



Original research

Effects of Chronic Brain Injury on Quality of Life: A Study in Patients With Left- or Right-Sided Lesion



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KEYWORDS

Quality of Life;
Chronic brain injury;
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Abstract Objectives: To test the hypothesis that quality of life (QOL) is made up of different components, and each of these has different anatomic and demographic contributors.

Design: Questionnaire-based study.

Setting: Center for Cognitive Neuroscience, University of Pennsylvania.

Participants: People with chronic brain injury (N = 52) volunteered for the study. After excluding patients with severe communication deficits, bilateral lesions, and incomplete data, 42 patients with focal lesions were included in the final study: 22 patients with left hemisphere injury (LHI) (9 women and 13 men; mean age \pm SD, 60.6 \pm 11.2y [range: 36-83]; mean chronicity \pm SD, 11.5 \pm 4.2y) and 20 patients with right hemisphere injury [RHI] (16 women and 4 men; mean age \pm SD [62.7 \pm 12.8y] [range: 31-79]; mean chronicity \pm SD 10.1 \pm 4.3y).

Interventions: Not applicable.

Main Outcome Measures: We administered the RAND36-Item Health Survey (RAND-Version-1.0), Stroke Impact Scale (version 3.0), Positive Affect and Negative Affect Scale, and Distress Thermometer to measure QOL in LHI and RHI patients. Exploratory factor analysis with principal component method reduced these measures to 5 factors, roughly categorized as—(1) physical functioning; (2) general health; (3) emotional health; (4) social functioning; and (5)

List of abbreviations: ANOVA, analysis of variance; FA, factor analysis; KMO, Kaiser-Meyer Olkin; LHI, left hemisphere injury; PANAS, Positive Affect and Negative Affect Scale; QOL, quality of life; RHI, right hemisphere injury; SIS, Stroke Impact Scale; ToM, theory of mind. Disclosures: A.C. served as a cognitive consultant for Genentec in the PRISMS stroke trial. M.C. is supported by USIEF Fulbright–Nehru Postdoctoral Award (no. 2172/FNPDR/2016). The other authors have nothing to disclose.

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cognitive functioning. Exploratory analyses attempted to relate these factor scores to demographic variables, neuroanatomical data, and neuropsychological measures.

Results: Physical functioning was the biggest contributor to reduced QOL, explaining 32.5% of the variance. Older age, less education, and larger lesion size predicted poorer physical functioning ($P < .001$). Age also affected emotional health. ($P = .019$). Younger patients reported poorer emotional health than older patients. LHI patients reported less satisfaction with their cognitive functioning ($P = .009$) and RHI patients with their physical functioning ($P = .06$). Exploratory neuroanatomical analyses hinted at brain areas that may be associated with the perception of disability in each QOL component.

Conclusions: QOL is composed of 5 components. Clinical and demographic factors appear to differentially affect these aspects of patients' perceived QOL, providing hypotheses for further testing and suggesting potential relations for therapeutic interventions to consider.

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Advances in medicine have allowed us to extend the length of life of people with neurologic illnesses. Health care professionals think beyond morbidity and mortality to include *well-being* as an end target of their treatment. Consequently, *well-year* is now recognized as a unit of health status.¹ Greater importance is being attached to patients' subjective assessments of well-being and their satisfaction with treatment, as distinct from objective clinical measures of their health status. Quality of life (QOL) is important for evaluating efficacy and cost utility of different treatment plans or interventions.

Recently, the mortality rates of patients with brain injury (eg, stroke,² traumatic brain injury,³ brain tumor⁴) have decreased. However, their health status is far from satisfactory.⁵ According to Lai et al,⁵ only 25% of stroke patients return to the level of everyday participation and physical functioning comparable to community-matched persons who have not had a stroke. Survivors of traumatic brain injury⁶ and brain tumors⁷ also have significant functional and psychosocial impairments, limiting them in everyday activity and participation. Identifying the different factors that affect QOL for patients with brain injury is necessary to guide focused rehabilitation strategies.

Laterality of lesion may be one such factor. Functional lateralization in human brain⁸ means that patients with left hemisphere lesions have different deficits than patients with right hemisphere lesions. However, few studies have investigated the effect of laterality on the QOL of patients with brain injury and their results are not consistent.⁹ Some reports support the idea that the right hemisphere is not as crucial as the left hemisphere for maintaining a good QOL.¹⁰⁻¹³ Others assert that lesions in the right hemisphere cause significant reductions in QOL.^{14,15} Several studies also report no differences based on the side of the lesion.¹⁶⁻¹⁹

The inconsistent results of studies regarding the role of laterality in determining QOL may stem from differences in the tools used to measure QOL. Notably, the same group of patients performed differently on different scales of QOL.¹⁹ Previous studies have also focused on particular etiologies rather than on the laterality of lesion, per se, making it unclear whether their results are tied to the particular etiology or reflect anatomy. In addition, most of these studies

considered patients either undergoing treatment or patients who had just completed a treatment plan or in whom recovery was not complete.^{12,15,18} Consequently, their reports on QOL were relatively unstable and likely to change with time and the acquisition of compensatory strategies. Only rare studies¹³ addressed the long-term effects of stroke. Dhamoon et al¹³ found a significant effect of lesion laterality on QOL. However, in this study¹³ the patient, family member, or health care provider rated the patient's QOL. Consequently, the study did not exclusively reflect the subjective experience or QOL perception of the patients themselves.

The present study is motivated to understand the neuroanatomic underpinnings of threats to QOL experienced by patients with focal brain injuries. At the coarsest level, we test the hypothesis that laterality of damage contributes differentially to QOL. However, for the reasons listed above, this hypothesis might be inadequately formulated if QOL cannot be reduced to a single construct. We also consider the possibility that laterality itself may be too coarse to assess brain-QOL relations. Consequently, our study is a preliminary investigation to test the hypothesis that QOL is made up of different components, each of which is associated with different locations of brain injury. We also considered how demographic variables and neuropsychological impairments might affect QOL.

To test these hypotheses: (1) we selected patients with chronic focal lesions broadly, because of stroke, tumor resection, hemorrhage, or aneurysmal rupture; (2) we assessed QOL in this group by administering a battery of relevant measures of QOL, 2 specific to QOL and 2 pertaining to mood; and (3) we used exploratory factor analysis with principal component method to distinguish different aspects of QOL and investigate the effects of lesion location on these components.

