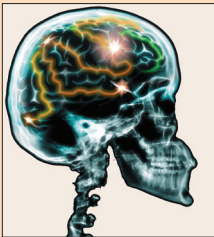


Cognitive Changes Associated With Cancer and Cancer Treatment: State of the Science

Diane Von Ah, PhD, RN, FAAN



© Digital Vision/Photodisc/Thinkstock

Background: Cognitive impairment is a distressing, disruptive, and potentially debilitating symptom that can occur as a direct result of cancer or its treatment. National organizations have identified cognitive impairment as a challenge many survivors face and call for research to address this problem. Despite the priority, research is still relatively limited and questions remain unanswered about prevalence and impact on survivors, as well as coping strategies and effective treatment options available to address this potentially debilitating problem.

Objectives: The purpose of this article is to (a) analyze the prevalence and types of cognitive impairment that commonly affect survivors; (b) delineate the impact that cognitive impairment after cancer and cancer treatment has on self-esteem, social relationships, work ability, and overall quality of life among survivors; and (c) synthesize and appraise commonly used coping strategies used by survivors to address cognitive impairment and evidence-based interventions that may be incorporated into clinical practice.

Methods: A comprehensive review and synthesis of the literature was conducted.

Findings: Evidence-based interventions to address cognitive changes after cancer and cancer treatment are limited. However, emerging research has demonstrated that nonpharmacologic treatments, such as cognitive training, are likely to be effective.

Diane Von Ah, PhD, RN, FAAN, is an associate professor in the School of Nursing at Indiana University in Indianapolis. The author takes full responsibility for the content of the article. As the recipient of the 2014 Trish Greene Memorial Quality-of-Life Lectureship, Von Ah presented this article at ONS Connections: Advancing Care Through Science in Phoenix, AZ. No financial relationships relevant to the content of this article have been disclosed by the author, planners, independent peer reviewers, or editorial staff. Von Ah can be reached at dvonah@iupui.edu, with copy to editor at CJONEditor@ons.org. (Submitted July 2014. Revision submitted July 2014. Accepted for publication July 18, 2014.)

Key words: cognitive impairment; evidence-based interventions; quality of life

Digital Object Identifier: 10.1188/15.CJON.19-01AP

The study of cognitive impairment as a late effect of cancer and its treatment has become a national research priority. The President's Cancer Panel, the National Cancer Institute Office of Cancer Survivorship, and the National Comprehensive Cancer Network Survivorship Panel have all identified emerging chronic and late effects of cancer and its treatment, such as cognitive impairment, as top research priorities (Hewitt, Greenfield, & Stovall, 2005). The National Coalition of Cancer Survivorship, a survivor-led cancer advocacy group, also has identified cognitive impairment as a challenge facing many cancer survivors and calls for research to address this problem. The Oncology Nursing Society Research Priority Survey identified cognitive impairment as one of the most distressing and difficult symptoms to treat (LoBiondo-Wood et al., 2014). Despite the priority, research in this area is relatively limited, with many unanswered questions regarding the prevalence and impact on

survivors as well as insufficient data to guide evidence-based interventions (Vardy, Wefel, Ahles, Tannock, & Schagen, 2008; Von Ah, Jansen, Allen, Schiavone, & Wulff, 2011; Von Ah, Storey, Jansen, & Allen, 2013).

Definition of Cognitive Impairment

Cognitive impairment has been defined as those cognitive changes that negatively affect higher-order mental processes (Hess & Insel, 2007). Although no single neurocognitive signature of cancer- and cancer treatment-related effects stands out (Castellon, Silverman, & Ganz, 2005), deficits in attention, memory, speed of processing, language (word finding), and executive functioning (problem solving) appear to be most common (Anderson-Hanley, Sherman, Riggs, Agocha, & Compas, 2003; Jansen, Miaskowski, Dodd, Dowling, & Kramer, 2005; Vardy et al., 2008). Cognitive deficits following diagnosis and

treatment of cancer may be subtle, yet may have a significant impact on quality of life in cancer survivors (Mehnert et al., 2007; Von Ah, Russell, Storniolo, & Carpenter, 2009).

