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Perceived Executive Functioning Deficits After Diagnosis in Women with Non-Metastatic Breast Cancer Prior to Adjuvant Therapies

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Abstract

Background Perceived deficits in executive functioning are among the many difficulties that women diagnosed with breast cancer experience. This study assessed the presence of perceived deficits in executive functioning among women with breast cancer prior to systemic treatment and radiation and associations between perceived deficits in executive function and comorbid fatigue, sleep, and mood disturbance.

Method Participants were recruited following their breast cancer diagnosis and assessed using the Behavior Rating Inventory of Executive Function for Adults (BRIEF-A), subjective and objective measures of sleep duration and efficiency, and self-report measures of insomnia severity, sleep quality, fatigue, and mood disturbance. Hierarchical regression was used to examine associations between symptoms, adjusting for age and education.

Results The final sample included 92 women with a mean age of 60.7 years and 13.5 years of education. Thirteen percent of participants reported global executive dysfunction. After partitioning out variability from other independent variables, fatigue ($p = < .001$), perceived sleep quality ($p = .030$), and symptoms of insomnia ($p = .008$) accounted for 13.3%, 5.7%, and 8.5% of unique variance in perceived executive functioning, respectively. Emotional fatigue was most strongly associated with perceived deficits in executive functioning. Neither subjective or objective sleep duration or efficiency was associated with perceived deficits in executive functioning.

Conclusion Fatigue, particularly emotional fatigue, insomnia, and poor sleep quality had the strongest associations with perceived deficits in executive functioning. Sleep interventions and fatigue management strategies may prove useful for women who seek to improve their perceived executive functioning.

Keywords Breast cancer · Executive functioning · Sleep disturbance · Insomnia · Fatigue · Mood

Introduction

Breast cancer is the most commonly diagnosed cancer type among women [1]. Therapeutic advances have led to a significant increase in the survival rate, but are often associated with short- and long-term side effects [2]. Perceived deficits in executive function and cognitive impairment can impact psychological, social, and occupational function [3–5] and have been reported by up to 75% of women undergoing active treatment for breast cancer [6, 7].

Few studies have investigated the presence of perceived deficits in executive function prior to initiating cancer treatment despite over a decade of research indicating that cognitive impairment can be present prior to the onset of such treatment [8]. Executive function is a broad term used to define a complex set of cognitive processes involved in day-to-day tasks, such as driving, cooking, and interacting with others. In addition to working memory, executive functioning is involved in inhibiting impulses, self-monitoring, and regulating emotions. Neuroimaging studies have demonstrated changes in executive functioning in individuals with breast cancer following chemotherapy [9, 10]. Executive functioning is seldom explored prior to treatment and is typically only investigated using objective neuropsychological

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tests or neuroimaging tools such as functional magnetic resonance imaging (fMRI). Recent research suggests that persistent self-reported cognitive problems among women with breast cancer are associated with neurocognitive changes warranting clinical attention [11].

Given that subjective reported cognitive complaints are more vigorously correlated with quality of life and emotional wellbeing than objective impairment [4, 12], it is important to capture the presence of perceived executive functioning difficulties prior to initiating treatment. The Behavior Rating Inventory of Executive Function for Adults (BRIEF-A) can help to understand the individual's perception of real-world manifestations of possible executive dysfunction and behavioral dyscontrol. The BRIEF-A has previously been used to study executive dysfunction in patients with brain tumors [13, 14], but has yet to be investigated in women diagnosed with breast cancer. Research is just beginning to explore the impact that psychological and behavioral factors (e.g., sleep quality, insomnia, fatigue, and mood disturbance) may have on the development and progression of pre-treatment perceived deficits in executive function among women with breast cancer. This is surprising given that between 30 and 60% of patients with cancer are affected by insomnia symptoms, with the highest rates being reported among women with breast cancer [15, 16]. Insomnia co-occurs with perceived cognitive impairment in roughly one in five people diagnosed with cancer and is most common at the beginning of cancer treatment [17]. Moreover, women with breast cancer are at increased risk of experiencing fatigue [18, 19]. Insomnia is a known contributing factor to, and predictor of, fatigue in patients and survivors of cancer [20–22]. Cognitive impairment, fatigue, and insomnia also frequently exist with other cancer side effects including depression. Using Bayesian network analysis in a sample of women prior to, after completing, and 1 year post chemotherapy, worse cognitive performance was significantly associated with worse sleep quality, fatigue, and mood [23]. This suggests that these symptoms may result from shared physiological and/or behavioral mechanisms that may also contribute to perceived deficits in executive function.

