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Vascular Aphasia Outcome after Intravenous Recombinant Tissue Plasminogen Activator Thrombolysis for Ischemic Stroke

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Key Words
Stroke · Thrombolysis · Conduction aphasia

Abstract
Introduction: No data about the specific outcome of aphasia after thrombolysis are available. Our aim was to describe the severity and type of aphasia after stroke thrombolysis. ***Methods:*** This retrospective cohort study included consecutive aphasic patients hospitalized in the Stroke Unit of Dijon (University Hospital, France) between 2004 and 2009 for a first-ever ischemic stroke of the left middle cerebral artery. Aphasic syndromes and their severity (French version of the Boston Diagnostic Aphasia Examination) were evaluated during the first week and 3 months after stroke. ***Results:*** In multivariate analyses, the severity of aphasia in the 37 thrombolysed patients was milder than in the 38 nonthrombolysed patients during the first week (adjusted OR = 10.13, 95% CI: 2.43–42.28, p = 0.002) and at 3 months (adjusted OR = 8.44, 95% CI: 2.76–25.80, p = 0.001). The frequency of mild aphasia (conduction or atypical) was not significantly higher in thrombolysed patients during the first week after stroke (adjusted OR = 5.80, 95% CI: 0.82–41.16, p = 0.079). ***Conclusion:*** The severity of aphasia during the first week and 3 months after stroke is milder in thrombolysed than in nonthrombolysed patients, perhaps because of a greater frequency of conduction and mild atypical aphasia.

Introduction

In the last decade, ischemic stroke patients have benefited from major improvements in acute management [implementation of stroke units, use of intravenous thrombolysis based on recombinant tissue plasminogen activator (rt-PA)]. Both have contributed to a reduction in mortality and functional impairment. Thrombolysis therapy has been shown to reduce the proportion of patients becoming dependent 3–6 months after ischemic stroke by 20% [1–3].

Contrasting with these well-documented results, no specific data are currently available about the specific effect of rt-PA thrombolysis on recovery from aphasia after ischemic stroke, even though vascular aphasia is a frequent condition affecting 21–38% of ischemic stroke patients [4, 5]. Moreover, stroke-related aphasia is a significant clinical issue as it persists in 1 out of 8 long-term stroke patient survivors [4], and is associated with more severe disability, worse recovery of social activities, and reduced probability to return to work [5–7]. Of note, recent studies have demonstrated that the prognosis of recovery from aphasia is better determined by clinical characteristics and the etiology of the cerebral lesion involved than by individual factors [8, 9]. Moreover, it is well known that the type of aphasia can change during the first week after stroke (e.g. nonfluent aphasia could evolve

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into fluent aphasia) [10]. However, as far as we know, no data about the neurobiological effects of rt-PA thrombolysis on aphasia after ischemic stroke have been published.

This study had 3 aims: (1) to compare the severity of aphasia and recovery from the condition in thrombolysed and nonthrombolysed aphasic ischemic stroke patients, (2) to describe and compare the clinical features of aphasia after stroke treated with and without thrombolysis, and (3) to compare the potential recovery of the previous activities 6 months and 1 year after stroke in the same sample.

Methods

Study Population and Case-Ascertainment

All patients hospitalized between 2004 and 2009 in the Stroke Unit of Dijon, France, with a diagnosis of first-ever ischemic stroke according to World Health Organization (WHO) recommendations and the International Classification of Diseases (ICD) [11] and alive 3 months after the index stroke were retrospectively identified. Only patients with ischemic stroke of the left middle cerebral artery and aphasia clinically documented by a speech therapist were included. Patients with a Neurological Institute of Health Stroke Scale (NIHSS) score >24, psychiatric disorders, dementia, or other neurological disease that could cause speech disorders were also excluded.

Left middle cerebral artery ischemic stroke was classified into 4 groups according to the location of the lesion assessed by either brain CT scan or MRI that were systematically performed: anterior (frontal, anterior temporal lobes), posterior (parietal, posterior temporal lobes), deep (basal ganglia and/or internal capsule), and whole (anterior + posterior). We distinguished classical ischemic stroke subtypes according to the TOAST classification [12].

