Title

Measuring cognitive complaints in breast cancer survivors: psychometric properties of the patient's assessment of own functioning inventory

Journal

Supportive Care in Cancer, 24(12)

ISSN

0941-4355

Authors

Van Dyk, Kathleen

Ganz, Patricia A

Ercoli, Linda

et al.

Publication Date

2016-12-01

DOI

10.1007/s00520-016-3352-6

Peer reviewed

Published in final edited form as:

Support Care Cancer. 2016 December ; 24(12): 4939–4949. doi:10.1007/s00520-016-3352-6.

Measuring Cognitive Complaints in Breast Cancer Survivors: Psychometric Properties of the Patient's Assessment of Own Functioning Inventory

Kathleen Van Dyk[1,2], **Patricia A. Ganz**[2,3,4], **Linda Ercoli**[1,2], **Laura Petersen**[3], and **Catherine M. Crespi**[3,4]

[1]UCLA Semel Institute for Neuroscience and Human Behavior, Los Angeles, CA, USA

[2]UCLA David Geffen School of Medicine, Los Angeles, CA, USA

[3]UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA

[4]UCLA Fielding School of Public Health, Los Angeles, CA, USA

Abstract

Purpose—Cognitive complaints are a concern for breast cancer survivors. Among various published measures for cognitive complaints, the Patient's Assessment of Own Functioning Inventory (PAOFI) is one of the few assessing a spectrum of cognitive abilities, including those most commonly reported by breast cancer survivors. This study aimed to examine the psychometric properties of the PAOFI in breast cancer survivors.

Methods—An exploratory factor analysis was conducted with a sample of breast cancer survivors (n=189) who had completed all primary cancer treatments. Construct validity was examined by correlating factor scores with valid measures of cognitive complaints, fatigue, and quality of life. Reliability was measured by internal consistency of the items in each factor within this sample, a separate sample of breast cancer survivors with high persistent cognitive complaints (n=72), and healthy controls (n=63). Factor scores were compared across the three samples.

Results—A five-factor structure similar to the PAOFI standardization study was found, with factors related to executive functioning (accounting for most of the variance), two aspects of memory functioning, language, motor/sensory-perceptual abilities. Factor scores highly correlated with measures of cognitive complaints, fatigue, and quality of life. Executive functioning and memory-related factors achieved adequate reliability across samples. Scores were significantly different across the three samples as expected.

Conclusions—The PAOFI is a reliable and valid tool for measuring cognitive complaints in breast cancer survivors.

Corresponding Author: Patricia A. Ganz, M.D., UCLA Jonsson Comprehensive Cancer Center, 650 Charles Young Drive South, Room A2-125 CHS, Los Angeles, CA 90095-6900, Phone: 310-206-1404, Fax: 310-206-3566, pganz@mednet.ucla.edu.

Conflict of Interest: The authors declare no conflict of interest. The authors have full control of all primary data and agree to allow the journal to review the data if requested.

Keywords

cognitive complaints; memory complaints; psychometric properties

Introduction

Cognitive dysfunction is now being recognized as a potential adverse effect of cancer treatment, often first detected by patient complaint. Both subjective cognitive changes (i.e. complaints) and objective neuropsychological declines following cancer treatment have been documented [1–3]; however, concordance between self-reported changes and formal cognitive testing in the literature is mixed [4]. Although this appears to be an important discrepancy, methodological considerations may help explain why researchers have been unsuccessful in documenting strong agreement between cognitive complaints and neuropsychological performance in cancer survivors.

Cognitive changes following cancer and its treatment are subtle and varied, making them susceptible to methodological limitations [5,6]. Assessment instruments for subjective awareness of cognitive decline must be finely tuned to capture varied cognitive complaints and varied severity of decline. Various subjective cognitive performance measures have been employed in cancer research studies including: The Cognitive Failures Questionnaire [7], The World Health Organization Quality of Life assessment instrument-100 [8], The Squire Memory Self-Rating Questionnaire [9], The Functional Assessment of Cancer Therapy–Cognitive Function instrument [10], among others. These instruments have established validity in measuring some aspects of subjective cognitive abilities, but their approaches vary and the scope of cognitive abilities queried is often limited to the domains of memory and attention, whereas executive functions are also important to assess in cancer-related cognitive decline [11].

The Patient's Assessment of Own Functioning Inventory (PAOFI) [12] offers a broader scope of assessment. The PAOFI has been widely used in other clinical populations, including HIV [13–15] and substance use [16], in which the nature of cognitive decline can be similarly subtle and challenging to characterize. The PAOFI was developed in consideration of both commonly reported patient complaints and the cognitive domains typically assessed in neuropsychological evaluations. This permits a more nuanced assessment of subjective cognitive decline, and allows researchers to investigate the relationship between domain-specific complaints and domain-specific cognitive performances. Further, the items query real-life examples of cognitive lapses, and the questions do not assume a common language for cognitive constructs, i.e., it does not directly ask the patient to rate their memory, attention, etc. The underlying cognitive constructs were first validated in the standardization study of a clinical sample [12].

The PAOFI is well-suited to assess cognitive complaints in cancer survivors; however, there has been limited study of its psychometric properties in this patient population. One other study examined the PAOFI in breast cancer patients [17] who had undergone surgery, but who had not yet undergone any adjuvant treatments (e.g., chemotherapy). The results of that exploratory factor analysis were largely consistent with those reported by Chelune and

colleagues [12] and supported the use of the PAOFI in that population. However, cognitive complaints are often reported *following* chemotherapy, therefore our study examined this measure in a sample of breast cancer survivors who had completed all primary treatments. Additionally, the scoring method applied in the standardization study [12] involved using cut-off scores for each item, i.e., only the most severe scores were counted in the tally of significant complaints, especially relevant for the detection of severe neuropsychological impairment. However, such a cut-off method may decrease granularity of complaint severity measurement, reducing the likelihood of characterizing more subtle cognitive changes such as those reported by breast cancer survivors. Therefore, we used the full range of scores in our analysis of this instrument. In this study we examined the factor structure, scaling, reliability and construct validity of the PAOFI in two samples of breast cancer survivors and a healthy comparison population to better understand its usefulness in this patient population.

