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THE RELATIONSHIP BETWEEN SOCIAL SUPPORT, OPTIMISM, AND COGNITION IN BREAST CANCER AND NON-HODGKIN'S LYMPHOMA SURVIVORS

by

Torricia Helena Yamada

An Abstract

Of a thesis submitted in partial fulfillment
of the requirements for the Doctor of
Philosophy degree in Psychological and Quantitative Foundations (Counseling Psychology)
in the Graduate College of
The University of Iowa

July 2011

Thesis Supervisors: Assistant Professor Natalie L. Denburg
Associate Professor Saba R. Ali

ABSTRACT

Cancer affects millions of people every year and survivorship has increased substantially recently. Two cancers that affect older adults is non-Hodgkin's lymphoma and breast cancer, yet very little research has focused on cancer and survivorship in late life. Emerging research has suggested that chemotherapy could have deleterious consequences on cognition, but few studies have considered the long-term neurocognitive sequelae of chemotherapy. Furthermore, social support and optimism have been independently examined as predictors of quality of life in cancer patients, but little research has considered the effects of these variables on other outcomes, such as cognition. The aim of this study was to gain a better understanding of the relationship between social support and optimism on cognition, specifically in non-Hodgkin's lymphoma (NHLS) and breast cancer survivors (BCS). It was hypothesized that social support and optimism would be positively related to cognition, and that social support would mediate the optimism-cognition relationship. Twenty-seven BCS (*M* age = 71.96), twenty-five female (*M* age = 69.76) and twenty-five male (*M* age = 65.28) NHLS groups were recruited. Each participant completed a three-hour standardized neuropsychological battery designed to evaluate a range of cognitive abilities involving attention, premorbid and current intellect, memory, language, visuospatial skills, and executive functioning, as well as self-report measures of mood, social support, and optimism. Performances on cognitive tests were within normal limits, but differences were found in aspects of executive functioning ($p < .01$) with the men outperforming women in the NHLS group. Women in the NHLS group performed better on a measure of executive functioning ($p < .05$) and visuospatial functioning ($p < .01$) than women in the BCS group. Women from both groups performed better than the male NHLS group on verbal learning and memory measures (all p's $< .05$). The groups did not differ on psychosocial variables. Correlations between psychosocial variables (i.e., social support and optimism) were variably related

to cognitive measures in both groups. Social support did not mediate the optimism-cognition relationship. This is the first study to consider the relationship between social support, optimism, and cognition and early interventions to improve cognition in cancer survivors is discussed.

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Graduate College
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CERTIFICATE OF APPROVAL

PH.D. THESIS

This is to certify that the Ph.D. thesis of

Torricia Helena Yamada

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To My Family -
My Mom and Dad, Pope and Darcie, Kirin, and the late Sora Jo

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ABSTRACT

Cancer affects millions of people every year and survivorship has increased substantially recently. Two cancers that affect older adults is non-Hodgkin's lymphoma and breast cancer, yet very little research has focused on cancer and survivorship in late life. Emerging research has suggested that chemotherapy could have deleterious consequences on cognition, but few studies have considered the long-term neurocognitive sequelae of chemotherapy. Furthermore, social support and optimism have been independently examined as predictors of quality of life in cancer patients, but little research has considered the effects of these variables on other outcomes, such as cognition. The aim of this study was to gain a better understanding of the relationship between social support and optimism on cognition, specifically in non-Hodgkin's lymphoma (NHLS) and breast cancer survivors (BCS). It was hypothesized that social support and optimism would be positively related to cognition, and that social support would mediate the optimism-cognition relationship. Twenty-seven BCS (*M* age = 71.96), twenty-five female (*M* age = 69.76) and twenty-five male (*M* age = 65.28) NHLS groups were recruited. Each participant completed a three-hour standardized neuropsychological battery designed to evaluate a range of cognitive abilities involving attention, premorbid and current intellect, memory, language, visuospatial skills, and executive functioning, as well as self-report measures of mood, social support, and optimism. Performances on cognitive tests were within normal limits, but differences were found in aspects of executive functioning ($p < .01$) with the men outperforming women in the NHLS group. Women in the NHLS group performed better on a measure of executive functioning ($p < .05$) and visuospatial functioning ($p < .01$) than women in the BCS group. Women from both groups performed better than the male NHLS group on verbal learning and memory measures (all p's $< .05$). The groups did not differ on psychosocial variables. Correlations between psychosocial variables (i.e., social support and optimism) were variably related

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CHAPTER I

INTRODUCTION

According to the American Cancer Society (ACS; American Cancer Society, 2010) it was estimated that there would be almost 1.5 million new cancer cases diagnosed in the United States in 2010, and over 570,000 American deaths the same year. Although these numbers are overwhelmingly bleak, survivorship has increased substantially in the past several years. Most currently, the 5-year survival rate for all diagnosed cancers rose to 68% between 1999 and 2005, a significant improvement from 50% in 1975-1977. Furthermore, in 2006, approximately 11.4 million Americans were living despite a history of cancer.

Seventy-eight percent of individuals diagnosed with cancer are over the age of 55 (ACS, 2010), and it is one of the leading causes of death in older adults, accounting for more than 22% of deaths in this population (U.S. Census, 2005). Furthermore, the probability of being diagnosed and treated for illness substantially increases with age, and 80% of older adults have at least one chronic health problem, including Alzheimer's disease (U.S. Census, 2005). Although there are a number of cancers that affect older adults, two cancers that are particularly prevalent in later adulthood are breast cancer and non-Hodgkin's lymphoma (NHL).

It was estimated that there would be over 207,000 and 60,000 new breast cancer and NHL diagnoses, respectively, in 2010 (ACS, 2010). Although mortality rates for cancer are, overall, decreasing based on early detection and technological advancements, it was anticipated that there would be almost 60,500 deaths as a result of these two cancers this past year. Survival rates are increasing for both of these cancers, but little has been done to examine survivorship.

Recently, evidence has emerged introducing and examining the phenomenon of "chemobrain," or possible cognitive dysfunction, as a result of chemotherapy treatments

for cancer. One recent example (Wefel, Witgert, & Meyers, 2008) from an online breast cancer survey found that of 471 respondents, 98% of participants reported a change in their thinking abilities during or after cancer treatment and 92% of five year survivors reported persistent problems. Furthermore, 62% of these respondents felt that this decline in their thinking abilities had an impact on their functioning and relationships, and they reported difficulty performing tasks on a daily basis.

A number of reviews have considered the effects of systemic therapies on all forms of cancer (Ahles & Saykin, 2001; Anderson-Hanley, Sherman, Riggs, Agocha, & Compas, 2003; Garofalo & Baum, 2001; Wefel, Kayl, & Meyers, 2004; Wefel et al., 2004; Wefel, et al., 2008). Unfortunately, very little research has highlighted NHL and, as a result, the limited studies in this population are forced to employ the breast cancer literature to support aims and hypotheses (e.g., Bellizzi, Miller, Arora, & Rowland, 2007). Auspiciously, breast cancer is likely examined more than any other cancer population, with many reviews featuring breast cancer alone (Bender, Paraska, Sereika, Ryan, & Berga, 2001; Falleti, Sanfilippo, Maruff, Weih, & Phillips, 2005; Olin, 2001; Reid-Arndt, 2006; Stewart, Bialajew, Collins, Parkinson, & Tomiak, 2006). Although all of these reviews have concluded that chemotherapy leads to cognitive decline in cancer patients, there are inconsistencies in both severity of dysfunction and cognitive domain affected. A thorough meta-analysis (Anderson-Hanley et al., 2003) examining all cancers and systemic treatments divided 29 studies and 838 patients into groups based on research method employed. Compared to published normative data, cancer patients performed worse in the domains of executive functioning (Cohen's d = -.93), verbal memory (Cohen's d = -.91), and motor functioning (Cohen's d = -.48); when compared to matched comparisons, cancer patients performed worse in the domains of information processing (Cohen's d = -.70) and executive functioning (Cohen's d = -.61). However, when being compared to oneself (i.e., longitudinal design), there were no significant differences in any cognitive domain, which the authors posited could be the result of

practice effects. Falleti and colleagues (2005) performed another meta-analysis with five cross-sectional studies that specifically examined cognition in breast cancer participants who had received chemotherapy. They found small to moderate effect sizes for multiple cognitive domains, including motor function (Cohen's d = -.51), spatial ability (Cohen's d = -.48), language (Cohen's d = -.41), memory (Cohen's d = -.26), executive functioning (Cohen's d = -.18), and attention (Cohen's d = -.03), but cautioned that the effect size findings of spatial ability and language were based on a small number of comparisons. A last meta-analysis (Stewart et al., 2006), also with breast cancer participants, evaluated seven studies and replicated the language and spatial ability findings. Additionally, declines in short-term memory were detected, though performances in all domains could not be classified as bona fide impairment (i.e., z-score < -2.0). Many of these studies examine cognition in cancer patients during or within a few months after treatment, and very few attempts have been made to examine cognition years after treatment.

Another review (Reid-Arndt, 2006) takes the extant breast cancer literature further and considers the neuropsychological implications of cancer treatments, such as vocational functioning and re-integration into the community. Not only does the review outline the possible cognitive consequences of chemotherapy, but it also highlights studies that have demonstrated returning to work as a predictive factor for positive experiences, and variables associated with returning to work, including disease severity, physical functioning, and fatigue. Furthermore, according to this review, changes in social and community functioning have been evaluated in breast cancer survivors, impacting both medical and psychological outcomes. Lastly, this review points to studies that assess quality of life in breast cancer patients post-treatment, many of which have shown that treatment, psychological, and interpersonal factors may predict quality of life in survivorship.

One recent qualitative study (Boykoff, Moieni, & Subramanian, 2009) interviewed 36 African-American and 38 White women who were at least one year post-

radiation and/or chemotherapy and 20 of these women were chosen for a focus group. Although data was collected via interview only, women who self-identified as experiencing chemobrain (e.g., increased forgetfulness and difficulties with abstract-reasoning) described frustration and fear about their diminished cognition. They additionally reported that they often felt that the medical community, friends, and family did not acknowledge the severity of their cognitive problems, which often left them feeling distressed, alone, and helpless. These survivors reported considerable difficulties returning to work, including decreased work efficiency, confusion, and memory loss. Another recent qualitative study (Munir et al., 2011) interviewed both breast cancer patients and health-care providers and found that perceived cognitive function is a serious concern for cancer survivors and there is a lack of information, advice, and support available to address these concerns. Furthermore, many of these breast cancer survivors felt that addressing their concerns regarding cognitive problems should be a priority.

Although these studies are promising in providing information about the needs and wants of cancer survivors, there is a clear lack of literature examining cognition in conjunction with quality of life and its causal variables. There is only one study (Reid-Arndt, Hsieh, & Perry, 2010) that has even considered the potential relationship between neuropsychological functioning and specific quality of life variables, including social support. This study evaluated women within one month post-chemotherapy, and then again at a 6-month and one-year follow-up. Each participant completed a neuropsychological battery and self-report questionnaires on perceived cognitive dysfunction, fatigue, and willingness to seek social support on three outcome variables: psychological functioning, social role functioning, and quality of life. It was found that self-reported cognitive difficulties were associated with poorer emotional well-being and individuals who demonstrated lower performances on verbal fluency tasks reported poorer functional well-being at 12 months post-chemotherapy. Less than 20% of the

cancer participants demonstrated decline over time and, in fact, most participants improved on neuropsychological tests by the 12 month post-chemotherapy time period.

Although the prior mentioned study is unique in its inclusion of neuropsychological testing data and specific quality of life variables, including social support, there still remains limited research in this area. Nine other studies (Downie, Mar Fan, Houede-Tchen, Yi, & Tannock, 2006; Hurria et al., 2006; Jenkins et al., 2006; Mar Fan et al., 2005; Mehnert et al., 2007; Quesnel, Savard, & Ivers, 2009; Schagen et al., 2002; Wefel, Lenzi, Thierault, Davis et al., 2004; Wefel, Saleeba, Buzdar, & Meyers, 2010) have examined quality of life and cognition, though there are a number of faults with the methodology of these studies. First, all of these studies equate functioning to quality of life, using a single measure of overall functioning and interpreting findings as quality of life, though functioning and quality of life are clearly not synonymous; rather functioning is simply one part of quality of life (e.g., Ware, 1991). Additionally, no research has considered how other specific variables of quality of life, such as social support and optimism, might correlate with or affect cognition in cancer patients and survivors. Due to this lack of information, therapeutic implications are often overlooked. Similar to the review studies, these specific evaluations of cognition in cancer patients yield inconsistent findings, but do provide a glimpse into the relationship between cognition and overall functioning. Specifically, all nine studies demonstrate cognitive changes in breast cancer patients, yet fail to directly relate cognitive decline with functional well-being.

Social support and optimism have been assessed thoroughly and individually in breast cancer patients (e.g., Carver et al., 2005; Mehnert & Koch, 2007), especially in terms of how these variables affect quality of life aspects. Overall, studies have shown that social support and optimism independently improve different aspects of quality of life in breast cancer patients. There have even been studies that specifically examined the relationship between social support and optimism on specific outcomes, such as distress

and functioning (Friedman et al., 2006; Shelby et al., 2008; Trunzo & Pinto, 2003). However, there are inconsistencies in this literature based on subpopulations within the breast cancer population. For example, Shelby and colleagues (2008) found that social support moderates the optimism-distress relationship in, specifically, African-American breast cancer patients, and does not mediate this relationship as another study has shown (Trunzo & Pinto, 2003). While it might seem intuitive that individuals who are optimistic attract more people, thus fostering social support, research (Brisette, Scheier, & Carver, 2002; Dougall, Hyman, Hayward, McFeeley, & Baum, 2001) has also specifically demonstrated this positive correlation in times of trauma. That is, individuals who are more optimistic utilize and identify social support more readily in times of trauma, such as a breast cancer diagnosis.

A last notable area of research has considered the role of social support and optimism on cognition in older adults. High levels of social support have been shown to promote successful aging (e.g., Fillit et al., 2002), in that individuals who have better social support not only age better, but also have less cognitive and functional difficulties throughout the lifespan. Although the reasoning for these findings is unknown, it has been postulated that social support and activity may stimulate mental processes, thus facilitating neural growth (Gow, Pattie, Whiteman, Whalley, & Deary, 2007; Zunzunegui, Alvarado, Del Ser, & Otero, 2003). The few studies that have incorporated optimism into cognitive research have focused mainly on how it might help individuals cope with cognitive impairment (McIlvane, Popa, Robinson, Houseweart, & Haley, 2008). One study, in particular, has considered the relationship between optimism and cognition (Bain et al., 2003), but focused only on the possibility that better cognition in childhood could lead to the development of optimism.

There is a clear lack of research examining cognition and quality of life variables, as well as long-term survivorship studies, especially with older adults. The aim of the present study was to gain a better understanding of the relationship between social

support, optimism, and cognition, specifically in NHL and breast cancer survivors. A better understanding of this relationship could help employ early interventions and provide additional information on the effects of chemotherapy and possible ways to influence cognition. It was hypothesized that both different aspects of social support and optimism would be positively related to cognition (i.e., attention, language, visuospatial skills, memory, and executive functioning), and that social support would mediate the optimism-cognition relationship. Furthermore, very little attention has been paid to long-term survivorship, and this study intended to add to the current breast cancer literature by describing both cognition and quality of life variables, specifically social support and optimism, in long-term survivorship. Lastly, based on the limited information on NHL, this study sought to provide additional descriptive and outcome data on NHL survivors.

CHAPTER II

LITERATURE REVIEW

The purpose of studying social support and optimism and the relationship of these variables to cognition is to help determine how to improve an aspect of quality of life in cancer patients. That is, what can be done from a therapeutic perspective to improve overall well-being in cancer patients by considering cognition? To better understand this relationship, it is important to delineate not only cognitive functioning, but also how social support and optimism affect quality of life in cancer patients.

Although it is notable that one recent study considered the impact of cognitive dysfunction on support seeking and social well-being (Reid-Arndt et al., 2010), to date, no other research has examined the influence of social support and optimism on cognition in cancer patients. Even generally examining the literature on cognition, cancer, and quality of life produces minimal results, as the majority of these studies focus on the health status and quality of life in pediatric cancer survivors (e.g., Pogany et al., 2006). In addition to the prior mentioned the study by Reid-Arndt and colleague (2010), there are a few exceptions to this; nine studies have examined cognition in conjunction with one aspect of quality of life, often using a single self-report measure of overall functioning (Downie et al., 2006; Hurria et al., 2006; Jenkins et al., 2006; Mar Fan et al., 2005; Mehnert et al., 2007; Quesnel et al., 2009; Wefel, Lenzi, Theriault, Davis et al., 2004; Wefel, et al., 2010). Although these studies will be detailed and are unique in their attempt to better understand cognition in conjunction with functioning, the use of a general functional questionnaire when assessing quality of life lacks the specificity necessary to guide therapeutic interventions. That is, although it is clearly important to identify how chemotherapy affects cognition and daily functioning, other psychosocial variables (e.g., social support) that can be easily altered in therapy should also be examined specifically. Furthermore, none of these studies question the relationship

between functioning and cognition, rather functioning is just another measurement variable. Because quality of life is a relatively broad domain, understanding the underlying variables that may improve quality of life is integral. Thus, the purpose of studying social support and optimism is to help determine how to improve another aspect of quality of life in cancer patients and survivors.

Furthermore, the term quality of life has begun to umbrella a variety of heterogeneous research topics, such as happiness, satisfaction, and functioning (Taillefer, Dupuis, Roberge, & May, 2003). For example, some current studies measure overall functional well-being (e.g., Downie et al., 2006) via self-report extract findings and make general assumptions regarding quality of life (i.e., higher functional well-being means better quality of life). Although this may seem logical and could potentially be true, this approach does not capture other underlying variables that affect quality of life and is methodologically limiting. Such faulty interpretations make research application challenging (Ware, 1991). Thus, examining and reviewing quality of life literature becomes a trial that must encompass not just quality of life, but interpretations that affect and correlate with quality of life. As such, not reviewing the literature that includes functioning as a measure of quality of life would be an injustice. Rather, this is just a criticism of the current literature, which too often uses quality of life interchangeably with other terms, such as satisfaction and functional well-being.

Research on adult cancer has focused mainly on breast cancer, which is helpful for only one group of this study. Research on NHL is negligible, with existing studies relying heavily on breast cancer studies to support their aims and hypotheses. Accordingly, the research available on NHL will be detailed, but general applications must be made based on thorough reviews of the breast cancer research.

Due to the extant research in this area, this literature review will highlight the relevant research of social support, optimism, and cognition in breast cancer patients predominantly since 2000. Since the research in NHL is so minute, it will be discussed

first, but latter research on breast cancer should be considered for this population. Accordingly, the breast cancer research will be evaluated. Specifically, emerging research examining cognition in breast cancer patients and short-term survivorship will be addressed first. Next, the effects of social support on quality of life in breast cancer patients will be highlighted, in conjunction with research on social support and cognition. Likewise, the effects of optimism on quality of life in breast cancer patients will then be addressed, along with the minimal available optimism and cognition research. Finally, studies explicitly exploring the relationship between social support and optimism will be detailed. Thus, this literature review will highlight relevant available research to extrapolate these findings into the aims and hypotheses of the present study.

Non-Hodgkin's Lymphoma

New diagnoses of NHL were expected to affect about 66,000 individuals in 2010 (ACS, 2010). It is additionally estimated that 20,200 individuals diagnosed with NHL died this past year. In most cases of NHL, risk factors are unknown, with the exception of higher prevalence in those individuals with reduced immune function due to auto-immune diseases, such as the Epstein-Barr virus. Interestingly, incidence rates for NHL have decreased in men and have slightly increased in women in the past 30 years. The five-year survival rate for all forms of NHL is 67%, though mortality rates differ based on specific lymphoma form. Individuals diagnosed are often treated with chemotherapy, yet sometimes radiation therapy is used either alone or in combination with adjuvant chemotherapy. Stem-cell transplantation is often considered if the cancer persists or recurs.

Even though the incidence rates of NHL have nearly doubled since the early 1970s (ACS, 2010), there is an underwhelming amount of research devoted to the disease. In fact, the limited research that has been done with NHL populations are forced to employ the breast cancer research to support aims and hypotheses (e.g., Bellizzi et al.,

2007). Furthermore, the minimal research that does exist generally includes a variety of lymphoma patients. It is important to note that NHL is just one form of lymphoma, and is oftentimes less fatal and treated differently than other lymphomas. Conclusions based on other lymphoma populations must also consider the comorbid confounding variables (e.g., HIV) that are difficult to parse out from results (i.e., whether observed cognitive decline is due to HIV-related symptoms, chemotherapy, or lymphoma itself). Too, some forms of lymphoma (central nervous system lymphoma) use a number of systemic interventions, including total brain irradiation, which likely affects cognitive functioning in a different manner than chemotherapy alone. Only three studies (Bellizzi et al., 2007; Beser & Oz, 2005; McIllmurray et al., 2001) examine quality of life, social support, optimism, and/or cognition in NHL patients. Of these studies, only two (Beser & Oz, 2005; McIllmurray et al., 2001) include all lymphoma patients and, accordingly, include NHL, yet neither separate out findings based on specific lymphoma diagnosis. Thus, the only study that focuses specifically on NHL will be detailed.