We distinguished between patients treated by intravenous rt-PA thrombolysis and those without thrombolysis. Of note, the decision for rt-PA thrombolysis treatment was always made by a neurologist according to French and international recommendations [1, 2, 13, 14].

The eligible thrombolysed patients were hospitalized between 2006 and 2009, whereas the nonthrombolysed patients were selected among the patients hospitalized in 2004 and 2005.

Language Assessment

Firstly, a bedside language examination was systematically done by a neurologist, based on the use of the standardized items for language testing of the NIHSS, which have good interrater reliability [15]. Aphasia was classified into 3 subgroups: fluent, nonfluent, and mutism.

Secondly, language was assessed during the first week after stroke by the speech therapist using subtests of the French version of the Boston Diagnostic Aphasia Examination (BDAE) [16] when the neurological condition became stabilized. The language assessment lasted 30–45 min and used some subtests of the short form of the BDAE. Five language domains were assessed: conversation and expository speech, auditory comprehension, oral expression, reading, and writing.

Thirdly, language was assessed 3 months after stroke, by a speech therapist, with the same method used during the first week after stroke.

In the course of the 2 assessments by the speech therapists, the severity of aphasia was graded into 6 categories according to the grades of the BDAE score (0 when both comprehension and expression were the poorest, and 5 when there was almost no audible language disability). Patients were then classified into 2 categories according to aphasia severity: severe aphasia (BDAE scores 0, 1, 2) and mild-to-moderate aphasia (BDAE scores 3, 4, 5). Aphasia was also classified according to the main classical aphasia syndromes: global, Broca's (motor), Wernicke's, conduction, amnesic and subcortical aphasia. Aphasia was considered atypical when the disorder did not meet the criteria for any of the classic aphasia syndromes. Patients were then classified into 2 categories: conduction and atypical aphasia versus other types of aphasia.

Variables of Interest

For each patient, data were retrospectively collected using the stroke unit files. Age, gender, NIHSS at stroke onset, education, handedness, type of speech rehabilitation, SSRI (selective serotonin reuptake inhibitor) before and after stroke, and prior transient ischemic attack were recorded.

Outcomes

The first outcome was the severity of the aphasia during the first week and 3 months after the index stroke (BDAE score). The second outcome was the type of aphasia diagnosed by the speech therapist during the first week after stroke onset and at 3 months. The third outcome was the potential recovery of the previous activities (work for younger patients, hobbies for retired patients) 6 months and 1 year after stroke.

Statistical Analysis

We compared the frequency of the type and the severity of aphasia during the first week and at 3 months between patients treated and untreated with rt-PA, using either a χ^2 test, Fisher's exact test, or t test (according to the type of the variables and the number of events). Trend analyses using likelihood ratios were performed. The odds ratio (OR) and confidence intervals (CI) were also computed using logistic regression.

In bivariate analyses, the associations between baseline characteristics and the type or severity of the aphasia during the first week and at 3 months were analyzed using logistic regression to estimate ORs and their 95% CIs. In multivariate analyses, we forced the treatment (rt-PA) and introduced all potential confounders into the models ($p < 0.20$ in univariate analyses). A stepwise selection procedure was then applied to obtain the final models.

A p value below 0.05 was considered statistically significant. SAS 9.2 (SAS Institute Inc., Cary, N.C., USA) was used for all analyses.

