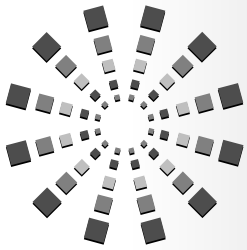

Mi Sook Jung, PhD, RN
Bernadine Cimprich, PhD, RN, FAAN

Cognitive Deficits in Korean Women Treated With Chemotherapy for Breast Cancer

KEY WORDS
Adjuvant chemotherapy
Breast cancer
Cognitive function
Culture

Background: Cognitive deficits have been reported as detrimental side effects in chemotherapy-treated breast cancer patients and survivors. Korean women treated for breast cancer may experience unrecognized cognitive deficits related to their treatment. However, no research has examined cognitive test performance in chemotherapy-treated Korean breast cancer survivors. **Objective:** The objectives of this study were 2-fold: (1) to examine differences in occurrence and severity of cognitive deficits in Korean women treated with adjuvant chemotherapy for breast cancer as compared with a control group of women without breast cancer and (2) to examine the relationship of selected demographic and cultural factors with cognitive test performance. **Methods:** Sixty-four Korean women, 32 women treated for localized breast cancer and 32 healthy controls, were enrolled. Breast cancer participants were assessed with established cognitive measures within 4 months after chemotherapy, and healthy controls, within 6 months after negative screening mammography. **Results:** The breast cancer group showed a significantly higher occurrence and greater severity of cognitive deficits than controls did. Importantly, older age, less education, greater collectivist tendency, and greater childrearing burden were reliably associated with poorer attention and working memory test performance. **Conclusions:** Cognitive deficits were found in chemotherapy-treated Korean women with moderate to large effect sizes compared with controls. Cultural characteristics contributed to worse cognitive performance. **Implications for Practice:** Healthcare providers should recognize that Korean women may be highly vulnerable to cognitive deficits. Cultural factors also need to be considered when assessing cognitive function and designing therapeutic interventions to counteract negative cognitive outcomes.

Author Affiliations: School of Nursing, University of Michigan, Ann Arbor.
The authors have no funding or conflicts of interest to disclose.

Correspondence: Mi Sook Jung, PhD, RN, School of Nursing, University of Michigan, 400 North Ingalls, Ann Arbor, MI 48109 (msjung@umich.edu).
Accepted for publication April 16, 2013.
DOI: 10.1097/NCC.0b013e3182980383

Breast cancer is the second most common cancer for Korean women, with an increasing prevalence rate observed over the last 10 years. According to recently available data, the average percentage change for breast cancer prevalence among Korean women was 6.5%, from 1999 to 2009.[1] This average percentage change score was higher than those of Western countries such as the United States (−2.0% from 1999 to 2004 and 0.9% from 2005 to 2009).[2] Of note, the highest prevalence rate of breast cancer in Korean women (40%) occurred between 40 and 49 years of age and more than half of new diagnoses of breast cancer (53%) were in women younger than 50 years.[1]

Korean women appear to experience significant burden related to the breast cancer illness and, at the same time, the need to fulfill role obligations to family regardless of health status. Specifically, middle-aged Korean women have a primary responsibility in performing traditionally ascribed family caregiving roles such as childrearing and household tasks.[3] The addition of a new breast cancer diagnosis and its treatment can add a heavy cognitive burden requiring increased mental efforts to maintain their usual level of functioning. As a result, it is possible that Korean women with breast cancer may experience an overuse of cognitive resources, leading to cognitive deficits and negative outcomes in personal and social functioning in their everyday lives.

Considerable attention has been devoted in recent years to the investigation of the distressing effects of breast cancer and its treatment and health-related quality of life among Korean women. At present, various studies have been conducted to develop interventions to relieve physical and psychological symptoms such as nausea, vomiting, pain, reduced arm movement, fatigue, anxiety and depression, and alopecia.[4] However, few studies have explored symptoms of compromised cognitive function in Korean breast cancer patients and survivors, let alone the design of culturally relevant therapeutic interventions to help restore cognitive function. Only 2 published studies have examined self-reported cognitive function in chemotherapy-treated Korean women with breast cancer.[5,6] For this reason, appropriate interventions are not yet available although women treated for breast cancer may experience reduced cognitive function in their daily lives. Thus, understanding cognitive deficits and culturally unique characteristics of cognitive problems is needed to develop more systematic assessment protocols and comprehensive care of Korean breast cancer survivors. The objectives of this study were (1) to examine differences in the occurrence and severity of cognitive deficits in Korean women treated with adjuvant chemotherapy for breast cancer as compared with a control group of women without breast cancer and (2) to examine the relationship of selected demographic and cultural factors with cognitive test performance.

■ Background

Empirical Evidence

There has been accumulating empirical evidence on treatment-related cognitive deficits in women with breast cancer in Western countries with predominantly white women.[7–11] Chemotherapy-treated breast cancer survivors have reported altered cognitive functioning, especially attention and working memory deficits with a reduced ability to focus, think clearly, multitask, and perform everyday duties.[12] This phenomenon has been labeled by breast cancer survivors as "chemobrain" or "chemofog" and has been associated with poorer functional outcomes in vocational performance, community involvement, and social role functioning.[13]

Overall, postchemotherapy cognitive deficits were reported in up to 75% of women after the completion of adjuvant chemotherapy for early-stage breast cancer.[8,9,14] A recently published study by Wefel and colleagues[9] is especially worthy of notice, as it provided evidence on changes in attention and working memory over the trajectory of chemotherapy for breast cancer. They reported that 21% of 42 participants had prechemotherapy cognitive deficits, which increased to 65% during and shortly after chemotherapy for breast cancer. Importantly, all participants who had prechemotherapy cognitive deficits developed some degree of decline in cognitive function over the course of chemotherapy, indicating that chemotherapy may be associated with an increased likelihood of failure to recover from alterations in cognitive function before treatment. Furthermore, approximately half of women who had unimpaired cognitive function before chemotherapy were classified as having postchemotherapy cognitive deficits. These findings suggest that chemotherapy-treated women may be at higher risk of cognitive deficits over time.

Certain individual factors such as age, educational level, menopausal status, and comorbidity have been suggested as contributory to cognitive deficits in women with breast cancer. Age is a well-known risk factor of posttreatment cognitive decline in women with breast cancer, and studies have observed that older women treated for breast cancer experienced lower posttreatment neuropsychological test performance compared with either younger women treated for breast cancer or age-matched healthy women without breast cancer.[11,15] Educational level can also influence cognitive function in healthy individuals as well as people with illness.[16] Higher education appears to buffer people from cognitive declines through more efficient utilization of brain networks as needed to enhance task performance.[17] A decline in reproductive hormone levels may lead to deteriorations in attention, memory, and learning in postmenopausal women treated for breast cancer.[18] Comorbidity is an important factor affecting cognitive function in women with breast cancer. Breast cancer patients with other chronic health problems showed lower performance on cognitive tests than did those without other chronic illness.[15] However, it has not been determined whether the above demographic, disease and treatment, and health factors might affect cognitive function, especially attention and working memory function, in middle-aged Korean women treated for breast cancer. Based on the above empirical literature review, it was hypothesized that the following factors would be significantly associated with attention and working memory deficits in women with breast cancer: demographics (age, education level), general health (comorbidity, menopausal status), and disease and treatment (cancer diagnosis, adjuvant chemotherapy) (Figure 1).

