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1 **New factors that affect quality of life in patients with aphasia**

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19

1 **Abstract**

2 **Background.** Aphasia severity is known to affect quality of life (QoL) in stroke patients as is
3 mood disorders, functional limitations, limitations on activities of daily life, economic status
4 and level of education. However, communication limitation nor fatigue has not been explored
5 in this specific population.

6 **Objective.** We aimed to investigate whether these factors were associated with QoL in
7 patients with aphasia after stroke.

8 **Methods.** Patients with aphasia were included from April 2014 to November 2017 after a first
9 stroke and were followed for 2 years post-stroke. QoL was assessed at follow-up by the
10 French Sickness Impact Profile 65 (SIP-65). We explored predictors such as mood disorders,
11 communication impairment, fatigue, limitations on activities of daily life, and aphasia severity
12 in addition to socio-demographic factors.

13 **Results.** We included 32 individuals (22 men; mean age 60.7 [SD 16.6] years) with aphasia
14 after a first stroke. Poor QoL as assessed by the SIP-65 was significantly associated (Pearson
15 correlations) with increased severity of aphasia initially ($p=0.008$) and at follow-up ($p=0.01$);
16 increased communication activity limitations at follow-up ($p<0.001$); increased limitations on
17 activities of daily life at baseline ($p=0.008$) and follow-up ($p<0.001$); increased fatigue at
18 follow-up ($p=0.001$); and increased depression symptoms at follow-up ($p=0.001$). On
19 multivariable analysis, QoL was associated with communication activity limitations,
20 limitations on activities of daily life, fatigue and depression, explaining more than 75% of the
21 variance (linear regression $R^2=0.756$, $p<0.001$). The relative importance in predicting the
22 variance was 32% for limitations on activities of daily life, 21% fatigue, 23% depression and
23 24% communication activity limitations.

1 **Conclusion.** Aphasia severity, mood disorders and functional limitations may have a negative
2 effect on QoL in patients with aphasia. Also, for the first time, we show that fatigue has an
3 important impact on QoL in this population. Specific management of this symptom might be
4 beneficial and should be explored in future studies.

5 **Keywords:** aphasia, quality of life, stroke, fatigue

6

7 **Introduction**

8 Quality of life (QoL) remains an important post-stroke outcome and a crucial challenge for
9 medical care. Special attention should be paid to QoL in post-stroke patients with aphasia
10 because it is a common post-stroke disorder with high prevalence [1]. Aphasia after a brain
11 lesion affects language production and/or comprehension, and the long-term consequences for
12 patients and their families are detrimental. Aphasia affects functional outcome, mood, QoL,
13 participation and the ability to return to work [2-5]. In recent studies, severity of aphasia
14 seemed strongly correlated with QoL, even more so than cancer or Alzheimer disease [6]
15 perhaps because our modern society relies on fast and efficient communication in the oral and
16 written modalities. Therefore, identifying and managing specific factors such as impaired
17 language and communication after stroke are essential to improve patients' QoL.

18 Previous studies identified several factors that affect QoL such as aphasia severity,
19 communication impairment, activity of daily life, economic status and level of education [7]
20 as well as mood disorders [5]. However, other hidden deficiencies have been poorly explored
21 in this specific population. This is the case for fatigue, known to have significantly higher
22 prevalence in individuals with stroke [8]. The prevalence of stroke-related fatigue is well
23 documented, but the factors contributing to fatigue and its resulting effects are still poorly

1 understood. Fatigue is known to affect function and QoL in non-aphasic post-stroke patients
2 [9 10] and interferes with the rehabilitation process. Indeed, recovery from stroke and aphasia
3 can be time- and energy-intensive, particularly when patients are under many different types
4 of therapy (i.e., speech therapy, physiotherapy, occupational therapy) on the same day, which
5 requires intense participation.

6 The aim of the present study was to investigate whether several relevant factors, including
7 unexplored ones such as fatigue, are associated with QoL of patients with post-stroke aphasia.

8 **Methods**

9 This was a retrospective analysis of the data collected for another prospective longitudinal
10 clinical trial from April 2014 to November 2017 that was approved by the local ethics
11 committee (CPP-SOOM3 University of Bordeaux). The consent of patients or their family
12 was obtained.

