Neuro-Oncology 14(12):1485–1502, 2012.
doi:10.1093/neuonc/nos244
Advance Access publication October 11, 2012

The effects of radiotherapy on psychosocial and cognitive functioning in adults with a primary brain tumor: a prospective evaluation†

Maria Kangas, Robyn L. Tate, Janet R. Williams, and Robert I. Smee

Centre for Emotional Health, Department of Psychology, Macquarie University, Sydney, Australia (M.K.); Rehabilitation Studies Unit, Northern Clinical School, Sydney Medical School, University of Sydney and Royal Rehabilitation Centre, Sydney, Australia (R.L.T.); The Prince of Wales Cancer Centre, Prince of Wales Hospital, Sydney, Australia (J.R.W., R.I.S.); The Prince of Wales Private Hospital, Sydney, Australia (R.I.S.)

A paucity of studies have evaluated the biopsychosocial factors contributing to quality of life (QoL) in adults with a primary brain tumor (BT). Our objective was to investigate (i) the effects of radiotherapy on the psychosocial (ie, posttraumatic stress symptoms [PTSS]) and cognitive functioning of adults with a primary BT, assessed preradiotherapy [T1] and postradiotherapy [T2], and (ii) predictors of PTSS and QoL postradiotherapy. Seventy adults with a BT were assessed at T1, and 67 patients were reassessed 3.5 months postradiotherapy. At each assessment, participants completed measures of PTSS, mood, QoL, and quality of social support and neurocognitive tests focusing on memory and executive functioning. Minimal differences in functioning were found between patients according to BT type (benign [$n = 45$] vs malignant [$n = 25$]) and tumor laterality (left vs right hemisphere), with 2 exceptions. Individuals with a left hemisphere benign BT experienced greater distress at T1, which declined at T2, whereas individuals with a left hemisphere malignant BT reported poorer social support at T2. The full sample performed poorly on tests of executive functioning, and 17% reported clinically elevated PTSS at T1, which reduced to 13% at T2. Younger age (<65 y), reduced QoL, and elevated anger symptoms at T1 predicted PTSS at T2, whilst having a benign BT, low PTSS, and depressive symptoms at T1 were predicted of improved QoL at T2. Findings highlight the importance of screening for psychosocial and cognitive disturbances in BT patients undergoing treatment to identify those at risk for acute and more prolonged problems.

Keywords: brain tumor, neurocognitive, quality of life, stress.

In the United States per annum, on average 209 per 100 000 individuals are diagnosed with a primary brain tumor (BT).[1] The average prevalence of benign BTs is much higher (166.5/100 000) than that of malignant BTs (42.5/100 000),[1] although both benign and malignant tumors can be life threatening and can cause neurocognitive and functional impairments[2,3] as well as psychosocial problems.[4–7] Indeed, being diagnosed with a BT can be a potentially traumatic experience due to a multitude of factors, which lends support to a biopsychosocial perspective pertaining to the quality of life (QoL) and emotional adjustment following a BT diagnosis.[8,9] This approach involves understanding the interplay between the biological/medical components of being diagnosed with a BT (eg, BT diagnosis, radiation dosage, BT laterality) and the psychological (eg, mood, affect, cognitive functioning) and social support effects.

The prevalence rates for clinical depression and anxiety have been found to be as high as 62.5% in adults treated for benign and malignant BTs.[6,7] This high prevalence rate accentuates the contribution of psychological components, particularly subjective appraisals of adjusting to having a BT. Notably, the person who internalizes a BT as life threatening or as a threat to physical integrity may elicit heightened posttraumatic stress symptoms (PTSS). This proposition is in line with cognitive models of trauma[10] and is supported by research showing that up to one-third of individuals

Received October 13, 2011; accepted August 13, 2012.

†Portions of these data were presented at the International Congress for Behavioral Medicine (ICBM), Washington DC, August 2010; and the annual convention of the American Psychological Association (APA)–Division 40 (Neuropsychology), San Diego, August 2010.

Corresponding Author: Maria Kangas, PhD, Centre for Emotional Health, Department of Psychology, Macquarie University, Sydney 2109, Australia (maria.kangas@mq.edu.au).

diagnosed with other types of neoplasms may experience posttraumatic stress disorder (PTSD) independent of cancer staging and medical treatments,[11] which has been found to compromise QoL.[12]

However, the majority of BT studies that have evaluated psychological problems in BT samples have assessed only "generic" anxiety or stress *not* specifically indexed to participants' BT experience. Hence, it is not possible to determine whether the anxiety symptoms are directly related to one's BT experience compared with generic stress arising from daily hassles and/or premorbid psychological problems. In fact, only 2 published studies have specifically assessed BT-related stress. In the first study, 19% of the adult patients met criteria for acute stress disorder (ASD) within 14 days following neurosurgical removal of their BT and within 3 months postdiagnosis.[13] However, the effects of ASD on cognitive functioning and QoL were not evaluated in the study. In the second study, 16% of adults who had been diagnosed and treated for a benign meningioma on average 4.4 years previously reported BT-related PTSS, which was significantly related to reduced QoL.[14] The findings from these studies suggest that 1 in 7 persons treated for a primary BT may be at risk for acute and more prolonged clinical stress reactions.

A notable gap in this field remains. The limited number of studies examining factors related to QoL outcomes in a biopsychosocial framework have utilized a cross-sectional design.[9] To this end, the term "predictor" has been regularly yet inappropriately used to identify factors that have simply been correlated with QoL. In fact there is a dearth of research with a prospective (pre-post treatment), longitudinal design to evaluate the effects of *both* cognitive and psychosocial functioning, including BT-related stress, in relation to QoL outcomes in adults who have been diagnosed with *either* a benign or a malignant BT. This line of inquiry has utility in further elucidating the factors contributing to poor QoL in BT survivors, as well as informing the advancement of assessment and rehabilitation approaches in working with BT patients. Accordingly, the first aim of this study was to examine whether there were any differences in neurocognitive and psychosocial functioning including BT-related stress and overall QoL between adults diagnosed with benign and with malignant BTs, prior to and following radiotherapy. The second aim was to investigate the incidence and predictors of BT-related PTSS and QoL in BT patients assessed pre- and postradiotherapy.

We chose to investigate predictors of BT-related PTSS as well as overall QoL in adults who were diagnosed with benign and malignant BTs and were recommended to receive radiotherapy, on the basis that radiotherapy is a common primary and adjuvant treatment for adult BTs. Specifically, some benign BTs are inoperable due to their size, site of the lesion, and proximity to surrounding structures. Hence, stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (FSRT) are the main forms of treatment to stabilize, reduce, or obliterate the tumor. Similarly, for malignant BTs, radiotherapy is commonly used as an adjunct to surgical excision, particularly if the tumor is only partially excised or has a high risk of recurrence. Hence, the impact of the potential neurotoxicity of radiation treatments in terms of psychological and cognitive functioning is important to further delineate, particularly considering that with the increasing advancements of stereotactic radiotherapy procedures, the risk for diffuse brain impairments is lessening relative to whole-brain radiation.[15] To this end, given the mixed findings that have emerged in the literature pertaining to BT characteristics (including radiation dosage and type and BT laterality) in relation to cognitive, emotional, and QoL outcomes, a third, exploratory aim of this study was to examine the effects of stereotactic radiotherapy (single-dose vs fractionated) and tumor laterality according to BT status (benign vs malignant) in relation to psychosocial and cognitive functioning.

Methods

Participants

Institutional ethics approval was provided by the South Eastern Area Health Service (Prince of Wales Hospital), Sydney, Australia, and Macquarie University, Sydney. Participants were recruited from a Sydney, Australia, hospital (between 2006 and 2009) into this longitudinal study, which was part of a larger research program. Eligibility criteria consisted of diagnosis of a primary BT and prescription to receive primary or adjuvant SRS or FSRT; age $\geq$18 years; ability to read and write English; and being deemed medically fit by medical staff to complete the assessment. Eligible participants completed 2 assessments; the first was conducted preradiotherapy [T1], and the second was scheduled on average 3 months postradiotherapy [T2]. A total of 70 people met eligibility criteria and consented to participate.

Measures

At T1, participants completed a scale to obtain demographic and BT-related information (see Table 1). BT-related details were also verified from medical records. At each assessment, participants were asked to complete the following set of questionnaires and neuropsychological tests.