Methods

Participants

Patients (N=52) enrolled in the Center for Cognitive Neuroscience Focal Lesion Database at the University of

Pennsylvania participated in the study. Database eligibility requirements include a diagnosis of a focal brain injury verifiable by magnetic resonance imaging or computed tomography scan, and absence of any other neurologic disorder or injury, learning disorder, or psychiatric condition. Additional requirements of this study included absence of moderate or severe aphasia that would make understanding the survey instruments difficult. All database volunteers meeting these criteria and active during the study recruitment period (May 2013–August 2014) were invited to participate. All participants signed an informed consent approved by the Institutional Review Board of the University of Pennsylvania and were compensated financially for their time. After excluding patients with severe communication deficits ($n=1$), bilateral lesions ($n=3$), and incomplete data ($n=6$), 42 focal lesion patients with unilateral injury were included in the analyses: 22 patients with left hemisphere injury (LHI) (9 women and 13 men; mean age \pm SD, $60.6\pm 11.2y$ [range: 36–83]; mean education \pm SD, $14.9\pm 2.7y$; mean lesion size \pm SD, 34.3 ± 44.9 cc; mean chronicity \pm SD, $11.5\pm 4.2y$) and 20 patients with right hemisphere injury (RHI) (16 women and 4 men; mean age \pm SD, $62.7\pm 12.8y$ [range: 31–89]; mean education \pm SD, $13.5\pm 2.3y$; mean lesion size \pm SD, 45.0 ± 53.2 cc; mean chronicity \pm SD, $10.1\pm 4.3y$). A total of 64% of the brain-injured patients considered in this study had experienced a stroke. The other patients had focal injuries resulting from tumor resections, hemorrhages, and ruptured aneurysms.

There were no significant differences in age, education, lesion size, and chronicity across LHI and RHI groups. The demographic and neurologic details of individual patients are presented in [table 1](#). Also included in [table 1](#) are scores from 4 neuropsychological tests collected as part of their database participation and reflective of their overall high level of cognitive function: Western Aphasia Battery,²⁰ American National Adult Reading Test,²¹ Philadelphia Brief Assessment of Cognition,²² and Mini-Mental State Examination.²³ All patients had their lesions mapped onto a standard brain template by a board-certified neurologist with the exception of 2 patients for whom films were not available. Data from these 2 patients were not included in the regression or exploratory lesion analyses.

QOL test materials

We administered the *RAND36-Item Health Survey* (RAND-version-1.0),²⁴ perhaps the most widely used general assessment of health-related quality of life,²⁵ and the *Stroke Impact Scale* (SIS-version 3.0),²⁶ the most widely used disease-specific health-related quality of life tool for stroke patients. We also included 2 standard depression scales—*Positive Affect and Negative Affect Scale* (PANAS)²⁷ and *Distress Thermometer*.²⁸ Depression and hopelessness have been associated with a poorer present QOL,²⁹ motivating our inclusion of the depression measures.

Procedure

Participants completed all 4 printed questionnaires in a single session either at the Hospital of the University of Pennsylvania or their homes. A researcher explained the

instructions for each questionnaire before presenting it to the participants to complete.

Statistical analyses

A factor analysis (FA) using principal component method with a varimax (orthogonal) rotation was conducted on data obtained from 42 patients. We obtained 21 measures per patient: PANAS (2), Distress Thermometer (1), RAND subscales (8), RAND health change (1), SIS subscales (8), and SIS stroke recovery (1). Because the sample size is smaller than typically obtained for FA, we calculated a recommended measure in designs where the ratio of cases to variables is less than 1:5—the Kaiser-Meyer Olkin (KMO) measure of sampling adequacy.³⁰ Examination of the KMO value indicated that the sample was factorable despite the small size ($KMO=.7$). Homogeneity of variance was confirmed by Bartlett's test (χ^2 [210]=511.6, $P<.001$). Communalities were above .5 for all items in the initial analysis. The diagonals of the anti-image correlation matrix were over .5 for all items except the positive and negative affects scores of the PANAS (PA_PANAS and NA_PANAS). We repeated the analysis after dropping PA_PANAS and NA_PANAS due to their low sampling adequacy. KMO of the new model was .7 and Bartlett's test was significant (χ^2 [171]=452.9, $P<.001$). One item (SIS-Handicap) did not load above .5 on any component and was dropped from the analysis. The final FA was conducted on 18 items. The KMO of the final model was .703 and Bartlett's test of sphericity was significant (χ^2 [153]=423.7, $P<.001$), again confirming that the data were factorable.³⁰ Communalities were above .5 for all items in the final analysis.

To anticipate the results, 5 factors were identified. A mixed-design analysis of variance (ANOVA) with group (LHI, RHI) as a between-participant variable and the 5 QOL components as within-participants variables was conducted to test for an interaction between group and QOL components. This analysis was followed by independent sample t tests to determine if LHI and RHI groups differed across the 5 QOL components. A discriminant analysis was performed to test how accurately patients' perceived QOL in the 5 domains could discriminate the LHI and RHI groups.

Stepwise regression was conducted to test if demographic (age, education) and neurologic factors (lesion size, chronicity) predicted the QOL components. Last, exploratory lesion analyses were conducted to consider whether injury to specific brain areas are associated with lower scores on any of the QOL components. To better understand the observed patterns and the potential effect of other participant differences, we also considered the effect of neuropsychological test performance and sex in post hoc analyses. Statistical analyses were done in SPSS Statistics^a and lesion analyses were done in MRICron.^b

Results

The final FA was done on 18 items. We extracted 5 components with eigenvalues above 1. The 5 components explained 32.5%, 16.3%, 9.8%, 7.4%, and 6.2% of the variance, respectively. The cumulative percentage of variance explained by the 5 components was 72.2%. The rotated component matrix with the communalities of the items is

Table 1 Demographic, neurologic, and neuropsychological details of LHI and RHI patients