Methods

Study Samples

Three study samples with varying degrees of cognitive complaints were used in this investigation: a large sample of female breast cancer survivors on which the factor structure is based; a sample of female breast cancer survivors with persistent, severe cognitive complaints; and a sample of healthy female controls.

The Mind Body Study—The Mind Body Study was a prospective longitudinal study in early-stage breast cancer patients after primary treatment (surgery, chemotherapy, or radiation) examining cognition and other outcomes before and after the introduction of adjuvant endocrine therapy. Baseline data collected from Mind Body Study participants (n=189) were used in the exploratory factor analysis, prior to the initiation of adjuvant endocrine therapy, providing a more uniform sample of post-treatment patients. Eligibility criteria included: age 21–65, newly diagnosed with stage 0, I, II, or IIIA breast cancer, completion of primary breast cancer treatments within the past 3 months and has not yet initiated endocrine therapy, available for 12-month follow-up, and English proficiency. Exclusion criteria included: previous cancer diagnosis or chemotherapy; whole brain irradiation or surgery; current or past central nervous system disorder or disease, epilepsy, dementia, head trauma with prolonged loss of consciousness; a current or past psychotic-spectrum disorder or major affective disorder including depression; a medical condition with known cognitive consequences; an active autoimmune disorder; insulin-dependent diabetes; uncontrolled allergic condition or asthma; chronic steroid use; and hormone therapy (estrogen, progestin compounds) other than vaginal estrogen.

Cognitive Rehabilitation Study—The Cognitive Rehabilitation Study sample (n=72) consisted of female breast cancer survivors with persistent cognitive complaints following primary treatment for cancer recruited for two separate clinical trials of a cognitive remediation protocol [18, 19]. Baseline data were used in the current study. Inclusion criteria were: age 21–75; history of stage I, II, or III breast cancer, primary treatments completed at least 18 months earlier and at most 5 years earlier (endocrine therapy permitted); self-

reported cognitive difficulties that interfered with daily activities; and proficiency in English. Further, inclusion required affirmative responses to all three of the following questions related to persistent cognitive difficulties: “Do you think or feel that your memory or mental ability has gotten worse since you completed your breast cancer treatment?,” “Do you think that your mind isn’t as sharp now as it was before your breast cancer treatments?” and “Do you feel like these problems have made it harder to function on your job or take care of things around the home?”. Exclusion criteria included: uncontrolled depression or current other psychiatric disorder; treatment with psychoactive medications (i.e., sedatives, hypnotics, or opiates); history of brain irradiation or intrathecal chemotherapy; history of a central nervous system disorder, head trauma, or seizure disorder; history of a learning disability; regular or heavy use of illicit substances or alcohol (i.e., 3 or more alcohol drinks per day).

Controls—Demographic and PAOFI data were obtained from a sample of healthy control volunteers (n=63) as part of a study conducted at the University of California, San Diego [20]. Participants were women without a history of breast cancer recruited to match a sample of women receiving adjuvant chemotherapy for breast cancer (S. Ancoli-Israel, NCI R01 CA112035). This sample has been previously described [21].

Studies were approved by the UCLA Institutional Review Board and all participants provided written informed consent.

Measures

Patient’s Assessment of Own Functioning Inventory (PAOFI)—The PAOFI consists of 33 items designed to capture self-assessed problems with different aspects of cognitive functioning including different aspects of cognitive complaints. Based on an initial factor analysis [12], items are aggregated into four subscales: Higher Level Cognitive and Intellectual Functions (HLC) tapping executive functioning (nine questions); Memory (ten questions); Language (nine questions); and Motor/Sensory-Perceptual (five questions), see Appendix 1 for items in each scale. Items are rated on a Likert scale from 1 (“almost always”) to 6 (“almost never”), and customary scoring involves summing only the number of items with high severity (i.e., scores of 1, 2, or 3) into a domain score. We were interested in examining the full range of scale scores, so to maintain directionality (i.e., higher scores indicate worse complaints), we reversed the Likert scale such that “almost never” was a score of 1, and “almost always” was a score of 6, and so forth.

Questionnaires—Participants in the Mind Body Study underwent assessment for memory complaints using the Squire Subjective Memory Questionnaire (SMQ; lower scores indicate worse memory complaints) [9] and fatigue was assessed using the Multidimensional Fatigue Inventory–Short Form (MFSI-SF) [22], which yields Mental, Physical, Emotional, Vigor, and General subscores, and Total. MFSI-SF Mental and General scores were used in this study (higher scores indicate worse complaints). Self-assessed health-related quality of life was assessed using the RAND36-item short form health survey (SF-36) Mental Component Summary score (MCS; higher scores indicate better health/functioning), the SF-36 Physical Component Summary score was not reported [23–25].

Data Analysis

Analysis of variance and chi square tests were used to examine group differences on demographic and clinical variables. Exploratory Factor Analysis: principal components analysis (PCA) was applied to the 33 PAOFI items from the Mind Body Study sample. The structure was set at five fixed factors consistent with Chelune's original structure [12], varimax rotation was applied as factors were assumed to be independent, and items with loadings greater than .5 were retained in the final structure [26]. Factor scores were calculated by averaging the items comprising each factor in the final factor structure. Thus, each factor score had a range of 1–6, with higher scores indicating more severe complaints, also see Appendix 1 for scoring.

