcentral gyrus, supramarginal gyrus, angular gyrus and insula were significantly associated with low fluency. Lesions involving the superior temporal gyrus, middle temporal gyrus, inferior temporal gyrus, middle frontal gyrus, inferior frontal gyrus, supramarginal gyrus and angular gyrus significantly resulted in auditory comprehension impairment. Lesions involving the superior temporal gyrus, middle temporal gyrus, middle frontal gyrus, inferior frontal gyrus, precentral gyrus, postcentral gyrus, supramarginal gyrus, angular gyrus and insula significantly resulted in repetition and naming deficits.

Conclusions: Our study suggests that focal lesion sites could lead to different language function impairments in the acute phase of post-stroke aphasia, which adds to our understanding of speech pathology and provides a direction for future research and treatment.

Key words: aphasia, stroke, brain imaging, lesion site, language function.

Introduction

Aphasia is a language disorder mainly caused by stroke. Approximately 21% to 38% of stroke patients

suffer from aphasia, which affects not only their daily communication, but also their social activities and quality of life [7]. The brain is a complex network structure that uses multiple regions to perform dif-

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ferent tasks, especially language tasks. Studies have shown that performing a language task requires the participation of multiple language-related brain regions, which means that different language regions may have different roles [24,29,30,36]. Therefore, damage to the focal language regions of the brain may cause specific language deficits. Researchers have also emphasised that understanding the role of the specific brain regions related to language after aphasia can help in understanding the pathophysiological mechanism of aphasia and serve as the basis for neuroregulatory strategies in aphasia [35].

Traditionally, Broca's area and Wernicke's area have been regarded as the classical language areas that play an important role in fluency and comprehension, respectively. However, existing studies have shown that other parts of these areas, such as the insula, also contribute to language deficits [6,14]. This indicates that understanding the role of broader language areas is crucial.

Recent studies have shown that focal lesion sites are related to specific language deficits [1,2,17]. For example, one study has shown that damage to the inferior triangularis and inferior operculum of the frontal cortex, supramarginal cortex and insula results in poor fluency and that lesions involving the parietal cortex, angular cortex, temporal middle cortex, sagittal stratum and temporal superior cortex are associated with poor comprehension [35]. However, these studies explored the relationship between lesion sites and language deficits in the subacute or chronic phases, while this relationship in the acute phase is still unknown. Therefore, the purpose of our study is to investigate the relationship between focal lesion sites and specific language deficits in the acute phase based on imaging data obtained within 1-2 days after stroke.

Material and methods

Participants

We retrospectively collected the data of individuals admitted to the Hebei General Hospital between June 2018 and June 2021. The inclusion criteria were as follows: 1) first-ever stroke, 2) aphasia, 3) lesions confined to the left hemisphere, 4) acute phase \leq 1 month, 5) native Chinese speaker, 6) right-handed, 7) age \geq 18 years and 8) imaging data obtained by either magnetic resonance imaging (MRI) or computed tomography (CT) within 1-2 days after stroke. Patients

were excluded if they had a prior history of psychological or neurological disease. We had no restrictions on the severity of the aphasia or type of aphasia. We followed the principles of the Strengthening the Reporting of Observational Studies in Epidemiology initiative (Supplementary Appendix A) [37].

Measures

Demographic information, including age, sex and education level, was extracted. Clinical features, including the time since onset, type of stroke (infarction or haemorrhage), type of aphasia (Broca's aphasia, Wernicke's aphasia, global aphasia, etc.), risk factors, stroke severity, language function, lesion site, dysphagia, dysarthria and cognitive impairment, were also extracted. The risk factors mainly involved high blood pressure, diabetes, hyperlipidaemia, coronary heart disease, atrial fibrillation, smoking and drinking.

Stroke severity was assessed by the Chinese version of the National Institute of Health Stroke Scale within 1-2 days after stroke. The scale consists of 15 items, including the level of consciousness, eye movements, integrity of visual fields, facial movements, arm and leg muscle strength, sensation, coordination, language, speech and neglect [21]. The score for each item ranges from 0 to 2, 0 to 3, or 0 to 4, and the total score ranges from 0 to 42. The higher the score, the more severe the stroke.