Bellizzi and colleagues (2007) posited that NHL survivors experience both positive and negative life changes, and appraised these changes and contributing factors. Particularly, the authors identified specific changes and how they related to sociodemographic, disease-related, psychosocial, physical, and mental factors. Participants were adult NHL survivors, at least two to five years since diagnosis, aged 23 to 85 (M = 60 years). Of 744 eligible participants, 308 completed a packet of questionnaires that included measures of positive and negative changes, physical and mental health, optimism, and social support. Respondents characterized both positive and negative life changes as a result of their NHL diagnosis treatment; the most positive changes were associated with relationships and spiritual changes, and the most negative changes were related to work, finances, and sex life. Interestingly, though current research focuses on the positive changes cancer patients experience, this study demonstrated that NHL survivors had an equal magnitude of both positive and negative

changes. It was also found that physical and mental functioning significantly decreased in those with more negative changes, but was not associated with positive life changes. As expected, increased availability of social support was associated with significantly greater levels of overall positive changes in both life and relationships, and significantly lower levels of negative life changes in relationships and finances. Ironically, though participants that scored higher in optimism were more likely to report lower levels of negative life changes, this variable was not associated with endorsements of higher positive changes. A last interesting finding of this study was that older adult participants were less likely to ascribe to more positive life changes and fewer negative life changes as a result of their cancer experience (i.e., older adults seemed to be less affected by their cancer experience).

This study highlights the importance of increasing social support and its possible beneficial impact on quality of life. However, the role of optimism is less apparent. Optimism might be a particularly salient characteristic to diminish negative reactions and thoughts, but does not necessarily amplify or increase the magnitude of positive reactions and thoughts.

Although the work of Bellizi and colleagues (2007) can be characterized as invaluable for its exclusive examination of quality of life in NHL, it is not without limitations. Through no fault of their own, the authors have no research with which to compare their study with, and the exploratory and cross-sectional nature of their study makes causal implications complex. Furthermore, even the authors posit that their choice measures, specifically their cancer-related life impact measure, had limited psychometric properties. Lastly, males and Hispanics were significantly less likely to participate in this study, a finding with implications that cannot be ignored considering that cancer census information demonstrates different incidence rates based on gender and ethnicity.

Breast Cancer

It was estimated that there would be 207,000 new breast cancer cases among women and almost 2,000 in men in 2010 (ACS, 2010). Though it was anticipated that there would be about 40,000 breast cancer deaths in that year, mortality rates in the breast cancer population have been decreasing since the 1990s due to earlier detection, more advanced treatment options, and the decrease of hormone therapy in women (which has been linked to increased risk in breast cancer). Based on disease stage, treatment may involve lumpectomy, mastectomy, removal of underarm lymph nodes, radiation therapy, chemotherapy, hormone therapy, and/or targeted biologic therapy. Most individuals diagnosed with breast cancer will have some sort of surgery (a lumpectomy or mastectomy with or without the removal of lymph nodes), but other treatments are frequently utilized. Systemic therapies (radiation, chemotherapy, hormone therapy, and biologic therapy) are chosen based on patient needs, tumor size, and disease stage. They are often used in combination with one another; that is, a breast cancer patient might have surgery, radiation therapy, and chemotherapy. The 5-year survival rate for breast cancer has increased to 98% if the cancer is localized, but decreases to 23% if the cancer has spread significantly (i.e., to other organs).

Cognition

Technological advancements have paved the way for more highly developed systemic interventions for the treatment of breast cancer. From a critical and acute care perspective, such advancements have increased survivorship for patients. However, there are still short- and long-term consequences to these innovations. “Chemobrain” or “chemofog” is a term that was coined by cancer patients, specifically breast cancer patients, to describe the memory loss and attentional difficulties as a result of chemotherapy. It is unknown who is responsible for the term, but research has attempted to develop a better understanding of these cognitive complaints and the inception and

progression of “chemobrain.” Since such modern phenomena in survivorship are rather new, this research is in its infancy, and the extant literature examining breast cancer and cognition has been produced mainly in the new millennium. While the cognitive complaints are pervasive throughout different cancers, especially after the receipt of chemotherapy, mostly breast cancer patients have been studied. However, more efforts to document illness progression, side effects, and consequences of treatment among all cancer groups are promising. In fact, a multidisciplinary workshop aimed to expand chemotherapy and cognition research has implored researchers to consider cognitive function in cancer populations other than breast cancer (Tannock, Ahles, Ganz, & van Dam, 2004).

Since breast cancer patients have been the target population for this research, a number of studies have focused on the cognitive consequences of specific treatments for breast cancer, such as chemotherapy and hormone therapy (tamoxifen), for example. The majority of research has focused on the use of chemotherapy in a variety of capacities. Many studies compare and contrast breast cancer patients who have received chemotherapy to those who have not, including breast cancer patients who have received other forms of treatment and healthy matched comparisons (Bender et al., 2006; Brezden, Phillips, Abdolell, Bunston, & Tannock, 2000; Castellon et al., 2004; Donovan et al., 2005; Stewart et al., 2008). Other studies have compared patients who have received standard-dose versus higher doses of chemotherapy (Mehnert et al., 2007, Schagen et al., 2002). The majority of these studies have been longitudinal (Bender et al., 2006; Collins, MacKenzie, Stewart, Bielajew, & Verma et al., 2009; Hermelink et al., 2007; Hurria et al, 2006; Jenkins et al., 2006; Mar Fan et al., 2005; Quesnel et al., 2009; Reid-Arndt et al., 2010; Stewart et al., 2008; Wefel, Lenzi, Theriault, Davis et al., 2004; Wefel et al., 2010) or retrospective (Ahles et al., 2002; Brezden et al., 2000; Castellon et al., 2004; Cimprich, So, Ronis, & Trask, 2005; Mehnert et al., 2007; Schagen et al., 2002; Scherwath et al., 2006; Yamada, Denburg, Beglinger, & Schultz, 2010). Although rare, because of the high

prevalence of chemotherapy in the treatment of breast cancer, there are some studies that have specifically examined treatments other than chemotherapy, such as hormone therapy alone (Jenkins, Shilling, Fallowfield, Howell, & Hutton, 2004), including tamoxifen (Paganini-Hill & Clark, 2000). Overall, the majority of studies have found cognitive dysfunction following chemotherapy, but the results have been inconsistent in terms of affected cognitive domains and severity of impairment. Furthermore, recent studies have even noted cognitive dysfunction in breast cancer patients before the start of any treatment (Ahles et al., 2008; Hermelink et al., 2007; Quesnel et al., 2009; Wefel et al., 2010). From the limited studies that have looked at cognitive sequelae more than two years post-chemotherapy, there have also been inconsistencies in whether cognitive impairment persists (Ahles et al., 2002; Mar Fan et al., 2005, Schagen, 2002; Yamada et al., 2010).

This section will first highlight a recent study that is the first to consider the implications of social support on cognitive status and quality of life together. Next, the cognitive studies that incorporate functioning as a measure of quality of life, including those that are both cross-sectional and prospective, will be detailed. Then the remaining prospective studies will be briefly outlined. Lastly, the retrospective studies examining the effects of chemotherapy on cognition will be addressed. Although studies involving hormone therapy and tamoxifen are important, they will not be specifically investigated. This latter research, though integral and increasingly examined, is not within the scope of this study.

Reid-Arndt and colleagues (2010) sought to explore the relationship between neuropsychological functioning and quality of life variables and, more specifically, it was hypothesized that executive functioning and memory deficits would affect social role functioning and quality of life negatively. They assessed breast cancer patients within one month of chemotherapy (N = 46), again at a 6-month follow- up (N = 39), and one-year follow-up (N = 33) with a neuropsychological test battery, in addition to self-report

questionnaires on perceptions of cognitive deficits and fatigue via the Profile of Mood States – Short Form (POMS-SF, Baker et al., 2002), social support seeking through the Hesitation Scale (Farmer, Clark, & Sherman, 2003), the Beck Depression Inventory – II (BDI-II, Beck, Steer, & Brown, 1996), the Social Role Functioning questionnaire (Bettencourt & Sheldon, 2001), and the Functional Assessment of Cancer Therapy – Breast (FACT-B; Brady et al., 1997), and a one-item question asking about overall quality of life (i.e., 'In general, how satisfied are you with your overall quality of life?'). The average study participant age was 53 years old. With regards to neuropsychological functioning, cognitive impairment was defined as one standard deviation below published normative data (and severe impairment as 1.5 to 2.0 standard deviations below published normative data). It was demonstrated that a modest number of individuals showed impairment (ranging from 6 to 25%) at both the 6 and 12 month testing periods. When comparing the two testing periods, the number of individuals who evidenced decline had decreased performances in verbal unstructured memory (i.e., list memory), an executive functioning task, and phonemic fluency, but also had better performances on a processing speed/attention task, an executive functioning task, and category fluency. Group performances between baseline and six months revealed statistically significant better performances on immediate memory, delayed memory, and verbal fluency tasks. These improvements were also seen across between baseline and the 12-month period, in addition to better response inhibition performances. Self-reported cognitive deficits was inversely correlated to immediate memory performances at both the 6 and 12-month testing period, and lower scores on a response inhibition task was correlated with the endorsement of fatigue, depression, and self-reported cognitive problems. Lastly, a regression analyses, in which depression, social role functioning, and overall functioning were used as outcome variables revealed that increased depression was related to greater hesitation to seek support and increased self-reported fatigue. As expected, greater hesitation to seek social support was the sole predictor of poorer social role functioning

and overall functioning, and fatigue was associated with different aspects of well-being. Individuals who endorsed a poor quality of life on the single-item question had more cognitive complaints, and better emotional well-being was related to less cognitive complaints.

This is the first (and only) study to consider specific quality of life variables (i.e., social support) with neuropsychological findings. Although the majority of their findings regarding quality of life variables are consistent with the literature (e.g., functioning and well-being is associated with fatigue), they provide an additional consideration by highlighting how individuals who endorse poor overall functioning are less likely to seek support and individuals who are less likely to seek support endorse poor social role functioning. With the exception of self-reported cognitive complaints (which is an important consideration), the authors do not find significant relationships between the neuropsychological variables and other outcomes. The participants in their study demonstrated limited cognitive decline and/or impairment as a group, with only a modest number of individuals exhibiting decline. Consequently, finding a potential relationship between, for example, social support, and cognition may have been limited in their study design. Furthermore, the authors highlight their inability to account for practice effects over time without a comparison group. Regardless, their findings warrant a further examination of specific psychosocial variables in conjunction with cognition in future studies, especially with other cancer populations, such as long-term survivors and older adults.

Other studies (Downie et al., 2006; Hurria et al., 2006; Jenkins et al., 2006; Mar Fan et al., 2005; Mehnert et al., 2007; Quesnel et al., 2009; Schagen et al., 2002; Wefel, Lenzi, Theriault, Davis et al. 2004; Wefel et al., 2010) that claim to measure quality of life are often truly measuring functioning as part of the broader “quality of life” concept and, thus, lack the specificity to draw any conclusions about other variables related to quality of life besides functioning. However, these studies are important to outline, as the

use of these functional questionnaires have become typical in this research. Furthermore, albeit through a functional questionnaire, these studies are the only ones to consider and examine a relationship between any perception of "quality of life" and cognition. Of note, all of these studies report on "quality of life" as another measured variable or how cognition affects "quality of life," and not how "quality of life" affects cognition.

The most recent study (Wefel et al., 2010) was a prospective longitudinal study that examined breast cancer patients before, shortly after, and one-year after receiving standard dose chemotherapy. Participants were, on average, 49 years old, and evaluated with a battery of cognitive tests that assessed attention, processing speed, learning and memory, and executive functioning; they were also administered mood measures (the Beck Depression Inventory and State-Trait Anxiety Inventory) and the Functional Assessment of Cancer Therapy – Breast Module (Brady et al., 1997). Participants were classified as impaired if their performance was less than 1.5 standard deviations below expectations based on normative data on one or more tests, or less than two standard deviations below expectations on one test. At baseline (N = 42), 21% of participants were classified as impaired with no significant correlations with self-reported mood symptomatology or functioning variables. At the acute interval (approximately 1.6 months following chemotherapy treatment, N = 37), 65% of the participants demonstrated decline with 38% declining on one measure, 58% declining on two measures, and 4% declining on three measures. At approximately 13 months post-baseline (almost 8 months post-chemotherapy, N = 28), 61% of the participants demonstrated cognitive decline, and of these participants 71% demonstrated continued decline (i.e., had decline at the acute interval as well), 29% demonstrated new decline, and 39% were stable compared to the acute testing time period. Throughout the three time points, only 27% of the participants who completed the study did not show any decline. Longitudinal analyses found that the Trail Making Test – Part B and a verbal list-learning task were the most predictive of later cognitive decline. Again, in these latter

two testing intervals, mood and functioning were not related to cognitive decline. The authors concluded that the most commonly affected cognitive domains were learning and memory, executive function, and processing speed, Furthermore, older participants and individuals who were classified as impaired at baseline were at greater risk for developing late cognitive decline.

Another study published by this same group earlier (Wefel, Lenzi, Theriault, Davis et al., 2004) used similar methods to evaluate the cognitive sequelae of standard-dose chemotherapy in breast cancer longitudinally. Participants (N = 18) were administered serial neuropsychological evaluations at the start of chemotherapy, about three weeks after starting chemotherapy, six months after baseline, and one year post-chemotherapy (about 18 months post-baseline) and were approximately 45 years old. In addition to assessing attention, processing speed, learning, memory, executive function, and motor skill, research participants also completed two scales of the Minnesota Multiphasic Personality Inventory (Greene, 1991) and the Functional Assessment of Cancer Therapy (Cella, 1996). Again, participants were classified as impaired if their performance was less than 1.5 standard deviations below expectations based on normative data on one or more tests, or less than two standard deviations below expectations on one test. At baseline, 33% of the participants were classified as having impairment, mostly in verbal learning and memory. Between baseline and short-term follow-up, 39% of the participants experienced a decline on one measure, 11% on two measures, and 11% on three measures. Specifically, there were significant differences in attentional and processing speed performance. At long-term follow-up, 45% of the participants had stable cognitive function, 45% had improved cognitive function, and 10% had a mixed pattern (i.e., improvement on some tests, but stabilization on others). Regarding quality of life, as measured by self-reported functioning, there were no differences between participants who experienced cognitive decline/impairment in comparison to participants who remained stable across the assessment periods. The

authors concluded that, although there were no significant mean group declines across time, a subset of women indeed experienced cognitive problems, specifically in the domains of attention, learning, and processing speed. Of note, declines in cognitive function were often subtle and still fell within normal limits, thus in a clinical assessment such changes may be overlooked.

The authors of these studies (Wefel et al., 2004; Wefel et al., 2010) tout being the first group to examine cognitive function with pre-chemotherapy baseline testing and quality of life longitudinally, which is not only unique and important, but also evidence to the infancy of considering quality of life variables with cognition in research. Unfortunately, the study remains slightly deficient. Though the authors include a functional and mood measure, they do little analyses with them. It would only be slightly exaggerative to note that their inclusion is limited to a description of the measures and a few sentences in both the results and discussion; clearly, functioning is not an integral part of their hypotheses or analyses. With regards to cognition, the authors may have benefited from a methodological design that utilized matched comparisons or controls who did not receive chemotherapy instead of relying on normative data. Regardless of the limitations, the authors do provide evidence that research with cancer populations and cognition needs to re-define impairment; that is, cognitive problems may exist but might not meet criteria for clinical impairment, which nevertheless affects the everyday activities of patients who live with or survive cancer. Furthermore, they additionally argue the need for more survivorship research and potential effects of chemotherapy long-term.

Another recent study (Quesnel et al., 2009) in Canada hypothesized that breast cancer patients receiving chemotherapy (N = 41) would perform worse on neuropsychological measures compared to women receiving only radiotherapy (N = 40) and healthy controls at three time points (N = 23 and N = 22 matched to chemotherapy and radiotherapy participants, respectively): prior to the start of chemotherapy, right after

chemotherapy, and at a three-month follow-up. The mean age range for the groups were 50 to 58 and each participant completed a neuropsychological battery, a self-report questionnaire on cognitive functioning (e.g., whether patients perceived themselves as experiencing cognitive dysfunction), and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (Aarons et al., 1993). Generally, there were mixed results with the breast cancer groups performing both better and worse on tests across the three testing time periods with the greatest amount of change between baseline and post-treatment (versus post-treatment and follow-up); declines were demonstrated on measures of attention, verbal memory, and verbal fluency. On subjective measures, only the chemotherapy group indicated decreased levels of cognitive functioning and quality of life from baseline to post-treatment, but self-reported quality of life improved at follow-up. Lastly, in comparison to healthy controls, there were mixed results with both the chemotherapy and radiotherapy groups performing better and worse than the healthy control group. Interestingly, the chemotherapy group reported better cognitive functioning than their controls and the radiotherapy group reported worse cognitive functioning than their controls.

As with other studies, the authors (Quesnel et al., 2009) questioned the ecological validity of some of the neuropsychological measures, especially based on the numerous mixed results. Specifically, although they were able to replicate some findings from other studies (e.g., decreased performances on measures of verbal memory and fluency), the authors were unable to explain significantly better performance than controls on other measures. Furthermore, the authors do not address potential differences between the two cancer groups and do not consider the relationship between subjective and objective measures.

Another study (Mehnert et al., 2007) examined perceptions about cognitive deficits, fatigue, and health-related quality of life in conjunction with cognition. Forty-seven women diagnosed with breast cancer and treated with either standard-dose (N = 23)

or high-dose chemotherapy in Germany were recruited (*N* = 24), in addition to breast cancer patients not treated with either radiation therapy or surgery (*N* = 29) and were ages 52 to 55. Every participant completed a cognitive battery of tests in 18 parameters examining three broad cognitive domains: attention, memory, and executive functioning. Additionally, participants completed a questionnaire on self-perceived deficits in attention, a fatigue inventory, and the European Organisation for Research and Treatment of Cancer Quality of Life-Core questionnaire (Aarons et al., 1993). Global cognitive impairment, as measured by a *z*-score < -1.4 in at least four parameters, was found in 13% of the standard-dose patients, 8% in the high-dose patients, and 3% in the comparison group, but there were no significant differences between groups based on parameter or domain. In terms of quality of life, emotional functioning was rated the lowest in all three groups and there were no significant differences between groups. In the standard-dose group, impairments in working and verbal memory were significantly correlated with lower levels of physical and emotional functioning, and difficulties on a simple reaction task significantly related to poorer social functioning. In the high-dose group, attentional difficulties correlated to problems in role, emotional, and social functioning, and cognitive problems in executive functioning were significantly related to physical and social functioning problems. Only verbal memory was associated with all three self-report questionnaires (self-perceived cognitive deficits, fatigue, and quality of life). The authors concluded that overall neuropsychological functioning was not directly and resolutely associated with health-related quality of life.

The findings of this study (Mehnert et al., 2007) are slightly concerning, especially since the results conveyed more cognitive difficulty in standard-dose versus higher-dose chemotherapy patients; it is intuitive that higher dose treatment would affect cognition more, a prediction that is consistent with other literature. Additionally, this study was retrospective and had a limited number of participants in each group. Lastly, and perhaps most important, the measures used to assess quality of life were not only

limited, but vague. Nevertheless, the authors should be commended in their attempt to tap into other variables that contribute to quality of life, including fatigue and personal perceptions about cognitive deficits. Furthermore, they are the only study to highlight a relationship between deficits in processing speed and executive functioning and social role functioning.

A prospective study (Jenkins et al., 2006) in the United Kingdom sought to compare breast cancer patients being treated with chemotherapy (*N* = 85), breast cancer patient being treated with radiotherapy (*N* = 43), and a healthy control group (*N* = 49) at baseline, one month post-chemotherapy (six months after baseline) and 12 months post-chemotherapy (18 months after baseline). Women were aged 51 through 59 across the groups and were given a neuropsychological battery, a general health questionnaire that screens for comorbid nonpsychotic psychiatric symptoms, the Functional Assessment of Cancer Therapy questionnaire (Cella, 1996), and an endocrine measure. There were no significant differences between the groups across the three testing periods and, in fact, performances on six measures were better. There were significant differences between the radiotherapy and control group on measures of memory and attention with the control group outperforming the former. However, all groups showed reliable decline on most neuropsychological measures: 20% of chemotherapy patients, 26% of radiotherapy patients, and 18% of healthy controls. In both cancer groups, increased psychological distress was reported at baseline and dropped during the second evaluation for the radiotherapy group and the third evaluation for the chemotherapy group. Lastly, both cancer groups reported less cognitive dysfunction in their daily life than the healthy control group at baseline, but reported more at the second time point; the chemotherapy group returned to baseline by the third time point, but the radiotherapy group continued to describe cognitive problems on a daily basis. Functioning and fatigue was better and stable across time for the radiotherapy group. In the chemotherapy group, fatigue increased and functioning decreased at the second time point, but significantly improved

at one-year follow-up. There were no correlations between functioning and cognitive variables.

