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Relationships between neurocognitive functioning, mood, and quality of life in patients with temporal lobe glioma

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Abstract

Objective—While neurocognitive functioning (NCF) and mood disturbance share a relationship with health-related quality of life (HRQOL), few studies have examined relationships between these constructs in glioma patients prior to treatment.

Methods—Newly diagnosed patients with glioma in the left (N=73; 49% glioblastoma) or right (N=30; 57% glioblastoma) temporal lobe completed neuropsychological testing and self-report measures of HRQOL (Functional Assessment of Cancer Treatment-General and Brain module) and mood (Beck Depression Inventory-Second Edition and State-Trait Anxiety Inventory).

Results—Verbal learning and memory, executive function, and language abilities were associated with various HRQOL scales. Stepwise linear regression showed that verbal learning predicted scores on the General Well-being scale and Brain module, processing speed predicted Social Well-being scores, and executive functioning predicted Functional Well-being scores on the FACT. Upper extremity strength also predicted scores on the Functional Well-being subscale and Brain module. Mood was more strongly associated with HRQOL domains than NCF, with depressive symptoms accounting for a large proportion of variance across most subscales.

Conclusions—In patients with temporal lobe glioma, depressive symptoms are strongly related to most aspects of HRQOL but not with NCF. NCF, specifically verbal learning and memory, executive functioning, and processing speed, also show direct relationships with numerous aspects of HRQOL. These findings underscore the importance of multimodal assessment of NCF and mood in this population.

Keywords

brain tumor; quality of life; mood; cognitive function; cancer; oncology

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Introduction

Glioma comprise approximately 80% of all primary brain tumors, affecting about 23,000 individuals in the United States per year.¹ In addition to poor prognosis, patients with glioma often face significant neurological deficits associated with tumor and treatment,² occupational disability,³ and future uncertainty,⁴ all of which may contribute to emotional and social complications.⁵ Given the detrimental impact of these factors upon patient well-being, issues pertaining to health-related quality of life (HRQOL) have garnered increased attention over the past decade.⁶

In addition to tracking patient HRQOL, monitoring neurocognitive functioning (NCF) and mood is also essential for optimal clinical care. The vast majority of patients with glioma exhibit cognitive impairment, which often presents early in the illness and is frequently progressive in nature.⁷ Such deficits can also impact the social and occupational functioning of glioma patients, with indication that NCF impairment influences HRQOL to a greater extent than physical symptoms.⁶ Mood disturbance, particularly symptoms of depression and anxiety, are also common in patients with glioma,^{5,8} with up to 48% exhibiting clinically significant symptoms during the course of illness.⁹ Importantly, symptoms of depression and neurocognitive impairment have been independently associated with reduced survival in patients with glioma, with emerging evidence suggesting that those exhibiting both have the worst prognosis.¹⁰⁻¹²

While it is known that NCF, mood, and HRQOL share a relationship, relatively little empirical work has examined the relationship between these factors in patients with glioma prior to initiation of treatment. Further, existing studies tend to collapse tumors of various cerebral regions and lobes into a single group, confounding the potential identification of patterns that may be specific to certain lesion locations. The present study aims to characterize relationships between NCF, mood, and HRQOL in newly diagnosed patients with glioma restricted to the temporal lobes. It is hypothesized that objective NCF, particularly memory performances, will be predictive of patient reported HRQOL, given the role of temporal lobe structures in learning and memory¹³ and the importance of such functions in successfully performing basic and instrumental activities of daily living.^{14,15} However, it is also expected that self-reported mood symptoms will be stronger predictors of HRQOL than NCF, as there is greater conceptual and methodological similarity between the constructs of HRQOL and mood, as well as between measurement instruments used to assess these constructs.

Materials and Methods

Participants

Newly diagnosed adult patients with glioma of the left temporal lobe (LTL) or right temporal lobe (RTL) who underwent comprehensive presurgical neuropsychological evaluation were identified in The University of Texas MD Anderson Cancer Center (MDACC) neuropsychology and neurosurgery databases. Those with history of other neurological disease were excluded, with the exception of seizure disorder secondary to tumor. Patients with a history of open surgical resection, radiotherapy, or any type of

chemotherapy prior to completion of neuropsychological assessment were also excluded. One hundred and three patients met criteria and completed presurgical neuropsychological evaluation between 2001 and 2010. The MDACC Institutional Review Board approved this retrospective study.

