

Assessing Discrepancies in Neurocognitive and Patient-Reported Measures of Brain Tumor Survivors

Deborah "Hutch" Allen, PhD, RN, CNS, FNP-BC, AOCNP®, Barbara W. Carlson, RN, PhD, FGSA,
John R. Carlson, MS, Renee H. Raynor, PhD, and Virginia J. Neelon, PhD, RN

OBJECTIVES: To examine the association between performance-based neurocognitive and patient-reported cognitive function tests and identify characteristics that may explain observed discrepancies as a means to advance intervention development.

SAMPLE & SETTING: 40 adults diagnosed with a primary brain tumor (PBT) (high-grade, $n = 35$) were recruited from two academic neuro-oncology clinics in North Carolina.

METHODS & VARIABLES: Eligibility included a Mini-Mental State Examination score of 24 or greater, having completed cancer treatment, and having tumor stability. Participants completed performance-based neurocognitive and patient-reported cognitive function, demographic, and symptom assessment tests at one time point.

RESULTS: Neurocognitive impairments included executive control, memory, and attention. Age, time since diagnosis, and tumor- or treatment-specific variables were not associated with neurocognitive or patient-reported cognitive function. Those reporting worse cognitive impairment tended also to report greater severity of PBT-specific and depressive symptoms.

IMPLICATIONS FOR NURSING: Patient-reported cognitive concerns warrant additional assessment for potential interventions to maintain function.

KEYWORDS primary brain tumor; adult patients with cancer; neurocognitive performance; survivors

ONF, 47(1), E1-E12.

DOI 10.1188/20.ONF.E1-E12

Adults diagnosed with a primary brain tumor (PBT) have benefited from advancements in cancer treatment with improved survival rates (Ostrom et al., 2018). As a result, survivors have an opportunity to voice their concerns about the impact of cancer and its treatment. Clinicians have been called on to assess and intervene as a means to improve their patients' quality of life. Because cognitive concerns are reported to be very distressing to cancer survivors (Allen & Loughan, 2018), they warrant exploration for development of cognitive interventions.

Performance-based neurocognitive impairment in survivors of adult PBT has been estimated to be as low as 32% for global impairment that occurs across many cognitive domains or as high as 93% for test-specific impairment (Dwan, Ownsworth, Chambers, Walker, & Shum, 2015). Tumor grade, location, and treatment have influenced these results (Dwan et al., 2015). Domains of cognitive function most commonly affected are of memory and executive control function (Dwan et al., 2015). The resulting deficits are recognized as a cause of disability, including the inability to return to work or participate in social activities, and pose long-term changes in daily lives (Allen & Loughan, 2018).

Self-reported cognitive complaints are often the first indicator of change in function or well-being (Ganz et al., 2013; Pranckeviciene, Deltuva, Tamasauskas, & Bunevicius, 2017). Although cognitive complaints have been more commonly reported during treatment or shortly after treatment completion (Savard & Ganz, 2016), Hendrix et al. (2017) found that patients newly diagnosed with brain tumors reported having problems with memory and language skills. Patient-reported cognitive concerns have been associated with shorter survival, worse functional status, and tumor progression (Pranckeviciene et al., 2017).

In addition, patient-reported cognitive complaints in survivors of PBT are associated with greater psychological distress (Pranckeviciene et al., 2017) and warrant further assessment, as well as monitoring over time.

Hendrix et al. (2017) recommend routine clinical inquiry of patient-reported cognitive concerns because impairments in cognitive function may be subtle. They did not find an association between patient-reported and neurocognitive function in adults newly diagnosed with PBT with good physical functioning prior to surgery. Likewise, discrepancies between patient-reported and neurocognitive tests have been observed across several cancer populations (Gondi et al., 2013; Savard & Ganz, 2016). Potential explanations include instrument psychometric issues (Hutchinson, Hosking, Kichenadasse, Mattiske, & Wilson, 2012; Meyers, 2013), variability in testing cut point scores used in defining cognitive impairment (Jones et al., 2011), type and staging of cancer (Dwan et al., 2015), type of cancer treatments (Gondi et al., 2013; Wefel, Kayl, & Meyers, 2004), and effects from aging or existing comorbidities (Ahles et al., 2010; Mandelblatt et al., 2013). Symptoms such as depression and fatigue also factor into the discrepancy because symptomatic patients may over-report cognitive complaints (Ganz et al., 2013; Ownsworth, Dwan, Chambers, Walker, & Shum, 2014). Lastly, Raffa (2010) suggests that the discrepancy reflects conscious and unconscious compensation that the patient may use to maintain function.

Although the discrepancy between neurocognitive and patient-reported cognitive function has been identified (Ahles et al., 2010; Ownsworth et al., 2014), there has been no systematic approach to exploring factors that may contribute to the issue in survivors with adult PBT. The current authors used the theory of unpleasant symptoms (TOUS) to provide a framework for exploring the patient's symptom experience throughout the illness trajectory (Lenz, Suppe, Gift, Pugh, & Milligan, 1995). Three major concepts frame the TOUS model: symptoms, influencing factors, and performance consequences that affect patient and family lives. Symptom manifestation is guided by physiological, psychological, and situational factors, which can serve as points for intervention to prevent or mitigate symptom development. Using TOUS to systematically examine the association between performance-based neurocognitive and patient-reported measures of cognitive function, the authors could explore factors that may contribute to congruence or discrepancy in survivors of adult PBT.

Methods

The aims of this study were to (a) examine the association between performance-based neurocognitive and patient-reported measures of cognitive function in survivors of adult PBT, and (b) explore factors that contribute to the discrepancy between neurocognitive function and patient-reported change in cognitive function since diagnosis.

Sample and Setting

Participants were recruited from the Preston Robert Tisch Brain Tumor Center at Duke University in Durham and the Lineberger Cancer Center in Chapel Hill, both in North Carolina, during a nine-month timeframe. Eligibility required that participants had completed PBT treatment (surgery, radiation therapy, and/or chemotherapy) one year prior to enrollment, were medically stable at the time of study participation, had no history of psychiatric diagnoses (including depression, alcohol, or substance abuse), had no history of comorbid neurologic diagnoses (except medically stable seizure disorder), and were not taking psychoactive medications. Of the 1,326 patients screened for study participation through scheduled clinic appointments at both cancer centers, 302 met eligibility criteria and were recruited through opt-in letters or in-clinic referrals. Of these, 62 indicated interest in participating. Twenty-two responders elected not to participate because of scheduling conflicts ($n = 12$) or presence of worsening neurologic symptoms and clinical instability ($n = 10$). This study had a final cohort of 40 community-dwelling participants.