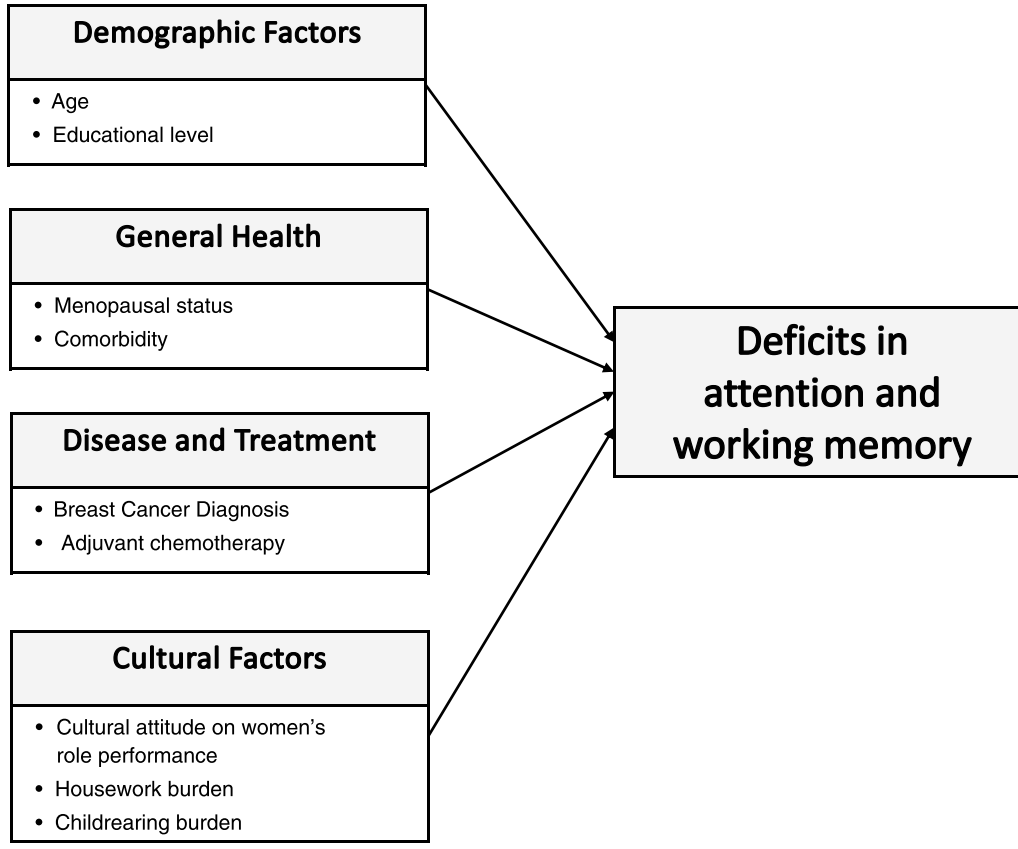

Figure 1 ■ Conceptual framework: factors influencing cognitive function in Korean women treated for breast cancer.

Theoretical Orientation: Attention and Working Memory

Cognitive deficits in breast cancer survivors have been frequently reported in attention and working memory systems, which are critical in integrating higher-order mental abilities.[19] Recent neuroimaging studies have supported that chemotherapy-treated breast cancer survivors had structural and functional changes in brain regions associated with attention and working memory processes compared with disease- and treatment-matched comparison groups.[10,19,20] Theoretically, attention is defined as the ability to effectively focus on information relevant to cognitive tasks through the active mental process of inhibiting competing or distracting stimuli from the internal or external environment.[21–23] Working memory is regarded as an ability to temporarily store and manipulate information for some purpose.[24] Both cognitive domains of attention and working memory are dependent on frontal lobe function of the brain and play an important role in efficiently and accurately carrying out planned activities and intended behaviors.[25,26] Increased use of cognitive effort not only facilitates appropriate responses to achieve specific goals but also can be costly in reducing cognitive reserves needed to attend. For example, if additional effort is continuously required to meet task demands without cognitive restoration, people are more prone to cognitive deficits, leading to relatively higher error rates and slower reaction times in performing intended tasks.[22,27]

Cultural Factors

Culture is thought to play an important role in attention and working memory function. Different cultural experiences and practices may impact these basic cognitive processes in different ways.[28] However, despite considerable evidence for the effect of cultural perspectives on cognition, culture has not been examined as an important factor contributing to breast cancer and its treatment-associated cognitive deficits. Culture is generally divided into 2 categories, collectivism and individualism.[29] Each of these produces meaningful distinctions in behavioral performance and preferences in cognitive and social processing through prolonged exposure to different cultural values, viewpoints, and behavioral practices. From a neurocultural point of view, East Asians in a collectivist culture acquire more holistic cognitive processing that has been related to greater attention to the relationships between different objects and to the interdependence of the individual object with the surrounding contexts. On the other hand, Westerners in an individualistic culture show more analytic cognitive processing that focuses on objects and their features rather than on relationships between objects and contexts surrounding them.[28] Thus, different patterns of attention and working memory may exist among women treated for breast cancer in collectivist versus individualist cultures.

Korean culture is characterized by collectivism and familism. Individuals with strong collectivist tendency are likely to (1) engage in holistic processing in perceiving self, others, and

the world, (2) have other-focused orientation rather than self-centered inclination in managing conflicts, and (3) emphasize self-control through the idea that people must suppress certain thoughts, feelings, and behaviors in sustaining in-group harmony.[30] Familism has also shared similar values with collectivism in terms of the emphasis on self-restraint, self-sacrifice, and family harmony.[31] Based on these cultural characteristics, a primary responsibility for the maintenance of family health and welfare relies heavily on women who engage in multiple family caregiving roles, including a mother, wife, daughter-in-law, and even shared breadwinner, as opposed to a single responsibility for family finance that is primarily imposed on married men in Korea.[32] It is reported that Korean women spend approximately 64 hours on housework and child care every week, and their level of fatigue was significantly correlated with the total mean hours of house work performance.[33] The imposition of family role obligations also can be a dual mental and physical burden on women who are employed outside the home,[32,34] and it may negatively affect Korean women's health outcomes and life satisfaction. Thus, Korean women's attitude and burden about culturally ascribed role performance need to be considered as possible contributory factors when examining attention and working memory deficits related to breast cancer and its treatment (see Figure 1).