Data Collection and Coding

Lesion Location and Size—As previously described,¹⁶ three distinct temporal lobe areas were defined to specify tumor location, including the lateral anterior, lateral posterior, and medial regions. Tumors with extension into 2 or more areas were considered multi-region. Volumetric analysis was performed on MRI scans with MedVision 1.41 software, as detailed elsewhere.¹⁷

Neurocognitive Testing—NCF testing was conducted as part of a comprehensive presurgical neuropsychological evaluation for clinical purposes. Table 1 lists the neuropsychological tests by domain that were routinely included in the clinical test battery and the source of normative comparison groups.¹⁸⁻²⁵ The number of patients administered a given NCF test differed by instrument, as the evaluations utilized a flexible battery and were performed for clinical purposes. Sample sizes are described by test in the table accompanying the results. Approximately half of the total sample did not have data for the HVLT-R DR and HVLT-R Rec variables, as clinic practices initially utilized an earlier version of the HVLT that did not include the delayed memory trials. Nonetheless, HVLT-R TR trials are identical between versions, and HVLT-R normative data were used for all HVLT variables, as indicated in Table 1.

All neurocognitive test scores were converted to z-scores ($M=0$, $SD=1$) using published normative data stratified by age, and other demographic characteristics when appropriate. Performance on an individual NCF test that fell at or below a z-score of -1.5 was considered impaired. Grip Strength Difference and Grooved Pegboard Difference scores were calculated as the z-score of the hand contralateral to the tumor minus the score of the hand ipsilateral to the tumor. Difference scores were considered impaired if the hand contralateral to the tumor was at least -1.5 below the hand ipsilateral to the tumor. The Clinical Trial Battery Composite (CTB Comp) is the mean of z-scores for COWA, TMTA, TMTB, HVLT-R TR, HVLT-R DR, and HVLT-R Rec. CTB Comp z-scores at or below -0.70 were considered impaired based on the results of prior receiver operating characteristic analyses (unpublished data).

Mood Questionnaires—Patients were also administered measures of mood at the time of NCF testing. Due to evolving clinical practice, only a subset of patients completed the following mood measures. The Beck Depression Inventory-Second Edition (BDI-II)²⁶ was administered ($N=40$) to measure the presence and severity of depressive symptomatology. The measure yields a total score, with higher scores reflecting greater depressive symptomatology. As recommended in the clinical manual, total scores of 14 or more were considered indicative of clinically significant elevations in depressive symptoms.²⁶

The State-Trait Anxiety Inventory (STAI)²⁷ Form Y was also administered to a subset of patients ($N=24$) to measure symptoms of current (state) and more longstanding (trait)

anxiety. The STAI yields 2 subscale scores, the total state anxiety score (STAI-S) and total trait anxiety score (STAI-T), with higher scores reflecting greater symptoms of anxiety. Scores of 44 or greater were considered indicative of clinically significant elevations in anxiety, which has been utilized as a cut-point in prior research regarding anxiety and cancer.²⁸⁻³⁰

Assessment of Health-Related Quality of Life—A subset of patients (N=96) completed the Functional Assessment of Cancer Therapy-General Version 4 (FACT-G)³¹ and Brain module at the time of NCF testing.³² From the FACT-G, four subscale scores are computed measuring Physical, Social, Emotional, and Functional Well-being. A total score is also calculated measuring General Well-being. The Brain module yields a total score from items reflective of cognitive and neurological symptoms characteristic of patients with brain tumors. Higher scores on all measures reflect greater HRQOL in the relevant domains. For the FACT-G, a healthy general U.S. population sample was used for determination of clinically significant deviations in patient HRQOL.³³ Consistent with recommendations regarding minimally important differences on the FACT-G,³⁴ subscale scores that fell at least 0.5 SDs below reference group means were considered clinically significant reductions in HRQOL. A healthy control reference group was unavailable for the Brain module.