Results

Baseline Characteristics

Among 118 ischemic stroke patients with aphasia between 2004 and 2005, and 163 ischemic stroke pa-

Table 1. Baseline characteristics of the ischemic stroke patients with aphasia (Dijon University Hospital, 2004–2009)

Age, years	67±13.9
Gender (male)	44 (58.7)
NIHSS (n = 74)	13±7
Intravenous rt-PA thrombolysis	37 (49.3)
Education (n = 56)	
Primary	28 (50.0)
Secondary	18 (32.1)
Higher	10 (17.9)
Handedness	
Right	71 (94.7)
Left	2 (2.7)
Ambidextrous	2 (2.7)
Sylvian stroke localization (n = 74)	
Anterior	9 (12.1)
Posterior	36 (48.7)
Anterior + posterior	17 (23.0)
Deep	12 (16.2)
Stroke subtypes	
TOAST 1	7 (9.3)
TOAST 2	31 (41.3)
TOAST 3	0 (0.0)
TOAST 4	5 (6.7)
TOAST 5	32 (42.7)
Acute aphasia (neurological examination; n = 74)	
Mutism	34 (46.0)
Fluent aphasia	24 (32.4)
Nonfluent aphasia	16 (21.6)
Aphasia subtype in the first week after stroke	
Conduction	6 (8.0)
Wernicke's	25 (33.3)
Motor aphasia (Broca's)	8 (10.7)
Global	23 (30.7)
Subcortical	3 (4.0)
Nonclassified	5 (6.7)
No aphasia	5 (6.7)
Aphasia severity during the first week (BDAE score)	
0	28 (37.3)
1	13 (17.3)
2	5 (6.7)
3	13 (17.3)
4	9 (12.0)
5	7 (9.3)
Speech rehabilitation after acute hospitalization	
Rehabilitation center	22 (29.3)
Speech therapist alone	25 (33.3)
No rehabilitation	28 (37.3)
Aphasia subtype 3 months after stroke	
Conduction	7 (9.3)
Wernicke's	18 (24.0)
Motor aphasia (Broca's)	10 (13.3)
Global	16 (21.3)
Subcortical	3 (4.0)
Non classified	0 (0.0)
Absence of aphasia	21 (28.0)
Aphasia severity at 3 months (BDAE score; n = 74)	
0	5 (6.8)
1	14 (18.9)
2	5 (6.8)
3	11 (14.0)
4	17 (23.0)
5	22 (29.7)
Recovery of the previous activities at 6 months (n = 73)	37 (50.7)
Recovery of the previous activities at 1 year (n = 73)	36 (49.3)
Death at 1 year	4 (5.3)
Prior TIA (n = 70)	11 (15.7)
Prior treatment with SSRI (n = 70)	4 (5.7)
Treatment with SSRI after stroke (n = 70)	20 (28.6)

Values are given as means ± SD or n (%). n = 75 patients unless otherwise indicated. TIA = Transient ischemic attack.

tients with aphasia between 2006 and 2009, we recorded 75 first-ever middle cerebral artery ischemic stroke patients according to the inclusion and exclusion criteria: 37 were treated with intravenous rt-PA thrombolysis (2006–2009) and 38 were not (2004–2005). The baseline characteristics of the patients are described in table 1. None of the patients underwent amnesic aphasia which was therefore not taken into account in the analyses.

The 37 thrombolysed patients differed from the 38 nonthrombolysed patients only in two baseline characteristics: they were significantly more likely to have a mutism than a fluent or nonfluent aphasia in the acute stage of the stroke (OR = 0.12, 95% CI: 0.04–0.40, p = 0.002, and OR = 0.22, 95% CI: 0.06–0.77, 0.018, respectively), and were more likely to be admitted to a rehabilitation center after their stroke (OR = 7.18, 95% CI: 2.01–25.66, p = 0.002; table 2). There was no significant difference in the mean NIHSS between these two groups (table 2).

Association between the Severity of Aphasia and rt-PA Thrombolysis during the First Week and 3 Months after Stroke

During the first week after stroke, aphasia was less severe in the thrombolysed (51.4% of the patients had grades 3, 4, or 5 at the BDAE score) than in the nonthrombolysed patients (26.3%). This significant relationship was not observed 3 months after the stroke. However, at 3 months, the trend analysis was significant (p = 0.011): aphasia seemed to be less severe in rt-PA-treated patients (table 3).