Language function was assessed by the Chinese version of the Western Aphasia Battery (WAB) scale when the patients came to the rehabilitation department within one month after stroke [34]. We mainly included fluency, auditory comprehension, repetition, naming ability and the aphasia quotient (AQ) in our study. The AQ was defined as the severity of the aphasia, ranging from 0 to 100. It was obtained by calculation. The formula was as follows: (spontaneous speech + auditory comprehension/20 + repetition/10 + naming/10) multiplied by 2.

Three professional speech and language pathologists blind to the results of the patients' language function independently assessed the lesion sites based on their experience and the patients' imaging data. Recognition of the lesion sites was mainly based on the main sulcus of the brain. During the above process, differing opinions were resolved through negotiation. The imaging data were derived from high-resolution MRI or CT scans. The main

areas of interest related to language that we chose were the superior temporal gyrus, middle temporal gyrus, inferior temporal gyrus, superior frontal gyrus, middle frontal gyrus, inferior frontal gyrus, precentral gyrus, postcentral gyrus, supramarginal gyrus, angular gyrus and insula.

Dysphagia was identified by the water swallow test [12]. Patients were given 3 oz of water and asked to drink from a cup without interruption. Coughing during the test or for one minute after completion or the presence of a post-swallow wet hoarse voice quality was scored as abnormal.

Dysarthria was assessed by the Chinese version of the Frenchay Dysarthria Assessment 2 [19]. This is a standardised tool for diagnosing dysarthria and contains seven sections: reflexes, respiration, laryngeal, lips, palate, tongue and intelligibility. Each section includes items that are assessed at rest, in motion and during speech. The result of each item contains five grades ranging from A to E, with A being considered normal and E considered the worst.

Cognitive impairment was assessed by the Chinese version of the Mini-Mental State Examination scale, which includes orientation, memory, attention and computation, recall and language ability [3]. A score of 25-30 is considered normal, and a score < 25 is considered to indicate cognitive deficits.

Statistical analysis

A descriptive analysis was used to analyse the baseline indicators of the patients, including their age, sex, education level, time since onset, type of stroke, type of aphasia, risk factors, stroke severity, dysphagia, dysarthria, cognitive impairment and language function. Since the age, time since onset, stroke severity and language function were continuous data, we used the mean (standard deviation) or median (interquartile range) to express these results.

The quantitative analysis methods used included the Wilcoxon rank sum test, the Kruskal-Wallis H test, Spearman's rank correlation test and multivariate linear regression analysis. The Wilcoxon rank sum test was used to analyse the relationship between lesion sites and fluency, auditory comprehension, repetition and naming deficits because each language score comprised continuous data and did not conform to the normal distribution. In order to further explore the influence of other variables on aphasia, the Wilcoxon rank sum test was used to explore the rela-

tionship between sex, type of stroke, risk factors, dysphagia, dysarthria and cognitive impairment and the AQ. The Kruskal-Wallis H test was used to explore the relationship between education level and the AQ. Spearman's rank correlation test was used to explore the relationship between age, stroke severity and total number of language-related lesion sites and the AQ. Multivariate linear regression analysis was used for risk factors that significantly affected AQ. The SPSS 21.0 software was used for the statistical analysis. A *P*-value < 0.05 was considered statistically significant.

Results

A total of 383 patients with aphasia were admitted to the rehabilitation department from June 2018 to June 2021. According to the inclusion and exclusion criteria, 52 patients were included in total. The reasons for exclusion in the screening process were as follows: 19 patients were non-stroke, 90 patients were non-first-stroke, 3 patients were not right-handed, 204 patients had no initial imaging data, 5 patients had lesions involving the right cerebral hemisphere, and 10 patients were not in the acute phase (Fig. 1).