Statistical Analysis

Independent-samples t-tests or Pearson χ^2 tests were used to compare demographic and clinical characteristics between LTL and RTL glioma patient groups to assess for potential biases in the sample. The potential impact of steroid and antiepileptic medication upon NCF and mood were determined with independent-samples t-tests. Associations between FACT scales and measures of mood and NCF were determined with Pearson product-moment correlations (r). Using Cohen's guidelines, correlation coefficients of .1, .3, and .5 corresponded to weak, moderate, and strong associations, respectively.³⁵ Separate stepwise multiple regression analyses were conducted with cognitive measures as predictors of each FACT scale. The HVLT-R DR, HVLT-R Rec, and CTB Comp variables were excluded due to the reduced sample sizes on these measures. Patients were included in these analyses only if they completed all other NCF measures and the FACT (N=83). Additional stepwise multiple regression analyses were performed with the BDI-II and STAI as the only predictors of each FACT scale. Patients were included in these analyses only if they completed the BDI-II, STAI, and FACT (N=24). For all regression procedures, a predictor was deleted if $\alpha > .10$ and added if $\alpha < .05$. Adjusted R^2 was utilized to determine the amount of variance accounted for by the models, correcting for the number of predictors in the model. All statistical analyses were performed with SPSS 21.0 (IBM Corp).³⁶ Two-sided tests were used with a significance level of $p < 0.05$.

Results

Patient Characteristics

Demographic and clinical characteristics are presented in Table 2. The majority of patients were diagnosed with glioblastoma (52%) and 71% of tumors were located in the LTL. Nearly 95% of the sample had Karnofsky Performance Status Scale scores (KPS) greater

than 80, indicating that physicians rated most patients as capable of completing normal activities with only minor signs or symptoms.³⁷ Demographic and clinical characteristics did not significantly differ between LTL and RTL patients.

Neurocognitive Impairment, Mood Disturbance, and Quality of Life

Descriptive data regarding NCF test performances, mood scales, and HRQOL measures are presented in Table 3. Most patients (74%) exhibited clinically significant NCF impairment on at least one measure. Rates of impairment were greatest on measures of verbal learning (HVLTR TR, 44%), memory (HVLTR DR, 37%), and executive functioning (TMTB, 36%). Performances did not differ by steroid use, though those taking antiepileptic medications performed better than those without on measures of auditory comprehension [Token: -0.02 (1.07) vs. -0.57 (1.34), $t(86)=-2.06$, $p=.043$] and executive function [TMTB: -0.68 (1.52) vs. -2.47 (3.48), $t(81)=-3.26$, $p<.001$]. Approximately 13% of patients who completed the BDI-II exhibited clinically significant depressive symptoms. Nearly 46% showed clinically significant state anxiety on the STAI-S, with only 17% exhibiting longstanding trait anxiety on the STAI-T. Regarding HRQOL on the FACT, clinically significant reductions were greatest in the domains of Emotional (54%) and Functional Well-being (24%).

Associations between Neurocognitive Functioning and Quality of Life

Pearson correlation coefficients describing associations between tests of NCF and HRQOL scales are displayed in the lower portion of Table 3. Moderate associations were found between the Emotional Well-being subscale, verbal learning and memory (HVLTR DR & HVLTR Rec), and overall cognitive functioning (CTB Comp); and between the Functional Well-being subscale and overall NCF (CTB Comp). A number of other weak but significant correlations were also identified.

Associations between Mood and Health-Related Quality of Life

All FACT scales were strongly associated with depression scores on the BDI-II (see Table 3). A few FACT scales also showed significant associations with anxiety on the STAI (see Table 3). Ratings of state anxiety (STAI-S) had moderate strength relationships with the General and Emotional Well-being scales, while trait anxiety (STAI-T) had a moderate relationship with the Brain module. Increased anxiety or depressive symptoms were not associated with worse NCF.

Predictors of Health-Related Quality of Life

Patient demographics and lesion volume (T1-weighted or FLAIR) were not associated with any FACT scales and were excluded from regression analyses. Results of stepwise linear regression analyses are summarized in Table 4. Verbal learning on HVLTR TR was the only significant predictor of the General Well-being scale [$F(1,81)=6.03$, $p=.016$]. None of the NCF tests were significant predictors of the Physical or Emotional Well-being subscales. For the Social Well-being subscale, only processing speed on TMTA was a significant predictor in the regression analysis [$F(1,81)=6.99$, $p=.010$]. Executive functioning on TMTB [$F(1,81)=7.82$, $p=.006$] and manual dexterity on Peg [$F(2,80)=6.46$, $p=.003$] were significant

predictors of the Functional Well-being subscale. Verbal learning on HVLT-R TR [F(1,81)=8.80, $p=.004$] and manual dexterity on Peg [F(2,80)=7.27, $p=.001$] were significant predictors of Brain Module scores.

