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► **To cite this version:**

Célise Haldin, Shenhao Dai, Céline Piscicelli, Valérie Marcon, Hélène Løevenbruck, et al.. Multifactorial interplay on language recovery following left-hemispheric stroke: A retrospective study. *Journal of neuropsychology*, 2024, 10.1111/jnp.12406 . hal-04856599

HAL Id: hal-04856599

<https://hal.science/hal-04856599v1>

Submitted on 27 Dec 2024

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RESEARCH ARTICLE

Multifactorial interplay on language recovery following left-hemispheric stroke: A retrospective study

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Abstract

Understanding the relative contribution of various factors influencing initial severity of aphasia and recovery after a stroke is essential for optimising neurorehabilitation programmes. We investigated how various significant sociodemographic, cognitive, clinical, stroke-related and rehabilitation-related factors modulate aphasia severity and language recovery following left-hemispheric stroke. Employing an innovative method, we conducted a retrospective analysis of 96 stroke participants to explore the combined impact of these factors. The initial severity of aphasia was categorised into severe, mild/moderate and no aphasia based on the severity of their language deficits in the subacute phase (Aphasia Severity Rating Scale, ASRS). To assess speech-and-language recovery, we classified 53/96 patients with aphasia into high and poor recovery categories using a gain score formula ($ASRS_{discharge} - ASRS_{admission} / ASRS_{admission}$). Subsequently, we performed statistical analyses (univariate analyses and forward stepwise logistic regression combined with bootstrap) to identify the determinants of the initial severity of aphasia and the degree of recovery. Our analyses unveiled that more severe aphasia initially was correlated with a more severe stroke (Odds Ratio, $OR = .90, p = .041$), moderate/severe executive dysfunction ($OR = .068, p < .001$) and larger lesion size ($OR = .068, p < .001$). Furthermore, the degree of recovery was associated with the intensity of speech-and-language therapy ($OR = 1.47, p = .043$). These findings enrich our understanding of the determinants of aphasia severity and

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language recovery, employing an original methodology to scrutinise the collective effect of multiple variables in a retrospective analysis of stroke participants. A better knowledge of these factors may help implement personalised language rehabilitation programmes to maximise speech-and-language recovery.

KEYWORDS

aphasia, language, multifactorial, recovery, stroke, subacute

INTRODUCTION

Aphasia, a frequent consequence of stroke, is a language disorder that disrupts communication, social interaction and quality of life. Early and intensive speech-and-language therapy (SLT) benefits people with post-stroke aphasia, but language recovery is heterogeneous among patients (Davis, 2007; Koleck et al., 2017). Recovery is influenced by various factors encompassing sociodemographic (gender, age, handedness, education level, social isolation, professional status, etc.), stroke-related (severity and type of stroke and aphasia, lesion size and location), clinical and cognitive (cognitive and language abilities) or rehabilitation-related (type, duration and intensity of rehabilitation) aspects (Gerstenecker & Lazar, 2019; Kiran & Thompson, 2019; Watila & Balarabe, 2015).

As concerns sociodemographic factors, studies indicate greater recovery in younger individuals, attributed to greater neuroplasticity (Boden-Albala et al., 2005; Kiran & Thompson, 2019), as well as in females and left-handers, explained by increased inter-hemispheric symmetry for language and higher involvement of the non-dominant hemisphere (Labache et al., 2020; Tzourio-Mazoyer et al., 2017). Education and psychosocial factors (mood, motivation, social support, etc.) have also modulated speech-and-language recovery and patients' quality of life (Boden-Albala et al., 2005; Bullier et al., 2020). These findings suggest that these factors may all contribute to recovery, but determining the independent predictive value of each is challenging due to confounding effects (Kristinsson et al., 2022).

Within stroke-related factors, the initial severity of aphasia is frequently highlighted as a crucial and consistent determinant of speech-and-language recovery (Gerstenecker & Lazar, 2019; Watila & Balarabe, 2015). Although the initial severity of aphasia is an important predictor of speech-and-language recovery, several other factors have also been shown to be critical. Several studies have reported that the evolution of aphasia is better explained by a combination of factors rather than a single predictor. A recent study on aphasia outcome at 3 months post-stroke shows that the initial severity of aphasia and lesion size and location are critical predictors of speech-and-language recovery (Benghanem et al., 2019). The important role of lesion size and location in speech-and-language recovery has also been acknowledged in studies (Harvey et al., 2022; Sul et al., 2019). Stroke severity also influences aphasia severity and speech-and-language recovery (Inatomi et al., 2008; Pedersen et al., 2004).

Non-linguistic cognitive factors, including visuospatial working memory, verbal short-term memory, problem-solving ability and executive functions, significantly affect speech-and-language recovery (Dignam et al., 2017; Gilmore et al., 2019; Seniów et al., 2009; Simic et al., 2020). More specifically, Simic et al. (2020) showed that maintaining flexibility and working memory updating abilities was associated with better speech-and-language recovery.

In the realm of rehabilitation-related factors, the intensity of SLT is generally identified as a key determinant, with high-intensity SLT (many hours over a short period) being more beneficial for patients' functional language skills than low-intensity SLT (Brady et al., 2016). More recent studies reveal that SLT is more effective when it is administered at high intensity, at an early stage (within one-month post-stroke), when it is tailored to the patient in terms of frequency and functional relevance, and when it can be implemented at home (Ali et al., 2021; Brady et al., 2022a, 2022b).

Despite numerous studies on the determinants of speech-and-language recovery, a consensus on their relative contributions remains elusive. Recovery depends on many variables and the interaction between these variables. The main focus is the complex relationship between the initial severity of aphasia after stroke and the degree of speech-and-language recovery (Døli et al., 2023; Lahiri et al., 2021). A better understanding of this relationship requires better insight into the determinants of the initial severity of aphasia. Moreover, Johnson et al. (2022) point out that studies should investigate beyond lesion location and examine the demographic and health factors that influence aphasia severity.

Based on these findings, our central hypothesis is that speech-and-language recovery is directly related to the initial severity of aphasia. However, some indirect factors could also come into play by modulating the initial severity of aphasia. The objective of this study was to assess multiple factors (sociodemographic, stroke-related, rehabilitation-related, clinical and cognitive) considered not in isolation but rather in combination since such an approach could provide more reliable insights into the determinants of initial severity of aphasia and speech-and-language recovery (Lai et al., 2021; Pustina et al., 2017). This could provide key variables to consider when implementing rehabilitation programmes to optimise speech-and-language recovery.