The authors (Jenkins et al., 2006) concluded that there is little evidence to suggest that there is meaningful change or impairment in cognition for women receiving chemotherapy in the UK. It is slightly concerning that the authors do not conjecture why their results are inconsistent with many studies that find some form of cognitive impairment; rather, they warn against over interpretation of cognitive findings in other studies. However, they do acknowledge that a small proportion of women do experience objective measurable change in concentration and memory. Although their quality of life measure was not correlated to any cognitive variables, it is unclear whether they attempted to analyze psychological distress in conjunction with cognition.

Another study (Hurria et al., 2006) highlighted the lack of current breast cancer research among older adults, and aimed to provide information on the longitudinal cognitive functioning in older breast cancer patients receiving chemotherapy. Twenty-eight patients with a mean age of 71 years were recruited and tested before and six months after chemotherapy; participants were given a 45-minute neuropsychological battery (initially two hours, but shortened based on patient feedback) and completed self-report measures regarding activities of daily living, comorbid conditions, general cognition, and the Functional Assessment of Cancer Therapy – Breast Module (Brady et al., 2007). The cognitive battery consisted of tests from seven domains: attention, verbal memory, visual memory, verbal, spatial, psychomotor, and executive function. Cognitive impairment was characterized as two standard deviations below the published normative mean on two or more measures. At baseline, 11% of the patients were impaired, compared to 29% after chemotherapy. Within-subject analyses revealed a two standard deviation decline on measures of visual memory, spatial function, psychomotor speed, and attention. Twenty-five percent of the patients demonstrated a one standard deviation decline since baseline in two or more domains, 21% in three or more domains, and 7% in

four or more domains compared to published normative data. Overall, there were no significant differences between baseline and after chemotherapy in functional status or any of the other self-report measures, with the exception of overall functioning, regardless of cognitive decline. The authors attributed this improvement in overall quality of life (as measured by functioning) to the termination of chemotherapy and the challenges associated with such treatment.

There are a number of limitations to this research (Hurria et al., 2006), including the minimal cognitive testing used to assess dysfunction. That is, although the battery was kept brief for the convenience of research participants, one measure was sometimes used to assess an entire domain, which is problematic. One test is not sensitive enough for researchers and clinicians to make attributions to an entire domain. Also, these authors used published normative data to characterize impairment instead of a control group matched across demographic characteristics; clearly the latter would be a more informative and sensitive characterization of possible dysfunction. Again, though standard, quality of life was measured via an overall functioning measure, which is not necessarily the same construct. Surprisingly, the authors do not report on baseline comorbid conditions, nor do they control for them; they only report that there were no significant mean changes longitudinally.

Downie and colleagues (2006) examined overall functioning, fatigue, menopausal symptoms, and cognitive complaints among breast cancer patients receiving chemotherapy. Twenty-one breast cancer participants with a median age of 47 years agreed to participate and were administered a thirty-minute fixed battery, completed an interview, and several self-report components of the Functional Assessment of Cancer Therapy scales, including the general questionnaire, and the fatigue and endocrine subscales (Cella, 1996). Fatigue was the most severe and frequently reported symptom, as well as menopausal symptoms. On the brief cognitive battery, participants had the most difficulty with language and memory, with language problems being more prevalent

and severe. However, cognitive problems self-reported during the interview in these domains were significantly higher than actual measured dysfunction. There was no correlation between functioning scores and cognitive problems. This study demonstrated that although cognitive problems do exist as a likely consequence of chemotherapy, they are not as severe or as frequent as self-reported problems.

A prior published study by this group (Mar Fan et al., 2005) evaluated breast cancer patients longitudinally shortly after the start of chemotherapy (*N* = 104) and at one- and two-year follow-up (*N* = 91 and *N* = 81, respectively) with matched controls (*N* = 102, *N* = 83, and *N* = 80, respectively). Each participant completed a functional assessment for fatigue, menopausal symptoms, and a general functional questionnaire (again, all self-report questionnaires were part of the Functional Assessment of Cancer Therapy questionnaire series; Cella, 1996), in addition to a short fixed neuropsychological battery, a sustained attention test, and the Trail Making Test. The median age of the patients and controls were 48 and 47 years, respectively. At baseline, patients experienced significantly more fatigue than controls, which improved over the two follow-ups, but continued to be significantly worse than controls over time. Similarly, because of chemotherapy-induced menopause, patients who received chemotherapy experienced significantly more menopausal symptoms than their matched comparison group. Quality of life, as assessed by the general functioning measure, was found to be worse for the cancer patients than for controls at the initial assessment, but resolved with similar levels reported by both groups at follow-up intervals. With regards to cognition, more cancer patients were classified as having moderate to severe cognitive dysfunction at baseline with improvement by the two year follow-up, as 16% of the sample were classified as having moderate to severe cognitive dysfunction at baseline (5% of controls), 4.4% at one-year follow-up (3.6% of controls), and 3.8% at two-year follow-up (0% of controls). Furthermore, 34.6% of the cancer patient sample was classified as having mild cognitive dysfunction at baseline (36.3% of controls), 30.8% at

one-year follow-up (19.3% of controls), and 21.3% at two-year follow-up (11.1% of controls). Patients also had poorer performance than controls on the Trails B subtest at the one- and two-year follow-up. Lastly, there was no relationship between fatigue, menopausal symptoms, and general functioning with any cognitive factors.

These studies (Downie et al., 2006; Mar Fan et al., 2005) successfully exemplify that perceptions of problems, including cognitive difficulties and fatigue, are quite high. However, in some cases, actual cognitive dysfunction does not match the severity of these complaints. Furthermore, though women continue to describe problems, actual cognitive dysfunction dissipates over time. This could be the result of a number of limitations of this study, particularly the abbreviated assessment battery that was used in both studies (i.e., sensitivity and specificity of the fixed battery and its use in a repeated measure design). It is also interesting that in the longitudinal study that uses a supposedly healthy control group, there is a significant amount of cognitive dysfunction found in this sample. The authors never posit why 36.3% and 5% of their controls demonstrate mild and moderate-severe cognitive dysfunction at baseline, respectively, which again points to the validity of the test battery to identify impairment and even potential confounding variables in recruitment and exclusionary methods.

A last study (Schagen et al., 2002) sought to delineate the late effects of adjuvant chemotherapy by exploring the effects of different chemotherapy regimens on neuropsychological functioning over time. Participants were enrolled from a prior study two years earlier and included three different chemotherapy groups, including patients who were treated with a high-dose cyclophosphamide, thiotepa, carboplatin chemotherapy (CTC, n = 22), a standard-dose flurorouracil, epirubicin, cyclophosphamide chemotherapy (FEC, n = 23), or a cyclophosphamide, methotrexate, 5-flourouracil chemotherapy (CMF, n = 31), and a control group that only received radiotherapy (n = 27). Each participant was evaluated approximately four years post-therapy and was given a neuropsychological battery, a questionnaire on cognitive

complaints, and a functional questionnaire (i.e., European Organisation for Research and Treatment of Cancer; Aarons et al., 1993) and the mean age range of the women was between 47 and 50. There were no differences between the three chemotherapy groups on subjective measures of cognitive complaints and functioning, and these reported complaints improved to the level of the control group compared to prior testing two years earlier (in which the FEC and CTC group endorsed more cognitive problems and the CTC group endorsed more functioning and mood problems). On neuropsychological testing, 3% of the CTC group was classified as impaired (compared to 11% on prior testing), 2% of the FEC group was classified as impaired (compared to 6% on prior testing), 4% of the CMF group was classified as impaired (compared to 8% on prior testing), and 3% of the control group was classified as impaired (compared to 2% on prior testing); furthermore, in general, all of the chemotherapy patients performances on cognitive testing improved, but the control group showed a slight deterioration. Consistent with prior testing, correlations between subjective and objective measures was low. The authors felt that objective cognitive problems throughout or shortly after chemotherapy are likely transient and do not differ significantly based on chemotherapy regimen received.

This study is an essential contribution to the extant research based on the need for more information about potential long-term cognitive sequelae of chemotherapy, but suffers from a number of challenges that researchers examining survivorship face. Not only is attrition high in this study, but almost half of the participants that were classified as impaired two years prior were unable/unwilling to be tested again for this study. The authors also expressed concern about practice effects, whether the neuropsychological measures chosen were sensitive enough for subtle changes, and small sample sizes.

The majority of the previously mentioned studies that incorporate some measure of functional well-being are longitudinal, and four other studies examine the effects of chemotherapy prospectively (Bender et al., 2006; Collins et al., 2009; Hermelink et al.,

2007; Stewart et al., 2008). The most recent study (Collins et al., 2009) evaluated the effects of chemotherapy in post-menopausal breast cancer patients before the start of chemotherapy (*N* = 45), one month after completing chemotherapy (*N* = 40), and approximately one year later (*N* = 40) by comparing them to breast cancer patients only receiving hormonal therapy (*N* = 34, *N* = 34, and *N* = 33, respectively). All of the women were between the ages of 50-65 with a mean age of 57. Each participant was given a neuropsychological battery that evaluated executive functioning, language, motor, processing speed, learning and memory, visuospatial function, working memory, and mood state. The two groups differed at baseline on some memory measures with the chemotherapy group outperforming the hormonal therapy group. Between the first two testing periods, the chemotherapy group demonstrated significantly higher rates of cognitive decline, specifically in the working memory and visual memory domains. By time three, there were no significant differences between the groups regarding decline or improvement across all domains. Additionally, there was only one significant difference on cognitive measures from baseline through one year follow-up, in which the chemotherapy group improved on measures of executive functioning. Lastly, a comparison between individuals receiving both chemotherapy and hormonal therapy was compared to individuals receiving chemotherapy only, and it was found that the individuals receiving both agents performed worse on processing speed and verbal memory tasks. The authors concluded that cognitive disruptions that are evidenced shortly after the completion of chemotherapy and/or through chemotherapy, generally, resolve after one year. Unfortunately, they do not discuss the potential everyday implications of the short-term dysfunction or why their one-year results are dissimilar to the limited retrospective studies that have found potential long-term impairment. Similar to other studies, the rate of attrition was high and, again, consistent with other studies, individuals who dropped out of the study were more likely to have performed poorer on neuropsychological tests at baseline.

Stewart and colleagues (2008) also found cognitive decline in breast cancer patients receiving chemotherapy with or without hormone therapy (*N* = 61) in comparison to patients receiving only hormonal treatment (*N* = 51). Participants were, on average, 58 and were given a cognitive assessment and a self-report measure of mood just prior to the start of chemotherapy (or hormone therapy) and following the last cycle of chemotherapy (or an equivalent time period for those receiving hormonal treatment). Although cognitive decline was three times more likely to occur in the patients who received chemotherapy, there were no mean differences between groups. Similar to other studies, individual cognitive declines were subtle and not likely to be characterized as bona fide cognitive impairment. Of note, stage of breast cancer clearly elicits specific treatments, such that individuals receiving chemotherapy as a treatment had a more advanced stage of breast cancer. A major limitation of this study was the time flexibility in the last testing session. Some participants were tested a mean 30.9 days after chemotherapy, but as little as six days after treatment lasting up to 179 days. There is minimal mention of how this discrepancy might affect cognition, and the researchers did not attempt to control for this variability.

Another study (Hermelink et al., 2007) in Germany conducted neuropsychological testing with breast cancer patients prior to the start of chemotherapy (*N* = 109) and approximately five months after baseline (n = 101), and also asked patients to report on perceived cognitive dysfunction and mood symptoms; the average age of the participants was 49. At baseline, 56% of patients were classified as having mild cognitive impairment (>1 test performance at least 1 standard deviation below published normative data) and 31% demonstrated moderate cognitive impairment (>1 test performance at least 2 standard deviations below published normative data). At the second testing period and after practice effects were taken into account, 22% of the patients showed deterioration, particularly on a fluency test, and 32% demonstrated improvement. Patients who performed well at baseline were at greater risk for showing decline over time. Although

subjective reports indicated greater perceived cognitive dysfunction over time, these reports were not significantly associated with poorer test performances, but were related to mood symptoms. Lastly, mood symptoms were also not related to cognitive deterioration. Based on baseline dysfunction, the authors questioned whether there is an alternative explanation for cognitive dysfunction in cancer patients beyond chemotherapy.

One last study (Bender et al., 2006) assessed the effects of adjuvant chemotherapy in three groups of breast cancer patients: those receiving chemotherapy, those receiving chemotherapy and tamoxifen, and those who did not receive chemotherapy or tamoxifen. The median age of the women were 43 to 44 years and cognition was assessed with a 90 minute battery of tests to assess attention, learning, memory, psychomotor speed, visuoconstructional ability, and executive function. Women who received chemotherapy both alone or in combination with tamoxifen demonstrated declines in memory compared to women who had not received chemotherapy, and there appeared to be more deleterious cognitive consequences with tamoxifen. This study was significantly limited by attrition. Specifically, by time three, over half of the participants had dropped out of the study or could not participate due to disease progression; subsequently, only 22 total participants of the original 46 from all three groups completed the entire study.

The remaining literature to be highlighted includes the retrospective studies, at least one year post-diagnosis, that examine cognition in breast cancer patients who received chemotherapy (Ahles et al., 2002; Brezden et al., 2000; Castellon et al., 2004; Scherwath et al., 2006; Yamada et al., 2010). The most recent study (Yamada et al., 2010) examined the neuropsychological outcomes of older breast cancer survivors, at least ten years post-chemotherapy. Breast cancer survivor participants (N = 30) were matched to a noncancer comparison group (N = 30) and administered a neuropsychological evaluation, in addition to a mood measure; the groups did not differ in terms of age (mean age 73), education, and estimates of premorbid intellect. The

noncancer comparison group outperformed the breast cancer survivor group in the domains of attention, psychomotor speed, and executive functioning, with the breast cancer survivor group performing .75 to 2.0 standard deviations below the comparison group. Notably, performances in both groups would not be considered impaired in a clinical setting (i.e., < 2.0 standard deviations below published normative data). The authors indicated that regardless of severity of impairment, the vulnerabilities that the cancer survivorship group demonstrated likely was noticeable and made everyday tasks more effortful. Although the authors are the first to look at long-term survivorship (e.g., more than ten years post-chemotherapy), there were a number of limitations to their study. First, there are methodological limitations, including no baseline data or comparisons to cancer survivors who have not received chemotherapy. Furthermore, the cancer survivor sample was highly educated and, thus, implications for the average cancer survivor are inferred.

Another recent study in Germany (Scherwath et al., 2006) examined the five-year cognitive effects of high-dose (N = 24) versus standard-dose chemotherapy (N = 23) in breast cancer survivors, in addition to a comparison breast cancer group only treated with surgery and radiation therapy (N = 29). Participants ranged in age from 52 to 55 and each participant was given a neuropsychological evaluation and survivors were classified as impaired if they performed < 1.4 standard deviations below published normative data. There were no differences between the three groups, but all groups were impaired on a simple reaction time attentional subtest and high-dose survivors demonstrated lower performance on a selective attention task. Furthermore, cognitive dysfunction was observed in about one-third of each patient group on memory tests. From a global neuropsychological impairment perspective, 13% of the standard-dose group was impaired, 8% of the high-dose group was impaired, and 3% of the comparison group. Notably, the standard dose group performed significantly better than normative data on reasoning subtests and the comparison group performed better on both a reasoning

subtest and a category fluency test, and no group showed impairment on tests of executive functioning. The authors concluded that the most frequently affected domain was attention.

Another study (Castellon et al., 2004) examined cognition in breast cancer survivors who had received chemotherapy with tamoxifen (*N* = 18) compared to survivors who had received chemotherapy without tamoxifen (*N* = 18), survivors who had received local therapy (*N* = 17), and matched comparisons without a history of breast cancer (*N* = 19) with a median age of 48. All breast cancer survivors were two to five years post-diagnosis. Participants completed a cognitive battery assessing verbal fluency, verbal learning, verbal memory, visual memory, visuospatial function, reaction time, psychomotor speed, and attention. They also completed self-report measures for mood and perceived cognitive function. Visual memory, visuospatial function, and verbal fluency differed between all groups, with survivors who had been treated with chemotherapy performing worse. There were also group differences between survivors who had additionally received tamoxifen compared to those who had not and matched comparisons in the domains of verbal learning, verbal fluency, and visuospatial functioning. Importantly, survivors who had not received chemotherapy at all performed as well, if not better, than matched comparisons. The ability for this study to evaluate so many different groups is invaluable, even though each group sample size is small. Unfortunately, the women in the study, on average, had a college education or higher and an estimated verbal intelligence quotient of 120 (over one standard deviation above average or 91st percentile), limiting generalizability.

Ahles and colleagues (2002) also examined long-term survivorship and cognition, at least five years post-diagnosis and on average 10 years post-treatment. Lymphoma survivors who had received chemotherapy (*N* = 36) and local therapy (*N* = 22), as well as breast cancer survivors who had received chemotherapy (*N* = 35) and local therapy (*N* = 35) were recruited, and completed a neuropsychological battery and a self-report measure

on perceived memory function; the mean age across groups ranged from 40 to 61. Those survivors who received chemotherapy performed significantly worse in the domains of verbal memory and psychomotor speed. Furthermore, for overall cognitive performance, survivors who had received chemotherapy were more than twice as likely to score in a low performance range; that is, 39% of participants who had received chemotherapy scored in the low performance range compared to only 14% of participants who received local therapy alone. Although this is one of the only studies to look at long-term survivorship, it suffers from the same pitfalls as other current literature. That is, there is no pre-diagnosis or pre-chemotherapy cognitive assessment, and the sample is heterogeneous in terms of treatment. Too, it is surprising that the authors failed to evaluate possible discrepancies between cancer populations, especially since their population is unique with the inclusion of lymphoma; rather, they limited their focus to treatment and global cognition only. Lastly, the authors did not consider potential gender differences between the two cancer populations, as the lymphoma group had both males and females while the breast cancer group only had females.

A last study (Brezden et al., 2000) that assessed the effects of chemotherapy on breast cancer patients compared three groups: women receiving chemotherapy (N = 31), women who had completed chemotherapy at least one year previously (N = 40), and matched comparisons (N = 36) with age range of 42 through 49 across all three groups. Participants completed a brief inclusive fixed-battery that evaluated memory, language, visual-motor, spatial, attention, components of executive function, and a self-report mood questionnaire. Women currently undergoing chemotherapy performed poorer in the domains of memory and language, and women who had already completed chemotherapy performed poorer in the domains of language and visual motor skills in comparison to matched comparisons. An obvious gap in this study is a comparison between women currently undergoing chemotherapy and women who had received chemotherapy; it is

surprising that the authors do not make this comparison limiting their analysis and discussion.

In sum, exciting new research has made great advances in exploring the effects of chemotherapy on cognition, but suffers from a number of pitfalls. First, the current literature is inconsistent. Most studies that assess executive functioning, memory, attention, and psychomotor speed find some sort of impairment. However, some studies find impairment in visual memory and not verbal memory or vice versa. Sometimes verbal learning is characterized as a part of memory, whereas in other cases it is considered a facet of attention. Also contributing to the inconsistency is the number of neuropsychological measures used; clearly, there are a number of validated measures which assess attention, so it is not surprising that studies use different measures. However, as mentioned above, some studies use short, fixed batteries that often utilize one test to define an entire cognitive domain, leading to a number of false positives or false negatives because of the lack of specificity and sensitivity of the measure. A final reason for inconsistency in the literature could be the general definition of impairment. For example, some studies specifically define impairment based on standard *z*-scores, but some studies define impairment as a *z*-score of -1.4 while others a *z*-score of -2.0. Too, some participant performances are compared to normative data, each other, other cancer populations, and/or matched comparisons. As some of the longitudinal studies address, definitions of impairment need to be constant across research and might even need to be distinct for cancer populations. Subtle impairments as a result of chemotherapy are worth investigating, even if such difficulties would not be classified as bona fide impairment in a clinical sense. Also, many of the longitudinal studies highlight how sometimes attrition rates are affected by cognitive dysfunction (i.e., individuals with the most impairment at baseline are less like to follow-up). Any change in cognition as a result of chemotherapy still has certain implications. It is not far-fetched to imagine, for example, a subtle difference in attention could make functioning particularly difficult when daily routines

necessitate organization. Or, from a psychological perspective, subtle changes in cognition could swell into concerns about possible dysfunction, leading to anxiety or even depression, affecting overall quality of life.

Although this research suffers from the challenges inherent in studying this population (e.g., heterogeneity of treatment and volunteer sample discrimination) and many clinical populations, it is disappointing that greater efforts have not been made to incorporate complex research designs. Namely, most studies examine cognition before, during, or after diagnosis or treatment of cancer and little else. The question should no longer solely be whether chemotherapy affects cognition, but rather how cognitive changes due to chemotherapy affect individual lives. Newer studies have attempted to address quality of life, but only through functioning. The functioning measures used in these studies are vague, and as it has been argued above, overall functioning is not synonymous with quality of life. Although the use of such functional questionnaires has become standard research practice, these questionnaires often do not provide the specificity to facilitate change, regardless of their intuitive relationship. Exploring specific factors that contribute to quality of life, like social support and optimism, provides better information which can be utilized to aid therapeutic interventions.