PTSD Checklist–Stressor Specific Version (PCL-S)[16].— The PCL-S was used to measure BT-related severity of PTSS. The PCL-S consists of 17 items in 3 subscales: re-experiencing, avoidance, and hyperarousal symptoms. Each item was rated on a 5-point scale, indicating the degree to which participants had been bothered by each symptom over the previous month in response to their "BT experience." Using the PCL-S symptom scoring method,[16] participants were classified as experiencing elevated BT-related PTSS (the *high PTSS* subgroup) if they reported, at minimum, a moderate level

Table 1. Demographic and clinical characteristics for the full sample ($n = 70$) and according to BT status and laterality

Variable	Full Sample ($n = 70$), M (SD)	Benign BT ($n = 45$), M (SD)	Malig. BT ($n = 25$), M (SD)	t or χ^2 t	LH Benign ($n = 23$), M (SD)	RH Benign ($n = 22$), M (SD)	t or χ^2 t	LH Malig. ($n = 11$), M (SD)	RH Malig. ($n = 11$), M (SD)	t or χ^2 t
Age, y & mo	50.57 (14.37)	54.36 (13.23)	43.74 (14.03)	***3.09*** **	58.35 (12.12)	50.18 (13.32)	−2.15	46.55 (12.67)	44.96 (15.06)	−0.27
Education, y	13.77 (3.2)	13.40 (3.25)	14.44 (2.96)	−1.32	13.70 (3.42)	13.09 (3.12)	−0.62	14.64 (2.20)	14.18 (3.94)	−0.33
Time since BT diagnosis, mo	27.62 (60.31)	29.63 (51.18)	23.95 (75.06)	0.38	19.42 (30.99)	40.37 (65.17)	1.39	9.33 (15.06)	41.44 (112.33)	0.94
T1: Time prior to RT treatment, days	15.22 (17.6)	17.91 (20.23)	10.48 (10.51)	2.01	21.96 (24.73)	13.48 (12.96)	−1.41	9.09 (8.74)	11.36 (13.03)	0.48
T2: Time since RT completion, mo ($n = 67$)	3.54 (0.84)	3.48 (0.85)	3.64 (0.84)	−0.74	3.48 (0.99)	3.48 (0.68)	−0.01	3.47 (0.83)	3.7 (0.76)	0.65
RT dosage (Gy)	44.63 (17.4)	39.62 (18.46)	53.47 (11.16)	***−3.88*** **	38.79 (19.50)	40.52 (17.67)	0.31	52.84 (13.44)	53.76 (10.63)	0.18
Fractionated treatment (Gy)		[$n = 34$] 47.06 (13.84)	53.47 (11.16)	−1.90						
	n (%)	***n (%)***	***n (%)***	χ^2/p	***n (%)***	***n (%)***		***n (%)***	***n (%)***	
Gender										
Male	32 (46)	17 (38)	15 (47)	3.20	8 (35)	9 (41)		7 (64)	5 (55)	
Female	38 (54)	28 (62)	10 (40)		15 (65)	13 (59)		4 (36)	6 (45)	
Age group										
<65 y (younger)	56 (80)	33 (73)	23 (92)	NA	15 (65)	18 (82)		10 (91)	10 (91)	
≥65 y (older)	14 (20)	12 (27)	2 (8)		8 (35)	4 (18)		1 (9)	1 (9)	
Education										
<High school	18 (26)	14 (31)	4 (16)	NA	7 (31)	7 (32)		1 (9)	3 (27)	
High school	9 (13)	6 (13)	3 (12)		4 (17)	2 (9)		1 99)	1 (9)	
Graduate degree	43 (61)	25 (56)	8 (72)		12 (52)	13 (59)		7 (64)	7 (64)	
Marital status										
Married/partnered	52 (74)	33 (73)	19 (76)	NA	15 (65)	18 (82)		11 (100)	7 (64)	
Single (incl. separated/divorced)	18 (26)	12 (27)	6 (24)		8 (35)	4 (18)		0 (0)	4 (36)	
Employment status										
Not working	39 (56)	27 (60)	12 (48)	0.94	14 (61)	13 (59)		5 (45)	5 (45)	
Working	31 (44)	18 (40)	13 (52)		9 (39)	9 (41)		6 (55)	6 (55)	
Type of treatments received										
1 treatment	26 (37)	24 (53)	2 (8)	NA	12 (52)	12 (54)		1 (9)	1 (9)	
>1 treatment	44 (63)	21 (47)	23 (92)		11 (48)	10 (46)		10 (91)	10 (91)	
RT										
Fractionated	60 (86)	35 (78)	25 (100)	NA	17 (74)	18 (82)		11 (100)	11 (100)	
Stereotactic (single dose; IMRS)	10 (14)	10 (22)	0 (0)		6 (26)	4 (18)		0 (0)	0 (0)	

Continued

Table 1. *Continued*

Variable	Full Sample ($n = 70$), M (SD)	Benign BT ($n = 45$), M (SD)	Malig. BT ($n = 25$), M (SD)	t or χ^2 t	LH Benign ($n = 23$), M (SD)	RH Benign ($n = 22$), M (SD)	t or χ^2 t	LH Malig. ($n = 11$), M (SD)	RH Malig. ($n = 11$), M (SD)	t or χ^2 t
Types of medical treatments										
RT only	26 (37)	24 (35)	2 (8)	NA	12 (52)	12 (55)		1 (9)	1 (9)	
Presurgical + RT	34 (49)	21 (47)	13 (52)		11 (48)	10 (46)		6 (55)	4 (36)	
Presurgical + RT+ chemotherapy	10 (14)	0 (0)	10 (40)		0 (0)	0 (0)		4 (36)	6 (55)	
Medication usage, yes	43 (61)	26 (58)	17 (68)	0.71	17 (74)	9 (41)		8 (73)	8 (73)	
Anticonvulsants	15 (21)	5 (11)	10 (40)	8.00** ($P = .007$)	3 (13)	2 (9)		4 (36)	5 (46)	
Pain medication	6 (9)	5 (11)	1 (4)	NA	4 (18)	1 (5)		0	1 (9)	
Concurrent medical conditions, yes	43 (61)	29 (64)	14 (56)	0.48	18 (78)	11 (50)		7 (64)	7 (64)	
Family history of cancer, yes	45 (65)	26 (59)	19 (76)	2	15 (65)	11 (52)		9 (82)	9 (82)	
History of psychological problems, yes	24 (35)	11 (26)	13 (52)	***4.83**** ***($P = .037$)***	9 (41)	2 (10)		5 (46)	6 (55)	
Stress as cause of BT, yes										
BT-related problems (ongoing at T2) ($n = 65$)	50 (77)	31 (74)	19 (83)	0.65	18 (82)	13 (65)		8 (80)	8 (80)	
Major stressors at T2 ($n = 65$)	35 (54)	23 (55)	12 (52)	0.04	13 (59)	10 (50)		5 (50)	5 (50)	

Abbreviations: RT, radiotherapy; IMRS, intensity-modulated radiosurgery.
*Statistically significant at $P < .05$.
**Statistically significant at $P < .01$.

of stress (score of ≥3) on at least 1 intrusion item, 3 avoidance items, and 2 hyperarousal items.

Impact of Event Scale–Revised (IES-R)[17].—The IES-R is comparable to the PCL-S because it also consists of 3 subscales; intrusion, avoidance, and hyperarousal. Participants were asked to complete the IES-R in reference to their "BT-experience," including diagnosis (T1) and postradiotherapy (T2), in terms of stress symptoms experienced over the preceding 7 days. Because the PCL-S was used as the dependent variable to test predictors of PTSS, the administration of the IES-R enabled an independent assessment of PTSS over a 7-day interval, which concurs with the standardized interval for the QoL and mood measures used in this study.

The Functional Assessment of Cancer Therapy (FACT)–General (G) and –Brain (Br)[18,19].—These scales were administered to assess participants' overall QoL. The FACT-G consists of 4 subscales: physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), and functional well-being (FWB). The FACT-Br is a supplement scale designed to measure BT-specific symptoms.[19] Each of the subscales is answered on a 5-point Likert scale, with higher scores denoting higher QoL. Participants rated each item in relation to how they had been feeling during the preceding 7 days.