This present study is the first to examine the effects of adjuvant chemotherapy for breast cancer in Korean women on attention and working memory function and the relationship between cultural factors (cultural attitude on women's role performance, housework burden, childrearing burden) and neurocognitive test performance. Findings of the study may contribute to a better understanding of cognitive deficits in Asian breast cancer survivors. Furthermore, this study may help healthcare providers identify women who are vulnerable to cognitive deficits and develop appropriate cultural interventions to improve cognitive function.

■ Methods

Design and Sample

This study used a cross-sectional, comparative design with a convenience sample of 64 Korean women, including 32 participants treated with adjuvant chemotherapy for newly diagnosed breast cancer (stage I to IIIa) at a university cancer center in South Korea and a comparison group of 32 healthy volunteers similar in age and educational background. Sample size was calculated by power analysis based on previous studies[15,35,36] with the nQuery Advisor version 7.[37] A sample of 64 subjects showed 85% power to detect a small to medium effect size for mean differences in the dependent variables between 2 groups at the 5% level of significance. The sample of 64 also provided 85% power to detect an R^2 of 0.29 with 6 predictors at the 5% level of significance in a multiple regression. All participants were screened with the Korean version of the Mini-Mental State Examination to exclude individuals with undiagnosed cognitive disorders such as dementia. Women were not included when they had (1) a total score of 24 or lower on the Mini-Mental State Examination and (2) a preexisting condition affecting the ability to perform cognitive tasks such as mental, psychiatric, or learning disorder; debilitating medical conditions; and currently prescribed medication known to influence cognitive function. No participants in the healthy control group had history of cancer diagnosis and its treatment.

Recruitment and Procedures

The breast cancer group was enrolled within 4 months after completing the last cycle of chemotherapy to assess the short-term treatment effect on cognitive function. This was consistent with other studies of short-term cognitive effects of chemotherapy. The mean time interval between chemotherapy completion and assessment was approximately 2 months (mean [SD], 70 [36] days). The healthy control group was recruited within 6 months after routine negative screening mammography to increase confidence of the absence of breast cancer. After written informed consent was obtained, testing was conducted by a trained research nurse in a quiet room using standard instructions. Neurocognitive tests and self-report questionnaires took about 45 to 60 minutes to complete. To limit the effects of fatigue on test performance, neurocognitive tests were administered before other measures and a short break was provided between tests. The study was approved by the institutional review board of 2 institutions located in the United States and South Korea.

Measures

Cognitive function was assessed with a brief battery of norm-referenced measures that were theoretically congruent with and sensitive to attention and working memory function, including the digit span and the controlled oral word association (COWA) tests. The attention network test (ANT) was also administered to measure both overall attention function and 3 specific components that make up the attention system. Cultural characteristics were measured in terms of cultural attitude toward women's role performance and perceived burden regarding housework and childrearing.

DIGIT SPAN TEST

The digit span test has been commonly used to evaluate attention and working memory function across countries.[16] This standardized test consisted of digit span forward (DSF) and backward (DSB). Participants were asked to recite a series of digits in the same order read by the examiner and the total number of digits correctly recited before 2 failed trials was recorded as DSF performance. The DSB requires more effort to sustain attention and working memory in recalling and manipulating a sequence of individual digits in reverse order. The DSB score was the number of digits correctly recited before 2 failed trials.

COWA TEST

The COWA test was originally developed to assess verbal fluency requiring attention and working memory function.[16,38] Neurologically, this test is known to be sensitive in measuring frontal lobe–dependent attention and working memory function.[36,39] Three target Korean letters were used to assess letter fluency (COWA test part A) and 2 categories were used to measure category fluency (COWA test part B). Participants were requested to verbally generate as many words beginning with each designated letter for the COWA test part A or appropriate to the target category for the COWA test part B as possible in a given time. For both part A and B performance, the score was the sum of words correctly generated in each trial. This measure has been found to be a valid and reliable tool in Korean healthy people (N = 451).[40]

ATTENTION NETWORK TEST

The ANT is a computerized measure that is easily administered to measure different types of attention, including alerting, orienting, and executive (controlled) attention.[27] Participants were asked to respond to the direction of the central target arrow as quickly and accurately as possible. The direction of the arrow to the left or right was randomly and equally assigned across all trials. Before starting the actual test, a brief practice session and standard instructions were provided to ensure that all participants had sufficient understanding of test procedures. Error rates and reaction times were recorded over 288 trials during a 15-minute test period.

WOMAN'S ATTITUDE ON TRADITIONAL GENDER ROLE

The Woman's Attitude on Traditional Gender Role was developed to describe Korean women's attitude between their subjective values and the normative expectations for performing women's roles traditionally ascribed, such as "A women should have a job that does not interfere with her taking care of children and doing housework."[41] This measure was used in a previous study to compare women's gender role attitude between 499 Korean women and 200 Korean men.[42] The Woman's Attitude on Traditional Gender Role consisted of 4 items rated from 1, "strongly agree," to 5, "strongly disagree."[41] Scores of all items were reversed so higher scores indicated greater tendency of collectivism-rooted values on women's role performance. Cronbach's α coefficient in the study was .61, which is considered a minimal acceptable level for scales with less than 10 items.[43]

LIFE STRESS FOR KOREAN HOUSEWIVES INSTRUMENT

The Life Stress for Korean Housewives Instrument was originally developed to assess the interpersonal and daily task–associated stress of Korean housewives.[44] The household chore subscale in this instrument was used to measure perceived burden associated with household affairs. This subscale consisted of 6 items (eg, I am always worn out because of performing household chores), with higher scores indicating greater housework burden. The satisfactory level of the reliability and validity of this instrument was confirmed in 1006 Korean women, and Cronbach's α coefficient was .86 for this household chore subscale.[44] In this study, Cronbach's α for internal consistency was .87.

THE MATERNAL STRESS INVENTORY

The Maternal Stress Inventory was used to assess women's burden about childrearing, which is culturally and socially considered as a primary responsibility of women in Korean society.[45,46] This measure consists of 7 items rated on a 4-point Likert scale. Higher scores indicate higher levels of burden in childrearing. The internal consistency coefficient in this study was 0.89.

Data Analysis

All procedures for statistical analyses were performed using the Statistical Package for the Social Sciences version 18 for Windows (SPSS Inc, Chicago, Illinois). To compute a composite cognitive score, raw scores of the cognitive measures were transformed to standardized z scores using the mean and the standard deviation for all participants. A total cognitive index (TCI) was derived from the sum of the z scores on the neurocognitive tests, including DSF, DSB, and COWA part A and part B.