Of the mood measures, depression on the BDI-II was the only significant predictor of all FACT scales, with the exception of Social Well-being, which was not significantly predicted by the BDI-II or the STAI. Specifically, ratings of depression on the BDI-II significantly predicted the General Well-being scale [F(1,22)=26.82, $p<.001$], the Physical Well-being subscale [F(1,22)=23.51, $p<.001$], the Emotional Well-being subscale [F(1,22)=20.63, $p<.001$], the Functional Well-being subscale [F(1,22)=6.21, $p=.021$], and Brain module scores [F(1,22)=26.85, $p<.001$].

Discussion

Neurocognitive dysfunction was common in the overall sample, with nearly three quarters of all patients with temporal lobe glioma exhibiting clinically significant impairment on at least one test. As hypothesized, impairment was most common on measures of verbal learning and memory, consistent with known neuroanatomical correlates implicating temporal lobe structures (especially medial regions) in memory processes.³⁸ However, a similar proportion exhibited executive impairment (about 40%) and mean performances fell below normative expectations on all other measures, with nearly 20% showing impairment on a composite. These findings indicate that glioma may result in more diffuse disruption of NCF than is often found with other focal neurological conditions, consistent with prior observations.³⁹

This study also adds to growing evidence implicating that NCF impairment is related to HRQOL deficits.^{6,39} Specifically, problems with verbal learning and memory, executive function, language comprehension, and upper extremity strength were significantly associated with worse HRQOL across various domains. Verbal learning was also a significant predictor of general HRQOL, as well as more brain tumor-specific concerns, including neurobehavioral complaints, difficulty with activities of daily living, and self-reported cognitive symptoms. Manual dexterity also contributed to the model predicting brain tumor-specific problems. Additionally, executive functioning and manual dexterity predicted functional aspects of HRQOL (e.g., occupational and recreational abilities), and processing speed was predictive of social HRQOL (e.g., relationship quality with friends and family). Taken together, greater deficits in learning and executive functioning are associated with reductions in numerous aspects of HRQOL in patients with temporal lobe glioma as hypothesized, in addition to indication that processing speed and motor functioning are also important contributors to HRQOL in this population.

Clinically significant depressive symptoms and characterological (trait) anxiety were relatively infrequent in the sample, while current (state) anxiety at the time of assessment was identified in nearly half of the sample. This is not entirely surprising given the fact that patients were newly diagnosed and awaiting neurosurgical intervention, which likely contribute to apprehension and future uncertainty. Ratings of both depression and anxiety were highly associated with emotional aspects of HRQOL (e.g., coping, nervousness, hope), on which over half of patients endorsed reductions in well-being. While similarity in items

across measures of mood and the Emotional Well-being subscale may contribute to the noted associations, the strength of the relationships suggest that symptoms of both anxiety and depression are important factors related to HRQOL. Indeed, depressive symptoms were strongly associated with reductions in all aspects of HRQOL, symptoms of state anxiety showed moderate relationships with general and emotional HRQOL, and more longstanding characterological anxiety was related to brain tumor-specific concerns. The importance of mood symptoms to patient HRQOL was further supported by the regression analyses, in which depression significantly predicted all HRQOL domains with the exception of social well-being. These findings echo prior studies asserting strong relationships between mood and HRQOL in patients with brain tumors at various stages of the disease course.^{40,41}

Differences in associations between HRQOL and performance-based tests of NCF compared to self-report measures of mood may relate to inherent differences between objective and subjective methods of assessment of disease burden. Depression, anxiety, and HRQOL are subjective phenomenological constructs, based on an individual's interpretation of their experiences. As HRQOL and mood states are private experiences, instruments measuring these constructs necessarily rely upon self-reports. Given these considerations, it is not surprising that most of the objective NCF measures were modest predictors of HRQOL in comparison with mood indices. Nonetheless, it should be emphasized that the variance in functional aspects of HRQOL accounted for by objective NCF measures (12%) was somewhat similar to that of depressive symptoms (19%), and a measure of processing speed was the only significant predictor of social HRQOL out of all NCF and mood measures. Thus, both self-reported measures of mood (particularly depression) and objective NCF tests are independently related to aspects of HRQOL.