Objectives

The first objective of the current study was to characterize the presence of perceived deficits in executive function among post-operative women with breast cancer prior to the onset of systemic treatment and radiation. The second objective was to examine the associations between perceived deficits in executive function and insomnia, sleep quality, subjective and objective total sleep time and sleep efficiency, fatigue, and mood disturbance before the onset of treatment for breast cancer.

Methods

Participants

The Human Research Ethics Board approved the research methods used in this study. One-hundred women with breast cancer were recruited from a regional cancer clinic after receiving their breast cancer diagnosis (i.e., after recovering from surgery but prior to beginning systemic treatment and radiation). Eligibility criteria were as follows: (1) female sex; (2) English-speaking; (3) over 18 years of age; (4) having a diagnosis of stage I–III breast cancer; and (5) scheduled to receive radiation and/or systemic therapy, including chemotherapy, endocrine therapy, and/or targeted therapies (i.e., trastuzumab). Exclusion criteria included the following: (1) previous treatment for cancer or currently undergoing treatment; (2) presence of a sleep disorder other than insomnia that was not currently managed, such as sleep apnea; (3) presence of a psychological disorder that was not stable and/or would impair the individual's ability to participate in the study, such as schizophrenia; and (4) a score lower than 24 on the Mini Mental State Examination (MMSE) (i.e., a score suggestive of severe cognitive impairment).

Procedure

The oncologists screened clinical charts to identify potentially eligible women prior to their appointment. Assessments with interested women were arranged to occur shortly after their clinic visit. After informed consent was obtained, a medical, psychological, and sleep disorder screen was administered to rule out the presence of one or more of the conditions specified above, and the MMSE [24] was administered to rule out the presence of severe cognitive impairment.

All assessments were conducted by trained graduate students and completed in person or remotely via telehealth for women located in rural areas. Self-report measures, an actigraph, and a postage paid return envelope were mailed to participants in rural settings.

Measures

All clinical variables were abstracted from medical charts, and a demographics questionnaire was used to characterize the sample (i.e., age, ethnicity, employment status, etc.).

Perceived Executive Function

The Behavior Rating Inventory of Executive Function for Adults (BRIEF-A) is a self-report measure composed of 75 items within nine non-overlapping theoretically and empirically derived clinical scales, three validity scales (Negativity,

Infrequency, and Inconsistency), two summary index scales (Behavioural Regulation and Metacognition), and an overarching summary score (Global Executive Composite). The Behavioral Regulation Index is composed of four scales (Inhibit, Shift, Emotional Control, and Self-Monitor) and captures the individual's ability to maintain appropriate inhibition of thoughts and actions, flexibility in shifting problem-solving set, modulation of emotional response, and monitoring of one's actions. The Metacognition Index is composed of five scales (Initiate, Working Memory, Plan/Organize, Task Monitor, and Organization of Materials) and captures the individual's ability to initiate activities and generate problem-solving ideas, sustain working memory, plan ahead, and organize one's materials and environment. Age-corrected *T* scores ($M = 50$, SD = 10) are used to interpret the individual's level of executive functioning on the BRIEF-A. These scores are transformations of the raw scale scores and *T* scores at or above 65 are considered clinically significant. Higher scores on the BRIEF-A reflect greater executive functioning difficulties. The test is normed to a sample of 1136 adults from a wide range of racial/ethnic backgrounds, educational backgrounds, and geographic locations. Reliability, validity, and clinical utility have been established, making the BRIEF-A an ecologically sensitive measure of executive functioning in individuals with a range of conditions [25].

Subjective Sleep Measures

The Insomnia Severity Index (ISI) [26] is a seven-item self-report questionnaire that assesses difficulty falling asleep, difficulty staying asleep, early morning awakenings, satisfaction with current sleep patterns, interference with daily functioning, sleep-related impairment, and distress level caused by sleep problems. The optimal cutoff scores are 0 to 7 (no clinically significant insomnia), 8 to 14 (sub-threshold insomnia), 15 to 21 (moderate insomnia), and 22 to 28 (severe insomnia).