ID	Sex	Age	Edu (y)	Lesion Side	Location	Lesion Size (CC)	Cause	Chronicity (y)	AQ	AMN/ART (Revised, 2/10)	PBAC-Memory (27)	PBAC-Visuospatial (18)	PBAC-Language (12)	PBAC-Executive (26)	PBAC-Behavior (24)	MMSE (30)
85	F	65	15	Left	Ins	13.1	Stroke	16.9	98.8	122.0	18	18	11	19.5	24	29
107	M	72	16	Left	FP	33.2	Stroke	16.2	N/A	103.0	N/A	N/A	N/A	N/A	N/A	N/A
141	F	54	16	Left	Ins	21.6	Stroke	14.0	98.8	113.0	N/A	N/A	N/A	N/A	N/A	N/A
215	M	64	14	Left	F	17.4	Stroke	14.5	94.4	106.0	18	17	11	18.5	24	29
236	M	68	19	Left	FP	156.0	Stroke	20.7	90.8	100.0	17.5	17	8.5	9.5	24	29
244	M	60	15	Left	T+Cer+ Pons	47.2	Stroke	13.9	98.4	109.0	N/A	N/A	12	18.5	24	27
318	F	63	12	Left	BG	20.7	Stroke	13.4	99	112.0	21.5	18	12	19	24	29
342	F	60	12	Left	O+T+Cs	42.1	Stroke	13.0	93.4	N/A	N/A	N/A	N/A	N/A	N/A	N/A
343	M	58	14	Left	T+Cer	20.1	Stroke	12.8	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
363	M	76	16	Left	F	16.8	Stroke	11.7	91.4	104.6	14	18	9	15.5	24	25
384	M	73	12	Left	F	11.3	Hemorrhage	12.3	93.1	102.4	14	13	10	19.5	24	22
428	M	58	12	Left	ACC+ F+CC	3.6	Stroke	12.2	95.5	109.4	15.5	12	10.5	17.5	24	30
493	M	70	14	Left	F	22.4	Aneurysm+ hemorrhage	10.3	92.1	104.0	10	18	10.5	15.5	24	24.5
529	F	68	12	Left	F	9.0	Stroke + aneurysm	10.4	94.9	95.0	13	13	8	17.5	23	26
534	F	63	16	Left	F	N/A	Aneurysm	10.1	N/A	120.0	N/A	N/A	N/A	N/A	N/A	N/A
541	M	49	19	Left	F	18.8	Tumour resection	10.4	N/A	122.0	21.5	18	11	22	24	25
565	M	56	12	Left	F	14.5	Aneurysm+ hemorrhage	10.6	N/A	121.0	N/A	N/A	N/A	N/A	N/A	N/A
642	M	79	12	Left	P	8.0	Stroke	11.4	96.8	N/A	16	18	11	19	24	25
755	F	50	16	Left	Cer	N/A	Stroke	3.9	N/A	120.0	20	18	12	21.5	24	30
775	M	45	20	Left	F	27.3	Aneurysm	6.1	99.2	110.4	13	16	11	20.5	24	29
792	F	31	14	Left	F	167.3	Tumor resection	2.2	99.6	106.2	14.5	14	10	17	24	27
795	F	52	20	Left	F	15.2	Tumor resection	6.6	96.0	124.8	21.5	18	12	20	24	30
83	M	72	12	Right	FTP	8.0	Stroke	16.6	99.8	114.0	17	16	12	23.5	24	29
87	F	74	15	Right	F	10.5	Stroke	16.7	99.1	113.0	23.5	17	10	20	24	28
112	F	50	16	Right	O+Th	4.7	Stroke	16.6	100	119.0	22	18	12	23	24	29
264	F	63	12	Right	F	45.3	Hemorrhage	14.5	N/A	116.0	N/A	N/A	N/A	N/A	N/A	N/A
444	F	82	12	Right	TP	15.5	Stroke	11.5	95.5	99.0	15	13	11.5	21.5	24	25
474	F	53	11	Right	P	22.2	Stroke	10.8	95.1	89.0	21	12	12	17.5	24	28
552	F	64	13	Right	F	4.1	Aneurysm	13.7	99.4	106.0	18.5	18	12	22	24	30
569	F	75	12	Right	FT+BG	37.4	Stroke	8.6	99.8	104.0	23	17	11	23	24	30
577	F	83	11	Right	Cer	4.2	Stroke	15.3	85.3	88.96	8.5	13	8	13	23	26
592	F	46	12	Right	FP	130.6	Stroke	11.8	97.8	110.0	19	14	12	19	22	29

(continued on next page)

Table 1 (continued)

ID	Sex	Age	Edu (y)	Lesion Side	Location	Lesion Size (CC)	Cause	Chronicity (y)	AQ	AMN/ART (Revised, 2/10)	PBAC-Memory (27)	PBAC-Visuospatial (18)	PBAC-Language (12)	PBAC-Executive (26)	PBAC-Behavior (24)	MMSE (30)
593	F	52	12	Right	FTP+BG+ Cau	170.1	Stroke	7.3	100	95.4	10.5	10	10	15.5	24	27
612	M	52	13	Right	Cer+Pons	27.8	Stroke	8.0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
640	F	72	18	Right	TP	64.6	Stroke	6.5	96.8	126.0	N/A	N/A	N/A	N/A	N/A	N/A
657	M	77	18	Right	PO	33.6	Stroke	5.6	99.2	126.2	21	18	12	21.5	24	28
665	F	54	14	Right	P	30.1	Tumor resection	4.7	N/A	110.0	22	18	12	22	24	30
694	F	36	12	Right	FP+BG+ Cau+Ins	46.5	Stroke	10.0	96.2	106.0	15.5	18	9	20.5	24	27
716	M	71	17	Right	F	182.1	Stroke+ aneurysm	6.0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
738	F	62	16	Right	Cer	32.2	Stroke	5.5	98.4	125.4	26	18	11.5	21	24	30
785	F	60	12	Right	F	7.7	Tumor resection	7.9	99.1	N/A	N/A	N/A	N/A	N/A	N/A	N/A
797	F	56	12	Right	T + brainstem	22.8	Tumor resection	4.6	N/A	114.7	16.5	14	10	20	24	30

Abbreviations: ACC, anterior cingulate cortex; AMNART, American National Adult Reading Test; BG, basal ganglia; Cau, caudate; CC, cingulate cortex; Cer, cerebellum; Cs, centrum semiovale; Edu, education; F, frontal (location); I, insula; MMSE, Mini-Mental State Examination; O, occipital; P, parietal; PBAC, Philadelphia Brief Assessment of Cognition; T, temporal; Th, thalamus; WAB, Western Aphasia Battery.

given in table 2. Based on inspection of the contributing individual items, we named the 5 factors: (1) physical functioning; (2) general health; (3) emotional health; (4) social functioning; and (5) cognitive functioning. Four items had cross-loadings >0.4 on other components, but they had primary loadings >0.6. The factors emotional health and cognitive functioning had <3 item loadings but we retained them as separate factors because (1) emotional health and cognitive functioning are theoretically different concepts, and (2) both RAND and SIS scales had fewer items measuring these 2 constructs.