This study focused exclusively on the relationships between NCF, mood, and HRQOL in newly diagnosed patients with temporal lobe glioma at a single time point in the presurgical period. It is likely that these factors and their interrelationships dynamically evolve throughout the disease course as the disease progresses and/or treatments are implemented or modified. Indeed, even in the presurgical period, our results show that medications may play an important role, as patients on antiepileptic medications performed better than those without on select NCF measures. While the significance of this finding is not entirely clear, de Groot et al (2013) recently reported that levetiracetam may in fact have a beneficial impact upon NCF in glioma patients, in contrast to the typically detrimental effects observed with the use of older antiepileptics.⁴² Similarly, relationships between psychosocial variables may be impacted by the implementation of other pharmacological and psychosocial interventions that specifically target mood and NCF problems (e.g., psychotherapy, cognitive rehabilitation, antidepressant and stimulant medications). Accordingly, future longitudinal study is needed to understand how these relationships may change following resection and during adjuvant therapy. To address these issues, we are routinely collecting these outcome data at regular intervals throughout the disease course. We also aim to develop more advanced neuroimaging protocols to better understand the etiology of observed impairments and symptoms in this population. Future studies are also needed to compare these results with analogous data regarding glioma of different cerebral regions, as the pattern of NCF impairment, mood symptoms, and relationships with HRQOL may vary by lesion location.

Perhaps the greatest limitation of the study pertains to the different sizes of subsamples included in analyses. Ideally, all patients would have completed each of the study measures, including NCF testing as well as measures of mood and HRQOL. However, patients were referred for clinical purposes, clinical practices changed over time, and the battery of measures was flexible to accommodate for unique referral questions and patient needs. Accordingly, separate regression analyses were conducted with those completing the NCF and HRQOL measures and those completing the mood and HRQOL measures. As such, slight differences between the results of correlational and regression analyses likely pertain to the different subsamples included. Nonetheless, subsamples were of similar composition regarding demographic and clinical characteristics, adding some support to their representativeness. Though replication is needed and future prospective studies would be helpful, the results generate preliminary evidence that both NCF and mood have important and independent associations with HRQOL in patients with glioma of the temporal lobes. In other words, when patients exhibit reductions in HRQOL following initial glioma diagnosis prior to any treatment, their NCF status should not be ignored or treated separately, but be considered a unique contributor to well-being alongside mood.

Overall, the findings support the primary study hypotheses, in that both NCF impairment and mood symptoms are primary contributors to reductions in the HRQOL of patients with temporal lobe glioma, even prior to treatment. Further, of the cognitive domains, learning and memory and executive function appear most important. Clinically, these findings support the routine assessment of NCF and mood in patients with glioma, even when performance status is relatively preserved. Specifically, neuropsychological evaluation may help identify targets for behavioral and/or pharmacological intervention, which may consequently improve patient well-being in the face of an ultimately fatal disease.

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Table 1

Neurocognitive tests grouped by principal domain

Test	Abbreviation	Norms
<i>Attention</i>		
WAIS-R/III Digit Span	Digit Span	Wechsler, 1981; Wechsler 1997
<i>Learning and Memory</i>		
HVLT-R Total Recall	HVLT-R TR	Benedict et al., 1998
HVLT-R Delayed Recall	HVLT-R DR	Benedict et al., 1998
HVLT-R Recognition Discrimination Index	HVLT-R Rec	Benedict et al., 1998
<i>Processing Speed</i>		
WAIS-R/III Digit Symbol	Digit Symbol	Wechsler, 1981; Wechsler, 1997
Trail Making Test Part A	TMTA	Tombaugh, 2004
<i>Executive Function</i>		
Trail Making Test Part B	TMTB	Tombaugh, 2004
WAIS-R/III Similarities	Similarities	Wechsler, 1981; Wechsler, 1997
MAE Controlled Oral Word Association	COWA	Ruff et al., 1996
<i>Language</i>		
MAE Token Test	Token	Benton et al., 2000
<i>Visuospatial Function</i>		
WAIS-R/III Block Design	Block Design	Wechsler, 1981; Wechsler, 1997
<i>Motor Function</i>		
Grip Strength Difference	Grip	Heaton et al., 2004
Grooved Pegboard Difference	Peg	Trites, 1977
Clinical Trial Battery Composite	CTB Comp	Mean of z-scores from the HVLT-R, COWA, and TMT using the above norms

Abbreviations: WAIS-R/III, Wechsler Adult Intelligence Scale-Revised or Third Edition; HVLT-R, Hopkins Verbal Learning Test-Revised; MAE, Multilingual Aphasia Examination.