Procedures, Measures, and Variables

The study received approval from both academic medical centers' institutional review boards. All participants provided informed consent in accordance with institutional review board protocols. After confirming eligibility, participants performed a screening Mini-Mental State Examination (MMSE) to assess cognitive capacity to participate in the study. A score of 24 or greater was required for participation; lower scores suggest presence of cognitive disorders, such as mild dementia (Folstein, Folstein, & McHugh, 1975). Thereafter, informed consent was obtained. Participants completed demographic and health information surveys, symptom questionnaires, and a standardized set of performance-based neurocognitive tests. The entire protocol took about 85 minutes to complete and included two five-minute breaks. All procedures for administering the standardized neurocognitive tests were performed by trained

personnel and supervised by a board-certified neuropsychologist. The standardized neurocognitive assessment included the Trail Making Tests Part A and B (Trails A and B), the Hopkins Verbal Learning Test–Revised (HVLTR), and the Multilingual Aphasia Examination–Controlled Oral Word Association Test (COWA). Designed by Meyers and Brown (2006) to reduce burden and fatigue in patients with cancer while obtaining meaningful data to determine cognitive function, this neurocognitive assessment has been used in adults with primary brain tumors (Hahn et al., 2009)

Trail Making Tests Part A and B: Trails A and B measure attention, sequencing, and mental flexibility during motor control and visual search tasks (Partington & Leiter, 1949). Individuals sequentially connect 25 numbers in Trail A and alternating sequential numbers and letters in Trail B; both are time-based tests. Trails A and B exhibit strong test-retest reliability ($r = 0.95$) and internal consistency (Cronbach alpha = 0.96) in determining attention and executive function impairments (Lezak, Howieson, & Loring, 2004), as well as discriminating between those with cognitive impairment and healthy controls ($p = 0.032$ and 0.02 , respectively) (Matuoka, Kurita, Nordly, Sjøgren, & de Mattos-Pimenta, 2019). Both tests moderately correlate with each other ($r = 0.49$), suggesting slightly different visual search and cognitive set-shifting functions (Lezak et al., 2004).

Hopkins Verbal Learning Test–Revised: The HVLTR measures three components of memory: new learning (immediate recall), short- and long-term memory (delayed recall), and word recognition (recognition discrimination index) (Shapiro, Benedict, Schretlen, & Brandt, 1999). Examiners read 12 words to participants for their immediate recall during three successive trials. Following a brief delay, the examiner reads 24 semantically related words for participant recognition of the original words. After a 25-minute delay, the participant freely recalls the original 12 words. HVLTR demonstrates moderate test-retest reliability ($r = 0.74$), internal consistency (Cronbach alpha = 0.74) (Mitrushina, Boone, Razani, & D’Elia, 2005), and good convergent validity with the Brief Visuospatial Memory Test–Revised in those with non-lateralized brain injuries ($r = 0.8$) (Benedict, Schretlen, Groninger, Dobraski, & Shpritz, 1996).

Multilingual Aphasia Examination–Controlled Oral Word Association Test: COWA assesses verbal fluency by asking the participant to say as many words as possible during 60 seconds that begin with a specific letter of the alphabet (Benton, Varney, & Hamsher,

1978). COWA has moderate test-retest reliability ($r = 0.74$), strong internal consistency (Cronbach alpha = 0.83) (Ruff, Light, Parker, & Levin, 1996), and moderate convergent validity with functional reading tasks for those diagnosed with Alzheimer disease ($r = 0.4$) (Lowenstein et al., 1992).

Patient-reported cognitive function was measured by the Everyday Cognitive Scale (ECog) (Farias et al., 2008). The ECog is a 39-item questionnaire with six subscales to compare participants’ perception of current cognitive ability during everyday activities to their ability prior to diagnosis. Using a four-point rating, the individual indicates the change in function by 1 (no change or better), 2 (a little worse), 3 (consistently worse), or 4 (much worse). ECog has good internal consistency (Cronbach alpha = 0.8), test-retest reliability (0.82 during a 29-day period), moderate convergent validity with a shared variance of 53% between ECog and MMSE ($p < 0.0001$), and sensitivity of 0.93 and 0.67 for discriminating dementia or mild cognitive impairment, respectively, from healthy controls (Farias et al., 2008).

Symptom assessment and functional abilities were measured using four instruments. The Functional Assessment of Cancer Therapy–Brain Tumor (FACT-BT) assesses well-being across domains of physical, social and family, emotional, and function, as well as cancer-specific concerns, with higher scores indicating greater well-being (Weitzner et al., 1995). FACT-BT has modest convergent validity ($r = 0.47$) with the Ferrans and Powers Quality of Life Index–Cancer (Weitzner et al., 1995). The current sample had a mean score of 139.6 (SD = 23, range = 85–183).

The MD Anderson Symptom Inventory–Brain Tumor (MDASI-BT) assesses severity and interference of six symptom domains (affective, generalized, constitutional, cognitive, gastrointestinal, and focal neurologic), with higher scores indicating greater daily symptom presence or life interference (Armstrong, Cohen, Eriksen, & Cleeland, 2005). MDASI-BT has high internal consistency (Cronbach alpha = 0.91) (Armstrong et al., 2006), test-retest reliability ($r = 0.8$) (Armstrong et al., 2005), and sensitivity to performance status, tumor recurrence, and mean symptom interference ($p < 0.001$, $p < 0.01$, and $p < 0.001$, respectively) (Armstrong et al., 2006). The current sample had a mean score of 1.25 (SD = 1.2, range = 0–5.7) for severity and 1.35 (SD = 1.9, range = 0–8.7) for interference.

The Older Adults Resource Services Activities of Daily Living Scale (OARS) elicits participants’ perception of their ability to perform activities of everyday

life, with higher scores indicating better function (Fillenbaum, 1978). OARS has moderate convergent validity with the Katz Activities of Daily Living Scale in community-dwelling older adults ($r = 0.33$, $p < 0.05$) (Rueben, Valle, Hays, & Siu, 1995). The current sample had a mean score of 27.1 (SD = 1.5, range = 23–28) for total, 13.9 (SD = 0.5, range = 12–14) for physical, and 13.2 (SD = 1.2, range = 11–14) for instrumental.

The Center for Epidemiological Studies Depression Scale–Revised (CESD-R) assesses presence of depressive symptoms by scores of 16 or greater (Burnam, Wells, Leake, & Landsverk, 1988;

Radloff, 1977). The CESD-R demonstrates high internal consistency (Cronbach alpha = 0.9) (Burnam et al., 1988) and moderate convergent validity with Hamilton's Rating Scale and the Raskin Rating Scale in adults with depression ($r = 0.44$ and $r = 0.54$, respectively) (Radloff, 1977). The current sample had a mean score of 10.4 (SD = 8.4, range = 0–39).

