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Changes in Attentional Function in Patients From Prior to Through 12 Months After Breast Cancer Surgery

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Abstract

Context.—While ~75% of breast cancer patients report changes in attentional function, little is known about how demographic, clinical, symptom, and psychosocial adjustment (e.g., coping) characteristics influence changes in the trajectories of attentional function over time.

Objectives.—This study evaluated inter-individual variability in the trajectories of self-reported attentional function and determined which demographic, clinical, symptom, and psychosocial adjustment characteristics were associated with initial levels and with changes in attentional function from prior to through 12 months after breast cancer surgery.

Methods.—Prior to surgery, 396 women were enrolled. Attentional Function Index (AFI) was completed prior to and nine times within the first 12 months after surgery. Hierarchical linear modeling (HLM) was used to determine which characteristics were associated with initial levels and trajectories of attentional function.

Results.—Given an estimated preoperative AFI score of 6.53, for each additional month, the estimated linear rate of change in AFI score was an increase of 0.054 ($p<0.001$). Higher levels of comorbidity, receipt of adjuvant chemotherapy, higher levels of trait anxiety, fatigue, and sleep disturbance, and lower levels of energy and less sense of control were associated with lower levels

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of attentional function prior to surgery. Patients who had less improvements in attentional function over time were Non-white, did not have a lymph node biopsy, had received hormonal therapy, and had less difficulty coping with their disease.

Conclusions.—Findings can be used to identify breast cancer patients at higher risk for impaired self-reported cognitive function and to guide the prescription of more personalized interventions.

Keywords

cancer-related cognitive impairment; attentional function, breast cancer, anxiety; fatigue; sleep disturbance; coping

INTRODUCTION

Cognition is a fundamental aspect of one's ability to engage in activities and accomplish goals. Cognition involves different inter-related functions, including attention, memory, comprehension, problem solving, verbal fluency, and decision-making.[1] Directed attention is connected to working memory and requires mental effort to actively inhibit irrelevant distractions for goal-directed tasks. Attentional function, supported by directed attention, may be among the most essential functions for cancer patients because it helps them acquire important information, make decisions, and carry out self-care-activities.[2] Impairments in attentional function may interfere with patients' self-care activities, such as their ability to adhere to treatment, manage side effects, and re-integrate into the workforce, which has a negative impact on their quality of life (QOL).[3,4]

Approximately 75% of breast cancer patients experience cancer-related cognitive impairment (CRCI) prior to, during, or after treatment.[5] In addition, CRCI remains a significant long-term problem for about 35% of survivors.[6-11] Determining the underlying mechanisms and risk factors for, as well as effective interventions for CRCI has been challenging. Findings from objective neuropsychological tests correlate poorly with self-report measures of CRCI,[2,12-16] and often do not detect deficits, even when patients have subjective complaints about difficulties with routine activities (e.g., problems with driving, inability to return to work).[13,17] Therefore, self-report measures are an essential component of the assessment of CRCI because they are better able to capture patients' experiences.[18,19]

Initially, CRCI was hypothesized to occur only with the administration of chemotherapy (CTX; i.e., "chemobrain"). However, accumulating evidence suggests that the etiology of CRCI in breast cancer patients is multi-factorial (e.g., the cancer itself,[8] neurotoxic effects of CTX;[20-26] chemically or surgically-induced menopause and the effects of hormone treatments on estrogen levels;[4,27-29] systemic immune responses induced by localized radiation therapy and subsequent elevation in plasma interleukin (IL)-6 levels;[30,31] delirium and stress associated with anesthesia and sugery;[32] chronic inflammation, dysregulation of cytokines, and premature aging due to telomere shortening induced by the cancer itself[7,32,33]) Because most of these data come from studies that evaluated CRCI following surgery,[33] additional research is warranted that addresses the occurrence of and risk factors for CRCI prior to and following breast cancer surgery.

A number of demographic and clinical characteristics, co-occurring symptoms, and psychosocial adjustment characteristics are associated with an increased risk for more severe CRCI. For example, while older breast cancer patients are presumed to be at a higher risk for CRCI because of age-related changes in cognition and the use of different coping mechanisms,[2] in some studies,[23,33-35] younger patients were at increased risk for CRCI during the survivorship period. Co-occurring symptoms, such as anxiety,[9,36,37] depressive symptoms,[6,36,37] fatigue,[6,8,9,37,38] neuropathy,[39] and sleep disturbance,[6,37,38] have been associated with CRCI both prior to and after breast cancer surgery.[13] In addition, in studies that evaluated patients prior to breast cancer surgery,[2,6,40] while CRCI was not associated with treatment modality, it was associated with pre-treatment levels of co-occurring symptoms. Of note, findings from recent studies suggest that associations between CRCI and anxiety and depressive symptoms may be related to challenges with emotional regulation, coping (e.g., avoidance), and psychosocial adjustment to breast cancer.[41-44] However, because of the observational nature of these studies, the relatively small sample sizes, and the lack of a comprehensive assessment of risk factors, these findings warrant replication to obtain a more comprehensive understanding of the risk factors associated with CRCI prior to and following breast cancer surgery.