Profile of Mood States (POMS)[20].—This is a well-validated 65-item measure of distress that consists of 6 subscales: anxiety/tension, depression/dejection, anger/hostility, vigor, fatigue/inertia, and confusion/bewilderment. Participants were asked to rate each item on a 5-point scale (with higher scores indicating greater distress) over the preceding 7 days. On the basis that the anxiety/tension subscale was redundant with the IES-R, this subscale was not included in the main analyses.

Partner Responses to Cancer Inventory (PRCI)[21].—The PRCI Emotional/Instrumental Support and Cognitive/Informational Guidance subscales were used to assess participants' perceived positive support received from their partners and family/friends during their BT experience. The 2 subscales were combined to form an aggregate positive social support score for the analyses.

Social Constraints Scale (SCS)[22].—The SCS has 9 items, adapted from the Cancer Rehabilitation Evaluation System,[23] and has been used to assess social constraints in cancer patients.[22] The same 9 items were used in this study to assess social constraints with family/friends (6-item subscale) and with one's partner/spouse (3-item subscale), with the exception that the term *cancer* was replaced by the phrase *brain tumor experience*. On a 4-point scale (with higher scores indicating greater constraint), participants rated how often they experienced communication difficulties with their family/friends and partners/spouses in the previous month.

Weschler Memory Scale, third edition (WMS-III)[24]***: Logical Memory (LM) I and II and Digit Span.***—The LM subtest was used to assess short-term recall. Digit Span was administered to test immediate attention span and working memory. Both tests were scored according to the WMS-III manual norms.

Executive tests.—Three tests, sensitive to executive impairments after brain injury, were selected.[25] The Weschler Adult Intelligence Scale, third edition (WAIS-III)[26]–Similarities subtest was administered to assess verbal concept formation. This test was scored according to the WAIS-III manual norms. The Controlled Oral Word Association Test (COWAT)[27] is a well-validated test of verbal fluency and mental flexibility. The standard instructions for the F-A-S version of the COWAT were used, and scores were scaled according to published norms. The Trail Making Test (TMT)[28,29] parts A and B were used to assess visual scanning and processing speed/cognitive flexibility, respectively. The scoring method by Strauss et al[29] was used, and raw scores were converted into percentiles according to normative data.[30]

Statistical Analysis

The association between high and low PTSS subgroups and categorical factors were tested using chi-square and Fisher exact tests; the latter were used for analyses conducted on smaller subsamples. Analyses of variance and repeated-measures general linear model (GLM) analyses (testing changes from T1 and T2) were conducted according to BT status (benign vs malignant) and laterality (left hemisphere [LH] vs right hemisphere [RH]), to test psychosocial and neurocognitive outcomes. Chi-square and Mann–Whitney *U* tests were used to examine whether there were any differences on any variables between PTSS subgroups. Repeated-measures GLM analyses were also conducted to test for changes according to PTSS status at T2. The alpha levels were adjusted due to the multiple comparisons between the 2 primary subgroups (benign vs malignant BTs). Because there were 16 specific variables tested for psychosocial functioning, adjusted alpha was set conservatively at $P < .003$. Similarly, because neurocognitive functioning was tested using 8 variables, adjusted alpha was set at $P < .006$.

Further, Pearson's bivariate correlations were conducted to assess severity of PTSS at T2 versus study variables indexed at T1. Two hierarchical linear regression models (where each variable was entered as a separate block) were conducted to test predictors of PTSS and QoL, respectively, at T2. Alpha was set at .05 for these 2 regression analyses, and variables with $P < .05$ in the final multiregression model were considered significant.

Results

Demographic and Medical Characteristics

Table 1 summarizes the variables at T1 for the full sample and according to BT status and laterality. Three participants with bilateral tumors were diagnosed with malignant BT. At T1, the sample was assessed on average 15.2 days prior to commencing SRS or FSRT, and the majority of the sample ($n = 67$) was reassessed on average 3.5 months postradiotherapy. Participants with malignant BTs were significantly younger than persons with benign BTs ($P = .003$). Most participants (92%) with malignant tumors were recommended to receive multiple medical treatments (including surgery and/or chemotherapy) compared with 47% of benign BT patients ($P < .001$). No further statistical differences were found between BT subgroups in relation to demographic and medical variables.

Psychosocial Functioning

Table 2 summarizes the scores for the psychosocial variables according to benign versus malignant BT subgroups. At T2, a number of participants had returned to their residence outside the Sydney region; hence, a number of participants synchronized their T2 assessments with medical follow-up visits in Sydney. However, due to time restrictions, several participants did not complete sections of the neurocognitive battery (see Table 2 for subsample sizes at T2).

A borderline significant interaction effect emerged between the benign and malignant BT subgroups and IES scores over time ($P = .003$). Persons with a benign tumor reported a significant decline in IES-R scores by T2 ($P < .001$) relative to the malignant BT subgroup. The exploratory analyses examining the effects of FSRT according to benign versus malignant subgroups also revealed that patients with a benign tumor reported a significant decline in IES scores over time ($P < .001$) (see Supplementary Table A for full summary of results for the FSRT subgroups). Furthermore, exploratory analyses examining the effects of tumor laterality within each of the benign and malignant subgroups revealed that patients with an LH benign tumor reported significant decline in IES-R scores relative to patients with an RH benign tumor ($P < .001$) (see Supplementary Tables B and C for full summary of results for laterality effects for benign and malignant BT subgroups, respectively).

There was also a strong trend toward significance between subgroups for the FACT-EWB scores at T2 ($P = .003$), with patients with a benign tumor reporting better emotional well-being at follow-up relative to patients with a malignant tumor. The follow-up analyses according to tumor laterality revealed that this effect was due to patients with an LH benign tumor reporting a greater improvement on FACT-EWB scores over time relative to patients with an RH benign tumor ($P = .004$).

A borderline significant interaction was also found between the benign and malignant BTs and SCS spousal scores over time ($P = .003$), with patients with a malignant tumor reporting a significant increase in scores at T2 ($P = .002$). Similarly, there was a trend toward significance in a reported decline in FACT-SWB scores at T2 for patients with a malignant tumor ($P = .009$). Exploratory analyses revealed that patients with an LH malignant BT reported a significant within-group decline in FACT-SWB scores over time ($P = .001$), whilst the scores for patients with an RH malignant BT remained stable ($P = .687$) (see Supplementary Table C). No further significant main effects, interactions, or within-group differences emerged for any other psychosocial variables examined between the BT subgroups, including supplementary analyses according to FSRT and tumor laterality.

An evaluation of POMS subscale *T*-scores below 40 for the vigor subscale and above 60 for the other 5 subscales was conducted to determine the proportion of participants who experienced clinically elevated PTSS. Fatigue was the most prevalent symptom experienced at both T1 and T2. Specifically, 10% ($n = 7$) of the sample (3 benign, 4 malignant) had clinically elevated fatigue scores at T1, and this increased to 20% ($n = 13$) at T2 (8 benign, 5 malignant). At T1, 7% of the sample (4 benign, 1 malignant) reported clinically elevated scores on the anger subscale, which reduced to 1.5% at T2. Only 1 participant experienced clinically elevated depression at both assessments.

Neurocognitive Functioning

The neurocognitive scores according to BT subgroups are also displayed in Table 2. The Supplementary Tables A–C summarize the neurocognitive scores according to FSRT and tumor laterality effects within each of the benign and malignant subgroups. Main effects were found on the LM I/II scores (all $P < .001$), indicating an improvement in short-term memory recall at follow-up, especially for patients with a benign tumor. Exploratory analyses showed that patients with both LH ($P = .001$) and RH ($P < .001$) benign tumors demonstrated a significant improvement in scores on the LM II test between the 2 assessments. In addition, patients with an RH benign tumor also demonstrated a substantial improvement in retention scores on the LM II test ($P = .006$). However, no significant differences in performance on the LM II test were found for patients with a malignant BT according to laterality effects.