Based on our hypothesis and considerations, we seek to identify the factors determining (a) initial severity of aphasia and (b) speech-and-language recovery in the first 6 months post-stroke. To this aim, we conducted a retrospective observational cohort study to assess the impact of a large number of modulatory factors. Using univariate and multivariate (forward stepwise logistic regression combined with bootstrap) analyses, we analysed data from patients with left-hemispheric stroke admitted to Grenoble Hospital over 7 years pre-COVID-19. It should be noted that the retrospective observational cohort design offers several advantages over randomised controlled trials (see Bosdriesz et al., 2020), particularly in allowing for more generalisable results.

MATERIALS AND METHODS

Study design and reporting

We conducted a monocentric observational study including participants with a left-hemispheric stroke, with or without aphasia, admitted to the neurological rehabilitation ward of the University Hospital Grenoble-Alpes between January 2012 and October 2019. Participants were assessed initially within the first 2 months post-stroke ('first assessment', FA) and finally, on discharge from the rehabilitation ward (before 180 days post-stroke; 'discharge assessment', DA). All data were collected from medical records and reports of neuropsychological, speech-and-language and neurological assessments carried out as part of clinical routine. These clinical assessments were conducted by trained and multidisciplinary therapists, including speech therapists, neuropsychologists, physical and rehabilitation medicine physicians, and cognitive neuroscientists. Speech therapists conducted speech-and-language assessments at FA and DA, neuropsychologists conducted neuropsychological assessments only at FA, and physical and rehabilitation medicine physicians and cognitive neuroscientists provided further diagnostic and interpretative input for overall neurological and cognitive evaluations. The reporting of the study follows STROBE guidelines (see [Table S1](#)).

Ethical and regulatory consideration

According to French law, observational studies with a retrospective data analysis do not require an ethics committee's approval as long as participants have been informed of the research and do not object to using their data. Therefore, all eligible participants were informed of their right to object via an information note, either mailed to their home or provided directly with an oral explanation of the procedure upon hospital admission. Those who declined to participate signed an objection form.

Participants

Inclusion criteria were age above 18 years old and a first left-sided mono-hemispheric stroke confirmed by the MRI, with a first speech-and-language assessment performed before 60 days post-stroke. Non-inclusion criteria were individuals over 80 years old, recurrent strokes, complications in the acute stage (malignant infarct, cerebral herniation, subarachnoid haemorrhage and hydrocephalus), dementia, unstable medical condition, severe psychiatric symptoms, inability to speak French and unavailability of MRI data.

A total of 136 individuals with a first left-hemispheric stroke were initially considered eligible and consented to participate in the study. Ninety-six participants were included in this study as they met the inclusion criteria (see Figure 1), including 72 individuals with aphasia and 24 without aphasia.

Outcome variables: Aphasia severity and recovery

The severity of aphasia was assessed, at both FA and DA, using the French version of the Aphasia Severity Rating Scale (ASRS), from the Boston Diagnostic Aphasia Examination (BDAE, Mazaux & Orgogozo, 1981). The BDAE is a widely used standard scale for the comprehensive assessment of aphasia in both English- and French-speaking individuals (Goodglass & Kaplan, 1983; Mazaux & Orgogozo, 1981). A score of 0 means 'no usable speech or auditory comprehension', 1 corresponds to 'all communication is through the fragmentary expression', 2 to 'conversation on familiar subjects is possible with help from listener', 3 to 'patient can discuss almost all everybody problems with little or no assistance', 4 to 'some obvious loss of fluency or facility of comprehension without significant limitation on the idea expressed' and 5 to 'minimal discernible speech handicaps' (Mazaux & Orgogozo, 1981). Based on the presence or absence of language disorders and the ASRS score measured at FA, three groups were constituted: severe ($ASRS_{FA} = 0-2$), mild/moderate ($ASRS_{FA} = 3-5$) and no aphasia.

All patients with aphasia followed a personalised SLT programme during their hospital stay. The degree of speech-and-language recovery was assessed based on ASRS scores measured at DA and FA,

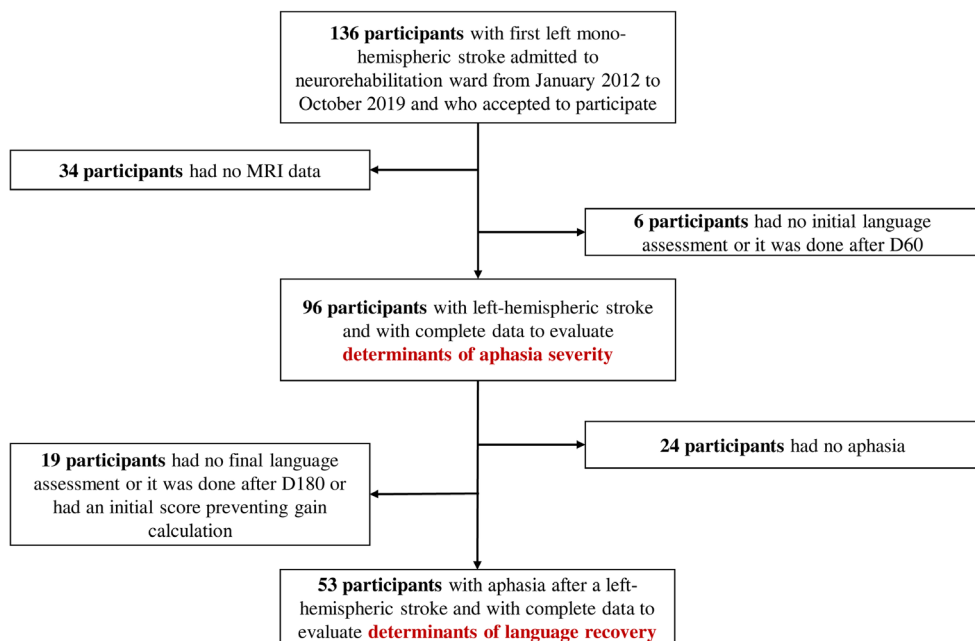


FIGURE 1 Flow chart of participants' inclusion in the study.

calculating a gain: $(ASRS_{DA} - ASRS_{FA}) / ASRS_{FA}$. Based on this gain, looking at the distribution of this variable (see [Figure S1](#)), two groups were constituted: patients with high recovery (gain $\geq .5$) and poor recovery (gain $< .5$).