Risk Factors

The exact etiology of cognitive deficits in cancer survivors is not fully understood and most likely is thought to be multifactorial (Bender & Thelen, 2013; Merriman, Von Ah, Miaskowski, & Aouizerat, 2013). Briefly, in cancer survivors, tumor- and/or treatment-related factors may directly or indirectly affect cognitive functioning through one or more of the following mechanisms: neurotoxic injury in the brain, microvascular injury, secondary central and/or systemic inflammatory processes, or dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in changes in endogenous hormones (estrogen and serotonin) (Merriman et al., 2013). In addition, it has been hypothesized that cancer treatment may accelerate cognitive aging by influencing aging at a cellular level, including inflammation, DNA damage, oxidative stress, telomere length, and cell senescence (Ahles, Root, & Ryan, 2012; Mandelblatt et al., 2013). Individual differences in age, education level, intelligence, menopausal status, comorbid conditions, medication usage, and genetics also may contribute to cognitive deficits in cancer survivors (Bender & Thelen, 2013). Cognitive deficits also may be compounded by other related symptoms, including fatigue, depression, and anxiety (Bender, Ergyn, Rosenzweig, Cohen, & Sereika, 2005; Bender & Thelen, 2013). A summary of cancer- and treatment-related and non-cancer treatment-related factors that may influence an individual's risk for cognitive impairment are displayed in Figure 1 (Bender & Thelen, 2013; Mandelblatt et al., 2013; National Comprehensive Cancer Network, 2013). The complexity associated with cognitive changes after cancer and cancer treatment contribute to the difficulty of understanding and effectively treating this symptom (Bender & Thelen, 2013).

Scope of the Problem

Seventeen percent (van Dam et al., 1998) to 75% (Wieneke & Dienst, 1995) of survivors report some level of cognitive impairment (Anderson-Hanley et al., 2003; Falleti, Sanfilippo, Maruff, Weih, & Phillips, 2005; Jansen et al., 2005; Stewart, Bielajew, Collins, Parkinson, & Tomiak, 2006; van Dam et al., 1998; Wieneke & Dienst, 1995). In Von Ah, Harvison, et al. (2009), the author's group found clinically significant memory deficits in 44% of breast cancer survivors ($n = 52$) who were, on average, 4.6 years ($SD = 2.76$) post-treatment. Five meta-analyses have also documented cognitive deficits that survivors experience, suggesting that impairments in memory, attention and concentration, speed of processing, and executive functioning are most common (Anderson-Hanley et al., 2003; Falleti et al., 2005; Jansen et al., 2005; Jim et al., 2012; Stewart et al., 2006). Although results of some prospective studies suggest cognitive impairment may attenuate over time (Jenkins et al., 2006; Tchen et al., 2003; Wefel, Lenzi, Theriault, Davis, & Meyers, 2004), researchers have found that a substantial number of survivors continue to have objectively measured memory deficits

for 5, 10, and even as long as 20 years post-treatment (Ahles et al., 2002; Jenkins et al., 2006; Koppelmans et al., 2012; Wefel et al., 2004).

In addition, researchers have explored cognitive changes associated with cancer using multiple neuroimaging techniques (Holohan, Von Ah, McDonald, & Saykin, 2013). Electrophysiologic and imaging studies reveal differences in central nervous system structure and function among survivors exposed to chemotherapy compared to baseline prechemotherapy or control participants (Brown et al., 1998; Ferguson, McDonald, Saykin, & Ahles, 2007; Inagaki et al., 2007; Kreukels et al., 2005; Saykin, Ahles, & McDonald, 2003; Schagen, Hamburger, Muller, Boogerd, & van Dam, 2001; Silverman et al., 2007). Results from imaging studies also have documented reduced regional volumes of gray and white matter, with studies demonstrating both short-term (Brown et al., 1998; Ferguson, McDonald, et al., 2007; Inagaki et al., 2007) and long-term effects (Saykin et al., 2003). In addition, in a review of the empirical literature, Holohan et al. (2013) identified 35 separate neuroimaging studies and noted that the majority identified structural and/or functional alterations which also were accompanied by increases in self-reported cognitive concerns, neuropsychological testing deficits, or both. Taken together, findings from these studies provide clear and convincing evidence that cognitive deficits are prevalent after cancer and cancer treatment.