The Pittsburgh Sleep Quality Index (PSQI) [27] is a 19-item measure that was used to assess subjective sleep quality. The PSQI probes seven areas related to sleep quality in the past month: sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, subjective sleep quality, use of sleeping medication, and daytime dysfunction. Global scores equal to or greater than 5 are indicative of poor sleep quality.

Sleep Measures

Participants completed a sleep diary and wore an actigraph over a 7-day period. The Consensus Sleep Diary (CSD) is a reliable and valid patient report of sleep [28]. The Micro Motionlogger sleep watches (Ambulatory Monitoring Inc., Ardsley, NY, USA) provide 95% sensitivity, 65% specificity, and 90% agreement to polysomnography, the current gold standard in objective sleep measurement [29]. Actigraphy data were analyzed using dedicated software from the manufacturer (ActionW, Version 2.7.2; Ambulatory Monitoring Inc., Ardsley, NY, USA) which uses the Cole-Kripke algorithm [30]. For the present analysis, only sleep efficiency and sleep duration were assessed as they encompass sleep onset latency and wake after sleep onset into their calculations, allowing for a more parsimonious, yet comprehensive evaluation of sleep.

Secondary Comorbid Symptom Measures

The Hospital Anxiety and Depression Scale (HADS) is a 14-item measure that was used to assess anxiety and depression symptoms in the past week. Established cutoffs are 0 to 7 (not significant), 8 to 10 (subclinical), and 11–21 (clinically significant) for anxiety and depression separately. The HADS has been used extensively in various cancer populations [31].

The Multidimensional Fatigue Inventory-Short Form (MFSI-SF) is a 30-item self-report measure and is comprised of five empirically derived subscales (general, emotional, physical, mental, vigor) and a total fatigue score. The measure does not have established cutoff scores; however, higher scores are reflective of greater levels of fatigue [32].

Data Examination

One participant was excluded from the analysis due to missing more than 50% of their data; all remaining participants were screened for potential outliers. Scores were winsorized for the 10 univariate outliers that exceeded the recommended cutoff *z*-score of 3.29 [33]. One participant was identified as a multivariate outlier (Mahalanobis distance exceeding the $\chi^2(9)$ critical of 37.70) [33], and their data was removed. An additional 6 participants were excluded because responses to the BRIEF-A were invalid. Skewness and kurtosis were evaluated by dividing estimates of skew and kurtosis by their respective standard errors [34]. Values in excess of 3.29 ($p < 0.001$) were considered to be skewed or kurtotic. Nine variables were considered to be significantly skewed. Non-linear transformations were used to create variables with normal distributions. Non-transformed variables were used in analyses to aid in interpretation given that the pattern of results was the same when using non-transformed variables or transformed variables.

Statistical Analyses

Presence of Perceived Deficits in Executive Function

Frequencies were tabulated to characterize the sample. Perceived executive functioning deficits were categorized into global executive functioning deficits, behavioral regulation

deficits, and metacognition deficits using the overarching summary score and the two summary index scores from the BRIEF-A. Perceived deficits in these areas were defined as scoring ≥ 1.5 SD *above* established cutoffs (i.e., *T* scores at or above 65).

Associations Between Perceived Deficits in Executive Function and Potential Confounding Factors

A hierarchical regression was used to examine associations between symptoms of insomnia, objective and subjective sleep duration and efficiency, sleep quality, fatigue, mood, and perceived deficits in executive function as measured by the Global Executive Composite score, after statistically adjusting for age and education. Zero-order and partial correlations were used to examine the relative importance of individual predictors. Statistical significance was set at $p < 0.05$ for all analyses. Practically significant results were defined as a partial $r \geq 0.2$ [35].