Determinants of aphasia severity and recovery

Sociodemographic factors

Demographic parameters included age, sex and handedness assessed by the French translation of the Edinburgh inventory (Oldfield, 1971). Social parameters included the education level (lower vs. higher than a high-school degree), the professional status (retired/unemployed vs. employed) and the isolation level, based on two items: living alone (yes vs. no) and family or friends support (absent/lower vs. strong). All of these parameters were determined at FA, and we collected them from medical records.

Cognitive and clinical factors

The naming abilities of patients with aphasia were assessed during speech-and-language assessments at FA and DA using picture naming tasks, either with the BDAE subtest (Mazaux & Orgogozo, 1981) or the DO80 (Deloche & Hannequin, 1997). We calculated a percentage of correct responses (%CR), ranging from 0 to 100%, to determine naming performance at FA and DA, and the change between FA and DA ('Naming change', $\%CR_{DA} - \%CR_{FA}$).

Depression was assessed during neuropsychological assessment at FA using the Aphasia Depression Rating Scale (ADRS), a depression scale designed to assess depression in patients with aphasia in the subacute phase, which has been validated in French-speaking individuals (Benaim et al., 2004). ADRS scores range from 0 to 32 (depression for a score higher than 9).

Other cognitive factors (global disability, executive dysfunction, upper limb apraxia, spatial neglect and motor weakness) were assessed during neuropsychological assessment at FA and detailed below.

Global disability was estimated with a modified Rankin scale (mRS; van Swieten et al., 1988). mRS scores range from 0 (no symptoms) to 6 (death). Participants were classified (cut-off at 2) as having no/mild and moderate/severe disability.

Executive functioning was estimated with an ad-hoc executive scale designed to classify post-stroke executive dysfunction based on several tests, including Trail Making Test, Stroop test, Wisconsin Card Sorting Test, verbal fluency (see Godefroy & GREFEX, 2008), digit span and code subtests of the Wechsler Adult Intelligence Scale-IV (Wechsler, 2011), tower of London (Coyette & Van der Linden, 1993; Culbertson & Zillmer, 2005) or Hanoi (Simon, 1975) and Rey complex figure test (Rey, 1959; Wallon & Mesmin, 2009). It should be noted that the tests performed by each participant were chosen by the neuropsychologist among the aforementioned tests, taking into account any co-existing disorders that could influence the results. Individuals were then classified, according to the test results and report from neuropsychological assessment, as having no/mild and moderate/severe executive dysfunction.

Upper limb apraxia was assessed with the Apraxia Screen of TULIA (AST; Vanbellinghen et al., 2011), ranging from 0 (severe apraxia) to 12 (no apraxia). Participants were classified (cut-off at 9) as having no/mild and moderate/severe upper limb apraxia.

Spatial neglect and limb motor weakness were assessed and classified into two groups (no/mild and moderate/severe disorders) as in Dai et al. (2021).

Stroke-related factors

Stroke severity was estimated 24h after the stroke using the National Institutes of Health Stroke Scale, NIHSS (Brott et al., 1989). The score ranges from 0 to 42, with higher scores indicating greater stroke severity. The type of stroke was also determined (ischemic or haemorrhagic).

The aphasia type was reported by a speech therapist, based on the speech-and-language assessment performed at FA, for patients with aphasia. Patients were categorised as having non-fluent (i.e. global, transcortical motor or Broca's aphasia) or fluent (i.e. transcortical sensory, conduction, subcortical, anomic or Wernicke's aphasia) aphasia (Damasio, 1998; Gerstenecker & Lazar, 2019).

The presence of white matter hyperintensities (WMHs) at FA was sought on MRI T2-FLAIR images. Participants were classified as having no/mild or moderate/severe WMHs (for details, see Dai et al., 2022).

Lesion size was extracted from lesion delineation on MRI T2-FLAIR as in Dai et al. (2022). Note that lesion size was normalised for multivariate statistical analyses (see the following section).

Finally, we calculated the delay between stroke onset and assessments of aphasia severity at FA and DA: 'First assessment time (in days post-stroke)' and 'Second assessment time (in days post-stroke)', respectively. We also considered the delay between these assessments ('Delay FA-DA').

Rehabilitation-related factors

For each patient with aphasia who received SLT during their hospital stay, we measured (i) the onset of SLT (in days post-stroke), which is defined as the delay between stroke onset and beginning of SLT, and (ii) the intensity of SLT (average number of sessions per week), which was calculated based on the number of sessions and the duration of rehabilitation (in weeks).

Statistical analyses

First, we aimed to assess the determinants of the initial severity of aphasia. We compared three groups of participants with various degrees of aphasia severity (severe, mild/moderate and no aphasia) using Kruskal–Wallis or chi-square tests, with $p < .05$ as a significant threshold. When test was significant, we used Mann–Whitney or chi-square tests to assess significant inter-group differences, with adjusted p -value using Bonferroni correction. The adjusted p -value was calculated as $p \times \text{number of statistical tests}$, and adjusted $p < .05$ was considered significant. Statistically significant factors were included stepwise in a multivariate ordinal logistic regression analysis (i.e. forward stepwise logistic regression) coupled with bootstrap resampling, with 1000 replications, to further explore their association with aphasia severity in the three groups mentioned above. More specifically, we used forward stepwise regression to build a model by sequentially adding variables until the Akaike information criterion (AIC) stopping rule was satisfied. To reduce the bias or error in the estimation of regression coefficients (risk of false positives or negatives) due to the multiple comparisons, we generated 1000 bootstrap samples by random resampling, which improves the robustness and validity of our results and interpretations.

Second, we assessed the determinants of speech-and-language recovery. We conducted analyses only for patients with aphasia who completed speech-and-language assessments at FA and DA and for whom it was possible to calculate a gain. Indeed, as division by 0 is mathematically impossible, we excluded patients with initial severity of aphasia at 0. We compared two groups of patients (poor and high recovery) using Mann–Whitney or chi-square test, with $p < .05$ as a significant threshold. Statistically significant factors were included stepwise in a multivariate binary logistic regression analysis coupled with bootstrap resampling, with 1000 replications, to explore their association with speech-and-language recovery, according to the two groups mentioned above.