A mixed ANOVA was conducted to assess the effect of laterality of lesion (LHI [n=22] vs RHI [n=20]) on the 5 factors. There was no significant main effect of group ($F_{1,40}=0.96, P=.333$) or factor scores ($F_{4,160}=.006, P=1$). However, there was a significant factor scores \times group interaction ($F_{4,160}=2.54, P=.042$; observed power=.7). Thus, the factor scores differed significantly in the LHI and the RHI groups (fig 1). An independent sample *t* test revealed that cognitive functioning was perceived as more impaired by the LHI group (mean \pm SD, $-.37\pm 1.1$) than the RHI group (mean \pm SD = $.40\pm .63$) [$t(33.44)=2.78, P=.009$, Cohen's $d=0.86$]. RHI patients reported lower perceived physical functioning than LHI patients, a difference that approached significance [$t(40)=-1.934, P=.06$, Cohen's $d=0.59$]. The results are summarized in table 3. To further explore the locus of the perceived difference in cognitive functioning between LHI and RHI patients, we conducted a post hoc comparison of the groups on 4 neuropsychological measures (Mini-Mental State Examination, American National Adult Reading Test, Western Aphasia Battery, Philadelphia Brief Assessment of the Cognition). No significant differences were observed (table 4).

In the discriminant analysis, the overall chi-square test was significant (Wilks $\lambda=.738, \chi^2=11.38, df=5$, canonical correlation = .51, $P=.04$). Cognitive functioning ($r=.82$) and physical functioning ($r=-.6$) were highly correlated with the discriminant function. Reclassification of cases based on the new canonical variable was successful. A total of 73.8% of the cases were correctly reclassified into their original categories. RHI and LHI groups were reclassified with 80% (16/20) and 68.2% (15/22) accuracy, respectively (table 5).

Given the uneven distribution of sex in the sample, we ran a post hoc analysis to consider its potential effect on the results. A mixed ANOVA examining the effect of sex (men [n=17] vs women [n=25]) on the principal component scores did not yield any significant differences. There was no significant main effect of sex ($F_{1,40}=.68, P=.416$), no significant main effect of principal component scores ($F_{4,160}=.06, P=.994$), and no significant sex \times principal component scores interaction ($F_{4,160}=1.51, P=.201$).

An exploratory stepwise regression analysis was conducted to predict the 5 factors. Education ($\beta=.567, t=4.68, P<.001$), lesion size ($\beta=-.452, t=-3.59, P=.001$), and age ($\beta=-.307, t=-2.47, P=.019$) predicted perceived physical functioning ($F_{3,39}=11.32, P<.001, R^2=.485$, Cohen's $f^2=.94$), indicating lesser education, larger lesion size, and older age were associated with worse perceived physical functioning after injury. Age ($\beta=.369, t=2.45, P=.019$) also predicted perceived

Table 2 Rotated component matrix with communalities of the items

Items	1. Physical Functioning	2. General Health	3. Emotional Health	4. Social Functioning	5. Cognitive Functioning	Communalities
SIS strength	0.92					0.9
RAND PF	0.863					0.834
SIS mobility	0.802					0.82
SIS ADL+IADL	0.767					0.827
SIS hand function	0.635		0.465			0.722
SIS stroke recovery	0.575				0.424	0.716
Distress		-0.716				0.733
RAND general health		0.706				0.681
RAND health change		0.675				0.544
RAND energy fatigue		0.638	0.421			0.73
SIS emotion			0.763			0.634
RAND EWB			0.625			0.522
RAND pain				0.701		0.791
RAND RLPF				0.681		0.7
RAND RLEP				0.66	0.42	0.781
RAND SF			0.474	0.639		0.642
SIS COMM					0.809	0.727
SIS memory					0.705	0.659

Abbreviations: ADL, activities of daily living; COMM, communication EWB, emotional well-being; IADL, instrumental activities of daily living; PF, physical functioning; RLPF, role limits physical functioning; RLEP, role limits emotional problems; SF, social functioning.

emotional health ($F_{1,39}=6.00$, $P=.019$, $R^2=.136$, Cohen's $f^2=.16$), indicating that younger patients reported worse perceived emotional health. However, none of these factors predicted perceived general health, social functioning, or cognitive functioning. Chronicity did not predict any of the 5 principal components.

To identify the brain areas associated with each of these factors, we conducted exploratory lesion subtraction analyses. First, factor scores were rank ordered from the smallest to the highest. Then, for each factor, we subtracted lesions of patients within the upper quartile (ie, top 25% on that factor) from the lesions of patients within the lower quartile (ie, bottom 25% who scored low on that factor). In this way, we plotted the brain areas that corresponded to the perception of dissatisfaction in each of these QOL factors. The lesion coverage map and subtraction plots for all 5 factors are shown in [fig 2A-F](#).

Discussion

Our study was motivated to understand the neuroanatomic and demographic variables that impair QOL in people with focal brain injury. We conducted a FA to identify components of QOL experienced by people with chronic focal lesions. Our study was motivated by the hypothesis that QOL is not a unitary construct and that people's QOL varies along different dimensions. A 5-factor model explained 72.2% of variance in QOL. Physical functioning was the most important QOL component that explained the most variance, followed by general health, emotional health, social functioning, and cognitive functioning.

We did not observe any effect of sex on the QOL components. In contrast to Drača,³¹ who reported that frequency of stroke in RH was significantly higher in men, we had few (4/20) male patients in the RHI group and a limited number of female patients in the LHI group (9/22).

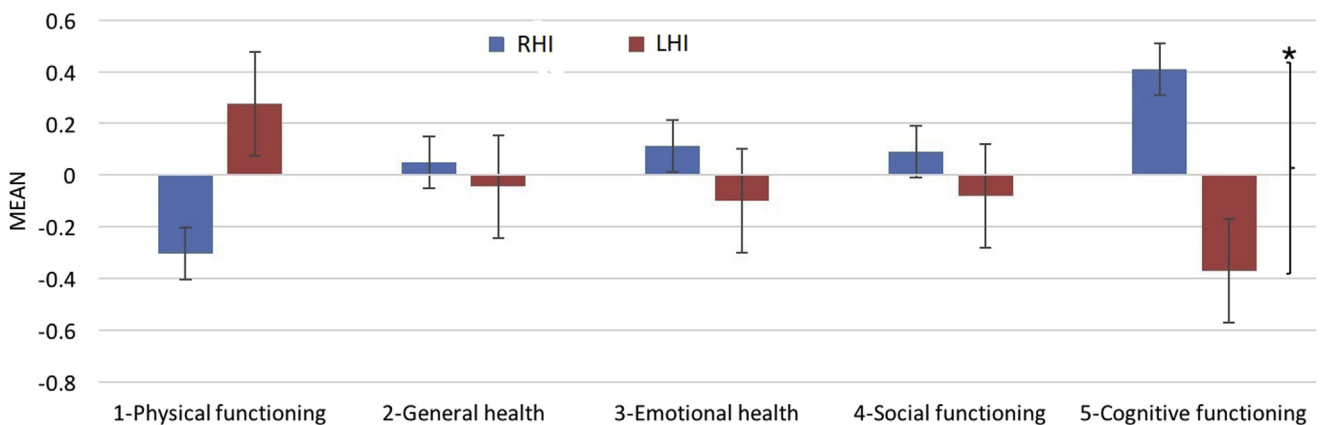


Fig 1 Mean and standard deviations of the 5 QOL factors in patients with RHI and LHI * $P<.05$.