Power Analysis

Type 1 error was restricted to 5%, test-wise, in two-sided tests for the power analysis. A sample size of 40 was determined to be sufficient to detect a minimum correlation of 0.41 between neurocognitive and patient-reported cognitive measures.

Data Analyses

To examine the congruence between performance-based neurocognitive and patient-reported cognitive measures, transformation of performance-based neurocognitive scores to standardized z scores using measure-specific age and education norms was required. The z scores were used to derive the Clinical Trials Battery (CTB) composite score (Johnson, Sawyer, Meyers, O'Neill, & Wefel, 2012). The authors defined normal neurocognitive function by composite scores greater than -1.3 SD, mild to moderate cognitive impairment as scores ranging from -1.3 to -3 SD, and severe cognitive impairment as scores of -3 or lower (Lezak et al., 2004). A total ECog score of 2 was used for the cut point to determine cognitive function; those with scores greater than 2 reported impairments in their cognitive ability. This cut point was chosen because the current sample's ECog scores were a mean of 1.87 (SD = 0.64), a median of 1.85, and a mode of 2. Setting cut points permitted additional investigation for discrepancies between neurocognitive and patient-reported scores through visual inspection. Descriptive statistics were used to explore relationships between patient-reported and neurocognitive function (Pearson correlations, t tests). Participant characteristics, including demographic and cancer-related variables, were explored to explain any differences in neurocognitive and patient-reported cognitive function (t tests, Kruskal-Wallis tests, chi-square tests).

Results

Demographics

The study sample consisted of 22 women and 18 men, predominately Caucasian, ranging in age from 30 to 64 years ($\bar{X} = 50.1$, SD = 9.7). All study participants had at least a high school education. The frontal ($n = 19$) and temporal lobes ($n = 10$) were the most common

TABLE 1. Sample Characteristics (N = 40)

Characteristic	\bar{X}	SD	Range
Time since diagnosis (years)			
All grades	8.4	6	1.3–25
Grade 2	5.1	2.4	2–7.4
Grade 3	10.9	7	2.4–25
Grade 4	3.9	4.1	1.3–11.8
Characteristic			n
Gender			
Female			22
Male			18
Race			
Caucasian			37
African American			3
Education			
High school			6
Technical/associate degree			12
Bachelor's degree			22
Tumor WHO grade			
2			5
3			25
4			10
Tumor location			
Frontal lobe			19
Temporal lobe			10
Other			11
Treatment			
Surgery/chemotherapy/radiation therapy			30
Radiation therapy/chemotherapy			4
Surgery/chemotherapy			3
Chemotherapy only			2
Surgery/radiation therapy			1
WHO—World Health Organization			

sites of tumor origin, and most of the participants were diagnosed with malignant brain tumors ($n = 35$). Hemispheric location was evenly split at 20 for each side. No participant had multiple tumor locations or a bi-hemispheric lesion. Time from original diagnosis until study ranged from 1.3 to 25 years (median = 6.7 years), with most having survived longer than five years (see Table 1).

Participants reported some impact of PBT-specific symptoms on their quality of life, including mild symptom severity, mild daily interference, and few symptoms of depression. Participants reported having good functional abilities and required little assistance with activities of daily living.

Cognitive Function

Scatterplots were used to examine the congruence of scores of neurocognitive performance (x axis) with patient-reported cognitive function (y axis). Table 2 contains performance-based neurocognitive and patient-reported cognitive function scores.

Performance-Based Neurocognitive Function

There was a wide range of CTB composite scores (-8.1 to 0.8). Ten participant scores indicated global cognitive impairment from mild to severe. The most commonly impaired domains were executive function (Trails B, $n = 19$) or memory (HVLT-R Delayed Recall, $n = 17$); 15 participants had impaired performances in both domains (delayed and recognition). Age, education, time since diagnosis, tumor characteristics, self-reported physical function, and depressive symptoms were not associated with performance scores for memory, attention, or CTB composite.

Patient-Reported Cognitive Function

Global patient-reported cognitive function for the 40 participants ranged from 1 to 3.29. Twenty-three reported no or little change in cognitive function since diagnosis (ECog scores less than 2), whereas 17 reported mild to severe changes in cognitive function since diagnosis (ECog scores between 2 [mild] and 4 [severe]). The domains most commonly reported as

TABLE 2. Neurocognitive and Patient-Reported Cognitive Function Scores (N = 40)

Domain	Test	Range	\bar{X}	SD	Freq (%) Impaired ^a
Neurocognitive performance scores^b					
CTB composite	HVLT-R, Trails, COWA	-8.10 to 0.8	-1.17	1.62	10 (25)
Memory and learning	HVLT-R Total Immediate Recall	-4.63 to 1.29	-0.98	1.48	15 (37.5)
Memory and learning	HVLT-R Delayed Recall	-4.95 to 1.07	-1.19	1.59	17 (42.5)
Memory and learning	HVLT-R Recognition	-5.07 to 0.8	-0.97	1.71	13 (32.5)
Processing speed	Trail A	-15.43 to 0.85	-1.67	2.77	12 (30)
Executive function	Trail B	-16.38 to 1.61	-2.17	3.47	19 (47.5)
Language	COWA	-3.19 to 2.48	-0.48	1.22	9 (22.5)
Patient-reported cognitive function scores^c					
Global	ECog Total	1 to 3.29	1.87	0.64	17 (42.5)
Attention	ECog Attention	1 to 4	2.32	1.05	24 (60)
Memory	ECog Memory	1 to 4	2.28	0.86	23 (57.5)
Language	ECog Language	1 to 3.5	1.93	0.71	18 (45)
Organizing	ECog Organizing	1 to 4	1.75	0.86	13 (32.5)
Planning	ECog Planning	1 to 3.2	1.49	0.61	7 (17.5)
Visuo-spatial	ECog Visuo-spatial	1 to 3.29	1.44	0.58	6 (15)

^a Impaired neuropsychological tests are -1.3 SD below norm data; ECog scores of 2 or greater

^b Neurocognitive-impaired participants are located in plotted groups C and D.

^c Self-reported impaired participants are located in plotted groups B and D.