Statistical analyses were conducted using the R software (R Core Team, 2020).

RESULTS

Participants

Ninety-six participants met the inclusion criteria (Figure 1) and were included in this study. Thus, the determinants of aphasia severity were analysed in 96 participants, whose sociodemographic, cognitive, clinical and stroke-related characteristics are presented in Table 1. Among these 96 participants, 24 had no aphasia (N-Aph), 31 had mild/moderate aphasia (M-Aph) and 41 had severe aphasia (S-Aph).

The median age was 65.59 (Q1–Q3 = 55.22–71.37), 61 (63.54%) participants were males, 90 were right-handed (93.75%), 30 had an education level higher than a high-school diploma (32.61%), 31 were employed (33.33%). Twenty-seven participants lived alone (29.35%), and 72 had strong family or friends support (78.26%). The majority had an ischemic stroke (78.13%), and stroke severity was moderate (median NIHSS of 11 [7–17.5]). The median score for mood disorders was 8.5 (6–12), suggesting no depression disorders. Participants' moderate/severe disorders included general disability (68.75%), limb weakness (39.58%), WMHs (39.58%), executive dysfunction (55.21%), upper limb apraxia (28.57%) and spatial neglect (29.47%). The median lesion size was 13,364 voxels (2674–37,824). Among patients with aphasia, 47 (65.28%) had fluent aphasia, their median %CR in naming was 70% (18.75–85) and the median severity of aphasia at FA was 2 (1–3).

There were missing data ($n = 40$, 2.16%) for the following factors: education level ($n = 4$), professional status ($n = 3$), living alone ($n = 4$), family/friends support ($n = 4$), naming-FA ($n = 11$), upper limb apraxia ($n = 5$), spatial neglect ($n = 1$), ADRS ($n = 7$) and NIHSS ($n = 1$).

Aphasia recovery was evaluated in 53 out of the 96 participants initially screened (see Figure 1). We considered only the 53 patients with aphasia who underwent two language assessments at FA and DA and for whom it was possible to calculate the gain. Based on the gain, these patients were divided into two groups: 22 with poor recovery and 31 with high recovery.

Determinants of the initial severity of aphasia

The group of patients with aphasia differed from the group without aphasia (Table 1) on several scores: higher stroke severity with a large effect size for S-Aph ($Z = 4.47$, $p < .001$, $r = .56$) and a moderate effect size for M-Aph ($Z = 2.66$, $p = .024$, $r = .36$); larger lesion size, with a large effect size, for S-Aph ($Z = 5.71$, $p < .001$, $r = .71$) and M-Aph ($Z = 3.82$, $p < .001$, $r = .52$); more participants with moderate/severe global disability among S-Aph ($\chi^2 = 7.93$, $p = .015$, $\nu = .29$, moderate effect size); more participants with moderate/severe executive dysfunction, with moderate effect size, among S-Aph ($\chi^2 = 30.62$, $p < .001$, $\nu = .56$) and M-Aph ($\chi^2 = 9.15$, $p = .007$, $\nu = .31$); more participants with moderate/severe upper limb apraxia among S-Aph ($\chi^2 = 13.03$, $p < .001$, $\nu = .38$, moderate effect size).

The group S-Aph differed from the group M-Aph on several scores (with small or moderate effect size): more severe stroke ($Z = 2.40$, $p = .049$, $r = .29$), larger lesion size ($Z = 4.00$, $p < .001$, $r = .47$), more severe naming deficits ($Z = -3.89$, $p < .001$, $r = .50$), less patients with fluent aphasia ($\chi^2 = 11.43$, $p < .001$, $\nu = .40$) and more patients with moderate/severe executive dysfunction ($\chi^2 = 8.16$, $p = .013$, $\nu = .29$).

For the multivariate analysis, we performed a forward stepwise logistic regression analysis with bootstrapping, testing significant variables from univariate analyses, except naming and aphasia type, since these data are not applicable for non-aphasia participants. There was no collinearity between variables selected by the univariate analyses and used in the multivariate analysis (Variance Inflation Factor < 10 ; see Table S2). Note that participants with missing data for any independent variable were removed from the sample before performing multivariate analyses ($N_{\text{final}} = 89$).

We showed that the most commonly occurring significant factors (selected more than 60% of the time; Austin & Tu, 2004) were lesion size (99.9%), executive dysfunction (99.6%) and stroke severity (67.2%). The signs of regression coefficients for these variables were all negative, suggesting the stability of our model. Finally, these factors (lesion size, executive dysfunction and stroke severity) were

TABLE 1 Sociodemographic, cognitive, clinical and stroke-related data for participants with severe (S-Aph), mild/moderate (M-Aph) and without (N-Aph) aphasia, as well as statistical comparisons between groups.

