Rehabilitation of cognitive dysfunction in survivors of breast cancer: A pilot study involving survivor-partner dyads

by

Katherine R.P. George

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Arts (MA) in Psychology

The Faculty of Graduate Studies
Laurentian University
Sudbury, Ontario, Canada

THESIS DEFENCE COMMITTEE/COMITÉ DE SOUTENANCE DE THÈSE
Laurentian Université/Université Laurentienne
Faculty of Graduate Studies/Faculté des études supérieures

Title of Thesis Titre de la thèse	Rehabilitation of cognitive dysfunction in survivors of breast cancer: A pilot study involving survivor-partner dyads
Name of Candidate Nom du candidat	George, Katherine R. P.
Degree Diplôme	Master of Arts
Department/Program Département/Programme	Psychology
Date of Defence Date de la soutenance	September 1, 2015

APPROVED/APPROUVÉ

Thesis Examiners/Examinateurs de thèse:

Dr. Matias Mariani
(Supervisor/Directeur(trice) de thèse)

Dr. Michael Persinger
(Co-supervisor/Co-directeur(trice) de thèse)

Dr. Adele Robinson
(Committee member/Membre du comité)

Dr. Barbara Collins
(External Examiner/Examinateur externe)

Approved for the Faculty of Graduate Studies
Approuvé pour la Faculté des études supérieures
Dr. David Lesbarrères
Monsieur David Lesbarrères
Acting Dean, Faculty of Graduate Studies
Doyen intérimaire, Faculté des études supérieures

ACCESSIBILITY CLAUSE AND PERMISSION TO USE

Abstract

Purpose: Cancer-related cognitive impairment (CRCI) has been associated with fatigue, emotional distress, reduced quality of life, and caregiver strain. A potential treatment option for those with CRCI is cognitive rehabilitation, a behavioural approach to improve cognitive skills and quality of life. There have been some studies that involve caregivers in aspects of rehabilitation. There are no studies in the literature however, that include direct retraining of survivors on lost functions and concurrent participation by their caregivers across all sessions. To fill this gap, a comprehensive 10-week cognitive rehabilitation program (CRP) was created, with aims to generalize improvement to everyday life in survivors of breast cancer.

Methods: A manualized CRP was developed and piloted with breast cancer survivors (BCSs) and their training partners. The program focused on psychoeducation and direct training on communication strategies, breathing/relaxation techniques, simple and complex attention, and higher-order thinking. Outcome measures included feasibility (retention and attendance rates), acceptability (homework compliance, session and program satisfaction), and measures of cognitive functioning and quality of life. BCSs and their individual partner underwent assessments at baseline, immediately after completing the program, and approximately 10 weeks later in order to investigate maintenance effects.

Results: Six BCSs (ages 44-59; ≥1 year post-chemotherapy) and their training partners enrolled and completed this study with a (100% retention rate). Rates of attendance were high for both BCSs and their training partners (94% and 92.5% respectively) with all participants indicating high levels of satisfaction with the

program. Repeated measures analyses of variance (ANOVAs) did not reveal a significant main effect for time on measures of sustained attention, processing speed, executive function, fluency (semantic and phonemic), verbal and visuospatial learning, recall and recognition. Repeated measures ANOVA revealed a significant main effect for time on measures of attentional capacity, focused attention, motor dexterity with the non-dominant hand, confrontation naming, and overall quality of life. Additionally, analyses using adjusted reliable change indices (RCI) were conducted on individual cases. RCIs yielded no change on most measures across time.

Conclusions: Findings suggest that a group-based CRP using a concurrent BCS /training partner approach was feasible, acceptable and proved beneficial to its participants. There were no significant main effects on most neuropsychological measures. Trends towards improvement on most measures across time seem to warrant further investigation, despite the small sample size and lack of statistical significance. The findings support a need to refine the intervention and to assess therapeutic efficacy with a planned randomized control trial.

Keywords

Breast cancer, cognition, rehabilitation, cancer-related cognitive impairment, neuropsychology, feasibility, pilot study

Acknowledgements

I would like to express the deepest appreciation to my supervisor, Dr. Matias Mariani, Ph.D., C.Psych., whose expertise, understanding, generous guidance and support made it possible for me to work on a topic that was of great interest to me. Without his guidance, persistent help and patience, this thesis would have not been possible.

I would like to thank my committee members, Dr. Adele Robinson, Ph.D., C.Psych. and Dr. Michael Persinger, Ph.D., C.Psych., for their interest in me at every stage of my academic journey. I appreciate their inspirations, timely suggestions with kindness, and enthusiasm.

I would like to give special thanks to Rhéal Huneault, Social Worker, for giving his time, providing input into the content of the cognitive rehabilitation program, and facilitating the caregiver group of this project.

I would like to express my gratitude to all my family and friends who put their faith in me, reviewed my drafts, and encouraged me as I completed this thesis!

Finally, I would like to thank the 12 participants of this study. This study opened my eyes to new perspectives about cancer-related cognitive impairment and the importance of caregiver support.

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction/Problem Statement

In recent years, cognitive functioning in individuals with cancer has been recognized as an important oncological outcome similar to survival and time to disease progression. Cancer-related cognitive impairment (CRCI) has emerged as a key focus of cancer survivorship research, with special focus on individuals with breast cancer. In conjunction, approximately 30% of breast cancer survivors (BCSs) report cognitive impairment. These cognitive deficits result in adverse impacts on the survivor's ability to complete activities of daily living and subsequently on their quality of life. Although programs geared at reversing cognitive decline in this population seem crucial, there is a paucity of research in this area, especially with respect to efficacy of rehabilitation protocols. The limited research conducted on this topic has focused on direct individual retraining rather than implementation of a concurrent individual and training partner (e.g. spouse, sibling, close friend) program that aims to generalize gains to the individual's everyday life. Caregivers are often used as proxy informants to report an individual's cognitive deficits and quality of life. There has been little consideration in the literature regarding the potential positive effects and therapeutic opportunities that may be derived from working simultaneously with the survivor and caregiver (the training partner). The purpose of this pilot study was to evaluate the feasibility and acceptability of a 10-week neuropsychological rehabilitation program designed for BCSs and their partners. The aims were to improve attention, problem-solving ability, planning and organization skills, self-efficacy, quality of life and communication in BCSs. Each BCS and their training partner partook in the rehabilitation program. The survivors underwent a baseline neurocognitive assessment (Time 0) as well as follow-up assessments at approximately

10 (Time 1) and approximately 20 (Time 2) weeks post-intervention to assess treatment effects, spontaneous recovery, and maintenance of effects over time.

A gap exists in the literature as how to best manage CRCI in BCSs and caregivers concurrently using a rehabilitation approach. The results of this pilot study may fill this gap by offering a CRP using direct retraining and compensatory strategies. One of the advantages of the CRP intervention is that it is manualized; therefore it is reproducible and may be adapted to various disease sites, and/or implemented in other cancer centres to rehabilitate cognitive deficits resultant from cancer treatment. Given the increasing prevalence of CRCI in BCSs, it is imperative that health care providers better equip themselves with the knowledge and skill to help BCSs and caregivers incorporate positive attitudes, thoughts, and beliefs about CRCI into behavioural changes that could improve aspects of attention and executive functioning.

Rationale for the Project

A number of published studies demonstrated the benefits of rehabilitation in individuals with traumatic brain injury who encounter cognitive challenges similar to those of BCSs (Cicerone et al., 2005; Cicerone et al., 2008). The cognitive deficits observed in BCSs are mild but nonetheless impact the survivors' activities of daily living, and subsequently, subjective quality of life (Kohli et al., 2009).

Although memory deficits are observed in the breast cancer population, the pattern of test results typically involves inefficient learning and retrieval rather than a primary memory deficit such as encoding and forgetfulness. Reid-Arndt et al. (2009) reported that executive functioning deficits were associated with declines in functional

outcomes, reduced engagement in social and community activities, and greater difficulties functioning effectively in important social roles such as spouse, parent, or employee among BCSs. They concluded that treatment efforts focusing to address cognitive, psychological, and physical issues show promise among cancer survivors. Improving executive abilities may help survivors across other functional domains. A need exists for rehabilitation programs that retrain, restore and/or remediate deficits in executive function and subsequently use these skills more effectively in servicing other cognitive functions. By extension, a rehabilitation program designed to address these executive deficits could result in improved everyday functioning in BCSs. The pilot program is designed to be a comprehensive model for treating BCSs who have objectively identified cognitive impairments following cancer treatment. While it may appear that the program is aimed at those with cognitive impairment, there can be a number of survivors with more extensive cognitive issues that could benefit from the cognitive rehabilitation program (CRP) as well.

Despite the importance of cognitive rehabilitation, currently there are no studies of cognitive rehabilitation in individuals with cancer that are designed with collateral partner or caregiver participation. Furthermore, Mosher et al. (2013) reported that family caregivers of cancer patients also suffered distress throughout the patient's journey of cancer treatment. The authors found that more than 50% of family caregivers reported reductions in time for social activities, low levels of energy, poor emotional well-being and an inability to cope with stress (Mosher et al., 2013). The least reported effects were on the caregivers' self-esteem, and relationships with patients and other family members. Interestingly, approximately 40% of caregivers, reported positive changes, in their

relationships with the patients and other family members as result of caregiving. Caregiver's mental health was strongly associated with life changes and more so than physical health (Mosher et al., 2013). Sherwood and colleagues (2008) propose that caregiver psychological health outcomes (defined as emotional distress, depressive symptoms, and anxious symptoms) are affected by both disease characteristics (e.g., disease stage, time since diagnosis, functioning and needs) and caregiver personal characteristics and resources (e.g., socio-demographic factors and social support). Caregivers are often involved in the rehabilitation of the deficits observed in their loved one with cancer. There has been little consideration in the literature concerning potential positive effects and therapeutic opportunities from working simultaneously with a survivor and caregiver. The few intervention studies conducted on this topic have done so with direct patient retraining. Implementation was not assessed on a concurrent program addressing the needs of both the affected individuals and their caregivers. Direct retraining is expected to help generalize strategies to the individual's everyday life.

Sohlberg and Mateer (2001) outlined three different phases of involvement in rehabilitation activities for families that were adapted for this study: 1) interviewing; 2) identifying and prioritizing goals; and 3) monitoring changes and revisiting goals. Caregivers can provide perspective around day-to-day difficulties experienced by the client, benefit from access to information, while helping to identify and work towards the goals of therapy.

An intervention aimed at improvement for BCSs with cognitive deficits has the potential to reduce everyday problems created by attention and memory lapses, reduce

secondary problems such as stress and/or fatigue, and improve well-being both for the caregiver and the survivor. An effective intervention with a training partner should help address the negative aspects of survivor-caregiver interactions and assist the training partner with empathizing with deficits of the survivors. For the training partners, these sessions should help identify, understand, normalize, and additionally help compensate for their partners breast-cancer-induced deficits. The proposed CRP aims to directly and indirectly address these issues. This pilot CRP is the suspected first use of a survivor-partner dyad beyond one session using this particular interventional format. This study is aimed at piloting the CRP in order to determine if the survivor-partner dyad interventional strategy could affect improvements to the functioning in the survivor's everyday life. These strategies include direct retraining of survivors on lost functions and concurrent participation by their caregivers across all sessions. To address this gap, a comprehensive 10-week cognitive rehabilitation pilot program (CRP) was created, with aims to generalize improvement to everyday life in survivors of breast cancer.

Aims and Research Hypotheses

The primary aim of this pilot study was to determine the feasibility and acceptability of a CRP to BCSs and their training partners. For this study, feasibility was defined by the ability to implement and complete a 10-week CRP. Feasibility was assessed by recruitment strategies, attrition rate, and attendance rates. Feasibility parameters would be accomplished by achieving the following targets:

1. Recruitment of 10 survivor-partner dyads within a 4- month recruitment period.

2. A minimum weekly attendance rate of 75% for all participants.
3. Retention of greater than 75% of participants at the end of the program.

The construct of treatment acceptability as defined by Kazdin (1980) involves the perceived appropriateness of treatment by potential clients or the degree to which individuals perceive a treatment to be appropriate, fair and reasonable (Kazdin, 1981, p. 493). For this study, acceptability was defined by the ease to which the participants used the CRP and how the participants felt the program fit their needs. Acceptability was assessed by homework compliance, responses from weekly session questionnaires and a final program satisfaction questionnaire administered to participants. The secondary aim of this study was to determine if the CRP resulted in improvement on objective and subjective neuropsychological outcomes. As the first pilot study in this area, it presented a unique opportunity to help guide procedures to implement a randomized control trial and/or larger, multi-centre trials in the future.

The proposed study addressed three primary hypotheses related to the possibility that short-term cognitive rehabilitation will result in:

1. measurable improvements in neuropsychological performance.
2. sustained improvements over time demonstrated through objective measurements.
3. concomitant with hypotheses 1 and 2, observable gains in the performance of activities of daily living.

Chapter 2: Literature Review

Cancer patients and survivors have reported numerous adverse symptoms associated with their disease and treatment including cognitive dysfunction, fatigue and affective distress. In particular, cognitive dysfunction has emerged as one of the most puzzling and concerning adverse effects in this population. The incidence of cognitive impairment varies by type of cancer, type of treatment, and time elapsed since diagnosis (Allen, 2011). Dietrich (2012) reported incidences ranging from 15% to 80%, and ranges were dependent on the study design and the sensitivity of neuropsychological tests used (Jansen, Miaskowski, Dodd, & Dowling, 2007).

Since the 1980's, there has been a burgeoning interest in CRCI in the literature (Ahles, Root & Ryan, 2012; Taillibert, 2010). CRCI has been colloquially termed "chemobrain" or "chemofog" and characterized by difficulty in memory, attention, concentration, processing speed, and executive functioning (Wefel, Kesler, Noll & Schagen, 2015). Although research has emerged in relation to cancer and cognition across various disease sites, breast cancer has been the major focus. This focus predominates due to the large breast cancer patient population who have received aggressive treatments, combined with continued improvements in survival rates (Siegel et al., 2012).

Worldwide, breast cancer is the most common type of cancer among women, accounting for 23% of the total number of cancer incidence (Jemal et al., 2011). Within Canada, one out of nine Canadian women is expected to develop breast cancer during their lifetime (Canadian Cancer Society's Advisory Committee on Cancer Statistics, 2014). As of 2014, the five-year relative survival rate for breast cancer in Canada was

88% for women and 80% for men (Canadian Cancer Society's Advisory Committee on Cancer Statistics, 2014). Adjuvant chemotherapy is a regimen involved in improving treatment outcomes with consistent reduction in mortality (Cold, Düring, Ewertz, Knoop & Møller, 2005) and increased rates of survival (Canadian Cancer Society, 2015). It is also known to have side-effects including, most commonly, fatigue, hair loss and depression (Azim Jr., Azambuja, Colozza, Bines & Piccart, 2011).

In breast cancer, CRCI research has largely focused on neurotoxicity associated with chemotherapy. Vodermaier (2009) reported that in most studies approximately 30% of individuals with breast cancer experience subtle cognitive decline after treatment with chemotherapy, with declines in cognitive functioning in survivors ranging from 17% to 75% (Wefel et al., 2004a). The range of cognitive complaints often attributed to CRCI has included: fatigue, lack of focus, mental confusion, inability to concentrate, inability to organize daily activities, loss of memory and memory lapses, decreased mental clarity, difficulties with concentrating and maintaining attention, remembering details, names and common words, multi-tasking and finishing certain tasks, learning new skills and slower thinking and processing (Taillibert, 2010). Perceived impairment of brain function can affect psychological well-being, the ability to perform usual activities of daily living, and the ability to perform in the workplace (Munir et al., 2011). CRCI has emerged as one of the most puzzling and concerning adverse effects of treatment in the breast cancer population.

Etiology of Cancer-related Cognitive Impairment

The pathological mechanisms of CRCI are not well understood. Many factors either independently or interdependently are hypothesized to influence cognitive function in individuals with breast cancer. Molecular and biological factors include direct injury to neurons due to chemotherapy induced brain toxicity (Yang & Moon, 2013). Physiological factors include cytokine deregulation, genetic susceptibility, cerebral white or gray matter microvasculature obstruction causing direct ischemia (Ahles & Saykin, 2007; Saykin, Ahles, & McDonald, 2003; Wefel et al., 2004), DNA damage and subsequent oxidative stress (Ahles & Saykin, 2007), integrity of the blood–brain barrier, and cognitive function prior to treatment initiation (Dietrich, 2012). Medical comorbidities and demographic factors that are hypothesized to influence and affect cognitive function related to CRCI have not been critically investigated in individuals with cancer (Mandelblatt et al., 2014; Wefel et al., 2015). These variables include: race, ethnicity, socioeconomic status, menopausal status, and the timing of treatment. Also incorporated are combinations of different treatment modalities: the disease state, fatigue, pain, psychological factors such as anxiety and depression, diet and body mass index (Janelsins, Keslet, Ahles & Morrow, 2014; Janz et al., 2007; Nguyen et al., 2013; Sherwin, 2012). During a 2003 workshop of oncologists, radiologists, psychologists and patient advocates, a consensus was developed to not only define and design treatment modalities but also develop methodological approaches around the existence of this clinical entity - CRCI (Tannock, Ahles, Ganz & Van Dam, 2004).

Radiation therapy is most often used in conjunction with other treatments to maintain control of the disease. It also decreases the chances of local recurrence for those

at higher risk (National Cancer Institute, 2014). Radiation to the breast, chest wall or regional lymph nodes, similar to surgery, produces localized effects that control the boundaries of the cancer. Unlike radiation to the brain, focal irradiation of the breast, chest-wall and regional lymph nodes have not been associated with changes in cognitive functioning (Shapiro & Recht, 2001). However, this relational association has not been tested in large sample size studies and has been confounded with individuals receiving chemotherapy and/or hormone treatments.

Neuropsychological Sequelae

Neuropsychological studies in individuals with breast cancer have been inconclusive regarding whether or not chemotherapy alone causes cognitive impairments (Collins, Mackenzie & Kyeremanteng, 2013). CRCI in this population was found in multiple functional domains. The neuropsychological sequelae observed typically include: inefficiencies in attention and concentration (the ability to focus on incoming stimuli); working memory (the ability to hold and manipulate information in the mind); information processing speed (the ability to sustain attention, engage in visual scanning, and activate and inhibit rapid responses); visual memory (immediate and delayed recall and recognition of visual information); verbal memory (immediate and delayed recall and recognition of word lists or stories); language (word finding, vocabulary, and speed and ease of word generation); visuospatial function (ability to copy a complex two-dimensional figure and reconstruct complex two-dimensional patterns); and organization (Correa & Ahles, 2008; Kayl et al., 2006; Lezak, 2004; Marin et al., 2009; Reid-Arndt et al., 2009; Stewart et al., 2006; Vodermaier, 2009; Wefel et al., 2004b).

Although currently there are no diagnostic criteria for CRCI in individual survivors, the advances described in the literature are helping move the field toward this goal (Edelstein & Bernstein, 2014). On an individual basis and similarly with other patient populations, a thorough evaluation should include an interview documenting change in functional status, self-reporting and family rating measures, and performance tests emphasizing attention, memory, processing speed, and executive functions. Neuropsychological tests should be valid, reliable and have good sensitivity and specificity (Lezak, 2004). The test battery selected should lead the clinician to the correct identification of individuals who have or do not have cognitive impairment (Vardy, Rourke & Tannock, 2007). In the context of clinical trials, interpretation of results has been complicated by a lack of standardization of the neuropsychological battery used, definitions of what constitutes cognitive impairment, and an understanding of how best to analyze the data (Tannock et al., 2004). To address this problem, the International Cognition and Cancer Task Force (ICCTF) provided research recommendations and guidelines to increase the homogeneity of studies and to facilitate comparisons among studies (Wefel et al., 2011). At a minimum, the ICCTF has recommended using a standardized core battery of tests that include measures of learning and memory, processing speed, and executive function (i.e., Hopkins Verbal Learning Test-Revised [HVLT-R], Trail-Making Test, and the Controlled Oral Word Association Test of the Multilingual Aphasia Examination [COWA]). These tests were selected because they have adequate psychometric properties and have been adapted to be used with other languages. In addition, the COWA and HVLT-R have alternative forms available that assist with serial testing. The ICCTF also recommended common criteria for defining

cognitive impairment and cognitive changes. Impaired cognitive performance can be defined as scoring 1.5 standard deviations (SDs) below published norms on two tests or scoring 2.0 SDs below published norms on one test (Wefel et al., 2011). The recommendations brought forth by the ICCTF could improve the homogeneity of study methods. Standardization and comparison among cognitive studies will provide more accurate information about incidence, severity, and risk factors for impairment.

Results of objective neuropsychological assessments have not always corroborated the deficits reported by individuals. Several studies (Biglia et al., 2012; Hutchinson, Hosking, Kichenadasse, Mattiske & Wilson, 2012; Pullens, De Vries, Van Warmerdam, Van De Wal, & Roukema, 2013; Shillings & Jenkins, 2007; Vardy & Dhillon, 2011) have reported a weak association between subjective reports of cognitive impairment and objective neuropsychological test results. Hutchinson, et al. (2012) reported the individual's perception of cognitive impairment was generally worse than that detected on objective assessment. Shilling and Jenkins (2007) suggested that self-reporting is necessary to define the impact of the subtle cognitive deficits caused by treatment on daily functioning and quality of life as exemplified by the impact of cognitive deficits on career and educational decisions, on activities of daily living, and on general quality of life. Vardy and Dhillon (2011) suggested the apparent disconnection between neuropsychological test performance and self-reported cognitive function exists because different constructs of cognitive impairment are measured. Although individuals' subjective perceptions of health are important, cognitive impairment is best measured by objective tests because subjective impairment is often associated with emotional components such as anxiety, depression and physical distress (e.g. pain).

Subjective cognitive complaints should be taken into account in the assessment of the individual's well-being, but it cannot be used as a substitute for objective cognitive measures, especially when making decisions about health, work and/or other major life decisions (Green, Pakenham & Gardiner, 2003).

Regardless of the objective-subjective assessment difference in measurement tools, cognitive impairment can cause substantial distress to many survivors (Schagen et al., 2014). A more comprehensive picture emerges with the combined incorporation of both subjective and objective measures of cognitive dysfunction. Simultaneously using both subjective and objective measures of cognitive dysfunction have provided a more complete picture of rehabilitation targets in cancer survivors (Gehring, Taphoorn, Sitskoorn & Aaronson, 2015).