Results

Demographic and Clinical Characteristics

Three hundred and forty-three women with breast cancer were approached between January of 2017 and February of 2019. Of these women, 205 refused study participation and 38 were ineligible for an overall recruitment rate of 29%. The main reason for refusal was that they did not want to participate (77%). Full details of the recruitment are reported in a separate publication [36]. One-hundred participants completed a baseline assessment and data was analyzed for 92. On average, participants were 60.7 years of age (range 29 to 83), had 13.5 years of education (range 7 to 25), and were 56.3 days post-surgery. Only two participants (2%) had surgery following their assessment. Small and unequal samples prevent formal statistical testing; however, executive functioning scores were similar regardless of disease severity or time since surgery. Compared to the normative sample for the BRIEF-A, the current sample had a larger proportion of Caucasian individuals, but according to the professional manual, there is a non-meaningful effect of race/ethnicity on scores. In addition, while levels of post-secondary education were similar, a larger proportion of the current sample had not completed high school than the BRIEF-A normative sample. Of the sample, 22.8% reported sub-threshold insomnia and 15.2% reported moderate to severe insomnia. The majority of the sample were deemed poor sleepers as characterized by the PSQI (71.7%). Clinically significant symptoms of anxiety or depression were reported by 14.1% and 2% respectively (refer to Table 1 for demographics and clinical characteristics for the entire group as well as women with and without perceived executive functioning difficulties).

Presence and Factors Associated with Perceived Executive Functioning Difficulties

As shown in Table 2, perceived deficits in global executive functioning were reported by twelve women, corresponding to 13.0% of the sample. Thirteen participants (14.1%) reported behavioral regulation deficits and nine (9.8%) reported metacognition deficits. Despite age being adjusted for during the scoring of the BRIEF-A, those with global executive functioning deficits were older (67.33 ± 8.75) than those without global executive functioning deficits (59.17 ± 10.80). Participants with perceived global executive functioning deficits also reported greater fatigue (30.25 ± 16.39) and depressive symptoms (4.67 ± 3.42) than participants without perceived global executive functioning deficits (fatigue; 16.64 ± 14.41; depressive symptoms; 2.75 ± 2.88). The groups appeared similar on measures of anxiety, sleep quality, insomnia, subjective or objective TST, or SE scores.

There was no significant effect of age and education on perceived deficits in global executive function in STEP1 of the hierarchical regression model (F (2, 89) = 1.28, $p = 0.284$), accounting for 2.8% of variance (Table 3). After adjusting for age and education, sleep, fatigue, and psychological predictors accounted for 31.8% of unique variance in perceived deficits in global executive functioning in STEP2 of the hierarchical regression model (F (11, 80) = 3.84, $p < 0.001$) (Table 3). Zero-order correlations indicated significant bivariate associations between perceived deficits in global executive functioning and insomnia severity ($r = 0.301$), sleep quality ($r = 0.214$), fatigue ($r = 0.477$), depressed mood ($r = 0.320$), and anxious mood ($r = 0.339$), demonstrating that as these symptoms increased, so did the perception of deficits in executive functioning. After partitioning out variability from other independent variables, fatigue ($b = 0.356$, SE = 0.101, $p = < 0.001$, $r_{partial} = 0.365$), perceived sleep quality ($b = -1.028$, SE = 0.466, $p = 0.030$, $r_{partial} = -0.239$), and symptoms of insomnia ($b = 0.717$, SE = 0.264, $p = 0.008$, $r_{partial} = 0.291$) remained significantly associated with perceived executive functioning accounting for 13.3%, 5.7%, and 8.5% of unique variance, respectively. Objective and subjective sleep duration and efficiency were not significantly or practically associated with perceived deficits in executive function ($p > 0.05$, $r_{partial} < 0.2$).

Considering the strength of the association between fatigue and perceived deficits in executive function, an exploratory hierarchical regression was performed to follow up on associations between perceived deficits and the specific dimensions of fatigue. General and physical fatigue were removed from the analysis due to multicollinearity.