Social Support

The definition of social support is negotiable, as this construct is generally categorized in two ways: functional (or qualitative) social support and structural (or quantitative) social support (Trunzo & Pinto, 2003). Functional support focuses more on emotional support, such as feeling cared for and being able to talk to someone about fears and feelings. Structural support, then, aims to identify whether individuals have the support of others for practical activities, such as rides to appointments. When social support is described in research, it is often functional support that is examined, as it is the complexity of feeling close to others that has apparent therapeutic implications. However,

though not as complex, a complete lack of structural social support clearly invokes certain challenges.

Cutrona and Russell (1987) provide another way to conceptualize interpersonal relationships based on a model that identifies specific provisions needed for individuals to feel supported, especially in times of stress (see Cutrona & Russell, 1987, for a more thorough review of different social support models). The first provision described is "guidance," which involves the availability of advice or information from another individual or support. "Reliable alliance" considers whether tangible assistance is met when the need or want exists. A third provision is "reassurance of worth," which highlights the individual need to feel competent based on others' perceptions lending better self-efficacy. The desire to feel others' reliance is specified as "opportunity for nurturance." "Attachment" is described as the sense of feeling close with others that enables a feeling of security. A last provision, "social integration," outlines the want to feel a sense of belonging with others. These six provisions may or may not be important in relationships based on individual needs and wants, thus perception of and satisfaction with such relationships plays a key role. Of note, not all interpersonal relationships necessitate fulfillment of all provisions. Rather, one individual might satisfy one provision or four, for example.

The aforementioned conceptualizations and definitions have driven social support research, though not always by the same name (for example, social networks, functional supports, and interpersonal relationships are terms used interchangeably). Social support research has demonstrated that breast cancer patients have specific social support needs (Aranda et al., 2005; Cappiello, Cunningham, Knobf, & Erdos, 2007; Hasson-Ohayon, Goldzweig, Braun, & Galinsky, 2010; Marlow, Cartmill, Cieplucha, & Lowrie, 2003; Mehnert & Koch, 2007), and social support can unequivocally improve the quality of life and psychosocial functioning of breast cancer patients by, for example, reducing distress and psychiatric problems (Arora, Rutten, Gustafson, Moser, & Hawkins, 2007; Baider,

Hadani, Goldzweig, Wygoda, & Peretz, 2003; Bloom, Stewart, Johnston, Banks, & Fobair, 2001; Lewis et al., 2001; Maly, Umezawa, Leake, & Silliman, 2005; Manne, Winkel, Ostroff, Grana, & Fox, 2005; Mehnert & Koch, 2007; Michael, Berkman, Colditz, Holmes, & Kawachi, 2002; Nosarti, Roberts, Crayford, McKenzie, & David, 2002; Talley, Molix, Schlegel, R., & Bettencourt, 2010). Beyond quality of life, one study (Weihs et al., 2005) even demonstrated that social support predicted overall survival in breast cancer patients. Another study (Reynolds & Perrin, 2004) not only showed that social support is important, but also matching the want and receipt of social support predicts better psychosocial adjustment (i.e., women who received unwanted support had poorer psychosocial adjustment).

Several other themes in the social support literature deserve mention, including the use of group therapy (e.g., Manne et al., 2005), online interventions (e.g., Gustafson et al., 2008), narrative and expressive writing (e.g., Gellaitry, Peters, Bloomfield, & Home, 2010) as a means to increase interpersonal relationships, in the hopes of improving quality of life as well. Emerging research has also focused on specific subpopulations within breast cancer patients, such as young women (e.g., Snyder & Pearse, 2010), sexual minority groups (e.g., Boehmer, Freund, & Linde, 2005) and Asian women (e.g., Lim & Zebrack, 2008), for example. Social support research is not limited to the field of psychology either; emerging qualitative and individual descriptive research in the field of social work has examined how social support impacts the breast cancer experience in a number of domains (e.g., Hirschman & Bourjolly, 2005).

The plethora of social support research in breast cancer populations is overwhelming, however, invaluable. For the purposes of this literature review, only the social support studies that generally evaluated the effects of social support on some aspect of quality of life will be discussed. Studies that examined social support in conjunction with other variables, such as the mediational role of social support in a coping-distress model are not examined, as coping, for example, was not evaluated in this

study (e.g., Junghyun, Han, Shaw, McTavish, & Gustafson, 2010). Too, studies with certain populations, such as low-income Hispanic women (Alferi, Carver, Antoni, Weiss, & Duran, 2001), though imperative in this field of research, are not detailed due to specificity. As such, only five studies (Arora et al., 2007; Bloom et al., 2001; Mehnert & Koch, 2007; Michael et al., 2002; Nosarti et al., 2002) are discussed explicitly based on their application of social support and its effects on quality of life in the breast cancer population in general. Two epidemiological studies will first be outlined (Michael et al., 2002; Mehnert & Koch, 2007), followed by two prospective studies (Arora et al., 2007; Nosarti et al., 2002). A final study (Bloom et al., 2001) will be featured based on its appraisal of multiple aspects of quality of life in breast cancer patients.

Both epidemiological studies (Michael et al., 2002; Mehnert & Koch, 2007) found that social support led to positive outcomes in breast cancer patients. Michael and colleagues (2002) aimed to better understand the impact of both medical characteristics and social networks on health-related quality of life. Breast cancer survivors (N = 699) completed information about their form of cancer and treatment, a questionnaire on social networks, and two questionnaires assessing general health- and cancer-related quality of life an average of four years post-diagnosis. Overall, social isolation was associated with lower quality of life, and social integration was an important predictor in all aspects of quality of life measured. Social networks also explained more of the variance of quality of life than disease and demographic specifics, with the notable exception that older age was associated with worse quality of life and functioning.

Another study (Mehnert & Koch, 2007) specifically identified the role of social support on psychological comorbidity and quality of life in breast cancer survivors. Breast cancer survivors (N = 1083), at least two years and less than 6.5 years post-diagnosis, were mailed a packet of questionnaires containing self-report measures on mood, post-traumatic stress symptoms, general health functioning, and social support. Interestingly, almost half of the participants would be classified as having moderate to

high levels of anxiety, and almost 20% moderate to high levels of depression. Too, almost half of the respondents did not feel they were adequately informed about professional support, and 15% identified a need for more psychosocial support. Overall, disease progress, less social support, lower educational attainment, and younger age predicted psychological comorbidity affecting quality of life. Specifically, older women with lower educational attainment were often more distressed and identified the need for support, yet were less likely to be informed about professional support interventions.

One prospective study (Arora et al., 2007) focused on social support available to women newly diagnosed with breast cancer. The authors specifically examined the support these women received, from whom, and the relationship between support and quality of life at both baseline and five months later via the internet. These breast cancer participants (N = 246) participated in an online support intervention, and completed surveys on social support, health-related quality of life, and self-efficacy. Results revealed specific patterns in support. Particularly, family and health care providers supplied the most support closer to diagnosis, and friends provided helpful emotional support. However, helpful emotional support significantly decreased over time.

Another prospective study (Nosarti et al., 2002) examined the relationship between pre-diagnostic factors, such as general health and psychiatric morbidity, and adjustment one year from diagnosis. Eighty-seven women were recruited just after diagnosis and completed a baseline general health questionnaire at the time of diagnosis. They then completed the same questionnaire plus other self-report measures assessing mood, adjustment to cancer, social support, and beliefs about breast cancer a little less than one year later at two other time points. Overall general health status, lack of social support, and an avoidant attitude predicted worse functioning at the first time point. Likewise, diffuse social support predicted psychological morbidity at the second time point.

Lastly, Bloom and colleagues (2001) hypothesized that the integration of a large social network would provide better emotional support, thus improving physical functioning in women with breast cancer. Three hundred and thirty six women diagnosed with breast cancer within seven months participated and completed an interview, as well as questionnaires evaluating general health status through physical and mental well-being, psychological resources, and three different measures of social support: social network, emotional support, and instrumental support. The authors' hypotheses were supported, and larger networks were related to individual feeling about the availability of emotional support. Furthermore, high self-esteem was related to greater emotional support, and emotional support significantly predicted well-being. However, the women that perceived greater instrumental support had poorer physical health. This study confirmed the importance of women's network and integration into support systems for improved well-being.

In conclusion, the social support literature is consistent: social support is important and can improve quality of life in breast cancer patients. Limitations of these studies are mainly concerned with generalizability to all breast cancer populations regardless of disease stage and receipt of variable systemic therapies. As is the case with many breast cancer studies, this research often involves heterogeneous treatment regimens, such that even a group of women who have only received chemotherapy likely have received a combination of other systemic treatments. Also, the aforementioned studies use a number of different social support measures that tap into different components of social support, forcing readers to rely on the interpretations of the authors to guide perceived implications. Based on convenience, many of these studies use cross-sectional or retrospective designs, meaning causal relationships can only be implied. Lastly, each study looks at a different aspect of the breast cancer experience, making comparison difficult. The ability to evaluate women before they are even diagnosed with cancer and follow them throughout treatment and survivorship would be ideal, but is

obviously impractical. However, promising national cohort studies, such as the Women's Health Initiative established in 1991 (National Institutes of Health, 2009), aim to better understand the development of specific diseases, including breast cancer.

Only one study (Reid-Arndt, 2010) considers the relationship between social support and cognition and there are no studies that examine the effects of social support on cognition in breast cancer or NHL survivors specifically, as is the aim of the present study. Conversely, trends to better understand the social functioning of breast cancer patients seem to be emerging, and provides a stepping stone to envision the possible implications of social support on cognition. Likewise, most social support research focuses on outcomes, such as quality of life. Thus, it is not a far leap to extrapolate the current social support findings and apply them to a different outcome, namely cognition.

Social support and successful aging

The review of social support literature based on the aims and hypotheses of the present study intentionally focuses on social support with breast cancer populations, and its implications for therapy. Thus, it is imperative to examine the effects of social support on quality of life in the manner previously addressed. However, exhausting and critiquing the literature in the area of social support and cognition is superfluous, as it has not been examined in breast cancer populations. However, it is important to address the possible implications of social support on cognition. The effects of social support on cognition, whether as a preventative or protective factor, serves to amplify the need to examine the relationship between social support and cognition in breast cancer populations.

A literature search on social support and cognition unveils thousands of research studies. This literature is important in focusing on the perceptions of social support with certain populations, as well as social support interventions with individuals who demonstrate cognitive impairment. For the purposes of the present study, however, only a

small minority apply. Based on the population of interest, only studies that examine the importance of social support for successful aging will be briefly highlighted.

Support has been shown to promote successful aging (Fillit et al., 2002; Fratiglioni, Paillard-Borg, & Winblad, 2004; Fratiglioni, Wang, Ericsson, Maytan, & Winblad, 2000; Gow et al., 2007; Hendrie et al., 2006; Menec, 2003; Seeman, Albert, Lusignolo, & Berkman, 2001; Zunzunegui et al., 2003). That is, individuals who have better social support age better and exhibit fewer cognitive and functional difficulties. Such research has posited that individuals who are more engaged and live an active lifestyle conserves cognitive ability. One review (Fillit et al., 2002) of factors that may contribute to cognitive decline in later life showed that social disengagement is a risk factor for cognitive dysfunction in older adults. Moreover, studies reviewed by the National Institutes of Health (Hendrie et al., 2006) demonstrated that psychosocial factors, such as emotional support and social networks, are significantly related to cognitive and emotional health in later life, suggesting such factors may have a protective effect. Fratiglioni and colleagues (2000 and 2004) used successful aging and social support to show that individuals who live alone and have fewer closer relationships were at higher risk for developing dementia. Another study (Gow et al., 2007) examined social support across the lifespan (once at the age 11 and again at age 79) and how it may predict cognition in later life, and it was found that individuals who reported loneliness had poorer cognitive function in old age. Additionally, it was found that individuals who could identify a key significant other (e.g., spouse or significant other) was also significantly related to cognitive outcome. Another study (Seeman et al., 2001) demonstrated that greater emotional support was significantly related to better cognition both at baseline and almost eight years later. A last study (St. John & Montgomery, 2010) found that older adults who endorsed better social life satisfaction (e.g., family relationships and friendships) were more likely to be women, more educated, less

depressed, less disability, and better cognition (as measured by the Mini-Mental State Examination).

This research demonstrates the importance of social support on cognition. The exact reasoning for why social support fosters successful aging is, at present, unknown. However, it has been postulated (Gow et al., 2007; Zunzunegui et al., 2003) that social support stimulates mental processes and facilitates neural growth through continued active engagement.

Optimism

The “glass is half full” colloquial expression used to describe optimism does not consider the expectations and consequences of perceiving a glass as full or empty. The definition of optimism has been investigated, including its differences from other personality characteristics, including neuroticism, trait anxiety, self-mastery, and self-esteem (Carver & Scheier, 2003; Scheier & Carver, 1992; Scheier, Carver, & Bridges, 1994). Dispositional optimism is generally defined as an expectation for a positive future (Carver & Scheier, 2003; Scheier & Carver, 1985; Scheier & Carver, 1992; Scheier et al., 1994), which affects how individuals approach and cope with challenges. Specifically, research has shown that optimists use more adaptive problem- and emotion-focused coping styles than pessimists (e.g., humor and positive reframing) when faced with adversity (Scheier et al., 1994). Furthermore, optimists usually approach challenges with both confidence and persistence, whereas pessimists are more likely to be doubtful and reluctant (Carver & Scheier, 2003; Scheier & Carver, 1985). Thus, dispositional optimism is relevant in predicting how an individual might confront health-related difficulties.

The most thorough review (Scheier & Carver, 1992) of the effects of optimism highlighted the importance of optimism on both psychological and physical well-being. In these studies, optimistic patients, regardless of disease or hospital setting, reported

lower levels of depression and distress and higher levels of satisfaction and quality of life. Furthermore, optimism predicted physical recovery in hospital settings; specifically, optimistic patients were more likely to have better recoveries and reach recovery milestones (e.g., walking after surgery or resuming everyday activities) more quickly than pessimistic patients. Of note, studies that focus on optimism as a predictor for better physical health are less consistent. This review is limited, not only because it is dated, but because it only incorporates one study about the effects of optimism in cancer patients.

The extant literature on optimism and breast cancer is surprisingly limited, especially in comparison to other quality of life variables, such as social support. In this research, optimism is often coupled with coping as a means to better understand how breast cancer patients and survivors adapt to their illness (David, Montgomery, & Bovbjerg, 2006; Karademas, Karvelis, & Argyropoulou, 2007; Shou, Ekeberg, & Ruland, 2005; Shou, Ekeberg, Ruland, Sandvik, & Karesen, 2004). Other research in optimism does not focus on how optimism affects coping, but rather how optimism affects specific outcomes, such as quality of life, psychiatric illness, and/or distress (Carver et al., 2005; Shou, Ekeberg, Sandvik, & Ruland, 2005; Tomich & Helgeson, 2006). Emerging research has shown that some therapeutic interventions might even alter and improve optimism (Antoni et al., 2001; Dubey & Sharma, 2006). Although this research is imperative, only a few of these studies will be outlined, based on their emphasis on how optimism affects quality of life in breast cancer patients throughout treatment and survivorship. First, longitudinal studies (Carver et al., 2005; Shou et al., 2004; Shou et al., 2005) assessing the effects of optimism on quality of life in breast cancer patients through survivorship will be detailed. Second, a prospective study (David et al., 2006) that examined optimism in newly diagnosed breast cancer patients before and after surgery will be addressed. Lastly, a retrospective study (Tomich & Helgeson, 2006) will be outlined.

Shou and colleagues (2004 and 2005) studied the relationship between optimism and both quality of life and emotional morbidity in breast cancer patients longitudinally up to one year after diagnosis. Participants were asked to appraise their cancer (e.g., to what degree breast cancer has been a challenge), and complete questionnaires on optimism, coping, positive expectations, psychiatric symptoms, and quality of life, among other measures. Longitudinal analyses showed that optimism was related to quality of life, and both emotional and social functioning, but not cognitive functioning (of note, cognitive function was assessed through five self-report items and not by formal cognitive evaluation). Specifically, optimistic women engage in a "fighting spirit" coping style, which is associated with better global health quality of life and functioning, whereas pessimistic women responded with a more hopeless and helpless coping style. Optimism was also inversely associated with emotional distress.

Carver and colleagues (2005) hypothesized that optimism would be a predictor of distress in early stage breast cancer patients. To longitudinally assess the effects of optimism, participants were recruited from previous studies (e.g., Carver et al., 1993), and 163 breast cancer survivors five to 13 years after treatment who had been diagnosed with Stage 0, I, or II breast cancer agreed to participate. This study used a repeated measure design to assess optimism, confidence about remaining cancer free, distress, depression, social disruption, and self-rated quality of life. It was found that there was continuity of well-being over time (i.e., if the participant had mood disturbances one year after treatment, there continued to be mood disturbances years later). Initial optimism predicted distress emotions, depression, quality of life, and social disruption longitudinally.

Another study (David et al., 2006) focused on anticipatory psychological distress in breast cancer patients just prior to surgery. Sixty women completed questionnaires assessing optimism and coping as part of a presurgical take home packet, and mood was assessed in the preoperative waiting area the day of surgery. Optimism and pessimism

were associated with specific and opposing coping responses, and higher optimism was associated with less distress before surgery.

A last study (Tomich & Helgeson, 2006) examined the effects of optimism in breast cancer patients who had been diagnosed five years previously. Participants were 35 breast cancer patients with recurrence who were matched with 35 disease-free breast cancer survivors. All participants completed questionnaires on self-esteem, optimism, personal control over illness, quality of life, and benefit finding. For participants with beliefs about perceived control over illness, the women who experienced recurrence reported a decline in physical and mental health, but there was no relationship for women who were disease-free. Contrary to other research, optimism and self-esteem were not related to physical or mental functioning, regardless of recurrence.

The literature on optimism regarding the breast cancer experience is hopeful. Optimism seems to play a role in improving quality of life, as well as similar constructs, including self-efficacy, coping, and perceptions of control. There are some inconsistencies in the research, but this can easily be attributed to the use of different measures to assess quality of life. A further limitation of these studies, in addition to the typical restrictions of working with a volunteer sample of breast cancer patients who have received combination treatments, is the difficulty in teasing out optimism from other similar variables. For example, some could argue that optimism is synonymous with specific forms of coping; therefore, analyzing both optimism and coping in the same study could unduly inflate significance. As such, the interrelationship between such variables must be considered.

Optimism and cognition

For the purposes of this literature review, understanding how optimism affects quality of life in breast cancer patients becomes an important component needed to extrapolate such findings to cognition; however, it is also necessary to consider any

literature that measures the effects of optimism on cognition in any population due to the complete lack of research in cancer populations. Unfortunately, the research is sparse in this arena as well. Research that does exist considers optimism as a quality of life predictor for healthy aging (Bain et al., 2003), postulating that higher cognitive ability in childhood could affect the development of optimism. Another study (McIlvane et al., 2008) incorporates optimism to determine how individuals cope and perceive cognitive impairments. The Big Five traits, which includes optimism, have also been examined in conjunction with cognitive ability in adolescents (Lounsbury, Welsh, Gibson, & Sundstrom, 2004), and were found to be significantly related. Regrettably, this research does not appreciably augment this review for the purposes of the present study.

Social Support and Optimism

There is surprisingly little information on the relationships between social support and optimism and their effect on quality of life outcomes in breast cancer patients. It would make sense that optimism would affect social support, as it can be argued that optimistic individuals likely attract more people, and thus are able to build more friendships, increasing available support during stressful situations and period (Brisette et al., 2002; Dougall et al., 2001; Shelby et al., 2008; Trunzo & Pinto, 2003). Specifically, it has been found that in traumatic times, such as breast cancer diagnosis and treatment, optimism and social support are positively related, and an optimistic disposition leads to less overall distress (Dougall et al., 2001; of note, the participants recruited for this study were rescue and recovery workers from the U.S. Air Flight 427 crash).

Although there is limited research, the studies that have examined the relationships between optimism and social support have extended beyond general quality of life outcomes, such as distress and psychosocial functioning (Friedman, et al., 2006; Shelby et al., 2008; Trunzo & Pinto, 2003), but have included specific factors, such as psychosexual well-being (Abend & Williamson, 2002; Wimberly, Carver, & Antoni,

2008) and stress response (Von Ah, Kung, & Carpenter, 2007) in breast cancer patients. Although the latter research is important to better understand specific outcomes and how such outcomes are related to social support and optimism, only studies that examine optimism and social support and their relationship to quality of life (e.g., overall well-being and psychological distress) as a whole in breast cancer patients will be discussed. These studies are meticulously detailed, because it is important to understand the relationships between social support and optimism for the purposes of the present study. Too, a specific depiction of the intercorrelations and analyses of these two variables in conjunction with an outcome measure guided the methodology of the proposed study.