Impact on Quality of Life and Work-Related Outcomes

Cognitive impairment can dramatically affect quality of life in survivors (Mehnert et al., 2007; Myers, 2013; Von Ah, Habermann, Carpenter, & Schneider, 2013). In a survey of 471 survivors, 62% stated that cognitive problems were disruptive to their functioning and relationships at home and at work (Hede, 2008). In qualitative interviews with 22 breast cancer survivors, cognitive impairment affected survivors' self-confidence, self-esteem, social relationships, and perceived work ability (Von Ah, Habermann, et al., 2013). Survivors related that they often were embarrassed when they could not remember names, dates, or places and often would withdraw from social situations. In addition, many identified that dealing with cognitive changes

Cancer- and Treatment-Related Factors:

- Cancer type, staging, disease trajectory: central nervous system primary or metastatic disease
- Cancer treatment: chemotherapy, intrathecal chemotherapy, brain irradiation

Non-Cancer Treatment-Related Factors:

- Demographic factors: age, education level, intelligence
- Life stage: menopausal status
- Comorbidities: cardiac toxicity, respiratory diseases
- Other medications: prescription, over-the-counter supplements
- Psychological distress: anxiety, depression
- Symptom burden: fatigue, sleep disturbances
- Genetics

FIGURE 1. Factors That Influence Cognitive Impairment Risk

Note. Based on information from Bender & Thelen, 2013; Mandelblatt et al., 2013; National Comprehensive Cancer Network, 2013.

after cancer and cancer treatment was most difficult when family, friends, or healthcare providers did not acknowledge or validate their concerns. Previous work by Von Ah, Russell, et al. (2009) with 135 African American (47%) and Caucasian (53%) breast cancer survivors also demonstrated that subjective cognitive impairment was related to poorer health-related quality of life, including more depressive symptoms, lower well-being, poorer physical functioning, and greater fatigue. Results from multiple studies also have shown that cognitive impairment, as demonstrated on objective neuropsychological tests, is associated with higher levels of depressive symptoms, fatigue, and anxiety (Bender et al., 2006; Cimprich, 1992, 1993; Mehnert et al., 2007; Stewart et al., 2008; Wefel et al., 2004). In preliminary work conducted by Von Ah et al. (2010), which included 444 breast cancer survivors compared to 355 healthy women, the authors found that cognitive impairment on neuropsychological tests (deficits in immediate [short-term] and delayed memory, processing speed, and executive functioning) was significantly related to depressive symptoms and fatigue. Findings are supported by research results in which cognitive impairment commonly co-occurs with fatigue and depressive symptoms across the cancer trajectory (Bender et al., 2005; Bender & Thelen, 2013). In addition, many researchers have demonstrated that cognitive impairment affects perceived work ability in survivors (Calvio, Peugeot, Bruns, Todd, & Feuerstein, 2010; de Boer et al., 2008; Feuerstein, Hansen, Calvio, Johnson, & Ronquillo, 2007; Hansen, Feuerstein, Calvio, & Olsen, 2008; Pryce, 2007; Taskila, Martikainen, Hietanen, & Lindbohm, 2007; Von Ah, Habermann, et al., 2013). In a large cohort study of 1,490 employed survivors and 2,796 reference participants, survivors had significantly lower levels of perceived work ability than healthy controls (Lindbohm et al., 2012). Perceived work ability, or the capability to manage job demands (Ilmarinen & Tuomi, 2004), has been associated with job stress (Kinnunen, Parkatti, & Rasku, 1994), and several studies have confirmed that poor work ability predicts loss of work productivity, retirement intentions, long-term absence, early retirement, need for rehabilitation, and work disability (Alavinia, de Boer, van Duivenbooden, Frings-Dresen, & Burdorf, 2009; Kuoppala, Lamminpaa, Vaananen-Tomppo, & Hinkka, 2011; Salonen, Arola, Nygard, Huhtala, & Koivisto, 2003; Sell et al., 2009). Overall, research has consistently documented the significant and negative impact of cancer- and cancer treatment-related cognitive impairment on survivor's self-confidence, social relationships, quality of life, and work-related outcomes (Myers, 2013).