To compare attention and working memory function and cultural characteristics between groups, independent t tests and Pearson χ^2 tests were conducted. Cohen d effect sizes were calculated for the differences in attention and working memory function. Pearson correlation coefficients were computed to examine which demographic and cultural variables were significantly associated with individual performance on cognitive measures. Multiple regression analyses were performed to determine possible predictors of attention and working memory function. Dependent variables consisted of TCI and mean reaction time in the ANT, respectively. The overall error rate in the ANT was not used as a dependent variable for the multiple regression analysis because the regression model on error rates in the ANT did not reach statistical significance ($P > .05$). The variance inflation factor and the Durban-Watson statistic were calculated as diagnostic approaches for evaluating the degree of multicollinearity, and all values were within the acceptable ranges, that is, less than 5 for variance inflation factor and close to 2 for the Durban-Watson statistic.

■ Results

Sample Characteristics

As presented in Table 1, most participants in this study were middle aged, well educated, and married. The overall mean (SD) age of the participants was 47 (8) years, and 62 women (97%) were younger than 60 years. The mean (SD) years of education was 12 (3) years, and 52 women (81%) were at least high school graduates. Most participants were married. Employment status was the only demographic variable showing a significant difference between groups ($\chi^2_{1,\ 64} = 12.70$, $P < .001$).

Table 1 • Sample Characteristics

	Total Sample (N = 64)	Breast Cancer Group (n = 32)	Healthy Control Group (n = 32)
Age, mean ± SD (range), y	47 ± 8 (31–61)	46 ± 8 (31–61)	48 ± 8 (31–59)
Education, mean ± SD (range), y	12 ± 3 (6–20)	12 ± 3 (6–16)	13 ± 3 (6–20)
Marital status			
Single[a]	15 (23)	6 (19)	9 (28)
Currently married	49 (77)	26 (81)	23 (72)
Employment status			
Employed outside home	26 (41)	6 (19)[b]	20 (62)
Unemployed	38 (59)	26 (81)	12 (38)
Menopausal status			
Premenopausal	34 (53)	17 (53)	17 (53)
Perimenopausal	9 (14)	4 (13)	5 (16)
Postmenopausal	21 (33)	11 (34)	10 (31)
Comorbidity[c]			
Yes	12 (19)	6 (19)	6 (19)
No	52 (81)	26 (81)	26 (81)
Stage of cancer			
I		10 (31)	
II		15 (47)	
IIIa		7 (22)	
Type of surgery			
Lumpectomy		7 (22)	
Mastectomy		25 (78)	
Chemotherapeutic regimen			
CEF[d]		13 (41)	
ACT[e]/AC[f]/TC[g]		19 (59)	
Radiation therapy			
Yes		5 (16)	
No		27 (84)	
Hormone therapy			
Yes		8 (25)	
No		23 (75)	

Values are presented as n (%), unless otherwise indicated.
[a]Includes never married, divorced, widowed, and separated.
[b]$P < .001$.
[c]Includes arthritis, diabetes, hepatitis, hypertension, or chronic pain due to intervertebral disc hernia.
[d]A combination of cyclophosphamide, epirubicin, and 5-fluorouracil.
[e]A combination of adriamycin, cyclophosphamide, and paclitaxel.
[f]A combination of cyclophosphamide and adriamycin.
[g]A combination of cyclophosphamide and docetaxel.

Specifically, most (81%) of the women in the breast cancer group were not employed outside of home, whereas more than 60% of the women in the healthy control group were employed as part-time or full-time workers. With regard to health-related characteristics, about 50% of women in each group were premenopausal, and most participants did not report any comorbid conditions. The majority (78%) of breast cancer participants had mastectomy, including simple or modified radical mastectomy. All breast cancer participants were newly diagnosed with localized breast cancer (stage I–IIIa) and were treated with at least 3 cycles of chemotherapy involving intravenous administration of a combination of cytotoxic agents such as cyclophosphamide (Cytoxan, Endoxan), doxorubicin (Adriamycin) or epirubicin, 5-fluorouracil, and paclitaxel (Genexol) or docetaxel (Taxotere, Monotaxel). Five (16%) women were receiving adjuvant radiation therapy at the time of testing and 8 (25%) women were being treated with hormonal therapy. Only 1 woman was receiving both radiation and hormonal therapy after completion of chemotherapy.

Attention and Working Memory Deficits

The occurrence of attention and working memory deficits was defined using a norm-referenced cutoff point for each single cognitive test.[16,47,48] As presented in Figure 2, the breast cancer group showed significantly higher proportions of mild to moderate deficits in individual performance on the DSF ($\chi^2_{1,64} = 4.66$, $P < .05$) and the DSB ($\chi^2_{1,64} = 5.32$, $P < .05$) than the healthy control group did. Similarly, the breast cancer group showed higher rates of mild to moderate deficits in the COWA test part A ($\chi^2_{1,64} = 5.34$, $P = .07$) and the COWA test part B ($\chi^2_{1,64} = 11.98$, $P < .001$) as compared with the healthy control group (Figure 3). Behavioral performance on the ANT was not used to define the occurrence of cognitive deficits

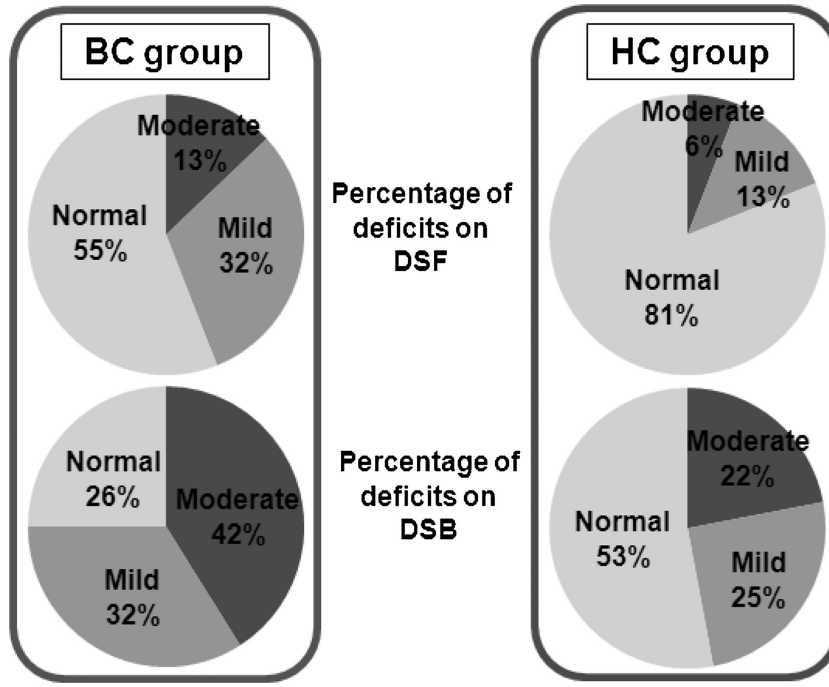

Figure 2 ■ Occurrence and severity of cognitive deficits related to digit span test performance in the breast cancer (BC) and healthy control (HC) groups. Mild deficits were defined by a cutoff score of 5 on the digit span forward (DSF) and 4 on the digit span backward (DSB); moderate deficits were defined by a cutoff score of 4 on the DSF and 3 on the DSB.

because of the absence of norm-referenced cutoff points for this test.