Table 1 Demographic and clinical characteristics

		Total sample ($N = 92$) N (%)	**Global executive function deficits** ($n = 12$) N (%)	**No global executive function deficits** ($n = 80$) N (%)
Age at enrollment (mean ± SD; years)		60.70 ± 10.82 (range = 29–83)	67.33 ± 8.75 (range = 50–80)	59.70 ± 10.80 (range = 29–83)
Marital status	Married/in a committed relationship	64 (69.6%)	8 (66.7%)	56 (70.0%)
	Divorced	7 (7.6%)	1 (8.3%)	6 (7.5%)
	Single	8 (8.7%)	0 (0.0%)	8 (10.0%)
	Widowed	12 (13.0%)	3 (25.0%)	9 (11.3%)
	Other	1 (1.1%)	0 (0.0%)	1 (1.3%)
Number of children	None	7 (7.6%)	0 (0.0%)	7 (8.8%)
	One to two	46 (50.0%)	6 (50.0%)	40 (50.0%)
	Three or more	39 (42.4%)	6 (50.0%)	33 (41.3%)
Race	White/Caucasian	88 (95.7%)	12 (100.0%)	76 (95.0%)
	Other	4 (4.3%)	0 (0.0%)	4 (5.0%)
Education (mean ± SD; years)		13.48 ± 3.67 (range = 7–25)	12.25 ± 3.60 (range = 8–19)	13.67 ± 3.67 (range = 7–25)
	Some high school (≤ 11 years)	33 (35.9%)	7 (58.3%)	26 (32.5%)
	High school (12 years)	13 (14.1%)	2 (16.7%)	11 (13.8%)
	College (13–15)	21 (22.8%)	1 (8.3%)	20 (25.0%)
	Post-secondary (≥ 16)	25 (27.2%)	2 (16.7%)	23 (28.7%)
Currently employed	Yes	34 (37.0%)	2 (16.7%)	32 (40.0%)
	No	58 (63.0%)	10 (83.3%)	48 (60.0%)
Pre-menopausal	Yes	22 (23.9%)	0 (0.0%)	22 (27.5%)
	No	68 (73.9%)	12 (100.0%)	56 (70.0%)
	Unsure	2 (2.2%)	0 (0.0%)	2 (2.5%)
Surgery	Lumpectomy	37 (40.2%)	5 (41.7%)	32 (40.0%)
	Simple mastectomy	47 (48.9%)	7 (58.3%)	40 (50.0%)
	Modified radical mastectomy	8 (8.7%)	12 (100.0%)	8 (10.0%)
	Sentinel node biopsy	72 (78.3%)	9 (75.0%)	63 (78.8%)
	Axillary lymph node dissection	12 (13.0%)	1 (8.3%)	11 (13.8%)
Time since surgery (mean ± SD; days)		56.25 ± 26.53 (range = − 120 to 118)	49.33 ± 19.61 (range = − 2 to 71)	57.29 ± 27.36 (range = − 120 to 118)
	No surgery before enrollment	2 (2.2%)	1 (8.3%)	1 (1.3%)
	Less than 1 month before enrollment	4 (4.3%)	1 (8.3%)	3 (3.8%)
	Less than 2 months	53 (57.6%)	8 (66.7%)	45 (56.3%)
	Less than 3 months	28 (30.4%)	2 (16.7%)	26 (32.5%)
	Less than 4 months	5 (5.4%)	0 (0.0%)	5 (6.3%)
T stage	T1	63 (68.5%)	8 (66.7%)	55 (68.8%)
	T2	23 (25.0%)	3 (25.0%)	20 (25.0%)
	T3	5 (5.4%)	1 (8.3%)	4 (5.0%)
	T4	1 (1.1%)	0 (0.0%)	1 (1.3%)
Estrogen receptor positive	Yes	92 (100.0%)	12 (100.0%)	80 (100.0%)
	No	0 (0.0%)	0 (0.0%)	0 (0.0%)
Progesterone receptor positive	Yes	85 (92.4%)	10 (83.3%)	75 (93.8%)
	No	7 (7.6%)	2 (16.7%)	5 (6.3%)
HER-2 positive	Yes	4 (4.3%)	0 (0.0%)	4 (5.0%)
	No	88 (95.7%)	12 (100.0%)	76 (95.0%)
Anxiety (mean ± SD)		5.73 ± 4.02 (range = 0–16)	7.83 ± 4.97 (range = 1–16)	5.41 ± 3.79 (range = 0–15)

Table 1 (continued)