In several longitudinal studies that evaluated for CRCI in women with breast cancer[6,8,9,11,36,45] findings suggest that cognitive function returns to presurgical levels at approximately 12 months. However, direct comparisons across studies are difficult because of the different aspects of CRCI that were evaluated (e.g., memory, verbal fluency); differences in the use of subjective versus objective measures; and differences in the number and timing of the assessments. In the one study that evaluated for inter-individual differences in CRCI trajectories,[6] the patients’ cancer diagnosis and/or co-occurring symptoms were associated with CRCI at each measurement point, from prior to through 24 months post-surgery. Of note, two recent reviews highlighted the paucity of research in this area and recommended that longitudinal studies examine the associations between CRCI and common co-occurring symptoms.[36,42]

Taken together these findings suggest that breast cancer patients are at relatively high risk for CRCI and that additional research is warranted on inter-individual differences in risk factors for this significant clinical problem. Given that no study has evaluated a comprehensive list of potential risk factors for CRCI from prior to through recovery after surgery, the purposes of this study, in a sample of patients who were assessed from prior to through 12 months after surgery (n=396), were to evaluate for inter-individual variability in the trajectories of self-reported attentional function and to determine which demographic, clinical, symptom and psychosocial adjustment characteristics were associated with initial levels and with changes in the trajectories of attentional function.

METHODS

Patients and settings

This descriptive, longitudinal study is part of a larger study that evaluated neuropathic pain and lymphedema in women who underwent breast cancer surgery whose methods were described in detail elsewhere.[47-49] In brief, patients were recruited from Breast Care Centers located in a Comprehensive Cancer Center, two public hospitals, and four community practices in Northern California. Patients were eligible to participate if they: were adult women (≥18 years) scheduled to have breast cancer surgery on one breast; were able to read, write, and understand English; agreed to participate; and gave written informed consent. Patients were excluded if they were having breast cancer surgery on both breasts and/or had distant metastasis at the time of diagnosis. A total of 516 patients were approached and 410 enrolled in the study (response rate 79.5%). For the current analysis, complete data from 396 women were available.

Instruments

Demographic and clinical characteristics—Patients completed a demographic questionnaire, the Karnofsky Performance Status (KPS) scale,[50] and the Self-Administered Comorbidity Questionnaire (SCQ).[51]

Attentional Function—The 16-item Attentional Function Index (AFI) is a commonly used self-report measure of attentional function.[18] Each item was rated on a 0 to 10 numeric rating scale (NRS). A higher mean score indicates greater capacity to direct attention.[18,52] AFI scores can be grouped into categories (i.e., <5.0 low attentional function, 5.0 to 7.5 moderate function, and >7.5 high function).[2] AFI has well established validity and reliability.[52,53] Its Cronbach's alpha was .95 in this study.

Symptom Measures—Spielberger State-Trait Anxiety Inventories (STAI-T, STAI-S) consist of 20 items that are rated from 1 to 4. Scores for each scale are summed and can range from 20 to 80. A higher score indicates greater anxiety. Cut-off scores of ≥31.8 and ≥32.2 indicate high levels of trait and state anxiety, respectively.[54] STAI-S and STAI-T inventories have well-established validity and reliability.[55,56] Cronbach's alphas for STAI-T and STAI-S were .88 and .95, respectively.

Center for Epidemiological Studies Depression Scale (CES-D) consists of 20 items assessing major symptoms of depression. Scores can range from 0 to 60, with scores of ≥16 indicating the need for clinical evaluation of major depression. The CES-D has well-established validity and reliability.[57-59] Its Cronbach's alpha was .90 in this study.

The 18-item Lee Fatigue Scale (LFS) assesses physical fatigue and energy.[60] Each item was rated on a 0 to 10 NRS. Total fatigue and energy scores were calculated as the mean of 13 fatigue items and 5 energy items. Higher scores indicate greater fatigue severity and higher levels of energy. Patients were asked to rate each item based on how they felt *"right now."* A cut-off score >4.4 indicates high levels of fatigue. A cut-off score ≤4.8 indicates low levels of energy.[61] LFS has well established validity and reliability. Cronbach's alphas for the fatigue and energy scales were .96 and .93, respectively.