CTB—Clinical Trials Battery; COWA—Controlled Oral Word Association Test; ECog—Everyday Cognitive Scale; Freq—frequency; HVLT-R—Hopkins Verbal Learning Test—Revised; Trail—Trail Making Test Part A or B

Note. COWA assesses verbal fluency and has an unlimited scoring range, with higher scores indicating greater verbal fluency skills; ECog is a 39-item questionnaire that compares participants' perceptions of current cognitive ability during everyday activities, with item scores ranging from 1 (no change or better) to 4 (much worse); HVLT-R measures three components of memory, with total immediate recall ranging from 0 to 36, delayed recall ranging from 0 to 12, and recognition ranging from -1 to 1 , with higher scores indicating better verbal memory; and Trails A and B measure attention, sequencing, and mental flexibility during motor control and visual search tasks, with faster times indicating better attention and cognitive flexibility.

changed were attention ($n = 24$), memory ($n = 23$), or language ($n = 18$). Nineteen participants reported changes in both attention and memory abilities.

Those with longer survival times since diagnosis were more likely to report greater difficulty performing tasks that require planning ($p < 0.05$). Individuals with right hemispheric lesions were more likely to report worsening cognitive function in all domains ($p < 0.05$). Those who reported more cancer-related symptoms or depressive symptoms indicated experiencing greater change in global, attention, memory, language, planning, and organizing domains of cognitive function ($p < 0.05$). Age, education, and other tumor characteristics were not associated with patient-reported cognitive function.

Congruence of Neurocognitive and Patient-Reported Cognitive Function by Participant Scores

Figure 1 illustrates participants' scores for neurocognitive versus patient-reported cognitive function. The scatterplot is depicted in groups to illustrate

neurocognitive and patient-reported cognitive function by normal or impaired scores. Groups A and B contain 30 participants with normal neurocognitive performance scores; groups C and D contain 10 participants with impaired neurocognitive performance scores. Those reporting little or no change in patient-reported cognitive function are in groups A and C, and those reporting substantial change in cognitive function are in groups B and D. The scatterplot demonstrates two congruent groups where neurocognitive and patient-reported measures agree (groups A and D, $n = 21$), and two incongruent groups where neurocognitive and patient-reported measures disagree (groups B and C, $n = 19$).

Congruent Groups

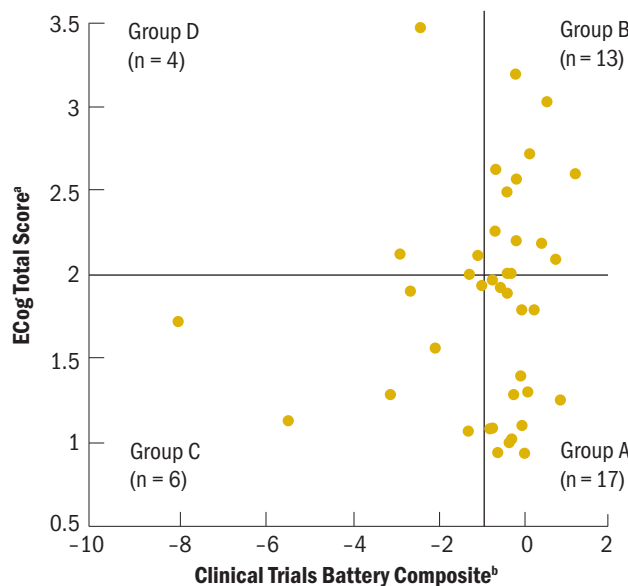
The 17 participants in Group A had congruent normal cognitive function scores—normal performance-based neurocognitive scores and little or no change in patient-reported cognitive function. Of these 17 participants, 4 had normal scores on all six neurocognitive tests. Participants in group A were mostly women ($n = 10$) and had the shortest time interval since diagnosis. Their tumors were located predominately in the frontal or temporal lobes ($n = 14$). These individuals reported significantly better quality of life than other groups ($p < 0.05$), fewer tumor-related symptoms, significantly fewer depressive symptoms ($p < 0.05$), and little need for physical assistance with activities of daily living (see Table 3).

The other congruent group, group D, had four participants with impaired cognitive function by performance-based and patient-reported measures. All were men with tumor location in the parietal and occipital lobes only. They tended to be older with longer time since diagnosis compared to other groups. These participants reported diminished quality of life, more tumor-related symptoms, and needing significantly more assistance with activities of daily living as compared to other groups ($p < 0.05$).

Incongruent Groups

There were 13 participants in group B, and all had normal performance-based neurocognitive function but patient-reported change of worsened cognitive function. Like group A, these were mostly women ($n = 10$) with tumors located predominately in the frontal or temporal lobes ($n = 11$). They reported impaired quality of life, more tumor-related symptoms, and significantly more depressive symptoms ($p < 0.05$) (five participants had CESD-R scores of 16 or greater).

FIGURE 1. Congruence of Neurocognitive and Patient-Reported Cognitive Function Scores



^a Range = 1–4

^b z scores

ECog—Everyday Cognitive Scale

Note. Group A indicates normal performance and self-report, congruent; group B indicates normal performance but report change in cognitive function, incongruent; group C indicates poor performance but report normal cognitive function, incongruent; and group D indicates poor performance and report change in cognitive function, congruent.

There were six participants in group C who had incongruent scores with impaired neurocognitive performance but patient report of little or no change in cognitive function. These were predominately men (n = 4) with tumor location primarily in the frontal or temporal areas (n = 4). They reported less impact of symptoms on their quality of life and less need for assistance in daily activities than participants in groups B and D.

Discussion

This study illustrates the association between performance-based neurocognitive and patient-reported cognitive measures and its contributing factors in adults with PBT. A discrepancy between measures of cognitive function was observed in about half of the sample. This discrepancy is concordant with reports

of cognitive functioning in adults newly diagnosed with PBT (Hendrix et al., 2017; Pranckeviciene et al., 2017). Likewise, discrepancies between patient-reported cognitive complaints and neurocognitive testing have also been observed in breast cancer survivors (Ahles et al., 2010; Ganz et al., 2013). The greatest discordance for these PBT survivors were found in the domains of attention and memory. This is similar to the discrepancy observed in breast cancer survivors (Ganz et al., 2013) and lung cancer survivors who had received prophylactic radiation therapy (Gondi et al., 2013).