Table 3 Result of independent sample *t* test of the 5 PCA components

Components	Group	n	Mean \pm SD	<i>t</i>	df	<i>P</i> Value
1-Physical functioning	RHI	20	-0.3 \pm 1.02	-1.934	40	.06
	LHI	22	0.28 \pm 0.92			
2-General health	RHI	20	0.05 \pm 1.01	0.304	40	.763
	LHI	22	-0.05 \pm 1.01			
3-Emotional health	RHI	20	0.11 \pm 0.98	0.681	40	.5
	LHI	22	-0.1 \pm 1.03			
4-Social functioning	RHI	20	0.09 \pm 1.03	0.543	40	.59
	LHI	22	-0.08 \pm 0.99			
5-Cognitive functioning	RHI	20	0.41 \pm 0.63	2.781	33.438	.009
	LHI	22	-0.37 \pm 1.14			

Larger sample size may be more sensitive for detecting potential differences in how men and women experience QOL after brain injury. If evident, determining neurologic, sociologic, or demographic factors that might underly sex differences in QOL would be an important area for future research.

Although cognitive functioning explained the least variance, it distinguished the left and right hemisphere injured patients. We assessed the effect of laterality on each factor of QOL and ran exploratory analyses to identify the predictors and brain-behavior correlates of these factors. Here we discuss these findings and their implications.

Physical functioning

In our sample, QOL was affected most by patients' perceived level of physical disability. We also found that age, education, and lesion size were predictors of perceived physical functioning.

Consistent with Jun et al,³² patients with higher education reported better perceived physical functioning. Without an objective measure of physical functioning, we cannot be certain of the relation between sociodemographic variables

and physical functioning, but the result clearly suggests that sociodemographic factors influence physical QOL—which in turn may affect prognosis and rehabilitation. People with higher education may have access to better medical care or be more likely to follow-up, thereby improving the odds of a better QOL. Adequate counseling sessions for patients with lower education levels and subsidized follow-up treatment may help improve their physical functioning—the most important component of QOL and, consequently, the one having a major effect on the QOL of caregivers as well.³³

Reports in the literature are inconsistent regarding the role of age and education in the health related QOL of brain-injured patients. Although some studies find age^{5,34,35} and education^{36,37} crucial, others do not.^{19,38-40} The effect of these factors may apply to specific QOL components, as found in our study. Global scores of QOL may be insensitive to the specificity of the effect.

Our exploratory lesion analyses indicated that lesions involving predominantly right motor cortex were associated with low perceived physical functioning. This observation is counterintuitive as the left hemisphere controls the dominant right hand and most of our patients were right-handed. However, the kinds of motor-intentional deficits associated with right frontal damage might account for this

Table 4 Comparison of standard neuropsychological tests in LHI and RHI patients

Cognitive Scales	Patient Group	n	Mean \pm SD	<i>t</i> Value	df	<i>P</i> Value
WAB-AQ	RHI	15	97.43 \pm 3.74	1.373	29	.18
	LHI	16	95.76 \pm 3.01			
AMNART	RHI	17	109.57 \pm 11.73	-0.354	34	.725
	LHI	19	110.78 \pm 8.69			
PBAC-memory	RHI	15	18.6 \pm 4.86	1.33	28	.194
	LHI	15	16.53 \pm 3.56			
PBAC-visuospatial	RHI	15	15.6 \pm 2.69	-0.886	28	.383
	LHI	15	16.4 \pm 2.23			
PBAC-language	RHI	15	11 \pm 1.3	0.892	29	.38
	LHI	16	10.59 \pm 1.24			
PBAC-executive	RHI	15	20.2 \pm 2.93	1.932	29	.063
	LHI	16	18.16 \pm 2.96			
PBAC-behavior	RHI	15	23.8 \pm 0.56	-0.892	29	.38
	LHI	16	23.94 \pm 0.25			
MMSE	RHI	15	28.4 \pm 1.59	1.496	29	.145
	LHI	16	27.28 \pm 2.45			

Abbreviations: AMNART, American National Adult Reading Test; AQ, aphasia quotient; MMSE, Mini-Mental State Examination; PBAC, Philadelphia Brief Assessment of Cognition; WAB, Western Aphasia Battery.

Table 5 Result of discriminant analysis

Standardized Canonical Discriminant Function Coefficients	Value
Function 1	
Physical functioning	−.636
General health	.109
Emotional health	.242
Social functioning	.194
Cognitive functioning	.824
Functions at Group Centroids	
RHI	.609
LHI	−.554

observation.⁴¹ Apart from lesions in the motor cortices, lesions in the bilateral-occipital lobe and the right superior temporal area were also associated with lower subjective ratings of physical functioning. One possibility is that lesions in these areas lead to difficulty in vision, exploration of objects, and processing of space-related information, all of which might restrict physical mobility and the activities of daily life.⁴²

General health

Age, education, lesion size, and chronicity did not predict levels of general health. Lesion side (left, right) also did not have any effect on this component. The exploratory subtraction plot suggests that many right hemisphere areas are important to general health—superior parietal, middle occipital, precentral, angular gyrus, thalamus, caudate, putamen, and insula—as well as the bilateral anterior cingulate. We could speculate how damage to these areas affects self-care and general health. For example, the right superior parietal-occipital region is usually associated with neglect. Lesions in the thalamus are reported to disturb the total sensory motor relay, attenuate the body's arousal system, disrupt emotion processing, and cause mood disorders. Acute poststroke depression is often associated with thalamic lesion.⁴³ Thalamic lesion can also cause pain or Dejerine-Roussy syndrome.⁴⁴ Lesions in the caudate⁴⁵ and anterior cingulum⁴⁶ may cause emotional disturbances. Lesions in the insula can affect awareness.⁴⁷ Future prospective studies could target the occurrence of these neurobehavioral symptoms with subjective reports of the quality of general health that patients with injuries in these areas experience.