The 21-item General Sleep Disturbance Scale (GSDS) assesses sleep quality in the past week. Each item was rated on a 0 (never) to 7 (everyday) NRS. The GSDS total score is the sum of 21 items, that ranges from 0 (no disturbance) to 147 (extreme sleep disturbance). A GSDS total score of ≥43 indicates a significant level of sleep disturbance.[62] The GSDS has well-established validity and reliability. Its Cronbach's alpha was .86 in this study.

The occurrence of breast pain prior to surgery was assessed with the question *"Are you experiencing pain in your affected breast?"* Patients who responded *"yes"*, rated the severity of their average and worst pain using a 0 (no pain) to 10 (worst imaginable pain) NRS. Patients were asked how many days per week and how many hours per day they experienced pain that interfered with function.

Psychosocial Adjustment Characteristics—Quality of Life Scale-Patient Version (QOL-PV) is a 41-item instrument that assesses four dimensions of QOL in cancer patients (i.e., physical, psychological, spiritual, social well-being), and a total QOL score. Each item was rated on a 0 to 10 NRS with higher scores indicating a better QOL. The QOL-PV has well established validity and reliability.[63,64] Cronbach's alpha for the QOL-PV total score was .86 in this study. Coefficients for the physical, psychological, spiritual and social well-being subscales were .70, .79, .75, and .61, respectively.

Individual items from the QOL-PV were used to assess psychosocial adjustment characteristics (i.e., distress, fear, coping, control). Patients were asked to rate their level of distress regarding their cancer diagnosis, fear of future diagnostic tests, fear of metastasis, level of control they felt over their lives, and difficulties coping as a result of cancer and its treatment. Each of these 5 items was rated using a 0 to 10 NRS with higher scores indicating a more positive appraisal of a particular characteristic. These specific items, that were used in our previous studies,[65,66] were chosen for evaluation based on literature reviews of psychosocial adjustment and attentional function in women with breast cancer.[44,67]

Study procedures

The Committee on Human Research at the University of California, San Francisco and the Institutional Review Board at each of the study sites approved the study protocol. During the patients' preoperative visit, a clinical staff member explained the study and introduced the patient to the research nurse, who determined eligibility and obtained written informed consent prior to surgery. Patients completed the enrollment questionnaires on average four days prior to surgery and follow-up questionnnaires at 1, 2, 3, 4, 5, 6, 8, 10, and 12 months after surgery. The research nurse met with participants in the Clinical Research Center or in their home. Medical records were reviewed for disease and treatment information.

Statistical analyses

Descriptive statistics and frequency distributions were generated on the sample characteristics, symptom severity scores, and psychosocial adjustment items using SPSS version 23.[68] AFI was assessed prior to surgery and at 1, 2, 3, 4, 5, 6, 8, 10, and 12 months after surgery. All other demographic, clinical, symptom and psychosocial adjustment characteristics that were evaluated as predictors in the hierarchical linear modeling (HLM) analysis were assessed prior to surgery.

HLM based on full maximum likelihood estimation was done using the software developed by Raudenbush and colleagues.[69,70] This analysis is discussed in detail in our previous publications.[61,71,72] In brief, during stage 1, intra-individual variability in AFI scores over time was examined. At this point, the model was constrained to be unconditional (i.e., no predictors) and likelihood ratio tests were used to determine the best fitting model.

The second stage of the HLM analysis examined inter-individual differences in the trajectories of AFI scores by modeling the individual change parameters (i.e., intercept, linear slope) as a function of proposed predictors at level 2. Table 1 presents a list of the proposed predictors that was developed based on a literature review about CRCI in breast cancer patients.[6,16,40,44,67,73,74] To improve estimation efficiency and construct a parsimonious model, an exploratory level 2 analysis was completed in which each potential predictor was assessed to determine whether it would result in a better model if it alone were added as a level 2 predictor. Predictors with a t-value of < 2.0 were dropped from subsequent model testing. All potential significant predictors from the exploratory analyses were entered into the model to predict each individual change parameter. Only predictors that maintained a statistically significant contribution in conjunction with other variables were retained in the final model. A p-value of <.05 indicated statistical significance.

RESULTS

Patient Characteristics

The demographic, clinical, symptom, and psychosocial adjustment characteristics for the patients (n=396) are summarized in Table 2. On average, patients were 55 years of age, well-educated, and underwent breast conserving surgery (80.3%). Most patients self-identified as White (64.9%), were post-menopausal (64.9%), and were unemployed (52.3%).