	All participants (N=96)	S-Aph (N=41)	M-Aph (N=31)	N-Aph (N=24)	Omnibus test	Group comparisons		
						N-Aph vs. M-Aph	N-Aph vs. Sev-Aph	M-Aph vs. Sev-Aph
Sociodemographic factors								
Age (years)	65.59 (55.22–71.37)	65.51 (59.75–72.38)	59.02 (49.72–69.47)	67.55 (58.23–72.65)	$\chi^2=6.99, p=.03,$ $\eta^2=.054$	$Z=-2.29,$ $p=.065$	$Z=-.49,$ $p=1$	$Z=2.25,$ $p=.073$
Sex, male (%)	61 (63.54)	30 (73.17)	17 (54.84)	14 (58.33)	$\chi^2=2.94, p=.23$			
Handedness, RH (%)	90 (93.75)	38 (92.68)	30 (96.77)	22 (91.67)	$\chi^2=.74, p=.69$			
Education level, >high-school (%)	30 (32.61)	12 (30.77)	12 (38.71)	6 (27.27)	$\chi^2=.87, p=.65$			
Professional status, employed (%)	31 (33.33)	15 (37.5)	13 (41.94)	3 (13.64)	$\chi^2=5.19, p=.075$			
Isolation level: Living alone (%)	27 (29.35)	13 (32.5)	6 (20)	8 (36.36)	$\chi^2=1.97, p=.37$			
Isolation level: Family/Friends support, strong (%)	72 (78.26)	29 (72.5)	26 (86.67)	17 (77.27)	$\chi^2=2.04, p=.36$			
Cognitive and clinical factors								
General disability, moderate/severe (%)	66 (68.75)	34 (82.93)	20 (64.52)	12 (50)	$\chi^2=8.02, p=.018,$ $v=.29$	$\chi^2=1.17,$ $p=.84$	$\chi^2=7.93,$ $p=.015,$ $v=.29$	$\chi^2=3.19,$ $p=.22$
Weakness of UL and LL, moderate/severe (%)	38 (39.58)	22 (53.66)	9 (29.03)	7 (29.17)	$\chi^2=5.93, p=.052$			
Naming-FA (0–100%) ^a	30.24 (7.5–74.3)	30.24 (7.5–74.3)	81.25 (68.75–96.25)	3 (12.5)	$\chi^2=30.60, p<.001,$ $v=.56$	$\chi^2=9.15,$ $p=.007,$ $v=.31$	$\chi^2=30.62,$ $p<.001,$ $v=.56$	$Z=-3.89,$ $p<.001,$ $r=.50$
Executive dysfunction, moderate/severe (%)	53 (55.21)	34 (82.93)	16 (51.61)	3 (12.5)	$\chi^2=15.25, p<.001,$ $v=.41$	$\chi^2=2.94,$ $p=.26$	$\chi^2=13.03,$ $p<.001,$ $v=.38$	$\chi^2=8.16,$ $p=.013,$ $v=.29$
UL Apraxia, moderate/severe (%)	26 (28.57)	19 (48.72)	6 (20.69)	1 (4.35)				$\chi^2=5.62,$ $p=.053$

TABLE 1 (Continued)

	All participants (N=96)	S-Aph (N=41)	M-Aph (N=31)	N-Aph (N=24)	Omnibus test	Group comparisons		
						N-Aph vs. M-Aph	N-Aph vs. Sev-Aph	M-Aph vs. Sev-Aph
Spatial neglect, moderate/severe (%)	28 (29.47)	17 (41.46)	8 (25.81)	3 (13.04)	$\chi^2 = 1.33$, $p = .75$	$\chi^2 = 5.54$, $p = .056$	$\chi^2 = 1.91$, $p = .50$	
Mood disorders, ADRS (0–32)	8.5 (6–12)	8 (5.75–12)	8 (6–10.5)	10 (4–12)	$\chi^2 = 6.02$, $p = .049$, $v = .25$	$\chi^2 = .19$, $p = .91$		
Stroke-related factors								
Type of stroke, infarct (%)	75 (78.13)	36 (87.80)	21 (67.74)	18 (75)	$\chi^2 = 4.34$, $p = .11$			
Stroke severity, NIHSS (0–42)	11 (7–17.5)	16 (12–21)	10.5 (7–15.75)	7 (5.75–9)	$\chi^2 = 22.02$, $p < .001$, $\eta^2 = .22$	$Z = 2.66$, $p = .024$, $r = .36$	$Z = 4.47$, $p < .001$, $r = .56$	
Lesion size (voxels)	13,364 (2674–37,824)	41,127 (19224–82,276)	11,689 (3412–21,556)	1656.5 (941.5–3050.5)	$\chi^2 = 41.71$, $p < .001$, $\eta^2 = .43$	$Z = 3.82$, $p < .001$, $r = .52$	$Z = 5.71$, $p < .001$, $r = .71$	
Type of aphasia, fluent (%) ^a		20 (48.78)	27 (87.10)				$\chi^2 = 11.43$, $p < .001$, $v = .40$	
Moderate/severe WMHs (%)	38 (39.58)	14 (34.15)	11 (35.48)	13 (54.17)	$\chi^2 = 2.86$, $p = .24$		$Z = 2.19$, $p = .14$	
FA time (days post-stroke) ^a		21 (15–25)	16 (8.5–27)					

Note: Data are presented as median with interquartile range (Q1–Q3) or as number with a percentage (%). A value of p -corrected $< .05$ (with Bonferroni correction) for inter-group comparison and $p < .05$ (without correction) for omnibus tests, and when we considered only aphasic participants (for the type of aphasia, FA time and naming), were considered statistically significant. Statistically significant results are presented in bold.

Abbreviations: ADRS, Aphasia Depression Rating Scale; FA, First Assessment; LL, Lower Limb; M-Aph, Mild/Moderate Aphasia; N-Aph, Non-Aphasic; NIHSS, National Institutes of Health Stroke Scale; RH, Right Handers; S-Aph, Severe Aphasia; UL, Upper Limb; WMHs, White Matter Hyperintensities.

^aData and statistical analyses presented only for participants with aphasia (N = 73).

statistically significant predictors in the model (at $\alpha = .05$) more than 50% of the time, respectively, 99.60%, 99.30% and 76.19% (see Table 2).

In the final model, a forward stepwise regression selected stroke severity, executive dysfunction, lesion size and general disability as determinants of the initial severity of aphasia. However, general disability was a noise predictor since it was selected less than 60% of the time (see Table 2). Finally, our analysis revealed that a 1-point increase in NIHSS (i.e. increase in stroke severity) decreases the odds of having mild/moderate or no aphasia by 10% (OR = .90, 95% CI = .82–.99, $p = .041$); the presence of moderate/severe executive dysfunction decreases the odds of having mild/moderate or no aphasia by 93.2% (OR = .068, 95% CI = .018–.22, $p < .001$); and an increase of 1 standard deviation in lesion size is associated with a 91% decrease in the odds of having mild/moderate or no aphasia (OR = .068, 95% CI = .013–.24, $p < .001$).

Determinants of speech-and-language recovery

Sociodemographic, cognitive, clinical, stroke-related and rehabilitation-related factors are presented in Table 3 for all 53 patients and each group (poor and high recovery). Among these 53 patients, 33 (62.3%) presented severe aphasia initially, with 30 (96.8%) patients in the group 'high recovery'.

Based on the univariate analyses, the group of patients with high recovery differed from those with poor recovery on several factors (with moderate effect size): larger lesion size ($Z = -2.31$, $p = .020$, $r = .32$), more intensive SLT ($Z = -3.05$, $p = .0023$, $r = .43$) and more participants with moderate/severe executive dysfunction ($\chi^2 = 4.16$, $p = .041$, $\nu = .28$).