Interventions

Interventions for CRCI can be pharmacological, non-pharmacological, or both. Pharmacologic management has been studied, and yet no known agent has been approved to combat these symptoms (Gehring, Roukema & Sitskoorn, 2012; Schagen et al., 2014). To date, the evidence does not support the efficacy of the pharmacological approaches of psychostimulants or erythropoietin (Von Ah, Storey, Jansen & Allen, 2014; Chan, McCarthy, Devenish, Sullivan & Chan, 2015). Research is limited regarding donepezil in individuals with cancer (Jatoi, Kahanic, Frytak, Schaefer, Foote, Sloan & Petersen, 2005; Rapp et al., 2015). Antioxidants, including vitamin E and *Ginkgo biloba*, were not efficacious in the limited trials conducted (Von Ah, Jansen, & Allen, 2014). Within the broader context of non-pharmacological interventions, cognitive rehabilitation

approaches are emerging as an important and viable treatment option for cancer survivors experiencing cognitive problems. The cognitive rehabilitation approaches will be the focus of the present review.

Cognitive Rehabilitation Therapy

The fundamental theory of cognitive rehabilitation therapy (CRT) was developed from the efforts to treat individuals who suffered from brain injury or stroke. The Brain Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine endorses the most commonly referenced definition of cognitive rehabilitation:

> Cognitive rehabilitation is defined as a systematic, functionally oriented service of therapeutic cognitive activities, based on an assessment and understanding of the person's brain-behaviour deficits. Specific interventions may have various approaches, which include: i) reinforcing, strengthening or re-establishing previously learned patterns of behaviour; ii) establishing new patterns of cognitive activity through compensatory cognitive mechanisms or impaired neurological systems; iii) establishing new patterns of activity through external compensatory mechanisms such as personal orthoses or environmental structuring and support; vi) enabling persons to adapt to their cognitive disability, even though it may not be possible to directly modify or compensate for cognitive impairments, in order to improve their overall level of functioning and quality of life. (Cicerone et al., 2000, p. 1596-1597)

This description allows for comprehensive, interdisciplinary rehabilitation programs with interventions to restore or reorganize function, compensates for impaired function through new cognitive patterns or external devices, and enables individuals to adapt to their new level of function.

The principles of CRT indicate that specific techniques alone are not adequate for effective rehabilitation. Instead, an integrated approach that addresses cognitive, emotional and motivational aspects of functioning is necessary (Clare, Wilson, Carter, & Hodges, 2003). CRT acknowledges the complex interactions among techniques including the social, emotional, and interpersonal contexts. These contextual aspects may help to target specific cognitive domains such as attention, memory, executive functioning. Various types of delivery models for cognitive rehabilitation methods should help target and improve the social, emotional, and interpersonal contexts. Cognitive rehabilitation strategies have been found to improve function in individuals with subtle to severe cognitive deficits (Cicerone et al., 2000; Sohlberg & Mateer 2001; Wilson, 2000).

Most research on the effectiveness of cognitive rehabilitation was directed towards improving neuropsychological and behavioural performance in adults. In two comprehensive reviews of evidence-based studies on brain injury rehabilitation, Cicerone and co-authors (Cicerone et al., 2000, 2005) determined that remediation, although typically characterized by small-to-moderate treatment improvements, is an effective therapeutic process. The National Academy of Neuropsychology and National Institute of Health published consensus statements that arrived at the same conclusion (National Academy of Neuropsychology, 2002; Ragnarsson, 2002).

Family Involvement in Cognitive Rehabilitation Therapy

Emotional stress, perceived burden of caretaking and disrupted family functioning, as well as the unmet needs of other family members may contribute to unhealthy family communication or functioning (Koehler, Wilhelm & Shoulson, 2011). Rummans et al., (2006) emphasized addressing the five key domains of quality of life (physical, mental, social, emotional, and spiritual) and developed an effective multidisciplinary intervention for patients with advanced cancer (Clark et al., 2013). Clark et al., (2013) conducted a study targeting the five domains of quality of life among caregivers and patients with advanced cancer who received radiotherapy. Dyads were randomly assigned to a 6-session, structured, multidisciplinary intervention arm or a standard care arm. Results demonstrated the multidisciplinary intervention was effective in maintaining the quality of life of patient participants; however, the intervention did not impact the quality of life for caregivers. Caregivers suggested that their needs could have been better addressed in a separate caregivers-only group. Many stated they did not want to discuss their challenges of cancer caregiving around their loved ones, or even in the presence of other cancer patients. They believed discussing their burden with other caregivers would have been beneficial to them. Based on a review by Hopkinson, Brown, Okamoto and Addington-Hall (2012), the authors concluded that if patient-family interventions included a component to facilitate interaction within the pair, a pattern of improvement emerged in the emotional health of both cancer patients and their caregivers.

A study evaluated a structured educational program directed to caregivers of patients diagnosed with a malignant glioma (Cashman et al., 2007). Program content

included brain tumor biology and treatment, symptom and adverse effect management, safety in the home, the role of palliative care, brain behavior relationships, understanding and coping with cognitive changes, and obtaining psychosocial support. Twenty-four caregivers participated, and assessment showed that knowledge was significantly improved. The program was favorably evaluated by participants. Participants also appreciated the opportunity to interact with other caregivers.

Achieving the goals of CRT involves working collaboratively with the client, family members or other support persons in the client's life and accommodating cognitive impairments and environmental variables relevant to the individual (Sohlberg & Mateer, 2001). Research has been limited regarding the benefits of actively including caregivers in oncological cognitive rehabilitation interventions. Locke et al., (2008) conducted a pilot study to determine the feasibility and tolerability of a combined cognitive-rehabilitation and problem-solving-therapy intervention for patients with brain tumors and their caregivers. Nineteen patient/caregiver pairs were enrolled and randomized. Thirteen pairs completed the 2-week trial. After receiving the intervention, 88% of patients used the study-specific strategies, and 88% indicated that they would recommend the intervention to other patients diagnosed with a brain tumor. The study intervention was described as "very helpful" or "somewhat helpful" by 88% of study participants. Caregivers were similarly enthusiastic about the intervention. The results showed that patients with brain tumors who have cognitive impairment can participate meaningfully in a structured intervention. Patients supported further research into the potential effectiveness of formal rehabilitation targeting cognitive and QOL symptoms for patients with brain tumors and their caregivers. The changes in cognitive and/or

behavioural functioning caused by brain injury, not only affects the individual, but also places enormous demands on families. The effects on individuals with breast cancer are just as challenging.

Successful rehabilitation for individuals with breast cancer involves cooperation, participation, and encouragement from the individuals' support network. Long-term treatment efforts require collaboration among health care professionals, clients, and their families (Levack et al., 2009). Garnering family support throughout the treatment process captures a unique resource to sustain treatment effects, provide generalization from theoretical and clinical application to real-life situations, and facilitates ongoing recovery. These partnerships can help ensure realistic treatment goals are met by valuing and acknowledging the expertise, needs and concerns of the individual and family (Sohlberg & Mateer, 2001).

Cognitive Rehabilitation and Cancer

As advances in medical treatments enable individuals with cancer to live longer, they allow health care providers to focus their attention on the individual's psychological state and quality of life. The need for psychosocial support for women with breast cancer has increasingly been recognized. As a result, a variety of interventions were developed to treat the emotional impact of the disease (Fors et al., 2010; Hoffman et al., 2012). In the last three decades, substantial growth in the number of support groups available to individuals with cancer has risen, mostly within hospital settings. Support groups have become increasingly popular, due to their cost-effectiveness, including the use of peer support. Cameron et al. (2005) studied women diagnosed with breast cancer and their

decisions to participate in group support programs. The authors concluded that psychosocial support programs and informational materials promoting their use may attract more participants if they are tailored to focus on resolving cancer-related distress rather than on general anxiety or depression. Cognitive rehabilitation is extensively used in many clinical populations that experience cognitive impairment; however, there is a scarcity of research regarding its use in individuals with cancer.

While cancer and cognition research has primarily been focused on elucidating the profile of CRCI in non-CNS tumours, few studies have focused on interventions to assist individuals once their cognitive deficits emerge. Schuurs and Green (2013) cited four published studies examining the true potential for cognitive rehabilitation to improve cognitive dysfunction in non-CNS tumours in adults. Gehring et al. (2009) posited that cognitive intervention programs may improve functioning and Von Ah et al. (2011) postulated against improvement. Closer examination of studies revealed that, to date, cognitive strategies or interventions tend to lead to improvements in subjective memory, but not necessarily objective memory test scores. Interventions based on self-regulatory cognitive rehabilitation show some promise. Additionally, interventions using relaxation techniques (e.g., meditation, exposure to the natural environment) may improve attention following breast cancer surgery.

A single-arm pilot study by Ferguson et al. (2007) also appeared to have potential to improve cognitive dysfunction in individuals with breast cancer who underwent chemotherapy. Twenty-nine BCSs underwent neuropsychological training using Memory and Attention Adaptation Training (MAAT) eight years after chemotherapy. The MAAT consists of a participant workbook, four individual monthly visits of 30–50

minutes and three telephone contacts among visits. Results demonstrated improvements in objective measures of cognitive function and improved stress management in dealing with memory problems in everyday life at a two-month, and a six-month follow-up interval. Similar results were found in a waitlist control trial. At the two-month follow-up, participants demonstrated significant improvements on the spiritual subscale of the quality-of-life measure and on verbal memory, relative to controls. However, changes in self-reported cognitive function were inconclusive.

Poppelreuter, Weis, and Bartsch (2009) compared the effects of group-based cognitive training and individualized training on cognitive impairment in individuals with breast cancer who received adjuvant chemotherapy. Neither form of training resulted in cognitive improvements equal to or greater than those observed over time in a non-treatment control group. Several factors may have contributed to the null results. Participants were recruited shortly after they completed chemotherapy which correlates with periods when spontaneous recovery of cognitive function is most likely to occur. On the contrary, Ferguson et al. (2007) evaluated participants who had completed chemotherapy at least 18 months (Ferguson et al., 2012) or 3 years previously (Ferguson et al., 2007). Poppelreuter et al. (2009) concluded that, during this narrow time frame immediately after chemotherapy, interventions aimed at improving cognitive outcomes may not be effective or necessary. Following completion of treatment, individuals are more likely to be dealing with many other important issues, and confronting cognitive deficits at this time may be psychologically disturbing (Fardell, Vardy, Johnston, & Winocur, 2011).

A recent study using a computerized cognitive training program (Kesler et al., 2013) included 41 BCSs who were randomly assigned to the active treatment group (n=21) and a 12-week waitlist (n=20). Inclusion criteria were a history of stages I-III breast cancer, a history of breast cancer treatment including surgery and adjuvant chemotherapy (participants were not excluded for radiation or hormonal therapies), a minimum age of 40, and at least 18 months post-chemotherapy to allow for neural stabilization. The participants completed a session of five exercises four times weekly for 12 weeks, with each session lasting approximately 20-30 minutes. Exercises included switching, mental rotation, working memory, spatial sequencing, word stem completion, route planning and rule-based puzzle solving. The active treatment group experienced significant improvements in cognitive flexibility, verbal fluency, processing speed, and a trending improvement on verbal memory as assessed by the Wisconsin Card Sorting Task, the letter fluency test from the Delis-Kaplan Executive Function System, the Symbol Search subtest of the Wechsler Adult Intelligence Scale 4th edition, and the Hopkins Verbal Learning Test-Revised, respectively. Although not significant, the active group also showed reduced self-rated symptoms of everyday executive function problems (i.e., the global executive composite score of the Behavioral Rating Inventory of Executive Function-Adult version).

Although CRCI has been described and investigated in many studies, there is a lack of information in specific neuropsychological training programs in cancer rehabilitation. More research is needed to systematically investigate the effects of specific neuropsychological rehabilitation strategies in individuals with breast cancer patients after completion of active treatment.

Chapter 3: Methods

This study was conducted in an ambulatory outpatient neuropsychology clinic in Northeastern Ontario, over the course of nine months. Participants were recruited via direct referrals from the cancer site, a newspaper advertisement, a breast cancer information website, and a radio interview. Study information was emailed to all staff and posted throughout the site. Methods were approved by the research ethics boards of the site where the research was conducted as well as from the affiliated university.

Participants

Six breast cancer survivors (BCSs) and their training partners participated in this study. Enrolment criteria specified that the BCSs:

1. had previously received a diagnosis of stages I - III breast cancer;
2. were between 18 and 60 years of age at time of recruitment;
3. were medically stable for a minimum of 3 months prior to the time of recruitment (i.e., no evidence of recurrent disease) or a secondary cancer diagnosis, and no anti-tumour treatment during that period of time (i.e., radiotherapy, chemotherapy, corticosteroids);
4. possessed adequate English proficiency to complete neuropsychological assessments;
5. reported at least one symptom of impaired cognitive functioning based on a self-report symptom checklist administered by the researcher;
6. demonstrated neuropsychological impairment at baseline, defined as a z-score $\leq$ -1.0 on two tests compared to the normative mean and,

7. were able to understand and be willing to sign a written informed consent document before enrolling in the study.

BCSs were required to have a designated training partner identified as:

1. a family member or close friend identified by the survivor;
2. having a minimum of a weekly face-to-face contact with the survivor;
3. at least 18 years of age;
4. having an adequate English proficiency to complete questionnaires;
5. available to come to the assessment and intervention sessions; and
6. able to provide written informed consent before enrolling in the study.

BCSs were excluded on the basis of the following criteria:

1. pre- and/or co-existing condition impairing cognition;
2. neurological or psychiatric condition sufficient to preclude providing informed consent;
3. poor proficiency in English;
4. history of mental retardation or IQ below 85;
5. life expectancy less than one year due to malignant disease;
6. recent and/or concurrent participation in cognitive rehabilitation, psychological intervention, drug trials, or neuropsychological testing.

Demographics/Clinical Characteristics

Demographic data for all participants collected through use of a self-report questionnaire at baseline included their age, gender, race/ethnicity, marital status, and education. The BCSs clinical characteristics were obtained through review of individual

medical charts. All variables obtained included: cancer type, date of diagnosis, type of treatments received (surgery, chemotherapy, and/or radiation), TMN (tumour, node and metastases) staging, current prescribed medications, and menstrual status.

Assessment of Neuropsychological Performance

Cognitive function was assessed using a battery of neuropsychological tests that were selected based on validity, reliability, and their use with BCSs in published literature. The tests and questionnaires were administered in a standardized fashion. Scoring followed standardized procedures. To minimize the influence of practice effects, alternate forms were used where available. Baseline assessments (T0) took place prior to the start of the cognitive rehabilitation program (CRP). Follow-up assessments were conducted directly after the 10-week treatment phase (T1) and approximately 20-weeks after baseline assessment (T2).

The assessment battery was designed to assess function across several cognitive domains: language skills, memory, attention, concentration, information processing speed, motor functioning, visuospatial functioning, problem solving, and mental flexibility. The assessment used the following tests: Benton's Judgement of Line Orientation (JOLO; Benton, Varney, & Hamsher, 1978); Boston Naming Test-Second Edition (BNT-2; Kaplan, Good glass, & Weintraub, 2001); Brief Visuospatial Memory Test-Revised (BVMT-R; Benedict, 1997); Conners' Continuous Performance Test-Second Edition (CPT-2; Conner's, 2004); Controlled Oral Word Association Task (COWAT; Spree & Strauss, 1998); Grooved Pegboard (GP; Reitman & Wolfsan, 1985); Grip Strength (Grip Strength; Reitman & Wolfsan, 1985); Hopkins Verbal Learning

Test-Revised (HVLT-R; Brandt & Benedict, 2001); Lateral Dominance Examination (LDE; Reitman & Wolfson,1985); Trail Making Test A and B (TMT-A/B; Reitman & Wolfsan, 1985); Wechsler Test of Adult Reading (WTAR; Pearson, 2001); Digit Span of the Wechsler Adult Intelligence Scale- Third Edition (WAIS-III) (DS; Wechsler, 1997); Digit Symbol-Coding of the WAIS-III (Cd; Wechsler, 1997); Letter-Number-Sequencing of the WAIS-III (LNS; Wechsler, 1997); Wisconsin Card Sorting Test, Computer Version 4 (WCST-CV4; Heaton & PAR Staff, 2003). Test descriptions are summarized in Table 1.

Self-reported Domains of Functioning

Self-reported cognitive dysfunction was measured using the Perceived Deficits Questionnaire (PDQ) and the Behavior Rating Inventory of Executive Function – Adult version (BRIEF-A) Self Report. The standardized self-report quality of life measures used included the European Organization for Research and Treatment of Cancer-Core Quality of Life Questionnaire (EORTC QLQ-C30) and breast cancer Specific Quality of Life Questionnaire (EORTC QLQ-BR23), Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventory (BAI), and the Brief Symptom Inventory-18 (BSI-18). The training partners were administered the Caregiver Quality of Life Index-Cancer (CQOLC) and the BRIEF-A, Informant Report.

The PDQ (Sullivan, Edgily, & Detox, 1990), consisting of 20 items, is part of the Multiple Sclerosis Quality of Life Inventory assessing self-perceived difficulties with organization, concentration, and memory during the previous month. Scores range from 20 to 100, with a higher score signifying greater perceived cognitive dysfunctions. The

PDQ has been shown to have good reliability and validity in persons with multiple sclerosis (Cronbach's alpha .77-.97). Although there is no psychometric data available for individuals with mild cognitive impairment, the questions are relevant to mild cognitive impairment (Dowdy et al., 2009).

The BRIEF-A (Roth, Squish, & Goya, 2005) is a 75-item questionnaire designed to assess executive functioning in daily life spanning the previous month. The inventory yields nine scales (Inhibit, Shift, Emotional Control, Self-Monitor, Initiate, Working Memory, Plan/Organize, Task Monitor, and Organization of Materials). T-scores are calculated for each of the clinical scales and indices (Metacognition and Behavioral Regulation) and for the summary (Global Executive Composite, GEC). T-scores are based on comparison to the normative sample comprised of 1050 self-reports, with higher scores reflecting greater difficulty. The BRIEF-A has been shown to have reliability and validity. Test-retest reliability across the clinical scales ranged from 0.82 - 0.93 over an average interval of 4.22 weeks for the Self-Report Form and from 0.91 - 0.94 over an average interval of 4.21 weeks for the Informant Report Form. Correlations between Self-Report ratings and Informant Report ratings were moderate, ranging from 0.44 - 0.68 for the clinical scales and from 0.61- 0.63 for the indexes and the GEC.

Psychological health status was evaluated using the Brief Symptom Inventory-18 (BSI-18). The BSI-18 is an 18-item version of the 53-item BSI that is derived from the Symptom Checklist-90. Items are rated on a five-point Likert scale items (0 = “not at all”; 4 = “extremely”) exploring the degree to which particular problems have distressed or bothered the respondent during the last seven days. These items constitute the standardized self-report symptom inventory designed to serve as a screen for depression,

somatization, and anxiety in medical and community populations (Derogates, 2000). Responses to all 18 items are summed to determine a Global Severity Index (GSI). Cronbach's alpha as a measure of internal reliability for this sample was 0.88 for the depression subscale, 0.70 for somatization, and 0.79 for anxiety.

The BAI (Beck & Steer, 1990) is a 21-item self-report measure designed to assess generalized anxiety. The respondent is asked to rate how much each symptom has bothered him or her in the past week. The symptoms are rated on a four-point scale, ranging from ‘‘not at all’’ (0) to ‘‘severely’’ (3). The BAI has a high internal consistency (Cronbach’s α= 0.92) and a test-retest reliability over one week of 0.75 (Beck, Epstein, Brown, & Steer, 1988). The reliability and validity of the BAI have been demonstrated in a variety of clinical populations, including individuals with cancer (Vodermaier, Linden, & Siu, 2009).

The BDI–II (Beck, Steer, & Brown, 1996) consists of 21 items designed to assess symptoms of depression based on the diagnostic criteria in the DSM-IV experienced during the previous two weeks. Each item contains four statements reflecting varying degrees of symptom severity. Respondents are instructed to circle the number (ranging from zero to three, indicating increasing severity) that corresponded with the statement that best described them. Ratings are summed to calculate a total BDI–II score. The BDI-II yields a coefficient alpha of 0.92 for the outpatient population (n = 500) in the sample referenced in the manual. In addition, a one-week test-retest correlation of 0.93 resulted from a study of 26 outpatients who had been referred for depression and took the BDI-II during their first and second therapy sessions (Beck, Steer & Brown, 1996).

Health-related quality of life was assessed with the EORTC QLQ-C30 and BR23 (Foyers, Aaronson, Boral, Groenvold, Curran & Bottomley, 2001), a questionnaire developed for use in clinical trials involving cancer patients. The validity, reliability, and sensitivity when administered to cancer patients are well established (Aaronson, Ahmedzi, Bergman, Bullinger, & Cull, 1993). The EORTC QLQ-30 is a 30-item questionnaire that consists of five functional scales (physical, role, cognitive, emotional, and social functioning), three symptom scales (fatigue, pain, nausea and vomiting), and a general health and quality-of-life scale. Five single items measure complaints often mentioned by cancer patients (loss of appetite, dyspnea, sleep disturbance, constipation, and diarrhea). The BR23 breast cancer module is designed to capture effects due to treatment. Twenty-three items are organized into four symptom scales (systemic therapy side effects, breast symptoms, arm symptoms, and upset by hair loss) and four functional subscales (body image, sexual functioning, sexual enjoyment, and future perspective). The scoring algorithm recommended by the EORTC is used to transform the responses to values on a scale of 0% to 100%. For the functional scales and global quality of life, a higher score corresponds to better functioning and quality of life. For symptom scales, a higher score corresponds to more frequent and/or more intense symptoms. The test-retest correlation over a four-day interval ranged from 0.82-0.91 (Aaronson, Ahmedzi, Bergman, Bullinger, & Cull, 1993).

The CQOLC (Weitzner, 1999) is a 35-item rating scale using a five point Likert-type scale to assess quality of life with family caregivers of cancer patients. The questionnaire was developed based on semi-structured interviews with patients, family caregivers and health care professionals. The instrument measures the impact of helping

a family member with cancer has on the caregiver's perception of quality of life. The CQOLC scales measure physical, emotional, family, and social functioning burden. It also includes items of spirituality, financial, and economic issues. The CQOLC scale is scored by adding up the score on each item to yield a total score for the instrument. Lower scores reflect better quality of life. The CQOLC has undergone formal psychometric testing demonstrating validity and reliability. Reliability was established by test-retest analysis over a period of three weeks at 0.95 and internal consistency measured by Cronbach's alpha was 0.91 (Weitzner, 1999).