Individual and mean change in attentional function

The first stage of HLM analysis examined how attentional function changed from prior to through 12 months after surgery. Table 3 presents the estimates of the unconditional, linear model. Because the model had no covariates, the intercept represents the estimated level of attentional function (i.e., 6.543 on a 0 to 10 scale) at the preoperative assessment. The estimated linear rate of change in attentional function, for each additional month, was .054 ($p<.001$). Figure 1A displays the trajectory for attentional function from the preoperative assessment through 12 months after surgery. Attentional function increased slightly over the course of 12 months. The mean attentional function scores for the various groups depicted in all of the figures are estimated or predicted means based on the HLM analysis.

Inter-individual differences in the trajectories of attentional function

The second stage of the HLM analysis evaluated how attentional function at the preoperative assessment and its change over time were associated with specific demographic, clinical, symptom, and psychosocial adjustment characteristics. As shown in the final model in Table 3, the characteristics that were associated with inter-individual differences in preoperative levels of attentional function were: level of comorbidity; receipt of adjuvant CTX; severity of trait anxiety, fatigue, energy, and sleep disturbance; and perception of control over things in one’s life. The characteristics that were associated with inter-individual differences in the linear slope for attentional function were ethnicity, having had a sentinel lymph node biopsy

(SLNB), receipt of hormonal therapy, level of attentional function prior to surgery, and difficulty coping with cancer and its treatment.

To illustrate the effects of each of these characteristics on patients' initial levels and trajectories of attentional function, Figures 1B and 1C display the adjusted change curves for attentional function that were estimated based on differences in level of comorbidity (i.e., lower/higher level of comorbidity calculated based on one standard deviation [SD] below and above the mean SCQ score) and receipt of adjuvant CTX (i.e., yes/no), respectively. Figures 2A through 2E display the adjusted change curves for attentional function that were estimated based on differences in trait anxiety, fatigue, energy, sleep disturbance and sense of control (i.e., higher/lower levels of each characteristic calculated based on one SD above and below the mean scores), respectively. Figures 3A through 3E display the adjusted change curves for attentional function that were estimated based on differences in ethnicity (White/Non-white), underwent SLNB (yes/no), receipt of hormonal therapy (yes/no), AFI score at enrollment, and difficulty coping with cancer and its treatments.

In summary, patients with lower levels of self-reported attentional function prior to surgery had a higher level of comorbidity; were scheduled to receive adjuvant CTX; had higher levels of trait anxiety, fatigue, and sleep disturbance and lower levels of energy; and reported less control over things in their life. In addition, patients with less improvement in AFI scores over time were more likely to be non-White, to have not had a SLNB, to have been prescribed hormonal therapy following surgery, and to have reported less difficulty coping as a result of their cancer and its treatments prior to surgery.

DISCUSSION

This study is the first to use HLM to examine inter-individual differences in the trajectories of attentional function and to evaluate whether a comprehensive list of demographic, clinical, symptom, and psychosocial adjustment characteristics were associated with AFI scores prior to surgery and over a period of 12 months. Prior to surgery, our patients had a mean AFI score of 6.5 which suggests that these women had some pre-existing impairments in attentional function. Our finding is consistent with a study by Cimprich and collegues (i.e., preoperative AFI score of 6.6)[2] but lower than the AFI score reported by Chen and colleagues (preoperative AFI score of 8.2).[6] While our sample's overall AFI score improved over the twelve months following surgery, at the end of one year, it remained in the moderate range (i.e., estimated at 7.18). However, as seen in Figure 3D, and consistent with a previous report,[75] patients in our study with lower preoperative AFI scores demonstrated greater improvements in attentional function in the 12 months following surgery. The minimal increase in AFI scores in our sample may be associated with inter-individual variability in the relatively large number of characteristics associated with decrements in attentional function that were identified in this study.

Consistent with previous reports,[9,36] no differences in preoperative AFI scores were found between our White and non-White patients. However, over the 12 months of the study, compared to the White patients, non-White patients had less improvements in their AFI scores over time. This association may be related to a number of factors including level of education,[76,77] employment status and ability to return to work,[78] and/or financial burden and high out-of-pocket costs associated with cancer and its treatments.[79] Our findings suggest that breast cancer patients from diverse ethnic backgrounds may need additional support and resources to improve their level of attentional function.

In terms of clinical characteristics and consistent with previous reports,[80-82] a higher level of comorbitiy was associated with lower preoperative AFI scores. In addition, while having an axillary lymph node dissection was not associated with changes in attentional function, patients who did not have a SLNB (i.e., 17.4% of the sample) reported worse AFI scores over time. This finding is most likely related to the fact that women who did not have a SLNB were most likely to be diagnosed with more advanced stage disease and had received neoadjuvant CTX and/or a mastectomy with an axillary lymph node dissection.