Regarding the 52 patients, the mean age was 57.40 (13.10). The gender distribution was 35 males, accounting for 67%, and 17 females, accounting for 33%. In terms of the education level, 8 patients had a bachelor's degree, 14 patients had a high school degree, 16 patients had a junior high school degree, 11 patients had a primary school degree, and 3 patients were illiterate. The median time since onset was 15.50 (9.00; 21.00) days. Regarding the type of stroke, 36 patients had cerebral infarction, accounting for 69%, and 16 patients had cerebral haemorrhage, accounting for 31%. For the type of aphasia, 12 patients had Broca's aphasia, 4 patients had Wernicke's aphasia, 3 patients had conduction aphasia, 1 patient had transcortical motor aphasia, 3 patients had transcortical sensory aphasia, 3 patients had mixed transcortical aphasia, 8 patients had anomia aphasia, 13 patients had global aphasia, and 5 patients had unclassified aphasia. Among the risk factors we included, hypertension was the most common risk factor, with 36 of 52 patients suffering from it. The stroke severity was assessed in only 32 of the 52 patients, with a median score of 4.50 (3.25; 10.75). Finally, 10 patients had dysphagia (account-

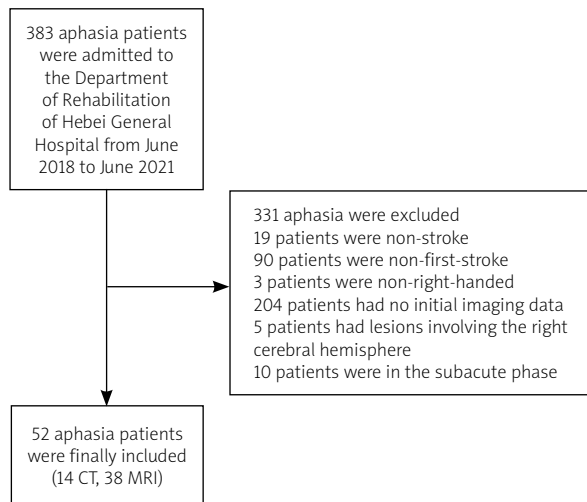


Fig. 1. Flowchart of the study.

ing for 19%), 5 patients had dysarthria (accounting for 10%), and 6 patients had cognitive impairment (accounting for 12%) (Table I).

The results of the Wilcoxon rank sum test showed that lesions involving the superior temporal gyrus ($p = 0.025$), middle frontal gyrus ($p = 0.014$), inferior frontal gyrus ($p = 0.002$), precentral gyrus ($p = 0.004$), postcentral gyrus ($p = 0.037$), supramarginal gyrus ($p = 0.043$), angular gyrus ($p = 0.044$) and insula ($p = 0.025$) were significantly associated with low fluency. Lesions involving the superior temporal gyrus ($p = 0.010$), middle temporal gyrus ($p = 0.035$), inferior temporal gyrus ($p = 0.032$), middle frontal gyrus ($p = 0.016$), inferior frontal gyrus ($p = 0.006$), supramarginal gyrus ($p = 0.002$) and angular gyrus ($p = 0.009$) significantly resulted in auditory comprehension impairment. Lesions involving the superior temporal gyrus ($p = 0.009$), middle temporal gyrus ($p = 0.037$), middle frontal gyrus ($p = 0.015$), inferior frontal gyrus ($p = 0.001$), precentral gyrus ($p = 0.012$), postcentral gyrus ($p = 0.006$), supramarginal gyrus ($p = 0.023$), angular gyrus ($p = 0.003$) and insula ($p = 0.018$) significantly resulted in repetition damage. Lesions involving the superior temporal gyrus ($p = 0.034$), middle temporal gyrus ($p = 0.034$), middle frontal gyrus ($p = 0.007$), inferior frontal gyrus ($p = 0.001$), precentral gyrus ($p = 0.007$), postcentral gyrus ($p = 0.017$), supramarginal gyrus ($p = 0.022$), angular gyrus ($p = 0.014$) and insula ($p = 0.004$) significantly caused a low naming ability (Table II).

The patients' age, sex, education level, type of stroke, risk factors included, stroke severity and cognitive