Table 1. *Neuropsychological Measures*

Test	Ability	Test Description	Test-retest reliability	Author
WTAR	Pre-morbid level of intellectual functioning	Reading test composed of a list of 50 words that have atypical grapheme to phoneme translations.	Ages 16-89 0.90-0.94	Psychological Corporation, 2001
WAIS-III DS	Immediate verbal attention span, verbal working memory	Involves forward and backward repetitions of series of digits	Ages 16-64 0.88	Weschler, D, 2001
WAIS-III Cd	Focused attention, graphomotor speed, visual scanning, incidental memory	Pairing numbers to nonsense symbols as quickly as possible	0.83	Weschler, D, 2001
WAIS-III LNS	Alternating attention; verbal working memory	Involves reading a sequence of numbers and letters and recalling the numbers in ascending order and the letter in alphabetical order	0.85	Weschler, D, 2001
CPT-2	Sustained attention, vigilance, reaction time	Computerized program that requires responding to the stimuli on a computer screen by pressing a space bar for every letter except for the letter "X."	Omissions – 0.84 Commissions – 0.65 Detectability - 0.76	Conners & MHS Staff, 2000
TMT-A	Focused visual attention	The examinee must draw lines to connect consecutively numbered circles on the work sheet	0.79 *	Strauss, Sherman, Spreen, 2006
TMT-B	Divided attention, cognitive flexibility	The examinee must draw lines to connect the same number of consecutively numbered and lettered circles on the worksheet by alternating between the two sequences	0.89*	Strauss, Sherman, Spreen, 2006

Table 1 (continued)

Test	Ability	Test Description	Test-retest reliability	Author
WCST:CV4	Novel problem-solving, concept formation, set maintenance	The examinee is asked to match a series of response cards that have various forms that vary in colour and number, to one of four static stimulus cards.	Across measures 0.12 - 0 .66	Heaton et al., 2003
COWAT	Phonemic fluency. semantic fluency	Phonemic - Examinees were required to generate orally as many words as possible that begin with the letters *F, A,* or *S* (1 min each). Semantic – The examinee is asked to generate as many names of animals as possible over a 1-min period.	>0.70	Strauss, Sherman, Spreen, 2006
BNT-2	Confrontation naming, object gnosis,	The examinee is presented with 60 drawings of objects and instructed to give the objects' names.	0.91	Strauss, Sherman, Spreen, 2006
HVLT-R	Verbal memory and recall	The examinee is required to recall of a series of 12 words over three learning trials, free recall after a delay, and a recognition trial	Total Recall 0.74 Delayed Recall 0.66	Brandt & Benedict, 2001
BVMT-R	Visuospatial learning and recall	The examinee is required to learn a matrix of six simple abstract designs (presented for 10 seconds) over three trials, and then delayed recall and recognition (yes/no) are assessed after 25 min.	Total Recall 0.80 Delayed Recall 0.79	Benedict, 1997
JOLO	Visuospatial judgment	The examinee is required to visually judge the angle between two full or partial lines, which is compared to a multiple choice display of 11 numbered lines carrying in their degree of angular orientation.	37 participants administered both versions; 6 hours – 21 days), 0.90	Benton, Hamsher, & Varney, 1983

Table 1 (continued)

Test	Ability	Test Description	Test-retest reliability	Author
Lateral Dominance Examination	Hand foot, and eye dominance	Consists of a series of performances used to determine the examinee's preference for use of hand, food and eye.		Reitan & Wolfson, 1985
Grooved Pegboard	Manual dexterity, visuomotor-coordination, speed	The examinee is asked to put pegs in holes as quickly as possible with their left and right hand. The number of pegs put in the pegboard is also counted also as an indication of motor speed.	0.67 – 0.86	Reitan & Wolfson, 1985; Strauss, Sherman, Spreen, 2006
Hand Dynamometer	Grip strength	The examinee squeezes the dynamometer to assess grip strength.	0.52 -.0.96	Reitan & Wolfson, 1985; Strauss, Sherman, Spreen, 2006

Note: WAIS-III Cd – US test-retest reliability coefficients reported; BNT = Boston Naming Test; BVMT-R = Brief Visuospatial Memory Test-Revised; COWAT = Controlled Oral Word Association Test - FAS and Animals; CPT-2 = Conners' Continuous Performance Test-2; HVLT-R = Hopkin's Verbal Learning Test –Revised; JOLO = Judgment of Line Orientation; TMT-A = Trail Making Test A; TMT-B = Trail Making Test B; WAIS-III Cd; Wechsler Adult Intelligence Scale - Third Edition Digit Symbol Coding; WAIS-III DS = Wechsler Adult Intelligence Scale - Third Edition Digit Span; WAIS-III LNS = Wechsler Adult Intelligence Scale - Third Edition Letter-Number Sequencing; WCST = Wisconsin Card Sorting Test; WTAR = Wechsler Test of Adult Reading

Cognitive Rehabilitation Program

Program development. A ten-week CRP was originally developed and piloted for relatives and patients with an acquired brain injury at the Glenrose Rehabilitation Hospital in Edmonton, Alberta. The purpose of the Glenrose Rehabilitation Hospital program was to improve cognitive functioning (attention, memory, and concentration) and participation in activities that may be due to the presence of a variety of cognitive and behavioural problems. Involvement of a family member or close friend helped to ensure that skills were maintained and applied to novel situations by using compensatory strategies. The involvement also facilitated communication about how current or possible future difficulties might be managed. The current CRP was further developed and enhanced, including the creation of a manual to guide the implementation of the CRP.

Goals of program. The goals of the program were 1) to teach, practice, and increase the use of strategies related to attention, executive functioning, memory and emotions for BCSs and their training partners; and 2) to help improve thinking and communication skills, and overall quality of life.

Program content. Survivors and their training partners were taught communication, relaxation and cognitive strategies. There were five pillars to the program (see Table 2).

Homework was an essential and effective component of therapy. Due to the condensed number of sessions in this CRP, homework such as reading, behaviour monitoring, and new skills were given to the participants to practice and use outside the sessions. Pre-planned homework exercises were designed for every sessions of the

program. The homework assignments were designed to help facilitate skill acquisition, treatment compliance and symptom reduction by integrating the concepts learned in sessions into daily life. The homework was a key mechanism for facilitating between-session work and progress. The following protocol was adapted from the original pilot study and used as a general guideline for the group sessions. Sessions did vary according to the specific needs of the participants.

Table 2. *Five Pillars of the Cognitive Rehabilitation Program*

1) *Communication and Relaxation Strategies* (2 Weeks) - Strategies for enhancing communication and improving social interactions
Week 1: Course review; Communication strategies
Week 2: Sleep hygiene; Breathing/Relaxation strategies
2) *Focused, Selective and Sustained Attention,* (2 Weeks) - Strategies for addressing and improving attention to tasks and behaviour
Week 3: Defining attention; Selective attention; Strategies to reduce distractions
Week 4: Sustained attention; Preparing to pay attention
3) *Inhibitory Control , Divided Attention, Task-Switching, and Multi-tasking* (2 Weeks) - Strategies for coping with many demands at the same time
Week 5: Implications of attention problems for daily functioning.
Week 6: Self-regulation; Impulse control/inhibition
4) *Organization, Problem-Solving, and Reasoning* (2 Weeks) - Strategies for solving problems as one encounters them on a daily basis
Week 7: Goal-setting – S.M.A.R.T. goals; Organization/Planning; Reasoning/Problem solving
Week 8: Goal management training
5) *Goal-Directed Behaviour, Planning, and Decision-making* (2 Weeks) - How to organize your thoughts to make decisions and generate, plan, and execute short- and long-term goals
Week 9: Goal management training continued
Week 10: Summary of the former sessions: general overview of the training

Baseline assessment (including pre-treatment interview and assessment). Participants arrived at the neuropsychology clinic at the cancer site to complete a two to three hour interview that included the neuropsychological battery and several

questionnaires as described previously. During this assessment, all participants signed an informed consent form after receiving both verbal and written information about the study procedures, confidentiality and privacy. The purpose of the initial assessment was to assess the participant's current problems and concerns. In addition to evaluating the BCS, the interview was used as an opportunity to start building rapport and interest in the CRP, and to instil hope. After completion of the interview, participants' tests were scored within 72 hours. The neuropsychological tests were used to determine participants' eligibility for program admission and to establish baseline data. Participants were informed of their eligibility via telephone and start date of the CRP.

Program delivery. The ten-sessions were designed to be conducted weekly in a group format. One main advantage in starting with a slightly higher group size than what is considered ideal was the issue of attrition. The groups were facilitated by a neuropsychologist and a master's level social worker, both having experience working in oncology. A psychology graduate student was also part of the facilitation team. Participants attended two-hour sessions with two breaks of 5-10 minutes midway in the session. The neuropsychologist also provided several hours of homework to the BCSs.

The CRP sessions consisted of three phases: 1) a check-in and teaching phase with the survivor and training partner; 2) a teaching and practice phase where the survivor and training partner groups separated (see Figure 1), the survivor group worked on direct metacognitive strategies; whereas, the training partner group worked on strategies to assist in compensating for deficits; and 3) a combined practice phase occurred where both groups reunited and there was a combined (survivor + partner) practice session.

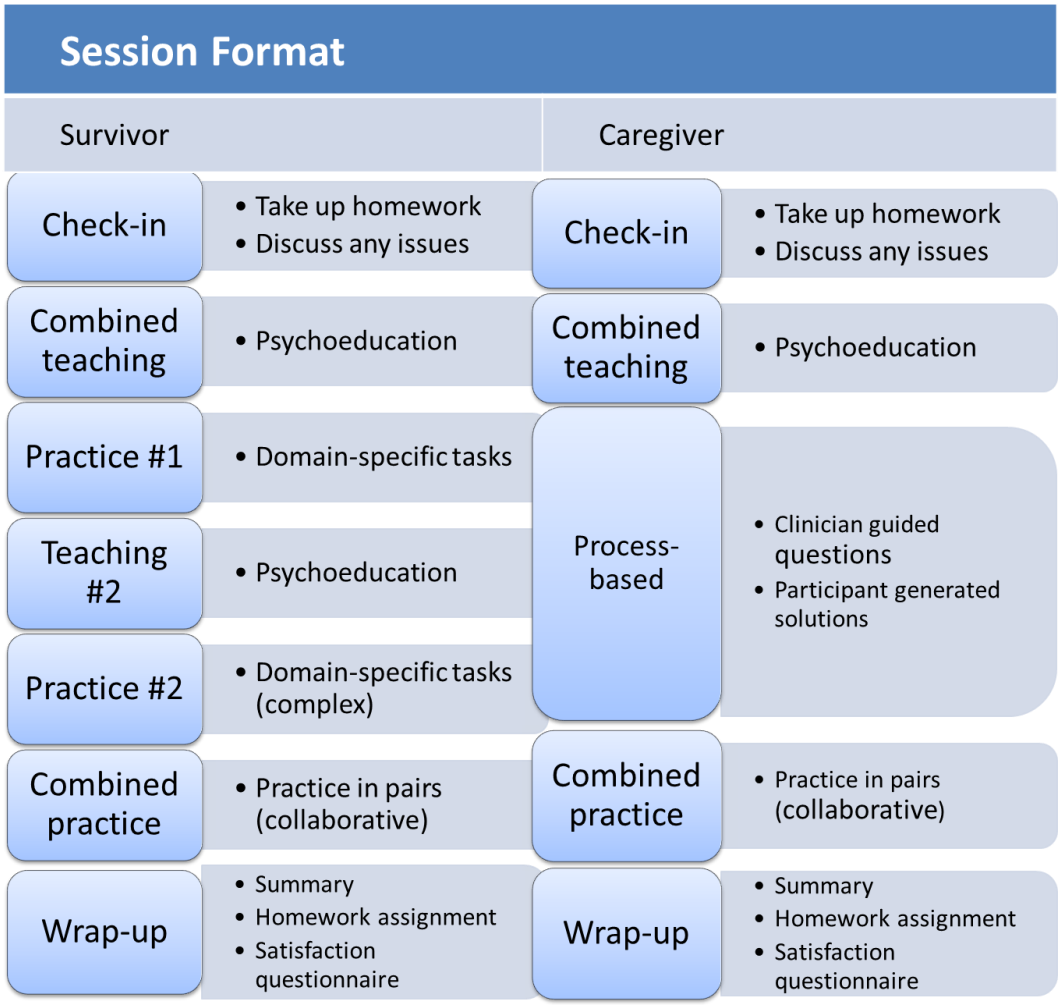


Figure 1. Schematic of cognitive rehabilitation session format.

The program maintained a consistent format. All sessions were held in the same room, on the same day of the week (with one exception due to a prior booking of the room at that time), and at the same time of day in order to provide enhanced structure for patients with mild cognitive deficits. Because participants could be easily distracted, facilitators needed to be active and directive in engaging the group in relevant discussions, setting limits, and adhering to the structure and format of the session. In addition, to ensure privacy and comfort, the group meetings were held in a quiet private meeting room that could be split into two sections with a dividing wall. The meeting

rooms were situated where participants would be free of distractions (i.e. staff interruptions, unit announcements) and there were no windows in order to help participants focus on the session content and maximize attention/concentration abilities.

It was also important that the facilitators limit the amount of time lecturing the participants. It was essential that the facilitators solicit input and reactions from the participants during the teaching sections to engage their interests and prevent distraction.

Material was presented using different modalities (visual, verbal, and written). The teaching sections were presented using Microsoft PowerPoint slides and handouts were provided for the participants to write notes and take home. Frequently engaging participant comprehension was important to verify understanding of the session materials. Since patients with mild cognitive deficits are less inclined to initiate discussions and/or ask questions when they do not understand a point, facilitators assessed group members' understanding by requesting that they describe or summarize the topic in their own words, give feedback and opinions, or provide concrete examples.

Session one. All subsequent sessions began with an agenda for the session. Members were introduced to one another and the purpose of the CRP was reviewed. The facilitators focused on introducing the nature of CRCI. A short video clip was presented to participants to facilitate a brief discussion of their own experience of CRCI. The facilitators assisted in discussion and guided discovery through questioning to help participants recognize that even small incremental changes in any one area of functioning (e.g. behaviour) could have an effect on many or all other areas of their experience. All participants were encouraged to present cognitive and daily life challenges experienced since BCSs completed their cancer treatment and identify their goals for completing the

CRP. There was only one teaching/practice module during this session and was presented to both the BCSs and training partners. Tips and techniques to communicate clearly and assertively with others were reviewed (see Figure 2). In the practice module, everyday scenarios were given to participants (e.g., job situation, physician's office) and participants were instructed to practice giving assertive responses to one another. Homework was assigned at the end of the session.

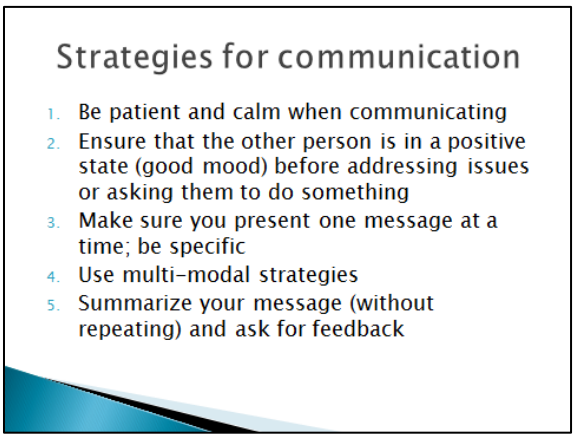
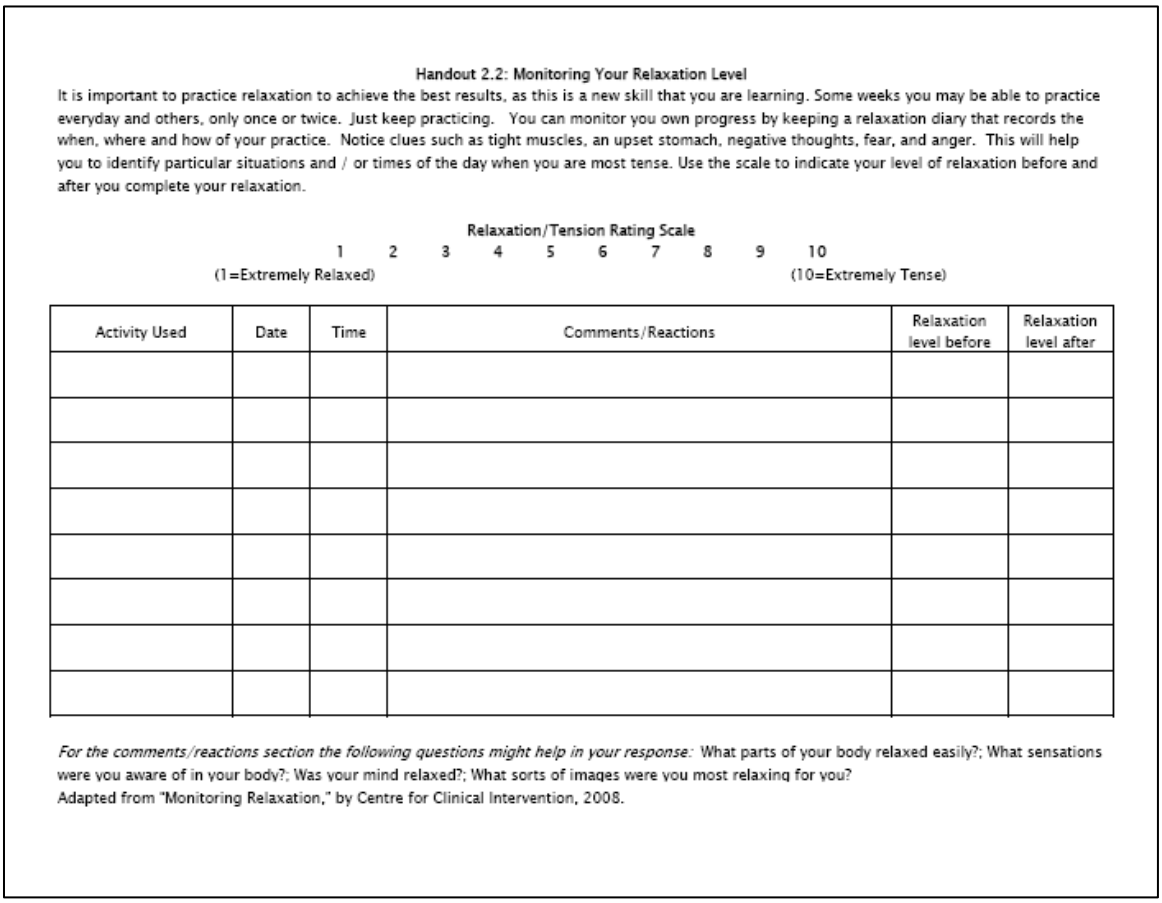


Figure 2. PowerPoint slide introducing strategies for improving communication.

Session two. After agenda setting, the facilitators and participants reviewed and discussed previously assigned homework. If problems arose, they were discussed briefly. This session consisted of two teaching/practice modules. The session was presented together for the BCSs and training partners. Cancer-related fatigue is one of the highest self-reported symptoms in cancer patients and survivors. For ongoing sleep difficulty, the most effective treatment is to alter sleep habits. The purpose of this session was 1) to discuss sleep hygiene and to learn and practice strategies that would help improve quality of sleep, and 2) to explore simple relaxation techniques to improve health and reduce

stress. The facilitator taught methods for promoting relaxation to self-regulate arousal and reduce cancer-related distress, including various forms of mindfulness and meditation. Practice exercises were 1) using the breath to create cognitive awareness and focus and 2) the raisin exercise and progressive muscle relaxation to facilitate mindfulness stress reduction. Homework exercises were to practice deep breathing, progressive muscle relaxation, and to monitor relaxation levels by keeping a weekly relaxation diary (see Figure 3).



Handout 2.2: Monitoring Your Relaxation Level

It is important to practice relaxation to achieve the best results, as this is a new skill that you are learning. Some weeks you may be able to practice everyday and others, only once or twice. Just keep practicing. You can monitor you own progress by keeping a relaxation diary that records the when, where and how of your practice. Notice clues such as tight muscles, an upset stomach, negative thoughts, fear, and anger. This will help you to identify particular situations and / or times of the day when you are most tense. Use the scale to indicate your level of relaxation before and after you complete your relaxation.

Relaxation/Tension Rating Scale

1 2 3 4 5 6 7 8 9 10

(1=Extremely Relaxed) (10=Extremely Tense)

Activity Used	Date	Time	Comments/Reactions	Relaxation level before	Relaxation level after

For the comments/reactions section the following questions might help in your response: What parts of your body relaxed easily?; What sensations were you aware of in your body?; Was your mind relaxed?; What sorts of images were you most relaxing for you?

Adapted from "Monitoring Relaxation," by Centre for Clinical Intervention, 2008.

Figure 3. Homework handout for week 2 – Monitoring Your Relaxation Level.

Session three. Agenda setting and review of homework occurred. This session consisted of three teaching/practice modules. The BCSs and training partners were separated into different rooms after the first teaching component of the session. All participants regrouped for the combined teaching/practice module. Attention difficulties are a major complaint associated with CRCI and has direct effects on other cognitive functions. The purpose of this session was to define attention and its subtypes. Elements of selective attention were taught and participants learnt strategies to overcome difficulties with selective attention. The exercises involved visual searches for letters in a letter array (letter find), and counting the number of words (i.e. "of" "the" "and") increasing in difficulty in different story passages. Training partners discussed healthy, adaptive and appropriate ways of responding to internal and external triggers (see Figure 4).

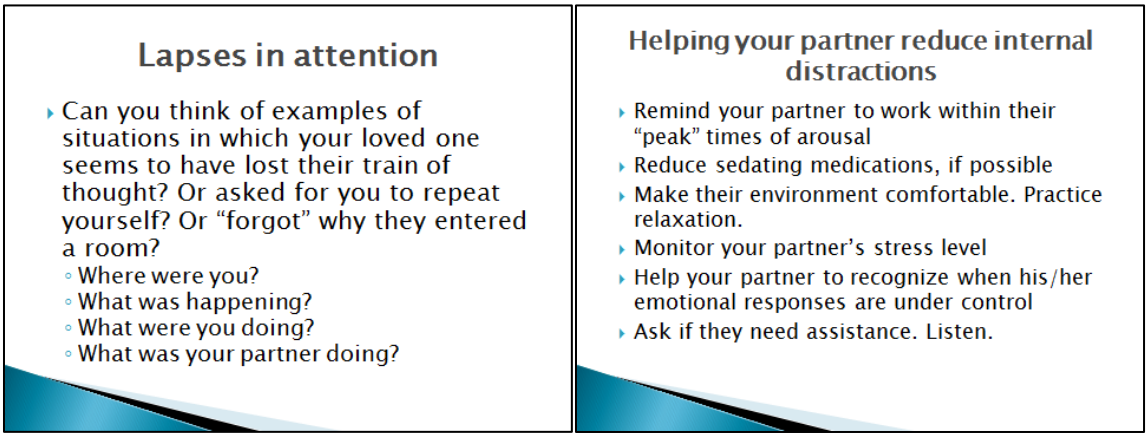


Figure 4. PowerPoint slides from week 3 - Training Partner Session.