Convergent construct validity was evaluated by examining Spearman's rho correlations between emergent factor scores and behavioral measures within the Mind Body Study sample: the SMQ, MFSI-SF scores, and the SF-36 MCS. Reliability was assessed by calculating Cronbach's alpha with the items that comprised each of the emergent factors within the three samples (i.e., Mind Body Study sample, Cognitive Rehabilitation Study sample, and healthy control sample). Factor scores were log10 transformed to correct skewness prior to conducting a univariate ANOVA to test for group differences on each emergent factor score among the three samples, controlling for age and education. Additional analyses included identifying potential cut-offs for clinical significance in the control group with the final factor scores (i.e., the average score of the items in each factor), set at the 85^{th} %ile, as well as examining the effects of education, employment status, and treatment on factors scores in the two BCS samples. Statistical significance was set at $p<.05$. Analyses were conducted using SPSS version 22 software.

We hypothesized that the instrument would demonstrate good reliability, and good convergent validity would be demonstrated by strong associations with other measures of self-assessed memory functioning. Additionally, we also hypothesized that factors would be positively associated with mental fatigue given its high correlation in breast cancer survivors [4]. Finally, we hypothesized that our scoring method (i.e., using the full range of scores) would show good discrimination among the three samples with varying degrees of cognitive complaints.

Results

Samples

See Table 1 for a summary of the characteristics of women in the three samples. Of note, the women in the breast cancer samples had higher education. Comparison of cancer treatment history between the Mind Body Study and Cognitive Rehabilitation Study samples indicated that the Cognitive Rehabilitation Study sample had a higher proportion of participants with a history of chemotherapy and radiation or chemotherapy only, whereas the Mind Body Study sample had a higher proportion of participants with a history of radiation only or neither chemotherapy nor radiation, reflecting the inclusion of women with stage 0 breast cancer in the Mind Body Study.

Exploratory Factor Analysis

Five factors with eigenvalues >1 were extracted with PCA using varimax rotation and accounted for approximately 57% of extracted variance. PAOFI items 14, 15, (language-related) and 24 (sensory/perceptual-related) had loadings <.05; a final PCA was conducted excluding these items and the five final factors accounted for approximately 60% of extracted variance. The final factor structure and item loadings are provided in Table 2. One item (25) related to confusion loaded on two factors and was retained in the factor with the higher loading (i.e., Factor 1). Factor structure was comparable to that of Chelune et al. [12]. One factor comprised mostly higher-level executive functioning cognition items (Factor 1; HLC). Two factors of memory-related items were identified: one comprised items mostly related to memory lapses possibly associated with attentional problems (Factor 2; Memory-Absent-Mindedness), and the other comprised items related to forgetting (Factor 3; Memory-Forgetfulness). We note that PAOFI standard scoring methods would combine the two memory factors into one Memory score, however we chose to keep the two memory related factors found in our analysis separate given the different aspects of cognitive difficulties they appeared to measure. We identified one factor of language and communication-related items, specifically expressive language abilities (Factor 4; Language Production). Finally, one factor of items related to motor behavior and perceptual abilities (Factor 5; Motor Perceptual) was found.

Our final structure departed from previously reported factor analyses in a few ways. First, three language items related to receptive language (items 11, 12, and 13) and one memory item related to failure to complete a task (item 8) loaded onto the factor with most of the HLC items; second, one HLC item related to distractibility (item 26) loaded onto one of the Memory factors along with items related to losing track of time, poor follow through on tasks, prospective memory difficulties, and misplacing things. (See Appendix 1 for comparison of Chelune et al.'s original factor structure to the factor structure found in this study.)

Construct Validity Analyses

We examined the correlations between the emergent factor scores and measures of memory, fatigue, and quality of life; see Table 3. As the factor scores were skewed, Spearman's rho correlations were used. Overall, all five factors demonstrated good convergent validity, and the strongest correlations were found between factors 1 (HLC), 2 (Memory-Absent-Mindedness), and 3 (Memory – Forgetfulness) and the MFSI Mental Subscale, and Factor 1 (HLC) and the Squire Memory Questionnaire.

Reliability Analyses

Reliability analyses were conducted using Cronbach's alpha within each of the three samples; see Table 2. Factors 1 (HLC), 2 (Memory-Absent-Mindedness), and 3 (Memory-Forgetfulness) achieved satisfactory or better reliability scores across the three samples if not better [27]. Factors 4 (Language Production) and 5 (Motor/Sensory-Perceptual) had at least acceptable reliability for all samples, with the exception of Factor 5 for the Control and Mind Body Study samples, and Factor 4 for the Cognitive Rehabilitation Study sample.

Group Comparisons & Additional Analyses

Factor scores were compared among the three samples controlling for age and education; see Table 4. The control group demonstrated the lowest scores across factors (i.e., fewest cognitive complaints), the Mind Body Study scores were mostly intermediate, and the Cognitive Rehabilitation Study scores were the highest. The two exceptions were that scores did not significantly differ between controls and the Mind Body Study sample on Factor 3 (Memory – Forgetfulness) or 5 (Motor/Sensory-Perceptual).

In subsequent analysis, we also examined potential cut-off scores in the control group to indicate significant cognitive dysfunction. We selected the 85th %ile (i.e., 1SD above the mean) of averaged factor scores in the control group, resulting in the following: HLC = 1.89; Memory-Absentmindedness = 2.6; Memory-Forgetfulness = 3.0; Language Production = 2.5; Motor/Sensory-Perceptual = 2.0; and Total = 10.78. As seen in Table 4, mean scores for both the Mind Body Study and the Cognitive Rehabilitation Study all fall above these cutoffs, with the exception of Language Production in the Mind Body Study.