While receipt of neoadjuvant CTX was identified as a potential predictor in the exploratory analyses, it was not included in the final model. However, consistent with previous reports,[23,36,75,83] receipt of adjuvant CTX was associated with lower AFI scores. In addition, patients who received hormonal treatment had a decline in attentional function over the 12 months of the study. The molecular mechanisms associated with CTX- and hormonally-induced changes in cognitive function are extremely complex and include: disruption of the blood-brain-barrier; deoxyribonucleic acid (DNA) damage and associated deficits in DNA repair mechanisms; telomere shortening; oxidative stress and associated inflammatory responses; polymorphisms in genes associated with neural repair; alterations in neural transmission; as well as changes in levels of sex steroid hormones that under physiologic conditions are neuroprotective and reduce oxidative stress (for reviews see 84-86). Additional research is warranted that examines associations between changes in attentional function and each of these molecular mechanisms. These types of investigations may identify potential therapeutic targets.

This study is the first to evaluate for associations between a comprehensive list of common co-occurring symptoms and changes in attentional function. Of note, in the exploratory analysis, all of the symptoms evaluated (i.e., trait anxiety, state anxiety, depression, fatigue, decrements in energy, sleep disturbance, pain, hot flashes) were associated with initial levels and/or the trajectories of attentional function. However, only trait anxiety, fatigue, decrements in energy, and sleep disturbance were retained in the final model. Consistent with previous studies,[6,8,36,87] higher levels of fatigue and lower levels of energy were associated with poorer attentional function at enrollment that persisted over the 12 months of the study. The association among these three symptoms may be related to a number of shared pathophysiologic mechanisms including: increases in inflammatory responses,[88], as well as the deleterious effects of cancer[87,89] and its treatments[8,9,87] on DNA repair mechanisms and neural transmission.

Consistent with previous studies,[2,6, 16,38,73,90] higher levels of sleep disturbance were associated with lower AFI scores. At enrollment, our patients reported relatively high levels of sleep disturbance (i.e., mean GSDS score 48.1 (α21.3); cut-off score of ≥43 indicates a significant level of sleep disturbance). Again, the association between decrements in attentional function and sleep disturbance may be due to decreases in the restorative processes associated with 6 to 8 hours of sleep[91,92] as well as excessive daytime sleepiness which is often associated with sleep disturbance. In addition, these two symptoms may share common underlying mechanisms including: increased levels of pro-inflammatory cytokines, changes in activity with the hypothalamic-pituitary adrenal axis, and alterations in DNA repair mechanisms.[33,87,93,94]

Consistent with other studies,[2,6,9,36,44,45,75,95,96] associations were found between higher preoperative levels of trait and state anxiety and lower levels of attentional function. Our patients reported levels of trait and state anxiety that were above the clinically meaningful cutoff scores for the instruments. In addition, findings from several longitudinal studies suggest that positive associations between anxiety and decrements in attentional function persist over time.[6,9,45] Of note, while anxiety and depressive symptoms often co-occur in cancer patients,[97] even though depressive symptoms were identified as a potential predictor in the exploratory analysis, it was not retained in the final model. Additional research is warranted on the co-occurrence of these two psychological symptoms and associated decrements in attentional function.

The relationship between higher levels of state anxiety and decrements in attentional function may be partially explained by women's use of disengagement coping strategies (e.g., avoidance, denial, self-blame).[41,44,98] This hypothesis is partially supported by our finding that women who reported that they perceived that they had less control over things in their life had lower levels of attentional function at enrollment. However, it is not readily apparent why an association was found with lower levels of difficulty with coping at enrollment and lack of improvements in attentional function over time. One could hypothesize that patients with more difficulties coping prior to surgery were more likely to seek and obtain support to improve their coping skills and had associated improvements in cognitive function. That said, our findings suggest that clinicians need to assess patients prior to surgery for anxiety, as well as various psychosocial adjustment characteristics (e.g., coping styles) so that patient education and/or appropriate referrals can be initiated.[99,100]

While this longitudinal study had numerous strengths including a relatively large sample size; a comprehensive evaluation of associations between demographic, clinical, symptom, and psychosocial adjustment characteristics and decrements in self-reported attentional function; as well as 12 months of follow-up, several limitations warrant consideration. The majority of our patients were White, well educated, and diagnosed with early stage disease, which limits the generalizability of our study findings. Despite the fact that findings from objective neuropsychological tests correlate poorly with self-report measures of CRCI,[2,12-16] and often do not detect deficits, even when patients have subjective complaints about difficulties with routine activities,[13,17] future studies should evaluate for longitudinal changes in CRCI using both types of measures. In addition, future studies should include age-matched controls without breast cancer. Our analysis focused on an evaluation of associations with preoperative levels of co-occurring symptoms. Given that symptom severity changes over time, future studies need to consider the use of statistical techniques like parallel process growth modeling to evaluate for changes over time in the severity of attentional function and each of the co-occurring symptoms.