Table 2. Bivariate association between the baseline characteristics and rt-PA therapy (Dijon University Hospital, 2004–2009)

	rt-PA thrombolysis present (n = 37)	rt-PA thrombolysis none (n = 38)	OR (95% CI)	p value (Khi-2 Wald)
Age, years	68±13.4	66±14.5	1.01 (0.98–1.04)	0.598
Gender (male)	25 (67.6)	19 (50.0)	2.08 (0.82–5.32)	0.125
NIHSS (n = 74)	15±7	12±7	1.07 (1.00–1.15)	0.050
Education (n = 56)				
Primary	19 (54.3)	9 (42.9)	reference	
Secondary	9 (25.7)	9 (42.9)	0.47 (0.14–1.60)	0.229
Higher	7 (20.0)	3 (14.3)	1.11 (0.23–5.30)	0.901
Handedness				
Right	35 (94.6)	36 (94.7)	reference	
Left	1 (2.7)	1 (2.6)	1.03 (0.06–17.10)	0.984
Ambidextrous	1 (2.7)	1 (2.6)	1.03 (0.06–17.10)	0.984
Sylvian stroke localization (n = 74)				
Anterior	4 (10.8)	5 (13.5)	0.56 (0.11–2.86)	0.486
Posterior	20 (54.1)	16 (43.2)	0.88 (0.27–2.82)	0.823
Anterior + posterior	10 (27.0)	7 (18.9)	reference	
Deep	3 (8.1)	9 (24.3)	0.23 (0.05–1.19)	0.079
Stroke subtypes				
TOAST 1	6 (16.2)	1 (2.6)	6.80 (0.73–63.05)	0.092
TOAST 2	13 (35.1)	18 (47.4)	0.82 (0.30–2.22)	0.693
TOAST 3	0 (0.0)	0 (0.0)	[a]	
TOAST 4	3 (8.1)	2 (5.3)	1.70 (0.25–11.59)	0.588
TOAST 5	15 (40.5)	17 (44.7)	reference	
Acute aphasia (neurological examination; n = 74)				
Mutism	25 (67.6)	9 (24.3)	reference	0.0005
Fluent aphasia	6 (16.2)	18 (48.7)	0.12 (0.04–0.40)	0.018
Nonfluent aphasia	6 (16.2)	10 (27.0)	0.22 (0.06–0.77)	
Speech rehabilitation after acute hospitalization				
Rehabilitation center	17 (46.0)	5 (13.2)	7.18 (2.01–25.66)	0.002
Speech therapist alone	11 (29.7)	14 (36.8)	1.66 (0.54–5.08)	0.376
No rehabilitation	9 (24.3)	19 (50.0)	reference	

Values are given as means ± SD or n (%). n = 75 patients unless otherwise indicated. [a] Missing values (inability of the logistic regression to calculate OR).

Additionally, in bivariate analyses, the NIHSS (OR = 0.92, 95% CI: 0.85–0.99, p = 0.026), admission to a rehabilitation center (OR = 0.22, 95% CI: 0.06–0.83, p = 0.025), and the prescription of an SSRI after stroke (OR = 0.10, 95% CI: 0.02–0.45, p = 0.003) were inversely associated with a favorable outcome of aphasia during the first week. At 3 months, fluent (OR = 4.04, 95% CI: 1.22–13.39, p = 0.023) or nonfluent (OR = 7.44, 95% CI: 1.46–37.99, p = 0.016) aphasia in the acute neurological examination was associated with a favorable outcome of aphasia, while the NIHSS (OR = 0.83, 95% CI: 0.75–0.91, $p < 10^{-4}$), the first grade of the TOAST classification (OR = 0.06, 95% CI: 0.01–0.53, p = 0.012), and the prescription of an SSRI after stroke (OR = 0.24, 95% CI: 0.08–0.72, p = 0.011) were inversely associated with a favorable outcome.

In multivariate analyses, rt-PA thrombolysis was significantly associated with a more favorable outcome of the aphasia (at the 1-week and 3-month language assessments; table 4).