Table 2

Demographic and clinical characteristics

	LTL (N=73)	RTL (N=30)	Total (N=103)
Age (years)			
Mean (SD)	51.3 (14.4)	53.6 (11.1)	52.0 (13.5)
Range	18–78	25–73	18–78
Gender, % Male	56.2	63.3	58.3
Race, % White	87.7	93.3	89.3
Handedness, % Right	86.3	83.3	85.4
Education (years)			
Mean (SD)	14.6 (2.6)	14.6 (2.0)	14.6 (2.4)
Range	7–20	11–19	7–20
Histology, %			
Glioblastoma	49.3	56.7	51.5
Astrocytoma	21.9	23.3	22.3
Oligodendroglioma	16.4	10.0	14.6
Other	12.3	10.0	11.7
Temporal Lobe Region, %			
Anterior	17.8	20.0	18.4
Posterior	30.1	23.3	28.2
Medial	37.0	46.7	39.8
Multi	15.1	10.0	13.6
Lesion Volume, cm ³			
T1-weighted, Mean (SD) ^a	24.8 (25.2)	32.6 (27.7)	27.1 (26.1)
FLAIR, Mean (SD) ^b	47.1 (44.1)	55.8 (47.2)	49.6 (45.0)
Seizure history, % yes	43.8	36.7	41.7
Antiepileptic Drug, % yes ^c	64.5	70.4	66.0
Steroid, % yes ^d	56.9	56.0	57.3
KPS ^b , %			
80	96.0	94.0	94.6

Abbreviations: LTL, Left temporal lobe; RTL, Right temporal lobe; KPS, Karnofsky Performance Status scale.

^aLTL N=72; RTL N=30.

^bLTL N=71; RTL N=29.

^cLTL N=62; RTL N=27.

^dLTL N=58; RTL N=25.

Table 3

Neurocognitive, mood, and quality of life scores and correlations

Test/Measure	N	Mean (SD)	Range	% Clinically Significant		
Neurocognitive Function ^a						
Digit Span	103	−0.43 (0.86)	−2.33–2.33	18.4		
HVLT-R TR	103	−1.28 (1.53)	−6.16–1.37	43.7		
HVLT-R DR	51	−1.22 (1.82)	−5.47–1.22	37.3		
HVLT-R Rec	51	−0.86 (1.84)	−7.71–0.86	18.4		
Digit Symbol	102	−0.04 (1.00)	−2.33–2.33	10.8		
TMTA	101	−0.30 (1.99)	−14.75–1.79	13.9		
TMTB	97	−1.26 (2.48)	−11.91–2.06	36.1		
Similarities	98	−0.21 (0.86)	−2.33–2.33	14.3		
COWA	102	−0.57 (1.13)	−3.66–1.61	15.7		
Token	97	−0.05 (1.11)	−2.33–0.92	17.6		
Block Design	101	−0.04 (0.92)	−2.00–2.67	6.9		
Grip	96	−0.11 (1.01)	−2.87–2.32	4.9		
Peg	99	−0.17 (1.32)	−4.18–3.25	11.7		
CTB Comp	49	−0.80 (1.03)	−3.86–1.06	19.4		
Mood ^b						
BDI-II	40	8.08 (7.00)	0.00–39.00	12.5		
STAI-S	24	40.58 (10.17)	24.00–62.00	45.8		
STAT-T	24	31.71 (8.72)	20.00–50.00	16.7		
Health-Related Quality of Life ^b						
General	95	83.53 (11.00)	49.00–104.00	12.6		
Physical	95	22.99 (4.14)	9.00–28.00	18.9		
Social	95	24.27 (3.95)	8.00–28.00	4.2		
Emotional	95	16.72 (4.39)	6.00–24.00	53.7		
Functional	95	19.56 (4.81)	9.00–28.00	24.2		
Brain	95	54.07 (12.11)	14.00–74.00	N/A		
FACT Scales						
Measure ^c	General	Physical	Social	Emotional	Functional	Brain
Neurocognitive Function						
Digit Span	−0.08	−0.00	0.02	−0.13	−0.08	0.12
HVLT-R TR	0.23 [*]	0.09	0.08	0.17	0.23 [*]	0.27 ^{**}
HVLT-R DR	0.09	0.03	−0.18	0.33 [*]	0.07	0.08
HVLT-R Rec	0.20	0.06	−0.10	0.40 ^{**}	0.22	0.15
Digit Symbol	0.08	−0.01	0.08	−0.06	0.19	0.13
TMTA	0.18	0.05	0.17	0.10	0.15	0.14
TMTB	0.23 [*]	0.10	0.22 [*]	−0.01	0.26 [*]	0.23 [*]