The severity of attention and working memory deficits was defined based on a comparison of raw scores on objective measures in breast cancer versus healthy control groups. Greater attention and working memory deficits were found in the breast cancer group than in the healthy control group. Specifically, women treated with chemotherapy for breast cancer showed lower scores on all cognitive tests than did healthy women without breast cancer (Table 2). Furthermore, the breast cancer

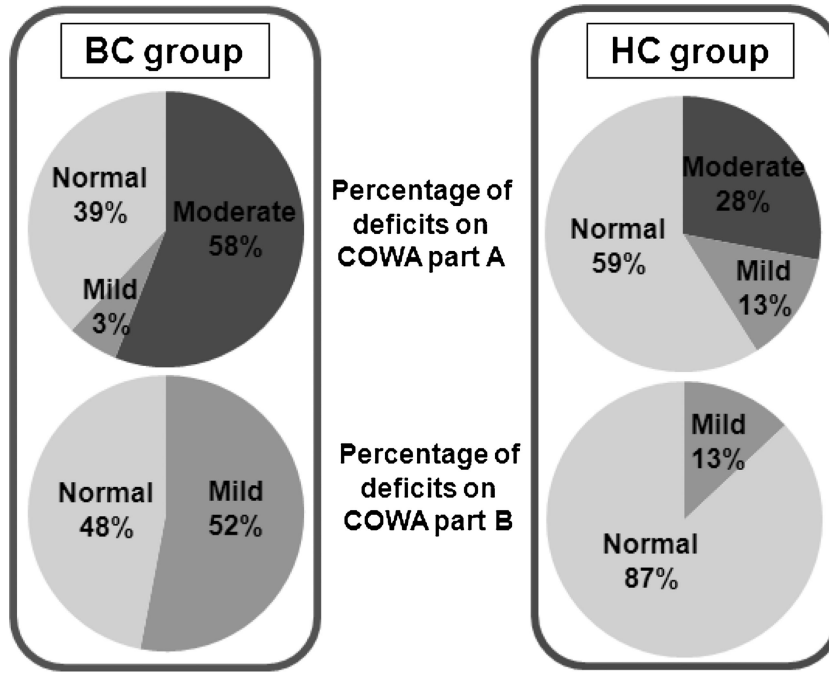

Figure 3 ■ Occurrence and severity of cognitive deficits related to controlled oral word association (COWA) test performance in the breast cancer (BC) and healthy control (HC) groups. Mild deficits were defined by a cutoff score of 28 for part A and 30 for part B; moderate deficits were defined by a cutoff score of 25 for part A. There is no suggested cutoff score for part B for defining moderate deficits.

Table 2 • Neurocognitive Performance on Attention and Working Memory Tasks

	Breast Cancer Group (n = 32)	Healthy Control Group (n = 32)
DSF	5.94 ± 0.26[a] (3.00 to 9.00)	6.81 ± 0.27 (4.00 to 9.00)
DSB	4.03 ± 0.24[a] (2.00 to 9.00)	4.81 ± 0.28 (3.00 to 9.00)
COWA part A	23.53 ± 1.85[b] (4.00 to 40.00)	33.81 ± 2.32 (13.00 to 67.00)
COWA part B	29.50 ± 1.49[b] (18.00 to 49.00)	39.84 ± 1.74 (22.00 to 63.00)
TCI	−2.50 ± 0.76[b] (−8.96 to 7.56)	2.50 ± 0.96 (−6.54 to 14.48)
ANT		
Overall error rate, %	4.70 ± 1.73[a] (0.00 to 31.67)	0.60 ± 0.13 (0.00 to 3.33)
Overall reaction time, ms	692.68 ± 22.21 (477.25 to 966.91)	636.64 ± 19.53 (464.31 to 891.98)

Values are presented as mean ± SD (range).
TCI = DSF + DSB + COWA part A + COWA part B (standardized scores).
Abbreviations: ANT, attention network test; COWA, controlled oral word association test; DSB, digit span backward; DSF, digit span forward; TCI, total cognitive index.
[a] $P < .05$.
[b] $P < .001$.

group had a significantly higher error rate across all trials in the ANT than the healthy control group did. A difference in mean reaction times between groups approached significance ($P = .06$). Cohen *d* effect size values for the group mean comparisons of cognitive test performance ranged from 0.53 to 1.13, suggesting medium to large effect sizes.

Relationships Between Neurocognitive Performance and Selected Factors

Older age was significantly related to worse performance on cognitive tests, except for error rates in the ANT, with moderate to moderately strong correlation coefficients ranging from 0.26 to 0.58 (Table 3). Higher education was also significantly associated with better performance on these selected tasks, and the strength of the relationships was moderately strong, ranging from 0.34 to 0.62. The presence of comorbidity was not associated with differences in neurocognitive test performance. Menopausal status was associated with cognitive performance, with postmenopausal women having lower mean scores on the TCI and slower mean reaction time on the ANT than the premenopausal women did ($P < .001$). However, these differences were no longer significant after controlling for age ($P > .1$).

Cultural characteristics were described in terms of cultural attitude on traditionally ascribed role performance, housework burden, and childrearing burden. As expected, the breast cancer and healthy control groups showed similar mean scores on these cultural characteristics. Specifically, the mean (SD) scores of cultural attitude on role performance were 3.23 (0.65) in the breast cancer group and 3.04 (0.72) in the healthy control group. The mean (SD) scores on the perceived burden associated with performing household tasks (Life Stress for Korean Housewives Instrument) were 2.09 (0.97) in the breast cancer group and 1.97 (0.84) in the healthy control group, representing an overall low level of housework burden. Mean (SD) childrearing burden scores were 2.03 (0.90) and 1.84 (0.62) in women treated for breast cancer and healthy women without cancer, respectively. Of note, stronger collectivistic attitude on women's role performance was significantly correlated with lower scores on the DSB and the COWA test part A and part B and poorer (slower) reaction time on the ANT. Small but significant correlations were found between childrearing burden and neurocognitive test performance. As presented in Table 3, greater childrearing burden was significantly related to worse performance on the COWA test part A and lower score on the TCI across all participants. A significant, positive correlation was found between housework burden and childrearing burden ($r = 0.63$, $P < .001$).

Table 3 • Correlations of Neurocognitive Measures With Selected Demographic and Cultural Variables

	Age	Education	Cultural Attitude on Role Performance	Housework Burden	Childrearing Burden
DSF	−0.33[a]	0.35[a]	0.02	0.08	−0.11
DSB	−0.38[a]	0.45[a]	−0.27[b]	−0.14	−0.24
COWA part A	−0.49[c]	0.62[c]	−0.33[b]	−0.15	−0.31[b]
COWA part B	−0.26[b]	0.34[a]	−0.26[b]	−0.02	−0.17
TCI	−0.46[c]	0.57[c]	−0.30[b]	−0.10	−0.28[b]
ANT error rate	0.16	−0.13	−0.04	−0.12	0.17
ANT reaction time	0.58[c]	−0.46[c]	0.37[a]	0.08	0.10

TCI = DSF + DSB + COWA part A + COWA part B (standardized scores).
Abbreviations: ANT, attention network test; COWA, controlled oral word association test; DSB, digit span backward; DSF, digit span forward; TCI, total cognitive index.
[a] $P < .01$.
[b] $P < .05$.
[c] $P < .001$.