Emotional health

Only age significantly predicted emotional health in the present study. Older patients reported better emotional health than younger patients. This finding is consistent with previous studies observing greater emotional well-being with age.⁴⁸ Others report that older adults move out of a negative emotional state faster than younger adults and are less likely to experience negative affect consistently.⁴⁹ Younger people may be burdened by liabilities like dependents to care for and these stresses may contribute to their low emotional health.⁵⁰ Younger patients may need counseling to boost

their emotional well-being and vocational rehabilitation for successful return to work⁵¹ and to alleviate their anxiety over financial insecurities. Most areas implicated in our exploratory anatomic analysis—left middle orbitofrontal cortex, left frontal areas, right frontal areas, bilateral insula, right caudate, right putamen, right thalamus, bilateral temporal cortex, right parietal cortex—are associated with the neural bases of emotion processing.⁵²

Social functioning

Age, education, lesion size, side, and chronicity did not predict social functioning. However, the subtraction plot included areas implicated in theory of mind (ToM) (right angular gyrus, right medial frontal areas, left temporal pole),⁵³ areas important for action observation (left inferior frontal gyrus, right inferior parietal lobule),^{53,54} and subcortical areas involved in social cognition (right cingulum and left caudate).^{55,56} ToM refers to the ability to understand and interpret another person's beliefs, emotions, and intentions. ToM requires both cognitive and emotional perspective taking and is necessary for social functioning.⁵⁷ Similarly, understanding the intentions of others while observing their actions is a fundamental aspect of social behavior.⁵⁸

Cognitive functioning

Age, education, lesion size, and chronicity did not predict the level of perceived cognitive functioning. However, patients with LHI reported significantly lower perceived cognitive functioning than patients with RHI. This subjective report was obtained despite LHI patients not exhibiting significant differences from RHI patients on standard neuropsychological measures of language, memory, visuospatial abilities, or executive function. One reason for this discrepancy between subjective and objective reports could be that although patients of both groups were able to answer with comparable accuracy, LHI patients may have had to exert greater cognitive effort. The lack of self-awareness generally associated with right hemisphere lesions is another possible explanation for this difference. Lunven et al¹⁹ observed that right-brain-injury patients, but not left-brain-injury patients, underestimated their difficulties when their scores were compared to scores provided by caregivers. Our subtraction analysis reveals that lesions primarily affecting language and memory areas of the brain (eg, bilateral angular gyrus and left inferior frontal cortex [pars triangularis], middle frontal, middle temporal gyrus, insula, putamen, caudate) were associated with subjective assessments of lower cognitive functioning. Although limited by reverse inference, this pattern is more consistent with a cognitive effort than an awareness-related interpretation of the laterality effect. Patients' perception of their abilities and disabilities appear more fine-grained than our rigorously designed clinical tests.

Study limitations

This study was conducted on a relatively small sample consisting of 42 patients, making our behavioral findings

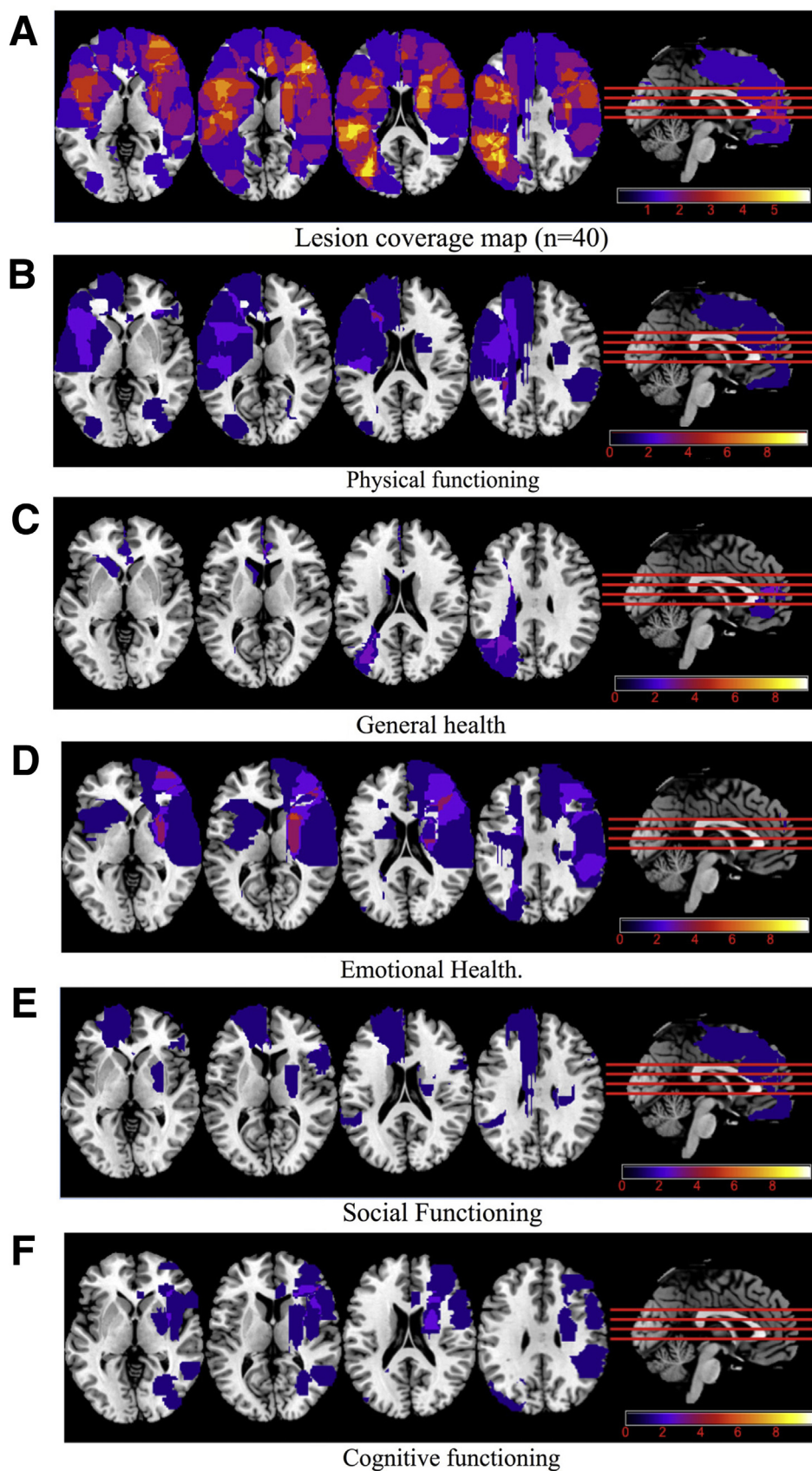


Fig 2 (A-F) The colored scale represents the number of lesions for each pixel. (A) Lesion coverage map; (B-F) subtraction plots (left side represents the right hemisphere and right side represents the left hemisphere).

preliminary and limiting our power to conduct detailed brain-behavior analyses. We consider the results of our lesion analyses to be hypothesis generating. Future studies are needed to verify these brain-behavior correlations. Although our sample size was smaller than typical of principal component analyses, the Kaiser-Meyer-Olkin measure of sampling adequacy and Bartlett's test of sphericity confirmed that the data set can be used for FA. We found a large effect size (Cohen's $d=.86$) for the difference in perception of cognitive functioning across the LHI and RHI groups. The effect size of the regression analysis for QOL component 1 (physical functioning) was also large (Cohen's $f^2=.94$). The regression analysis for QOL component 3 (emotional health) had a small but nontrivial effect size (Cohen's $f^2=.16$). Thus, the effect size measures reassure that the study reports significant and relevant information on patients with brain injury despite having a low sample size.