While the clinical characteristics associated with deficits in attentional function (i.e., level of comorbidity, receipt of adjuvant CTX, receipt of hormonal therapy) cannot be changed, many of the other characteristics can be assessed and addressed with appropriate pharmacologic and non-pharmacologic interventions. The initiation of these interventions, in the perioperative period, may result in a decrease in patients' overall symptom burden, as well as improvements in attentional function. In addition, timely referrals to mental health professionals and/or social workers may decrease patients' levels of anxiety and stress, as well as improve their ability to cope with their cancer treatment(s) and maintain their level of cognitive function.

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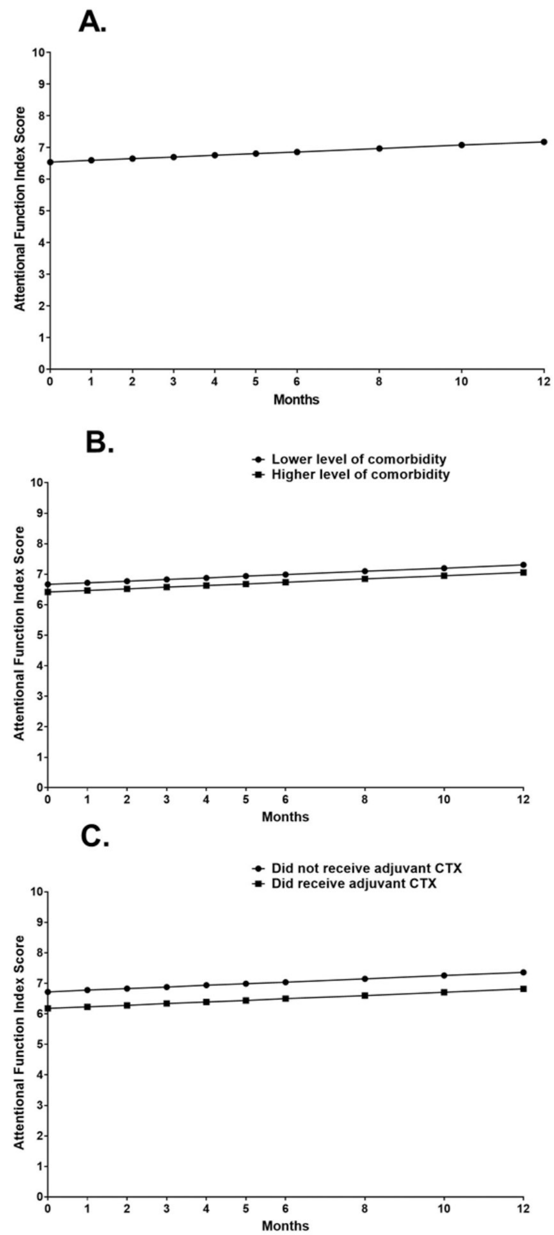

Figure 1.

Trajectory of cognitive function evaluated using the Attentional Functional Index over the 12 months (A). Influence of comorbidity (B) and receipt of adjuvant chemotherapy (CTX) (C) on interindividual differences in the severity of attentional function over 12 months.