A modified version of the Seashore Rhythms Test (Reitan & Wolfson, 1985) was developed and presented to participants for the combined exercise. Complex musical

patterns increasing in difficulty were given in an auditory presentation over three trials consisting of 10, 15 and 30 musical pairs. Participants had to indicate whether the pairs sounded the same or different. The combined exercise was designed to facilitate discussion about the differences between auditory memory and attentional abilities. Homework included completing two "I Spy" activities, and having a conversation in a distracted environment (while watching television). Partners were to review the MESSAGE strategy handout for supportive effective communication (adapted from Smith, Broughton et al., 2011).

Session four. Session four followed the usual format and focussed on helping the participants to understand the prerequisites for attention: arousal and alertness. Sustained attention is the ability to maintain attention to sensory events for prolonged period of time. Sustained attention is an important cognitive domain that is crucial to daily functioning, and can have a substantial impact on numerous other areas of cognitive functioning. The facilitators discussed elements of sustained attention and barriers that impede concentration (see Figure 5).

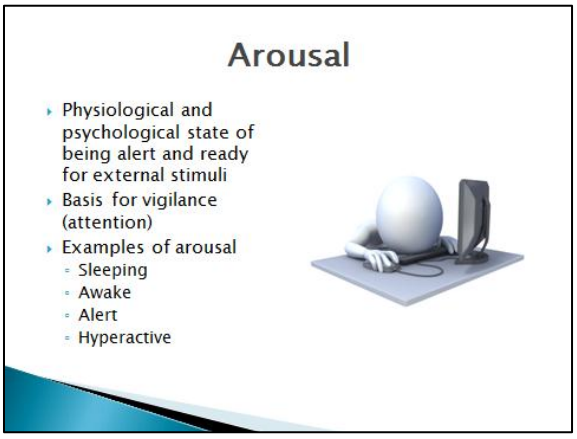


Figure 5. PowerPoint slide from week 4 - Survivor Teaching Session.

In the first practice activity, BCSs performed a computerized task of sustained visual attention. Participants were instructed to watch a clock and tick on a piece of paper when it skipped a beat. The second activity required listening to 60-second podcasts and providing synopses of the information heard. The 60-second synopses provided an approach to practicing concentration and comprehension of spoken information. The purpose of the training partner module was to review the MESSAGE handout, with particular emphasis on encouraging and engaging communication. Strategies to reinforce their partner's progress throughout the program and beyond were also discussed (see Figure 6).

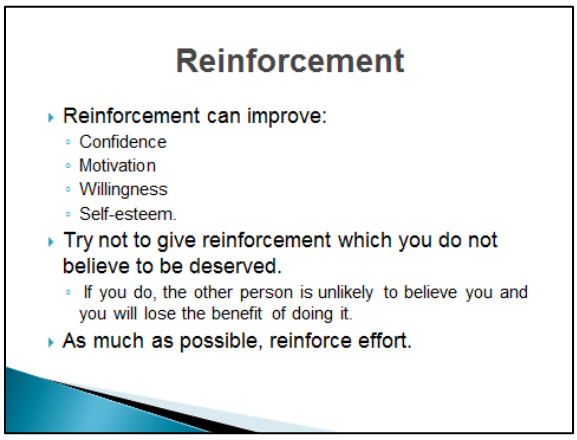


Figure 6. PowerPoint slide from partner session week 4 – Teaching Reinforcement.

The combined module provided teaching about reinforcing attention. The practice activity involved the training partners to read an article to the survivors. The survivors were instructed to capture important issues and recite as much of the story as possible to their training partner. The training partners provided cued recall questions if salient points were missed. The homework assigned to the BCSs included reading and the summarizing an article without any assistance. Training partners were assigned to observe a mistake in their partner's daily or weekly routine. Their homework assignment involved not taking any action on correcting the mistake. The mistake was discussed during the next training partner session. The combined homework activity involved reading and/or listening to an article in a distracting environment. Each person could be either the reader or the listener. The listener was to summarize the article to their partner and the reader was to provide them with reinforcement.

Session five. Session five followed the established pattern: agenda setting, homework review, discussion of the session topics and homework assignment. The purpose of this session was to understand the difference between divided and alternating

attention (see Figure 7). In the practice sessions, BCSs performed exercises that required them to 1) alphabetically alternate between boy and girl names (see Figure 8), 2) perform mental mathematical operations and 3) perform alternating actions on a set of embedded words (e.g., circle "stripy" words – wasp or barcode , underline "sticky" words – glue or toffee) while ignoring irrelevant words. The partner homework from session 4 (observing a mistake) was reviewed and provided an introduction to discussing strategies to help with divided attention.

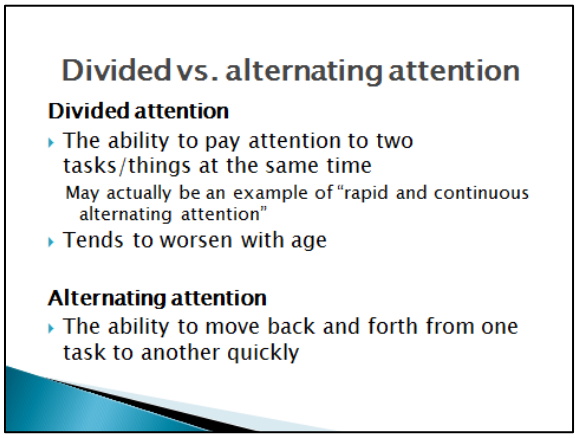


Figure 7. PowerPoint slide from breast cancer survivor session week 5– Defining Divided vs Alternating Attention.

The combined practices were alphabetical N-back activities. The N-back activities require temporary storage, and training might increase short-term storage capacity in either the verbal or the spatial domain (Lilienthal, Tamez, Talley, Shelton, Myerson, & Hale, 2013). In the first activity, participants thought of the name of a food beginning with the next letter of the alphabet and were to name the previous person's food (e.g. Person 1 would say "apple", Person 2 would say "apple, banana" and so forth). In the second activity, the category was changed to animals. Each person was instructed to say the name of an animal and the response from two people back (Person 1 would say "ant", Person 2 would say "bear", Person 3 would say "ant, cat" and so forth).

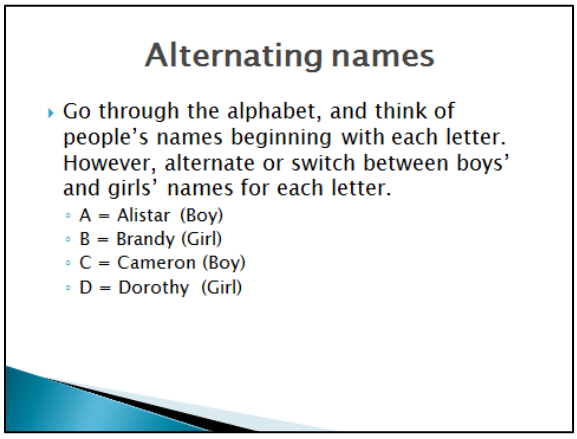


Figure 8. PowerPoint slide from breast cancer survivor session – Alternating Name Practice Activity

Session six. Session six followed the established pattern: agenda setting, homework review, discussion of the session topics and homework assignment. The purpose of this session was to provide a brief overview of three main areas of self-regulation (self-awareness/self-monitoring, impulse control/inhibition and emotional control/frustration tolerance) and to learn how to anticipate emotional triggers. Participants were taught healthy, pro-active ways to be successful in regulating their own physical, emotional and cognitive processes. The training partner session started with the weekly review of successes and difficulties (see Figure 9). Strategies to help training partners cope with impulsivity and managing anger were discussed. The combined teaching/practice module focused on emotional control and anger triggers. One of the practice activities instructed the BCSs to identify a recent situation where they became frustrated. The training partners facilitated a discussion about possible strategies and solutions that could help their partners in the future. Homework was assigned at the end of the session.

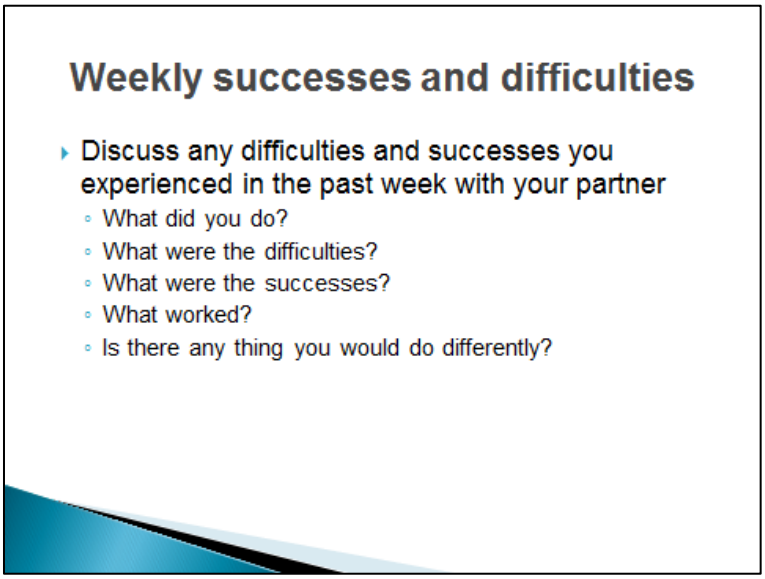
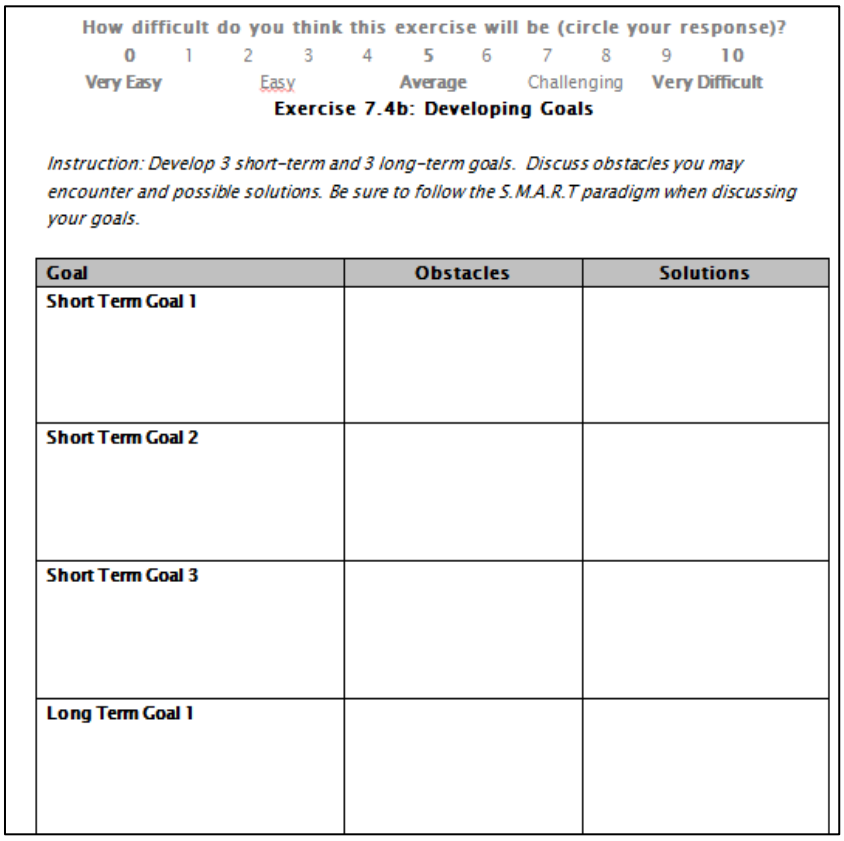


Figure 9. PowerPoint slide from training partner session 6 – Weekly Successes and Difficulties.

Session seven. Session seven followed the established pattern and focused on the processes used to set goals and how to develop action plans. The main theme for this session was goal-setting, planning (reasoning) and organization. Participants were taught the S.M.A.R.T. (Specific, Measurable, Attainable, Reliable, and Timely) goal criteria to ensure that the goals created were within reason and attainable. Practice exercises for the BCSs included chunking and categorization in order to retain longer sets of information. The training partners discussed unrealistic goal setting and ways to help their partner and themselves achieve S.M.A.R.T. goals. The session did not have a combined teaching module. The combined practice included activities of reasoning and problem-solving. Homework assigned to the BCSs was to develop actions plans. An example of a plan would be to write at least ten steps required to complete a task, such as putting up a shelf in the kitchen. Another homework assignment required the development of short- and long-term goals including obstacles and possible solutions (see Figure 10).



How difficult do you think this exercise will be (circle your response)?

0 1 2 3 4 5 6 7 8 9 10

Very Easy Easy Average Challenging Very Difficult

Exercise 7.4b: Developing Goals

Instruction: Develop 3 short-term and 3 long-term goals. Discuss obstacles you may encounter and possible solutions. Be sure to follow the S.M.A.R.T paradigm when discussing your goals.

Goal	Obstacles	Solutions
Short Term Goal 1		
Short Term Goal 2		
Short Term Goal 3		
Long Term Goal 1		

Figure 10. Homework sample from session 7 – Developing Goals.

Session eight and nine. Both sessions followed the established pattern of agenda setting, homework review, discussion of the session topics and homework assignment. The purpose of sessions eight and nine was to teach the strategies of goal management training; that is to improve an individual's ability to complete everyday tasks. The goals of these sessions were for participants to 1) identify and evaluate daily life difficulties, 2) review problem solving strategies and action planning, and 3) learn how to manage conflicts more effectively.

Session ten. After agenda setting, the facilitators and participants reviewed and discussed previously assigned homework. Session ten was a review of the program content and discussion of future steps beyond the program.

Analyses

Feasibility and acceptability. One of the evaluation goals was to provide demonstrated evidence of the feasibility and acceptability of the CRP. Another goal was to determine methods to improve the program in the future,

Recruitment and retention. Recruitment took place at tertiary cancer site. Documentation included methods for referral, a log of participant inquiry, and strategies to increase participant enrolment. A retention log was developed to record if participants left the study and included the date and reasons for leaving.

Attendance rate. An attendance log was maintained at each CRP session and assessment. Documentation included the number of sessions and assessments attended for each participant and reasons for absence.

Homework compliance. BCSs and training partners completed a weekly evaluation form about their homework. At each check-in, the homework evaluation form was discussed. All participants were asked the following questions:

1. What did we talk about last session that was important?
2. What do you foresee getting in the way of completing your homework?
3. What homework did you do? (If you didn't do it, what got in the way?)
4. What did you learn?

5. What happened (positive and negative) this week that the facilitators should know?
6. What important issue do you want to bring up during check-in?

Directly after the end of the program, BCSs were asked:

7. How often did you complete your homework?

Homework compliance was assessed based on the responses from questions 3, and 7 noted above.

Program evaluation. Information about the acceptability of the CRP was obtained from BCS and training partners. A Session Satisfaction Questionnaire was distributed weekly to all participants for feedback on the modules. Participants were asked to rate the following questions on a five-point Likert scale (strongly disagree to strongly agree):

1. The session objectives were clear to me.
2. The session activities stimulated my learning.
3. The activities in this session gave me sufficient practice and feedback.
4. The difficulty level of this session was appropriate.
5. The pace of this session was appropriate.
6. The handouts provided were useful.
7. The instructors were well prepared.
8. The instructors were helpful.
9. Please rate the overall quality of the session (excellent, very good, good, fair or poor).

Qualitative questions included:

10. Things I liked about this sessions.
11. Things I would change about this session.
12. Additional information I would like on this topic.
13. Additional comments.

At the end of the CRP, two different versions of a Cognitive Rehabilitation Program Satisfaction Questionnaire were given to BCSs and training partners respectively, regarding their experiences with the program: All participants were asked the following questions:

1. The program objectives were clear to me.
2. The program activities stimulated my learning.
3. The activities in this program gave me sufficient practice and feedback.
4. The difficulty level of this program was appropriate.
5. The length of this program appropriate.
6. The handouts provided were useful.
7. The presentations had enough information.
8. The instructor (lead facilitator) was well prepared.
9. The instructor (lead facilitator) was helpful.
10. Overall quality of the session.
11. Did you receive the kind of service you expected?
12. To what extent has our program met your needs?
13. How satisfied are you with the quality of help you received during the program?

14. How satisfied are you with the amount of help you received during the program?
15. Has the program helped you to deal more effectively with you and/or your partner's difficulties?
16. Overall, if a friend were in need of similar help, would you recommend our program to him or her?
17. Overall, how satisfied are you with the CRP?

Qualitative questions included:

18. Things I liked about this program.
19. Things I would change about this program.
20. What changes if any have you noticed in yourself since the CRP program started.
21. What changes if any have you noticed in your partner since the CRP program started?
22. Can you sum up what have you found helpful about the program for you?
23. Can you sum up what have you found helpful about the program for your partner?

Additional questions asked specifically to BCSs included:

1. How often did you practice the activities (beyond the completion of homework)?
2. Do you feel you are more informed about the cognitive changes you experienced following chemotherapy?
3. Compared to how I felt before beginning this study, now I am.

4. How do you rate your current quality of life?
5. What were the strengths of the breast cancer survivor group?
6. What were the weaknesses of the breast cancer survivor group?
7. What topics should be more discussed within the breast cancer survivor group?
8. What topics should be more reduced within the breast cancer survivor group?

Questions to training partners about the program included:

1. The instructors for the caregiver group were well prepared.
2. The instructors for the caregiver group were helpful.
3. What were the strengths of the caregiver group?
4. What were the weaknesses of the caregiver group?
5. What topics should be more discussed within the caregiver group?
6. What topics should be more reduced within the caregiver group?

Statistical analyses. Descriptive statistics were used to summarize demographic variables, neuropsychological functioning and cancer characteristics. Published normative data adjusted for age, education and gender where appropriate were used to convert participants raw cognitive test scores into standardized scores (z-scores; mean [M] = 0, standard deviation [SD] = 1; T-scores; M = 50, SD = 10). Scores were adjusted for sign according to performance direction (with higher values indicating better performance for all variables.

The study had a within-group, repeated measures design that allowed for significant effects to be measured despite low sample size. One-way repeated measures ANOVAs with the within-subjects factor "time" (baseline, post-intervention and maintenance) were conducted for each of the neuropsychological measures. Degrees of freedom were adjusted via the Greenhouse-Geisser method. Post-hoc pairwise comparisons were calculated using the Bonferroni correction to evaluate whether differences in outcome scores for the different times of measurement were significant. Statistical analyses were performed with the Statistical Package for Social Sciences (version 19.0) with an alpha level set at .05 for all analyses. Estimates of effect size were reported using partial eta squared. These estimates were defined as small ($\eta 2 = 0.01$), medium ($\eta 2 = 0.06$), and large ($\eta 2 = 0.15$) effects (Cohen, 1988).

Reliable change indices. The reliable change analysis allows the researcher or clinician to reduce the adverse impact of measurement error on test interpretation on an individual's score and to determine if a change in the score is due to real change or chance variation. In other words, is the difference in score clinically meaningful or due to random error. Tests with published test-retest reliability possess inherent error; therefore, the RCI allows identification of changes in test scores that are clinically and statistically meaningful for each patient. The RCI represented the 90% confidence interval for the difference in performance between two evaluations that would be expected if no real change occurred. Importantly, the level of analysis for the RCI encompassed each individual patient, not the group as a whole. Reliable change estimates were derived from a modification of the method proposed by Jacobson and Truax (1991).

The reliable change methodology allows the clinician to estimate measurement error surrounding test-retest difference scores. Specifically, the standard error of difference (S_{diff}) is used to create a confidence interval for the baseline-retest difference score. The steps for calculating the S_{diff} are provided below. Note that the test-retest reliability coefficient is used in these formulae to make them more relevant to the interpretation of change over time. Most researchers and test publishers use internal consistency reliability coefficients in their SEM formulas; internal consistency reliability is almost always higher than test-retest, making the SEM smaller. In this study, RCI was computed by dividing the difference between pre-treatment and post-treatment scores by the standard error of measurement (RCI = [post-test – pretest] / SE_{meas}). SE_{meas} = SD* (1-r) 1/2 where SD = standard deviation of pretest and r = the reliability (test-retest reliability) of measure. The difference was categorized as "reliable increase" (RCI > +1.64), "uncertain change" (-1.64 ≤ RCI ≤ +1.64) and "reliable decrease" (RCI < -1.64). In the present study, test-retest reliability and SDs for each test score were derived from published data—typically from information provided in the test manual.

Chapter 4: Results

Demographics/Clinical Characteristics

Demographic data and clinical characteristics for the six BCS and the six training partners are provided in Table 3. All BCS were female with a mean age of 52.3 years (standard deviation [SD] = 7.0, range 43-59). All BCS underwent surgery pre-chemotherapy and received local radiation therapy (5000cGy, 25 fractions). Four of the training partners were spouses and the remaining two were adult children. The mean age of the training partners was 48.0 years of age (SD = 14.7, range 30-67).

One BCS had a recurrence of cancer at the time of the first follow-up assessment. In addition, her training partner did not attend the last three sessions of the CRP due to work commitments and was unable to complete the first follow-up assessment questionnaires. A second BCS had ongoing chronic pain, and related health concerns that could have impacted the results of her neuropsychological assessments. In addition, there was a protocol deviation in the standardization of the neuropsychological battery with this participant in that the incorrect alternate form of the Brief Visuospatial Memory Test-Revised (BVMT-R) was administered on the second follow-up assessment. The correct alternate form was administered at the end of the assessment and the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) Vocabulary subtest was administered during the delay. Additionally, one BCS was seen for clinical purposes one year prior to the beginning of this study. The alternate forms used were not the same alternate forms used for the other participants (i.e. this participant was administered HVLT-R Forms 2,4 and 3, while the other participants were administered HVLT-R Forms 1, 2 and 4).