The varied etiologies of the patient population are both a strength and weakness of the design. Postinjury reorganization may differ between stroke and tumor patients, and different risk profiles and medications may contribute differently to their postinjury recovery and cognitive profiles. However, the inclusion of aneurysm and tumor patients allows us to sample the brain more broadly, because stroke lesions are limited by the vascular distribution. Limiting our analysis to stroke patients would have weakened our statistical power unnecessarily given that we do not have clear reasons to predict differences between stroke and the other patient subtypes.

We consider the results of our PCA and lesion analyses to provide preliminary support for our hypotheses: that QOL is a multifaceted construct, and injury to different brain areas can differentially affect these facets. To strategically target therapeutic interventions based on injury site, and to establish the possible effects of lesion cause, confirmation with a larger sample size and more even distribution of etiologies will be an important next step.

Conclusions

Since 1980, fatalities from heart disease and stroke have decreased by more than half,⁵⁹ and the cancer death rate dropped by 26% from 1991 to 2005.⁶⁰ These advances raise the importance of assessing QOL associated with these conditions after rehabilitation. We found that perception of physical disability had the greatest effect on patients' QOL. Education, lesion size, and age predicted perceived physical functioning. Older patients were more satisfied with their emotional health than younger patients. Patients with left hemisphere lesions were less satisfied with their cognitive functioning and had lesions in the areas of the brain typically implicated in language and memory functions. In summary, our study provides preliminary support for our hypothesis that different factors contribute to different components of QOL experienced by patients with neurologic injury. Our exploratory lesion analyses also generated a rich set of hypotheses for future testing. Closer attention to these domains can help guide rehabilitation and restorative efforts in this growing population of people.

Suppliers

- a. IBM SPSS Statistics version 25.0; IBM Corp.
- b. MRICron software; NeuroDebian.

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References

1. Kaplan RM, Bush JW. Health-related quality of life measurement for evaluation research and policy analysis. *Health Psychol* 1982;1:61-80.
2. Koton S, Schneider AL, Rosamond WD, et al. Stroke incidence and mortality trends in US communities, 1987 to 2011. *JAMA* 2014;312:259-68.
3. Coronado VG, Xu L, Basavaraju SV, et al. Surveillance for traumatic brain injury-related deaths—United States, 1997–2007. *MMWR Surveill Summ* 2011;60:1-32.
4. Porter KR, McCarthy BJ, Freels S, Kim Y, Davis FG. Prevalence estimates for primary brain tumors in the United States by age, gender, behavior, and histology. *Neuro Oncol* 2010;12:520-7.
5. Lai SM, Studenski S, Duncan PW, Perera S. Persisting consequences of stroke measured by the stroke impact scale. *Stroke* 2002;33:1840-4.
6. Di Battista A, Godfrey C, Soo C, Catroppa C, Anderson V. Depression and health related quality of life in adolescent survivors of a traumatic brain injury: a pilot study. *PLoS One* 2014;9:e101842.
7. Liu R, Page M, Solheim K, Fox S, Chang SM. Quality of life in adults with brain tumors: current knowledge and future directions. *Neuro Oncol* 2009;11:330-9.
8. Corballis MC. Lateralization of the human brain. *Prog Brain Res* 2012;195:103-21.
9. Palese A, Lamanna F, Di Monte C, Calligaris S, Doretto M, Criveller M. Quality of life in patients with right- or left-sided brain tumours: literature review. *J Clin Nurs* 2008;17:1403-10.
10. Trojanowski T, Peszynski J, Turowski K, et al. Quality of survival of patients with brain gliomas treated with postoperative CCNU and radiation therapy. *J Neurosurg* 1989;70:18-23.
11. Giovagnoli AR, Tamburini M, Boiardi A. Quality of life in brain tumor patients. *J Neurooncol* 1996;30:71-80.
12. Hahn CA, Dunn RH, Logue PE, King JH, Edwards CL, Halperin EC. Prospective study of neuropsychologic testing and quality-of-life assessment of adults with primary malignant brain tumors. *Int J Radiat Oncol Biol Phys* 2003;55:992-9.
13. Dhamoon MS, Moon YP, Paik MC, et al. Quality of life declines after first ischemic stroke: the Northern Manhattan Study. *Neurology* 2010;75:328-34.
14. Salo J, Niemela A, Joukamaa M, Koivukangas J. Effect of brain tumour laterality on patients' perceived quality of life. *J Neurol Neurosurg Psychiatry* 2002;72:373-7.