Performances on the Digit Span remained relatively stable (in the average range) for all subgroups. Although no significant main or interaction effects were found for performances on the Similarities test ($P > .01$), a significant within-group difference was found over time for patients with malignant tumors, demonstrating an improvement in scores over time ($P = .001$). However, no significant difference was found for this subgroup according to tumor laterality

Table 2. Psychosocial and neurocognitive functioning at T1 and T2 according to BT diagnosis: benign vs malignant tumor

	Benign, M (SE)	Malignant, M (SE)	Main Effect Observed *P*	Signature Adjusted *P* (<.003)	Between-Groups Observed *P*	Signature Adjusted *P* (<.003)	Benign Within-Group Observed *P* (adjusted) (<.003)	Malignant Within-Group Observed *P* (adjusted) (<.003)
Psychosocial variables								
PCL-S[a]								
T1	29.3 (1.9)	29.1 (2.6)			.965	NS		
T2	24.8 (1.4)	29.1 (1.8)	.067	NS	.065	NS	***.003***[#]	.982
N	44	23						
IES[a] total								
T1	20.8 (2.5)	19.4 (3.5)			.762	NS		
T2	12.9 (2.3)	21.7 (3.2)	.093	***NS***[++]	.025	NS	***.000*****	.399
N	44	23						
FACT-PWB								
T1	22.7 (0.7)	21.9 (1.1)			.533	NS		
T2	22.9 (0.8)	21.5 (1.1)	.959	NS	.315	NS	.764	.783
N	44	22						
FACT-SWB								
T1	22.6 (0.6)	23.0 (0.9)			.727	NS		
T2	22.0 (0.7)	20.7 (1.0)	.008	***TR***[#]	.273	NS	.349	***.009***[#]
N	44	22						
FACT-EWB								
T1	17.7 (0.7)	16.3 (1.0)			.267	NS		
T2	19.4 (0.7)	15.7 (1.0)	.4	NS	***.003***	***TR***[#]	.031	.605
N	44	22						
FACT-FWB								
T1	21.3 (0.8)	19.8 (1.1)			.271	NS		
T2	21.4 (0.8)	18.5 (1.2)	.466	NS	.055	NS	.826	.295
N	44	22						
FACT-G total								
T1	84.1 (2.0)	80.9 (2.8)			.345	NS		
T2	85.8 (2.3)	76.5 (3.2)	.421	NS	.022	NS	.412	.120
N	44	22						
FACT-Br								
T1	59.6 (1.7)	56.8 (2.5)			.366	NS		
T2	59.9 (1.6)	53.9 (2.3)	.252	NS	.039	NS	.780	.112
N	44	22						
POMS depression[a]								
T1	39.2 (1.2)	40.7 (1.7)			.465	NS		
T2	37.9 (1.0)	42.0 (1.4)	.967	NS	.019	NS	.329	.458
N	44	22						

Continued

Table 2. *Continued*

	Benign, M (SE)	Malignant, M (SE)	Main Effect Observed *P*	Signature Adjusted *P* (<.003)	Between-Groups Observed *P*	Signature Adjusted *P* (<.003)	Benign Within-Group Observed *P* (adjusted) (<.003)	Malignant Within-Group Observed *P* (adjusted) (<.003)
POMS anger[a]								
T1	43.9 (1.2)	46.7 (1.7)			.171	NS		
T2	43.1 (0.9)	45.0 (1.3)	.212	NS	.238	NS	.495	.294
N	44	22						
POMS vigor[a]								
T1	57.8 (1.7)	61.6 (2.2)			.159	NS		
T2	57.2 (1.7)	59.9 (2.4)	.434	NS	.36	NS	.732	.474
N	44	22						
POMS fatigue[a]								
T1	45.9 (1.3)	48.6 (1.9)			.249	NS		
T2	46.6 (1.5)	50.4 (2.1)	.274	NS	.144	NS	.587	.338
N	44	22						
POMS confusion[a]								
T1	41.8 (1.3)	43.1 (1.8)			.54	NS		
T2	40.9 (1.2)	43.6 (1.7)	.828	NS	.204	NS	.441	.78
N	44	22						
PRCI positive support								
T1	46.76 (1.7)	51.50 (2.4)			.109			
T2	43.78 (1.7)	47.00 (2.3)	.012		.269	NS	.086	.058
N	41	22		NS		NS		
SCS friends/family[a]								
T1	.56 (0.1)	.69 (0.2)			.521	NS		
T2	.49 (0.1)	.67 (0.1)	.608	NS	.253	NS	.463	.916
N	43	22						
SCS spouse/partner[a]								
T1	.46 (0.1)	.55 (0.2)			.664	NS		
T2	.36 (0.1)	1.03 (0.2)	.048	***NS***$^{++}$	***.002***	**	.367	***.003***$^{\#}$
N	43	22						
Neurocognitive tests (signature adjusted $P < .006$)								
LM I recall[b]								
T1	9.7 (0.5)	10.3 (0.7)			.508	NS		
T2	11.4 (0.6)	11.4 (0.8)	***.001***	*	.995	NS	***.001****	.092
N	42	23						
LM II recall[b]								
T1	10.0 (0.6)	10.0 (0.8)			.982	NS		

T2	12.2 (0.6)	11.0 (0.8)	***.000***	*	.245	NS	***.000****	.092
N	42	23						
LM II retention[b]								
T1	10.8 (0.6)	9.4 (0.8)			.187	NS		
T2	12.7 (0.5)	11.0 (0.6)	***.000***	*	.025	NS	***.000****	.033
N	42	23						
Digit Span[b]								
T1	10.5 (0.5)	11.2 (0.7)			.424	NS		
T2	11.3 (0.5)	11.2 (0.7)	.325	NS	.923	NS	.098	1.00
N	43	23						
Similarities[b]								
T1	10.8 (0.5)	10.9 (0.7)			.916	NS		
T2	10.7 (0.6)	12.6 (0.9)	.011	NS	.086	NS	.794	***.001****
N	43	21						
COWAT[c]								
T1	35.2 (4.1)	27.0 (5.5)			.233	NS		
T2	41.0 (4.3)	30.0 (5.8)	.082	NS	.132	NS	.057	.447
N	42	23						
TMT-A[c]								
T1	52.7 (5.6)	44.4 (6.2)			.326	NS		
T2	63.6 (5.7)	48.9 (6.3)	.053	NS	.089	NS	.041	.44
N	22	18						
TMT-B[c]								
T1	24.1 (5.5)	27.8 (6.1)			.658	NS		
T2	40.5 (7.0)	35.0 (7.8)	.024	NS	.606	NS	.02	.339
N	22	18						

Abbreviations: NS, not significant at adjusted *P* values; TR, statistical significant trend; Sig. = Statistical Significance (with adjusted *P* value
[a]High score denotes poorer performance; for all other scores, the reverse applies.
[b]Age-matched scaled scores used according to validated Wechsler manuals.
[c]Percentile scores calculated on age and gender according to validated norms.
*Neurocognitive tests adjusted $P < .006$.
**Psychosocial variables adjusted $P < .003$.
[#]Psychosocial and neurocognitive variables significant trend $P < .01$.
[++]Significant interaction effect: IES total, $P = .003$; SCS spouse, $P = .003$.

($P > .03$). Additionally, although no significant effects were found for performances on the COWAT, all subgroups performed below the average level. Similarly, scores on the TMT part B were well below average at T1; however, a significant main effect was found ($P = .005$) for the benign subgroup, which demonstrated an improvement of scores over time, especially for participants with an RH tumor ($P = .005$).

Incidence and Predictors of BT-Related PTSS

Table 3 summarizes the study variables according to participants' PTSS status. At T1, 17% of the sample reported high PTSS, whilst at T2, 13% reported high PTSS. Over half (56%) of the individuals with high PTSS at T2 had also reported high PTSS at T1. However, no differences were found between PTSS subgroups at either assessment in relation to demographic and medical variables including BT type and laterality effects.

At T1, the high PTSS subgroup reported significantly elevated scores on the subscales for POMS depression ($P = .003$), POMS anger ($P = .001$), and SCS family/friends ($P < .001$); significantly lower scores on the FACT-G ($P = .002$); and a strong trend toward significantly reduced scores on the FACT-EWB ($P = .005$) and FACT-Br ($P = .007$).

Individuals with high PTSS at T2 also reported lower scores on most of the QoL subscales (notably, FACT-EWB, FACT-FWB, FACT-G, and FACT-Br; $P < .003$) and higher scores on the SCS scales ($P < .001$) and the subscales for POMS depression ($P = .001$) and POMS confusion ($P = .000$). Further, the low PTSS subgroup at T2 reported a significant decline in PTSS over time as assessed by the PCL-S and IES-R ($P < .001$). Conversely, the mean scores for the PCL-S and IES-R remained stable for the high PTSS subgroup at T2.