Measure ^c	FACT Scales					
	General	Physical	Social	Emotional	Functional	Brain
Similarities	0.04	−0.06	−0.01	0.17	−0.00	0.14
COWA	0.10	0.10	0.07	−0.01	0.11	0.16
Token	0.22 [*]	0.07	0.12	0.15	0.20	0.22 [*]
Block Design	0.04	0.06	−0.01	0.10	−0.04	0.06
Grip	0.15	0.22 [*]	0.01	0.02	0.20	0.17
Peg	0.05	0.14	−0.01	−0.19	0.18	0.19
CTB Comp	0.29	0.11	0.04	0.38 [*]	0.31 [*]	0.21
<i>Mood</i>						
BDI-II	−0.79 ^{***}	−0.72 ^{***}	−0.58 ^{***}	−0.52 ^{***}	−0.50 ^{***}	−0.64 ^{***}
STAI-S	−0.42 [*]	−0.20	−0.05	−0.45 [*]	−0.34	−0.28
STAT-T	−0.33	−0.14	−0.15	−0.26	−0.31	−0.46 [*]

Abbreviations: See Table 1 for abbreviations of neurocognitive measures. BDI-II, Beck Depression Inventory-Second Edition; STAI-S, State subscale of the State-Trait Anxiety Inventory; STAI-T, Trait subscale of the State-Trait Anxiety Inventory.

^a z-scores.

^b Raw scores.

^c Data represent Pearson product-moment correlation coefficients (r).

^{*} p<0.05.

^{**} p<0.01.

^{***} p<0.001.

Table 4

Predictors of FACT scales

FACT Scale	Neurocognitive Predictor(s) [†]	Unstandardized B	Standard Error B	Standardized β	p-value	Adjusted R ²
<i>General</i>	HVLT-R TR	1.91	0.78	0.26	0.016	0.06
<i>Physical</i>	No significant predictors					
<i>Social</i>	TMTA	0.97	0.37	0.28	0.010	0.07
<i>Emotional</i>	No significant predictors					
<i>Functional</i>						
Model 1	TMTB	0.56	0.20	0.30	0.006	0.08
Model 2	TMTB	0.58	0.20	0.31	0.003	0.12
	Peg	0.94	0.43	0.23		
<i>Brain</i>						
Model 1	HVLT-R TR	2.48	0.84	0.31	0.004	0.09
Model 2	HVLT-R TR	2.15	0.83	0.27	0.001	0.13
	Peg	2.51	1.09	0.24		
FACT Scale	Mood Predictor(s) ^{††}	Unstandardized B	Standard Error B	Standardized β	p-value	Adjusted R ²
<i>General</i>	BDI-II	-1.58	0.30	-0.74	<0.001	0.53
<i>Physical</i>	BDI-II	-0.45	0.09	-0.72	<0.001	0.50
<i>Social</i>	No significant predictors					
<i>Emotional</i>	BDI-II	-0.62	0.14	-0.70	<0.001	0.46
<i>Functional</i>	BDI-II	-0.46	0.19	-0.47	0.021	0.19
<i>Brain</i>	BDI-II	-1.74	0.34	-0.74	<0.001	0.53

Note. See tables 1 and 3 for abbreviations.

[†] HVLT-R DR, HVLT-R Rec, and CTB Comp excluded due to reduced sample size for these variables. N=83.

^{††} BDI-II, STAI-S, and STAI-T included as the only predictors. N=24.