All significant variables from univariate analyses were kept for the multivariate analysis (stepwise logistic regression analysis with bootstrapping). There was no evidence of collinearity between variables selected by the univariate analyses (Variance Inflation Factor < 10 ; see Table S3). Participants with missing data for any independent variable were removed from the sample before performing multivariate analyses ($N_{\text{final}} = 51$).

We showed that all three factors were selected more than 60% of the time: 83.5% for SLT intensity, 72.1% for executive dysfunction and 67.5% for lesion size (Table 4). The regression coefficients were mainly positive (between 99.72% and 100%), suggesting the stability of our model. Only SLT intensity and executive dysfunction were significant predictors ($> 50\%$ of the time): 68.26% and 67.55%, respectively.

Moreover, based on statistical results from forward stepwise regression, only SLT intensity was significant in the final model (the p -value observed for executive dysfunction is tendential with $p = .052$).

TABLE 2 Results of stepwise logistic regression analysis with bootstrap to find determinants of initial severity of aphasia.

	Covariates selected (%)	Coefficients' sign		Statistical significance (%)
		+	-	
Lesion size (normalised)	99.9	.00	100.00	99.60
Executive dysfunction	99.6	.00	100.00	99.30
Stroke severity, NIHSS	67.2	.00	100.00	76.19
General disability	48.4	99.38	.62	66.12
Age	26.5	87.17	12.83	41.89
Spatial neglect	24.2	18.60	81.40	58.26
UL Apraxia	21.9	41.10	58.90	52.51

Note: For each variable, which was significant in the univariate analyses, we present the percentage of times that the variable was selected as an independent predictor, the sign of the regression coefficient was positive or negative, and the variable was significant in the model.

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; UL, Upper Limb.

TABLE 3 Sociodemographic, cognitive, clinical, stroke-related and rehabilitation-related data for aphasic participants with poor and high recovery, as well as statistical comparisons between groups.

	All participants (N=53)	Poor recovery (N=22)	High recovery (N=31)	Poor vs. high recovery
Sociodemographic factors				
Age (years)	62.5 (54–70.6)	57.15 (49.10–70.45)	64.30 (59.20–70.50)	$Z = -1.60, p = .11$
Sex, male (%)	36 (67.92)	12 (54.55)	24 (77.42)	$\chi^2 = 3.09, p = .079$
Handedness, RH (%)	50 (94.34)	21 (95.45)	29 (93.54)	$\chi^2 = .088, p = .77$
Education level, > high school diploma (%)	15 (28.85)	7 (31.82)	8 (26.67)	$\chi^2 = .16, p = .69$
Professional status, employed (%)	23 (44.23)	10 (45.45)	13 (43.33)	$\chi^2 = .023, p = .88$
Isolation level: Living alone (%)	15 (29.41)	5 (23.81)	10 (33.33)	$\chi^2 = .54, p = .46$
Isolation level: Family/Friends support, strong (%)	40 (78.43)	18 (85.71)	22 (73.33)	$\chi^2 = 1.12, p = .29$
Cognitive and clinical factors				
General disability, moderate/severe (%)	39 (73.58)	14 (63.64)	25 (80.65)	$\chi^2 = 1.92, p = .17$
Weakness of UL and LL, moderate/severe (%)	21 (39.62)	6 (27.27)	15 (48.39)	$\chi^2 = 2.40, p = .12$
Naming change (0–100%)	17.5 (3.75–40)	17.08 (1.88–26.46)	21.25 (7.19–49.07)	$Z = -.99, p = .33$
Executive dysfunction, moderate/severe (%)	37 (69.81)	12 (54.55)	25 (80.65)	$\chi^2 = 4.16, p = .041, v = .28$
UL Apraxia, moderate/severe (%)	16 (32.65)	6 (30.00)	10 (34.48)	$\chi^2 = .11, p = .74$
Spatial neglect, moderate/severe (%)	16 (30.19)	6 (27.27)	10 (32.36)	$\chi^2 = .15, p = .70$
Mood disorders, ADRS (0–32)	8 (5.25–11)	7.5 (5.75–9.25)	8 (5.25–11.75)	$Z = -.43, p = .67$
Stroke-related factors				
Type of stroke, infarct (%)	45 (84.91)	17 (77.27)	28 (90.32)	$\chi^2 = 1.71, p = .19$
Stroke severity, NIHSS (0–42)	13 (8.75–18)	11 (8–20)	13 (9–17.5)	$Z = -.13, p = .90$
Lesion size (voxels)	23,300 (7833–45,637)	17,646 (5012–31,529)	33,484 (13530–75,011)	$Z = -2.31, p = .020, r = .32$
Type of aphasia, fluent (%)	36 (67.92)	18 (81.82)	18 (58.06)	$\chi^2 = 3.33, p = .068$
Moderate/severe WMHs (%)	15 (28.30)	6 (27.27)	9 (29.03)	$\chi^2 = .020, p = .89$
DA time (days post-stroke)	82 (62–123)	81 (64.75–105)	82 (61.5–135.50)	$Z = -.43, p = .67$
Delay FA-DA	59 (44–101)	60 (45,25–92,25)	59 (43–106,50)	$Z = -0, 53, p = 0, 59$
Rehabilitation-related factors				
SLT onset (days post-stroke)	17 (13–24)	14.5 (1.25–22.25)	21 (15–24)	$Z = -1.91, p = .058$
SLT intensity (sessions/week)	4.4 (2.4–5)	3.5 (1.53–4.63)	5 (4–5)	$Z = -3.05, p = .0023, r = .43$

Note: Data are presented as median with interquartile range (Q1–Q3) or as number with a percentage (%). A value of $p < .05$ was considered statistically significant, and significant results are presented in bold. Missing data concerned: Education level ($n = 1$), Professional status ($n = 1$), Living alone ($n = 2$), Family support ($n = 2$), NIHSS ($n = 1$), SLT onset ($n = 2$), SLT intensity ($n = 2$), Naming change ($n = 12$), UL Apraxia ($n = 4$), ADRS ($n = 3$).