The analysis of plotting patient-reported (ECog scores) versus neurocognitive (CTB z scores) allowed for the recognition of the patterns of congruent (agreement between neurocognitive and patient-reported assessment) and incongruent (disagreement

TABLE 3. Subject and Tumor-Related Characteristics by Congruence Group (N = 40)

Variable	\bar{X}	SD	\bar{X}	SD	\bar{X}	SD	\bar{X}	SD
Age (years)	50.3	9.7	46.1	9.7	53.5	8.7	57.5	6.5
Education (years)	15.3	2	14.6	1.8	14.7	2.1	16.5	1
Time since diagnosis (months)	82.7	75.3	98.6	70.5	119.8	96.3	160.3	104
CESD-R	6.4	5.7	15.5	10.7	10.5	6.3	10.3	4.4
FACT-BT*	152.4	18.6	128.2	20.5	136.8	29.1	126.8	14.5
MDASI-BT severity	0.8	0.6	1.5	1	1.8	2	1.7	1.8
MDASI-BT interference	0.6	0.6	1.5	1.5	1.3	1.5	4.1	4.5
OARS total	27.4	1.4	26.8	1.5	27.3	1	26	2.3
OARS physical*	13.9	0.5	13.9	0.3	14	0	13.3	1
OARS instrumental	13.5	1	12.9	1.3	13.3	1	12.8	1.5
	Group A (n = 17)		Group B (n = 13)		Group C (n = 6)		Group D (n = 4)	
Variable	n		n		n		n	
Male gender*	7		3		4		4	
Frontal lobe tumor	9		7		3		-	
Temporal lobe tumor	5		4		1		-	
Other tumor location	3		2		3		4	
Score of 16 or greater ^a	2		5		1		1	

*p < 0.05 difference across groups

^aBased on the CESD-R

CESD-R—Center for Epidemiological Studies Depression Scale—Revised; FACT-BT—Functional Assessment of Cancer Therapy—Brain Tumor; MDASI-BT—MD Anderson Symptom Inventory—Brain Tumor; OARS—Older Adults Resource Services Activities of Daily Living Scale

Note. Group A indicates normal performance and self-report, congruent; group B indicates normal performance but report change in cognitive function, incongruent; group C indicates poor performance but report normal cognitive function, incongruent; and group D indicates poor performance and report change in cognitive function, congruent.

Note. The CESD-R assesses presence of depressive symptoms by scores of 16 or greater; the FACT-BT assesses physical, social, and family relationships and emotional and functional domains of well-being, with higher scores (range = 0–132) indicating greater well-being; the MDASI-BT assesses severity (range = 0–220) and interference (range = 0–60) of six symptom domains, with higher scores indicating greater daily symptom presence or life interference; and OARS elicits participants' perception of their ability to perform activities of everyday life, with higher scores for physical (range = 0–14), instrumental (range = 0–14), and total (range = 0–28) indicating better function.

between neurocognitive and patient-reported assessment) scores. A key advantage of this technique is the observation of two groups with congruent (groups A and D) or incongruent (groups B and C) scores. Most of the current sample (groups A and B) had performance-based neurocognitive scores within normal parameters, indicating no impairment in cognitive performance. Individuals in group B indicated their awareness of change in cognitive function, although neurocognitive testing could not detect significant impairments. This group warrants attention to prevent and mitigate cognitive concerns. The smaller cohorts of groups C and D often get overlooked and warrant additional exploration to understand their functional experiences and the caregiver burden imposed by their documented cognitive limitations. Although both groups C and D demonstrated performance-based neurocognitive impairment, group D reported awareness of their change in cognitive function and impact on their quality of life in contrast to group C, who reported little or no change in cognitive function. Although participants in group C were diagnosed with frontal or temporal tumors, potentially contributing to their reduced awareness, they also warrant attention because further decline may occur at any time, with serious implications to patient functionality and caregiver burden.

The TOUS framework informed the authors' exploration using the four-quadrant plotting technique for physiologic, psychological, and situational factors that may contribute to congruence or incongruence between neurocognitive and patient-reported cognitive responses. The current study documents discrepancies between cognitive performance and patient-reported cognitive function in 19 of 40 survivors of PBT who had undergone cancer treatment with chemotherapy or radiation therapy. The current sample reflects a diversity of ages ranging from 31 to 64 years, with only six being older than age 60 years. This may explain why the current findings did not substantiate an association between age and cognitive function, as previously reported in survivors of PBT (Gehring, Aaronson, Gundy, Taphoorn, & Sitskoorn, 2011; Zucchella, Bartolo, Di Lorenzo, Villani, & Pace, 2013). Several studies have noted an association between time elapsed since diagnosis and neurocognitive impairment in survivors of PBT (Correa et al., 2008; Klein, 2012; Moretti et al., 2005; Scheibel et al., 2007); however, the current authors did not observe this in the study. This may be related to the sample having a wide range of time elapsed since diagnosis

KNOWLEDGE TRANSLATION

- Cognitive impairment in adults with cancer, particularly in those with primary brain tumors, can be a distressing and persistent symptom.
- Survivors often report cognitive concerns when signs of cognitive impairment may not be apparent to clinicians and warrant further investigation.
- Performance-based neurocognitive testing should be considered at time of diagnosis and intermittently through the cancer trajectory to track changes in cognitive function over time and offer potential interventions that may prevent or reduce cognitive impairment.

(as many as 25 years) and the fact that all were otherwise healthy, community-dwelling adults.

In addition, those with congruent cognitive responses tended to report fewer cognitive complaints (fewer symptoms and less symptom severity). In contrast, participants with incongruent cognitive responses tended to report greater symptom severity, greater impact on quality of life, and the presence of depressive symptoms. Similarly, Ownsworth et al. (2014) observed that adults with PBT who reported depressive symptoms also reported greater symptom impact on emotional well-being. It should be noted that 22% of the current sample reported depressive symptoms on the CESD-R during the time of study participation, which can confound cognitive function.

Limitations

The cross-sectional study design limits the generalizability of the findings, and the lack of longitudinal data prevents describing how a given participant's reported cognitive function and neurocognitive trajectory may change over time. Although several criteria were used to control factors that might influence cognitive function and to ensure a healthy community-dwelling cohort of participants, these exclusions limit generalizability. In addition, the sample is heterogeneous in regard to tumor grade, location, and treatment. Because of this diversity and the sample size, the authors were unable to control for or explore the effect of tumor location, grade, recurrence, and treatments on cognitive function (Davidson, Gao, Mason, Winocur, & Anderson, 2008; Hodgson, Hutchinson, Wilson, & Nettelbeck, 2013; Mandelblatt et al., 2013; Nokia, Anderson, & Shors, 2012; Robertson, 2014). The authors did not find any significant effect of these factors on neurocognitive

testing scores. This is similar to findings of Hendrix et al. (2017) who did not find an association with type of tumor and cognitive function; however, tumor volume and location were contributing factors for worsening cognitive function. Likewise, other reports also found tumor location or type (Hahn et al., 2009; Johnson et al., 2012; Satoer et al., 2012; Zucchella et al., 2013), or treatment modalities (Moretti et al., 2005; Zucchella et al., 2013) were associated with impaired cognitive function in PBT survivors. Other explanations for these differences may relate to the different neurocognitive tests used to determine cognitive performance, lack of sensitivity by neurocognitive tests to determine mild cognitive impairments, or the cut points used to define impairment (Caine, Mehta, Laack, & Gondi, 2012; Jones et al., 2011; Mandelblatt et al., 2013). Lastly, despite organizational recommendations, cognitive function measures have not been routinely implemented as a standard of practice for adults newly diagnosed with cancer to determine baseline cognitive function and monitor change over time (Wefel, Vardy, Ahles, & Schagen, 2011).