13 *Participants*

14 We included 32 individuals with aphasia after a first stroke who were followed 2 years post-
15 stroke. Inclusion criteria were aphasia after a first ischemic or haemorrhagic stroke of the left
16 hemisphere, usable auditory comprehension (see below) that permitted understanding basic
17 questions from questionnaires, French-speaking and right-handed. Exclusion criteria were
18 impairment of consciousness or coma, illiteracy, pre-stroke dementia, severe dysarthria, and
19 psychiatric disorders. Participants were followed by a physician specialised in physical
20 medicine and rehabilitation and received multidisciplinary rehabilitation (e.g., physiotherapy
21 and/or occupational therapy) according to the French and International guidelines and
22 depending on their initial deficiencies. Hence, if needed, patients had physiotherapy 4 to 5
23 times a week the first months and occupational therapy to train upper-limb motor impairment

1 or limitations in daily life activities. To treat aphasia, all patients received conventional
2 speech therapy at least for the first 6 months after the stroke, as much as possible depending
3 on their tolerance and at least 3 sessions a week. Figure 1 presents the overlap of the lesions.

4 *Measures*

5 In addition to socio-demographic information, the following instruments were administered to
6 each participant at the 2 time points (i.e., as soon as possible in the first 14 days post-stroke
7 and 2 years post-stroke [± 3 months]), during a face-to-face interview by a trained physician
8 and a speech therapist at baseline and by 2 speech therapists at follow-up, who were blinded
9 to baseline results.

10 QoL was assessed at follow-up by Sickness Impact Profile (SIP-65), the French short version
11 of the SIP-136, a specific scale for patients with aphasia [11]. The SIP-65 is feasible and
12 recommended to assess health-related functional status and QoL of French people with
13 aphasia, excluding those without reliable comprehension (i.e., patients with Z-score less than
14 the mean in comprehension subtests). This survey can be completed by patients themselves,
15 with the speech therapist to assist comprehension impairment, and consists of 65 items
16 divided into 8 categories exploring physical, psychological and social components of QoL.

17 The severity of aphasia was determined by using the French version of the Goodglass and
18 Kaplan's Boston Diagnostic Aphasia Examination (BDAE) and its severity subscore, the
19 Aphasia Severity Rating Scale (ASRS) [12]. The ASRS is rated on a 6-point Likert scale from
20 0, no usable speech or auditory comprehension, to 5, very slight language impairment. This
21 measure was performed in the acute phase (i.e., as soon as possible in the first 14 days post-
22 stroke) and at follow-up. Aphasia severity was considered mild with ASRS score 4-5,
23 moderate with ASRS score 3, and severe with ASRS score < 3 . Good outcome at month 6 was

1 defined as ASRS score 4 or 5. Hence, to explore the impact of good recovery on QoL, we
2 were able to distinguish between 3 categories based on the initial severity: 1) patients with
3 mild or moderate aphasia initially, known to have good outcomes [13] and who all recovered,
4 2) patients with severe aphasia who did not recover and 3) patients with severe aphasia who
5 recovered.

6 Comprehension subscores allowed for screening impairments in comprehension for reliable
7 assessment at follow-up. On the basis of the Z-score of the BDAE, we excluded patients with
8 scores $< 56/72$ for the subscore picture recognition “words discrimination” (mean 68.4 [SD
9 5]), $< 10/15$ for the item order execution “commands” (mean 13.2 [SD 2.4]) or $< 6/12$ for the
10 item complex material (mean 9.5 [SD 1.9]).

11 Communication activity limitation was assessed by the Verbal Communication Scale of
12 Bordeaux (VCSB) [14], exploring current communication behaviours in daily life. It also
13 includes questions about motivation for communication and strategies implemented by the
14 patient to cope with their difficulty. Several aspects of communication were explored: basic
15 communication, conversation, phone use, shopping, social communication, reading and
16 writing. This measure was performed only at follow-up because of the lack of relevancy in the
17 acute phase.

18 Fatigue was assessed by the French version [15] of the Fatigue Severity Scale (FSS) [16], a
19 self-administered questionnaire consisting of 9 items that identifies features of fatigue. Each
20 item is graded from 1, strongly disagree, to 7, strongly agree. The scale was validated in
21 stroke [17]. It was performed only at follow-up because of its lack of relevancy in the acute
22 phase.

1 Limitations on activities of daily life were assessed at baseline and at follow-up by the Barthel
2 index (scored from 0, no functional abilities, to 100, no limitation). This measure was
3 performed in the acute phase and at follow-up. Initial stroke severity was assessed by the US
4 National Institutes of Health Stroke Score (NIHSS) at baseline.