Friedman and colleagues (2006) examined the role of optimism, social support and psychosocial functioning among women with breast cancer, postulating that age, marital status, optimism, and social support would account for quality of life, distress, and mood disturbance. Eighty-one women participated in the study and completed a number of self-report questionnaires. Health-related quality of life was measured using the Functional Assessment of Chronic Illness Therapy – General (FACIT-G; Cella, 1997), and cancer-specific distress was measured using the Impact of Events Scale (IES; Horowitz, Wilner, & Alvarez, 1979), which identifies feelings and thoughts about a stressful event. The Profile of Mood States-Short Form (POMS-SF; Curran, Andrykowski, & Studts, 1995) was used to assess mood disturbance. Dispositional Optimism was measured using the LOT (Scheier & Carver, 1985), and social support was assessed through the Social Support Questionnaire (SSQ; Sarason, Levine, Basham, & Sarason, 1983). Finally, participants were asked if they had a family history of cancer. Descriptive statistics, Pearson correlations, one-way ANOVAS, and multiple regression analyses were performed to analyze and interpret data.

The mean age of participants was 52 (*SD* = 10.2) years of age, with an average of 26 months (*SD* = 33.5) since their initial diagnosis (Friedman et al., 2006). Demographic characteristics were more diverse than in most other research samples: only 24% of the

participants had less than a high school degree and 9% were college graduates. Fifty-six percent of the subjects were African-American, 27% Hispanic, and 17% Caucasian. The women had been received varying treatment as well, with the majority of women undergoing a mastectomy (62%), as well as adjuvant chemotherapy, hormonal treatment, and/or in combination with radiation within the past six months (65%) or more than six months previous to the study (24%); of note, the researchers did not specifically parse out systemic treatments. Eleven percent of the sample had not yet been treated for breast cancer. Older women reported better emotional well-being (EWB) than younger women; optimistic women reported better EWB, functional well-being (FWB), and social well-being (SWB), as well as overall less distress and lower mood disturbance than pessimistic women. Women who reported better social support also endorsed greater FWB and SWB. Women with a family history of breast cancer reported lower EWB and FWB, and women currently receiving treatment reported greater EWB and fewer intrusive stressful thoughts than women who had not received treatment. Finally, there was no between-group difference for race/ethnicity or marital status, and time since diagnosis was not related to either quality of life or psychological adjustment.

Using multivariate analyses, it was found that older age, receipt of treatment, and greater optimism accounted for 41% of the variance in EWB (Friedman et al., 2006). Furthermore, no family history of breast cancer treatment, receipt of treatment, and optimism accounted for 43% of the variance in FWB. Optimism and satisfaction with social support accounted for 43% of the variance in SWB. Pessimistic women who had not yet been treated for their cancer accounted for 31% of the variance in distress. Lastly, women who were pessimistic and had a family history of cancer accounted for 41% of mood disturbance.

This study (Friedman et al., 2006) considered how the relationship between social support and optimism affects a number of outcomes; findings indicated optimism and satisfaction with social support are important for social well-being and preventing

distress. However, due to the cross-sectional design of the study, causal relationships between independent variables, such as optimism and social support, and dependent variables, such as quality of life, could not be determined. Furthermore, though the authors should be applauded for recruiting such a diverse sample in terms of race, ethnicity, and education, the heterogeneity of disease stage and treatment makes interpretation challenging.

Another study (Trunzo & Pinto, 2003) examined the effects of psychosocial variables on distress in breast cancer survivors prospectively. This study hypothesized that functional social support (i.e., how emotionally supported an individual feels) mediates the relationship between optimism and distress. Breast cancer survivors diagnosed within one year were recruited (N = 69), and were given an initial interview and four follow-up assessments every three months. Participants completed the Duke-UNC Functional Social Support Scale (Broadhead, Gelbach, de Gruy, & Kaplan, 1988), the LOT-R (Scheier & Carver, 1985) and the POMS-SF to assess mood (McNair, Lorr, & Droppelman, 1992). To examine the relationships between the predictor, hypothesized mediator, and criterion variables, zero-order correlational analyses were performed at baseline, six- and 12-month assessments, followed by multiple regressions analyses. Lastly, ANOVAs and independent samples t-tests were conducted to compare responses to questionnaires and demographic and descriptive information (e.g., education level, marital status, disease stage, and treatment).

The mean age of the participants (Trunzo & Pinto, 2003) was 57.5 (SD = 13.2) years of age, and all participants were Caucasian. Fifty-seven percent were married and/or living with a partner. Most participants (68%) had at least some college education. Regarding the details of breast cancer diagnosis, the mean number of days since diagnosis was 247.3 (SD = 106), and participants had been diagnosed with Stage 0 (16%), I (52%), or II (32%) breast cancer. Participants had received combination treatments, including surgery and chemotherapy, radiation, and/or hormonal therapy.

Trunzo and Pinto (2003) found no significant differences in distress based on disease stage and treatment at baseline and six-months. At 12 months, however, Stage 0 patients and those receiving surgery with and without other adjuvant regimens reported greater distress than Stage I and II patients receiving surgery in conjunction with radiation or hormonal treatment. No significant differences were found for other demographic information. Most importantly, social support mediated the negative association between optimism and emotional distress at baseline and six months, but not at one year.

This study (Trunzo & Pinto, 2003) highlights the importance of considering the relationships between optimism (thought to be a relatively stable trait) and other psychosocial variables, such as social support. However, there are some limitations to the study, including some of its findings. It is unclear why, for example, the mediation model was not significant at 12 months. Furthermore, it is also puzzling that disease stage and treatment were related to distress at 12 months, but not at earlier assessment periods. Although assessments were performed five times, it is odd that only results from three assessments are reported with no mention of either the three-month or nine-month assessments. Lastly, this study suffers from the same dilemma that most breast cancer studies face: an overwhelmingly well-educated and Caucasian sample.

A final study (Shelby et al., 2008) examined the effects of optimism and social support on adjustment, specifically among African-American women diagnosed with nonmetastatic breast cancer. Women were recruited for a randomized clinical trial of a psychosocial support group intervention, but the data presented in this specific article were derived from baseline assessment prior to randomization. It was exploratory in nature, trying to determine whether the relationships between social support, optimism, and adjustment would be maintained in an African-American sample. Too, the authors hypothesized that social support would buffer, and thereby reduce, the negative impact of lower optimism on adjustment in this sample. Each participant completed the LOT

(Scheier & Carver, 1985) to measure optimism, the Interpersonal Support Evaluations List – Short Form (ISEL-SF; Cohen & Hoberman, 1983) to assess social support, the Mental Health Inventory (MHI; Veit & Ware, 1983) to appraise psychological distress, and the Cancer Rehabilitation Evaluation System – Short Form (CARES-SF; Schag, Ganz, & Heinrich, 1991) to evaluate quality of life in cancer patients. Descriptive statistics, intercorrelations, and both linear and multiple regression analyses were used to analyze the data.

All women (N = 77) had been diagnosed with breast cancer stages 0 – IIIA, had completed surgical treatment a mean of 3.4 (SD = 2.4) months prior to the baseline assessment, and were on average 53.5 (SD = 12.8) years of age (Shelby et al., 2008). Age and income were negatively associated with psychological distress and concerns, and being employed was associated with lower psychological distress and physical and psychosocial concerns. Participants who had received chemotherapy were in significantly greater psychological distress.

Optimism was negatively associated with psychological distress and positively associated with social support and well-being (Shelby et al., 2008). Social support was negatively associated with distress. Optimism continued to be significantly associated with distress after including social support in the regression model. For all of these models, social support was not a mediator for the optimism-distress and optimism-well being relationship. Optimism and social support were not related to psychosocial and physical functioning, respectively. Lastly, moderator analyses demonstrated that social support moderated the relationship between psychological distress, psychological well-being, and psychosocial functioning, and buffered the impact of low optimism on adjustment.

This study (Shelby et al., 2008) is important not only because of its uncommonly diverse sample, but also because of its oppositional results to the limited previous research highlighting social support as a potential mediator of the optimism-well-being

relationship. Specifically, the findings suggest that social support is only an important resource for women with low optimism. Thus, social support does not explain the relationship between optimism and well-being, rather influences it. However, one limitation of the study was the presence of significant differences between those individuals who decided to participate, and those that did not. Specifically, individuals who declined participation were older. Additionally, this study used only baseline assessment data, thus cause and effect relationships should be interpreted with caution.

Overall, emerging evidence demonstrates cognitive decline as a result of chemotherapy in breast cancer patients, but little research has focused on cognition in survivorship or older cancer patients. Too, the literature is inconsistent in terms of findings, which is likely the result of small sample size, varying definitions of impairment, and a general lack of uniformity among samples and measures. Some limitations cannot be avoided due to the nature of convenient samples and cancer treatment. For example, volunteer samples oftentimes have higher educational attainments, perhaps enabling them to more readily participate in studies. Also, the heterogeneity of systemic treatments is common, as combination therapies are utilized based on patient needs. Obviously, some of these limitations are difficult to overcome, and the proposed study will, unfortunately, face similar challenges. Nevertheless, that does not lessen the reality of the limitation in terms of generalizability.

Social support and optimism independently have demonstrated considerable effects on quality of life. The relationship between social support and optimism has been featured in the recent breast cancer literature in conjunction with specific outcomes, such as quality of life. Although there has been one study that has sought to determine how neuropsychological functioning and support seeking affects social role functioning, no studies to date have considered cognition as an outcome that may be affected by such variables. To date, limited research has, generally, examined how cognition affects quality of life using only functional measures. Problems with these studies are multi-

faceted. First, overall functioning cannot be equated to quality of life. Although, some may defend the logic in using these terms synonymously, the implications of such an exchange negates the possible explanation of other variables and renders other definitions of quality of life useless. Second, such analysis restricts therapeutic implications by highlighting mostly stable characteristics, as opposed to ones that might be changed. Lastly, social support and optimism have demonstrated benefits for successful aging and less cognitive decline, indicating that research should consider topics that might foster early interventions to improve outcome, especially in cognition.

There is an obvious gap in the literature in terms of variables associated with quality of life in conjunction with cognition, as no studies to date have examined such relationships. The aim of the present study to evaluate the relationship between social support, optimism, and cognition is therefore warranted and needed. A better understanding of this relationship could encourage early interventions and provide additional information on the effects of chemotherapy and the possible ways to influence cognition.

CHAPTER III

METHODS

Participants

Two groups of cancer survivors were recruited for this study. Breast cancer survivor participants (hereafter referred to as BCS) were recruited in collaboration with the Iowa Cancer Registry starting in 2007. Letters were sent inviting potential participants to partake in a larger study entitled "Elderly Cancer Survivors: Cognitive Outcomes and Markers of Neurodegeneration," which assesses genetic polymorphisms and neuroimaging in conjunction with cognition in breast cancer survivors. Research to date from this study has included pilot data for neuroimaging and comparisons between a sample of breast cancer survivors to healthy adults with no history of cancer. Enrollment criteria of this study specified that women had to be over the age of 65 years of age, at least 50 years of age at the time of breast cancer diagnosis and treatment, and 10 years post-treatment. Additionally, participants had to be diagnosed with early malignant breast cancer stages I through IIIA with no evidence of metastasis. All breast cancer survivor participants were treated with a combination chemotherapy regimen involving cyclophosphamide, methotrexate and 5-fluorouracil, or an anthracycline.

The non-Hodgkin's Lymphoma survivor participants (hereafter referred to as NHLS) were recruited in collaboration with the Holden Comprehensive Cancer Center (HCCC) and the Specialized Program for Research Excellence (SPORE), a registry that focuses on research with lymphoma and is based at the University of Iowa in collaboration with the Mayo Clinic and the National Cancer Institute starting in 2005. Potential participants were identified by a physician at the HCCC, and were invited to participate in a larger study entitled "Effects of Chemotherapy on Thinking and Function," which compares cognition in NHL survivors who have received adjuvant anthracycline- or non-anthracycline-based chemotherapy. Research to date has

considered comorbid illnesses and cognition in this sample. Enrollment criteria specified that the participants had to be at least 48 years of age and diagnosed and treated for NHL at least 18 months previously. All participants were treated with either an anthracycline-based combination chemotherapy regimen, such as with adriamycin in some combination with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone, or a non-anthracycline- based chemotherapy regimen, such as cyclophosphamide alone or in some combination with vincristine and prednisone.

Participants were excluded from both groups if they had a cancer recurrence, another type of cancer, or central nervous system (CNS) disease. Furthermore, participants were also excluded if they had been diagnosed with a psychiatric or neurological disorder. All participants signed a written informed consent document approved by the University of Iowa Institutional Review Board.

Procedures

Each participant completed a standardized neuropsychological battery of approximately three hours in length designed to evaluate a broad range of cognitive abilities involving premorbid and current intellect, attention, language, visuospatial skills, memory, and executive functioning (for a thorough review of neuropsychological tests, including psychometric properties, and their utility in examining cognitive domains, please see Lezak, Howieson, & Loring, 2004 and Tranel, 2009). Participants also completed self-report measures of mood, social support, and optimism.

Measures

Premorbid Intelligence

Premorbid intellectual ability was measured using the Wide Range Achievement Test – III Reading subtest (WRAT-III; Wilkinson, 1993), a 42-item single-word reading task. Raw scores are converted to standard scores (or percentiles and grade equivalents)

and it has been shown to be highly correlated (.62) with vocabulary, as measured by formal intellectual testing (e.g., Wechsler Adult Intelligence Scale; WAIS), and is a valid measure of reading ability. Reading subtests are often used to determine premorbid intellectual ability, as it has been demonstrated that, with the exception of severe neuropsychiatric disease and focal brain insult, reading ability remains unaffected in spite of neurodegeneration. To illustrate, if an individual can read the word "efficacious" as a young adult, they should be able to read this same word at the age of 75 regardless of a possible dementia (Lezak et al., 2004).

Attention

Both simple and divided attention (also referred to as working memory) was measured using the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III; Wechsler, 1997) Digit Span subtest. In this task, participants are asked to repeat strings of numbers both forward up to nine digits (simple auditory attention) and backward up to eight digits (divided attention/working memory). Scores range from 0 to 30 with higher scores indicative of better attention and the average score for individuals aged 65-79 is 15-16 points. From the original subtest (prior to subsequent revisions), 89% of the normative sample had spans within the 5 to 8 digit range and the normal range for digits forward is 6 +/- 1; generally; spans of 6 or better are within normal limits and a span lower than 4 is borderline to impaired. For digits backward, a span of 4 to 5 is usually within normal limits and anything less than 4 is considered impaired. As individuals normally age, forward and backward span only changes minimally (Lezak et al., 2004).

Trail Making Test part A (Spreen & Strauss, 1998) is both a simple attention and psychomotor task, and participants connect dots in numerical order as quickly as they can, without making errors. Scores consist of time to complete the task and number of errors. An average raw score on this test for individuals ages 56 to 66 is 30-33 seconds and up to 43-52 seconds for adults up to the age of 86 (Steinberg, Bieliauskas, Smith, &

Ivnik, 2005). Reliability coefficients vary, but most are in the .80s or .90s depending on neuropsychiatric or neurodegenerative illnesses (e.g., schizophrenia and vascular disease), and performance time increases significantly with each succeeding decade (Lezak et al., 2004).

Language

The Controlled Oral Word Association Test (COWAT; Benton, Hamsher, & Sivan, 1994) measures verbal fluency, and participants are given one minute to say as many words as they can that begin with a specific letter. The raw score consists of all acceptable words that are produced and is adjusted based on age, sex, and education. Average scores for 56- to 66-year olds is 34-39 words across the three trials; for individuals up to the age of 86, a total score of 30-35 is considered average (Steinberg, Bieliauskas, Smith, & Ivnik, 2005). Test-retest reliability after one year is around .70 for the letters “F” and “S,” and the letter “A” has the lowest reliability; it has also been shown to have a moderate correlation (.41-.45) for the Digit Span and Vocabulary subtests of the WAIS and is not correlated with memory (.17-.22; Lezak et al., 2004).

For the Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1983), a confrontation naming task, participants are shown a series of 60 line drawings of simple objects and asked to name them (a short form of 20 items also exists). Average scores for individuals aged 60-69 is 53 and for individuals aged 70-79, the average naming score is 49. If an individual has difficulties spontaneously naming the object, they are provided with semantic and then phonemic cues. Practice effects are minimal over one year, but appreciable decline has been found starting at the age of 70. Education is a predictive variable and there are high correlations with verbal ability (e.g., r = .65 with the WAIS Vocabulary subtest). The BNT is a sensitive indicator of cognitive deficits and, for example, individuals with Alzheimer’s disease often perform poorly on this task as they demonstrate lexical retrieval and semantic deficits (Lezak et al., 2004).

Visuospatial

The Rey-Osterrieth Complex Figure Test-Copy Condition (Rey, 1941) is a detailed drawing that participants must copy while looking at the stimuli. There are 18 items, each worth two points (maximum total score = 36), that must be drawn correctly in terms of placement and accuracy. Difficulties with this task can be indicative of a neurodegenerative disease, such as Alzheimer's disease, and/or lateralized or focal deficits (Lezak et al., 2004).

Participants must identify and discriminate photographs of unfamiliar faces on the Facial Recognition Test (FRT; Benton, Sivan, Hamsher, Varney, & Spreen, 1994). There are 13 items; for 6 items, participants are asked to match identical faces, and for the other 7 items, participants are asked to match 3 faces that are oriented and shaded differently to a sample face. Raw scores are the number of correct items and corrections are made based on age and years of education; a score of 41-54 is considered to be within normal limits. Test-retest reliability was .60 with older adults at a one year interval and practice effects have been shown to be minimal, and older age is negatively associated with test success (Lezak et al., 2004).

Memory

The Rey Auditory-Verbal Learning Test (AVLT; Rey, 1964) is a verbal learning and memory task in which participants are given five trials to learn a list of 15 words, and are then asked to recall the words following a 30-minute delay period. There is high test-retest reliability in both learning (.61-.86) and memory (.51-.72) over a one-month time period. Individuals are given one point for each correctly recalled item in both an immediate and delay condition (Lezak et al., 2004). An average learning score across the five trials is 15-17 for individuals aged 59-69 with a delayed recall of 9, and a learning score of 11-14 for individuals aged 83-99 with a delayed recall of 5 (Steinberg, Bieliauskas, Smith, Ivnik, & Malec, 2005).

Visual memory was assessed with the Rey-Osterrieth Complex Figure Test-Delay Condition (Rey, 1941), and participants must reproduce the complex figure they were asked to draw 30 minutes previously from memory. Both the AVLT and the Rey-Osterrieth Complex Figure Test are incidental memory tasks, thus participants are not told that a delayed condition with the same stimuli will be administered to evaluate memory.

Participants look at simple geometric figures for 10 seconds, and are asked to draw from immediate memory what they saw for the Benton Visual Retention Test (BVRT; Sivan, 1992). An item is considered correct if all items are fully accurate in the drawing, but a participant can make multiple errors in one drawing through, for example, omissions, rotations, and substitutions. The average correct score for individuals aged 65-69 is 6.39 down to 4.47 for individuals aged 85-89, and the average number of errors for these age ranges is 5.32 and 10.00, respectively. It has high reliability in repeat administrations with no significant differences in correct or error means. In factor analytic studies, loadings on visuospatial ability, memory, and concentration were .55, .45, and .42, respectively. The BVRT has been shown to be sensitive to cognitive decline in early Alzheimer's disease (Lezak et al., 2004).

Executive Functioning

The Intra-dimensional/Extra-dimensional Shift (ID/ED Shift; Sahakian & Owen, 1992) task is a computerized task in which compound stimuli are presented in two stages (intra- and extra-dimensional shift) as shapes overlaid with lines on a computer screen. Participants must be able to set-shift by learning rules through computer feedback to change between intra- and extradimensional stages. This test has been shown to be sensitive to deficits, as well as progressive decline, especially in patients with an early course of Alzheimer's disease or Parkinson's disease.

In the Trail Making Test part B task (Spreen & Strauss, 1998), participants connect dots consecutively and in alternating order between numbers and letters (i.e., connecting dots from 1 to A and then 2 to B). An average raw score on this test for individuals ages 56 to 66 is 64-77 seconds and up to 115-141 seconds for adults up to the age of 86 (Steinberg, Bieliauskas, Smith, & Ivnik, 2005). As a secondary component to Trail Making Test part A, reliability coefficients are, again, in the .80s or .90s depending on neuropsychiatric illnesses. This test is sensitive to cognitive inflexibility and difficulties with set-shifting (Lezak et al., 2004).