		Total sample ($N=92$) N (%)	**Global executive function deficits** ($n=12$) N (%)	**No global executive function deficits** ($n=80$) N (%)
	Non-significant anxiety	67 (72.8%)	7 (58.3%)	60 (75.0%)
	Sub-threshold anxiety	12 (13.0%)	1 (8.3%)	11 (13.8%)
	Clinically significant anxiety	13 (14.1%)	4 (33.3%)	9 (11.3%)
Depression (mean ± SD)		3.00 ± 3.00 (range = 0–12)	4.67 ± 3.42 (range = 0–12)	2.75 ± 2.88 (range = 0–11)
	Non-significant depression	81 (88.0%)	10 (83.3%)	71 (88.8%)
	Sub-threshold depression	9 (9.8%)	1 (8.3%)	8 (10.0%)
	Clinically significant depression	2 (2.2%)	1 (8.3%)	1 (1.3%)
Fatigue (mean ± SD)		18.41 ± 15.29 (range = 0–66)	30.25 ± 16.39 (range = 7–66)	16.63 ± 14.41 (range = 0–57)
Insomnia (mean ± SD)		6.70 ± 5.80 (range = 0–22)	8.33 ± 5.80 (range = 1–22)	6.45 ± 5.80 (range = 0–22)
	No insomnia	57 (62.0%)	5 (41/7%)	52 (65.0%
	Sub-threshold insomnia	21 (22.8%)	6 (50.0%)	15 (18.8%)
	Moderate insomnia	12 (13.0%)	0 (0.0%)	12 (15.0%)
	Severe insomnia	2 (2.2%)	1 (8.3%)	1 (1.3%)
Sleep quality (mean ± SD)		7.09 ± 3.86 (range = 1–19)	7.42 ± 3.75 (range = 1–15)	7.04 ± 3.90 (range = 1–19)
	Good sleepers	26 (28.3%)	3 (25.0%)	23 (28.7%)
	Poor sleepers	66 (71.7%)	9 (75.0%)	57 (71.3%)
Sleep duration (mean ± SD)	Objective/Mins	397.14 ± 84.53 (range = 190–593)	439.71 ± 82.10 (range = 312–593)	390.75 ± 83.51 (range = 190–592)
	Subjective/Mins	410.19 ± 85.96 (range = 164–649)	416.58 ± 111.13 (range = 186–649)	409.23 ± 82.37 (range = 164–594)
Sleep efficiency (mean ± SD)	Objective	78.86 ± 10.91 (range = 49–97)	82.25 ± 10.86 (range = 65–97)	78.35 ± 10.89 (range = 49–96)
	Subjective	80.34 ± 11.78 (range = 44–98)	77.33 ± 12.81 (range = 44–93)	80.79 ± 11.64 (range = 46–98)

HER-2 human epidermal growth factor receptor-2

After adjusting for age and education, the remaining dimensions of fatigue accounted for 22.3% of unique variance in perceived executive functioning (F (7, 84) = 5.754, $p < 0.001$) (Table 4). Zero-order correlations revealed significant bivariate associations between perceived deficits in executive functioning and emotional fatigue ($r = 0.423$), mental fatigue ($r = 0.381$), and vigor ($r = -0.307$). After partitioning out variability from other independent variables, only emotional fatigue ($b = 0.702$, SE = 0.316, $p = 0.029$, $r_{partial} = 0.233$) remained significantly and practically associated with perceived executive functioning, accounting for 5.4% of unique variance.

Table 2 Presence of perceived executive functioning deficits as measured by the BRIEF-A (participants were considered to have perceived executive functioning deficits if they received scores ≥ 1.5 standard deviations above established cutoffs)

		(*N* = 92) N (%)
Global Executive Composite	Global executive functioning deficits	12 (13.0%)
	No global executive functioning deficits	80 (87.0%)
Behavioral Regulation Index	Behavioral regulation deficits	13 (14.1%)
	No behavioral regulation deficits	79 (85.9%)
Metacognition Index	Metacognition deficits	9 (9.8%)
	No metacognition deficits	83 (90.2%)

BRIEF-A Behaviour Rating Inventory of Executive Function-Adult

Table 3 Hierarchical regression examining associations between the Global Executive Composite score and comorbid symptoms