Table I. Clinical data of 52 patients with aphasia after stroke

Items		$\bar{x} \pm s/n$ (%)
Age (years)		57.40 (13.10)
Sex	Female	17 (33)
	Male	35 (67)
Education level	Bachelor degree	8 (15)
	High school degree	14 (27)
	Junior high school degree	16 (31)
	Primary school degree	11 (21)
	Illiterate	3 (6)
Duration of disease (days)		15.50 (9.00; 21.00)
Type of stroke	Ischemic	36 (69)
	Haemorrhagic	16 (31)
Type of aphasia	Broca's aphasia	12 (23)
	Wernicke's aphasia	4 (7)
	Conduction aphasia	3 (6)
	Transcortical motor aphasia	1 (2)
	Transcortical sensory aphasia	3 (6)
	Mixed transcortical aphasia	3 (6)
	Anomia aphasia	8 (15)
	Global aphasia	13 (25)
	Unclassified	5 (10)
Risk factors	Hypertension	36 (69)
	Diabetes	10 (19)
	Hyperlipidaemia	12 (23)
	Coronary heart disease	4 (8)
	Arrhythmia	4 (8)
	Smoking	17 (33)
	Drinking	14 (27)
	Stroke severity	4.50 (3.25; 10.75)
	Dysphagia	10 (19)
	Dysarthria	5 (10)
Cognitive impairment	6 (12)	
WAB	Fluency	4.50 (0.25; 6.00)
	Auditory comprehension	97.00 (22.5; 164.25)
	Repetition	56.50 (0; 83.75)
	Naming	24.50 (0; 62.75)
	AQ	39.40 (12.80; 68.53)

Table II. Quantitative analysis of the relationship between lesion site and language function

Variable	Fluency (<i>P</i> -value ^a)	Auditory comprehension (<i>P</i> -value ^a)	Repetition (<i>P</i> -value ^a)	Naming (<i>P</i> -value ^a)
Superior temporal gyrus	0.025	0.010	0.009	0.034
Middle temporal gyrus	0.249	0.035	0.037	0.034
Inferior temporal gyrus	0.363	0.032	0.093	0.054
Superior frontal gyrus	0.188	0.984	0.257	0.266
Middle frontal gyrus	0.014	0.016	0.015	0.007
Inferior frontal gyrus	0.002	0.006	0.001	0.001
Precentral gyrus	0.004	0.071	0.012	0.007
Postcentral gyrus	0.037	0.313	0.006	0.017
Supramarginal gyrus	0.043	0.002	0.023	0.022
Angular gyrus	0.044	0.009	0.003	0.014
Insula	0.025	0.086	0.018	0.004

^a Wilcoxon rank sum test**Table III.** Quantitative analysis of the influence of factors other than the lesion site on aphasia

Items	<i>P</i> -value	<i>R</i> or <i>Z</i> or χ^2
Age ^a	0.960	<i>R</i> = 0.007
Sex ^b	0.310	<i>Z</i> = -1.014
Education level ^c	0.930	χ^2 = 0.861
Type of stroke ^b	0.519	<i>Z</i> = -0.644
Risk factors		
High blood pressure ^b	0.613	<i>Z</i> = -0.506
Hyperlipidaemia ^b	0.602	<i>Z</i> = -0.521
Diabetes ^b	0.437	<i>Z</i> = -0.778
Atrial fibrillation ^b	0.481	<i>Z</i> = -0.704
Coronary heart disease ^b	0.548	<i>Z</i> = -0.601
Smoking ^b	0.383	<i>Z</i> = -0.872
Drinking ^b	0.128	<i>Z</i> = -1.522
Stroke severity ^a	0.151	<i>R</i> = -0.260
Dysphagia ^b	< 0.001	<i>Z</i> = -3.715
Dysarthria ^b	0.009	<i>Z</i> = -2.623
Cognitive impairment ^b	0.943	<i>Z</i> = -0.072
Total number of language-related sites ^a	< 0.001	<i>R</i> = -0.508

^a Spearman rank correlation, ^b Wilcoxon rank sum test, ^c Kruskal-Wallis *H* test

impairment were not significantly related to the AQ, while dysphagia ($p < 0.001$), dysarthria ($p = 0.009$) and the total number of language-related lesion sites ($p < 0.001$) were significantly related to a low AQ (Table III). Multivariate linear regression analysis further showed that dysphagia and the total number of language-related lesion sites were significantly related with a low AQ, while dysarthria was not related with AQ.