5 Anxiety and depression were assessed by the French version of the Hospital Anxiety and
6 Depression Scale (HADS) [18], with 2 subscores assessing depression (HADS-D) and anxiety
7 (HADS-A). Each subscore includes 7 items scored from 0 to 3; a score >7 indicates anxiety or
8 depression [19]. This measure was performed only at follow-up because of its lack of
9 relevancy in the acute phase.

10 *Statistical analysis*

11 First, we explored the association between QoL and age, sex, completed speech therapy, level
12 of education, antidepressant treatment, ASRS at baseline and 2 years post-stroke, the category
13 of patients taking into account initial severity, VCSB, FSS, Barthel Index, NIHSS, and
14 HADS-A and HADS-D. Pearson and Spearman correlations, one-way ANOVA for multiple
15 groups and independent *t* tests for binary variables (normal distribution) were used. We then
16 used multivariable analysis (linear regression, backward method) with SIP-65 as the
17 dependent variable and significant factors assessed at follow-up. Regarding aphasia, the
18 category of patients taking into account initial severity or VCSB were added to the model.
19 This method first placed all variables in the model and calculated the contribution of each of
20 them. Their contribution was then compared against a removal criterion. The variable with the
21 least contribution to the model was subsequently removed and the reduced model re-estimated
22 for the remaining variables. The contribution of the remaining variables was reassessed in an
23 iterative way until the model reached statistical significance. Moreover, for each predictor, the
24 relative importance and contribution percentages of the predictors were calculated [20]; p-

1 values were adjusted for multiplicity to control the overall type I error rate [21]. Finally, all
2 subscores of VCSB were added in a model with SIP-65 as a dependent variable by using the
3 same approach to explore which subscore was the most predictive. All statistical analyses
4 were performed with R3.5.0 (www.R-project.org). $P < 0.05$ was considered statistically
5 significant.

6 **Results**

7 Among the 32 individuals with aphasia after stroke included (22 men; mean age 60.7 [SD
8 16.6] years, range 23–94), at follow-up, 13 with mild aphasia (10 with ASRS=5 and 3 with
9 ASRS=4) ended speech therapy, considering that they no longer needed it. Other participants
10 had from 1 to 5 sessions/week since the initial stroke hospitalisation: 3 had 1 session/week (3
11 with ASRS score 5), 4 had 2 sessions/week (4 with ASRS score 4-5), 7 had 3 sessions/week
12 (3 with ASRS score 4-5, 2 with ASRS score 3, and 2 with ASRS score 1) and 3 had 4
13 sessions/week (3 with ASRS score 1). We found no significant correlation between SIP-65
14 score and number of sessions (Spearman $r(30)=0.151$, $p=0.409$). Inter-rater reliability was
15 perfect regarding aphasia severity ($\kappa=1$). Characteristics of the included patients are in
16 Table 1.

17 Nine patients took antidepressants (7 selective serotonin reuptake inhibitors) at follow-up. We
18 found no association between this medication and HADS ($t(30)=1.446$, $p=0.158$).

19 On univariate analyses, poor QoL assessed by the SIP-65 was significantly associated with
20 increased severity of aphasia (ASRS) initially ($r(30)=-0.458$, $p=0.008$) and at follow-up
21 ($r(30)=-0.451$, $p=0.010$), increased communication activity limitation (VCSB) at follow-up
22 ($r(30)=-0.650$, $p<0.001$), increased severity of stroke (NIHSS) initially ($r(30)=0.408$,
23 $p=0.020$), increased limitations on activities of daily life (Barthel Index) at baseline ($r(30)=-$

1 0.458, $p=0.008$) and follow-up ($r(30)=-0.657$, $p<0.001$), increased fatigue at follow-up
2 ($r(30)=0.572$, $p=0.001$), and increased depression symptoms (HADS-D) at follow-up
3 ($r(30)=0.549$, $p=0.001$) (Table 2). A significant association was also found for the category of
4 patients regarding the initial severity ($F(2)=4.208$, $p=0.025$), and patients who did not recover
5 showed poor QoL (Bonferroni post-hoc analysis, 95% confidence interval [-22.02 to -0.76]
6 $p=0.033$).