However, housework burden was not significantly correlated with objective test performance.

Predictors of Attention and Working Memory Function

Multiple regression analyses were performed to determine the possible predictors of cognitive performance, using the composite score of TCI and the overall mean reaction time on the ANT as dependent variables. Based on the correlation analyses, cultural attitude on women's role performance and childrearing burden were selected as independent variables in the regression models with 4 other variables, breast cancer (patient, healthy control), age, years of education, and employment status (employed, unemployed). As shown in Table 4, these 6 variables accounted for 56% of the variance in scores on the TCI (multiple $R = 0.75$, $F_{6, 57} = 12.04$, $P < .001$). Being in the breast cancer group ($t = -4.00$, $P < .001$), older age ($t = -2.58$, $P < .05$), and less education ($t = 2.41$, $P < .05$) were found to be significant predictors of lower scores on the TCI. Similarly, the same 6 variables explained 52% of the variance in the overall mean reaction time on the ANT (multiple $R = 0.72$, $F_{6, 57} = 10.13$, $P < .001$). In this regression model, being in the breast cancer group ($t = 2.23$, $P < .05$), older age ($t = 4.80$, $P < .001$), and strong cultural attitude of women's role performance ($t = 2.32$, $P < .05$) were found as significant predictors of slower reaction times on the ANT (Table 5). Taken together, being in the breast cancer group was found to be a significant predictor of attention and working memory deficits. As expected, older age and less education were important factors to explain worse cognitive test performance. Of the cultural characteristics, collectivism-based attitude toward women's role performance contributed to poorer performance on attention and working memory tests in Korean women.

Discussion

The present study is the first to describe cognitive deficits in Korean women treated with chemotherapy for early-stage breast cancer. Findings from this study demonstrate that chemotherapy-treated Korean breast cancer survivors had a higher occurrence and greater severity of deficits in attention and working memory function than did healthy Korean women not exposed to cancer diagnosis and treatment. This finding is consistent with previous studies conducted in other ethnic/racial populations indicating that women exposed to chemotherapy for breast cancer may be susceptible to posttreatment cognitive deficits.[8,9,11,14] However, the effect sizes for cognitive deficits were different from those reported in studies conducted in Western countries. Mild to moderate cognitive deficits were commonly reported in studies with Western women treated for breast cancer as compared with matched controls.[49] In contrast, medium or large effect sizes for cognitive deficits were found in this study with Korean women. Taken together, these results reflect the presence of cognitive deficits in women treated for breast cancer across studies, but the magnitude of the deficits is larger among Korean women, relative to Western women, after breast cancer treatment.

The observed higher severity of cognitive dysfunction in Korean breast cancer survivors suggests the possibility of cultural differences in postchemotherapy cognitive deficits. Specifically, Korean women may have greater deficits in attention and working memory function than do women in Western countries. In addition to the differences in effect sizes noted above, it measures was previously found that performance on the same cognitive was different between these culturally separated groups. In a study performed by Vearncombe et al,[7] Western women exhibited better performance on the DSB and COWA tests 1 and 6 months after chemotherapy when compared with the Korean breast cancer participants in this study. Interestingly, these differences in cognitive responses were shown regardless of sample similarities in age, years of education, stage of cancer, receiving chemotherapy, and time since treatment.

A recently published study by Cheung et al[50] provided evidence of qualitatively different experiences with cognitive deficits depending on cultural contexts. They reported that *chemobrain* or even *cognitive function* was not a familiar term in Asian women, unlike Western women with breast cancer. Furthermore, Asian women reported that cognitive deficits were closely related to frustration or guilt about their functional inability to perform their duties for spouse and children as expected. Future research is needed to examine both actual and perceived cognitive function in Eastern and Western women treated for breast cancer.

Table 4 • Multiple Regression Analysis of TCI to Identify Demographic and Cultural Predictors

	Scores of the TCI		
	b (SE)	β	*P*
Breast cancer	−4.53 (1.13)	−.42	.000
Age	−0.21 (0.08)	−.31	.012
Education	0.55 (0.23)	.28	.019
Employment status	0.65 (1.11)	.06	.559
Cultural attitude on women's role performance	−0.86 (0.74)	−.11	.250
Childrearing burden	−0.41 (0.68)	−.06	.544

Multiple $R = 0.75$, $R^2 = 0.56$, $F_{6,57} = 12.04$, $P < .001$.
TCI = DSF + DSB + COWA part A + COWA part B (standardized scores).
Abbreviations: ANT, attention network test; COWA, controlled oral word association test; DSB, digit span backward; DSF, digit span forward; TCI, total cognitive index.

Table 5 • Multiple Regression Analysis of Reaction Time on the ANT to Identify Demographic and Cultural Predictors

	Scores of the ANT		
	b (SE)	β	*P*
Breast cancer	58.29 (26.15)	.24	.030
Age	9.05 (1.88)	.59	.000
Education	−1.50 (5.29)	−.03	.777
Employment status	−24.29 (25.59)	−.10	.346
Cultural attitude on women's role performance	39.49 (17.05)	.22	.024
Childrearing burden	−19.27 (15.63)	−.12	.223

Multiple $R = 0.72$, $R^2 = 0.52$, $F_{6,57} = 10.13$, $P < .001$.
Abbreviation: ANT, attention network test.

Chemotherapy may contribute to the observed cognitive deficits after breast cancer treatment in Korean women. Even after controlling for possible covariates, worse cognitive test performance was still found in the chemotherapy-treated breast cancer group than in the healthy women not exposed to any cancer diagnosis and treatment. However, because of an absence of a treatment-matched breast cancer control group, it is not clear whether cognitive function was affected by disease, treatment, or combined effects. Nevertheless, this finding still provides important evidence that chemotherapy-treated Korean breast cancer survivors are vulnerable to negative cognitive outcomes. Therapeutic interventions to counteract cognitive problems need to be considered for Korean breast cancer survivors over the course of treatment.

As expected, age and education were found to be significant predictors of cognitive function. Previous studies in Western women with breast cancer reported that older age and lower educational level yielded worse cognitive performance after and even before breast cancer diagnosis and treatment.[11,15] Interestingly, the effect of age on cognitive function was moderate to large in this study despite the absence of participants 65 years or older. The participants of this study consisted of middle-aged women ranging in age from 31 to 61 years, whereas the above-noted studies showed a relatively wide range of age distribution of participants. This finding highlights a need to identify a "critical age" at which cognitive vulnerability may develop even in middle-aged Korean women with breast cancer.