We were also interested in examining the effects of education and cancer treatment on these new factor scores. Within each sample we compared factor scores between those who achieved a college degree or higher versus those who achieve less formal education. Within each sample, no differences were found between education groups on factor scores (p's >. 05) with one exception: in the control group, those with at least a college degree had higher (i.e., worse) scores on the Memory-Forgetfulness factor (mean = 2.29, SD = .69) versus those who did not (mean = 1.88, SD = .73; F(1,61) = 5.47, p=.02). We also examined employment status and found that within the Mind Body Study those who were employed at least part-time (n=122) had lower (i.e., better) scores on the factors Memory-Absentmindedness (F(1,187)=14.36, p<.01), Memory-Forgetfulness (F(1,187)=7.57, p<.01), as well as the Total score (F(1,187)=10.24, p<.01) compared to those who were not employed at least part-time (n=67). There were no differences found on any scores within the Cognitive Rehabilitation Study sample between those who were employed at least part-time (n=49) and those who were not (n=20; p's <.05).

Within the Mind Body Study and Cognitive Rehabilitation Study samples we also examined if cognitive complaints were related to the type of cancer treatment received. Within the Mind Body Study, again a cohort collected immediately following primary cancer treatment, we found that those who underwent chemotherapy (with or without radiation; n=97) reported significantly higher (i.e., worse) cognitive complaints on factor scores HLC (F(1,187)=17.89, p<.01)

Memory-Absentmindedness (F(1,187)=21.46, p<.01), Memory-Forgetfulness (F(1,187)=7.22, p<.01), Language Production (F(1,187)=19.60, p<.01), and Total (F(1,187)=22.05, p<.01) but not Motor/Sensory Perceptual (p>.05) compared to those who did not undergo chemotherapy (n=92). There were no differences on any factor score or the Total between those who underwent radiation (with or without chemotherapy; n=141) and those who did not (n=48; p's>.05). Within the Cognitive Rehabilitation Study sample, there were no differences found on any factor score or the Total score between those who underwent chemotherapy (with or without radiation; n=65) and those who did not (n=13;

p's>.05). There were similarly no differences between those who received radiation (with or without chemotherapy; n=54) versus those who did not (n=20) on any factor score or the Total score (p's>.05).

Discussion

The primary goal of this study was to examine the PAOFI as a measure of cognitive complaints in breast cancer survivors after completion of primary cancer treatments. We conducted an exploratory analysis to determine if the factor structure was comparable to the original structure in a non-cancer population [12], and used a scoring system that took advantage of the full severity rating of each item, rather than applying cutoff scores to indicate clinical significance based on the original Chelune et al. analyses. We found similar factors to Chelune and colleagues on the whole, but there were a few important differences. First, three items traditionally included in the Language and Communication score loaded onto the HLC score; these three items seem to tap receptive language abilities and "understanding" verbal or visual information (see Appendix 1). Since executive functioning difficulties are one of the more common areas susceptible to changes following cancer treatment, these items may be capturing difficulties associated with higher level processing of information and working memory versus problems with the immediate reception of language (i.e., an aphasia). Additionally, an item traditionally included in the Memory score (item 8) loaded on the HLC score; this item captured difficulty completing tasks and suggests it may be capturing aspects of attentional capacity. Another item traditionally included in the HLC score querying distractibility (item 26) loaded onto one of the memory factors with items assessing memory lapses related to absent-mindedness and attention. This finding may highlight the role of attentional difficulties in perceived memory problems in this population.

One other study has examined the psychometric properties of the PAOFI in breast cancer patients. Bell and colleagues [17] looked at the factor structure of the PAOFI in women with early-stage breast cancer, after surgery and before any adjuvant treatments (e.g., chemotherapy). The results of their exploratory factor analysis were also largely consistent with those reported by Chelune and colleagues [12]. Similar to their results [17], we also found that the HLC factor accounted for most of the explained variance, suggesting similar types of complaints in both populations, however there are important differences in the composition of the HLC factor. The Bell et al. PAOFI item numbers were not identical to the Chelune et al. numbering (used in this study), so direct comparison of individual item content is not possible. However, they did provide the original domain for each item from which we are able to broadly draw comparisons. In our sample, three Language items and one Memory item loaded onto the HLC factor, whereas no other domain items loaded on the HLC factor in Bell et al.'s results. One explanation for this discrepancy is that attention and executive difficulties may be more pervasive, driving other observed cognitive difficulties in the post-primary treatment population, which may not have yet developed in those yet to undergo chemotherapy or radiation. Thus, since our scoring method is more tailored to this population, it will likely be more sensitive to post-treatment cognitive complaints than that of Chelune's or Bell's analyses.

This study supports the use of the PAOFI as a valid, reliable tool for assessment of cognitive complaints in breast cancer survivors. Reliability was generally adequate or better for the Mind Body Study, control, and Cognitive Rehabilitation Study samples. Good convergent validity was demonstrated in the Mind Body Study sample, and the new factor scores correlated with a self-assessment of memory decline, fatigue, and mental health-related quality of life, consistent with our predictions. The HLC factor demonstrated the strongest relationships with each validating instrument, supporting its strength as a sensitive measure. As predicted, the new PAOFI factors scores were significantly different between controls, Mind Body Study, and Cognitive Rehabilitation Study samples, supporting the precision of this new structure to gauge the severity of cognitive complaints. Further, the Cognitive Rehabilitation Study sample was composed of breast cancer survivors with persistent cognitive complaints 18 months to 5 years post treatment, thus our results indicate that this scoring method is sensitive to the severity of persistent cognitive complaints in this population.

We also examined relevant factors to cognitive complaints and found largely no effect of education on the new factors, supporting its use in an educationally diverse population. There was an effect of employment status on the two memory-related factors scores in the Mind Body Study sample, but not on any other scores and there was no such effect seen in the Cognitive Rehabilitation Study sample. It’s possible that worse memory was affecting ability to work or return to work for some as those with higher complaints tended to not have full or part-time employment in this sample of recently treated patients, but that cannot be confirmed.

When we examined treatment effects of the new factor scores, we found that those who underwent chemotherapy had much higher levels of complaints compared to those who did not in the Mind Body Study sample whereas there were no treatment effects found in the Cognitive Rehabilitation study sample. This finding likely reflects complaints captured during the period of recovery from the effects of chemotherapy in the Mind Body Study since subjects were within 3 months of treatment. In the Cognitive Rehabilitation Study most of the sample had a history of chemotherapy, so it’s likely we are underpowered to observe any effects if they exist.