Association between the Type of Aphasia and rt-PA Thrombolysis during the First Week and 3 Months after Stroke

In bivariate analyses, conduction and atypical aphasia were significantly more frequent after thrombolysis during the first week after stroke (24.3% of the thrombolysed vs. 5.3% of the nonthrombolysed patients), while there was no significant difference at 3 months (10.8% of the thrombolysed vs. 7.9% of the nonthrombolysed patients had conduction aphasia; table 3). The mean NIHSS was

Table 3. Bivariate association between the type or severity of aphasia and rt-PA therapy (n = 75, Dijon University Hospital, 2004–2009)

	rt-PA thrombolysis present (n = 37)	rt-PA thrombolysis none (n = 38)	OR (95% CI)	p value (Khi-2 Wald)	p value for trend
During the first week after stroke					
Aphasia severity (BDAE score)					
0	13 (35.1)	15 (39.5)	0.35 (0.06–2.10)	0.249	0.215
1	4 (10.8)	9 (23.7)	0.18 (0.02–1.34)	0.094	
2	1 (2.7)	4 (10.5)	0.10 (0.01–1.54)	0.099	
3	8 (21.6)	5 (13.2)	0.64 (0.09–4.66)	0.659	
4	6 (16.2)	3 (7.9)	0.80 (0.09–6.85)	0.834	
5	5 (13.5)	2 (5.3)	reference		
Aphasia severity					
Severe aphasia	18 (48.7)	28 (73.7)	reference		
Mild-to-moderate aphasia	19 (51.4)	10 (26.3)	2.96 (1.12–7.79)	0.028	
Aphasia subtype					
Conduction	4 (10.8)	2 (5.3)	1.33 (0.19–9.31)	0.288	0.138
Wernicke's	10 (27.0)	15 (39.5)	0.80 (0.17–3.77)	0.900	
Motor aphasia	3 (8.1)	5 (13.2)	reference		
Global	11 (29.7)	12 (31.6)	0.46 (0.09–2.32)	0.614	
Subcortical	2 (5.4)	1 (2.6)	2.00 (0.13–29.80)	0.399	
Atypical	5 (13.5)	0 (0.0)	[a]	0.967	
Absence of aphasia	2 (5.4)	3 (7.9)	1.63 (0.36–7.43)	0.928	
Aphasia subtype					
Conduction + atypical aphasia	9 (24.3)	2 (5.3)	5.79 (1.16–28.94)	0.033	
Others	28 (75.7)	36 (94.7)	reference		
3 months after stroke					
Aphasia severity (BDAE score; n = 74)					
0	0 (0.0)	5 (13.2)	[a]	0.967	0.011
1	9 (25.0)	5 (13.2)	1.03 (0.26–4.16)	0.969	
2	3 (8.3)	2 (5.3)	0.86 (0.12–6.26)	0.879	
3	2 (5.6)	9 (23.7)	0.13 (0.02–0.74)	0.022	
4	8 (22.2)	9 (23.7)	0.51 (0.14–1.84)	0.303	
5	14 (38.9)	8 (21.1)	reference		
Aphasia severity					
Severe aphasia	12 (33.3)	12 (31.6)	reference		
Mild-to-moderate aphasia	24 (66.7)	26 (68.4)	0.92 (0.35–2.44)	0.872	
Aphasia subtype					
Conduction	4 (10.8)	3 (7.9)	1.33 (0.19–9.31)	0.772	0.521
Wernicke's	8 (21.6)	10 (26.3)	0.80 (0.17–3.77)	0.778	
Motor aphasia	5 (13.5)	5 (13.2)	reference		
Global	5 (13.5)	11 (29.0)	0.46 (0.09–2.32)	0.343	
Subcortical	2 (5.4)	1 (2.6)	2.00 (0.13–29.80)	0.615	
Unclassifiable	0 (0.0)	0 (0.0)	[a]		
Absence of aphasia	13 (35.1)	8 (21.1)	1.63 (0.36–7.43)	0.532	
Aphasia subtype					
Conduction aphasia	4 (10.8)	3 (7.9)	1.41 (0.29–6.80)	0.665	
Others	33 (89.2)	35 (92.1)	reference		

Values represent n (%) unless otherwise indicated. [a] Missing values (inability of the logistic regression to calculate OR).

not statistically different between these two groups: NIHSS (mean ± SD) = 11 ± 7 in the group of patients with conduction or atypical aphasia, NIHSS (mean ± SD) = 14 ± 7 in the other group of patients; OR = 0.94, 95% CI: 0.85–1.04, p = 0.195.