The presence of comorbid condition was not significantly associated with neurocognitive test performance. However, the small number of women with comorbidity in this study might not be sufficient to detect an effect on neurocognitive performance. In addition, menopausal status was not related with performance on objective measures after controlling for age, suggesting that in this sample, age per se was a stronger predictor of neurocognitive functioning than menopausal status was.

A significant relationship between childrearing burden and cognitive function was found across all participants. That is, Korean women who perceived greater childrearing burden showed worse cognitive performance and vice versa. In contrast, housework burden was not significantly correlated with cognitive test performance, although it was highly correlated with childrearing burden. This finding can be interpreted as follows. Both doing housework and rearing children have been regarded as perceived burden associated with women's primary responsibility. However, the level of mental effort required to perform these duties may be different. Possibly, childrearing is more likely than housework to require considerable mental energy and therefore affect actual responses in attention and working memory. This may be an appreciable issue in explaining the uniqueness of greater cognitive deficits in Asian, especially Korean, women treated for breast cancer. Although it is not clear whether childrearing burden resulted from lack of support for childrearing or from an overwhelming sense of responsibility for such duties, nursing interventions targeting women's childrearing burden can be useful in supporting their attention and working memory function.

Collectivism-based attitude on women's role performance was also significantly correlated with performance on cognitive tasks. Stronger tendency toward collectivism was a significant predictor of cognitive deficits in Korean women. The prime cultural value of collectivism is self-restraint in thoughts, feelings, and actions to support in-group harmony.[28,30] When women encounter life challenges such as having breast cancer, this cultural perspective may be an additional cognitive burden requiring more mental effort in attempting to perform their usual activities and responsibilities for their families. Thus, a collectivist tendency may help explain the differences in cognitive function between Western and Eastern women with breast cancer. However, to understand the uniqueness of cognitive deficits in Asian women with breast cancer, a foremost research priority is to further explore how cultural attributes might increase risk for neurocognitive alterations in attention and working memory processes over the entire course of cancer diagnosis and treatment.

Certain limitations need to be considered when interpreting the findings in this study. First, this study used a cross-sectional design, which limits the investigation of cognitive changes over time owing to an absence of baseline data before initiation of any treatment. Therefore, it is not possible to verify the changing pattern of cognitive function across the overall trajectory from diagnosis through treatment. Second, this study did not have a treatment-matched comparison group of women with breast cancer not treated with chemotherapy. Our findings were obtained from women treated with varying chemotherapy regimens, and thus, it remains unclear whether cognitive deficits may be associated with a specific drug regimen or even other

treatment modalities. Finally, a small number of women in this study were treated with radiation therapy and endocrine therapy in addition to chemotherapy, and the possible influence of such combination therapies on neurocognitive function needs to be examined in larger samples.

Despite the above limitations, this study provides first evidence of attention and working memory deficits in Korean women after chemotherapy for breast cancer and highlights the necessity of assessing cultural characteristics to design appropriate interventions to improve cognitive function in breast cancer patients and survivors from a collectivist culture. These findings also underscore the importance of gaining a deeper understanding of chemobrain in varying ethnic minority women with breast cancer.

■ Clinical Implications

The results emphasize the need for awareness of cognitive deficits in breast cancer patients and survivors from non-Western countries such as South Korea. Cognitive test performance observed in Korean women treated with chemotherapy for breast cancer was poorer than that of disease- and race-matched controls, and the effect sizes for cognitive deficits were moderate to large. The findings indicate that healthcare providers need to seriously recognize that chemotherapy-treated Korean breast cancer survivors may be at high risk for cognitive deficits and thus precisely assess changes in their cognitive performance over time. Next, the findings can be used to improve patient education about cognitive symptoms that can occur after treatment. As yet there, is little awareness of compromised cognitive function in relation to breast cancer and its treatment among Korean women. The occurrence and severity of cognitive deficits reported in this study can be used to help Korean women with breast cancer realize the importance of being active in monitoring their cognitive function. Last, this study demonstrates that cultural characteristics may be important factors affecting reduced cognitive function. Healthcare providers need to consider that women may differently experience cognitive deficits as a result of being confronted with differing cognitive and behavioral demands naturally ascribed from their cultural contexts. Especially, women with a strong tendency toward collectivism and who have childrearing burden are likely to experience poor cognitive performance after treatment. Healthcare providers need to assess the unmet need for support and provide appropriate interventions to these groups of women. To this end, effort needs to be made to develop, implement, and evaluate appropriate cultural interventions to counteract cognitive deficits and associated detrimental effects on intended behaviors in everyday situations.

ACKNOWLEDGMENTS

We thank the Behavioral Cooperative Oncology Group, Mary Margaret Walther Program for Cancer Care Research, which provided a predoctoral and postdoctoral fellowship for financial support and research training.