The relationships observed between the new factor scores and validity measures highlight that cognitive complaints are multifaceted: among the strongest relationships observed were those between the HLC factor score and a specific memory complaint measure, the Squire Memory Questionnaire, followed by mental scores on the MFSI-SF. The mental score items on the MFSI-SF directly assess similar content to the PAOFI HLC (e.g., “I have trouble remembering things”, “I am confused”, “I have trouble paying attention”), so it is not surprising that there is a strong correlation between the two scales.

The utility of self-assessed cognitive functioning has long been debated in various clinical populations. In theory, cognitive complaints indicate neuropsychological decline but efforts to establish this relationship in cancer survivors have produced ambiguous results [4]. It has long been maintained that subjective cognitive assessment is not a substitute for objective performance [28], but a distinct construct on its own with useful applications. The lens

through which patients self-reflect to assess their own abilities is inextricably colored by self-beliefs [29]. Thus, patients' self-assessment of cognitive functioning represents judgment of cognitive decline in the context of their psychological state. Mood is a known relevant factor in cognitive complaints; self-report assessments of mood and cognitive decline likely share capturing loss of self-esteem, grief over loss of functioning, and worry about recovery to baseline functioning.

The value of cognitive complaints has been widely recognized in other clinical populations. For example, cognitive complaints in absence of impairment predict progression to Alzheimer's disease dementia [30]; complaints in non-demented older adults are associated with Alzheimer's disease-related patterns of brain activity on neuroimaging [31]; and complaints are in fact a diagnostic *requirement* for the prodromal stage of Alzheimer's disease dementia, Mild Cognitive Impairment [32,33]. We propose that efforts to examine cognitive decline in cancer survivors similarly treat cognitive complaints as a distinct symptom that offers valuable and clinically meaningful insight into the patient's experience of cognitive decline.

The sensitivity of neuropsychological performance to reveal functional abilities has been described as only "moderate" [34], whereas cognitive complaints may be more sensitive to functional problems. Cognitive complaints offer a unique insight into which aspects of cognitive decline are most noticeable or are having the greatest impact, even if objective performances are technically within a "normal" range. Such discrepancies can expose the most important cognitive targets to prioritize for rehabilitative strategies by efficiently identifying the abilities needed for daily functioning that survivors find lacking. Cognitive complaints can also identify those who may have cognitive vulnerability under stress [28], which is difficult to detect in a laboratory setting. Since complaints are inextricably tied to mood and psychological processes, they can signal coincident mood symptoms. Effective intervention approaches may include cognitive rehabilitation [19], and Cognitive Behavioral Therapy [35] such as addressing harmful or negative thought patterns, and cognitive complaints may be the best measures to assess intervention efficacy.

Among limitations of this study, the Mind Body Study and Cognitive Rehabilitation Study groups in general were middle-aged, highly educated, and were predominantly white, limiting generalizability of results. An argument can be made that cognitive complaint domains may be correlated and an oblique rotation would be more appropriate in factor analysis. We did examine the factor structure using an oblique rotation, but the results were difficult to interpret in contrast to the straightforward and readily interpretable results using the varimax rotation, suggesting the latter is a more appropriate choice. In addition, applying a varimax rotation is consistent with previous reports [17,12].

In this study, we established a more refined scoring method for the PAOFI that captures complaints in cognitive constructs specific to breast cancer survivors. Overall, our findings support the use of this scoring method for the PAOFI in breast cancer survivors as a valid and reliable tool for assessing cognitive complaints. Cognitive complaints likely comprise detection of true cognitive changes and also physical, psychological and emotional factors, all of which are critical to address. This new scoring method may better correlate with

neuropsychological functioning, which future studies should explore. Future research that further reveals the multifactorial nature of cognitive complaints will help expose targets for cognitive and psychological intervention strategies. Cognitive complaints in breast cancer survivors are a unique, meaningful symptom that alerts clinicians to threats to poor functioning, and future directions include establishing the predictive value of cognitive complaints on functional decline, such as productivity at work, social engagement, and self-care.

Acknowledgments

This research was supported by funding from the National Cancer Institute R01 CA 109650, P30 CA16042 and the Breast Cancer Research Foundation (to PAG). We would also like to acknowledge sharing of data from the National Cancer Institute R01CA112035 (to S. Ancoli-Israel) for data on healthy women used in this report.