No significant differences in neurocognitive functioning were found between PTSS subgroups at T1. However, the high PTSS subgroup at T2 had substantially lower scores on the TMT part B at T2 ($P = .005$) compared with the low PTSS subgroup. There was also a significant main effect for LM I/II scores over time, in accordance with status of PTSS at T2 ($P < .003$). Specifically, participants with low PTSS at T2 experienced an improvement in immediate and delayed memory recall and retention (all $P < .01$). No further differences were found on any other tests according to status of PTSS at T2.

Table 4 presents the bivariate correlation coefficients between independent variables (at T1) and severity of PTSS at T2 for the full sample and BT subgroups, in order to select the optimal set of predictors of PTSS. A regression model was then tested in order to determine which variables at baseline predicted severity of PTSS at T2. An initial hierarchical linear regression model was tested that included the following variables assessed at T1, with each variable entered as a separate block in the model: age; and scores on the PCL-S, FACT-G/Br, POMS depression, POMS anger, SCS family/friends, and COWAT. Results indicated that scores on POMS depression and COWAT did not contribute any unique variance; therefore, these variables were removed and the analysis was rerun on the remaining 5 variables. In the final model, 3 variables (younger age [<65 y], elevated POMS anger, and lower FACT-G/Br scores at T1) were uniquely, significantly predictive of heightened severity of PTSS at T2 (see Table 5).

Predictors of QoL

A linear regression model was also conducted to test which variables at baseline predicted QoL at T2. BT status was included in this model along with T1 scores on the PCL-S, FACT-G/Br, POMS depression, SCS family/friends, and COWAT, which were entered separately in blocks in a hierarchical model. Benign BTs, higher FACT-G/Br, and lower PCL-S and POMS depression scores at T1 were each found to be significantly associated with better QoL at T2 (see Table 6).

Discussion

Three key patterns of results emerged in relation to neuropsychosocial functioning according to BT type and laterality effects. First, participants with a benign tumor had substantially elevated PTSS and general distress at baseline relative to patients with a malignant tumor. However, the benign subgroup experienced a significant reduction in PTSS and an improvement in emotional well-being postradiotherapy, especially for persons with an LH tumor. Although there are mixed findings pertaining to BT laterality and the effects on anxiety and mood,[9] our results support previous studies that have found that BT patients with an LH tumor are more susceptible to mood disturbances.[31] The present findings also concur with the interhemispheric emotional balance theory, which posits that the RH processes negative emotional information, whilst the LH processes positive emotional content.[32–34]

The second pattern of findings further concurs with this theory[32–34] and lends support to the biopsychosocial model.[8,9] In particular, participants with a malignant BT reported a significant reduction in social well-being and heightened social constraints in their interpersonal relationships postradiotherapy relative to participants with a benign BT. Moreover, persons with an LH malignancy reported substantially lower social well-being at follow-up compared with persons with an RH malignancy. Social support and particularly lower levels of social constraints are robust findings in the oncology[21,22] and trauma[35] literature in terms of buffering against adverse psychological effects in adapting to a potentially life-threatening crisis.

The third pattern of findings pertains to cognitive functioning postradiotherapy. At baseline, short-term memory functioning was found to be in the average range for the majority of the sample, with the exception that participants with an LH malignancy performed

Table 3. Demographic and clinical characteristics and psychosocial and neurocognitive functioning at T1 and T2 according to subgroups of PTSS at T1 and T2

Variables	T1		χ^2/P^a	T2		χ^2/P^a
	High PTSS ($n = 12$) n (%)	Low PTSS ($n = 58$) n (%)		High PTSS ($n = 9$) n (%)	Low PTSS ($n = 58$) n (%)	
Gender						
Male	4 (33)	28 (48)	0.9	3 (33)	27 (47)	0.55
Female	8 (67)	30 (52)		6 (67)	31 (53)	
Age group						
<65 y (younger)	9 (75)	47 (81)	NA	7 (78)	47 (81)	NA
≥65 y (older)	3 (25)	11 (19)		2 (22)	11 (19)	
Education						
<High school	4 (33)	14 (24)	NA	2 (22)	16 (28)	NA
High school	2 (17)	7 (12)		1 (11)	7 (12)	
Graduate degree	6 (50)	37 (64)		6 (67)	35 (60)	
Marital status						
Married/partnered	7 (58)	45 (78)	1.93	5 (56)	44 (76)	NA
Single (incl. separated/divorced)	5 (42)	13 (22)		4 (44)	14 (24)	
Employment status						
Unemployed	9 (75)	30 (52)	NA	7 (78)	31 (53)	NA
Employed	3 (25)	28 (48)		2 (22)	27 (47)	
BT type						
Benign	9 (75)	36 (62)	NA	4 (44)	40 (69)	NA
Malignant	3 (25)	22 (38)		5 (56)	18 (31)	
Laterality						
Left hemisphere	8 (67)	26 (45)	NA	3 (33)	30 (52)	NA
Right hemisphere	3 (25)	30 (52)		4 (44)	27 (47)	
Bilateral	1 (8)	2 (3)		2 (22)	1 (1)	
Type of treatments received						
1 treatment	5 (42)	21 (36)	0.13	4 (44)	22 (38)	NA
>1 treatment	7 (58)	37 (64)		5 (56)	36 (62)	
RT						
Fractionated	9 (75)	51 (88)	1.36	8 (89)	49 (85)	NA
Stereotactic (single dose; IMRS)	3 (25)	7 (12)		1 (11)	9 (15)	
Types of medical treatments						
RT only	5 (42)	21 (36)	0.28	4 (44)	22 (38)	0.83
Presurgical + RT	5 (42)	29 (50)		3 (33)	28 (48)	
Presurgical + RT + chemotherapy	2 (17)	8 (14)		2 (22)	8 (14)	

Continued

Table 3. *Continued*

Variables	T1		χ^2/P^a	T2		χ^2/P^a
	High PTSS ($n = 12$) *n* (%)	Low PTSS ($n = 58$) *n* (%)		High PTSS ($n = 9$) *n* (%)	Low PTSS ($n = 58$) *n* (%)	
Medication usage, yes	7 (58)	36 (62)	0.06	6 (67)	35 (60)	0.13
Anticonvulsants	2 (17)	13 (22)	NA	2 (22)	12 (21)	NA
Pain medication	3 (25)	3 (5)	NA	2 (22)	3 (5)	NA
Concurrent medical conditions, yes	7 (58)	36 (62)	0.06	5 (56)	36 (62)	0.14
Family history of cancer, yes	8 (67)	37 (65)	0.01	4 (44)	39 (68)	NA
History of psychological problems, yes	5 (42)	19 (34)	0.26	5 (56)	19 (34)	1.56
Stress as cause of BT, yes	6 (50)	5 (9)	***12.85**** (***P* = ***.002)***	2 (22)	9 (16)	NA
PTSS at T1						
No/low PTSS	NA	NA	NA	4 (44)	51 (88)	***10.02**** (*P* = ***.007)***
Yes/high PTSS				5 (56)	7 (12)	
BT-related problems (ongoing at T2)	NA	NA	NA	8 (89)	42 (75)	0.84
Major stressors at T2	NA	NA	NA	6 (67)	29 (52)	0.69
	M (SD)	***M (SD)***	***Z (obs. P)***[1]	***M (SD)***	***M (SD)***	***Z (obs. P)***[1]
Age, y & mo	52.25 (14.39)	50.22 (14.46)	−0.59	46.89 (15.77)	50.75 (14.34)	−0.72
Education, y	13.25 (3.49)	13.88 (3.12)	−0.56	13.33 (3.64)	13.76 (3.16)	−0.24
Time since BT diagnosis, mo	9.5 (13.48)	31.37 (65.46)	−0.94	4.21 (3.76)	28.36 (58.34)	−1.32
T1: Time prior to RT, days	19.33 (19.79)	14.35 (17.21)	−1.36	NA	NA	NA
T2: Time since RT completion, mo ($n = 67$)	3.46 (0.77)	3.55 (0.86)	−0.17	3.54 (0.79)	3.54 (0.85)	−0.09
RT dosage (Gy)	43.53 (18.06)	44.87 (17.47)	−0.14	45.16 (15.34)	43.54 (17.62)	0.17
Expected prognosis (T1)	7.54 (2.11)	7.05 (2.34)	−0.56	7.22 (2.44)	7.21 (2.20)	−0.11
Psychosocial variables						
PCL-S[a]						
T1	50.83 (12.95)	25.28 (6.21)	−5.10** *[P = .000]*	46.22 (17.68)	26.59 (9.09)	−3.47** *[P = .000]*
T2	NA	NA		43.00 (8.87)	23.67 (5.70)	−4.62** *[P = .000]*
IES[a] total						
T1	44.83 (19.51)	15.79 (10.53)	−4.16** *[P = .000]*	42.67 (20.08)	16.83 (13.26)	−3.58** *[P = .000]*
T2	NA	NA		43.89 (17.52)	11.57 (9.46)[#]	−4.39** *[P = .000]*
FACT-PWB						
T1	19.83 (4.57)	22.99 (4.68)	−2.21 *[P = .026]*	20.44 (4.95)	22.77 (4.84)	−1.50 *[P = .135]*
T2	NA	NA		19.56 (7.30)	22.92 (4.70)	−1.72 *[P = .087]*
FACT-SWB						
T1	22.22 (4.64)	22.74 (4.12)	−0.31 *[P = .761]*	23.11 (3.44)	22.55 (4.38)	−1.61 *[P = .881]*
T2	NA	NA		19.33 (5.0)	21.93 (4.52)	−1.04 *[P = .109]*