Table 3. Demographic and Clinical Characteristics of Participant

Breast Cancer Survivors			
	Mean	SD	Range
Age at baseline (years)	52.3	7.0	43 - 59
Education (years)	15.7	3.9	12 - 23
Estimated FSIQ (baseline)	107.5	5.9	100 - 115
Months between last chemotherapy treatment and baseline testing	71.5	73.6	12 - 212
Training partners			
Age at baseline (years)	48.0	14.7	30 - 67
Years of Education	15.2	1.1	12 - 20
Relationships to	4 spouses; 2 children		
Cancer Characteristics			
	N		
Type of Cancer			
Infiltrating Duct Carcinoma, Nos	3		
Carcinoma, Nos	1		
Infiltrating Duct And Lobular Carcinoma	1		
Infiltrating Duct Mixed With Other Types	1		
Stage of Disease			
II	2		
III	2		
Unknown	2		
Type of chemotherapy			
FEC-D x 6 cycles	2		
ACT x 4 cycles	1		
AC x 4 cycles	1		
CMF x 6 cycles	1		
ZOL x 10 cycles	1		
Surgery	6		
Hormonal Therapy	2		
Local Radiation (5000cGy, 25 fractions)	6		
Estrogen Receptor - Positive	4		
Progesterone Receptor - Positive	5		
Menopausal Status			
Pre-menopausal	2		
Post-menopausal	4		

Note. AC = Adriamycin, Cytoxan; ACT = Adriamycin, Cytoxan, Taxol; CMF = Cyclophosphamide IV or PO, methotrexate, fluorouracil; FEC-D = 5-fluorouracil–epirubicin–cyclophosphamide followed by docetaxel; SD = Standard Deviation; ZOL= Zoledronic Acid

Aim 1: Feasibility and Acceptability

Recruitment and retention. Oncologists were emailed about the study objectives and a meeting was requested to discuss whether patients could be referred to the study from their clinic. One oncologist responded to a request for a meeting and indicated that their current patient population did not meet the inclusion criteria. Several health care professionals were also contacted and asked to post posters in clinic areas and/or mention to support group meetings in hopes of reaching a wider audience. Recruitment for the study lasted 4 months. Posters were displayed in the cancer site patient library, patient education bulletin boards in the site and clinic waiting rooms. Posters were sent to the Editorial Committee of the Breast North Info website, promoted at the local Run for the Cure and to facilitators of a breast cancer support group. Recruitment efforts were unsuccessful after 2 months, and as such a more intensive recruitment regimen initiated. A brief article appeared in a local newspaper discussing the study. The study was mentioned during a radio interview with the principal investigator, and individuals were referred from the neuropsychology clinic of the cancer site. Three individuals did inquire about the study, one via telephone and two via email. After the study was explained, two of the three individuals did not meet the initial screening criteria. Although recruitment efforts were slow, six breast cancer survivors (BCS) and their training partners were recruited.

Baseline assessments took place within a 2-month period. Each baseline assessment was scored within 48 hours and results were discussed with the neuropsychologist to determine the presence of neuropsychological impairment.

Participants were notified by telephone of their results and asked if they were interested in participating in the study.

The cognitive rehabilitation program (CRP) was delivered to participants in the winter. Six BCS and their training partners enrolled in the CRP study. Another element of feasibility for any intervention research protocol is that of attrition. Once recruited, are participants compliant in completing the protocol? All the participants who entered into this pilot study completed. This represents a 0% attrition rate or conversely, a 100% retention rate.

Attendance. The overall attendance rate for participants was high at 93% (BCS = 94% and training partners = 92.5%). Fifty-eight percent (n=7) of the participants attended all sessions, three participants missed one session (one BCS and two training partners), and two participants missed two sessions (one BCS and one training partner). Participants who missed sessions worked through the manual and received briefings from the facilitators.

Homework compliance. BCSs and training partner completed a weekly evaluation form about their homework. At each check-in, the homework evaluation form was discussed. Weekly, participants were asked "what homework did I do? (If I didn't do it, what go in the way?)" Qualitative responses indicated that for session 1, most participants reported they completed all the homework. One BCS commented that she and her partner had discussions every night at supper while another stated she practiced trying to be assertive instead of aggressive when speaking to her spouse. For session 2, participants reported they practiced the 10-count most often. For sessions 3 through 7 the majority of participants indicated they completed all assigned homework. For sessions 8

and 9, participants reported completing fewer activities. Participants reported reasons for not completing homework were feeling overwhelmed, stressed, tired, lacking motivation and having other personal commitments.

Directly after the end of the program, BCSs were asked how often they did the homework assigned to them by the facilitators. Five of the participants reported they always completed their homework (all of it, at every session). BCSs were also asked how often they practiced the activities (beyond the completion of homework). Half of the BCSs indicated sometimes, two BCSs indicated often and 1 BCSs reported always.

Program evaluation.

Weekly Session Questionnaire. All participants were encouraged to complete the session questionnaire despite their absence if they were away for a particular session to allow for feedback of the materials presented. Positive results (strongly agreed/agreed and excellent/very good) for each of the questions are presented in Table 4.

Clarity of session objectives. The majority of the participants "strongly agreed" or "agreed" the session objectives were clear to them for each of the weekly sessions (range 75% - 100%). For sessions 5 and 9 respectively, 2 participants (1 BCSs and 1 training partner in each session) rated the objectives as not appropriate or not applicable. Three participants (1 BCS and 2 training partners) rated session 7 objectives as not appropriate or not applicable.

Activities stimulated learning. The majority of the participants "strongly agreed" or "agreed" the session activities stimulated their learning for each of the weekly sessions (range 75% - 100%). For session 1, a BCS indicated they "neither agreed or nor

disagreed" that session activities stimulated their learning. For session 5, 1 training partner indicated they "disagreed" and 2 participants (1 BCS and 1 training partner) rated the question as not appropriate or not applicable. For session 7, three participants (1 BCS and 2 training partners) rated the question as not appropriate or not applicable

Activities provided sufficient feedback. On most sessions, participants indicated they "strongly agreed" or "agreed" the activities gave them sufficient practice and feedback (range 58%-92%). Specifically on session 8, four participants (3 BCSs and 1 training partner) rated that they "neither agreed nor disagreed". One BCS remarked that relaxation and breathing awareness (session 2) was an area of concern and was looking forward to implementing what was learned in class to reach "a positive outcome".

Difficulty level of session. The majority of the participants "strongly agreed" or "agreed" the session activities stimulated their learning for each of the weekly sessions (range 75% - 100%). Two participants (1 BCS and 1 training partners) rated they "neither agreed or nor disagreed" the difficulty level was appropriate for session 2. For session 7, three participants (1 BCS and 2 training partners) rated the question as not appropriate or not applicable.

Pace of session. Across all sessions, most participants "strongly agreed" or "agreed" the pace of the sessions were appropriate (range 75% - 100%). For session 7, three participants (1 BCS and 2 training partners) rated the question as not appropriate or not applicable. For session 8, one training partner "disagreed, one BCS rated they "neither agreed nor disagreed" and one training partner rated the question as not appropriate or not applicable In addition, participants indicated session 8 felt rushed and too much information was presented.

Usefulness of handouts. The majority of the participants "strongly agreed" or "agreed" the handouts provided were useful for each of the sessions (range 75% - 100%). For session 7, 3 participants (1 BCS and 2 training partners) rated the question as not appropriate or not applicable. Participants commented that they found the handouts very useful and would like to know where to access additional activities

Preparedness of instructors. Across all sessions, most participants "strongly agreed" or "agreed" the preparedness of the sessions were appropriate (range 75% - 100%). For session 7, three participants (1 BCS and 2 training partners) rated the question as not appropriate or not applicable. Participants provided feedback about areas to improve which included reviewing grammar, producing better audio quality of recordings and hole-punching their handouts for their binders.

Helpfulness of instructors. Across all sessions, most participants "strongly agreed" or "agreed" the helpfulness of the sessions were appropriate (range 75% - 100%). For session 7, three participants (1 BCS and 2 training partners) rated the question as not appropriate or not applicable.

Overall quality of session. Across all sessions, most participants rated the overall quality of the sessions as "excellent" or "very good" (range 73 - 100%). Most sessions had a rating of 91% or 100% with the exception of session 8. For session 8, three participants (2 BCSs and 1 training partner) rated the overall quality as "good". Participants indicated they thoroughly enjoyed the review session and activities (session 10) and "felt it was a good wrap up to the classes.

Table 4. Positive results (strongly agreed/agreed and excellent/very good) for Weekly Session Questionnaire for all sessions

	Session 1		Session 2		Session 3		Session 4		Session 5		Session 6		Session 7		Sessions 8 & 9		Session 10	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
The session objectives were clear to me.	12	100	12	100	11	92	11	92	10	83	11	92	9	75	11	92	10	83
The session activities stimulated my learning.	11	92	12	100	11	92	12	100	9	75	11	92	9	75	10	83	10	83
The activities in this session gave me sufficient practice and feedback.	10	83	11	92	10	83	11	92	9	75	11	92	9	75	7	58	10	83
The difficulty level of this session was appropriate.	12	100	10	83	11	92	11	92	9	75	11	92	9	75	10	83	10	83
The pace of this session was appropriate.	12	100	12	100	10	83	11	92	10	83	11	92	9	75	9	75	10	83
The handouts provided were useful.	12	100	12	100	11	92	12	100	10	83	11	92	9	75	11	92	10	83
The instructors were well prepared	12	100	11	92	11	92	12	100	10	83	10	83	9	75	11	92	10	83
The instructors were helpful	12	100	12	100	11	92	12	100	10	83	11	92	9	75	11	92	10	83
Overall quality of the session[a]	10	83	11	92	11	92	12	100	9	75	10	83	9	75	8	67	10	83

[a]– Response options included “excellent” or “very good”

Cognitive Rehabilitation Program Satisfaction Questionnaire. Measures of acceptability of the CRP were at a 100% positive response rate for the majority of the questions on the program satisfaction questions (see Figure 11).

The majority of the participants, "strongly agreed" or "agreed" the session objectives were clear to them for each of the weekly sessions. All of the participants "strongly agreed" or "agreed" the program activities stimulated learning and 100% indicated the difficulty level of the program was appropriate. Ninety-two percent (n=11) felt the program contents (handouts and presentations) were useful. One participant remarked "I liked the presentations that were followed by the practical exercises". Nine participants (5 BCSs and 4 training partners) "strongly agreed" or "agreed" the activities provided sufficient practice and feedback. Two training partners endorsed a neutral response and 1 BCS disagreed. Sixty- six percent (4/6) of the BCSs thought the length of the program was appropriate; one participant was neutral and the other participant did not agree. All the training partners "strongly agreed" or "agreed" the program length was appropriate. Participants included comments such as "sometimes sessions felt rushed, would maybe lengthen the number of weeks to ensure ample time to explore all activities". Furthermore, all of the participants "strongly agreed" or "agreed" that the lead facilitator (the principal investigator) was well prepared and helpful throughout the CRP.

Overall, ninety-two percent (n=11) rated the overall quality of the program as "excellent" or "very good. All of the participants (n=12) were "very satisfied" or "satisfied" with the program and would recommend the treatment to a friend ("Yes, definitely" or "Yes, generally"). Participants included comments such as:

> "The program covered a range of the problems we were experiencing and gave us proactive solutions when they occurred BUT also provided awareness strategies to recognize the beginning of a situation and prevent it before it happened". - *Breast Cancer Survivor*

> "The caregiver group was very comforting and reassuring. It was a support group for us to release our frustrations and build ourselves up to help our partners". - *Training partner*

> "I found it [the program] inspired and refreshed me in my ongoing support through my partner's rehabilitation". - *Training partner*

> "It [the training partner group] was supportive. There was no competition - everyone was there for the same reasons and looking for the best solution for their loved one. I found it inspired and refreshed me in my ongoing support through my partner's rehabilitation". - *Training partner*

All of the participants (n=12) indicated the program helped them deal more effectively with themselves or their partner's difficulties ("very satisfied" or "satisfied"),

> "It was relevant [the program]. Immediately we could begin using the strategies this program covered". – *Breast Cancer Survivor*.

> "It was interesting to hear solutions and problems of other people in the same or similar situation" - *Training partner*

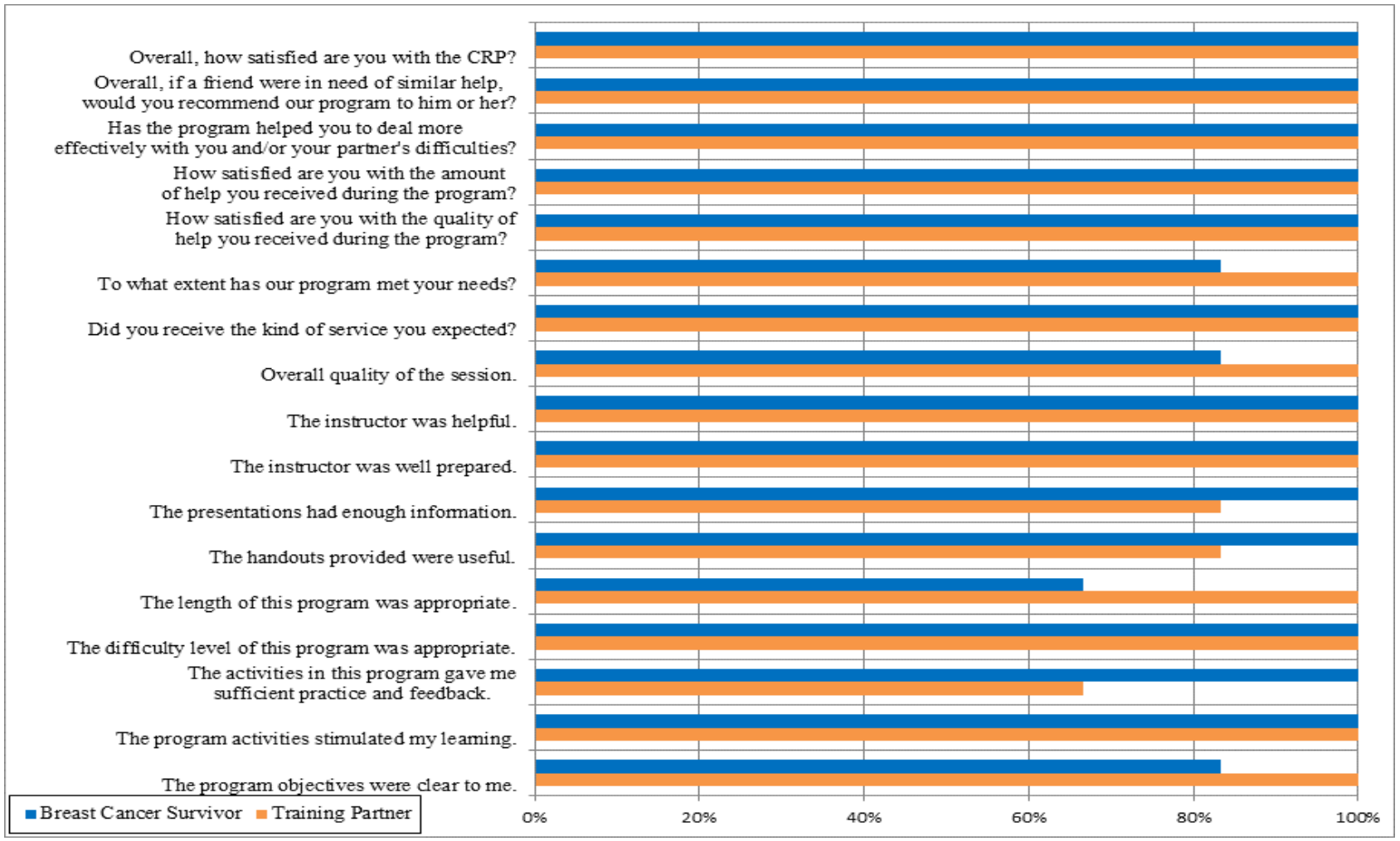


Figure 11. Program satisfaction results - ratings (agree and strongly agree)

Participants were asked what enjoyed most and least about the CRP. In answer to the question concerning the best features, the common themes reported were the a) information and activities provided; b) group dynamics and c) inclusion of a partner group. One participant said [they] "loved the concept; Love believing we can regain some of what was lost". When asked what the weaknesses of the CRP were, participants stated a) time of year; b) length of sessions; and c) the amount of homework. Participants indicated the time of the year was not optimal due to weather conditions (program was offered in winter); have an earlier start time (6:00pm instead of 6:30pm) and/or offer classes during the day as well. After completion of the program participants also agreed it would be better not to condense two sessions into one;

> "Not to put the classes together; there was so much information just for one session", and
>
> "Understanding we had to condense a couple of sessions - we found we were so focused on the homework, we did not have time to fully absorb it and apply it to our everyday lives."

Questions addressed specifically to BCSs:

Practicing activities. The BCS responses were variable when asked how often they practiced the activities beyond the completion of homework. Three BCSs (50%) reported sometimes, two reported often (33%) and one BCS (17%) indicated always.

Feeling informed about cognitive changes. All of the BCS (n=6) reported they felt more informed about the cognitive changes they experienced following chemotherapy. Two BCSs indicated they felt the information was too generalized and

would have liked a discussion about each individual's cognitive issues and experiences following cancer treatment.

Subjective ratings of improvement and quality of life. Four of the BCSs reported they felt "much improved" compared to how they felt before beginning this study and five BCS rated their current quality of life as somewhat better.

Strengths and weaknesses of BCS group. Most of the BCSs indicated they felt the program had no weakness. One participant indicated:

> "participants should have expressed exactly what problems they were experiencing so that we could determine if we all had the same thing (problem) in common".

BCSs stated they enjoyed the camaraderie, openness, positive attitudes and "willingness to stay in the study".

Additional topics for discussion. BCSs indicated they would like more discussion on each BCS's experience and coping mechanisms, more in-depth teaching module for memory/concentration, and differences between CRCI and dementia.

Questions addressed specifically to training partners:

Preparedness and helpfulness of instructors for caregiver group. All of the training partners "strongly agreed" or "agreed" the instructors (Social Worker and graduate student) were well prepared and helpful throughout the CRP

Strengths and weaknesses of caregiver group. The training partners did not report many weaknesses. Two training partner felt the information presented was repetitive and another felt the length of the caregiver sessions was long enough to allow for discussion

on a meaningful topic. Training partner's comments about the strengths of the caregiver group are outlined below:

> "Every week [the instructors] had us talk about our [weekly] positive/negative experiences, which were beneficial in the sense that some of the experiences were similar".
>
> "They allowed us to express our concerns about our partners and offered suggestions that were very helpful".
>
> "Great alternative methods to approach situations".
>
> "It was supportive. There was no competition - everyone was there for the same reasons and looking for the best solution for their loved one. I found it inspired and refreshed me in my ongoing support through my partner's rehabilitation".
>
> "Was able to be with others who were dealing with the same problems as me".
>
> "Camaraderie; ability to learn from each other".

Additional topics for discussion. Training partners indicated they would appreciate more discussion on each of the BCSs' specific cognitive issues, additional compensatory strategies, and to incorporate ways younger children could be involved and exercises adults could do with them.

Aim 2: Improvement and Maintenance of Neuropsychological Outcome Measures

Neuropsychological performance. All BCSs scored within the impaired range on at least one measure at baseline. Areas of impairments were variable for the BCSs at baseline. Impairments were most commonly seen on a test of verbal fluency (FAS), a test of list-learning and memory (Hopkins Verbal Learning Test-Revised, HVLT-R), a test of visuospatial- learning and memory (Benton Visuospatial Memory Test-Revised, BVMT-R), and a test of sustained attention (Connors' Continuous Performance Test-II, CPT-2). Based on BCSs' demographics variables and their performance on a word recognition test insensitive to neuronal injury, BCSs had average pre-morbid intellectual ability (M = 107.50, SD = 5.86). Descriptive statistics for the standardized neuropsychological measures for the BCSs are displayed in Table 5. Means at baseline and follow-up assessments fell within the normative range across tests. In general, the effect of time was not significant for most of the cognitive abilities measured. Upward trends across time, although not statistically significant were observed on most of the neuropsychological measures.

Attentional capacity/working memory. In terms of attentional capacity, a repeated-measures ANOVA revealed a significant main effect for digit span (F (2,10) = 3.91, p = 0.01, ${}_p\eta^2$ = .59). Bonferroni post hoc test did not show ($p > .05$) the source of differences between the assessment times. The first trial of the HVLT-R and BVMT-R can be utilized as measures of focused attention. Repeated measures ANOVA for HVLT-R Trial 1 and BMVT-R Trial 1 were not significant for main effects (p's >.05). Effect sizes across all measures ranged from 0.03 to 0.59.

Concentration/focused attention. On a measure of inattentiveness (CPT-2: Omissions), a one-way repeated measures ANOVA revealed significant main effects for time (F (2, 10) = 4.224, p = 0.085, $_p\eta^2$ = .46). Bonferroni post hoc test did not show (p > .05) the source of differences between the assessment times. On a measure of impulsivity (CPT-2: Commissions), a one-way repeated measures ANOVA revealed a significant main effect for time (F (2, 10) = 6.357, p = 0.017, $_p\eta^2$ = .56). Bonferroni post hoc test did not reveal (p > .05) the source of differences between the assessment times. The detectability (CPT-2: d') provides information on how well the examinee discriminates between targets and non-targets. A one-way repeated measures ANOVA revealed a significant main effect for time (F (2, 10) = 7.451, p = 0.01, $_p\eta^2$ = .60). Post-hoc analysis showed that there was a significant difference (p = .05) between post-intervention scores (T1) and at maintenance (T2). Effect sizes across all measures were large and ranged from 0.46 to 0.60.

Sustained attention (vigilance). On measures of vigilance, one-way repeated measures ANOVA did not reveal a significant main effect for time (p's >.05). Effect sizes across all measures ranged from 0.06 to 0.33.

Processing speed. One-way repeated measures ANOVA did not reveal any significance main effects for time on measures of processing speed (p's >.05). Effect sizes across all measures ranged from 0.01 to 0.26.

Executive functioning. On a measure of cognitive flexibility, divided attention and perceptual motor functioning under time pressure (Trails Making B), a repeated measures ANOVA did not reveal a significant main effect for time (p >.05). Similarly, one-way repeated measures ANOVAs did not reveal significant main effects for time (p's

>.05) on measures of the WCST (total errors, preservative responses, preservative errors and conceptual level responses). Effect sizes across all measures ranged from 0.10 to 0.27.

Motor functioning. There were no statistically significant improvements with visuomotor- coordination, dexterity and hand strength in the BCSs' dominant hand. Motor dexterity with the non-dominant hand indicated a significant main effect for time (F (2, 10) = 103.34, p = 0.01, ${}_p\eta^2$ = .59). Bonferroni post hoc test did not reveal (p > .05) the source of differences between the assessment times. However a difference between baseline and the 20-week follow-up assessment approached significance (p = 0.065). Hand strength with the non-dominant hand indicated a significant main effect for time (F (2, 10) = 6.364, p = 0.016, ${}_p\eta^2$ = .56). Bonferroni post hoc test did not reveal (p > .05) the source of differences between the assessment times. Effect sizes across all measures ranged from 0.25 to 0.59.

Language. One-way repeated measures ANOVA did not reveal any significant for main effects for time on measures of semantic and phonemic fluency (p's >.05). On a measure of confrontation naming (Boston Naming Test-2 [BNT-2]), a one-way repeated measures ANOVA revealed a significant main effect for time (F (2, 10) = 250.39, p = 0.005, ${}_p\eta^2$ = .65). Bonferroni post hoc test did not reveal (p > .05) the source of differences between the assessment times. Effect sizes across all measures ranged from 0 to 0.65.

Memory: learning. One-way repeated measures ANOVA did not reveal any significant main effects for time (p's >.05) on measures of verbal (HVLT-R Total Recall)

and visuospatial learning (BVMT-R Total Recall). Effect sizes for verbal learning was 0.18 and visual memory was 0.27.