Implications for Nursing

A patient-reported change in cognitive function is a distressing symptom for adult survivors of PBT (Allen & Loughan, 2018), and patient-reported cognitive symptoms often precede performance-based neurocognitive decline (Ganz et al., 2013). A change in patient-reported cognitive function should prompt a thorough neurocognitive assessment; likewise, a lack of awareness of cognitive function change also warrants additional assessment to mitigate further decline and promote functional capabilities. The simultaneous assessment of patient-reported and neurocognitive function provides a framework for understanding factors that contribute to cognitive trajectory of PBT survivors. Although simultaneous assessment of performance-based neurocognitive and patient-reported cognitive function in the current study was performed at only one time point, longitudinal assessments could aid in the identification of those at risk for cognitive problems and prompt implementation of targeted interventions to mitigate or prevent cognitive decline. Interventions may include, but are not limited to, cognitive training programs, cognitive rehabilitation programs, and exercise as tailored to patient needs (Loughan, Allen, Von Ah, & Braun, 2018).

Lastly, longitudinal changes in cognitive function via neurocognitive performance and/or patient-reported cognitive function should be monitored. The authors'

scatterplot technique can be used to monitor change over time and may provide a means to identify those at risk for cognitive decline. Additional study using these techniques to explore use over time is warranted.

Conclusion

Cognitive impairment in adults with cancer, and particularly those with PBT, can be a distressing and persistent symptom. This study illustrates a discrepancy in patient-reported and performance-based cognitive function in survivors of adult PBT. Contributing factors include the impact of PBT-associated symptoms on quality of life and the presence of depressive symptoms. As patient-reported cognitive concerns may be precursors for performance-based cognitive decline, clinicians should routinely assess cognitive concerns throughout their patient's illness trajectory. When concerns are voiced, additional assessment should be performed and monitored over time with appropriate evidence-based cognitive interventions offered to mitigate or prevent cognitive decline.

Deborah "Hutch" Allen, PhD, RN, CNS, FNP-BC, AOCNP®, is the director of nursing research and evidence-based practice at Duke University Health System in Durham, NC; **Barbara W. Carlson, RN, PhD, FGSA**, is the Robert and Doris Klabzuba Professor of Nursing Science and assistant director of translational research at the Donald W. Reynolds Center for Geriatric Nursing Excellence in the Fran and Earl Ziegler College of Nursing at the University of Oklahoma Health Science Center in Oklahoma City; the late **John R. Carlson, MS**, was a statistician in Edmond, OK; **Renee H. Raynor, PhD**, is an assistant clinical professor in the Department of Psychiatry and Behavioral Sciences and Department of Neurosurgery and is a clinical neuropsychologist in the Preston Robert Tisch Brain Tumor Center at Duke University; and **Virginia J. Neelon, PhD, RN**, is a retired assistant professor from the School of Nursing at the University of North Carolina at Chapel Hill. Allen can be reached at hutch.allen@duke.edu, with copy to ONFEditor@ons.org. (Submitted January 2019. Accepted July 10, 2019.)

The authors gratefully acknowledge the assistance of Cheryl Koenig, research assistant, and Merle Mishel, PhD, RN, FAAN, dissertation committee member, both in the School of Nursing at the University of North Carolina.

Funding for this study was provided by an American Cancer Society Doctoral Scholarship award (DSCNR-08-201-03-SCN) to Allen.

Allen, B.W. Carlson, Raynor, and Neelon contributed to the conceptualization and design. Allen and B.W. Carlson completed

the data collection. Allen and J.R. Carlson provided statistical support. All authors provided analysis. Allen, B.W. Carlson, Raynor, and Neelon contributed to the manuscript preparation.