FACT-EWB						
T1	13.42 (5.65)	17.95 (3.92)	−2.76* *[P = .005]*	12.89 (4.34)	17.86 (4.35)	−3.20** *[P = .001]*
T2	NA	NA		11.56 (5.79)	19.21 (3.82)	−3.42** *[P = .000]*
FACT-FWB						
T1	17.67 (6.29)	21.09 (4.61)	−1.81 *[P = .070]*	14.56 (5.36)	21.71 (4.22)	−3.28** *[P = .001]*
T2	NA	NA		15.22 (4.99)	21.28 (5.43)	−2.91* *[P = .003]*
FACT-G total						
T1	73.14 (13.74)	84.76 (11.64)	−2.96** *[P = .002]*	71.00 (10.52)	84.89 (12.29)	−3.05** *[P = .001]*
T2	NA	NA		65.67 (14.34)	85.34 (14.16)	−3.16** *[P = .001]*
FACT-Br						
T1	49.42 (11.45)	59.84 (10.93)	−2.66* *[P = .007]*	48.56 (12.38)	60.09 (10.65)	−2.50 *[P = .011]*
T2	NA	NA		44.78 (10.95)	59.98 (9.94)	−3.39** *[P = .000]*
POMS depression/dejection[a,d]						
T1	48.83 (10.54)	37.79 (5.51)	−2.91* *[P = .003]*	47.22 (9.48)	38.40 (6.96)	−2.75* *[P = .005]*
T2	NA	NA		47.56 (9.94)	37.98 (5.01)	−3.20** *[P = .001]*
POMS anger/hostility[a,d]						
T1	53.83 (11.15)	43.07 (5.58)	−3.14** *[P = .001]*	53.44 (10.79)	43.38 (6.47)	−2.99** *[P = .002]*
T2	NA	NA		50.78 (9.47)	42.65 (4.81)	−2.53 *[P = .010]*
POMS vigor[a,d]						
T1	60.58 (9.19)	59.33 (10.42)	−0.56 *[P = .574]*	63.67 (9.92)	58.52 (10.23)	−1.41 *[P = .163]*
T2	NA	NA		67.44 (9.75)	56.65 (10.69)	−2.63* *[P = .007]*
POMS fatigue/inertia[a,d]						
T1	54.08 (8.51)	45.53 (8.24)	−2.97* *[P = .003]*	54.11 (6.05)	45.64 (8.29)	−2.42 *[P = .014]*
T2	NA	NA		51.44 (9.79)	47.33 (9.85)	−1.18 *[P = .245]*
POMS confusion[a,d]						
T1	54.17 (7.93)	40.16 (6.17)	−4.45** *[P = .000]*	52.11 (6.05)	40.66 (7.47)	−3.63** *[P = .000]*
T2	NA	NA		50.89 (8.02)	40.37 (7.12)	−3.44** *[P = .000]*
PRCI positive support						
T1	49.42 (12.97)	48.86 (10.70)	0.36 *[P = .717]*	55.00 (9.11)	47.64 (11.17)	1.92 *[P = .055]*
T2	NA	NA		50.11 (8.22)	44.25 (11.16)	1.41 *[P = .158]*
SCS friends/family[a]						
T1	1.50 (0.93)	0.46 (0.56)	−3.76** *[P = .000]*	1.20 (0.95)	0.52 (0.66)	−2.52 *[P = .012]*
T2	NA	NA		1.14 (0.66)	0.41 (0.50)	−3.86** *[P = .000]*
SCS spouse/partner[a]						
T1	1.14 (1.09)	0.35 (0.58)	−2.82* *[P = .005]*	0.96 (1.05)	0.40 (0.68)	−2.13 *[P = .033]*
T2	NA	NA		1.67 (1.15)[#]	0.41 (0.67)	−3.55** *[P = .000]*
Neurocognitive tests						
LM I recall[b]						
T1	8.50 (4.17)	10.21 (3.21)	−1.50 *[P = .135]*	9.00 (3.71)	10.03 (3.46)	−0.77 *[P = .452]*
T2[##]	NA	NA		11.44 (2.79)	11.43 (3.82)[#]	−0.22 *[P = .833]*

Continued

Table 3. *Continued*

Variables	T1		χ^2/P^a	T2		χ^2/P^a
	High PTSS ($n = 12$) *n* (%)	Low PTSS ($n = 58$) *n* (%)		High PTSS ($n = 9$) *n* (%)	Low PTSS ($n = 58$) *n* (%)	
LM II recall						
T1	8.92 (3.12)	10.19 (3.96)	−1.12 *[P = .263]*	10.00 (3.40)	9.98 (3.93)	−0.18 *[P = .867]*
T2[##]	NA	NA		12.33 (3.05)	11.68 (3.84)[#]	−0.30 *[P = .775]*
LM II retention[b]						
T1	9.50 (3.45)	10.29 (3.84)	−0.56 *[P = .573]*	10.78 (3.87)	10.14 (3.84)	−0.50 *[P = .627]*
T2[##]	NA	NA		12.67 (2.18)	12.04 (3.13)[#]	−0.16 *[P = .876]*
Digit Span[b]						
T1	9.25 (4.39)	10.88 (3.03)	−1.91 *[P = .056]*	9.33 (4.15)	10.90 (3.17)	−1.66 *[P = .099]*
T2	NA	NA		9.11 (3.26)	11.61 (3.29)	−2.31 *[P = .019]*
Similarities[b]						
T1	9.42 (3.61)	10.91 (2.92)	−1.35 *[P = .177]*	10.11 (3.98)	10.83 (2.97)	−0.17 *[P = .875]*
T2	NA	NA		9.67 (3.54)	11.56 (4.22)	−1.29 *[P = .202]*
COWAT[c]						
T1	20.83 (18.32)	32.93 (27.53)	−1.25 *[P = .292]*	16.67 (20.62)	33.97 (26.68)	−1.86 *[P = .063]*
T2	NA	NA		24.44 (28.77)	39.11 (27.52)	−1.48 *[P = .144]*
TMT-A[c]						
T1	[$n = 12$] 40.00 (29.85)	[$n = 50$] 52.20 (27.65)	−1.29 *[P = .197]*	[$n = 9$] 38.89 (25.22)	[$n = 50$] 53.00 (27.94)	−1.46 *[P = .147]*
T2	NA	NA		[$n = 8$] 42.25 (32.49)	[$n = 32$] 59.69 (25.72)	−1.06 *[P = .300]*
TMT-B[c]						
T1	[$n = 12$] 11.67 (11.15)	[$n = 50$] 28.98 (26.71)	−1.92 *[P = .053]*	[$n = 9$] 7.78 (8.33)	[$n = 50$] 29.80 (26.18)	−2.48 *[P = .012]*
T2	NA	NA		[$n = 8$] 10.00 (14.14)	[$n = 32$] 45.00 (32.33)	−2.72* *[P = .005]*

Abbreviations: obs., observed; NA, not applicable.
[a]High score denotes poorer performance; for all other scores, the reverse applies.
[b]Age-matched scaled scores used according to validated Wechsler manuals.
[c]Percentile scores calculated on age and gender according to validated norms.
[d]POMS scores reflect *T*-scores.
*Statistically significant at $P < .01$ (adjusted $P < .003$ means that this is a trend toward significance)
**Statistically significant at $P < 002$.
[#]$P < .01$ with adjusted $P < .003$, trend toward statistically significant simple effects/within-group differences.
[##]GLM statistically significant main and/or interaction effects for PTSS at T2 with $P < .003$.