Abbreviations: ADRS, Aphasia Depression Rating Scale; DA, Discharge Assessment; FA, First Assessment; LL, Lower Limb; NIHSS, National Institutes of Health Stroke Scale; RH, Right Handers; SLT, Speech-and-Language Therapy; UL, Upper Limb; WMHs, White Matter Hyperintensities.

TABLE 4 Results of stepwise logistic regression analysis with bootstrap, to find determinants of language recovery.

	Covariates selected (%)	Coefficients' sign		Statistical significance (%)
		+ (%)	- (%)	
SLT intensity	83.5	100.00	.00	68.26
Executive dysfunction	72.1	99.72	.28	67.55
Lesion size (normalised)	67.5	99.85	.15	45.04

Note: For each variable, which was significant in the univariate analyses, we present the percentage of times that the variable was selected as an independent predictor, the sign of the regression coefficient was positive or negative, and the variable was significant in the model.

Abbreviations: SLT, Speech-and-Language Therapy.

This result suggests that a 1-point increase in SLT intensity (i.e. an increase of one session/week) increased the odds of having high recovery by 47% (OR = 1.47, 95% CI = 1.04–2.21, $p = .043$).

DISCUSSION

We explored the multimodal (sociodemographic, cognitive, clinical, stroke-related and rehabilitation-related) determinants of the initial severity of aphasia and the degree of speech-and-language recovery in participants with left-hemispheric stroke. Our results showed that stroke severity, lesion size and executive dysfunction were significant determinants of the initial severity of aphasia. At the same time, SLT intensity was the most significant determinant of speech-and-language recovery.

Our results are in agreement with previous studies reporting that a severe stroke is more often related to aphasia (Inatomi et al., 2008; Wilson et al., 2019). A consensus exists on the initial stroke severity being a predictor of the post-stroke outcome of aphasia (El Hachoui et al., 2013; Pedersen et al., 2004). Moreover, the relation between lesion size and initial severity of aphasia has also been reported (Doli et al., 2021; Lahiri et al., 2021). A recent study highlighted that haemorrhagic stroke, non-fluent aphasia and larger lesions were associated with more severe aphasia initially (Lahiri et al., 2021).

We also report that executive dysfunction determines the initial severity of aphasia. Indeed, univariate analyses revealed that executive functions were more severely impaired in patients with aphasia than in those without aphasia, and all the more, the aphasia was severe. This result, in line with previous reports (Bonini et al., 2015; Fonseca et al., 2019; Simic et al., 2020), highlights that executive functions are the most impaired cognitive skills in patients with aphasia and language disorders. This result also reflects an essential principle of cognitive organisation, that of cognitive interaction (Roger et al., 2022), between language and non-linguistic or general domain represented by executive functions and cognitive control. To maintain a correct level of language abilities, the integrity of the neurolinguistic system is insufficient. Still, other cognitive components should come into play, including working memory, long-term memory, executive functions and attention (Herbet & Duffau, 2020; Roger et al., 2022) within large anatomic-functional connectomic networks. Indeed, a large lesion-inducing aphasia, situated in the proximity of the substrates of executive functions, leads to a disruption of the anatomic-functional interactions between language and executive functions. The extension of lesions towards the prefrontal cortices underlying executive processes and cognitive control explains language and executive dysfunction (Olsson et al., 2019). Thus, executive functions and language abilities seem closely related, and according to some authors, executive functioning can be considered an appropriate indicator of communication abilities (Gonçalves et al., 2018; Olsson et al., 2019).

Altogether, these results imply that the relationship between stroke severity, executive dysfunction and aphasia severity may be related to the lesion extent and its location. Our results suggest that a more severe stroke and greater executive dysfunction are associated with a larger lesion, with a higher probability of impacting regions that are crucial for language and other cognitive processes, resulting in more severe aphasia (Inatomi et al., 2008; Kiran & Thompson, 2019; Lahiri et al., 2021). We plan to examine the role of lesion location in a future study.

Regarding determinants of speech-and-language recovery, we showed that the most robust determinant was SLT intensity. Several studies have evaluated the impact of sociodemographic, clinical, cognitive, stroke-related and rehabilitation-related factors on language recovery and aphasia outcomes. Indeed, in the literature, among the determinants associated with speech-and-language recovery, some are more consensual, such as aphasia severity (Lahiri et al., 2021; Ramsey et al., 2017) and lesion size and location (Benghanem et al., 2019; Harvey et al., 2022; Sul et al., 2019), and others are more debated, such as sex, age, handedness or education level (Ellis & Urban, 2016; Kristinsson et al., 2022; Wallentin, 2018). In our study, because of the use of the initial severity of aphasia in the calculation of gain that quantifies recovery, we cannot directly assess the role of the initial severity of aphasia on speech-and-language recovery. However, it should be noted that the group with high recovery consisted of 96.8% of patients with severe aphasia initially, suggesting a greater gain in patients with severe aphasia. This may be explained by the fact that patients with severe aphasia initially have a larger 'space' for improvement than those with mild/moderate aphasia (Lee et al., 2009; Osa García et al., 2020). Indeed, for patients with severe aphasia initially, the ASRS is low (between 0 and 2) and can increase by 1 to 5 points between FA and DA. In contrast, for patients with mild/moderate aphasia, the ASRS is higher (between 3 and 5), and it can thus increase only by 1 or 2 points.

Therefore, our results showed that more intensive SLT is associated with higher recovery in the sub-acute phase, particularly for patients with severe aphasia. These findings are consistent with previous studies showing that intensive rehabilitation, which boosts neuroplasticity, leads to better recovery than low-intensity rehabilitation (Brady et al., 2016, 2022b; Dignam et al., 2016). It has been suggested that repetition and intensity of SLT positively influence learning (or relearning) and consolidation (Kiran & Thompson, 2019). Another study showed that intensive rehabilitation for patients with more severe aphasia correlated with better recovery in terms of content (%words in the training script; Lee et al., 2009). So, knowledge of the prognosis for recovery may encourage the inclusion of some patients with severe aphasia in intensive therapies (Glize et al., 2017).