Coping Strategies to Address Cognitive Impairment

Although cognitive impairment after cancer and cancer treatment is a prevalent and significant problem, little research has focused on addressing these cognitive changes. Interviews with survivors provide some insight regarding how survivors live with and manage cognitive changes after cancer (Myers, 2013; Von Ah, Storey, et al., 2013). Figure 2 displays a summary of positive and potentially negative coping strategies used by survivors to address cognitive impairment. The majority of the research reviewed identified positive methods for coping with cognitive changes after cancer. In previous work (Von Ah, Storey, et al., 2013), the author's group was able to identify and

Examples of Positive Coping Strategies

- Writing things down
- Using reminder cues (e.g., calendar, notes)
- Develop a routine schedule.
- Focus on one task at a time; do not rush tasks.
- Give oneself permission to make mistakes.
- Keep items and belongings in the same place.
- Surround self with supportive family and friends.
- Ask for help when necessary.
- Humor
- Seek stress-reduction activities, such as exercise, meditation, yoga.
- Obtain plenty of rest; adequate sleep
- Mind-stimulating activities: crossword puzzles, word games, sudoku

Examples of Potentially Negative Coping Strategies

- Withdrawal from social activities
- Avoiding substantive social interactions
- Leaving employment

FIGURE 2. Coping Strategies to Address Cognitive Impairment After Cancer

classify these positive coping strategies into five overarching and distinct categories: organizational and self-management, management of the physical environment, management of the social environment, stress and attentional fatigue-reducing methods, and engaging in mind-stimulating activities. However, the literature also reported that survivors identified potentially negative coping strategies, such as avoiding social activities, avoiding substantive social interactions, and leaving demanding employment situations (Myers, 2013). Although removal from a stressful social or work situation may be appropriate depending on the context and extent used, these avoidant strategies may not produce the long-term positive adjustment that is necessary to address cognitive changes after cancer.

Interventions for Cognitive Changes After Cancer and Its Treatment

Evidence-based interventions for cognitive impairment after cancer and cancer treatment remain limited. Researchers have explored pharmacologic and nonpharmacologic approaches to address cancer- and cancer treatment-related cognitive impairment (Von Ah et al., 2011; Von Ah, Jansen, & Allen, 2014). Table 1 displays the pharmacologic interventions trialed, including the use of donepezil, an acetylcholinesterase inhibitor often used for Alzheimer disease (Jatoi et al., 2005; Shaw et al., 2006); methylphenidate, a psychostimulant often used in children with attention deficit hyperactivity disorder (Bruera, Miller, Macmillan, & Kuehn, 1992; Butler et al., 2007; Escalante et al., 2014; Gagnon, Low, & Schreier, 2005; Gehring et al., 2012; Lower et al., 2009; Mar Fan et al., 2008; Meyers, Weitzner, Valentine, & Levin, 1998; Schwartz, Thompson, & Masood, 2002); memantine, an N-methyl-D-aspartate receptor antagonist, which has been shown to be neuroprotective in preclinical trials (Brown et al., 2013); and modafinil, a psychostimulant often used for narcolepsy (Blackhall, Petroni, Shu, Baum, & Farace, 2009; Gehring et al., 2012; Kohli et al., 2009; Lundorff, Jonsson, & Sjogren, 2009). Table 2 highlights the nonpharmacologic treatments used to address cognitive impairment, including