References

1. Jung KW, Park S, Kong HJ, et al. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2009. *Cancer Res Treat*. 2012;44(1):11–24.
2. Surveillance, Epidemiology, and End Results (SEER) Program. SEER stat fact sheets: breast 2012. http://seer.cancer.gov/statfacts/html/breast.html. Accessed July 27, 2012.
3. Im EO, Lee EO, Park YS. Korean women's breast cancer experience. *West J Nurs Res*. 2002;24(7):751–765.
4. Choi KS, Kim MS, Lee IJ, Han SY, Park JA, Lee J. Analysis of nursing intervention studies on patients with breast cancer in Korea. *J Korean Oncol Nurs*. 2011;11(1):74–82.
5. Lee E. Relationships of mood disturbance, symptom experience, and attentional function in women with breast cancer based upon the theory of unpleasant symptoms. *J Korean Acad Nurs*. 2005;35(4):728–736.
6. Moon S, Kim S, Kim S. Perceived cognitive function and related factors in Korean women with breast cancer. *Asian Nurs Res*. 2011;5(2):141–150.
7. Vearncombe KJ, Rolfe M, Wright M, Pachana NA, Andrew B, Beadle G. Predictors of cognitive decline after chemotherapy in breast cancer patients. *J Int Neuropsychol Soc*. 2009;15(6):951–962.
8. van Dam FS, Schagen SB, Muller MJ, et al. Impairment of cognitive function in women receiving adjuvant treatment for high-risk breast cancer: high-dose versus standard-dose chemotherapy. *J Natl Cancer Inst*. 1998;90(3):210–218.
9. Wefel JS, Saleeba AK, Buzdar AU, Meyers CA. Acute and late onset cognitive dysfunction associated with chemotherapy in women with breast cancer. *Cancer*. 2010;116(14):3348–3356.
10. Saykin AJ, McDonald BC, Ahles TA, et al. Altered brain activation following systemic chemotherapy for breast cancer: interim analysis from a prospective study. *J Int Neuropsychol Soc*. 2006;12:131.
11. Ahles TA, Saykin AJ, McDonald BC, et al. Longitudinal assessment of cognitive changes associated with adjuvant treatment for breast cancer: impact of age and cognitive reserve. *J Clin Oncol*. 2010;28(29):4434–4440.
12. Boykoff N, Moieni M, Subramanian SK. Confronting chemobrain: an in-depth look at survivors' reports of impact on work, social networks, and health care response. *J Cancer Surviv*. 2009;3(4):223–232.
13. Reid-Arndt SA, Yee A, Perry MC, Hsieh C. Cognitive and psychological factors associated with early posttreatment functional outcomes in breast cancer survivors. *J Psychosoc Oncol*. 2009;27(4):415–434.
14. Wieneke MH, Dienst E. Neuropsychological assessment of cognitive functioning following chemotherapy for breast cancer. *Psychooncology*. 1995;4(1):61–66.
15. Cimprich B, So H, Ronis DL, Trask C. Pre-treatment factors related to cognitive functioning in women newly diagnosed with breast cancer. *Psychooncology*. 2005;14(1):70–78.
16. Lezak MD, Howieson DB, Loring DW. *Neuropsychological Assessment*. 4th ed. Oxford, UK: Oxford University Press; 2004.
17. Stern Y. What is cognitive reserve? Theory and research application of the reserve concept. *J Int Neuropsychol Soc*. 2002;8(3):448–460.
18. Bender CM, Paraska KK, Sereika SM, Ryan CM, Berga SL. Cognitive function and reproductive hormones in adjuvant therapy for breast cancer: a critical review. *J Pain Symptom Manage*. 2001;21(5):407–424.
19. Wefel JS, Schagen SB. Chemotherapy-related cognitive dysfunction. *Curr Neurol Neurosci Rep*. 2012;12(3):267–275.
20. McDonald BC, Conroy SK, Ahles TA, West JD, Saykin AJ. Gray matter reduction associated with systemic chemotherapy for breast cancer: a prospective MRI study. *Breast Cancer Res Treat*. 2010;123(3):819–828.
21. James W. *The Principles of Psychology*. New York, NY: H. Holt and Company; 1890.
22. Kaplan S, Kaplan R. *Cognition and Environment*. Ann Arbor, MI: Ulrich; 1989. Original work published in 1982, New York, NY: Praeger.
23. Posner MI. *Attention in Cognitive Neuroscience: An Overview*. Cambridge, MA: MIT Press; 1995.
24. Smith EE, Jonides J. Storage and executive processes in the frontal lobes. *Science*. 1999;283(5408):1657–1661.
25. Awh E, Vogel EK, Oh SH. Interactions between attention and working memory. *Neuroscience*. 2006;139(1):201–208.

26. Knudsen EI. Fundamental components of attention. *Annu Rev Neurosci*. 2007;30:57–78.
27. Fan J, McCandliss BD, Sommer T, Raz A, Posner MI. Testing the efficiency and independence of attentional networks. *J Cogn Neurosci*. 2002; 14(3):340–347.
28. Nisbett RE, Peng K, Choi I, Norenzayan A. Culture and systems of thought: holistic versus analytic cognition. *Psychol Rev*. 2001;108(2): 291–310.
29. Hofstede G. *Cultures and Organizations: Software of the Mind*. London, England: McGraw-Hill; 1991.
30. Cho GH. The Confucian origin of the East Asian collectivism. *Korean J Soc Pers Psychol*. 2007;2(4):21–53.
31. Suh S. A study of the meaning and the change of familism in Korea. *J Korean Home Manag Assoc*. 2003;21(4):93–101.
32. Moon EH. Women's attributes expected at home and at work. *Yonsei J Womans Stud*. 1995;1:76–99.
33. Park CS, Oh JA, Suh SR. A study of the housework hours and fatigue levels in middle-aged women. *J Korean Acad Womens Health Nurs*. 2000; 6(3):398–412.
34. Lu K, Lee K. A study of dual-earner couple's household work time and life satisfaction. *J Korean Home Manage Assoc*. 2004;22(5):265–281.
35. Cimprich B. Development of an intervention to restore attention in cancer patients. *Cancer Nurs*. 1993;16(2):83–92.
36. Ahn KH, Kim MS, Kim YS, et al. A neuropsychological study of frontal lobe function in obsessive-compulsive disorder. *J Korean Neuropsychiatr Assoc*. 2000;39(3):598–609.
37. Elashoff JD. *nQuery Advisor Version 7.0 User's Guide*. Boston, MA: Statistical Solutions; 2007.
38. Benton AL, Hamsher K. *Multilingual Aphasia Examination*. Iowa City, IA: AJA Associates; 1989.
39. Kim M. Impairment of working memory in patients with schizophrenia. *Korean J Health Psychol*. 2005;10(1):17–30.
40. Kang Y, Chin J, Na DL, Lee J, Park JS. A normative study of the Korean version of Controlled Oral Word Association Test (COWAT) in the elderly. *Korean J Clin Psychol*. 2000;19(2):385–392.
41. Kang IS. Research on the attitudes of work-family relationship and gender roles: comparative analysis between employed. *Democr Soc Policy Stud*. 2009; 15:237–274.
42. Park K. A study on the factors affecting time conflict of married women workers between work and family: focusing on the differences according to age groups and gender role attitude. *J Korean Women Stud*. 2009;25(2): 37–71.
43. Loewenthal KM. *An Introduction to Psychological Tests and Scales*. London, England: UCL Press; 1996.
44. Chon K, Kim K. Life stress and coping styles of Korean housewives. *Korean J Health Psychol*. 2003;8(1):1–39.
45. Pearlin LI, Scholler C. The structure of coping. *J Health Soc Behav*. 1978; 19(1):2–12.
46. Chun SY. *Relationship Between Stress Levels in Mothers of Disabled Children and Child's Dependence in Activities of Daily Living* [master's thesis]. Seoul, Korea: Sookmyung Women's University; 1984.
47. Ruff RM, Light RH, Parker SB, Levin HS. Benton Controlled Oral Word Association Test: reliability and updated norms. *Arch Clin Neuropsychol*. 1996;11(4):329–338.
48. Tombaugh TN, Kozak J, Rees L. Normative data stratified by age and education for two measures of verbal fluency: FAS and animal naming. *Arch Clin Neuropsychol*. 1999;14(2):167–177.
49. Falleti MG, Sanfilippo A, Maruff P, Weih L, Phillips KA. The nature and severity of cognitive impairment associated with adjuvant chemotherapy in women with breast cancer: a meta-analysis of the current literature. *Brain Cogn*. 2005;59(1):60–70.
50. Cheung YT, Shwe M, Tan YP, Fan G, Ng R, Chan A. Cognitive changes in multiethnic Asian breast cancer patients: a focus group study. *Ann Oncol*. 2012;23(10):2547–2552.