Table 4. Bivariate correlations with PCL-S score at T2 according to full sample and BT subgroups

Variable	Full Sample		Benign BT Sample		Malignant BT Sample	
	N	*r*	*N*	*r*	*N*	*r*
BT type, benign vs malignant	67	0.06		NA		NA
Gender[a]	67	0.07	44	−0.08	23	−0.32
Age	67	−0.28***	44	−0.11	23	−0.37
Years of education	67	0.11	44	0.15	23	−0.04
Laterality (LH vs RH)[b]	64	0.03	44	0.06	20	−0.06
Radiation dosage	67	0.02	44	−0.11	23	0.01
Medical treatments received[c]	67	−0.06	44	−0.17	23	−0.28
Anticonvulsant medication[d]	67	0.00	44	0.24	23	−0.44***
Psychiatric history[e]	67	0.20	44	−0.01	23	0.35
Psychosocial variables at T1						
PCL-S	67	0.64**	44	0.69**	23	0.63**
IES total	67	0.57**	44	0.57**	23	0.64**
FACT-PWB	67	−0.44**	44	−0.49**	23	−0.36
SWB	67	−0.09	44	−0.11	23	0.06
EWB	67	−0.37*	44	−0.35***	23	−0.34
FWB	67	−0.43**	44	−0.37***	23	−0.48***
G/total	67	−0.49**	44	−0.50**	23	−0.46***
Br	67	−0.43**	44	−0.51**	23	−0.25
G/Br total	67	−0.52**	44	−0.57**	23	−0.40
POMS depression	67	0.45**	44	0.40*	23	0.59*
Anger	67	0.61**	44	0.67**	23	0.48***
Vigor	67	0.12	44	0.04	23	0.14
Fatigue	67	0.48**	44	0.40*	23	0.57**
Confusion	67	0.56**	44	0.48**	23	0.73**
PRCI positive support	65	0.31***	42	0.31***	23	0.23
SCS friends/family	67	0.45**	44	0.43*	23	0.48***
Spouse/partner	67	0.34*	44	0.35***	23	0.33
Neurocognitive variables at T1						
LM I recall	67	−0.00	44	−0.10	23	0.08
LM II recall	67	0.03	44	0.10	23	−0.11
Retention	67	−0.05	44	0.06	23	−0.15
Digit Span	67	−0.13	44	−0.19	23	−0.11
Similarities	67	−0.03	44	−0.08	23	0.04
COWAT	67	−0.27***	44	−0.23	23	−0.29
TMT-A	59	−0.18	38	−0.02	21	−0.30
B		−0.30***		−0.22		−0.44***
Major stressors between T1 and T2[f]	65	0.18	44	0.14	23	0.27

[a]Gender scored 1 = female, 2 = male.
[b]Laterality scored 1 = RH, 2 = LH.
[c]Medical treatments received scored 1 = received only radiation treatment, 2 = received multiple treatments (radiation as well as surgery and/or chemotherapy).
[d]Anticonvulsant medication: whether person is taking anticonvulsants, scored 0 = no, 1 = yes.
[e]Psychiatric history: whether person reported history of psychological problems prior to BT diagnosis, scored 0 = no, 1 = yes.
[f]Major stressors: whether person reported experiencing concurrent major (non-BT) stressors between T1 and T2 assessments, scored 0 = no, 1 = yes.
*Statistically significant with adjusted alpha at $P < .006$.
**$P < .002$.
***Trend toward significance with $P < .05$.

slightly below average on the LM test. Indeed, all participants performed significantly better on this test at follow-up, particularly persons with a benign tumor. Although the improvement in memory scores at T2 may in part be due to practice effects, this result may also, in part, be due to an improvement in brain function. In contrast, all subgroups performed poorly on the executive tests at both assessments. This pattern of

Table 5. Regression analysis for variables predicting PTSS[a] at T2 ($n = 66$)

Variable	R^2	B	β	t	P
Age	0.076	−0.16	−0.25	−2.60	.012*
PCL-S T1	0.281	2.41	0.1	0.85	.399
FACT-G/Br T1	0.445	−0.13	−0.31	−2.83	.006**
POMS anger T1	0.503	0.36	0.31	2.56	.013*
SCS friends/family T1	0.507	1.05	0.09	0.74	.463

[a]PTSS at T2 assessed by PCL-S.
*Statistically significant at $P < .05$.
**Statistically significant at $P < .01$.

Table 6. Regression analysis for variables predicting QoL[a] at T2 [$n = 65$]

Variable	R^2	B	β	t	P
BT group status	0.086	−11.75	−0.23	−2.61	.011*
PCL-S T1	0.214	−0.62	−0.31	−2.09	.041*
FACT-G/Br T1	0.485	0.85	0.76	6.79	.000**
POMS depression T1	0.567	−1.46	−0.46	−3.37	.001**
SCS friends/family T1	0.57	2.75	0.08	0.7	.487
COWAT T1	0.587	0.13	0.14	1.56	.124

BT group status coded as 0 = benign BT, 1 = malignant BT.
[a]QoL at T2 assessed by FACT-G/Br combined total score.
*Statistically significant at $P < .05$.
**Statistically significant at $P < .01$.

findings is comparable to a number of studies that have found that BT patients are most susceptible to incurring deficits in executive functioning whilst memory and attentional skills remain relatively intact.[2,3,36] Indeed, memory performance may improve following BT treatment, especially for patients with low-grade/benign tumors,[2,36] who represented 65% of the current sample. It is also possible that improvement in memory may have been in part facilitated by an improvement in emotional well-being. That is, patients may have come to terms with their BT experience during the early stages of treatment recovery at the follow-up assessment.

The findings further highlight that 1 in 7 patients may be experiencing PTSS as a result of their BT experience, which is compatible with the incidence of PTSS documented by longer-term survivors of benign BTs[14] and by other oncology populations.[11] Moreover, whereas 44% of individuals with PTSS at T1 no longer reported heightened PTSS postradiotherapy, 56% of patients experienced chronic PTSS. This waxing and waning effect of PTSS is consistent with findings of other oncology studies[37] and concurs with research demonstrating that PTSS stabilize over time.[12] Importantly, a high level of PTSS was associated with reduced QoL and poor perceived quality of social support, both pre- and postradiotherapy. Following radiotherapy, PTSS were also related to a significant reduction in executive functioning. Collectively, these findings lend support to the cognitive model of trauma.[10] Moreover, elevated anger, reduced health-related QoL preradiotherapy, and younger age (<65 y) were each found to uniquely predict PTSS postradiotherapy. These variables have been found to be vulnerability factors in developing mood and stress disorders in other oncology[11,38] and civilian trauma[35] populations.

The finding that persons with malignant BTs and persons with elevated PTSS and depressive symptoms post–BT diagnosis are more vulnerable to experiencing reduced QoL posttreatment further lends support to the biopsychosocial model. Moreover, the most prevalent problem posttreatment was fatigue. This result concurs with research documenting that fatigue is the most frequently reported symptom associated with cancer and its treatment, which may further hamper one's general QoL.[39,40]

There are several methodological issues that need to be considered in interpreting study outcomes. Although the prospective design was a strength, the follow-up assessment was relatively short. Second, although well-validated measures were used, case diagnosis of PTSD and depression cannot be solely inferred from self-report measures. Future studies need to utilize multimodal assessments. Third, a more comprehensive battery of neurocognitive tests is warranted in future studies, particularly tests of nonverbal skills. Fourth, given the heterogeneity of the sample in terms of BT type, the sample size for the malignant BT subgroup was relatively small. Hence, the findings are preliminary, although they can facilitate future research in this field using larger samples. Finally, the findings may not necessarily generalize to non-Caucasian BT samples.

Notwithstanding these limitations, the present study lends support to a biopsychosocial framework[8,9] in furthering our understanding of the neuropsychosocial effects of BTs. Considering that persons diagnosed with benign/low-grade BTs have a relatively good prognosis in terms of survival rates, early and accurate identification of adult BT patients who are at risk for developing psychosocial and neurocognitive problems is warranted in order to prevent chronic psychosocial disturbances. Our findings support a growing body of research that has found that adult BT patients are at risk for experiencing both acute and chronic psychosocial disturbances,[4,6,13,14] although it is surprising that to date, there are no published controlled trials for the treatment of psychosocial and/or cognitive problems in this population.[14] The present findings attest to the need for the development of validated interventions to manage the psychological and neurocognitive sequelae of being diagnosed and treated for a BT with good medical prognosis, in order to enhance patients' QoL.