Participants must correctly categorize cards based on verbal feedback from the administrator in the Wisconsin Card Sorting Test (WCST; Heaton, Chelune, Talley, Kay, & Curtiss, 1993). This task requires both problem-solving ability and mental flexibility and perseverative errors and categories completed are sensitive to cognitive deficits, especially in older adults. Retest correlations are low (i.e., most correlations at or below .34) because scores often improve with repeat testing; thus, though it is a good measure of executive dysfunction, it should not be administered multiple times. Reliability coefficients vary, but most are in the .80s or .90s depending on neuropsychiatric illnesses, and performance time increases significantly with each succeeding decade. For this study, participants were given the short version of the task and were only given one deck of cards to sort (64 cards instead of the usual 128 cards), but it has been demonstrated to be a good predictor of performance for the full version (Lezak et al., 2004).

Manual Dexterity

Participants put grooved pegs into a 5 x 5 board with slotted holes oriented in different directions for the Grooved Pegboard task (Pegs; Klove, 1963). Participants must pick up the pegs individually and insert them in the pegboard as quickly as possible using only their dominant and then non-dominant hand as quickly as possible. Response time and number of drops are recorded. Men take, on average, 5 seconds longer to complete

the task and normative data indicates that it takes women 65.2 +/- 12.3 seconds and men 70.2 +/- 13.2 seconds to complete the task with their dominant hand (for ages 16 to 70). For the non-dominant hand, it takes women 72.0 +/- 15.1 seconds and men 76.3 +/- 15.3 seconds to complete the task. The test is particularly sensitive to potential slowing due to medications, diffuse brain dysfunction, and neurodegenerative disease progression (Lezak et al., 2004).

Quality of Life Variables

The Beck Depression Inventory – II (BDI-II; Beck, Steer, & Brown, 1996) is a 21-item self-report mood measure of depressive symptomatology. It was developed based on criteria from the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR; American Psychiatric Association, 2000) as a measure of depression. Item content includes statements about, for example, worthlessness (e.g., I feel like a complete failure as a person), loss of pleasure (e.g., I don't enjoy things as much as I used to), suicidality (e.g., I have thoughts of killing myself, but would not carry them out), and loss of interest (e.g., It's hard to get interested in anything). Cutoff scores to differentiate depressive symptom endorsement are 0-13 (minimal depression), 14-19 (mild depression), 20-28 (moderate depression), and 29-63 (severe depression). The scale has demonstrated both internal consistency reliability in outpatients (r = .92) and test-retest reliability (r = .93).

Social support was measured using the Social Provisions Scale (SPS; Cutrona & Russell, 1987), a 24-item measure that assesses relationships with other people in the form of six factors: *guidance, reliable alliance, reassurance of worth, attachment, social integration,* and *opportunity for nurturance*. The *guidance* subscale evaluates an individual's ability to gain advice or information from a support (e.g., "There is no one I can turn to for guidance in times of stress"). The *reliable alliance* subscale studies whether there are tangible supports (e.g., "There are people I can count on in an

emergency"). *Reassurance of worth* is a subscale that assesses whether an individual recognizes their own skills and competencies (i.e. "Other people do not view me as competent"). *Opportunity for nurturance* considers whether an individual feels that others need them (e.g., "There are people who depend on me for help"). The *attachment* subscale examines whether an individual feels emotionally close with another resulting in a sense of security (e.g., "I feel a strong emotional bond with at least one other person"). Lastly, the *social integration* subscale determines whether an individual feels a sense of belonging to others (i.e. "There is no one who likes the things I do"). Each factor is loaded with four items, two of which are reverse scored, and statements are rated on a 1 (strongly disagree) to 4 (strongly agree) point Likert scale. The total score of the SPS has demonstrated reliability (r = .915) and appropriate discriminant validity with self-report measures that evaluate, for example, introversion-extraversion (r = .289), depression (r = -.278), and neuroticism (r = -.199).

Optimism was measured using the Life Orientation Test – Revised (LOT-R; Scheier & Carver, 1985), a 10-item measure (including 4 filler items) designed to assess individual differences in optimism versus pessimism. Items are rated on a 0 (strongly disagree) to 4 (strongly agree) point Likert scale to specify agreement with statements that identify trait optimism (e.g., "In uncertain times, I expect the best"). Higher scores indicate greater optimism, while lower scores are indicative of pessimism. The measure is widely used, and demonstrates internal consistency (r = .76) and test-retest reliability (r = .79). Furthermore, the LOT-R has shown appropriate convergent and divergent validity with, for example, self esteem (r = .48), internal-external control (r = .34), and private self-consciousness (r = -.04).

Statistical Analyses

The present study aimed to examine social support, optimism, and cognition in breast cancer and NHL survivors. First, descriptive statistics were used to describe social

support, optimism, and cognition. Second, analysis of variance (ANOVA) was used to compare social support, optimism, demographic characteristics (i.e., age, gender, and education), and survivorship status between the BCS and NHLS groups. Third, multivariate analysis of variance (MANOVA) was used to compare cognition (i.e., premorbid intellect, attention, language, visuospatial functioning, memory, and executive functioning) across the groups. Lastly, Pearson correlations and hierarchical multiple regression analyses were used to assess the relationships between social support, optimism, and cognition in both participants groups.

Although mediational analyses were used to specifically assess whether social support mediates the optimism-cognition relationship, it is important to note that the present study did not utilize longitudinal data. As such, causal inferences, such as interpretations that quality of life variables predict cognition, cannot be made. However, performing such analyses was used to better understand the relationship between these variables. There are conditions that must be met for a variable to be considered a mediator (Baron & Kenny, 1986; Frazier, Tix, & Barron, 2004). First, the independent variable (optimism) must be related to the mediator (social support). Second, the independent variable (optimism) must be related to the criterion or outcome variable (cognition); likewise, the mediator (social support) must be related to the outcome (cognition). Lastly, the relationship between the independent variable (optimism) and outcome (cognition) significantly decreases when the mediator (social support) is controlled. Based on these criteria, linear regression analyses were completed to assess the relationships between 1) optimism and cognition; 2) social support and cognition; 3) optimism and social support and; 4) optimism and cognition while controlling for social support.

CHAPTER IV

RESULTS

This chapter will outline the statistical results of the study. First, a description of demographic variables of the sample and then both psychosocial variable and cognitive score information will be addressed. Differences between the NHLS and BCS groups on all variables will then be outlined. Lastly, bivariate correlations of psychosocial and cognitive variables are delineated and, subsequent, hierarchical regressions.

Demographics

The nature of this study relied on a volunteer sample and each participant completed the study in a single test session. If a participant was missing a data point from a neuropsychological measure, a sample imputed mean was calculated; notably, no subject was missing more than two data points. A total of 77 participants completed the standardized battery, 50 in the NHLS group and 27 in the BCS group. The participants in the NHLS group were approximately 6.75 years post-diagnosis (*SD* = 5.2, range = 1.6-30 years) and the participants in the BCS group were approximately 16.8 years post-diagnosis (*SD* = 2.8, range = 13.8-22.5 years). Based on the mixed gender of the NHLS group, demographic and cognitive variables are reported as three separate groups: the BCS group, the female NHLS group, and the male NHLS group. Demographic information is presented in Table 1. The average age and education of the BCS group (*N* = 27) was 71.96 *(4.89)* and 14.59 *(2.82)* years, respectively. In the female NHLS group (*N* = 25), the average age was 69.76 *(8.18)* and average education was 13.64 *(1.93)* years. Lastly, the male NHLS group (*N* = 25) had an average age of 65.28 *(9.89)* and average education of 15.12 *(2.39)* years.

Table 1. Demographic Characteristics of the Patient Groups

BCS Group (N = 27)

	Minimum	**Maximum**	**Mean**	**SD**
Age	66	85	71.96	4.89
Education	11	22	14.59	2.82
WRAT Reading	87	115	105.04	7.61
Handedness	**Right**	**Left**	**Mixed**	
	92.6%	7.4%	0%	

Female NHLS Group (N = 25)

	Minimum	**Maximum**	**Mean**	**SD**
Age	56	86	69.76	8.18
Education	11	18	13.64	1.93
WRAT Reading	78	120	104.16	9.06
Handedness	**Right**	**Left**	**Mixed**	
	92%	8%	0%	

Male NHLS Group (N = 25)

	Minimum	**Maximum**	**Mean**	**SD**
Age	50	84	65.28	9.89
Education	12	20	15.12	2.39
WRAT Reading	94	117	104.13	6.72
Handedness	**Right**	**Left**	**Mixed**	
	88%	8%	4%	

Group Characteristics

Three separate analyses were completed to examine the potential differences between groups. First, an ANOVA was done to compare differences between men and women in the NHLS group (Table 2). There were significant group differences in education (p = 020), but premorbid intellect (WRAT-III; p = .488) and age (p = .087) were not different between the two genders. Differences were also found in aspects of executive functioning, including number of stages completed in the ID/ED Shift (p = .004) and categories completed on WCST (p = .012) with men outperforming women on both of these tasks. Additionally, verbal memory encoding as measured by the learning trials of the AVLT (p = .043) and verbal memory retention as measured by the delayed trials of the AVLT (p = .029) were different between the two groups with women outperforming men. There were no differences between men and women in aspects of attention, language, visuospatial ability, manual dexterity, and psychosocial variables.

Second, an ANOVA was used to compare women in the BCS and NHLS group (Table 3). The women did not differ on age (p = .240), education (p = .165), or estimates of premorbid intellect (WRAT-III Reading, p = .933). Women in the NHLS group performed better on one measure of executive functioning (Trails B; p = .049) and on a measure of visuospatial functioning (FRT; p = .001). Notably, social integration endorsement was approaching significance, with the BCS group indicating higher levels of social integration as measured by the SPS. The two groups of women performed similarly in other aspects of executive functioning and visuospatial ability, as well as on tasks of attention, language, memory, manual dexterity, and psychosocial variables.

Table 2. ANOVA Comparing Men and Women NHLS Groups

VARIABLES	FEMALE MEAN *(SD)*	MALE MEAN *(SD)*	F	SIG.
Age	69.76 *(8.177)*	65.28 *(9.885)*	3.049	.087
Education	**13.64 *(1.934)***	**15.12 *(2.386)***	**5.085**	**.020**
Premorbid Intellect				
WRAT-III Reading	104.16 *(9.063)*	104.13 *(6.720)*	.489	.489
Attention				
Digit Span – Forward	9.8 *(2.380)*	10.48 *(1.939)*	1.226	.274
Digit Span – Reverse	6.72 *(2.011)*	6.56 *(2.485)*	.063	.803
Digit Span – Total	16.52 *(3.84)*	17.04 *(3.713)*	.237	.629
Trail Making Test – part A	34.76 *(16.566)*	32.55 *(10.245)*	.321	.574
Trail Making Test – part A errors	.24 *(.436)*	.08 *(.277)*	2.4	.128
Language				
COWAT	43.48 *(13.153)*	39.92 *(8.441)*	1.297	.260
BNT	54.84 *(6.336)*	56. 50 *(3.841)*	1.254	268
Visuospatial				
Complex Figure Copy	32.20 *(3.969)*	32.28 *(2.578)*	.007	.933
FRT	47.64 *(3.499)*	46.16 *(3.078)*	2.522	.119
Memory				
AVLT – Trial 1	6.16 *(1.463)*	5.52 *(1.122)*	3.012	.089
AVLT – Trial 5	11.72 *(2.525)*	10.40 *(2.309)*	3.720	.060
AVLT – Total Trials	**46.56 *(9.988)***	**41.28 *(7.802)***	**4.339**	**.043**
AVLT – Delay	**10.08 *(2.957)***	**8.26 *(2.701)***	**5.051**	**.029**
Complex Figure Delay	15.76 *(4.592)*	17.14 *(5.729)*	.883	.352
BVRT – Correct Score	6.64 *(1.497)*	6.40 *(1.500)*	.321	.574
BVRT – Error Score	4.68 *(2.428)*	6.12 *(2.833)*	3.724	.060

Table 2 continued

Executive Functioning				
ID/ED Stages	**7.44 *(1.653)***	**8.42 *(.902)***	**9.389**	**.004**
Trail Making Test – part B	79.12 *(27.668)*	88.12 *(29.397)*	1.243	.271
Trail Making Test – part B errors	.64.00 *(.952)*	1.12 *(1.166)*	2.541	.117
WCST – Perseverative Errors	11.00 *(7.314)*	8.52 *(9.136)*	1.246	.270
WCST – Categories	**2.44 *(1.609)***	**3.52 *(1.436)***	**6.809**	**.012**
Manual Dexterity				
Pegs - Dominant Hand	86.82 *(25.152)*	83.40 *(25.746)*	.226	.637
Pegs – Nondominant Hand	93.96 *(24.719)*	89.08 *(26.215)*	.459	.502
Psychosocial Variables				
BDI-II	7.73 *(5.487)*	7.00 *(7.461)*	.157	.693
SPS- Guidance	14.48 *(1.896)*	13.63 *(2.281)*	2.130	.151
SPS – Reasurrance of Worth	13.16 *(1.841)*	13.83 *(2.057)*	1.522	.223
SPS – Social Integration	13.48 *(2.417)*	13.88 *(1.941)*	.413	.523
SPS – Attachment	14.00 *(1.848)*	13.29 *(2.579)*	1.281	.263
SPS – Nurturance	11.80 *(3.329)*	12.42 *(1.954)*	.645	.426
SPS – Reliable Alliance	14.52 *(1.610)*	13.96 *(1.922)*	1.286	.262
SPS – Total	81.44 *(9.592)*	81.00 *(9.409)*	.027	.869
LOT	19.28 *(4.179)*	18.26 *(4.845)*	.666	.418

A last analysis compared the BCS group with the female NHLS and male NHLS groups on cognitive and psychosocial variables (Table 4). Because there were differences in age (p = .018) between the BCS and male NHLS groups (p = .015) with the breast cancer participants being older, a MANCOVA was used. Age was controlled for and the cognitive variables were used as dependent variables (i.e., Digit Span raw scores, Trail Making Test parts A and B, COWAT, BNT, Complex Figure Copy and Delay, FRT, AVLT, BVRT, ID/ED Stages, and WCST). The overall MANCOVA group effect was

Table 3. ANOVA Comparing Women in NHLS and BCS Groups

VARIABLES	NHLS FEMALE MEAN *(SD)*	BCS FEMALE MEAN *(SD)*	F	SIG.
Age	69.76 *(8.177)*	71.96 *(4.887)*	1.415	.240
Education	13.64 *(1.934)*	14.59 *(2.818)*	1.988	.165
Premorbid Intellect				
WRAT-III Reading	104.16 *(9.063)*	105.04 *(7.613)*	.007	.933
Attention				
Digit Span – Forward	9.8 *(2.380)*	9.41 *(2.258)*	.373	.544
Digit Span – Reverse	6.72 *(2.011)*	6.07 *(1.615)*	1.642	.206
Digit Span – Total	16.52 *(3.84)*	15.48 *(3.367)*	1.079	.304
Trail Making Test – part A	34.76 *(16.566)*	37.81 *(8.867)*	.702	.406
Trail Making Test – part A errors	.24 *(.436)*	.26 *(.447)*	.025	.876
Language				
COWAT	43.48 *(13.153)*	39.41 *(15.093)*	1.069	.306
BNT	54.84 *(6.336)*	56.96 *(2.457)*	2.611	.112
Visuospatial				
Complex Figure Copy	32.20 *(3.969)*	33.33 *(1.961)*	1.744	.193
FRT	**47.64 *(3.499)***	**44.41 *(3.434)***	**11.298**	**.001**
Memory				
AVLT – Trial 1	6.16 *(1.463)*	5.48 *(1.553)*	2.619	.112
AVLT – Trial 5	11.72 *(2.525)*	12.41 *(1.886)*	1.249	.269
AVLT – Total Trials	46.56 *(9.988)*	48.59 *(8.271)*	.643	.427
AVLT – Delay	10.08 *(2.957)*	10.22 *(2.621)*	.034	.855
Complex Figure Delay	15.76 *(4.592)*	15.870 *(5.095)*	.007	.935
BVRT – Correct Score	6.64 *(1.497)*	6.67 *(1.488)*	.004	.949
BVRT – Error Score	4.68 *(2.428)*	5.26 *(2.229)*	.805	.374

Table 3 continued

Executive Functioning				
ID/ED Stages	7.44 *(1.653)*	8.00 *(1.732)*	1.699	.198
Trail Making Test – part B	**79.12 *(27.668)***	**97.04 *(35.467)***	**4.079**	**.049**
Trail Making Test – part B errors	.64.00 *(.952)*	.52 *(.700)*	.278	.601
WCST – Perseverative Errors	11.00 *(7.314)*	11.00 *(5.685)*	.000	1.00
WCST – Categories	2.44 *(1.609)*	2.92 *(1.598)*	1.201	.278
Manual Dexterity				
Pegs - Dominant Hand	86.82 *(25.152)*	93.30 *(18.786)*	1.117	.296
Pegs – Nondominant Hand	93.96 *(24.719)*	104.81 *(25.365)*	2.484	.121
Psychosocial Variables				
BDI-II	7.73 (5.487)	5.73 (5.064)	1.944	.169
SPS- Guidance	14.48 (1.896)	14.70 (1.964)	.177	.675
SPS – Reasurrance of Worth	13.16 (1.841)	13.57 (1.532)	.804	.374
SPS – Social Integration	13.48 (2.417)	14.57 (1.590)	3.907	.054
SPS – Attachment	14.00 (1.848)	14.17 (1.696)	.134	.716
SPS – Nurturance	11.80 (3.329)	12.78 (2.131)	1.711	.197
SPS – Reliable Alliance	14.52 (1.610)	15.04 (1.770)	1.353	.250
SPS – Total	81.44 (9.592)	84.83 (6.617)	2.347	.132
LOT	19.28 (4.179)	18.45 (3.839)	.608	.439

significant (Wilk's λ p = .003). Follow-up ANOVAs showed that, after controlling for age, differences were found between the three groups in aspects of visuospatial ability and memory; by contrast, there were no differences between the three groups on tasks measuring attention, language, executive functioning, and manual dexterity, as well as the psychosocial variables, including depression (BDI-II), optimism (LOT-R), and social support (SPS). A Bonferroni procedure (to correct for Type I error rate inflation) was then used for pairwise comparisons for each cognitive variable that demonstrated

Table 4. MANCOVA Group Comparisons Covarying for Age

VARIABLES	NHLS MALE ADJ. MEAN	NHLS FEMALE ADJ. MEAN	BCS FEMALE ADJ. MEAN	F	SIG.
Premorbid Intellect					
WRAT-III Reading	104.608	104.072	104.66	.045	.956
Attention					
Digit Span – Forward	10.202	9.550	9.619	.430	.652
Digit Span – Reverse	6.466	6.737	6.146	.527	.593
Digit Span – Total	16.667	16.587	15.765	.473	.625
Trail Making Test – part A	35.633	34.207	35.474	.137	.872
Trail Making Test – part A errors	.087	.239	.254	1.224	.300
Language					
COWAT	39.322	43.587	39.862	.842	.435
BNT	55.723	54.980	57.553	2.522	.087
Visuospatial					
Complex Figure Copy	32.129	32.227	33.448	1.522	.225
FRT	**46.034**	**47.663**	**44.503**	**5.678**	**.005**
Memory					
AVLT – Trial 1	5.418	6.178	5.559	2.099	.130
AVLT – Trial 5	**10.084**	**11.777**	**12.647**	**8.260**	**.001**
AVLT – Total Trials	**40.077**	**46.776**	**49.507**	**7.545**	**.001**
AVLT – Delay	**7.898**	**10.149**	**10.513**	**6.416**	**.003**
Complex Figure Delay	16.793	15.822	16.134	.215	.806
BVRT – Correct Score	6.257	6.666	6.775	.786	.460
BVRT – Error Score	6.332	4.642	5.098	2.874	.063
Executive Functioning					
ID/ED Stages	8.382	7.450	8.030	2.948	.059

Table 4 continued

Trail Making Test – part B	94.148	78.037	92.458	2.374	.100
Trail Making Test – part B errors	1.139	.637	.504	2.765	.070
WCST – Perseverative Errors	9.272	10.865	10.431	.319	.728
WCST – Categories	3.353	2.471	3.052	2.261	.112
Manual Dexterity					
Pegs - Dominant Hand	89.911	85.653	88.350	.306	.737
Pegs – Nondominant Hand	95.545	92.799	99.897	.700	.500
Psychosocial Variables					
BDI-II	7.257	7.683	5.535	.893	.414
LOT	18.683	19.204	18.133	.452	.638
SPS- Guidance	13.646	14.476	14.680	1.707	.189
SPS – Reasurrance of Worth	13.874	13.153	13.535	.989	.377
SPS – Social Integration	13.880	13.479	14.562	1.971	.147
SPS – Attachment	13.372	13.986	14.112	.875	.421
SPS – Nurturance	12.195	11.840	12.951	1.360	.263
SPS – Reliable Alliance	14.044	14.505	14.978	1.720	.186
SPS – Total	81.011	81.438	84.819	1.478	.235

significance (Table 5). The results of this procedure indicate that there were differences in the domain of visuospatial ability, as measured by a facial recognition task (FRT, p = .005) and pairwise comparisons showed significant differences between the BCS and female NHLS group (p = .004) with the female NHLS group outperforming the BCS group (similar to the prior mentioned results). There were also significant group differences in aspects of learning and memory, including number of items named after five learning trials (AVLT – Trial 5, p = .001) and total items named (AVLT – Total Trials, p = .001). Verbal memory was also significantly different between groups (AVLT

Table 5. Pairwise Comparisons with Bonferroni Correction

	SIGNIFICANCE			MEANS (SD)
	BCS	**NHLS FEMALE**	**NHLS MALE**	
Visuospatial				
FRT				
BCS		**.004**	.378	44.503
NHLS FEMALE	**.004**		.297	47.663
NHLS MALE	.378	.297		46.034
Memory				
AVLT-Trial 5				
BCS		.463	**.000**	12.647
NHLS FEMALE	.463		**.026**	11.777
NHLS MALE	**.000**	**.026**		10.084
AVLT – Total Trials				
BCS		.749	**.001**	49.507
NHLS FEMALE	.749		**.023**	46.776
NHLS MALE	**.001**	**.023**		40.077
AVLT-Delay				
BCS		1.00	**.004**	10.513
NHLS FEMALE	1.00		**.014**	10.149
NHLS MALE	**.004**	**.014**		7.898

– Delay, p = .003). Each pairwise comparison was significant for the BCS group outperforming the male NHLS group, in addition to the female NHLS group performing better than the male NHLS group. Specifically, the BCS and female NHLS group performed better than the male NHLS group (AVLT – Trial 5, p = .00 and p = .026, respectively; AVLT – Total Trials, p = .001 and p = .023, respectively; AVLT – Delay, p

= .004 and p = .014, respectively); there were no significant differences between the BCS and female NHLS groups on these tasks (all p's > .05).