REFERENCES

- Ahles, T.A., Saykin, A.J., McDonald, B.C., Li, Y., Furstenberg, C.T., Hanscom, B.S., . . . Kaufman, P.A. (2010). Longitudinal assessment of cognitive changes associated with adjuvant treatment for breast cancer: Impact of age and cognitive reserve. *Journal of Clinical Oncology*, 28, 4434–4440. <https://doi.org/10.1200/JCO.2009.27.0827>
- Allen, D.H., & Loughan, A.R. (2018). Impact of cognitive impairment in patients with gliomas. *Seminars in Oncology Nursing*, 34, 528–546. <https://doi.org/10.1016/j.soncn.2018.10.010>
- Armstrong, T.S., Cohen, M.Z., Eriksen, L., & Cleeland, C. (2005). Content validity of self-report measurement instruments: An illustration from the development of the Brain Tumor Module of the M.D. Anderson Symptom Inventory. *Oncology Nursing Forum*, 32, 669–676. <https://doi.org/10.1188/05.ONF.669-676>
- Armstrong, T.S., Mendoza, T., Gning, I., Coco, C., Cohen, M.Z., Eriksen, L., . . . Cleeland, C. (2006). Validation of the M.D. Anderson Symptom Inventory Brain Tumor Module (MDASI-BT). *Journal of Neuro-Oncology*, 80, 27–35. <https://doi.org/10.1007/s11060-006-9135-z>
- Benedict, R.H.B., Schretlen, D., Groninger, L., Dobraski, M., & Shpritz, B. (1996). Revision of the brief visuospatial memory test: Studies of normal performance, reliability, and validity. *Psychological Assessment*, 8, 145–153.
- Benton, A.L., Varney, N.R., & Hamsher, K.D. (1978). Visuospatial judgment. A clinical test. *Archives of Neurology*, 35, 364–367. <https://doi.org/10.1001/archneur.1978.00500300038006>
- Burnam, M.A., Wells, K.B., Leake, B., & Landsverk, J. (1988). Development of a brief screening instrument for detecting depressive disorders. *Medical Care*, 26, 775–789. <https://doi.org/10.1097/00005650-198808000-00004>
- Caine, C., Mehta, M.P., Laack, N.N., & Gondi, V. (2012). Cognitive function testing in adult brain tumor trials: Lessons from a comprehensive review. *Expert Review of Anticancer Therapy*, 12, 665–667. <https://doi.org/10.1586/era.12.34>
- Correa, D.D., Shi, W., Thaler, H.T., Cheung, A.M., DeAngelis, L.M., & Abrey, L.E. (2008). Longitudinal cognitive follow-up in low grade gliomas. *Journal of Neuro-Oncology*, 86, 321–327. <https://doi.org/10.1007/s11060-007-9474-4>
- Davidson, P.S., Gao, F.Q., Mason, W.P., Winocur, G., & Anderson, N.D. (2008). Verbal fluency, trail making, and Wisconsin Card Sorting Test performance following right frontal lobe tumor resection. *Journal of Clinical and Experimental Neuropsychology*, 30, 18–32. <https://doi.org/10.1080/13803390601161166>
- Dwan, T.M., Ownsworth, T., Chambers, S., Walker, D.G., & Shum, D.H. (2015). Neuropsychological assessment of individuals with brain tumor: Comparison of approaches used in the classification of impairment. *Frontiers in Oncology*, 5, 56. <https://doi.org/10.3389/fonc.2015.00056>
- Farias, S.T., Mungas, D., Reed, B.R., Cahn-Weiner, D., Jagust, W., Baynes, K., & Decarli, C. (2008). The measurement of everyday cognition (ECog): Scale development and psychometric properties. *Neuropsychology*, 22, 531–544. <https://doi.org/10.1037/0894-4105.22.4.531>
- Fillenbaum, G. (1978). *Center for the Study of Aging and Human Development: Multifactorial Functional Assessment Questionnaire*. Durham, NC: Duke University Press.
- Folstein, M.F., Folstein, S.E., & McHugh, P.R. (1975). “Mini-mental state”. A practical methods for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189–198. [https://doi.org/10.1016/0022-3956\(75\)90026-6](https://doi.org/10.1016/0022-3956(75)90026-6)
- Ganz, P.A., Kwan, L., Castellon, S.A., Oppenheim, A., Bower, J.E., Silverman, D.H., . . . Belin, T.R. (2013). Cognitive complaints after breast cancer treatments: Examining the relationship with neuropsychological test performance. *Journal of the National Cancer Institute*, 105, 791–801. <https://doi.org/10.1093/jnci/djt073>
- Gehring, K., Aaronson, N.K., Gundy, C.M., Taphoorn, M.J., & Sitskoorn, M.M. (2011). Predictors of neuropsychological improvement following cognitive rehabilitation in patients with gliomas. *Journal of the International Neuropsychological Society*, 17, 256–266. <https://doi.org/10.1017/S13556177100001530>
- Gondi, V., Paulus, R., Bruner, D.W., Meyers, C.A., Gore, E.M., Wolfson, A., . . . Movsas, B. (2013). Decline in tested and self-reported cognitive functioning after prophylactic cranial irradiation for lung cancer: Pooled secondary analysis of Radiation Therapy Oncology Group randomized trials 0212 and 0214. *International Journal of Radiation Oncology, Biology, Physics*, 86, 656–664. <https://doi.org/10.1016/j.ijrobp.2013.02.033>
- Hahn, C.A., Zhou, S.M., Raynor, R., Tisch, A., Light, K., Shafman, T., . . . Marks, L.B. (2009). Dose-dependent effects of radiation therapy on cerebral blood flow, metabolism, and neurocognitive dysfunction. *International Journal of Radiation Oncology, Biology, Physics*, 73, 1082–1087. <https://doi.org/10.1016/j.ijrobp.2008.05.061>
- Hendrix, P., Hans, E., Griessenauer, C.J., Simgen, A., Oertel, J. & Karbach, J. (2017). Neurocognitive status in patients with newly-diagnosed brain tumors in good neurological condition: The impact of tumor type, volume, and location. *Clinical Neurology and Neurosurgery*, 156, 55–62. <https://doi.org/10.1016/j.clineuro.2017.03.009>
- Hodgson, K.D., Hutchinson, A.D., Wilson, C.J., & Nettelbeck, T. (2013). A meta-analysis of the effects of chemotherapy on cognition in patients with cancer. *Cancer Treatment Reviews*, 39, 297–304. <https://doi.org/10.1016/j.ctrv.2012.11.001>
- Hutchinson, A.D., Hosking, J.R., Kichenadasse, G., Mattiske, J.K., & Wilson, C. (2012). Objective and subjective cognitive impairment following chemotherapy for cancer: A systematic review. *Cancer Treatment Reviews*, 38, 926–934. <https://doi.org/10.1016/j.ctrv.2012.05.002>