7 On multivariable analysis, the model was significant [$R^2=0.756$, $F(4,27)=20.87$, $p<0.001$],
8 when including HADS-D, FSS, Barthel index and VCSB at follow-up as predictors and when
9 including the category of patients regarding the initial severity instead of VCSB [$R^2=0.815$,
10 $F(5,26)=22.18$, $p<0.001$]. The predictor with the most relative importance in predicting the
11 variance in the first model was the Barthel index (32%), followed by FSS (21%), HADS-D
12 (23%), and VCSB (24%) and in the second model, the Barthel index (31%), FSS (22%),
13 HADS-D (29%), and the category of patients regarding the severity initially (18%). The
14 detailed models are presented in supplementary results.

15 Regarding VCSB subscores, a model including writing and conversation subscores was
16 significant [$R^2=0.432$, $F(2,29)=11$, $p<0.001$] and other subscores were excluded.

17 **Discussion**

18 The present study confirms that aphasia severity, mood disorders and functional limitations
19 are associated with poor QoL and that fatigue may play an important part to explain poor QoL
20 in individuals with aphasia after stroke.

21 These findings agree with previous studies [5]. Regarding aphasia severity and functional
22 limitations, these factors are predictive of QoL. However, only severity at follow-up was
23 associated with QoL. For the same severity at follow-up, patients with great improvement

1 from baseline did not have better QoL than patients with mild improvement or no
2 improvement. Therefore, patients may consider only the symptoms but not all the progress
3 since the stroke. Mood disorders, communication abilities and fatigue were assessed only in
4 the chronic phase because of their early fluctuations and lack of relevance.

5 The relevance of communication abilities suggests specific approaches for speech therapy.
6 Indeed, the VCSB scale assesses behaviours in daily life and is not necessarily associated with
7 aphasia severity [22] despite a strong correlation [3]. Of note, poor QoL was associated with
8 difficulties in conversation skills and writing. The latter is known to be one of the most
9 affected abilities [3]. Hence, rehabilitation targeting these specific abilities and based on
10 activity limitations and participation restrictions might affect QoL [7 23].

11 Mood disorders and fatigue are a hidden handicap and are often underestimated by healthcare
12 providers in post-stroke patients [24]. Special attention should be paid to patients with
13 aphasia, who are known to have more anxiety and depression symptoms [25]. In our
14 population, antidepressant medication was not associated with mood disorders, which
15 suggests either under-diagnosis [24] or negative connotations of these medications in patients.

16 To the best of our knowledge, this is the first report of QoL affected by chronic fatigue in
17 patients with aphasia. Fatigue symptoms in our sample were broadly similar to those found in
18 post-stroke patients without aphasia [26]. We found no significant correlation between fatigue
19 and other variables in the multivariable models, which suggests an independent effect of
20 fatigue on QoL. Fatigue is known to be associated with poor QoL in non-aphasic post-stroke
21 patients [9]. Regarding the specific population of patients with aphasia, fatigue could also be
22 due to mood disorders or language impairment. Moreover, a consistent protocol for fatigue
23 management is needed in aphasia rehabilitation, and fatigue should be considered by speech

1 therapists who have to take into account its impact on rehabilitation [27], even if this
2 symptom remains difficult to treat.

3 Our study has several limitations. First, the sample size was small and patients with impaired
4 comprehension that did not permit understanding basic questions from the questionnaires
5 were excluded. However, this limitation is due to the SIP-65, validated in patients with
6 aphasia, excluding patients with impaired comprehension. To our knowledge, no tool exists to
7 explore QoL in patients with severe comprehension impairment. QoL remains difficult to
8 explore without a communication skill, and severe comprehension impairment is a major
9 limitation of communication and cognitive abilities [28]. Severe production impairment can
10 be overpassed by using non-verbal communication, but this is not possible for severe
11 comprehension impairment, and domains that require communication skill cannot be
12 explored.

13 Our population seemed to be similar to previous large cohort regarding age, educational level
14 and aphasia severity[29]. Moreover, results with the HADS for patients with the most severe
15 disease were the same as with the ADRS, a specific tool validated in severe aphasia, based on
16 sympatric symptoms. Moreover, patients should have more anterior lesions and therefore be
17 more exposed to mood disorders and less anosognosia because of the exclusion of patients
18 with severe comprehension impairment. However, lesions were localised in perisylvian
19 regions, similar to a previous large cohort, and the correlation between lesion and linguistic
20 impairment remains difficult (for more details, see [30]).