References

1. Ahles TA. Brain vulnerability to chemotherapy toxicities. Psychooncology. 2012; 21(11):1141–1148. DOI: 10.1002/pon.3196 [PubMed: 23023994]
2. Ahles TA, Root JC, Ryan EL. Cancer- and cancer treatment-associated cognitive change: an update on the state of the science. J Clin Oncol. 2012; 30(30):3675–3686. JCO.2012.43.0116 [pii]. DOI: 10.1200/JCO.2012.43.0116 [PubMed: 23008308]
3. Wefel JS, Kesler SR, Noll KR, Schagen SB. Clinical characteristics, pathophysiology, and management of noncentral nervous system cancer-related cognitive impairment in adults. CA Cancer J Clin. 2015; 65(2):123–138. DOI: 10.3322/caac.21258 [PubMed: 25483452]
4. Pullens MJ, De Vries J, Roukema JA. Subjective cognitive dysfunction in breast cancer patients: a systematic review. Psycho-Oncology. 2010; 19(11):1127–1138. [PubMed: 20020424]
5. Jim HS, Phillips KM, Chait S, Faul LA, Popa MA, Lee YH, Hussin MG, Jacobsen PB, Small BJ. Meta-analysis of cognitive functioning in breast cancer survivors previously treated with standard-dose chemotherapy. J Clin Oncol. 2012; 30(29):3578–3587. JCO.2011.39.5640 [pii]. DOI: 10.1200/JCO.2011.39.5640 [PubMed: 22927526]
6. Ono M, Ogilvie JM, Wilson JS, Green HJ, Chambers SK, Ownsworth T, Shum DH. A meta-analysis of cognitive impairment and decline associated with adjuvant chemotherapy in women with breast cancer. Frontiers in oncology. 2015; 5
7. Broadbent DE, Cooper PF, FitzGerald P, Parkes KR. The Cognitive Failures Questionnaire (CFQ) and its correlates. Br J Clin Psychol. 1982; 21(Pt 1):1–16. [PubMed: 7126941]
8. The WHOQOL Group. The World Health Organization quality of life assessment (WHOQOL): development and general psychometric properties. Social Science & Medicine. 1998; 46(12):1569–1585. [PubMed: 9672396]
9. Squire L, Wetzel C, Slater P. Memory complaint after electroconvulsive therapy: assessment with a new self-rating instrument. Biological Psychiatry. 1979; 14(5):791–801. [PubMed: 497304]
10. Wagner LI, Sweet J, Butt Z, Lai J-s, Cella D. Measuring patient self-reported cognitive function: development of the functional assessment of cancer therapy-cognitive function instrument. J Support Oncol. 2009; 7(6):W32–W39.
11. Wefel JS, Vardy J, Ahles T, Schagen SB. International Cognition and Cancer Task Force recommendations to harmonise studies of cognitive function in patients with cancer. Lancet Oncol. 2011; 12(7):703–708. S1470-2045(10)70294-1 [pii]. DOI: 10.1016/S1470-2045(10)70294-1 [PubMed: 21354373]
12. Chelune, GJ.; Heaton, RK.; Lehman, RA. Advances in clinical neuropsychology. Springer; 1986. Neuropsychological and personality correlates of patients' complaints of disability; p. 95-126.
13. Blackstone K, Moore D, Franklin D, Clifford D, Collier A, Marra C, Gelman B, McArthur J, Morgello S, Simpson D. Defining neurocognitive impairment in HIV: deficit scores versus clinical ratings. The Clinical Neuropsychologist. 2012; 26(6):894–908. [PubMed: 22708483]

14. Heaton RK, Franklin DR, Ellis RJ, McCutchan JA, Letendre SL, Leblanc S, Corkran SH, Duarte NA, Clifford DB, Woods SP, Collier AC, Marra CM, Morgello S, Mindt MR, Taylor MJ, Marcotte TD, Atkinson JH, Wolfson T, Gelman BB, McArthur JC, Simpson DM, Abramson I, Gamst A, Fennema-Notestine C, Jernigan TL, Wong J, Grant I. HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature, and predictors. J Neurovirol. 2011; 17(1):3–16. DOI: 10.1007/s13365-010-0006-1 [PubMed: 21174240]
15. Thames AD, Becker BW, Marcotte TD, Hines LJ, Foley JM, Ramezani A, Singer EJ, Castellon SA, Heaton RK, Hinkin CH. Depression, cognition, and self-appraisal of functional abilities in HIV: An examination of subjective appraisal versus objective performance. The Clinical Neuropsychologist. 2011; 25(2):224–243. [PubMed: 21331979]
16. Richardson-Vejlgaard R, Dawes S, Heaton RK, Bell MD. Validity of cognitive complaints in substance-abusing patients and non-clinical controls: the Patient's Assessment of Own Functioning Inventory (PAOFI). Psychiatry Res. 2009; 169(1):70–74. S0165-1781(08)00186-8 [pii]. DOI: 10.1016/j.psychres.2008.06.018 [PubMed: 19619901]
17. Bell MJ, Terhorst L, Bender CM. Psychometric Analysis of the Patient Assessment of Own Functioning Inventory in Women With Breast Cancer. Journal of nursing measurement. 2013; 21(2):320. [PubMed: 24053059]
18. Ercoli LM, Castellon SA, Hunter AM, Kwan L, Kahn-Mills BA, Cernin PA, Leuchter AF, Ganz PA. Assessment of the feasibility of a rehabilitation intervention program for breast cancer survivors with cognitive complaints. Brain Imaging Behav. 2013; 7(4):543–553. DOI: 10.1007/s11682-013-9237-0 [PubMed: 23955490]
19. Ercoli L, Petersen L, Hunter A, Castellon S, Kwan L, Kahn-Mills B, Embree L, Cernin P, Leuchter A, Ganz P. Cognitive rehabilitation group intervention for breast cancer survivors: results of a randomized clinical trial. Psycho-Oncology. 2015
20. Liu L, Rissling M, Neikrug A, Fiorentino L, Natarajan L, Faierman M, Sadler GR, Dimsdale JE, Mills PJ, Parker BA. Fatigue and circadian activity rhythms in breast cancer patients before and after chemotherapy: a controlled study. Fatigue: biomedicine, health & behavior. 2013; 1(1–2):12–26.
21. Ganz PA, Kwan L, Castellon SA, Oppenheim A, Bower JE, Silverman DH, Cole SW, Irwin MR, Ancoli-Israel S, Belin TR. Cognitive complaints after breast cancer treatments: examining the relationship with neuropsychological test performance. Journal of the National Cancer Institute. 2013:djt073.
22. Stein KD, Martin SC, Hann DM, Jacobsen PB. A multidimensional measure of fatigue for use with cancer patients. Cancer Pract. 1998; 6(3):143–152. [PubMed: 9652245]
23. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care. 1992; 30(6):473–483. [PubMed: 1593914]
24. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Medical care. 1993:247–263. [PubMed: 8450681]
25. McHorney CA, War JE Jr, Lu JR, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. Medical care. 1994:40–66. [PubMed: 8277801]
26. Costello AB. Getting the most from your analysis. Pan. 2009; 12(2):131–146.
27. Nunnally, J. Psychometric methods. New York: McGraw-Hill; 1978.
28. Herrmann DJ. Know thy memory: The use of questionnaires to assess and study memory. Psychological Bulletin. 1982; 92(2):434.
29. Hertzog C, Park DC, Morrell RW, Martin M. Ask and ye shall receive: Behavioural specificity in the accuracy of subjective memory complaints. Applied Cognitive Psychology. 2000; 14(3):257–275.
30. Geerlings MI, Jonker C, Bouter LM, Adèr HJ, Schmand B. Association between memory complaints and incident Alzheimer's disease in elderly people with normal baseline cognition. 1999