- Johnson, D.R., Sawyer, A.M., Meyers, C.A., O'Neill, B.P., & Wefel, J.S. (2012). Early measures of cognitive function predict survival in patients with newly diagnosed glioblastoma. *Neuro-Oncology*, 14, 808–816. <https://doi.org/10.1093/neuonc/nos082>
- Jones, R.N., Manly, J., Glymour, M.M., Rentz, D.M., Jefferson, A.L., & Stern, Y. (2011). Conceptual and measurement challenges in research on cognitive reserve. *Journal of the International Neuropsychological Society*, 17, 593–601. <https://doi.org/10.1017/S1355617710001748>
- Klein, M. (2012). Neurocognitive functioning in adult WHO grade II gliomas: Impact of old and new treatment modalities. *Neuro-Oncology*, 14(Suppl. 4), iv17–iv24. <https://doi.org/10.1093/neuonc/nos161>
- Lenz, E.R., Suppe, F., Gift, A.G., Pugh, L.C., & Milligan, R.A. (1995). Collaborative development of middle-range nursing theories: Toward a theory of unpleasant symptoms. *Advances in Nursing Science*, 17, 1–13.
- Lezak, M.D., Howieson, D.B., & Loring, D.W. (Eds.) (2004). *Neuropsychological assessment* (4th ed.). Oxford, UK: Oxford University Press.
- Loughan, A.R., Allen, D.H., Von Ah, D., & Braun, S. (2018). Neuropsychology of chemotherapy in brain tumor patients. In H.B. Newton (Ed.), *Handbook of brain tumor chemotherapy, molecular therapeutics, and immunotherapy* (2nd ed., pp. 783–810). London, England: Elsevier.
- Lowenstein, D.A., Rubert, M.P., Berkowitz-Zimmer, N., Guterman, A., Morgan, R., & Hayden, S. (1992). Neuropsychological test performance and prediction of functional capacities in dementia. *Behavior, Health, and Aging*, 2, 149–158.
- Mandelblatt, J.S., Hurria, A., McDonald, B.C., Saykin, A.J., Stern, R.A., VanMeter, J.W., . . . Ahles, T. (2013). Cognitive effects of cancer and its treatments at the intersection of aging: What do we know; what do we need to know? *Seminars in Oncology*, 40, 709–725. <https://doi.org/10.1053/j.seminoncol.2013.09.006>
- Matuoka, J.Y., Kurita, G.P., Nordly, M., Sjøgren, P., & de Mattos-Pimenta, C.A. (2019). Validation of a battery of neuropsychological tests for patients with metastatic cancer. *Clinical Nursing Research*. Retrieved from <https://doi.org/10.1177/1054773819831210>
- Meyers, C.A. (2013). Cognitive complaints after breast cancer treatments: Patient report and objective evidence. *Journal of the National Cancer Institute*, 105, 761–762. <https://doi.org/10.1093/jnci/djt091>
- Meyers, C.A., & Brown, P.D. (2006). Role and relevance of neurocognitive assessment in clinical trials of patients with CNS tumors. *Journal of Clinical Oncology*, 24, 1305–1309. <https://doi.org/10.1200/JCO.2005.04.6086>
- Mitrushina, M., Boone, K.B., Razani, J., & D'Elia, L.F. (2005). *Handbook of normative data for neuropsychological assessment* (2nd ed.). New York, NY: Oxford University Press.
- Moretti, R., Torre, P., Antonello, R.M., Cattaruzza, T., Cazzato, G., Bava, A., . . . Korczyn, A.D. (2005). Neuropsychological evaluation of late-onset post-radiotherapy encephalopathy: A comparison with vascular dementia. *Journal of the Neurological Sciences*, 229–230, 195–200. <https://doi.org/10.1016/j.jns.2004.11.027>
- Nokia, M.S., Anderson, M.L., & Shors, T.J. (2012). Chemotherapy disrupts learning, neurogenesis and theta activity in the adult brain. *European Journal of Neuroscience*, 36, 3521–3530. <https://doi.org/10.1111/ejn.12007>
- Ostrom, Q.T., Gittleman, H., Truitt, G., Boscia, A., Kruchko, C., & Barnholtz-Sloan, J.S. (2018). CBTRUS statistical report: Primary brain and other central nervous system tumors diagnosed in the United States in 2011–2015. *Neuro-Oncology*, 20(Suppl. 4), iv1–iv86. <https://doi.org/10.1093/neuonc/noy131>
- Ownsworth, T., Dwan, T., Chambers, S., Walker, D.G., & Shum, D.H. (2014). The moderating effect of estimated pre-morbid IQ on the relationship between neuropsychological status and subjective well-being after brain tumour. *Journal of Psychosomatic Research*, 76, 257–260. <https://doi.org/10.1016/j.psychores.2013.12.008>
- Partington, J.E., & Leiter, R.G. (1949). Partington's pathway test. *Psychological Service Center Bulletin*, 1, 11–20.
- Pranckeviciene, A., Deltuva, V.P., Tamasauskas, A., & Bunevicius, A. (2017). Association between psychological distress, subjective cognitive complaints and objective neuropsychological function in brain tumor patients. *Clinical Neurology and Neurosurgery*, 163, 18–23. <https://doi.org/10.1016/j.clineuro.2017.10.007>
- Radloff, L.S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, 1, 385–401. <https://doi.org/10.1177/014662167700100306>
- Raffa, R.B. (2010). Is a picture worth a thousand (forgotten) words?: Neuroimaging evidence for the cognitive deficits in 'chemo-fog'/'chemo-brain.' *Journal of Clinical Pharmacy and Therapeutics*, 35, 1–9. <https://doi.org/10.1111/j.1365-2710.2009.01044.x>
- Reuben, D.B., Valle, L.A., Hays, R.D., & Siu, A.L. (1995). Measuring physical function in community-dwelling older persons: A comparison of self-administered, interviewer-administered, and performance-based measures. *Journal of the American Geriatrics Society*, 43, 17–23. <https://doi.org/10.1111/j.1532-5415.1995.tb06236.x>
- Robertson, I.H. (2014). Right hemisphere role in cognitive reserve. *Neurobiology of Aging*, 35, 1375–1385. <https://doi.org/10.1016/j.neurobiolaging.2013.11.028>
- Ruff, R.M., Light, R.H., Parker, S.B., & Levin, H.S. (1996). Benton Controlled Oral Word Association Test: Reliability and updated norms. *Archives in Clinical Neuropsychology*, 11, 329–338.
- Satoer, D., Vork, J., Visch-Brink, E., Smits, M., Dirven, C., & Vincent, A. (2012). Cognitive functioning early after surgery of gliomas in eloquent areas. *Journal of Neurosurgery*, 117, 831–838. <https://doi.org/10.3171/2012.7.JNS12263>
- Savard, J., & Ganz, P.A. (2016). Subjective or objective measures of cognitive functioning—What's more important? *JAMA Oncology*, 2, 1263–1264. <https://doi.org/10.1001/jamaoncol.2016.2047>

- Scheibel, R.S., Newsome, M.R., Steinberg, J.L., Pearson, D.A., Rauch, R.A., Mao, H., . . . Levin, H. (2007). Altered brain activation during cognitive control in patients with moderate to severe traumatic brain injury. *Neurorehabilitation and Neural Repair*, 21, 36–45. <https://doi.org/10.1177/1545968306294730>
- Shapiro, A.M., Benedict, R.H., Schretlen, D., & Brandt, J. (1999). Construct and concurrent validity of the Hopkins Verbal Learning Test-Revised. *Clinical Neuropsychologist*, 13, 348–358.
- Wefel, J.S., Kayl, A.E., & Meyers, C.A. (2004). Neuropsychological dysfunction associated with cancer and cancer therapies: A conceptual review of an emerging target. *British Journal of Cancer*, 90, 1691–1696. <https://doi.org/10.1038/sj.bjc.6601772>
- Wefel, J.S., Vardy, J., Ahles, T., & Schagen, S.B. (2011). International Cognition and Cancer Task Force recommendations to harmonise studies of cognitive function in patients with cancer. *Lancet Oncology*, 12, 703–708. [https://doi.org/10.1016/S1470-2045\(10\)70294-1](https://doi.org/10.1016/S1470-2045(10)70294-1)
- Weitzner, M.A., Meyers, C.A., Gelke, C.K., Byrne, K.S., Cella, D.F., & Levin, V.A. (1995). 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*, 75, 1151–1161. [https://doi.org/10.1002/1097-0142\(19950301\)75:5<1151::aid-cnrcr2820750515>3.0.co;2-q](https://doi.org/10.1002/1097-0142(19950301)75:5<1151::aid-cnrcr2820750515>3.0.co;2-q)
- Zucchella, C., Bartolo, M., Di Lorenzo, C., Villani, V., & Pace, A. (2013). Cognitive impairment in primary brain tumors outpatients: A prospective cross-sectional survey. *Journal of Neuro-Oncology*, 122, 455–460. <https://doi.org/10.1007/s11060-013-1076-8>