21

22 **Conclusions**

23 Our findings confirm the possible negative effect of aphasia severity, mood disorders and
24 functional limitations on QoL in patients with aphasia after stroke. For the first time, the
25 present study highlights that fatigue has an important impact on QoL in this specific

1 population. Fatigue should be considered part of the speech rehabilitation process, and speech
2 therapists should take it into account.

3

4 **Conflict of interest.** None declared.

5

6 **Legend**

7 Figure 1. Overlap of brain lesions of 30/32 patients with aphasia after stroke. Two patients
8 presented contraindications for MRI.

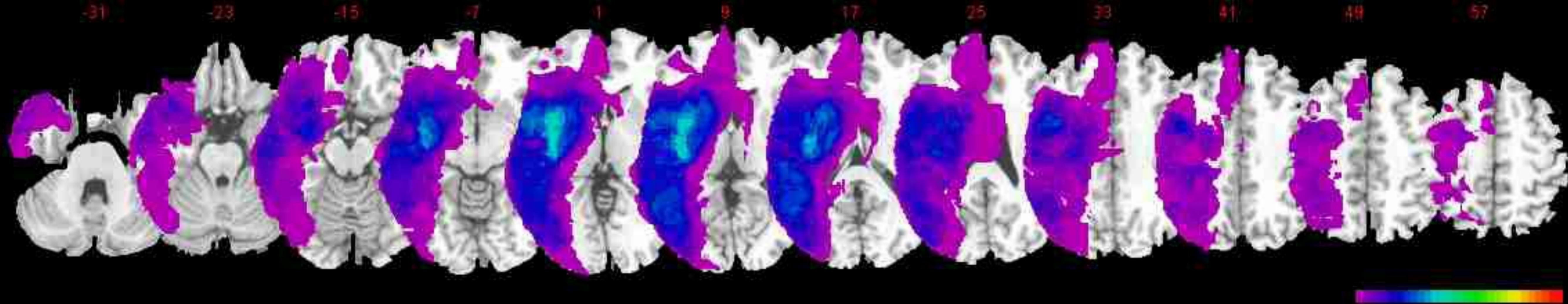
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7



1 **Table 1.** Characteristics of the 32 patients with aphasia after stroke.

Female	10 (31)
Age (years), mean (SD)	60.7 (16.6)
Level of education	
Less than lower secondary school	5 (16)
Vocational certificate	14 (43)
High school degree or university degree	13 (41)
Aphasia severity at baseline	
Severe (ASRS score 0-1-2)	20 (63)
Moderate (ASRS score 3)	4 (12)
Mild (ASRS score 4-5)	8 (25)
Aphasia severity at follow-up	
Severe (ASRS score 0-1-2)	5 (16)
Moderate (ASRS score 3)	4 (12)
Mild (ASRS score 4-5)	23 (72)
SIP-65 score, median (Q1–Q3)	15 (9–22.5)

2 Data are n (%) unless indicated.

3 ASRS, Aphasia Severity Rating Scale; SIP-65, Sickness Impact Profile 65

Table 2. Assessment at baseline and follow-up and association between these factors and quality of life assessed by the SIP-65.

		p-value*
<i>Acute phase</i>		
Stroke severity (NIHSS)	7.6 (7.5)	0.020
Barthel index	65.8 (35.6)	0.008
ASRS	2 (1.8)	0.008
<i>Follow-up</i>		
Antidepressant treatment, n (%)	9 (28)	0.160
Speech therapy, n (%)	19 (59)	0.118
Barthel index	95 (13)	<0.001
ASRS	3.9 (1.4)	0.010
VCSB	69.1 (27.3)	<0.001
Fatigue Severity Score	2.7 (1.7)	0.001
HADS anxiety subscore	4.5 (3.8)	0.472
HADS depression subscore	4.8 (4.3)	0.001
Category of patients		0.025
Mild or moderate aphasia initially and good outcome (n=12), median (Q1–Q3)	11 (4.5–21.75)	
Severe initially and poor outcome (n=9), median (Q1–Q3)	26 (14–32.5)	
Severe initially and good outcome (n=11), median (Q1–Q3)	14 (9–19)	

Data are mean (SD) unless indicated.

NIHSS, US National Institutes of Health Stroke Score; HADS, Hospital Anxiety and Depression Scale; ASRS, Aphasia Severity Rating Scale; VCSB, Verbal Communication Scale of Bordeaux,

* Pearson correlation or ANOVA