Memory: recall/recognition. One-way repeated measures ANOVA did not reveal any significant main effects for time (*p*'s >.05) on measures of verbal recall (HVLT-R Delayed Recall), retention discrimination (HVLT-R Recognition Discrimination Index), and visuospatial- recall (BVMT-R Delayed Recall). Effect sizes were small ranging from 0.02 to 0.03.

Visuospatial Perception. Raw scores on the JOLO were corrected for age and gender. A one-way repeated measures ANOVA revealed a significant main effect for time (F (2, 10) = 5.0674, p = 0.030, ${}_p\eta^2$ = .50). Bonferroni post hoc test did not show (p > .05) the source of differences between the assessment times. Scores also indicated that at baseline, two participants scored within the average range, one participant scored within the high average range, and three participants scored in the superior range. Post-intervention scores indicated marked improvement in visuospatial perception (five of the participants had scores within the superior range) and at 20-weeks after intervention, all six participants had scores within the superior range.

Reliable change indices. Normative data were not available for the BNT-2 and JOLO test, and RCI were not calculated for these tests. Reliable change indices are presented for all tests (see Table 6). Examination of individual scores across this group revealed no change in most cognitive domains. Three BCS showed reliable improvements on a measures of working memory (Digit Span), from baseline to maintenance, processing speed (CPT-2 Hit Reaction time) post-intervention to maintenance and focused attention (CPT-2: Commissions) from baseline to maintenance.

Four BCSs showed worsening on measures of visuospatial learning (BVMT-R Total) from follow-up to maintenance and three BCSs worsened on a measure of visuospatial recall (BVMT-R Delayed Recall) from baseline to post-intervention.

Table 5. Mean (Z-scores) and Standard Deviations for Neuropsychological Tests Across Assessments

Cognitive Domain	Baseline		Post-Treatment		Follow-up Treatment		*p*	Effect Size
	M	***SD***	***M***	***SD***	***M***	***SD***		
Attentional Capacity/Working Memory								
Digit Span: Total	-0.11	0.98	0.83	1.01	0.94	1.18	.011	0.592
HVLT-R: Trial 1	-0.80	0.71	-0.25	0.86	-0.33	0.82	.484	0.135
BVMT-R: Trial 1	-0.35	1.05	0.03	0.88	-0.05	0.81	.665	0.078
LNS: Total	0.44	1.47	0.67	0.97	0.61	1.57	.860	0.030
Concentration/Focused Attention								
CPT-2: Omissions (Inattention)[a]	0.27	0.46	0.71	0.01	0.65	0.15	.047	0.458
CPT-2: Commissions (Impulsivity)[a]	-0.48	0.84	0.59	0.92	0.81	1.11	.017	0.560
CPT2d (inattention)[a]	-0.33	0.90	0.88	1.16	1.58	1.35	.010	0.598
Sustained Attention (Vigilance)								
Hit RT Block Change[a]	-0.29	1.35	0.56	0.85	0.01	1.17	.135	0.330
Hit SE Block Change[a]	-0.39	0.40	0.28	0.91	-0.20	0.82	.350	0.189
Hit RT ISI Change[a]	0.32	0.99	0.15	0.78	0.15	0.52	.731	0.061
Processing Speed								
Coding	0.44	1.11	1.22	0.91	0.72	0.77	.219	0.262
Trail Making Test – A	0.73	1.03	1.03	0.89	1.17	0.99	.509	0.126
CPT-2: HitRT[a]	0.35	0.85	0.43	1.29	0.43	1.05	.955	0.009
Executive Functioning								
Trail Making Test – B	-0.17	1.11	-0.03	0.94	0.15	0.79	.595	0.099
WCST:CV4: Total Errors	-0.72	1.00	-0.27	1.28	0.08	0.78	.277	0.227
WCST:CV4: Preservative Responses	-0.67	1.05	-0.35	1.35	0.27	0.77	.224	0.259
WCST:CV4: Preservative Errors	-0.60	1.02	-0.32	1.28	0.25	0.83	.263	0.234

Table 5 Continued

Cognitive Domain	Baseline		Post-Treatment		Follow-up Treatment		*p*	Effect Size
	Mean	SD	Mean	SD	Mean	SD		
WCST:CV4: Conceptual Level Responses	-0.77	0.88	-0.30	1.41	0.20	0.76	.201	0.274
Motor Functioning								
Grip Strength – Dominant	-0.40	0.88	-0.73	0.95	-1.07	1.05	.065	0.421
Grip Strength – Non-dominant	-0.10	0.50	-0.68	0.73	-0.75	0.94	.016	0.560
Grooved Pegboard – Dominant	0.62	1.20	-0.03	1.00	0.65	1.03	.231	0.254
Grooved Pegboard – Non-dominant	0.37	1.03	0.30	1.35	1.05	1.21	.012	0.586
Language								
Verbal Fluency	-0.67	0.96	-0.62	0.67	-0.32	0.73	.222	0.260
Animals	0.58	0.65	0.60	0.61	0.62	1.12	.996	0.001
Boston Naming Test	-0.45	0.71	0.50	0.50	0.78	0.89	.005	0.653
Memory: Learning								
HVLT-R: Total	-0.45	0.92	-0.03	0.62	0.05	0.72	.364	0.183
BVMT-R: Total	-0.62	1.07	0.08	0.87	-0.27	0.57	.194	0.279
Memory: Recall/Recognition								
HVLT-R: Delayed Recall	0.07	0.83	0.08	0.87	0.23	0.50	.902	0.020
BVMT-R: Delayed Recall	-0.18	1.08	-0.03	1.09	-0.22	0.59	.901	0.021
HVLT-R: RDI	0.07	0.14	0.18	0.88	-0.02	0.65	.859	0.030
Visuospatial Perception								
JOLO (corrected raw values)	27.67	2.80	29.17	0.75	30.00	0.89	.030	.503

Note. CPT-2 = Connors Performance Test - 2; HVLT-R = Hopkins Verbal Learning Test-Revised; BVMT-R = Benton Visual Memory Test – Revised; LNS = Letter Number Sequencing; RDI – Recognition Discrimination Index; RT = Reaction Time; WCST = Wisconsin Card Sorting Test

[a] Reversed scored so that for all variables higher means indicate better performance

Table 6. Individuals Evidencing Reliable Change Between Sessions

Cognitive Domain	T0 vs T1			T1 vs T2			T0 vs T2		
	Worsen	No Change	Improve	Worsen	No Change	Improve	Worsen	No Change	Improve
Attentional Capacity/Working Memory									
Digit Span: Total	0	5	1	0	6	0	0	3	3
HVLT-R: Trial 1	0	4	0	1	5	0	0	6	0
LNS: Total	0	5	1	2	3	1	2	3	1
Concentration/Focused Attention									
CPT-2: Omissions (Inattention)[a]	0	6	0	0	6	0	0	6	0
CPT-2: Commissions (Impulsivity)[a]	1	3	2	0	6	0	0	3	3
CPT2d (inattention)[a]	0	6	0	0	6	0	0	6	0
Sustained Attention (Vigilance)									
Hit RT Block Change[a]	0	6	0	0	6	0	0	6	0
Hit SE Block Change[a]	0	6	0	0	6	0	0	6	0
Hit RT ISI Change[a]	0	6	0	0	6	0	0	6	0
Processing Speed									
Coding	0	4	2	0	6	0	0	6	0
Trail Making Test – A	0	5	0	0	6	0	1	5	0
CPT-2: HitRT [a]	0	6	0	2	1	3	0	4	2
Executive Functioning									
Trail Making Test - B	0	6	0	0	6	0	1	5	0
WCST:CV4: Total Errors	0	6	0	0	6	0	0	6	0
WCST:CV4: Preservative Responses	0	6	0	0	6	0	0	6	0
WCST:CV4: Preservative Errors	0	6	0	0	6	0	0	6	0

Table 6 Continued

Cognitive Domain	T0 vs T1			T1 vs T2			T0 vs T2		
	Worsen	No Change	Improve	Worsen	No Change	Improve	Worsen	No Change	Improve
WCST:CV4: Conceptual Level Responses	0	6	0	0	6	0	0	6	0
Motor Functioning									
Grip Strength – Dominant	0	6	0	0	6	0	0	6	0
Grip Strength – Non-dominant	0	6	0	0	6	0	0	6	0
Grooved Pegboard – Dominant	0	5	1	1	5	0	0	6	0
Grooved Pegboard – Non-dominant	0	6	0	0	6	0	0	6	0
Language									
Verbal Fluency	0	6	0	0	6	0	0	6	0
Animals	0	6	0	0	6	0	1	5	0
Boston Naming Test[b]	-	-	-	-	-	-	-	-	-
Memory: Learning									
HVLT-R: Total	0	6	0	0	6	0	1	5	0
BVMT-R: Total	0	6	0	4	2	0	2	3	1
Memory: Recall/Recognition									
HVLT-R: Delayed Recall	0	6	0	0	6	0	0	6	0
BVMT-R: Delayed Recall	3	2	1	1	5	0	2	3	1
HVLT-R: RDI	0	6	0	0	6	0	0	6	0
Visuospatial Perception									
JOLO[b]	-	-	-	-	-	-	-	-	-

Note. CPT-2 = Connors Performance Test - 2; HVLT-R = Hopkins Verbal Learning Test-Revised; BVMT-R = Benton Visual Memory Test – Revised; LNS = Letter Number Sequencing; RDI – Recognition Discrimination Index; RT = Reaction Time; WCST = Wisconsin Card Sorting Test

[a]Reversed scored for all variables; higher means indicate better performance

[b]Unable to find data to calculate RCI

Self-reported domains of functioning. A one-way repeated measure ANOVA did not reveal a significant main effect for time on the Beck Depression Inventory-II (BDI-II). However, mean BDI-II raw scores indicated there was a decline in self-reported depressive symptoms from baseline (M = 15.17; SD=5.70) to T2 (M = 8.3; SD=5.53). A one-way repeated measures ANOVA revealed a significant main effect for time on the Beck Anxiety Inventory (F (2, 2) = 5.632, $p < .05$, ${}_{p}\eta^2 = .53$). Bonferroni post hoc test did not show ($p > .05$) the source of differences between the assessment times. There was a pattern of a decline in self-reported symptoms of anxiety across time. The global severity index (GSI) from the Brief-Symptom Inventory-18 indicated participants did not report distress and there no were significant main effects across testing times (p's >.05) for the GSI and the three clinical subscales

Examination of the Working Memory subscale of the BRIEF-A Self-report revealed a significant main effect for time relating directly to the participants ability to sustain working memory (F(2,10) = 4.970, $p > .05$, ${}_{p}\eta^2 = .49$). Bonferroni post hoc test did not show ($p > .05$) the source of differences between the assessment times. The Metacognitive Index, a measure of the ability to actively problem solve in a variety of contexts, revealed a significant main effect for time (F (2, 6) = 6.43, $p > .05$, ${}_{p}\eta^2 = .68$) (see Table 7). Bonferroni post hoc test did not show ($p > .05$) the source of differences between the assessment times. No significant improvements were observed on the other self-report subscales or the indices.

A repeated measures ANOVA determined that the mean total on the Perceived Deficit Score Questionnaire was not statistically significant between testing sessions but scores showed a trend in improvement for perceived cognitive functioning over time

($F(2,10)= 3.91$, $p = .06$, ${}_p\eta^2 = .44$). The greatest impairment in self-perceived cognition at baseline was observed in the attention/concentration and retrospective memory subscale scales. All the PDQ subscales indicated improvement across time, although not statistically significant.

A one-way repeated measures ANOVA did not reveal any significant main effects for time on a measure of overall quality of life ($p > .05$). On a measure of subjective cognitive functioning, a one-way repeated measures ANVOA revealed a significant effect for time (F (2, 10) = 5.40, $p > .05$, ${}_p\eta^2 = .51$). Bonferroni post hoc test did not show ($p > .05$) the source of differences between the assessment times. Although not significant, mean scores indicated that the BCSs felt cognitive function improved between baseline and post-intervention. This feeling was maintained 20-weeks later. All other subscales of the EORTC did not reveal any significant main effects, $p > .05$.

Caregiver measures. One training partner was not able to attend the post-assessment (T1) due to work commitments. Repeated measures analyses for the BRIEF-A informant report and CQOLC included five training partners.

On the BRIEF-A Informant report, a one-way repeated measures ANOVA revealed a significant main effect for time on the emotional control subscale ($F(2,8) = 25.877$, $p < 0.001$, ${}_p\eta^2 = .86$). Bonferroni post hoc test results revealed that the difference was between baseline and post intervention ($p = 0.002$) ¸ and between baseline and the 20-week follow-up assessment ($p = 0.03$). A one-way repeated measures ANOVA revealed significant main effects for time on the planning/organization subscale (F (2, 8) = 20.044, $p < 0.001$, ${}_p\eta^2 = .83$). Bonferroni post hoc test results revealed that the difference was between baseline and post intervention ($p = 0.011$), and between baseline

and the 20-week follow-up assessment ($p = 0.05$). A one-way repeated measures ANOVA revealed significant main effects for time on the behavioral regulation index (F (2, 8) = 9.492, $p = 0.008$, $_p\eta^2 = .70$). Bonferroni post hoc test revealed the difference was between baseline and post intervention ($p = 0.05$). A one-way repeated measures ANOVA revealed significant main effects for time on the metacognition index (F (2, 8) = 4.654, $p = 0.046$, $_p\eta^2 = .54$). Bonferroni post hoc test revealed that the difference was between baseline and post intervention ($p = 0.05$). A one-way repeated measures ANOVA revealed significant main effects for time on the global executive composite index (F (2, 8) = 9.386, $p = 0.008$, $_p\eta^2 = .70$). Bonferroni post hoc test revealed that the difference was between baseline and post intervention ($p = 0.02$).

There were no significant changes in the total CQOLC score. However, mean scores decreased across time indicating that training partners were reporting a better quality of life.

Table 7. Mean and Standard Deviations for Self-Reported Measures Across Assessments

Subjective Measure	**Baseline**		**Post-Treatment**		**Follow-up Treatment**		***p***	**Effect Size**
	M	***SD***	***M***	***SD***	***M***	***SD***		
BAI (raw scores)	12.17	7.8	6.17	4.5	4.17	2.3	.023	0.530
BDI-II (raw scores)	15.17	5.7	10.00	4.1	8.33	5.55	.096	0.374
BSI-18 (T-Score) [a]								
Somatization	47.17	8.5	49.83	9.7	51.00	9.4	.282	0.223
Depression	40.83	10.7	47.00	8.9	48.17	3.9	.129	0.336
Anxiety	48.17	11.3	52.83	9.5	52.83	9.5	.587	0.101
Global Severity Index	45.33	13.2	49.50	10.1	46.67	9.1	.351	0.189
BRIEF-A Self Report (T-scores)[a]								
Behavioral Regulation Index	46.67	11.67	46.50	13.47	56.67	10.23	.556	0.111
Inhibit Subscale	53.50	2.59	50.50	9.61	49.67	7.60	.510	0.126
Shift Subscale	44.17	10.63	39.67	12.64	56.50	12.42	.141	0.324
Emotional Control Subscale	39.83	13.38	46.50	12.33	62.67	10.07	.117	0.349
Self-Monitor Subscale	52.50	9.27	50.67	10.35	48.33	11.33	.857	0.030
Metacognition Index	42.00	7.80	44.50	5.86	56.83	7.67	.032	0.499
Initiate Subscale	46.67	12.14	46.00	9.12	56.50	10.96	.556	0.440
Working Memory Subscale	27.33	13.66	34.00	5.02	60.17	6.39	.032	0.499
Plan/Organize Subscale	45.67	7.63	44.50	10.48	59.50	8.80	.271	0.230
Task Monitor Subscale	46.83	6.91	45.33	2.58	53.50	6.38	.213	0.266
Organization of Materials Subscale	53.50	6.57	55.67	7.01	49.83	7.47	.556	0.441
Global Executive Composite	43.50	8.87	45.17	8.28	57.00	8.02	.162	0.305
Perceived Deficits Questionnaire (raw scores)								
Attention/Concentration	10.33	5.3	9.33	3.1	7.67	2.3	.223	0.259
Prospective Retrospective Memory	10.67	3.9	8.33	2.0	6.67	3.0	.065	0.484
Memory	8.00	4.4	5.50	1.9	4.17	2.3	.029	0.509
Planning/Organization	9.00	4.4	8.17	3.5	5.83	2.3	.084	0.391
Total	38.00	16.5	31.33	8.6	24.33	6.4	.056	0.439
EORTC QLQ C30								
Global Health Status/Quality of Life	61.11	14.6	58.33	13.9	59.72	15.3	.881	0.25
Physical Function	65.55	22.1	66.66	18.4	72.22	21.7	.314	0.207
Role Function	69.44	26.7	69.44	40.0	86.11	16.4	.413	0.162

Subjective Measure	Baseline		Post-Treatment		Follow-up Treatment		*p*	Effect Size
	M	***SD***	***M***	***SD***	***M***	***SD***		
Emotional Function	65.27	23.2	81.4	12.3	69.44	17.2	.112	0.355
Cognitive Function	47.22	24.5	72.22	13.6	72.22	8.6	.026	0.519
Social Function	58.33	36.1	61.11	25.1	72.22	25.1	.265	0.233
BRIEF-A Informant Report (T-scores)[a]								
Behavioral Regulation Index	56.67	7.47	50.80	6.14	57.17	8.40	.008	0.704
Inhibit Subscale	49.67	9.61	45.40	1.34	51.33	5.61	.164	0.363
Shift Subscale	56.50	13.13	54.20	15.21	59.17	12.70	.051	0.525
Emotional Control Subscale	62.67	6.31	52.00	7.11	59.17	11.16	< .001	0.866
Self-Monitor Subscale	48.33	6.98	48.40	4.72	53.33	6.53	.383	0.213
Metacognition Index	56.83	9.26	51.60	9.58	55.50	9.81	.046	0.538
Initiate Subscale	56.50	10.25	51.80	8.20	55.17	9.83	.194	0.336
Working Memory Subscale	60.17	15.55	52.60	10.62	60.33	11.18	.551	0.135
Plan/Organize Subscale	59.50	11.50	51.60	8.96	55.33	9.59	< .001	0.834
Task Monitor Subscale	53.50	5.99	53.20	10.01	53.17	7.81	.742	0.072
Organization of Materials Subscale	49.83	10.74	47.00	8.92	50.00	8.17	.703	0.084
Global Executive Composite	57.00	8.46	51.20	7.16	56.50	8.83	.008	0.701
Caregiver Quality of Life Questionnaire – Cancer (raw scores)								
Burden	15.5	4.3	10.60	6.2	15.00	6.7	.416	0.197
Disruptiveness Scale	7.17	2.8	5.40	4.8	4.83	5.5	.671	0.095
Positive Adaptation	10.83	2.8	10.60	4.8	10.83	5.0	.859	0.037
Financial	2.50	2.3	1.60	1.8	2.00	2.4	.305	0.257
Total	48.33	9.5	39.20	11.7	45.17	18.4	.369	0.205

Note. BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory-II; BSI-18 – Brief Symptom Inventory-18; BRIEF- The Behavior Rating Inventory of Executive Function – Adult Version; EORTC - European Organization for Research and Treatment of Cancer-Core Quality of Life Questionnaire

[a] Reversed scored so that for all variables higher means indicate better performance

Chapter 5: Discussion and Conclusions

The literature is burgeoning with studies that have primarily focused on identifying CRCI and its impact on quality of life of the affected individual. While limited, research has begun to focus on the management of CRCI and the identification of appropriate interventions to alleviate symptoms and improve quality of life in individuals with cancer (Von Ah, Storey, Jansen, & Allen, 2014). A 10-week, face-to-face cognitive rehabilitation program (CRP) was developed to support both survivors of breast cancer and training partners to cope with cancer-related cognitive changes. The purpose of the CRP was 1) to teach, practice, and increase the use of strategies related to attention and executive functioning for BCSs and their training partners; and 2) to help improve thinking, communication skills, mood, and overall quality of life. What made the CRP unique was that training partners were integrated in all sessions, their perspective on BCSs everyday functioning was measured, and their own quality of life was evaluated. The aims of this pilot study were: 1) to determine the feasibility and acceptability of a brief CRP to BCSs and their training partners and 2) to determine if neuropsychological outcomes improved and were maintained following completion of the CRP.

Aim 1: Feasibility and Acceptability

This pilot study provided useful data concerning the feasibility of our CRP. Feasibility was assessed in a number of ways: ease of recruitment, retention, attendance rates, homework compliance, and participant satisfaction.

Recruitment and retention. We were able to successfully recruit six survivors of breast cancer and training partners to participate in a group intervention. Few studies

exist to compare this CRP. Julious (2005) recommended a minimum sample size of 12 per group as a rule of thumb and justified this based on rationale about feasibility and precision around the mean and variance. The originally proposed sample size was 10 dyads and future studies should aim for a minimum of 10-12 dyads per group.

Barriers to recruitment in our study included system-level (e.g. research strategy procedures), clinician-level (e.g. lack of time) and participant-level factors such as BCSs unawareness of shortcoming, misattributing cognitive impairments to fatigue or stress and perhaps not having an available support system. Although we recruited 6 dyads, the process was not easy. BCSs were required to have a designated training partner identified at the beginning of the study. There may have been BCSs who were interested in this study but lacked a partner. The requirements for a partner may have been a deterrent or obstacle to potential study participants. Without a partner it could be perceived that they could not participate in the CRP. This may have contributed to low study enrollment. According to Standard II.43 of the Canadian Psychological Association Code of Ethics (Canadian Psychological Association, 2000) psychologists must "not place an individual, group, family, or community needing service at a serious disadvantage by offering them no service in order to fulfill the conditions of a research design, when a standard service is available". One needs to ethically consider avoiding bias to individuals who do not have a partner but would still benefit from the CRP. We did not receive any inquiries from potential participants without partners, perhaps for the reason previously stated; participants who met the BCS inclusion criteria but lacked a partner would have been invited to participate in the CRP. Several actions were taken to address our main recruitment challenges such as referrals from health care professions

and providing adequate information to the community. Recommendations for future iterations of this study are provided below.

Health care professionals were informed of the study via mass email sent to all staff accounts at the cancer site. Often email is used a viable outlet for communication and collaboration in a work environment. However, our email may have been overlooked due to communication overload when inboxes are flooded by other mass. Although the intention was to reach as many staff as possible, mass emailing may no longer be the most effective way. Additionally, meeting invitations to oncologists to request referrals and provide them with the necessary contact information for enrolment was unsuccessful. Several of the oncologists were on vacation or unavailable during that time. Given the busy practices of oncologists, it may have been more beneficial to provide written information (not email) on study information and eligibility criteria. For many BCSs, follow-up care is provided by primary care providers who work outside of a cancer centre. Given these scenarios, recommendations would be 1) to present study information to health care providers in a forum where they are together (e.g. rounds, program meetings) and 2) to mail study information to primary care providers in the community.