Supplementary Material

Supplementary material is available online at Neuro-Oncology (http://neuro-oncology.oxfordjournals.org/).

Acknowledgments

We wish to thank the patients of Prince of Wales Hospital, Sydney, for their time in this study. We wish to also thank the research assistants who worked on this project, including J Belcher, A Sparks, E Stanton, K Xavier, and E Zelestis.

Conflict of interest statement. None declared.

Funding

This work was partially supported by a grant from the Macquarie University awarded to M. K.

References

1. Porter KR, McCarthy BJ, Freels S, et al. Prevalence estimates for primary brain tumors in the United States by age, gender, behaviour, and histology. *Neuro-Onc*. 2010;12:520–527.
2. Costello A, Shallice T, Gullan R, et al. The early effects of radiotherapy on intellectual and cognitive functioning in patients with frontal brain tumours: the use of a new neuropsychological methodology. *J Neuro-Onc*. 2004;67:351–359.
3. Dijkstra M, van Nieuwenhuizen D, Stalpers LJA, et al. Late neurocognitive sequelae in patients with WHO grade I meningioma. *J Neurol Neursurg Psychiatry*. 2009;80:910–915.
4. Mainio A, Tuunanen S, Hakko H, Niemela A, et al. Decreased quality of life and depression as predictors for shorter survival amon patients with low-grade gliomas: a follow-up from 1990 to 2003. *Eur Arch Psych Clin Neuro*. 2006;256:516–521.
5. Ownsworth T, Hawkes AL, Chambers S, et al. Applying a biopsychosocial perspective to investigate factors related to emotional adjustment and quality of life for individuals with brain tumour. *Brain Imp*. 2010;11:270–280.
6. Arnold SD, Forman LM, Brigidi BD, et al. Evaluation and characterization of generalized anxiety and depression in patients with primary brain tumors. *Neuro-Onc*. 2008;10:171–181.
7. D'Angelo C, Mirijello A, Leggio L, et al. State and trait anxiety and depression in patients with primary brain tumors before and after surgery: 1-year longitudinal study. *J Neurosurg*. 2008;108:281–286.
8. Liu R, Page M, Solheim K, et al. Quality of life in adults with brain tumors: current knowledge and future directions. *Neuro-Onc*. 2008;11:330–339.
9. Ownsworth T, Hawkes AL, Steginga S, et al. A biopsychosocial perspective on adjustment and quality of life following a brain tumor: a systematic evaluation of the literature. *Disability Rehab*. 2009;31:1038–1055.
10. Ehlers A, Clark DM. A cognitive model of posttraumatic stress disorder. *Behav Res Ther*. 2000;38:319–345.
11. Kangas M, Henry J, Bryant R. Posttraumatic stress disorder following cancer: a conceptual and empirical review. *Clin Psych Rev*. 2002;22:499–524.
12. Kangas M, Henry J, Bryant R. The course of psychological disorders in the 1st year after cancer diagnosis. *J Cons Clin Psych*. 2005;73:763–768.
13. Goebel S, von Harscher M, Mehdorn HM. Comorbid mental disorders and psychosocial distress in patients with brain tumours and their spouses in the early treatment phase. *Sup Care Cancer*. 2010;19:1797–1805.
14. Kangas M, Williams JR, Smee RI. The association between posttraumatic stress and health-related quality of life in adults treated for a benign meningioma. *Applied Res Qual Life*. 2012;7:163–182.
15. Jagannathan J, Petit JH, Balsara K, et al. Long-term survival after gamma knife radiosurgery for primary and metastatic brain tumors. *Am J Clin Oncol*. 2004;27:441–444.
16. Weathers FW, Litz BT, Huska JA, et al. *PTSD Checklist–Civilian Version*. Boston: National Center for PTSD, Behavioral Science Division; 1994.
17. Weiss DS, Marmar CR. The Impact of Event Scale–Revised. In: Wilson, JP, Keane, TM, eds. *Assessing Psychological Trauma and PTSD*. New York: The Guildford Press; 1997.
18. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy Scale: development and validation of the general measure. *J Clin Onc*. 1993;11:570–579.
19. Weitzner MA, Meyers CA, Gelke C, et al. The Functional Assessment of Cancer Therapy (FACT) scale: development of a brain subscale and revalidation of the general version (FACT-G) in patients with primary brain tumors. *Cancer*. 1995;75:1151–1161.
20. McNair DM, Lorr M, Droppleman LF. *EdITS Manual: Profile of Mood States.* San Diego: Educational & Industrial Testing Service; 1971.
21. Manne S, Schnoll R. Measuring supportive and unsupprtive responses during cancer treatment: a factor analytic assessment of the partner responses to cancer inventory. *J Behav Med*. 2001;24:297–321.
22. Lepore SJ, Helgeson VS. Social constraints, intrusive thoughts, and mental health after prostate cancer. *J Soc Clin Psych*. 1998;17:89–106.
23. Schag CA, Ganz PA, Henrich RL. Cancer Rehabilitation Evaluation System–Short Form (CARES-SF): a cancer specific rehabilitation and quality of life instrument. *Cancer*. 1991;68:1406–1413.
24. Wechsler D. *Wechsler Memory Scale*. 3rd ed. San Antonio, TX: The Psychological Corporation; 1997.
25. Lezak MD, Howieson DB, Loring DW. *Neuropsychological Assessment*. 4th ed. New York: Oxford University Press; 2004.
26. Weschler D. *Wechsler Adult Intelligence Scale*. 3rd ed. San Antonio, TX: The Psychological Corporation; 1997.
27. Spreen O, Strauss E. *A Compendium of Neuropsychological Tests*. New York: Oxford University Press, Inc; 1991.
28. Reitan RM, Wolfson D. *The Halstead–Reitan Neuropsychological Test Battery*. 2nd ed. Tucson, AZ: Neuropsychology Press; 1993.
29. Strauss E, Sherman EMS, Spreen O. *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary*. 23rd ed. New York: Oxford University Press; 2006.
30. Tombaugh TN. Trail Making Test A and B: normative data stratified by age and education. *Arch Clin Neuropsych*. 2004;19:203–214.
31. Hahn CA, Dunn RH, Logue PE, et al. Prospective study of neuropsychological testing and quality-of-life assessment of adults with primary malignant brain tumours. *Int Journal Rad Onc Biol Phys*. 2003;55:992–999.
32. Burton LA. Emotional status after right vs. left temporal lobectomy. *Seizure*. 1999;8:116–119.
33. Heller W, Etienne MA, Miller GA. Patterns of perceptual asymmetry in depression and anxiety: implications for neuropsychological models of emotion and psychopathology. *J Abn Psych*. 1995;104:327–333.
34. Mainio A, Hakko H, Niemela A, et al. The effect of brain tumour laterality on anxiety levels among neurosurgical patients. *J Neuro Neurosurg Psych*. 2003;74:1278–1282.

35. Ozer EJ, Best SR, Lipsey TL, et al. Predictors of posttraumatic stress disorder and symptoms in adults: a meta-analysis. *Psych Bull*. 2003;129:52–73.
36. Tucha O, Smely C, Lange KW. Effects of surgery on cognitive functioning of elderly patients with intracranial meningioma. *Brit J Neurosurg*. 2001;15:184–188.
37. Andrykowski MA, Cordova MJ, McGrath PC, et al. Stability and change in posttraumatic stress disorder symptoms following breast cancer treatment: a 1-year follow-up. *Psycho-Onc*. 2000;9:69–78.
38. Kangas M, Henry JL, Bryant RA. The relationship between acute stress disorder and posttraumatic stress disorder following cancer. *J Cons Clin Psych*. 2005;73:360–364.
39. Kangas M, Bovberg DH, Montgomery GH. Cancer-related fatigue: a systematic and meta-analytic review of non-pharmacological therapies for cancer patients. *Psych Bull*. 2008;134:700–741.
40. Young KE, White CA. The prevalence and moderators of fatigue in people who have been successfully treated for cancer. *J Psychosom Res*. 60:29–38.