Variable Relationships

To assess the relationship between social support, optimism, and cognition, a bivariate correlation matrix was calculated separately for both the NHLS group and the BCS group. In the NHLS group (Table 6), age was not related to any of the psychosocial variables, but education was positively related to several aspects of social support, including Reassurance of Worth (r = .389, p = .005), Social Integration (r = .294, p = .038), Nurturance (r = .327, p = .020), and the SPS total score (r = .299, p = .035). Premorbid intellect was negatively related to depression (r = -.325, p = .023). On measures of attention, performance on repeating digits backward (Digit Span – Reverse) was related to both optimism (r = .298, p = .043) and Reassurance of Worth (r = .295, p = .039). Number of errors on Trail Making Test – part A was also significantly and positively related to Nurturance (r = .330, p = .020). Aspects of visuospatial ability, including scores of a complex figure copy (Reliable Alliance, r = -.336, p =.018; SPS Total, r = - .322, p = .024) and facial recognition were negatively related to social support (Nurturance, r = -.310, p = .030). Social support was also related variably to memory. Specifically, on AVLT – Trial 5, Guidance (r = .293, p = .041) and Attachment (r = .325, p = .023) were positively related. Guidance (r = -.290, p = .049), Attachment (r = -.344, p = .015), Reliable Alliance (r = -.316, p = .027), and Total SPS score (r = -.290, p = .049) were negatively related to the Complex Figure Delay total copy score. Lastly, depression was negatively related to the BVRT correct score (r = -.292, p = .042) and positively related to the BVRT error score (r = .326, p = .022). Time on the Grooved Pegs task with the dominant hand was positively related to depression (r = .334, p = .019). With regards to the psychosocial variables, BDI was negatively related to optimism (r = -.338, p = .020) and social support on the subscales Reassurance of Worth (r = -.368, p = .010) and

Social Integration (r = -.363, p = .011). Lastly, optimism was positively related to aspects of social support, including Guidance (r = .293, p = .043), Reassurance of Worth (r = .354, p = .014), Social Integration (r = .415, p = .003), Attachment (r = .430, p = .002), Reliable Alliance (r = .433, p = .002), and Total Score (r = .431, p = .002). There were no significant correlations between executive functioning and the psychosocial variables.

In the BCS group (Table 7), Nurturance was negatively related to education (r = -.392, p = .043). Facial recognition was negatively related to depression (r = -.408, p = .038). In the domain of learning and memory, optimism was negatively related to AVLT – Trial 1 (r = -.465, p = .029) and AVLT – Total Trials (r = -.438, p = .042), and Guidance was positively related to the BVRT Error Score (r = .427, p = .042). The relationship between executive functioning and psychosocial variables was inconsistent, and only categories completed on WCST was negatively correlated to Reliable Alliance (r = -.462, p = .031). Lastly, depression was negatively related to optimism (r = -.507, p = .016) and Reassurance of Worth (r = -.548, p = .007); optimism was positively related to Reassurance of Worth (r = .599, p = .003) and Reliable Alliance (r = .517, p = .014). There were no correlations between the psychosocial variables and other cognitive variables, including attention, language, executive functioning, and manual dexterity.

There were limited similarities of variable relationships across the two groups. For example, in the NHLS group, education was significantly and positively related to Nurturance, but in the BCS group, education was significantly and negatively related to Nurturance. With regards to the relationships between cognitive and psychosocial variables, some of the variable relationships were consistently positive or negative between the two groups, but the degree of significance differed. For example, in the NHLS group, total social support was negatively related to the complex figure copy raw score (r = - .322, p = .024), but not in the BC group (r = -.059, p > .05), Lastly, some of the variable relationships were inconsistent and, for example, AVLT Total Trials was

Table 6. Bivariate Correlations for NHLS Group

VARIABLES	BDI	LOT	SPS – Guidance	SPS – Reassurance of Worth	SPS – Social Integration	SPS – Attachment	SPS – Nurturance	SPS – Reliable Alliance	SPS - Total
Demographics									
Age	.156	.261	.003	.014	-.065	.068	-.276	.114	-.054
Education	-.313	.058	.078	**.389****	**.294***	.114	**.327***	.053	**.299***
Premorbid Intellect									
WRAT-III Reading	**-.325***	.267	-.045	.122	.020	.063	.105	.027	.073
Attention									
Digit Span – Forward	-.227	.133	.182	.124	.088	.201	.119	.215	.210
Digit Span – Reverse	-.155	**.298***	.122	**.295***	.039	.192	.132	.257	.231
Digit Span – Total	-.223	.252	.179	.248	.074	.231	.149	.278	.260
Trail Making Test – part A	.141	.151	-.224	-.125	-.055	-.167	-.223	.005	-.193
Trail Making Test – part A errors	-.024	-.004	.145	.145	.067	.144	**.330***	.064	.221
Language									

Table 6 continued

COWAT	-.229	.089	.188	.007	.120	.177	.213	.085	.192
BNT	**-.308***	-.011	.201	.222	-.009	.155	.089	.032	.159
Visuospatial									
Complex Figure Copy	.098	-.160	-.182	-.151	-.278	-.271	-.197	**-.336***	**-.322***
FRT	.128	-.036	-.004	-.174	**-.310***	-.059	-.106	-.126	-.178
Memory									
AVLT – Trial 1	.025	-.125	-.075	-.104	-.199	-.013	-.039	-.016	-.079
AVLT – Trial 5	-.122	.075	**.293***	.129	.009	**.325***	-.018	.237	.218
AVLT – Total Trials	-.123	.028	.212	.120	-.072	.265	.055	.175	.168
AVLT – Delay	.022	-.116	.120	.045	-.167	.125	.031	.153	.065
Complex Figure Delay	-.067	-.234	**-.290***	-.077	-.161	**-.344***	-.103	-.316*	**-.290***
BVRT – Correct Score	**-.292***	.114	.042	.024	-.123	-.046	-.130	-.104	-.082
BVRT – Error Score	**.326***	-.199	-.029	-.042	.094	.018	.079	.003	.034
Executive Functioning									
ID/ED Stages	-.177	-.164	,073	.281	.098	.103	.124	.201	.193
Trail Making Test – part B	-.034	-.101	-.123	-.110	-.017	-.122	-.017	-.046	-.098
Trail Making Test – part B errors	-.094	-.080	-.034	-.152	.030	-.041	.095	-.182	-.049
WCST – Perseverative Errors	.180	-.175	.115	.039	-.256	.031	-.292	.074	-.090
WCST – Categories	-.101	-.080	-.164	-.023	.118	-.066	.186	-.183	-.009

Table 6 continued

Manual Dexterity									
Pegs – Dominant Hand	**.334***	.131	-.063	-.199	-.173	-.025	-.031	.040	-.103
Pegs – Nondominant Hand	.010	.171	.155	.035	-.032	.199	-.015	.197	.115
Psychosocial Variables									
BDI-II	--	**-.338***	-.132	**0.368***	**-.363***	-.143	-.156	-.079	-.281
LOT		--	**.293***	**.354***	**.415****	**.430****	.047	**.433****	**.431****
SPS- Guidance			--	**.475****	**.374****	**.822****	.157	**.618****	**.769****
SPS – Reasurrance of Worth				--	**.569****	**.547****	.158	**.468****	**.712****
SPS – Social Integration					--	**.419****	**.383****	**.532****	**.746****
SPS – Attachment						--	.149	**.745****	**.818****
SPS – Nurturance							--	**.304***	**.540****
SPS – Reliable Alliance								--	**.814****
SPS – Total									--

* $p < .05$. ** $p < .01$

Table 7. Bivariate Correlations for BCS Group

VARIABLES	BDI	LOT	SPS – Guidance	SPS – Reassurance of Worth	SPS – Social Integration	SPS – Attachment	SPS – Nurturance	SPS – Reliable Alliance	SPS – Total
Demographics									
Age	-.169	.102	.309	-.002	.256	.342	.148	.210	.344
Education	-.265	.261	-.097	.246	.218	-.244	**-.392***	-.107	-.137
Premorbid Intellect									
WRAT-III Reading	-.177	-.066	-.271	.032	.045	-.130	-.001	-.168	-.141
Attention									
Digit Span – Forward	-.003	.025	-.369	-.136	.061	-.131	.118	-.293	-.200
Digit Span – Reverse	-.253	.248	-.096	.202	.034	-.103	.050	.002	.017
Digit Span – Total	-.116	.126	-.294	-.005	.057	-.134	.103	-.199	-.129
Trail Making Test – part A	.156	-.041	.131	-.126	.046	.171	-.020	.136	.094
Trail Making Test – part A errors	-.334	.007	.249	.040	.166	.176	-.176	.214	.169
Language									
COWAT	-.277	.128	.052	.171	-.045	-.307	-.063	-.077	-.075
BNT	-.093	-.056	-.008	.216	.127	-.103	-.199	-.231	-.074

Table 7 continued

Visuospatial									
Complex Figure Copy	-.037	-.045	-.088	-.028	-.206	-.171	.077	.157	-.059
FRT	**-.408***	.182	.154	.307	.160	-.057	-.228	.141	.105
Memory									
AVLT – Trial 1	-.112	**-.465***	-.240	-.367	-.249	-.118	-.248	-.212	-.383
AVLT – Trial 5	.052	-.368	-.181	-.215	-.031	.102	.251	-.242	-.069
AVLT – Total Trials	-.037	**-.438***	-.169	-.342	.015	.229	.032	-.163	-.100
AVLT – Delay	.048	-.345	-.067	-.227	.094	.252	-.113	-.237	-.085
Complex Figure Delay	-.203	-.130	-.389	-.234	-.120	-.218	-.181	-.159	-.355
BVRT – Correct Score	.023	.111	-.262	-.093	.172	.051	-.061	-.210	-.121
BVRT – Error Score	.238	-.077	**.427***	.169	-.012	-.003	-.004	.289	.238
Executive Functioning									
ID/ED Stages	.083	.211	-.135	.051	.000	-.185	.416	-.254	-.012
Trail Making Test – part B	.277	-.102	.245	-.041	.075	.335	.057	.152	.226
Trail Making Test – part B errors	.128	-.008	.179	-.113	.048	.254	-.041	.157	.132
WCST – Perseverative Errors	-.019	-.035	.200	.004	-.332	-.021	-.184	.369	.010
WCST – Categories	.030	-.321	-.221	-.252	.196	.201	.219	**-.462***	-.073

Table 7 continued

Manual Dexterity									
Pegs – Dominant Hand	.141	.046	-.108	-.026	.196	.122	.001	-.362	-.056
Pegs – Nondominant Hand	.023	.231	.072	.035	.262	.146	-.028	-.030	.116
Psychosocial Variables									
BDI-II	--	**-.507***	-.179	**-.548****	-.273	-.062	.328	-.324	-.243
LOT		--	.397	**.599****	.256	-.080	-.206	**.517***	.372
SPS- Guidance			--	**.483***	**.480***	**.467***	-.017	**.631****	**.807****
SPS – Reasurrance of Worth				--	**.478***	.188	-.086	.225	**.571****
SPS – Social Integration					--	**.653****	.185	.072	**.740****
SPS – Attachment						--	.275	.164	**.728****
SPS – Nurturance							--	-.118	.381
SPS – Reliable Alliance								--	**.528****
SPS – Total									--

* $p < .05$. ** $p < .01$

negatively related to Guidance in the BCS group ($r = -.438$, $p = .042$), but had a positive relationship in the NHLS group ($r = .028$, $p > .05$).

Regression Analyses

As outlined, bivariate correlations were used to determine which cognitive variables were related to both social support and optimism to identify potential variables to include in the hierarchical regression analyses for meditational analyses. Optimism was related to Reassurance of Worth, the mediator ($r = .354$, $p < .05$). Only one cognitive variable (Digit Span – Reverse) in one group (NHLS) significantly correlated to both optimism ($r = .298$, $p < .05$) and social support ($r = .295$, $p < .05$). To test for mediation, three regression equations were used and education was entered into the first step in all three models (to account for the correlation between the social support measure and education). Regression analyses are detailed in Table 8. In equation one, working memory (Digit Span – Reverse) was regressed on optimism and the overall model was significant [$F = 3.454$, R^2 change = .078, $p = .040$]. The R^2 change refers to the amount of variance accounted for by that variable after controlling for the initial variable entered into the equation. That is, after controlling for education, optimism accounted for almost 8% of the variance of working memory performance. In the second regression equation, education was entered in the first step and then Reassurance of Worth was regressed on optimism. The overall model was significant [$F = 8.059$, R^2 change = .104, $p = .001$]. In this model, Reassurance of Worth accounted for an extra 10% of the variance in optimism after education was entered. In the last equation, again education was entered in the first step, social support (mediator) was entered in the second step, and optimism was entered in the final step. The overall model was not significant [$F = 2.644$, R^2 change = .046, $p = .060$]. In terms of mediation, the relationship between optimism and working memory performance was not significantly smaller when Reassurance of Worth was in the equation (equation three) compared to when Reassurance of Worth was not in the equation (equation one). More importantly, after education was entered, social support was no longer significantly related to the working memory task at all. Therefore, the

analyses did not support the hypothesis that social support mediates the optimism-cognition relationship after controlling for education.

As mentioned previously, certain conditions must be met for a variable to be considered a mediator, including relationships between the independent variable, mediator, and outcome variable. Based on the bivariate correlations, there were no other outcome variables (cognitive variables) that were related to both the independent variable (optimism) and mediator (social support). As such, no further analyses were conducted to explore the relationship between these variables.

Table 8. Mediational Analysis

Analysis of Digit Span (Reverse) Regressed on Optimism

VARIABLES	B	B	SE	R^2 Change	F	R^2	p
Step 1				.050	2.529	.050	.118
Education	.224	.220	.138				.118
Step 2				.078	3.454	.128	.040
Education	.208	.204	.134				.135
LOT	.280	.142	.069				.046

Analysis of Social Support (Reassurance of Worth) Regressed on Optimism

VARIABLES	B	B	SE	R^2 Change	F	R^2	P
Step 1				.152	8.578	.152	.005
Education	.389	.332	.113				.005
Step 2				.104	8.059	.255	.001
Education	.371	.316	.107				.005
LOT	.323	.142	.056				.014

Table 8 continued

Analysis of Digit Span (Reverse) Regressed on Social Support (Reassurance of Worth) and Optimism

VARIABLES	B	B	SE	R^2 Change	F	R^2	p
Step 1				.050	2.529	.050	.118
Education	.224	.220	.138				.118
Step 2				.051	2.652	.101	.081
Education	.129	.126	.148				.399
SPS – R	.246	.284	.173				.108
Step 3				.046	2.644	.147	.060
Education	.148	.146	.146				.323
SPS-R	.159	.184	.182				.318
LOT	.228	.116	.074				.123

CHAPTER V

DISCUSSION

There have been great strides in chemobrain research in the past decade, but few attempts have been made to examine the long-term effects of chemotherapy on cognition, especially in older adult survivorship. Furthermore, even fewer studies have considered quality of life variables in conjunction with cognition in cancer patients or survivors. The aim of the present study was to gain a better understanding of the relationship between social support, optimism, and cognition, specifically in older adult NHL and breast cancer survivors. Cognitive and psychosocial variables were first examined in the sample. It was hypothesized that both social support and optimism would be positively related to cognition, and this hypothesis was only partially supported. The hypothesis that social support would mediate the optimism-cognition relationship was not supported. It was hoped that a better understanding of these relationships could help employ early interventions and provide additional information on the effects of chemotherapy and possible ways to influence cognition.

The results of this study are discussed in this chapter, in addition to comparing the current results to the extant literature. New research that considers potential physiological mechanisms of how chemotherapy affects the brain is then outlined. Next, limitations of the study are addressed. Lastly, implications for clinical practice are presented.

Study Findings

Discussion of Cognitive and Psychosocial Variables

Generally, in this study, neuropsychological test performances were within normal limits compared to published normative data (Spreen & Strauss, 1998 Steinberg, Bieliauskas, Smith, & Ivnik, 2005; Steinberg, Bieliauskas, Smith, Ivnik, Malec, 2005) Unfortunately, there are no studies to date that have specifically examined the potential

effects of chemotherapy in an NHL population, thus comparisons are difficult. In spite of this, when employing the breast cancer literature, the findings of this study are consistent with other studies that have questioned the potential long-term effects of chemotherapy. For example, one study concluded (Jenkins et al., 2006) that approximately 18 months from baseline, there was little to suggest meaningful change in cognition in breast cancer patients, and another study found that cognitive problems resolve within one year post-treatment (Collins et al., 2009). Schagen and colleagues (2002) even noted cognitive improvements in a two-year follow-up of breast cancer survivors.

However, this research has been largely inconsistent. Some researchers that have failed to demonstrate cognitive changes after chemotherapy have found that a subset of women do demonstrate decline when their individual performances are compared over time (e.g., Reid-Arndt et al., 2010; Wefel et al., 2010). Two studies, in particular, that are important to highlight because they are the most similar to this study based on their want to examine longer-term survivors, found that approximately 2 to 5 years post-diagnosis, breast cancer survivors that had been treated with chemotherapy performed worse on measures of visual memory, visual function, and verbal fluency (Castellon et al., 2004). Another study examined both breast cancer and lymphoma survivors treated with chemotherapy approximately 10 years prior and these participants performed worse on measures of verbal memory and psychomotor speed (Ahles et al., 2002). Unlike the present study, in both of these studies, the researchers had a comparison group; namely, cancer survivors with a history of chemotherapy were compared to cancer survivors without a history of chemotherapy. (Furthermore, upon closer inspection and when compared to normative published data, their samples also performed, generally, within normal limits regardless of statistically significant differences between groups).

In terms of specific group differences, it was found that the men in the NHLS group outperformed the women in the NHLS group in aspects of executive functioning (i.e., stages completed on the ID/ED and WCST measures), while the women in this

group performed better on verbal learning and memory tasks.. There were no differences between men and the women in the NHLS group in aspects of attention, language, visuospatial ability, manual dexterity, and psychosocial variables. Gender differences are sometimes found on neuropsychological tasks, but often not to the degree that performance is significantly affected. For example, on the most popular intelligence measures (Wechsler Adult Intelligence Scales), there is no correction for gender when computing raw scores to standard scores. Too, normative published data for older adults, for example the Mayo's Older American Normative Studies (Steinberg, Bieliauskas, Smith, & Ivnik, 2005), considers only age and predicted full scale IQ before converting raw scores to standard scores. However, there have been some individual studies that have examined potential gender differences in neuropsychological test performance (e.g., Roivainen, 2011).

The finding that men in the NHLS group outperformed women in the NHLS group on executive functioning tasks is surprising and likely represents a true vulnerability for these women, as one research study found that in older adults, women outperform men on the WCST task, including percentage of perseverative errors and categories completed (Boone, Ghaffarian, Lesser, Hill-Gutierrez, & Berman, 1993). This finding implicates potential frontal neural system disruption, and the ability to form new concepts, benefit from feedback, and cognitive flexibility. Since gender differences on neuropsychological testing likely cannot solely explain the difference between these two groups, possible mechanisms for differences include an interaction between gender and chemotherapy regimen and/or survivorship status.