There were also efforts to inform community members of the study. Support group facilitators were contacted through email and were asked to print and hand-out materials about the study. To improve recruitment efforts for support groups and community organizations, we recommend delivering a brief in-person presentation containing information about CRCI, information about the CRP, and how participants can enrol in the study. After 2 months of no enrolment, print and broadcast media was

used as an additional strategy to support recruitment efforts. These efforts proved successful and several individuals contacted the study coordinator. Based on the success of media recruitment, we would recommend finding cost-effective strategies utilizing media. These could include paid radio advertisements, radio public service announcements, public service announcements through local newspapers, print and online newsletters, and use of social media (Facebook or Twitter).

Retention and attrition are important elements of feasibility in any intervention study. Despite the recruitment challenges, all the participants who enrolled completed the study and a subsequent return for two additional post-intervention assessments. Factors that were associated with retention included the duration of the sessions (2 hours in person with homework), the length of the intervention was brief (10 weeks), and the time year the CRP was offered (winter in Northern Ontario). Retention information was valuable because it provided the research team with information about what was acceptable or unacceptable about the intervention, and if any modifications should be made for future studies.

The weekly session format of the CRP was beneficial for participants because it allowed an opportunity for education followed by practical activities that could be applied in real-life contexts. Sessions were promoted as 1.5 hours in length but in most cases they lasted 2 hours. One of the participants suggested offering the CRP in the afternoon; however, a systematic review by Islam et al (2014) indicated that the prevalence of BCSs returning to work varies from 43% to 93% following completion of active treatment. In addition, caregivers (training partners) are more likely employed in daytime jobs. We would not change the time of day when the CRP was offered (evening

versus afternoon); however, we would recommend beginning earlier (i.e. 5:30 p.m. or 6:00 p.m.) and extending to session time from 1.5 hours to 2 hours. This would allow participants to better absorb the content, ask questions, and allow for more discussion.

There was variability in responses from the BCSs in terms of the length of sessions. Most of the participants felt the length of the sessions was appropriate. However one felt there was too much information and the number of sessions should be increased. In hindsight, the teaching modules of sessions six through nine were content heavy and subsequently many of the practice sessions were given as homework. Due to inclement weather, it was necessary to cancel one of the sessions. Subsequently sessions 8 and 9 were combined into one session to ensure the CRP program finished on its intended date. The combined session resulted in the teaching modules that were loaded in content and one of the participants commented that "having the two sessions at the same time was too much and the homework was intense" for them.

Although there is no evidence to support the effects of duration and intensity of CRPs, Cicerone et al. (2000) reported that "maintenance and generalizations of benefits from cognitive rehabilitation are greatest when treatment is provided for approximately long periods of time". Similar to cognitive behavioural therapy, this CRP was time-limited. Cognitive behavioural therapies usually have a course of weekly therapy sessions lasting 12-16 weeks. Therefore if the CRP were to run again, duration of 12-16 weeks is recommended to allow the content to be spread over more sessions.

Attendance. The high attendance rate for participants would support the idea that physically attending treatment may be therapeutic in a manner that promotes maintenance of gains in some patients, compared to a telephone- or internet based intervention. Mohr

and colleagues (2012) postulated that attending face-to-face therapy may serve as a form of behavioural activation. Another possibility that Mohr et al., (2012) suggested was that "the physical presence of the therapist, although not having an effect during treatment, contributes to the maintenance of gains, which suggests that human contact may have unique qualities that exert their effects and contribute to resilience after contact has ceased." Although support does not necessarily have to be provided face-to-face, the structure of the CRP (i.e., group based) does not permit using a videoconferencing or telephone based approach. Moreover, the high attendance rates provide support that the structure of the CRP was important and beneficial to BCSs and training partners.

Homework compliance. Participants were assigned between-session homework that involved practice of the previous session's content. We thought that the use of between-session homework activities would likely promote the use of skills learned during the sessions. Participants often reported that they completed their homework, suggesting that homework was acceptable. Homework has an extensive history in the broader psychotherapy literature (Kazantzis Whittington & Dattillio, 2010) and is primarily used to help generalise skills developed in session to the participant's broader world and prolong "symptom improvement by extending therapeutic aspects of treatment beyond the completion of therapy" (Kazantzis & Lampropoulos, 2002; Mausbach, Moore & Patterson, 2009). Participants may have been inclined to report completing homework in a socially desirable fashion. Participants may be exaggerating their degree of compliance with homework assignments. Future iterations of the study could add a clinician-rated homework scale to allow for comparisons of homework compliance.

Program evaluation. There were several benefits to offering a group-based intervention in addition to cost-effectiveness: 1) a group format can also reduce an individual's sense of alienation by allowing them to feel part of a cohesive group of participants (Yalom, 2005) and; 2) the group-based intervention created a forum for educational sessions and the exchange of ideas regarding coping strategies and compensatory techniques. Positive feedback indicated that survivors of breast cancer found the intervention helpful in dealing more effectively with their difficulties. Training partners were similarly enthusiastic about the intervention strategies and rated instructors for the caregiver group sessions as well-prepared and helpful. Furthermore, participants often remarked that there was an increased, positive ability to cope with CRCI issues, and that the discussion of issues and coping strategies were important to them. Mateer and Sohlberg (2001) stated that rehabilitation success depends on a true collaboration with the client and family members in the client's life. Upon completion of the study, all the BCSs felt they were more informed about the cognitive changes they experienced following chemotherapy, and four of them felt they were much improved compared to their feeling prior to beginning this study. Overall, all the participants were satisfied with the CRP and indicated that they would recommend the intervention to others if offered again.

Aim 2: Improvement and Maintenance of Neuropsychological Outcome Measures

The participants tolerated the three-hour test battery of neuropsychological measures during all assessment sessions. The test battery was deemed suitable for use as a comprehensive assessment that could be repeated with minimal practice effects

(alternate forms were used where available) and minimal patient fatigue. The addition of a control group could possibly clarify any practice effects and the differences observed in the CRP group. Despite their common use, cognitive screeners such as the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) are not sensitive enough to detect the presence and breath of subtle cognitive impairment commonly seen in individuals breast cancer (Baschnagel, Wolters, & Camphausen, 2008; Root, Ryan, & Ahles, 2015; Lange et al., 2014). On the opposite side of the spectrum, traditional neuropsychological batteries such as the Halstead-Reitan Neuropsychological Battery, Luria-Nebraska (Lezak et al., 2004) are generally time-consuming to administer in a research setting – they can take up to 8-10 hours to administer. The compromise is having a brief test battery that is reliable and sensitive to detect meaningful neuropsychological change. The study's test battery not only proved suitable in a research setting, but, given the breath of cognitive areas it covers, it would likely be useful to evaluate cognitive changes and predict outcome in a clinical setting.

Hypothesis I sought to evaluate the effects of the CRP through analyzing baseline measures versus the post-intervention assessment. At baseline, the mean test scores from the BCS group were within normal limits for all measures. This data is consistent with results reported by Reid-Arndt, Hsieh, and Perry (2010) that cognitive abilities are within normal limits for a majority of breast cancer survivors in the year following active treatment. On self-report measures, BCSs reported mild anxiety, mild depression, low levels of psychological distress and low levels of impairments on executive function behaviour in their everyday environment.

The results of the current study revealed few significant findings in support of the hypothesized relationship between short term cognitive rehabilitation and measurable improvements in neuropsychological measures. Repeated measures ANOVAs did not demonstrate significant effects for time on most measures. Significant main effects and moderate effect sizes for time were noted on measures of attentional capacity, impulsivity, detectability, motor dexterity and grip strength of the non-dominant hand, confrontation naming, and visuospatial perception. Additionally, statistical evidence in this pilot study does not provide solid evidence of supporting the original pilot hypothesis that a CRP is efficacious in improving and/or maintaining cognitive impairments following a brief CRP.

Hypothesis II evaluated whether the CRP resulted in sustained improvements over time on neuropsychological measures. Similar to hypothesis I, repeated measures ANOVAs did not demonstrate significant effects for time on most measures. A main effect for time was demonstrated on a measure of detectability (CPT-2: d'), suggesting that BCSs improved their ability to distinguish relevant from irrelevant information. This ability is related to the concepts of executive control and inhibition. According to Fernandez-Duque, Baird and Posner (2000), this type of executive functioning relates to better metacognitive monitoring, which involves control processes such as conflict resolution and emotional regulation. At the very least, these result suggest that the BCSs may have utilized the strategies taught from the CRP and developed the confidence to attempt to use them.

Hypothesis III sought to evaluate if the CRP resulted in observable gains in the performance of activities of daily living. Specifically, results of this pilot study indicate

that the CRP is associated with improvements in self-reported subjective cognition, psychosocial distress, social functioning, and fatigue. Differences of at least 10 points (on a 0-100 scale), are classified as the minimum clinically meaningful change in a health related quality of life parameter (Osoba, Rodrigues, Myles, Zee & Pater, 1998). Comparing baseline to 20-weeks after completion of the program, large improvements (greater than 20 points change) were reported on the following functional and symptom scales of the EORTC QLQ-C30: Role (the ability to work or participate in leisure activities); Cognitive (the ability to concentrate or remember things); Social (physical conditions or medical treatments interfering with family life or social activities); Fatigue (the need for rest, feeling of weakness or tiredness) and future perspectives (worries about health in feature. The large change in these scales suggests that the content, activities, and discussions that occurred during the CRP provided an important framework for the participants' self-awareness. Low scores over time on the Perceived Deficits Questionnaire indicated that the BCSs perceived fewer deficits both immediately after the intervention and at 20-week follow-up. Program evaluation and subjective measures indicated the participants felt better. This suggests that the CRP has some beneficial influence on mood and on quality of life.

Additionally, the pilot study was not able to tease out the relative effectiveness of cognitive retraining versus the use of compensatory strategies. Given the small sample size, it is reasonable to take note of data trends that could become statistically significant, in a study with a greater sample size. For example, trends were found in a review of neuropsychological measures of sustained attention, measures of executive functioning, semantic and phonemic fluency, verbal learning and delayed recall. Self-report measures

demonstrated trends in the areas of psychological health status (BSI-18), declines in self-reported depressive symptoms, (BDI-II), declines in anxious symptoms (BAI), and improvements in perceived difficulties with organization, concentration, and memory (PDQ). Although the above data are trending in a positive direction (from the perspective of intervention effectiveness) these changes remain marginal and to some degree uncertain because of the small sample size. The trends towards improvement on objective and self-report measures could be considered as an indirect cue of the importance of direct and compensatory training in everyday life. Furthermore, mean scores fell within the normative range across measures and across time. This finding conceals the heterogeneity in recovery outcomes and underscores the limitations of examining only group data with a small sample size.

Cicerone et al., (2000) emphasized that regardless of the specific approach or area of intervention, cognitive rehabilitation should be directed at promoting changes that improve functioning in areas of relevance to an individual‘s everyday life. There is evidence to indicate that the effect sizes from cognitive rehabilitation are largest when the training closely resembles outcomes measures, suggesting task-specific or skill-specific effects. Despite moderate to large effect sizes on many of the objective and subjective measures, given the small sample size many of the comparisons failed to reach significance. On objective measures that were statistically significant, large effect sizes for changes across time were observed in the areas of attentional capacity ($_p\eta^2 = .59$), inattentiveness ($_p\eta^2 = .45$), detectability ($_p\eta^2 = .59$), non-dominant grip strength ($_p\eta^2 = .59$), non-dominant manual dexterity ($_p\eta^2 = .65$), confrontation naming ($_p\eta^2 = .65$), and visuospatial perception ($_p\eta^2 = .50$). Moderate effect sizes for changes across time were

also observed on self-reported measures of generalized anxiety ($_p\eta^2$ = .53), an index score on the ability to cognitively self-manage tasks and to monitor performance ($_p\eta^2$ = .49), perceived retrospective memory dysfunction ($_p\eta^2$ = .48), perceived prospective memory dysfunction ($_p\eta^2$ = .51), and subjective cognitive functioning ($_p\eta^2$ = .52). The preliminary data indicated that improvements were observed in the rehabilitated neuropsychological domains and may provide a focal point to optimize the design of subsequent studies.

Reliable change indices (RCIs) were calculated to assess if there were changes at the individual level that would be *clinically* meaningful. RCIs did not confirm if the CRP induced improvement at the individual level on most measures. The test-retest reliability and SD for each objective measure were derived from published data. Perhaps the lack of change can be attributed to the difficulty in finding normative data for the breast cancer population or having a local control group.

Caregivers. In addition, caregivers of individuals with cancer can be faced with substantial challenges. An illness, such as breast cancer, can cause a major disruption in lives of individuals and their families. Aspects of this disruption, in turn, can impact the behaviours, roles, and responsibilities held by the individual with breast cancer and their partner in the family unit (Northouse, 1989; Northouse, Katapodi, Song, Zhang, & Wood, 2010). Caregivers may be faced with role adjustments that can culminate in problems managing responsibilities at work, home and in other family relationships (Girgis, Lambert, Johnson, Waller & Currow, 2013). Perceived quality of life for the training partners was evaluated using the Caregiver Quality of Life Index-Cancer (CQOLC) questionnaire. The training partners rated their mental/emotional burden, lifestyle disruption, financial concerns, hopefulness as low. The scores remained relatively stable

across assessments suggesting low caregiver burden in our training partners. Although this is a pilot study, the results highlight the importance of enlisting caregivers to help incorporate cognitive strategies and exercises into the survivor's everyday life. There also seems to be a direct benefit to the training partner in terms of reduced caregiver burden and improved quality of life. Despite the positive findings, the results are limited to a pilot study design and cannot be generalized to all populations. Further evaluation is warranted in order to help rule out confounds such as training partner demographics.

Limitations

The pilot study had several limitations. The small sample size may limit the interpretability of the results. The sample size was far too small to address potentially confounding factors such as chemotherapy treatments, concurrent medication use, and fatigue. Similar to other studies, the sample of BCSs was heterogeneous in terms of disease, treatment and demographics, and therefore, the effects of these variables on intervention efficacy could not be addressed due to the lack of statistical power. It is known that comparison of uneven group sizes is not methodologically ideal (Meyers, Gamst, Guarino, 2006). To address the issues of small and uneven group numbers and lack of a control comparison group, interpretation of results incorporated effect sizes that are independent of group size. Reliable change indices used information available from general population studies and did not have a control group for which to compare changes. Participants served as their own controls. Unpublished data (Mariani, 2014) indicated that the baseline premorbid full-scale IQ was nearly the same for participants in this pilot study compared to local BCSs. The baseline cognitive profile indicated that the

participants in the CRP had lower mean T-scores in visual and verbal memory and executive function compared to the local sample.

There was a relatively large number of neuropsychological and subjective measures. The test battery was comprehensive and administration time was approximately 2-3 hours. This comprehensive test battery and time were necessary given the complex nature of the phenomena under investigation. Further studies may want to reduce the number of neuropsychological tests within the battery used and select tests that are initially known to be sensitive and specific to detect changes in CRCI. An assessment should have a comprehensive battery that is sensitive and specific to detect minimal impairments and include the areas known to be involved with CRCI. Analysing cognitive domains (domain specific) and an overall impairment (global deficit) could be used as an approach to focus on the most reliable and salient measures and to reduce the number of statistical tests performed in this relatively small sample. However, ICCTF (Wefel et al., 2011) recommends against this approach to longitudinally monitor changes in cognitive function since declines from a higher level to the average range would be ignored.

Another potential criticism of this study was the use of self-reports to gather data. Self-report questionnaires are widely used as proxy measures of clinical outcomes. Unfortunately, bias associated with self-report questionnaires is quite common and can potentially influence the outcome of the targeted construct. An advantage of self-reporting is that it gives the researcher, the respondents' own perspective. The disadvantage is that there are potential validity problems such as truthfulness or deception. Patient reported outcomes are a necessity for research, thus it is paramount

that researchers and clinicians utilize effective methods for controlling bias in a study. Although data collection was not blind in this study, self-report measures were written to deter the possibility of interviewer bias (Tourangeau & Smith, 1996).

There were challenges with the development of the CRP (manual and content). The manual was not completed in its entirety prior to the start of the first session and posed a weekly challenge to complete session content. Each weekly session was completed a few hours or 1 day prior to delivery. Rarely do interventions run exactly as it is written in the manual, and facilitation can be unpredictable. Several of the session activities and homework used audio and sound quality proved suboptimal. The attention-based activities were read by one of the facilitators and the participants indicated there was difficulty in listening (i.e. rate of speech was too fast and speaker would pause abruptly). In addition, several of the handouts had grammatical errors. Regardless of these procedural issues, participants did rate the facilitators as well-prepared. This preparedness can be attributed to the facilitator's years of experience in group facilitation, and working with individuals diagnosed with cancer and their families. Given this is the first time the pilot study occurred, the CRP manual was completed in draft format simultaneously while running the program.

Finally, the study results can only be generalized to BCSs in Northern Ontario who report having cognitive symptoms and score(s) below a predetermined cut-off on objective neuropsychological tests. Results may not apply to survivors who have significant cognitive impairment on the basis of objective test results. Subsequently, results may apply only to survivors with relatively mild deficits, similar to the group studied, who have sufficient cognitive resources and motivation to follow the

rehabilitation program and report cognitive symptoms. Similar to most studies with BCSs, the inherent heterogeneity of this sample in terms of disease and treatment factors may limit the generalizability of these results to other cancer populations. These factors will need to be addressed in further, larger studies. Nonetheless, this was a pilot study and to our knowledge, the first study to implement a concurrent cognitive rehabilitation approach with BCS and training partners.

Conclusion

CRPs are increasingly recognized as beneficial alternatives and/or as adjunctive therapy to medications for improving specific types of cognitive dysfunction in individuals with neurological disorders or maintaining individuals at their current level. There is limited evidence for the effectiveness of cognitive rehabilitation in BCSs. The cognitive training programs for traumatic brain injury and Alzheimer's disease that utilize the well-developed programs have shown a number of improvements. Improvements occur in memory, attention, executive functioning, and problem solving (Cicerone et al., 2005). The improvements demonstrated the feasibility of these retraining programs. Despite the increasing concern regarding cognitive changes associated with CRCI, few studies have been designed and conducted to evaluate interventions to treat cognitive changes. If cognitive impairment is detected or reported by survivors of breast cancer, strategies to help them and their family members cope with these changes may be useful. The results of the study contribute to the literature on cognitive rehabilitation for the cancer population.

Irrespective of the shortcomings, the BCSs reported subjective improvement in cognition, mood and quality of life, and training partners reported reduced burden. All participants reported improved communication, were satisfied with the program, and indicated that they would participate in the program again and recommend it to a friend.

References

Aaronson, N. K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N. J., . . . de Haes, J. C. (1993). The European organization for research and treatment of cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute, 85*(5), 365-376.

Ahles, T. A., Root, J. C., & Ryan, E. L. (2012). Cancer- and cancer treatment-associated cognitive change: An update on the state of the science. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 30*(30), 3675-3686.

Ahles, T. A., & Saykin, A. J. (2007). Candidate mechanisms for chemotherapy-induced cognitive changes. *Nature Reviews.Cancer, 7*(3), 192-201.

Azim, H. A.,Jr, de Azambuja, E., Colozza, M., Bines, J., & Piccart, M. J. (2011). Long-term toxic effects of adjuvant chemotherapy in breast cancer. *Annals of Oncology : Official Journal of the European Society for Medical Oncology / ESMO, 22*(9), 1939-1947.

Baschnagel, A., Wolters, P. L., & Camphausen, K. (2008). Neuropsychological testing and biomarkers in the management of brain metastases. *Radiation Oncology (London, England), 3*, 26-717X-3-26.

Beck, A.T., Steer, R.A. (1990). *Manual for the beck anxiety inventory*. San Antonio, TX: Psychological Corporation.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for the Beck depression inventory-II*. San Antonio, TX: Psychological Corporation.

Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988). An inventory for measuring clinical anxiety: Psychometric properties. *Journal of Consulting and Clinical Psychology, 56*(6), 893-897.

Benedict, R. H. B.*The Brief Visuospatial Memory Test-revised: Professional manual*. Odessa, FL: Psychological Assessment Resources, Inc.

Benton, A. L., Varney, N. R., & Hamsher, K. D. (1978). Visuospatial judgment. A clinical test. *Archives of Neurology, 35*(6), 364-367.

Biglia, N., Bounous, V. E., Malabaila, A., Palmisano, D., Torta, D. M., D'Alonzo, M., . . . Torta, R. (2012). Objective and self-reported cognitive dysfunction in breast cancer women treated with chemotherapy: A prospective study. *European Journal of Cancer Care, 21*(4), 485-492.

Brandt, J., & Benedict, R. H. B. (2001). *Hopkins Verbal Learning Test-revised. Professional Manual.* Lutz, FL: Psychological Assessment Resources, Inc.

Cameron, L. D., Booth, R. J., Schlatter, M., Ziginskas, D., Harman, J. E., & Benson, S. R. (2005). Cognitive and affective determinants of decisions to attend a group psychosocial support program for women with breast cancer. *Psychosomatic Medicine, 67*(4), 584-589.

Canadian Cancer Society. (2015). *Risk of breast cancer recurrence and adjuvant therapy*. Retrieved from http://www.cancer.ca/en/cancer-information/cancer-type/breast/treatment/risk-of-breast-cancer-recurrence-and-adjuvant-therapy/?region=on#ixzz3fVMiqxbp

Canadian Cancer Society's Advisory Committee on Cancer Statistics. (2014). *Canadian cancer statistics 2014*. Toronto, Ontario: Canadian Cancer Society.

Canadian Psychological Association. (2000). *Canadian code of ethics for psychologists, third edition.* Ottawa, Ontario. Retrieved from http://www.cpa.ca/cpasite/UserFiles/Documents/Canadian%20Code%20of%20Ethics%20for%20Psycho.pdf

Cashman, R., Bernstein, L.J., Bilodeau, D., Bovett, G., Jackson, B., Yousefi, M. et al, (2007). Evaluation of an educational program for the caregivers of persons diagnosed with a malignant glioma. *Canadian Oncology Nursing Journal, 17,* 6–15.

Chan, R. J., McCarthy, A. L., Devenish, J., Sullivan, K. A., & Chan, A. (2015). Systematic review of pharmacologic and non-pharmacologic interventions to manage cognitive alterations after chemotherapy for breast cancer. *European Journal of Cancer (Oxford, England : 1990), 51*(4), 437-450.

Cicerone, K. D., Dahlberg, C., Kalmar, K., Langenbahn, D. M., Malec, J. F., Bergquist, T. F., . . . Morse, P. A. (2000). Evidence-based cognitive rehabilitation: Recommendations for clinical practice. *Archives of Physical Medicine and Rehabilitation, 81*(12), 1596-1615.