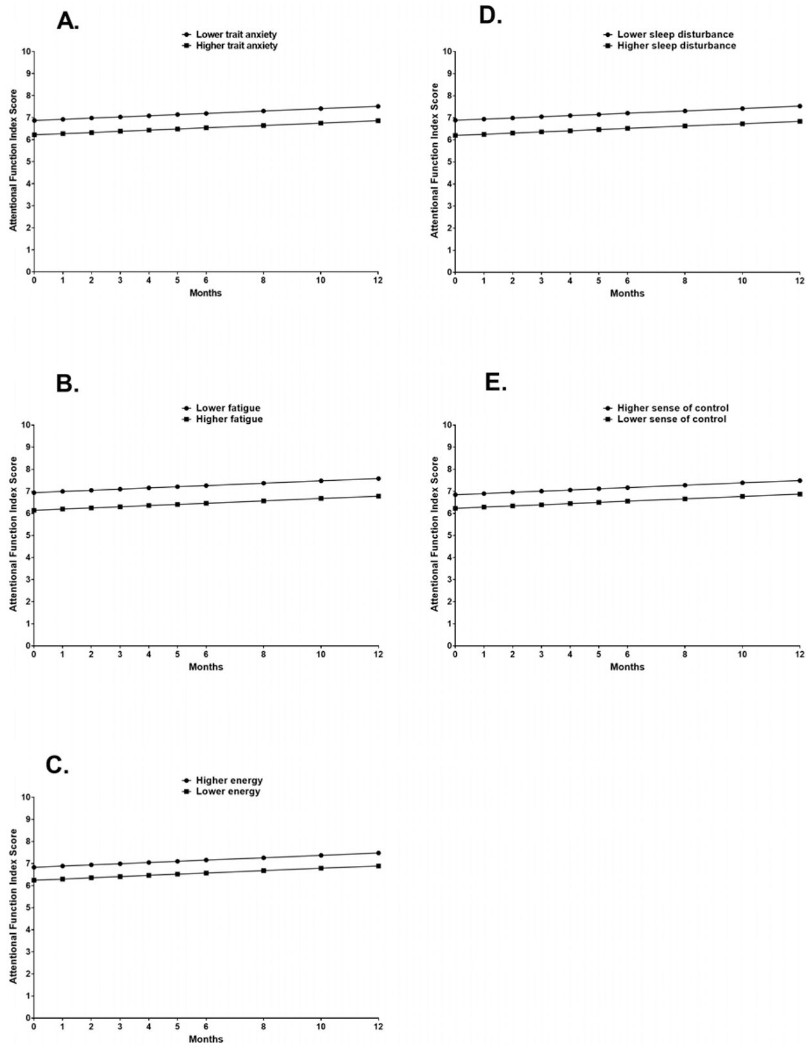

Figure 2.

Influence of levels of trait anxiety (A), fatigue (B), energy (C), sleep disturbance (D), and sense of control (E) on interindividual differences in the severity of attentional function over 12 months.

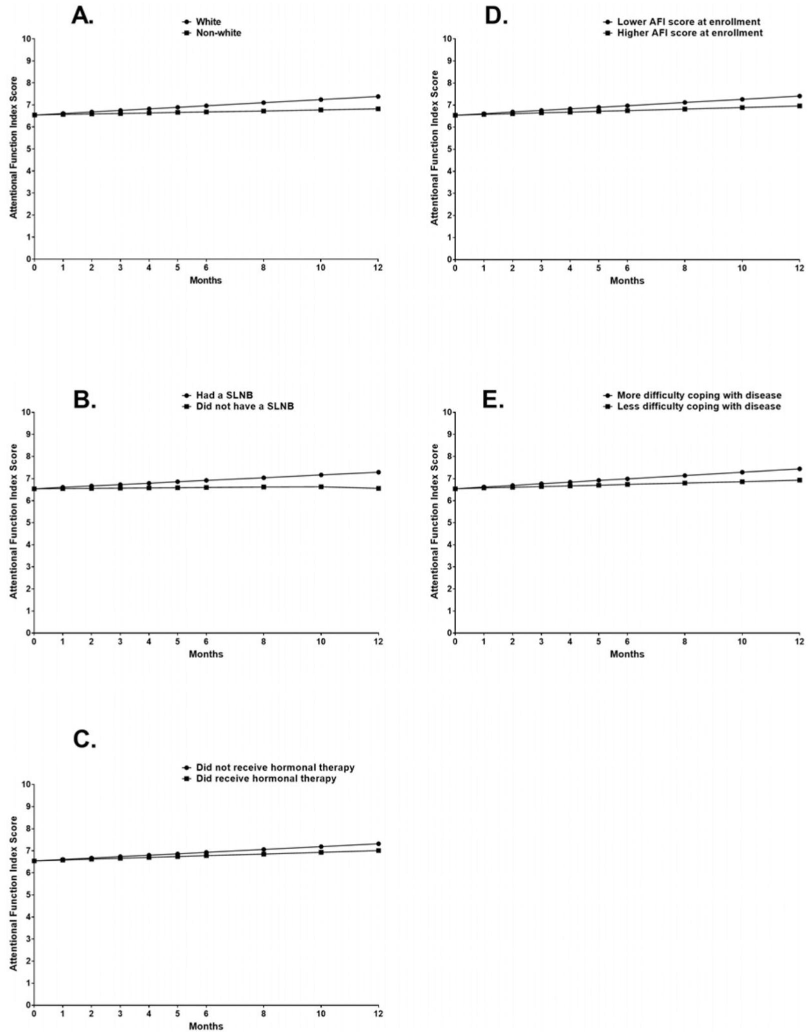

Figure 3.

Influence of race/ethnicity (A), receipt of a sentinel lymph node biopsy (B), receipt of hormonal therapy (C), preoperative level of attentional fuction (D), and level of difficulty coping with the disease (E) on interindividual differences in severity of attentional fatigue over 12 months.