31. Ercoli L, Siddarth P, Huang S-C, Miller K, Bookheimer SY, Wright BC, Phelps ME, Small G. Perceived loss of memory ability and cerebral metabolic decline in persons with the apolipoprotein E-IV genetic risk for Alzheimer disease. Archives of general psychiatry. 2006; 63(4):442–448. [PubMed: 16585474]
32. Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, Gamst A, Holtzman DM, Jagust WJ, Petersen RC. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's & Dementia. 2011; 7(3):270–279.
33. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. Arch Neurol. 1999; 56(3):303–308. [PubMed: 10190820]
34. Marcotte, TD.; Cobb Scott, J.; Kamat, R.; Heaton, RK. Neuropsychology and the Prediction of Everyday Functioning. In: Marcotte, TD.; Grant, I., editors. Neuropsychology of everyday functioning. Guilford Press; 2009.
35. Ferguson RJ, Ahles TA, Saykin AJ, McDonald BC, Furstenberg CT, Cole BF, Mott LA. Cognitive-behavioral management of chemotherapy-related cognitive change. Psycho-Oncology. 2007; 16(8):772. [PubMed: 17152119]

Appendix 1: Patient's Assessment of Own Functioning Inventory Item Factors Grouped by Original Chelune et al. Scoring [12]

Items and Original Factor/Subscore	New Factor
MEMORY	
1. How often do you forget something that has been told to you within the last day or two?	Memory - Forgetfulness
2. How often do you forget events which have occurred in the last day or two?	Memory - Forgetfulness
3. How often do you forget people whom you met in the last day or two?	Memory - Forgetfulness
4. How often do you forget things that you knew a year or more ago?	Memory - Forgetfulness
5. How often do you forget people whom you knew or met a year or more ago?	Memory - Forgetfulness
6. How often do you lose track of time, or do things either earlier or later than they are usually done or are supposed to be done?	Memory – Absent-Mindedness
7. How often do you fail to finish something you start because you forgot that you were doing it? (Include such things as forgetting to put out cigarettes, turn off stove, etc.)	Memory – Absent-Mindedness
8. How often do you fail to complete a task that you start because you have forgotten how to do one or more aspects of it?	HLC
9. How often do you lose things or have trouble remembering where they are?	Memory – Absent-Mindedness
10. How often do you forget things that you are supposed to do or have agreed to do (such as putting gas in the car, paying bills, taking care of errands, etc.)?	Memory – Absent-Mindedness
LANGUAGE	
11. How often do you have difficulties understanding what is said to you?	HLC
12. How often do you have difficulties recognizing or identifying printed words?	HLC
13. How often do you have difficulty understanding reading material which at one time you could have understood?	HLC
14. Is it easier to have people show you things than it is to have them tell you about things?	*Excluded*
15. When you speak, are your words indistinct or improperly pronounced?	*Excluded*
16. How often do you have difficulty thinking of the names of things?	Language – Production

Items and Original Factor/Subscore	New Factor
17. How often do you have difficulty thinking of the words (other than names) for what you want to say?	Language – Production
18. When you write things, how often do you have difficulty forming the letters correctly?	Language – Production
19. Do you have more difficulty spelling, or make more errors in spelling, than you used to?	Language – Production
MOTOR/SENSORY-PERCEPTUAL	
20. How often do you have difficulty performing tasks with your right hand (including such things as writing, dressing, carrying, lifting, sports, cooking, etc.)?	Motor/Sensory-Perceptual
21. How often do you have difficulty performing tasks with your left hand?	Motor/Sensory-Perceptual
22. How often do you have difficulty feeling things with your right hand?	Motor/Sensory-Perceptual
23. How often do you have difficulty feeling things with your left hand?	Motor/Sensory-Perceptual
24. Lately, do you have more difficulty than you used to in seeing all of what you are looking at, or all of what is in front of you (in other words, are some areas of your vision less clear or less distinct than others)?	*Excluded*
HIGHER LEVEL COGNITIVE FUNCTIONS	
25. How often do your thoughts seem confused or illogical?	HLC
26. How often do you become distracted from what you are doing or saying by insignificant things which at one time you would have been able to ignore?	Memory – Absent-Mindedness
27. How often do you become confused about (or make a mistake about) where you are?	HLC
28. How often do you have difficulty finding your way about?	HLC
29. Do you have more difficulty now than you used to in calculating or working with numbers (including managing finances, paying bills, etc.)?	HLC
30. Do you have more difficulty now than you used to in planning or organizing activities (i.e., deciding what to do and how it should be done)?	HLC
31. Do you have more difficulty now than you used to in solving problems that come up around the house, at your job, etc.? (In other words, when something new has to be accomplished, or some new difficulty comes up, do you have more trouble figuring out what should be done and how to do it)?	HLC
32. Do you have more difficulty now than you used to in following directions to get somewhere?	HLC
33. Do you have more difficulty now than you used to in following instructions concerning how to do things?	HLC

HLC = Higher Level Cognitive Functions

Likert Scale for each item (scale numbers used in this study):

6 almost always

5 very often

4 fairly often

3 once in a while

2 very infrequently

1 almost never

New Factor Scoring

Average responses across factor items to obtain the factor score (range 1–6):