Predictor	*b*	SE *b*	*t*	*p*	R^2	R^2 change	Zero-order correlation	Partial correlation
Step 1					.028			
Age	0.018	0.102	0.175	.861			.078	.019
Education	−0.427	0.302	1.415	.160			−.166	−.148
Step 2					**.345**[b]	**.318**[b]		
Insomnia	0.717	.264	**2.719**[a]	**.008**			**.301**[a]	**.291**[a]
Sleep quality	−1.028	.466	**2.205**	**.030**			**.214**[a]	**−.239**[a]
Sleep duration (objective)	0.022	.018	1.244	217			.118	.138
Sleep duration (subjective)	−0.008	.021	0.373	.710			−.071	−.042
Sleep efficiency (objective)	0.000	.141	0.003	.998			−.010	.000
Sleep efficiency (subjective)	0.022	.153	0.143	.887			−.202	.016
Fatigue	0.356	.101	**3.511**[b]	**< .001**			**.477**[b]	**.365**[b]
Depression	−0.084	.506	0.166	.868			**.320**[a]	−.019
Anxiety	0.033	.343	0.096	.924			**.339**[b]	.011

Bold indicates statistical significance

[a] $p < .05$

[b] $p < .001$

Discussion

This study is one of the first to investigate the perception of executive functioning deficits before systemic treatment and radiation among women with breast cancer, and possible associations with sleep quality, insomnia, mood, and fatigue. Prior to initiating other treatments, 13.0% of the sample reported global deficits in executive functioning, 14.1% reported behavioral regulation deficits, and 9.8% reported metacognition deficits. Recent evidence suggests that assessing perception of cognitive and executive function prior to initiating systemic therapy has clinical utility. In a 2-year longitudinal study of 397 women with non-metastatic breast cancer, those who reported poor pre-treatment cognitive function had a clinically meaningful decline in global wellbeing even 24 months later [37]. Pre-adjuvant therapy cognition has also been associated with features of tumor aggressiveness including stage of disease, HER2 positivity, and tumor size [38]. Including routine assessment of cognitive function in cancer care may help to identify those women who may be at risk of poorer cancer recovery.

Given that this is the first time the BRIEF-A has been used to assess perceived deficits in executive function in women with breast cancer, it is not possible to compare our results to other published research using this measure. However, there is evidence that patients diagnosed with other cancer types also report what has been referred to as "neurobehavioral problems." These neurobehavioral problems have been described as both apathy (e.g., loss of initiation and loss of spontaneity) and disinhibition (e.g., impulsivity,

Table 4 Hierarchical regression examining associations between Global Executive Composite score and fatigue

Predictor	*b*	SE *b*	*t*	*p*	R^2	R^2 change	Zero-order correlation	Partial correlation
Step 1					.028			
Age	0.018	0.102	0.175	.861			.078	.019
Education	−0.427	0.302	1.415	.160			−.166	−.148
Step 2					**.251**[b]	**.223**[b]		
General fatigue	-	-	-	-			-	-
Physical fatigue	-	-	-	-			-	-
Emotional fatigue	0.702	0.316	2.218	**.029**			**.423**[b]	**.233**[a]
Mental fatigue	0.419	0.283	1.483	.142			**.381**[b]	.158
Vigor	−0.150	0.245	0.611	.543			**−.307**[b]	−.066

Bold indicates statistical significance

[a] $p < .05$

[b] $p < .01$

irritability, and impaired social judgment), which overlap with mood symptoms [39]. In a recent study that used the BRIEF-A to compare a sample of healthy adults to cohorts of non-cancer patients with neurological and neuropsychiatric disorders, 7.8% of the healthy control group reported symptoms that were 1.5 SD above the mean of 50 on the global executive composite [40]. These authors suggest that the BRIEF-A might not be a pure measure of everyday executive functioning, but rather also reflect general psychological adjustment. Considering that our estimates of perceived executive functioning deficits are only slightly higher that what may be observed in healthy populations, more research utilizing matched non-cancer control groups is needed to understand the relationship of these perceived deficits to actual impairments in daily life.