Discussion

Our study found that the focal lesion locations were related to specific language deficits in the patients with acute aphasia after stroke (≤ 1 month). Damage to the superior temporal gyrus, middle frontal gyrus, inferior frontal gyrus, precentral gyrus, postcentral gyrus, supramarginal gyrus, angular gyrus and insula was associated with poor fluency. Lesions including the superior temporal gyrus, middle temporal gyrus, inferior temporal gyrus, middle frontal gyrus, inferior frontal gyrus, supramarginal gyrus and angular gyrus were associated with poor auditory comprehension. Lesions involving the superior temporal gyrus, middle temporal gyrus, middle frontal gyrus, inferior frontal gyrus, precentral gyrus, postcentral gyrus, supramarginal gyrus, angular gyrus and insula were associated with poor repetition and poor naming ability. These findings suggested that the execution of each language task may require the participation of multiple language regions and that each language region may also participate in multiple language tasks. That is, language is a complex system, and each language task is completed via the cooperation of multiple language functions. Therefore, the injury of any function will lead to certain language deficits, which helps us further understand the neural mechanism of aphasia. Moreover, our study showed that the severity of aphasia in the acute phase was not associated with age, sex, education level, type of stroke, risk factors included, stroke severity or whether there was cognitive impairment. However, if a patient had dysphagia, dysarthria or a higher number of lan-

Table IV. Indigenous test results of multivariate linear regression independent variables ($R^2 = 0.449$)

	Unstandardized β value	Sx value	Standardized β value	t value	P-value
Intercept	57.452	4.235		13.567	0.000
Dysphagia	-23.544	10.855	-0.318	-2.169	0.035
Dysarthria	-12.021	14.292	-0.121	-0.841	0.404
Number of lesions	-4.677	1.101	-0.464	-4.246	0.000

guage-related lesion sites, the degree of aphasia in the acute phase was more serious.

Fluency involves a series of cognitive functions, including semantic memory, grammatical knowledge, working memory, articulatory planning and executive function. In one study [28], in order to explore the influencing factors of fluency, the deficits were simplified and divided into articulatory deficits and grammatical deficits. Articulatory deficits, assessed by the phonetic error proportion, were strongly correlated with the WAB fluency score as well as with the postcentral gyrus and supramarginal gyrus. The results regarding the grammatical deficits showed that the proportion of words in sentences is significantly related to the middle frontal gyrus and inferior frontal gyrus. Working memory is associated with the supramarginal gyrus, which is responsible for mapping phonology to articulation [22]. Phonetic articulatory planning and execution are related to the postcentral gyrus and supramarginal gyrus [28]. Several other research works have also shown that fluency is associated with the superior temporal gyrus [8], angular gyrus [1], precentral gyrus [15,18], anterior insula [4] and some white matter tracts [1,10,15,25], corresponding to the anterior segment of the arcuate fasciculus (AF), frontal aslant tract, uncinate fasciculus, superior longitudinal fasciculus and inferior fronto-occipital fasciculus. In particular, the posterior superior temporal gyrus plays a role in phonological recognition, self-monitoring of speech and retrieval of semantic information [8]. The angular gyrus is involved in phonological production and retrieval [1]. The precentral gyrus supports executing speech mouth movements [15]. The anterior insula is a key area of the brain, which coordinates complex articulatory movements [4]. The above results were consistent with our study – except for those concerning the white matter tracts because we did not explore the relationship between white matter tracts and language function.

There are three subsets of auditory comprehension on the WAB scale, including single-word recognition, yes/no questions and sequential commands. Lwi *et al.* [26] used lesion-symptom mapping to investigate the relationship between specific lesion sites and these three subsets in patients with chronic aphasia. The results showed that the mid-to posterior middle and inferior temporal gyrus and the angular and inferior-middle occipital gyrus were related to poor performance on single-word recognition. The posterior superior temporal gyrus, mid- to posterior middle temporal gyrus and posterior inferior temporal gyrus were associated with poor performance on yes/no questions. The superior temporal gyrus, posterior middle temporal gyrus and angular gyrus were involved in poor performance on sequential commands. These results suggested that auditory comprehension deficits are mainly caused by injury of the superior temporal gyrus, middle temporal gyrus, inferior temporal gyrus and angular gyrus, especially injury of the posterior temporal lobe. However, the role of the posterior temporal lobe in comprehension remains controversial. Some studies have suggested that the anterior temporal lobe – rather than the posterior temporal lobe – is important for comprehension [13]. Since our study did not refer to the role of the anterior or posterior temporal lobe in comprehension, future studies are needed to further explore this issue. In addition to the areas mentioned above, some studies have also suggested that middle frontal gyrus [31], inferior frontal gyrus [20,27] and supramarginal gyrus [27,32] play a role in auditory comprehension. In particular, researchers have indicated that the middle frontal gyrus plays an important role in word comprehension [31]. The inferior frontal gyrus is associated with grammar, lexical retrieval and sentence comprehension [27]. The supramarginal gyrus is involved in auditory and phonological short-term memory related to sentence comprehension [32]. Regarding white matter tracts, Xing *et al.* [38] have shown that the uncinate fasciculus is related to word-level comprehension