In terms of verbal learning and memory, the women in both the NHLS and BCS group outperformed the men in the NHLS group, which also likely reflects a true difference and weakness in the men, although there has been some evidence of small gender effects that indicate women perform better on verbally mediated tasks, but this research has been largely inconsistent (Schmidt, 1996; Steinberg, Bieliauskas, Smith,

Ivnik, & Malec, 2005). On average, the women in this study did not differ from men in their ability to immediately recall a list of words after a single exposure, but were able to recall (encode) more words across the five trials. Furthermore, the women were able to recall more words from the list in a delayed condition. However, it is likely that the women's better memory performance is related to better encoding performance; that is, the women were able to recall more words from the list in a delay condition because they learned more words from the list across the five trials. Again, performances in all three groups were within normal limits. Clearly, based on the age of the group, this is an area of interest, as performance on this task could implicate dysfunction in the memory system (e.g., hippocampus and fronto-subcortical regions), a hallmark symptom in some neurodegenerative diseases (e.g., Alzheimer's disease).

Lastly, the BCS group performed worse on an ecologically valid measure of executive functioning (i.e., Trails B) and a facial recognition task compared to the women in the NHLS group. Again, though all of these performances were within normal limits, there is little evidence to suggest that the BCS group should perform poorer on these tasks than women in the NHLS group beyond a true difference between these groups. The differences could be attributable to the specific chemotherapy regimen employed, menopausal status, or point to potential effects of hormone therapy that breast cancer patients often receive for many years post-diagnosis.

It is notable that there were no differences on self-reported mood, social support, and optimism between groups. Scores on social support measures in the sample were also comparable, if not slightly better, to the published means (Cutrona & Russell, 1987) and a study that specifically examined social support in older adults (Cutrona, Russell, & Rose, 1986). Interestingly, the sample in this study endorsed significantly higher dispositional optimism compared to older community dwelling adults (Isaacowitz, 2005) and more comparably to the original norms based on undergraduate students (Scheier & Carver, 1985).

Cognitive and Psychosocial Variable Relationships

Correlations in both groups ranged from small to medium correlations with small, medium, and large correlations identified by an *r* of .10, .30., and .50, respectively (Cohen, 1992). This is the first study of its kind to consider social support and optimism together with cognition and correlational analyses were meant to be exploratory; consequently, based on the number of comparisons, some correlations could be attributable to Type I error and only correlations that reflected a medium correlation ($r > .30$) that were significant at a *p*-value of $< .01$ are highlighted. However, future studies with larger sample sizes might offer additional support for the small correlations that were found in this study. Furthermore, social support has only been considered simultaneously with cognition in one study (Reid-Arndt, 2010) and, unfortunately, a different measure of social support was used, making comparisons difficult. Thus, explanations regarding the correlations between psychosocial variables and cognition is unique, but hypothetical.

Only education was positively related to Reassurance of Worth from the SPS in the NHLS group. Reassurance of Worth measures an individual's ability to recognize their own skills, thus it is not surprising that individuals who have more education are more adept at recognizing their competencies. Individuals with a higher education likely have more opportunity to test their skills and have them evaluated. Interestingly, Reassurance of Worth, specifically in older adults, has been found to be related to health outcomes (e.g., 'I have relationships where my competence and skill are recognized'; Cutrona & Russell, 1987). It is believed that since older adults often feel a sense of role loss, particularly in the context of retirement, children growing up, and the loss of independence, feeling competent and worthy evokes a want to care for oneself better.

It is not surprising that social support, as measured by the total score of SPS, was inversely correlated with depression and positively correlated with optimism. Additionally, optimism was negatively correlated to depression (both *p*'s $< .05$).

However, the positive correlation between optimism and the SPS was only significant in the NHLS group ($p < .01$). Although, the SPS is not utilized extensively in the current social support literature, through the use of other social support measures, the positive relationship between social support and optimism, as well as the negative relationship between mood and both social support and optimism is consistent with extant literature (e.g. Shelby et al., 2008).

Lastly, this study was the first to look at the potential relationship between social support, optimism, and cognition; more specifically, it was hypothesized that social support mediated the optimism-cognition relationship. Unfortunately, there was only one cognitive variable that significantly correlated with both optimism and social support, a working memory measure (Digit Span Reverse raw score). It is notable that these correlations did not meet the criterion specified prior to adjust for Type I error, however, as this is the one of the first studies to examine these variables together, especially in a meditational analysis, its value for discussion is important. Education was significantly related to Reassurance of Worth in this group, thus it was controlled for in all regression analyses. Subsequent analysis revealed that after controlling for education, Reassurance of Worth was no longer significantly related to Digit Span Reverse performance. The present study's hypothesis that social support would mediate the optimism-cognition relationship, consequently, was not supported. Not only was Reassurance of Worth not predictive of Digit Span performance after controlling for education, the relationship between optimism and working memory performance was not significantly smaller when Reassurance of Worth was in the equation versus when Reassurance of Worth was not in the equation.

These results are particularly intriguing and suggest that education affects the relationship between Reassurance of Worth and working memory performance. Much attention has been paid to education and its effects on cognition recently in the context of the cognitive reserve theory (Stern, 2009). This is particularly interesting research,

especially for considering potential predisposing factors as to why some individuals, like cancer survivors, may show greater cognitive impairment than others. In a review of cognitive reserve research, Stern (2009) posits that the brain actively copes with brain damage through pre-existing cognitive processes or by recruiting compensatory processes. That is, two individuals may have the same amount of brain damage, but can demonstrate different levels of cognitive impairment. Education has been shown to influence cognitive reserve above and beyond innate intelligence, and it has also been confirmed that higher educational attainment, occupational attainment, and leisure activities produce synergistic effects on cognitive reserve and, thus, cognitive reserve is not fixed. Studies have consistently found that higher educational attainment is a protective factor in demonstrable behavioral changes as a result of neurodegenerative disease. However, though individuals with higher cognitive reserve may chronologically experience symptom onset differently (than those with lower reserve), it has also been shown that these individuals with hypothesized higher cognitive reserve will show decrements in cognitive functioning more quickly. Taken together, individuals with less cognitive reserve may experience symptom onset earlier, but often have a slower progressive decline in cognitive function as the result of a neurodegenerative disease. In the present study, participants performed within normal limits per normative data on neuropsychological testing, but based on their demographic information, including higher educational attainment, they may be at particular risk for developing late-onset symptoms regardless of chemotherapy status. Too, even though they do not show impairment on behavioral tests, chemotherapy could have affected brain structures nonetheless, and these cancer survivors may be recruiting broader neural networks to complete tasks effectively.

In conclusion, these findings are promising as they indicate potential differences between cancer survivor groups. These differences could be attributable to the chemotherapy regimen that each cancer survivor receives or to the type of cancer itself.

Unfortunately, social support and optimism was not significantly correlated to as many of the cognitive variables as was hypothesized, and the correlations were not consistent within domain or between groups. That is, groups demonstrated different correlations between cognitive and psychosocial variables, and no two tests within a single cognitive domain demonstrated significant correlations with either optimism or social support. This complication makes it difficult to posit that, for example, better social support was related to better cognition. However, the relationship between some cognitive and psychosocial variables is valuable in providing a foundation for future studies that may be able to include larger sample sizes. This study is one of the first of its kind to consider beyond the effects of chemotherapy on cognition and consider potential predictive and/or protective factors of chemobrain. This is also the first study to examine cognition in NHL specifically, and consider potential effects of gender.

Even though there was no evidence of cognitive impairment in either cancer group, research has demonstrated that cognitive dysfunction has been found in long-term survivorship when a control group is used (e.g., Ahles et al., 2002; Castellon et al., 2004), although the group performances would not be classified as clinical impairment. The inconsistency in the literature begs the question as to whether there are truly long-term cognitive consequences of chemotherapy. Although behaviorally (via neuropsychological testing), the research has been variable, new research that highlights potential physiological changes as a result of chemotherapy are promising.

Mechanisms of Change in the Brain after Chemotherapy

Although it was initially believed that antineoplastic agents of chemotherapy could not pass the blood-brain barrier, recent evidence has suggested that chemotherapy has been associated with both acute and chronic encephalopathy, cerebrovascular complications, and toxic leukoencephalopahy leading to white matter disease (Deprez et al., 2011; Myers, 2009; Raffa, 2010; Saykin, Ahles, & McDonald, 2003; Saykin, Ahles,

Schoenfeld et al., 2003). Specifically, it is believed that chemotherapy can cause direct neurotoxic injury to the cerebral parenchyma, an inflammatory response, and/or microvascular injury leading to the obstruction of blood vessels, thrombosis, infarction, and parenchymal necrosis. Additionally, it has been postulated that chemotherapy can alter neurotransmitter levels. Clearly, such adverse effects depend on specific chemotherapy agents, doses, and combination treatments that are tailored based on individual needs and, as such, detailed investigations of any regimen in isolation is nearly impossible. However, it is known that some specific agents are more toxic than others. For example, methotrexate, an antimetabolite that is a common chemotherapy agent due to its disruption of DNA synthesis (and used in this study's breast cancer group), has demonstrated decreased hippocampal concentrations of neurotransmitters affecting cognition.

More recent studies have considered the use of neuroimaging techniques to capture a better understanding of how chemotherapy may affect the brain, however, this research has been minimal. Through structural imaging analyses, Saykin and colleagues (2003) found reductions in bilateral neocortical gray matter and cortical and subcortical white matter in long-term survivors (> 5 years) of breast cancer and lymphoma in comparison to healthy controls. Several researchers (Castellon, Silverman, & Ganz, 2005; Silverman et al., 2007) found altered cerebral blood flow in the frontal cortex in breast cancer patients who had received chemotherapy compared to breast cancer patients who had not received chemotherapy five to ten years previously while performing a short-term recall task. Additionally, with a short-term visual memory task, resting metabolism was decreased and severity of hypometabolism in the frontocortical areas was correlated to severity of cognitive dysfunction. Women treated with both chemotherapy and tamoxifen demonstrated decreases in basal ganglia activity.

Internationally, a group of researchers performed structural imaging on Japanese breast cancer survivors, approximately three years post-surgery, who received

chemotherapy compared to women who did not receive chemotherapy (Yoshikawa et al., 2005). They found no significant differences in hippocampal volume between the two groups as measured by an 8% difference, even though the chemotherapy group performed slightly worse on an attentional measure in a laboratory setting. This same group, however, did find smaller right prefrontal and parahippocampal gyrus in cancer survivors exposed to chemotherapy within four months of their adjuvant treatment, but not again at a mean of 4 years later (Inagaki et al., 2007).

A last interesting research study (Ferguson, McDonald, Saykin, & Ahles, 2007) evaluated monozygotic twins that were reared together, one of whom had been diagnosed with cancer and treated with chemotherapy and the other with no remarkable medical history. The twin with a history cancer and chemotherapy was three times more likely to endorse cognitive problems, though neuropsychological testing did not differ between the twins. It was found that the twin with a history of cancer and chemotherapy had more white matter lesions on structural imaging and had increased brain activation on functional imaging than her twin. Although neuropsychological performances were comparable in the twins, it was concluded that the higher endorsement of cognitive problems in the twin with the history of cancer and chemotherapy was likely attributable to the recruitment of broader neural networks to accomplish tasks comparably to the unaffected twin.

In animal studies, it has been found that mice treated with clinically relevant levels of 5-fluorouracil (also part of the chemotherapy regimen for the breast cancer survivors in this study) demonstrate both in vitro and in vivo changes to central nervous system (CNS) white matter tracts. Specifically, CNS progenitor cells and oligodendrocytes are particularly vulnerable after exposure and induced delayed degeneration of CNS white matter tracts (Han et al., 2008). The implications of this research highlight the possibility of delayed damage to the white matter tracts of individuals treated with chemotherapy. A last study (Janelsins et al., 2009) aimed to show

that chemotherapy agents that are known to cross the blood-brain barrier, such as cyclophosphamide (part of the chemotherapy regimen in both of the cancer survivor groups in this study) and fluorouracil, would more likely affect neurogenesis than agents that do not (paclitaxel and doxorubicin) in mice. It was found that all four chemotherapy agents resulted in reduction of newly divided cells in the dentate gyrus, which is part of the memory system.

Although this neuroimaging research is in its infancy and there is some variability in findings, it is integral in highlighting potential long-term physiological effects of chemotherapy. Potential physiological changes to the brain as a result of chemotherapy, clearly, has important implications for clinical practice and informed consent for cancer treatment. Furthermore, based on the cognitive reserve theory, it has served to explain why individuals often endorse cognitive problems, but perform within expectations on current neuropsychological tests (e.g., monozygotic twin study; Ferguson et al., 2007). This research also accounts for why there may be inconsistencies regarding the existence of cognitive impairment in the chemobrain research, as delayed physiological changes to the brain have been demonstrated.

Study Limitations

There are a number of limitations to this study due in part to the methodological design, but also in part to cancer research and cognition research on their own. First, the retrospective design of this study made it difficult to conclude the trajectory of cognitive impairment over time. Baseline data with neuropsychological evaluations throughout survivorship would have allowed for a better understanding of how chemotherapy affects cognition in the long-term and in older adults. The present study suffered from a small sample size. Furthermore, within this sample, the individual participants themselves were homogenous in terms of educational background and race. This study relied on a volunteer sample, which likely positively biased responses for both the cognitive and

psychosocial variables (i.e., volunteer participants are more likely to be cognitively intact and less likely to have psychosocial distress). Lastly, this study was the first study to consider both social support and optimism with cognition, but these psychosocial measures may lack the sensitivity and specificity to be useful and predictive of outcome in this sample population.

Similar to other research in this area, the heterogeneity of cancer disease and combination chemotherapy regimens makes it difficult to parse out the exact effects of specific chemotherapy agents. Even though longitudinal research seems to be the most beneficial in terms of understanding the course of cancer and the effects of chemotherapy, such prospective studies often suffer from high attrition rates. Too, these attrition rates are often the result of the mechanism being studied, such as cognitive status, chemotherapy regimen used, or disease stage. For example, if cognition is being evaluated longitudinally, it is concerning if the participant who demonstrates the most cognitive impairment drops out of the study, because of dysfunction severity. Likewise, a participant drops out of the study because of fatigue and illness associated with adjuvant treatment, but effects of adjuvant treatment is what is being examined.

Lastly, cognition research is infused with a plethora of instruments with different tests being used across different studies and cognitive domains. In addition to a variety of neuropsychological test batteries being employed, methodologically, research designs have also been heterogeneous. For example, some studies examine cancer patients and survivors cross-sectionally, retrospectively, and/or prospectively, which makes it difficult to compare results. Furthermore, definitions of impairment are not consistent across studies. Lastly, it has also been questioned whether the neuropsychological measures used in chemobrain research are sensitive enough to pick up on mild cognitive impairment and the potential implications on everyday functioning.

Implications for Clinical Practice

The results of the current study raise a number of important clinical implications. Current chemobrain research has found that cancer patients and survivors often report cognitive dysfunction on a daily basis, but do not necessarily demonstrate bona fide (or clinically relevant) cognitive impairment on neuropsychological tests (e.g., Reid-Arndt et al., 2010; Quesnal et al., 2009). Furthermore, qualitative research has shown that breast cancer survivors consistently report that managing their cognitive problems is a priority and health care workers often fail to provide information and support for their cognitive complaints (Boykoff et al., 2009; Munir et al., 2011). As such, psychologists are in a particularly unique position to offer both support and intervention for these complaints.

Very recently, research aimed to help alleviate cognitive complaints in cancer survivors has emerged. Though extremely limited at this time, studies have considered the effects of Tai Chi (Reid-Arndt, Matsuda, & Cox, in press), meditation (Biegeler, Chaoul, & Cohen, 2009), and in-patient rehabilitation (Poppelreuter, Weis, & Bartsch, 2009) on cognition, for example. One promising study (Ferguson et al., 2007) presented data on a pilot study of cognitive-behavioral management of chemotherapy-related cognitive change. Women who received chemotherapy (N = 29) for stage I or II breast cancer three years post-cancer treatment and complained of memory and attentional problems were recruited. The cognitive-behavioral intervention included a workbook, the Memory and Attention Adaptation Training (MAAT), and four individual monthly visits (30-50 minutes in length) with phone contacts once between visits for support and review. The four cognitive-behavioral components of the workbook included education on memory and attention, self-awareness training, self-regulation (through relaxation training, activity scheduling, and pacing), and cognitive compensatory strategies training. Participants were assessed after recruitment, and at a two- and 6-month follow-up with self-reported cognitive function, breast cancer survivor quality of life, and mood questionnaires, in addition to standardized neuropsychological tests. Improvements in

self-reported cognitive function and quality of life were observed among the group. Furthermore, participants rated the MAAT as helpful and reported high treatment satisfaction. Better performances on neuropsychological measures were also found, but the authors cautioned against this finding, as they did not take into consideration practice effects or repeated exposure to the test materials. Unfortunately, in a more recent randomized clinical trial (Ferguson et al., in press) using this same intervention, there were no significant differences in self-reported complaints between individuals receiving the intervention versus a waitlist control group, even though individuals receiving the intervention performed better on a verbal learning task and endorsed greater spiritual growth. Nevertheless, the authors caution that the small sample size in the study should not render the intervention ineffective; rather, research with larger sample sizes and intensified treatment to include more sessions could prove the intervention efficacious. These interventions are invaluable based on providing a service that is apparently needed by cancer survivors.

Cognitive rehabilitation and remediation as an intervention could prove extremely beneficial to cancer survivors, not only to address the cognitive complaints shortly after chemotherapy, but especially for long-term survivors and older adults. As individuals age, concerns about cognition often increase due to normal aging and the implications of cognitive decline, such as a neurodegenerative disease. Therefore, these interventions could prove useful for cancer survivors regardless of age or time since treatment.

In addition to interventions aimed to address cognitive complaints, it is important to also consider clinical interventions prior to the onset of cognitive problems. Although this study found minimal significant correlations between psychosocial variables and cognition, this could be the result of methodological design flaws and power restrictions. This study relied on volunteers and it is not difficult to imagine that such an individual likely is functioning better, both socially and cognitively. Therefore, one must consider

the individuals who do not volunteer for studies and how their specific needs could be met.

It is difficult to believe that providing social support could have a negative impact on cancer survivors, especially since an overwhelming amount of research indicates that social support unequivocally improves quality of life and leads to positive outcomes (e.g., Mehnert & Koch, 2007; Talley et al., 2010) and also supports successful aging (e.g., Fillit et al., 2002). Too, emerging research has demonstrated that chemotherapy might cause diffuse brain changes for which individuals compensate differently. Providing support to cancer patients and survivors seems intuitive, but the importance of this could play a pivotal role in specific outcomes, such as cognition, even if the exact mechanism of improvement remains unknown.

Based on the extant literature, it is prudent for health care workers, including psychologists, to support cancer survivors in every capacity, as well as normalize their concerns about cognitive impairment. An ideal intervention would provide education about the potential effects of chemotherapy on cognition and how this may affect everyday tasks. Furthermore, support groups that work together to solve potential everyday challenges could prove fruitful in both improving social networks and identifying compensatory strategies for cognitive complaints, as well as addressing everyday challenges. Lastly, these relationships could affect neural systems through activity in the hopes of decelerating cognitive decline.

Conclusions

A recent workshop (Tannock et al., 2004) sought to bring researchers from a variety of disciplines to discuss the extant chemobrain research and future directions. The following priorities were established for future research: 1) to conduct large-scale clinical studies that are longitudinal in design that compare cancer patients based on receipt of chemotherapy; 2) to explore discrepancies between subjective reports of cognitive

problems with objective measures of cognition; 3) to examine cognitive dysfunction in more than breast cancer patients and women to address underlying mechanisms that may relate to changes in serum levels of sex hormones and chemotherapy-induced menopause; 4) to consider interventions to alleviate these problems; and 5) to develop more animal studies and utilize more imaging techniques to facilitate understanding of underlying mechanisms that cause cognitive impairment as a result of chemotherapy. This particular study has served to consider cognitive dysfunction in more than just a breast cancer population, as it included NHL survivors as well. Additionally, within the entire sample, a new demographic has been examined, namely older adult survivors. Lastly, within the NHL group, a glimpse into potential gender differences in cognition as a result of cancer disease and/or chemotherapy regimen has been highlighted. Even though this study was unsuccessful in demonstrating a significant relationship among psychosocial and cognitive variables, it was successful in considering potential protective factors from cognitive dysfunction as a means to employ interventions. Regardless of whether cognitive dysfunction was found in this sample of long-term survivors, there is a clear need to address the cognitive complaints of cancer patients and survivors.

Based on the limitations of this study and other chemobrain research, future research considerations should include longitudinal studies with larger sample sizes across different cancer groups. A systems level approach (e.g., epidemiological studies) that would enable researchers to gather data prior to cancer diagnosis would be ideal. Furthermore, it is necessary to re-define cognitive impairment to reflect the cognitive complaints that cancer patients and survivors describe. Additionally, research to validate a clinical tool specifically designed for cancer patients that is sensitive enough to be used across research designs could be particularly helpful. Such a tool would allow for comparisons across cancer groups and enable more specific designs to parse out the effects of disease, stage of disease, and the toxicity of specific chemotherapy agents. Lastly, greater efforts must be made to consider the predictive factors associated with

cognitive impairment, such as psychoeducation and support groups. Interventions that aim to protect cancer patients from cognitive impairment throughout treatment could be the key to psychological health in survivorship.

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