Table 1 –

Potential predictors of the intercept (I) and linear coefficient (LC) for attentional function using preoperative characteristics

Characteristic	I	LC
Demographic characteristics		
Age	■	
Lives alone		
Education		■
Marital status		
Ethnicity	■	■
Employment status		
Clinical characteristics		
Body mass index	■	
Karnofsky Performance Status score	■	
Self-administered Comorbidity Questionnaire score	■	
Neoadjuvant chemotherapy	■	
Type of surgery		
Sentinel lymph node biopsy		■
Axillary lymph node dissection	■	
Breast reconstruction at the time of surgery		■
Menopausal status		
Adjuvant radiation therapy in the first six months after surgery		
Adjuvant chemotherapy in the first six months after surgery	■	
Use of complementary therapy in first six months after surgery	■	
Use of hormonal therapy in the first six months after surgery		■
Symptoms		
Trait anxiety score	■	
State anxiety score	■	■
Center for Epidemiological Studies Depression Scale score	■	■
General Sleep Disturbance Scale score	■	■
Lee Fatigue Scale score	■	■
Lee Energy Scale score	■	
Attentional Function Index score		■
Presence of breast pain prior to surgery	■	
Worst pain	■	
Average pain	■	
Number of days per week in pain	■	
Number of hours per day in pain	■	

Characteristic	I	LC
Severity of hot flashes	■	
Psychosocial adjustment characteristics		
Distress at initial cancer diagnosis	■	■
Fear of future diagnostic tests	■	■
Fear of metastasis	■	■
Difficulty coping as a result of disease/treatment	■	■
Control of things in your life	■	

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Table 2 –

Demographic, clinical, symptom, and psychosocial adjustment characteristics of the patients prior to surgery (n=396)

Demographic and clinical characteristics	**Mean (SD)**
Age (years)	54.9 (11.6)
Education (years)	15.7 (2.6)
Karnofsky Performance Status score	93.2 (10.3)
Self-Administered Comorbidity Questionnaire score	4.3 (2.8)
	%
Non-white	35.1
Married or partnered	41.4
Working for pay	23.7
Postmenopausal	47.7
Stage of disease	
0	18.4
I	38.4
IIA and IIB	34.8
IIIA, IIIB, IIIC, and IV	8.4
Received neoadjuvant chemotherapy	19.9
Type of surgery	
Breast conservation surgery	80.3
Mastectomy	19.7
Sentinel lymph node biopsy	82.6
Axillary lymph node dissection	37.1
Underwent reconstruction at the time of surgery	21.7
Received adjuvant radiation therapy in the first six months	56.6
Received adjuvant chemotherapy in the first six months	33.6
Symptom severity scores prior to surgery	**Mean (SD)**
Attentional Function Index score	6.6 (1.9)
Trait Anxiety Inventory score	35.3 (8.8)
State Anxiety Inventory score	41.6 (13.3)
Center for Epidemiological Studies-Depression score	13.7 (9.7)
Lee Fatigue Scale - Fatigue score	3.1 (2.3)
Lee Fatigue Scale - Energy score	4.9 (2.5)
General Sleep Disturbance Scale score	48.1 (21.3)
Pain in affected breast prior to surgery (% yes)	27.5
Psychosocial adjustment characteristics	
Distress at initial cancer diagnosis	8.1 (2.7)
Fear of future diagnostic tests	5.2 (3.3)
Fear of metastasis	6.0 (3.5)
Difficulty coping as a result of disease/treatment	3.3 (2.6)
Control of things in your life	6.1 (2.6)

Abbreviation: SD = standard deviation

Table 3 –

Hierarchical linear model of attentional function

	Coefficient (SE)	
	Unconditional Model	**Final Model**
Fixed effects		
Intercept	6.543 (.084)[+]	6.543 (.057)[+]
Time[a] (linear rate of change)	.054 (.007)[+]	.053 (.006)[+]
Time invariant covariates		
Intercept		
Level of comorbidity		−.044 (.020)[*]
Receipt of adjuvant chemotherapy		−.547 (.116)[+]
Trait anxiety		−.038 (.007)[+]
Fatigue		−.171 (.029)[+]
Energy		.118 (.024)[+]
Sleep disturbance		−.016 (.003)[+]
Control of things in life		.117 (.024)[+]
Linear		
Non-white ethnicity x time		−.047 (.012)[+]
Sentinel lymph node biopsy x time		.053 (.015)[**]
Receipt of hormonal therapy x time		−.025 (.012)[*]
Attentional function x time		−.010 (.003)[**]
Difficulty coping x time		.008 (.002)[**]
Variance components		
In intercept	2.401[+]	.922[+]
In slope	.007[+]	.004[+]
Goodness-of-fit deviance (parameters estimated)	11649.144 (6)	11290.122 (18)
Model comparison (X^2)		359.021 (12)[+]

[a]Time was coded as zero at the time of the preoperative visit

Abbreviation: SE = standard error

[*]p<.05

[**]p<.01

[+]p<.001