deficits. The posterior temporal white matter tracts, inferior longitudinal fasciculus and AF are related to sentence-level comprehension deficits. The inferior fronto-occipital fasciculus is related to both word- and sentence-level comprehension. These results were consistent with our results, except for those regarding the white matter tracts.

Repetition concerns auditory processing, phonological analysis, output mapping and speech production [5]. In one study, in order to investigate the neural correlates of repetition, Dell and colleagues [11] explored the connections between auditory input and phonological units as well as between the lexical system and phonological system. It turned out that the superior temporal gyrus, postcentral gyrus and supramarginal gyrus are associated with the process from the auditory input to phonological units and play a role in auditory discrimination. The precentral gyrus, postcentral gyrus, supramarginal gyrus and insula are associated with lexical-phonological connections and are responsible for auditory-motor integration. Moreover, Baldo *et al.* [5] suggested that the middle temporal gyrus and angular gyrus are related to single-word repetition and are responsible for lexical semantic retrieval. Regarding white matter tracts, some studies have shown that the superior longitudinal fasciculus [35], inferior fronto-occipital fasciculus [9,40] and AF [9] are related to repetition. However, the role of the AF in repetition remains controversial. Some researchers believe that the AF is crucial for repetition [9], while others suggest that repetition is only associated with the cortex around perisylvian regions rather than the AF [5]. Therefore, the role of the AF in repetition needs to be further explored. These results were consistent with ours, except for those regarding the middle frontal gyrus, inferior frontal gyrus and white matter tracts. One possible reason for this is that the previous research only involved word repetition and not sentence repetition, whereas we covered both with the WAB scale. Mirman *et al.* [28] have shown that grammatical sentence structuring relies on frontal regions, particularly the inferior and middle frontal gyrus. Schwart *et al.* [33] have also suggested that the middle frontal gyrus plays an important role in verbal working memory, which is essential for long sentence repetition.

To investigate the neural correlates of naming, one study divided naming into a semantic system and phonetic system [11]. The semantic system was the process from semantic units to lexical units, and

the phonetic system was the process from lexical units to phonological units. The results showed that the semantic process was related to the anterior superior and middle temporal gyrus, temporal pole, middle frontal gyrus, inferior frontal gyrus and angular gyrus. The phonetic system was related to the precentral gyrus, postcentral gyrus, supramarginal gyrus and insula. These results were the same as our results – except for those concerning the temporal pole because we did not include the temporal pole as an area of interest. Specifically, the anterior superior and middle temporal gyrus and angular gyrus are responsible for semantic representation, and the middle and inferior frontal gyrus play a role in the attentional or working memory processes that control such representations. In terms of white matter tracts, the superior longitudinal fasciculus [23], inferior fronto-occipital fasciculus [23], AF [23] and uncinate fasciculus [39] are related to naming ability.

There were some limitations in our study. First, the study was a retrospective analysis, so it was inevitable that there would be incomplete data, such as the data regarding stroke severity. Second, the sample size was small, with only 52 patients included. Third, we did not analyse the role of the right cerebral hemisphere in language because it was involved in only 5 of 385 patients in our study, nor did we study the effect of white matter tracts on aphasia. Fourth, we analysed the relationship between lesion site and language function but did not analyse the role of lesion volume because some studies have shown that the specific damaged structure rather than the lesion volume has been identified as a more accurate specific injury index [16,36]. In view of the above, prospective and large sample studies are needed in the future to further explore the relationship between lesion site and language function in patients with acute aphasia. Special attention should also be paid to the role of language function in the right cerebral hemisphere, the subcortical structure and the lesion volume.

Conclusions

Our study suggests that the brain is a complex network structure and that damage to different areas of the brain can lead to specific language impairments, which adds to our understanding of language pathology and provides a direction for future research and treatment.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Hebei General Hospital.

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Disclosure

The authors report no conflict of interest.

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