Memory – Forgetfulness: Items 1, 2, 3, 4, 5

Memory – Absent-Mindedness: Items 6, 7, 9, 10, 26

HLC: Items 8, 11, 12, 13, 25, 27, 28, 29, 30, 31, 32, 33

Language Production: Items 16, 17, 18, 19

Motor/Sensory-Perceptual: Items 20, 21, 22, 23

Table 1

Characteristics of Samples

	Healthy Controls (n = 63)	Mind Body Study Sample (n = 189)	Cognitive Rehabilitation Study Sample (n = 72)
Age, years mean (SD)	51.96 (9.35)	51.84 (8.32)	53.70 (7.93)
Race, % white (n)	79% (50)	80% (151)	87% (63)
Education*, % (n)			
H.S.	8% (5)	0% (0)	1% (1)
Some College	29% (18)	19% (35)	25% (18)
College Degree or more	63% (40)	81% (154)	74% (53)
Received Chemotherapy and Radiation*, % (n)	--	41% (77)	58% (45)
Received Chemotherapy Only*, % (n)	--	10% (20)	25% (28)
Received Radiation Only*, % (n)	--	34% (64)	11% (9)
Neither Chemotherapy nor Radiation*, % (n)		15% (28)	5% (4)

H.S. = High School;

* $p<.05$, group differences

Table 2

Final Structure Factor Loadings for PAOFI items with Loadings <.50 in the Mind Body Study Sample and Reliability (Cronbach's Alpha) for the Mind Body Study, Cognitive Rehabilitation Study, and Healthy Control samples

	Factor				
Item Number (Original Subscore)	**1 (HLC)**	**2 (Memory – Absent-Mindedness)**	**3 (Memory - Forgetfulness)**	**4 (Language Production)**	**5 (Motor/Sensory Perceptual)**
13 (Language)	.78				
32 (HLC)	.78				
33 (HLC)	.73				
28 (HLC)	.69				
31 (HLC)	.66				
27 (HLC)	.64				
11 (Language)	.64				
29 (HLC)	.58				
30 (HLC)	.58				
25 (HLC)	.57	.51			
12 (Language)	.57				
8 (Memory)	.51				
6 (Memory)		.74			
10 (Memory)		.68			
7 (Memory)		.65			
26 (HLC)		.60			
9 (Memory)		.51			
5 (Memory)			.76		
3 (Memory)			.73		
4 (Memory)			.72		
2 (Memory)			.64		
1 (Memory)			.55		
16 (Language)				.75	
17 (Language)				.67	
18 (Language)				.64	
19 (Language)				.61	
22 (Motor/Sensory-Perceptual)					.81

	Factor				
Item Number (Original Subscore)	**1 (HLC)**	**2 (Memory – Absent-Mindedness)**	**3 (Memory - Forgetfulness)**	**4 (Language Production)**	**5 (Motor/Sensory Perceptual)**
23 (Motor/Sensory-Perceptual)					.76
20 (Motor/Sensory-Perceptual)					.61
21 (Motor/Sensory-Perceptual)					.55
Total Variance Explained (60%)	37%	8%	6%	5%	4%
Cronbach's α, MBS Sample	.92	.80	.84	.77	.59
Cronbach's α, CRS Sample	.90	.81	.78	.56	.84
Cronbach's α, Healthy Control Sample	.87	.76	.83	.70	.36

PAOFI = Patient's Assessment of Own Functioning; HLC = Higher Level Cognition

Excluded items: 14, 15, 24

Support Care Cancer. Author manuscript; available in PMC 2017 December 01.

Table 3

Spearman's rho Correlations with PAOFI Factors and Health Questionnaires in the Mind Body Study sample

	Squire Memory Questionnaire Total Score	SF-36 MCS score	MFSI-SF Mental Subscore	MFSI-SF General Subscore
Factor 1 (HLC)	−.65**	−.47**	.71**	.47**
Factor 2 (Memory – Absent-Mindedness)	−.56**	−.47**	.66**	.42**
Factor 3 (Memory - Forgetfulness)	−.43**	−.30**	.61**	.34**
Factor 4 (Language Production)	−.50**	−.36**	.59**	.33**
Factor 5 (Motor/Sensory-Perceptual)	−.20**	−.15*	.21**	.27**
Total Score	−.62**	−.48**	.76**	.48**

* $p<.05$,

** $p<.01$

HLC = Higher Level Cognition; SF-36 MOS = Medical Outcomes Study, Short Form; Second Edition; MFSI-SF = Multidimensional Fatigue Symptom Inventory – Short Form

Table 4

Group Comparisons of Factor Scores

	A: Healthy Control Sample Mean (SD)	B: Mind Body Study Sample Mean (SD)	C: Cognitive Rehabilitation Study Sample Mean (SD)	*Omnibus F test*	*Pairwise Tests p*<.05
Factor 1 (HLC)	1.32 (.40)	1.55 (.67)	2.68 (.90)	$F(2,319) = 86.29$, $p<.01$	A<B<C
Factor 2 (Memory – Absent- Mindedness)	1.86 (.66)	2.11 (.84)	3.76 (.93)	$F(2,319) = 99.70$, $p<.01$	A<B<C
Factor 3 (Memory - Forgetfulness)	2.14 (.73)	2.37 (.93)	3.59 (.83)	$F(2,319) = 52.46$, $p<.01$	A<C, B<C
Factor 4 (Language Production)	1.89 (.69)	2.11 (.80)	3.36 (.75)	$F(2,319) = 70.17$, $p<.01$	A<B<C
Factor 5 (Motor/Sensory- Perceptual)	1.35 (.47)	1.38 (.60)	1.87 (1.04)	$F(2,319) = 13.03$, $p<.01$	A<C, B<C
Total Score	8.57 (1.96)	9.52 (2.89)	15.25 (3.21)	$F(2,319) = 111.60$, $p<.01$	A<B<C

HLC=Higher Level Cognition

Presented means and standard deviations are of untransformed, unadjusted scores.

F and p values reflect group comparisons conducted on log 10 transformed factor scores, adjusted for age and education.