Cicerone, K. D., Dahlberg, C., Malec, J. F., Langenbahn, D. M., Felicetti, T., Kneipp, S., . . . Catanese, J. (2005). Evidence-based cognitive rehabilitation: Updated review of the literature from 1998 through 2002. *Archives of Physical Medicine and Rehabilitation, 86*(8), 1681-1692.

Clare, L., Wilson, B. A., Carter, G., & Hodges, J. R. (2003). Cognitive rehabilitation as a component of early intervention in Alzheimer's disease: A single case study. *Aging & Mental Health, 7*(1), 15-21.

Clark, M. M., Rummans, T. A., Atherton, P. J., Cheville, A. L., Johnson, M. E., Frost, M. H., Miller, J. J., Sloan, J. A., Graszer, K. M., Haas, J. G., Hanson, J. M., Garces, Y. I., Piderman, K. M., Lapid, M. I., Netzel, P. J., Richardson, J. W. and Brown, P. D. (2013). Randomized controlled trial of maintaining quality of life during radiotherapy for advanced cancer. *Cancer, 119,* 880–887.

Cohen, J. (1988). Chapter 8 - The Analysis of Variance. In Cohen, J. , *Statistical power analysis for the behavioral sciences (2nd ed.)* (273 – 406) . New Jersey: Lawrence Erlbaum.

Cold, S., During, M., Ewertz, M., Knoop, A., & Moller, S. (2005). Does timing of adjuvant chemotherapy influence the prognosis after early breast cancer? results of the Danish breast cancer cooperative group (DBCG). *British Journal of Cancer, 93*(6), 627-632.

Collins, B., Mackenzie, J., & Kyeremanteng, C. (2013). Study of the cognitive effects of chemotherapy: Considerations in selection of a control group. *Journal of Clinical and Experimental Neuropsychology, 35*(4), 435-444.

Conners, C. K., & MHS Staff (Eds.). (2000). *Conners' Continuous Performance Test II: Computer program for windows technical guide and software manual.* North Tonawanda, NY: Multi-Health Systems.

Correa, D. D., & Ahles, T. A. (2008). Neurocognitive changes in cancer survivors. *Cancer Journal (Sudbury, Mass.), 14*(6), 396-400.

Derogatis, L. R. (2000). *Brief Symptom Inventory 18*. Minneapolis: National Computer Systems Pearson, Inc.

Dietrich, J. (2012). Cognitive impairment in patients with cancer. *The ASCO Post, 3*(15)

Doody, R. S., Ferris, S. H., Salloway, S., Sun, Y., Goldman, R., Watkins, W. E., . . . Murthy, A. K. (2009). Donepezil treatment of patients with MCI: A 48-week randomized, placebo-controlled trial. *Neurology, 72*(18), 1555-1561.

Edelstein, K., & Bernstein, L. J. (2014). Cognitive dysfunction after chemotherapy for breast cancer. *Journal of the International Neuropsychological Society : JINS, 20*(4), 351-356.

Fardell, J. E., Vardy, J., Johnston, I. N., & Winocur, G. (2011). Chemotherapy and cognitive impairment: Treatment options. *Clinical Pharmacology and Therapeutics, 90*(3), 366-376.

Fayers, P. M., Aaronson, N. K., Bjordal, K., Groenvold, M., Curran, D., Bottomley, A., on behalf of the EORTC Quality of Life Group. (2001). *The EORTC QLQ-C30 scoring manual (3rd edition).* Brussels: European Organisation for Research and Treatment of Cancer.

Ferguson, R. J., Ahles, T. A., Saykin, A. J., McDonald, B. C., Furstenberg, C. T., Cole, B. F., & Mott, L. A. (2007). Cognitive-behavioural management of chemotherapy-related cognitive change. *Psychooncology, 16*(8), 772-777.

Ferguson, R. J., McDonald, B. C., Rocque, M. A., Furstenberg, C. T., Horrigan, S., Ahles, T. A., & Saykin, A. J. (2012). Development of CBT for chemotherapy-related cognitive change: Results of a waitlist control trial. *Psycho-Oncology, 21*(2), 176-186.

Fernandez-Duque, D., Baird, J. A., & Posner, M. I. (2000). Executive attention and metacognitive regulation. *Consciousness and Cognition, 9*, 288–307

Fors, E. A., Bertheussen, G. F., Thune, I., Juvet, L. K., Elvsaas, I. K., Oldervoll, L., . . . Leivseth, G. (2011). Psychosocial interventions as part of breast cancer rehabilitation programs? results from a systematic review. *Psycho-Oncology, 20*(9), 909-918.

Gehring, K., Roukema, J. A., & Sitskoorn, M. M. (2012). Review of recent studies on interventions for cognitive deficits in patients with cancer. *Expert Review of Anticancer Therapy, 12*(2), 255-269.

Gehring, K., Sitskoorn, M. M., Gundy, C. M., Sikkes, S. A., Klein, M., Postma, T. J., . . . Aaronson, N. K. (2009). Cognitive rehabilitation in patients with gliomas: A randomized, controlled trial. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 27*(22), 3712-3722.

Gehring, K., Taphoorn, M. J., Sitskoorn, M. M., & Aaronson, N. K. (2015). Predictors of subjective versus objective cognitive functioning in patients with stable grades II and III glioma. *Neuro-Oncology Practice, 2*(1), 20-31.

Girgis, A., Lambert, S., Johnson, C., Waller, A., & Currow, D. (2013). Physical, psychosocial, relationship, and economic burden of caring for people with cancer: A review. *Journal of Oncology Practice, 9*(4), 197-202.

Green, H.J., Pakenham, K.I. and Gardiner, R.A. (2003). *Objective and Subjective Cognitive Deficits Associated with Cancer: Implications for Health Professionals*. Manuscript submitted for publication.

Heaton, R., Chelune, G., Talley, J., Kay, G., & Curtiss, G. (1993). *Wisconsin Cart Sorting Test Manual. Revised and Expanded*. Odessa, FL: Psychological Assessment Resources, Inc.

Hoffman, C. J., Ersser, S. J., Hopkinson, J. B., Nicholls, P. G., Harrington, J. E., & Thomas, P. W. (2012). Effectiveness of mindfulness-based stress reduction in mood, breast- and endocrine-related quality of life, and well-being in stage 0 to III breast cancer: A randomized, controlled trial. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 30*(12), 1335-1342.

Hopkinson, J.B., Brown, J.C., Okamoto, I., & Addington-Hall, J.M. (2012). The effectiveness of patient–family carer (couple) intervention for the management of symptoms and other health-related problems in people affected by cancer: A systematic literature search and narrative review. *Journal of Pain and Symptom Management, 43,* 111–142.

Hutchinson, A. D., Hosking, J. R., Kichenadasse, G., Mattiske, J. K., & Wilson, C. (2012). Objective and subjective cognitive impairment following chemotherapy for cancer: A systematic review. *Cancer Treatment Reviews, 38*(7), 926-934.

Islam T, Dahlui M, Majid H.A., Nahar A.M., Taib, N.A.M., Su., T.T, & MyBCC study group (2014). Factors associated with return to work of breast cancer survivors: a systematic review. *BMC Public Health,14*:S8

Jacobson, N. S., & Truax, P. (1991). Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology, 59*(1), 12-19.

Janelsins, M. C., Kesler, S. R., Ahles, T. A., & Morrow, G. R. (2014). Prevalence, mechanisms, and management of cancer-related cognitive impairment. *International Review of Psychiatry (Abingdon, England), 26*(1), 102-113.

Jansen, C. E., Miaskowski, C. A., Dodd, M. J., & Dowling, G. A. (2007). A meta-analysis of the sensitivity of various neuropsychological tests used to detect chemotherapy-induced cognitive impairment in patients with breast cancer. *Oncology Nursing Forum, 34*(5), 997-1005.

Janz, N. K., Mujahid, M., Chung, L. K., Lantz, P. M., Hawley, S. T., Morrow, M., . . . Katz, S. J. (2007). Symptom experience and quality of life of women following breast cancer treatment. *Journal of Women's Health (2002), 16*(9), 1348-1361.

Jatoi, A., Kahanic, S. P., Frytak, S., Schaefer, P., Foote, R. L., Sloan, J., & Petersen, R. C. (2005). Donepezil and vitamin E for preventing cognitive dysfunction in small cell lung cancer patients: Preliminary results and suggestions for future study designs. *Supportive Care in Cancer : Official Journal of the Multinational Association of Supportive Care in Cancer, 13*(1), 66-69.

Jemal, A., Bray, F., Center, M. M., Ferlay, J., Ward, E., & Forman, D. (2011). Global cancer statistics. *CA: A Cancer Journal for Clinicians, 61*(2), 69-90.

Julious S.A. (2005) Sample size of 12 per group rule of thumb for a pilot study. *Pharmaceutical Statistics, 4*, 287–291.

Kaplan, E. F., Goodglass, H., & Weintraub, S. (1983). *The Boston Naming Test* (2nd ed.). Philadelphia, PA: Lea & Febiger.

Kayl, A. E., Wefel, J. S., & Meyers, C. A. (2006). Chemotherapy and cognition: Effects, potential mechanisms, and management. *American Journal of Therapeutics, 13*(4), 362-369.

Kazantzis, N., & Lampropoulos, G. K. (2002). Reflecting on homework in psychotherapy: What can we conclude from research and experience? *Journal of Clinical Psychology, 58*(5), 577-585.

Kazantzis, N., Whittington, C., & Dattilio, F. (2010). Meta-analysis of homework effects in cognitive and behavioral therapy: A replication and extension. *Clinical Psychology: Science and Practice, 17*(2), 144-156.

Kazdin, A. E. (1981). Acceptability of child treatment techniques: The influence of treatment efficacy and adverse side effects. *Behavior Therapy*, 12, 493-506.

Kempfert, J., Rastan, A., Holzhey, D., Linke, A., Schuler, G., Mohr, F. W., & Walther, T. (2012). The learning curve associated with transapical aortic valve implantation. *Annals of Cardiothoracic Surgery, 1*(2), 165-171.]

Kesler, S., Hadi Hosseini, S. M., Heckler, C., Janelsins, M., Palesh, O., Mustian, K., & Morrow, G. (2013). Cognitive training for improving executive function in chemotherapy-treated breast cancer survivors. *Clinical Breast Cancer, 13*(4), 299-306.

Kohli, S., Fisher, S. G., Tra, Y., Adams, M. J., Mapstone, M. E., Wesnes, K. A., . . . Morrow, G. R. (2009). The effect of modafinil on cognitive function in breast cancer survivors. *Cancer, 115*(12), 2605-2616.

Lange, M., Giffard, B., Noal, S., Rigal, O., Kurtz, J. E., Heutte, N., . . . Joly, F. (2014). Baseline cognitive functions among elderly patients with localised breast cancer. *European Journal of Cancer (Oxford, England : 1990), 50*(13), 2181-2189.

Levack, W. M., Siegert, R. J., Dean, S. G., & McPherson, K. M. (2009). Goal planning for adults with acquired brain injury: How clinicians talk about involving family. *Brain Injury, 23*(3), 192-202.

Lezak, M., Howieson, M., & Loring, D. (2004). *Neuropsychological Assessment* (Forth Edition ed.). New York: Oxford University Press

Locke, D. E. C., Cerhan, J. H., Wu, W., Malec, J. F., Clark, M. M., Rummans, T. A., & Brown, P. D. (2008). Cognitive rehabilitation and problem-solving to improve quality of life of patients with primary brain tumors: A pilot study. *Journal of Supportive Oncology, 6*(8), 383-391.

Mandelblatt, J. S., Stern, R. A., Luta, G., McGuckin, M., Clapp, J. D., Hurria, A., . . . Ahles, T. (2014). Cognitive impairment in older patients with breast cancer before systemic therapy: Is there an interaction between cancer and comorbidity? *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 32*(18), 1909-1918.

Marin, A. P., Sanchez, A. R., Arranz, E. E., Aunon, P. Z., & Baron, M. G. (2009). Adjuvant chemotherapy for breast cancer and cognitive impairment. *Southern Medical Journal, 102*(9), 929-934.

Mausbach, B. T., Moore, R., Roesch, S., Cardenas, V., & Patterson, T. L. (2010). The relationship between homework compliance and therapy outcomes: An updated meta-analysis. *Cognitive Therapy and Research, 34*(5), 429-438.

Meyers, L. S., Gamst, G., & Guarino, A. J. (2006). *Applied multivariate research. Design and interpretation* (1st ed.). Thousand Oaks, California: Sage Publications Inc.

Mosher, C. E., Bakas, T., & Champion, V. L. (2013). Physical health, mental health, and life changes among family caregivers of patients with lung cancer. *Oncology Nursing Forum, 40*(1), 53-61.

Munir, F., Kalawsky, K., Lawrence, C., Yarker, J., Haslam, C., & Ahmed, S. (2011). Cognitive intervention for breast cancer patients undergoing adjuvant chemotherapy: A needs analysis. *Cancer Nursing, 34*(5), 385-392.

National Academy of Neuropsychology. (https://www.nanonline.org/docs/PAIC/PDFs/NANPositionCogRehab.pdf). Cognitive rehabilitation: Official statement of the national academy of neuropsychology. Retrieved from 2002

Nguyen, C. M., Yamada, T. H., Beglinger, L. J., Cavanaugh, J. E., Denburg, N. L., & Schultz, S. K. (2013). Cognitive features 10 or more years after successful breast cancer survival: Comparisons across types of cancer interventions. *Psycho-Oncology*, *22*(4), 862-868.

Northouse, L. L. (1989). The impact of breast cancer on patients and husbands. *Cancer Nursing, 12*(5), 276-284.

Northouse, L. L., Katapodi, M. C., Song, L., Zhang, L., & Mood, D. W. (2010). Interventions with family caregivers of cancer patients: Meta-analysis of randomized trials. *CA: A Cancer Journal for Clinicians, 60*(5), 317-339.

Osoba, D., Rodrigues, G., Myles, J., Zee, B., & Pater, J. (1998). Interpreting the significance of changes in health-related quality-of-life scores. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 16*(1), 139-144.

Poppelreuter, M., Weis, J., & Bartsch, H. H. (2009). Effects of specific neuropsychological training programs for breast cancer patients after adjuvant chemotherapy. *Journal of Psychosocial Oncology, 27*(2), 274-296.

Pullens, M. J., De Vries, J., Van Warmerdam, L. J., Van De Wal, M. A., & Roukema, J. A. (2013). Chemotherapy and cognitive complaints in women with breast cancer. *Psycho-Oncology, 22*(8), 1783-1789. Ragnarsson, K. T. (2002). Results of the NIH consensus conference on "rehabilitation of persons with traumatic brain injury". *Restorative Neurology and Neuroscience, 20*(3-4), 103-108.

Rapp, S. R., Case, L. D., Peiffer, A., Naughton, M. M., Chan, M. D., Stieber, V. W., . . . Shaw, E. G. (2015). Donepezil for irradiated brain tumor survivors: A phase III randomized placebo-controlled clinical trial. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 33*(15), 1653-1659.

Reid-Arndt, S. A., Hsieh, C., & Perry, M. C. (2010). Neuropsychological functioning and quality of life during the first year after completing chemotherapy for breast cancer. *Psycho-Oncology, 19*(5), 535-544.

Reid-Arndt, S. A., Yee, A., Perry, M. C., & Hsieh, C. (2009). Cognitive and psychological factors associated with early posttreatment functional outcomes in breast cancer survivors. *Journal of Psychosocial Oncology, 27*(4), 415-434.

Reitan, R. M., & Wolfson, D. (1993). *The Halstead-Reitan neuropsychological test battery: Theory and clinical interpretation* (2nd ed.). South Tucson, Arizona: Neuropsychology Press.

Root, J. C., Ryan, E., Barnett, G., Andreotti, C., Bolutayo, K., & Ahles, T. (2015). Learning and memory performance in a cohort of clinically referred breast cancer survivors: The role of attention versus forgetting in patient-reported memory complaints. *Psycho-Oncology, 24*(5), 548-555.

Roth, R. M., Isquith, P. K., & Gioia, G. A. (2005). *BRIEF-A. behavior rating inventory of executive function-adult version professional manual*. Lutz, FL: Psychological Assessment Resources, Inc.

Rummans, T.A., Clark, M.M., Sloan, J.A., et al. Impacting quality of life for patients with advanced cancer with a structured multidisciplinary intervention: a randomized controlled trial (2006). *Journal of Clinical Oncology, 24,* 635-642.

Saykin, A. J., Ahles, T. A., & McDonald, B. C. (2003). Mechanisms of chemotherapy-induced cognitive disorders: Neuropsychological, pathophysiological, and neuroimaging perspectives. *Seminars in Clinical Neuropsychiatry, 8*(4), 201-216.

Schagen, S. B., Klein, M., Reijneveld, J. C., Brain, E., Deprez, S., Joly, F., . . . Wefel, J. S. (2014). Monitoring and optimising cognitive function in cancer patients: Present knowledge and future directions. *European Journal of Cancer Supplements, 12*(1), 29-40.

Schuurs, A., & Green, H. J. (2013). A feasibility study of group cognitive rehabilitation for cancer survivors: Enhancing cognitive function and quality of life. *Psycho-Oncology*, *22*(5), 1043-1049.

Shapiro, C. L., & Recht, A. (2001). Side effects of adjuvant treatment of breast cancer. *The New England Journal of Medicine, 344*(26), 1997-2008.

Sherwin, B. B. (2012). Estrogen and cognitive functioning in women: Lessons we have learned. *Behavioral Neuroscience, 126*(1), 123-127.

Sherwood, P. R., Given, B. A., Donovan, H., Baum, A., Given, C. W., Bender, C. M., & Schulz, R. (2008). Guiding research in family care: A new approach to oncology caregiving. *Psycho-Oncology*, *17*(10), 986-996.

Shilling, V., & Jenkins, V. (2007). Self-reported cognitive problems in women receiving adjuvant therapy for breast cancer. *European Journal of Oncology Nursing, 11*(1), 6-15.

Siegel, R., DeSantis, C., Virgo, K., Stein, K., Mariotto, A., Smith, T., . . . Ward, E. (2012). Cancer treatment and survivorship statistics, 2012. *CA: A Cancer Journal for Clinicians, 62*(4), 220-241.

Sohlberg, M. M., & Mateer, C. A. (2001). *Cognitive rehabilitation: An integrative neuropsychological approach.* New York, USA: The Guilford Press.

State of practice and Providers of cognitive rehabilitation therapy. (2011). In R. Koehler, E. E. Wilhelm & I. Shoulson (Eds.), *Cognitive rehabilitation Therapy for traumatic brain Injury Evaluating the evidence* (pp. 80-112). Washington, D.C.: The National Academic Press. Retrieved from http://www.nap.edu/openbook.php?record_id=13220

Stewart, A., Bielajew, C., Collins, B., Parkinson, M., & Tomiak, E. (2006). A meta-analysis of the neuropsychological effects of adjuvant chemotherapy treatment in women treated for breast cancer. *The Clinical Neuropsychologist, 20*(1), 76-89.

Strauss, E., Sherman, E. M. S., & Spreen, O.*A compendium of neuropsychological tests: Administration, norms, and commentary* (3rd ed.). NY, USA: Oxford University Press.

Sullivan, J. J. L., Edgley, K., & Dehoux, E. (1990). A survey of multiple sclerosis part 1: Perceived cognitive problems and compensatory strategy use.*4*, 99-105.

Taillibert, S. (2010). Is systemic anti-cancer therapy neurotoxic? does chemo brain exist? and should we rename it? *Advances in Experimental Medicine and Biology, 678*, 86-95.

Tannock, I. F., Ahles, T. A., Ganz, P. A., & Van Dam, F. S. (2004). Cognitive impairment associated with chemotherapy for cancer: Report of a workshop. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 22*(11), 2233-2239.

Vardy, J., Rourke, S., & Tannock, I. F. (2007). Evaluation of cognitive function associated with chemotherapy: A review of published studies and recommendations for future research. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 25*(17), 2455-2463.

Vardy, J., & Dhillon, H. (2011). 43 - cognitive function in cancer survivors. *Supportive oncology* (pp. 448-455). Saint Louis: W.B. Saunders.

Vodermaier, A. (2009). Breast cancer treatment and cognitive function: The current state of evidence, underlying mechanisms and potential treatments. *Women's Health (London, England), 5*(5), 503-516.

Vodermaier, A., Linden, W., & Siu, C. (2009). Screening for emotional distress in cancer patients: A systematic review of assessment instruments. *Journal of the National Cancer Institute, 101*(21), 1464-1488.

Von Ah, D., Jansen, C., Allen, D. H., Schiavone, R. M., & Wulff, J. (2011). Putting evidence into practice: Evidence-based interventions for cancer and cancer treatment-related cognitive impairment. *Clinical Journal of Oncology Nursing, 15*(6), 607-615.

Von Ah, D., Jansen, C. E., & Allen, D. H. (2014). Evidence-based interventions for cancer- and treatment-related cognitive impairment. *Clinical Journal of Oncology Nursing, 18 Suppl*, 17-25.

Wechsler, D. (2001). *WAIS-III Canadian technical manual*. Toronto, Ontario, Canada: The Psychological Corporation, A Harcourt Canada Assessment Company.

Wechsler, D. (2001). *Wechsler test of adult reading (WTAR)*. San Antonio, TX: Psychological Corporation.

Wefel, J. S., Kesler, S. R., Noll, K. R., & Schagen, S. B. (2015). Clinical characteristics, pathophysiology, and management of noncentral nervous system cancer-related cognitive impairment in adults. *CA: A Cancer Journal for Clinicians, 65*(2), 123-138.

Wefel, J. S., Lenzi, R., Theriault, R., Buzdar, A. U., Cruickshank, S., & Meyers, C. A. (2004). 'Chemobrain' in breast carcinoma?: A prologue. *Cancer, 101*(3), 466-475.

Wefel, J. S., Lenzi, R., Theriault, R. L., Davis, R. N., & Meyers, C. A. (2004). The cognitive sequelae of standard-dose adjuvant chemotherapy in women with breast

carcinoma: Results of a prospective, randomized, longitudinal trial. *Cancer, 100*(11), 2292-2299.

Wefel, J. S., Vardy, J., Ahles, T., & Schagen, S. B. (2011). International cognition and cancer task force recommendations to harmonise studies of cognitive function in patients with cancer. *The Lancet.Oncology, 12*(7), 703-708.

Weitzner, M. A., Jacobsen, P. B., Wagner, H.,Jr, Friedland, J., & Cox, C. (1999). The caregiver quality of life index-cancer (CQOLC) scale: Development and validation of an instrument to measure quality of life of the family caregiver of patients with cancer. *Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation, 8*(1-2), 55-63.

Wilson, B. A. (2000). Compensating for cognitive deficits following brain injury. *Neuropsychology Review, 10*(4), 233-243.

Yang, M., & Moon, C. (2013). Neurotoxicity of cancer chemotherapy. *Neural Regeneration Research, 8*(17), 1606-1614.