15. de Haan RJ, Limburg M, Van der Meulen JHP, Jacobs HM, Aaronson NK. Quality of life after stroke. *Stroke* 1995;26:402-8.
16. Rogers MP, Orav J, Black PM. The use of a simple Likert scale to measure quality of life in brain tumor patients. *J Neuro-oncology* 2001;55:121-31.
17. Pelletier G, Verhoef MJ, Khatri N, Hagen N. Quality of life in brain tumor patients: the relative contributions of depression, fatigue, emotional distress, and existential issues. *J Neuro-oncology* 2002;57:41-9.
18. Drewes C, Sagberg LM, Jakola AS, Solheim O. Quality of life in patients with intracranial tumors: does tumor laterality matter? *J Neurosurg* 2016;125:1-8.
19. Lunven M, Correia S, Migliaccio RD, et al. Recuperation of daily activities and quality of life after stroke: the EAVQ-QdV scale. *Ann Phys Rehabil Med* 2015;58:e7-8.
20. Kertesz A. *The Western Aphasia Battery*. New York: Grune & Stratton; 1982.
21. Grober E, Sliwinski M, Korey SR. Development and validation of a model for estimating premorbid verbal intelligence in the elderly. *J Clin Exp Neuropsychol* 1991;13:933-49.
22. Libon DJ, Massimo L, Moore P, et al. Screening for frontotemporal dementias and Alzheimer's disease with the Philadelphia brief assessment of cognition: a preliminary analysis. *Dement Geriatr Cogn Disord* 2007;24:441-7.
23. Folstein MF, Folstein SE, McHugh PR. A practical state method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189-98.
24. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-Item Health Survey 1.0. *Health Econ* 1993;2:217-27.
25. Hays RD, Morales LS. The RAND-36 Measure of Health-Related Quality of Life (The Finnish Med Soc Duodecim). *Ann Med* 2001;33:350-7.
26. Duncan PW, Bode RK, Lai SM, Perera S. Rasch analysis of a new stroke-specific outcome scale: the stroke impact scale. *Arch Phys Med Rehabil* 2003;84:950-63.
27. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol* 1988;54:1063-70.
28. Roth A, Kornblith A, Batel-Copel L, Peabody E, Scher H, Holland J. Rapid screening for psychologic distress in men with prostate carcinoma. *Cancer* 1998;82:1904-8.
29. de Leval N. Quality of life and depression: symmetry concepts. *Qual Life Res* 1999;8:283-91.
30. Field A. *Discovering statistics using SPSS*. Thousand Oaks, CA: Sage; 2009.
31. Drača S. Gender and stroke lateralization: factors of functional recovery after the first-ever unilateral stroke? *Neuro-Rehabilitation* 2012;30:247-54.
32. Jun HJ, Kim KJ, Chun IA, Moon OK. The relationship between stroke patients socio-economic conditions and their quality of life: the 2010 Korean Community Health Survey. *J Phys Ther Sci* 2015;27:781-4.
33. Pucciarelli G, Vellone E, Savini S, et al. Roles of changing physical function and caregiver burden on quality of life in stroke: a longitudinal dyadic analysis. *Stroke* 2017;48:733-9.
34. Gurcay E, Bal A, Cakci A. Health related quality of life in first-ever stroke patients. *Ann Saudi Med* 2009;29:36-40.
35. Nichols-Larsen DS, Clark PC, Zeringue A, Greenspan A, Blanton S. Factors influencing stroke survivors' quality of life during subacute recovery. *Stroke* 2005;36:1480-4.
36. Lailaturrahmi, Armenia, Armal K, Akmal. Education determines the health related quality of life on the stroke patients of the National Stroke Hospital, West Sumater, Indonesia. *World J Pharm Pharm Sci* 2014;3:1369-77.
37. Din NC, Ahamat MH, Mukahar R, Basri H. Health-related quality of life in stroke patients. Available at: https://www.researchgate.net/publication/236024118_Health-related_quality_of_life_in_stroke_patients. Last accessed December 30, 2019.
38. Langton HR. Rehabilitation after stroke. *Q J Med* 1990;76:659-74.
39. Gokkaya NK, Aras MD, Cakci A. Health-related quality of life of Turkish stroke survivors. *Int J Rehabil Res* 2005;28:229-35.
40. Abubakar SA, Isezuo SA. Health related quality of life of stroke survivors: experience of a stroke unit. *Int J Biomed Sci* 2012;8:183-7.
41. Na DL, Adair JC, Williamson DJ, Schwartz RL, Haws B, Heilman KM. Dissociation of sensory-attentional from motor-intentional neglect. *J Neurol Neurosurg Psychiatry* 1998;64:331-8.
42. Marx MS, Werner P, Cohen-Mansfield J, Feldman R. The relationship between low vision and performance of activities of daily living in nursing home residents. *J Am Geriatr Soc* 1992;40:1018-20.
43. Omura T, Kimura M, Kim K, et al. Acute poststroke depression is associated with thalamic lesions and clinical outcomes: a case-control study. *J Stroke Cerebrovasc Dis* 2018;27:499-505.
44. Nasreddine ZS, Saver JL. Pain after thalamic stroke: right diencephalic predominance and clinical features in 180 patients. *Neurology* 1997.
45. Cheng YC, Liu HC. Psychotic symptoms associated with left caudate infarction. *Int J Gerontol* 2015;9:180-2.
46. Yücel M, Wood SJ, Fornito A, Riffkin J, Velakoulis D, Pantelis C. Anterior cingulate dysfunction: implications for psychiatric disorders? *J Psychiatry Neurosci* 2003;28:350-4.
47. Craig AD. How do you feel — now? The anterior insula and human awareness. *Nat Rev Neurosci* 2009;10:59.
48. Charles ST. Strength and vulnerability integration: a model of emotional well-being across adulthood. *Psychol Bull* 2010;136:1068-91.
49. Carstensen LL, Pasupathi M, Mayr U, Nesselroade JR. Emotional experience in everyday life across the adult life span. *J Pers Soc Psychol* 2000;79:644-55.
50. Morris R. The psychology of stroke in young adults: the roles of service provision and return to work. *Stroke Res Treat* 2011;2011:1-10.
51. Matérne M, Lundqvist L-O, Strandberg T. Opportunities and barriers for successful return to work after acquired brain injury: a patient perspective. *Work* 2017;56:125-34.
52. Etkin A, Büchel C, Gross JJ. The neural bases of emotion regulation. *Nat Rev Neurosci* 2015;16:693-700.
53. Yang DY, Rosenblau G, Keifer C, Pelphrey KA. An integrative neural model of social perception, action observation, and theory of mind. *Neurosci Biobehav Rev* 2015;51:263-75.
54. Rosa S De, Schillinger FL, Bühlhoff HH. fMRI adaptation between action observation and action execution reveals cortical areas with mirror neuron properties in human. *Neurosci Biobehav Rev* 2010;34:1-10.
55. Fujiwara H, Hirao K, Namiki C, et al. Anterior cingulate pathology and social cognition in schizophrenia: a study of gray matter, white matter and sulcal morphometry. *Neuroimage* 2007;36:1236-45.
56. Kemp J, Berthel MC, Dufour A, et al. Caudate nucleus and social cognition: neuropsychological and SPECT evidence from a patient with focal caudate lesion. *Cortex* 2013;49:559-71.
57. Doherty MJ. *Theory of mind: how children understand others' thoughts and feelings*. Hove, United Kingdom: Psychology Press; 2008.
58. Ge S, Liu H, Lin P, Gao J, Xiao C, Li Z. Neural basis of action observation and understanding from first- and third-person perspectives: an fMRI study. *Front Behav Neurosci* 2018;12:283.
59. Mensah GA, Wei GS, Sorlie PD, et al. Decline in cardiovascular mortality: possible causes and implications. *Circ Res* 2017;120:366-80.
60. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin* 2018;68:7-30.