Severity of fatigue symptoms had the strongest relationship with perceived executive functioning, after partitioning out variability from other variables. Fatigue is one of the most common symptoms experienced by cancer patients, can present prior to diagnosis and treatment [41, 42], and tends not to be improved by adequate sleep or rest [18]. Emotional fatigue (e.g., I feel upset) had the strongest associations with perceived executive functioning deficits. Considering that measures of depression and anxiety were not directly associated with perceived deficits in executive function, this suggests that emotional distress may contribute to the perception of fatigue severity, which then influences how one feels about their executive function. Fatigue is associated with reduced quality of life and has a profound impact on everyday functioning, with depression, pain, and a decline in both physical and cognitive functioning implicated in patients affected [43, 44]. A recent prospective longitudinal study assessing 75 women with breast cancer over 2 years demonstrated that fatigue severity was significantly associated with compromised attention and lower processing speed throughout the entire 2-year period, including prior to treatment commencement [45]. A 2015 cross-sectional study of 204 women with breast cancer demonstrated that after controlling for chemotherapy, age, and education, fatigue, in addition to hyperarousal symptoms, accounted for the largest proportion of variance in perceived executive functioning [46]. The relationship between fatigue and perceived executive functioning may be explained by their shared underlying mechanisms (e.g., cellular inflammation). The identification of fatigue, specifically emotional fatigue, as a factor associated with perceived executive functioning deficits may help researchers and clinicians develop more targeted and effective interventions.

Insomnia symptoms and poor sleep quality, but not sleep duration or efficiency, were also significantly associated with perceived executive functioning deficits. Insomnia is a dissatisfaction with one's sleep characterized by difficulty falling or staying asleep despite adequate opportunity. A large majority of the sample (71.7%) were characterized as poor sleepers and over a third reported sub-threshold or moderate to severe insomnia. Research in breast cancer populations has demonstrated an association between insomnia symptoms and severity of reported cognitive impairment [47]. In non-cancer patients with insomnia, those with short sleep duration (defined as total polysomnographic sleep time < 6.5 h and sleep efficiency < 85%) demonstrate worse objectively measured executive function compared to those with insomnia and normal sleep duration and healthy sleepers [48]. Both insomnia groups, regardless of sleep duration, reported worse cognitive problems and mood disturbance than healthy sleepers. The lower presence of anxiety (14.1%) and depressive (2.2%) symptoms in our sample might have limited our ability to be able to detect smaller magnitude associations between mood disturbance, sleep, and perceived executive functioning. Studies with larger samples are needed to better understand the relative influence of these contributing factors.

Strengths

This study is characterized by several strengths, including the use of a valid and reliable measure of perceived executive functioning in combination with objective and subjective sleep outcomes and measures of fatigue and mood that are empirically supported and frequently utilized in breast cancer populations. Together, the utilization of the measures in this study will facilitate comparison to future studies, which will allow for an enriched discussion of perceived executive functioning and associated factors in women with breast cancer. This study also controlled for confounding factors that can impact the assessment of cognitive functioning, including age, education, depression, fatigue, insomnia, and sleep disturbance.

Limitations

The results of this study must also be interpreted with limitations in mind. First, the percentage of women who consented to the study was lower than desirable. Recruiting women with breast cancer for non-clinical trials around the time of their diagnosis is challenging and women with high distress burden may not have been as willing to participate in the research. Further, the treating oncologists identified women to approach for the study. This method of recruitment may have introduced unintentional selection bias. Further, we were not able to collect clinical or demographic information from women who did not consent to participate in the study to assess this hypothesis. This means that individuals who opted to participate may differ systematically from the larger breast cancer population. This may have contributed to difficulty assessing

the associations between mood disturbance and perceived executive dysfunction. Second, the cross-sectional design does not allow for the inference of causality or the ability to determine the direction of the observed associations. Third, racial and ethnic minorities were under-represented, which may impact the generalizability of our findings to the larger population of women with breast cancer. Fourth, the populations norms for the BRIEF-A consist of both women and men, which does not allow us to isolate the potential influence of gender on scores. Finally, results from regression analyses may be impacted by common method variance. This may influence the strength of associations relying on self-report and reflect a patient's propensity to respond in a certain manner.

Conclusion

The present study suggests that fatigue, insomnia symptoms, and poor sleep quality significantly contribute to a perception of executive dysfunction, above that of objective and subjective sleep disruption and mood disturbance. As such, interventions designed to improve fatigue and/or sleep may represent meaningful, first-line treatment targets in women with breast cancer and perceived executive dysfunction, prior to commencing cancer treatment.

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Declarations

Ethics Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to Participate Informed consent was obtained from all individual participants included in the study.

Conflict of Interest The authors declare no competing interests.

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