In multivariate analyses, conduction and atypical aphasia during the first week after stroke seemed to be more frequent in patients treated with thrombolysis than in those without, but this relationship was not significant (table 5).

Table 4. Multivariate association between baseline characteristics and the severity of aphasia (n = 69, Dijon University Hospital, 2004–2009)

	OR	95% CI	p value
During the first week after stroke			
rt-PA thrombolysis: yes vs. no	10.13	2.43–42.28	0.002
NIHSS	0.90	0.82–0.99	0.028
Rehabilitation center vs. no rehabilitation	0.10	0.02–0.60	0.011
Speech therapist vs. no rehabilitation	0.65	0.17–2.54	0.540
3 months after stroke			
rt-PA thrombolysis: yes vs. no	8.44	2.76–25.80	0.001
NIHSS	1.20	1.11–1.30	$<10^{-4}$
Rehabilitation center vs. no rehabilitation	5.23	1.42–19.36	0.013
Speech therapist vs. no rehabilitation	1.51	0.49–4.69	0.476

Table 5. Multivariate association between baseline characteristics and conduction + atypical aphasia during the first week after stroke (n = 56, Dijon University Hospital, 2004–2009)

	OR	95% CI	p value
rt-PA thrombolysis: yes vs. no	5.80	0.82–41.16	0.079
NIHSS	0.86	0.75–0.99	0.033
Education: secondary vs. primary	0.10	0.01–1.01	0.051
Education: higher vs. primary	0.11	0.01–1.26	0.076

All of the patients with conduction aphasia had mild-to-moderate aphasia thanks to the BDAE score during the first week after stroke and at 3 months (data not shown).

Potential Recovery of the Previous Activities 6 Months and 1 Year after Stroke

Conduction and atypical aphasia were associated with better recovery of the previous activities 6 months (OR = 12.96, 95% CI: 1.56–107.48, p = 0.002) and 1 year (OR = 13.84, 95% CI: 1.67–114.86, p = 0.015) after stroke. A similar relationship between the mild aphasia during the first week after stroke and the resumption of previous activities at 6 months (OR = 13.14, 95% CI: 3.83–45.13, $p < 10^{-4}$) and 1 year (OR = 10.06, 95% CI: 3.16–31.97, $p < 10^{-4}$) was found. Moreover, all the patients who resumed their activities a few months after the stroke had mild aphasia at 3 months.

Discussion

Our study demonstrated that the aphasia after ischemic stroke treated with rt-PA thrombolysis was less severe than in nonthrombolysed patients at the 1-week and 3-month language assessments by the speech therapist. It also highlights that the frequency of conduction and mild atypical aphasia is greater after a thrombolysed than a nonthrombolysed stroke.

The classification of the patients into two categories according to the type of aphasia was made after observational consideration in the clinical practice of the neurologist and the speech therapist.

Our study has several strengths. First, speech was systematically evaluated using constant methodology based on standardized tests. The baseline characteristics of thrombolysed and nonthrombolysed patients were similar, thus making the two groups comparable. Secondly, data were collected in a stroke unit, which ensures the reliability of the information. Thirdly, the different periods of admission between thrombolysed and nonthrombolysed patients were chosen to avoid a selection bias: the nonthrombolysed patients were not contraindicated patients for rt-PA thrombolysis because this drug was less widespread before 2005 than after this year. In fact, none of the aphasic ischemic stroke patients was treated by rt-PA thrombolysis in Dijon in 2004 and 2005 (data obtained from the Dijon Stroke Registry) because the indications of such a treatment were more restrictive than today.