In this study, we also showed that executive dysfunction potentially plays a role in speech-and-language recovery, as shown by the selection of executive dysfunction variable in the bootstrap analysis but the tendential p -value in the final model. Although this result is tendential and in line with the influence of executive dysfunction on initial severity of aphasia, it seems that the assessment of executive functions is necessary and essential to consider in the implementation of personalised rehabilitation (Gilmore et al., 2019; Olsson et al., 2019; Simic et al., 2019; Varkanitsa & Kiran, 2022). Indeed, tailored SLT, based on functional relevance or difficulties, contributes to speech-and-language outcomes with the aim of maximising each patient's potential speech-and-language recovery (Brady et al., 2022a; Kristinsson et al., 2022). Moreover, as Gilmore et al. (2019) point out, targeting non-linguistic cognitive skills, such as executive functions, may be effective for improving language abilities (see also Mayer et al., 2017). Indeed, as mentioned in previous studies, the integrity of executive functions sustains the transfer of compensatory mechanisms acquired during SLT to activities of daily life, including communication (Simic et al., 2019, 2020). Moreover, building on the association between executive (or non-linguistic cognitive) functions and language, Herbet and Duffau (2020) have proposed multimodal rehabilitation strategies which target both affected language processes and functions associated with language (working memory, executive functions and attention). This can lead to a reconfiguration of functional networks, ultimately establishing a new state of functional equilibrium capable of compensating for language impairment.

Overall, our findings are beneficial regarding clinical applications. Indeed, identifying factors associated with the initial severity of aphasia and speech-and-language recovery is crucial for tailoring rehabilitation, maximising treatment effectiveness and establishing realistic recovery expectations for patients and their families (Doogan et al., 2018; Kristinsson et al., 2022, 2023; Simic et al., 2019; Varkanitsa & Kiran, 2022). Our results confirm previous findings in the literature, highlighting the influence of key factors, such as stroke severity, lesion size, executive dysfunction and SLT intensity, on aphasia severity and speech-and-language recovery. Based on these results, we suggest that to implement the most appropriate rehabilitation programme and guarantee the best long-term outcome, the SLT should be

frequent (i.e. intensive rehabilitation) and personalised (i.e. adapting rehabilitation to the patients' skills and difficulties) (Brady et al., 2022a, 2022b). Thus, we propose that intensive and adapted rehabilitation in patients with severe aphasia could optimise their language rehabilitation and guide future recommendations for patient care in hospital settings or elsewhere. Concerning intensive therapy, studies do not agree on an optimal intensity (Dignam et al., 2016) and 'intensive rehabilitation' is not defined in the same way across studies (e.g. number of hours per session, duration of therapy or total hours; Kiran & Thompson, 2019). Thus, in this study, we associate the term 'intensive rehabilitation' with an intensity of five sessions/week, as this is the median observed in the high recovery group. Moreover, for 'adapted rehabilitation', we support rehabilitation programmes combining executive function training and SLT (Bontemps et al., 2024; Herbet & Duffau, 2020; Simic et al., 2022). Recently, Bontemps et al. (2024) proposed a new method combining executive function training and anomia therapy for patients with chronic aphasia. This rehabilitation programme improves naming abilities and also allows the generalisation of trained strategies to untrained linguistic levels, with an improvement in discourse abilities. In another study, authors proposed a multimodal rehabilitation protocol which includes working memory training and phonological components analysis naming therapy (Simic et al., 2022). They showed that combined programme increases treatment efficacy and allows generalisation to language and communication abilities.

Several limitations of this study should be mentioned. First, the cohort size and missing values in the data lead to the need to validate these results in a larger cohort with complete data. Second, in this work, the assessment of executive functions is based on a single global score proposed by neuropsychologists and grouping different executive skills (i.e. flexibility, attentional control, inhibition, working memory and planning). Thus, we propose that an assessment of executive skills, with a more detailed score, would provide a more accurate indication of executive functioning in patients, and a more informative initial clinical assessment. Third, the use of the gain and its calculation only allows interpretations of recovery relative to the aphasia severity and not in terms of functional use of language. Despite recognising this limitation, we find it the most appropriate approach due to considerations of cohort size and available data on aphasia severity (ASRS score), as it incorporates the initial severity of aphasia in its calculation, enabling the measurement of relative improvement. Additionally, categorising patients into equivalent groups based on recovery levels (high and poor recovery) enables us to maintain a balanced dataset. Future investigations will supplement these findings by examining the potential influence of lesion location on the initial severity of aphasia and speech-and-language recovery.

CONCLUSION

In summary, while validation in a larger sample is needed due to missing data in our cohort, our findings enhance the understanding of aphasia severity and speech-and-language recovery in French patients. The study introduces an original method for analysing multiple variables collectively. This insight may aid in personalised language rehabilitation, guiding the selection and adapting methods for optimal recovery based on individual profiles and needs. Indeed, we propose that intensive tailored rehabilitation, with five sessions/week and a combination of executive function training and SLT, could maximise speech-and-language recovery for patients with severe aphasia initially.

AUTHOR CONTRIBUTIONS

Céline Haldin: Conceptualization; data curation; formal analysis; investigation; methodology; visualization; writing – original draft; writing – review and editing. **Shenhao Dai:** Conceptualization; data curation; formal analysis; investigation; methodology; resources; visualization; writing – original draft; writing – review and editing. **Céline Piscicelli:** Conceptualization; data curation; investigation; methodology; resources; writing – review and editing. **Valérie Marcon:** Conceptualization; data curation; resources; methodology; writing – review and editing; investigation. **Hélène Løvenbruck:** Conceptualization; methodology; resources; supervision; writing – original draft; writing – review

and editing. **Dominic Pérennou:** Conceptualization; methodology; project administration; resources; supervision; writing – original draft; writing – review and editing. **Monica Baciú:** Conceptualization; methodology; project administration; supervision; resources; writing – original draft; writing – review and editing.

CONFLICT OF INTEREST STATEMENT

No commercial or financial conflict of interest was identified for this research.

DATA AVAILABILITY STATEMENT

As the data presented in this article constitute patient health data, in accordance with French regulation and ethical rules, we cannot make this dataset available.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Data S1.

How to cite this article: Haldin, C., Dai, S., Piscicelli, C., Marcon, V., Lævenbruck, H., Pérennou, D., & Baciú, M. (2024). Multifactorial interplay on language recovery following left-hemispheric stroke: A retrospective study. *Journal of Neuropsychology*, *00*, 1–18. <https://doi.org/10.1111/jnp.12406>