Mild aphasia was significantly associated with more complete resumption of the previous daily activities 6 months and 1 year after stroke. This interesting finding underlines the impact of rt-PA thrombolysis because patients with aphasia but without thrombolysis are considered to have more severely disabling strokes than patients without aphasia [5], and aphasia may be associated with a lower likelihood of resuming usual social activities and returning to work [4, 6]. Our results are consistent with the previous reports of the effects of rt-PA thrombolysis on functional outcome 3 months after stroke [1, 2]. Our study also highlights that conduction aphasia is milder than the other types of aphasia. This result is also consistent with a previous study which demonstrated stroke patients with conduction aphasia had better recovery [8, 9]. Moreover, aphasia described as unclassifiable by the speech therapist, such as mild paraphasia and paragraphia, which occurred in the aftermath of mutism, was not severe: all the patients who suffered from them during the first week after their stroke resumed a normal language

network at 3 months. Indeed, this atypical aphasia was diagnosed only after stroke treated with thrombolysis, which suggests a relationship between atypical aphasia and rt-PA thrombolysis, even though our sample size was too small to confirm this hypothesis.

From a physiopathological point of view, it is well established that aphasia improves after stroke due to the plasticity of language-related brain functions [17, 18] and penumbra dynamics [19]. Recovery from aphasia is concomitant with an activation pattern that changes from a left to a homologous recruited right hemispheric pattern [17]. This recovery is improved by the restoration of damaged left hemisphere language networks and activation in left hemisphere border zones [18]. A bilaterally reorganized language network is therefore the most effective [18]. However, no data about outcomes following aphasia in thrombolysed patients are currently available in the literature. How does rt-PA modify language patterns in stroke patients?

Our first hypothesis is that rt-PA leads to selective reperfusion of the cerebral blood flow: some cerebral areas may be less sensitive to this drug and thus more vulnerable to ischemia [20]. It is well known that conduction aphasia is associated with lesions of the left arcuate fasciculus [21, 22], which is a deep brain white-matter tract connecting Broca's area (in the frontal lobe) to Wernicke's area (in the parietal lobe) [23]. Some authors have also put forward the notion of associations between conduction aphasia and lesions of the left supramarginal gyrus, sometimes extending to the temporal cortex [24], but this concept is not supported by all researchers [21]. Indeed, a previous study demonstrated that thrombolysis in rats with focal ischemia leads to incomplete reperfusion, with moderate recovery in the periphery only [24]. Therefore, if cerebral reperfusion is selective, we could expect that the rt-PA would be less efficient in the deep cerebral areas, especially the deep white matter such as the arcuate fasciculus. As a consequence, lesions of the left arcuate tract, leading to conduction aphasia, would be the only residual sign after stroke treated with thrombolysis.

Our second hypothesis to explain the modification in language patterns by rt-PA relies on the potential neuroprotective effect of rt-PA: several studies have suggested that rt-PA could contribute to brain plasticity after ischemic stroke by leading to the synthesis of neurotrophic factors including brain-derived neurotrophic factor [25, 26].

Our study has several methodological limits. It is a retrospective cohort study with a potential selection bias (patients lost to follow-up and a great number of excluded patients), differential misclassification bias (reminder bias), and small sample size. These could have led to decreased power of the study and to an underestimation of the relationships between rt-PA thrombolysis and conduction or atypical aphasia, and could explain why some of the results of our study were not statistically significant. Therefore, this may have diminished the representativeness of our cohort and thus limited the generalization of the results and conclusion.

To conclude, our study demonstrates that beyond its favorable effect on motor recovery, intravenous rt-PA thrombolysis in ischemic stroke is an effective treatment to improve recovery from aphasia. This improvement might rely on the greater frequency of conduction and mild atypical aphasia after stroke thrombolysis. Further studies are needed to understand the physiopathological mechanisms involved.

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Disclosure Statement

None.

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