TABLE 1. Pharmacologic Interventions for Cognitive Impairment in Survivors

| Study | Intervention | Findings |
|---|--|---|
| Donepezil | | |
| Jatoi et al., 2005 ^a | 5 mg per day for four weeks increased to 10 mg per day plus vitamin E 1,000 IU per day | No treatment effect |
| Shaw et al., 2006 | 5 mg per day for six weeks; 10 mg per day for 18 weeks; followed by six weeks washout | Improvement on attention and concentration, verbal memory, and figural memory |
| Methylphenidate/Dexamethylphenidate (MPH/dMPH) | | |
| Bruera et al., 1992 | 10 mg per day for two days | Improvement in alertness, attention, and memory |
| Butler et al., 2007 | 10–30 mg per day during and eight weeks after radiation therapy | No treatment effect |
| Escalante et al., 2014 | 18 mg per day for two weeks followed by placebo for two weeks | Improvement in speed of processing and recall |
| Gagnon et al., 2005 | 10 mg test dose; increased to 20 mg per day and increased by 5 mg per day until resolution of delirium or maximum tolerated dose | Improvement in overall cognitive functioning alertness, psychomotor functioning, and slurred speech |
| Gehring et al., 2012 ^a | 20 mg per day MPH or 18 mg per day sustained release MPH versus 200 mg per day modafinil for four weeks | Improvement in speed of processing and executive function; MPH improved attention, modafinil improved processing speed |
| Lower et al., 2009 | 10 mg per day | No treatment effect |
| Mar Fan et al., 2008 | 10 mg per day for one week; if tolerated, increase up to 20 mg per day | No treatment effect |
| Meyers et al., 1998 | 10 mg per day; increase by 5 mg BID until response or dose-limiting toxicity | Improvement in psychomotor speed, memory, visual-motor function, executive function, motor speed, and dexterity |
| Schwartz et al., 2002 ^a | 20 mg per day, long-acting, for four months and 15–20 minutes of exercise | Improvement in perceived mental health and executive function in MPH group |
| Memantine | | |
| Brown et al., 2013 | Total dose of 20 mg per day | Reduced decline in memory processing speed and executive function; no improvement in delayed recall |
| Modafinil | | |
| Blackhall et al., 2009 | 100 mg per day for two weeks; 200 mg per day for two weeks | Improvement in cognitive flexibility; no intervention effect on verbal learning, memory, verbal fluency, motor and eye-hand coordination, attention, or motor speed |
| Gehring et al., 2012 | 20 mg per day MPH or 18 mg per day sustained release MPH versus 200 mg per day modafinil for four weeks | Improvement in speed of processing and executive function; MPH improved attention, modafinil improved processing speed |
| Kohli et al., 2009 | 200 mg day for four weeks; responders continued 200 mg day or placebo for four weeks | Improvement in speed of memory and episodic memory but not working memory |
| Lundorff et al., 2009 | 200 mg per day for four days | Improvement noted in attention and psychomotor speed |
| ^a Indicates interventions that combine pharmacologic and nonpharmacologic approaches | | |

cognitive behavioral training (Cherrier et al., 2013; Ferguson et al., 2007, 2012; Goedendorp, Knoop, Gielissen, Verhagen, & Bleijenberg, 2014; Locke et al., 2008; McDougall, 2001; McDougall, Becker, Acee, Vaughan, & Delville, 2011; Schuurs & Green, 2012; Sherer, Meyers, & Bergloff, 1997), cognitive training (Gehring et al., 2009; Hassler et al., 2010; Kesler et al., 2013; Miotto et al., 2013; Poppelreuter, Weis, & Bartsch, 2009; Von Ah et al., 2012; Zucchella et al., 2013), electroencephalography (EEG)/neurofeedback (Alvarez, Meyer, Granoff, & Lundy, 2013), exercise (Baumann et al., 2011; Korstjens, Mesters, van der Peet, Gijzen, & van den Borne, 2006; Oh et al., 2011; Reid-Arndt, Matsuda, & Cox, 2012; Schwartz et al., 2002), ginkgo biloba (Attia et al., 2012; Barton et al., 2012), meditation (Milbury et al., 2013), mindfulness-based stress reduction (Hoffman et al., 2012), natural restorative environment (Cimprich, 1993; Cimprich & Ronis, 2003), structured rehabilitation (Rottmann et al., 2012), and vitamin E (Chan, Cheung, Law, & Chan, 2004; Jatoi et al., 2005).

The emerging empirical research has demonstrated the most support for nonpharmacologic treatments, such as cognitive training. In fact, the Oncology Nursing Society's Putting Evidence Into Practice (PEP) resource identified cognitive training programs as likely to be effective for addressing cognitive impairment in survivors (Von Ah et al., 2014). However, additional research is needed to fully understand the benefits of interventions designed to reduce stress and improve attention, such as cognitive behavioral training, mindfulness-based stress reduction, and exercise. Research regarding pharmacologic treatments has yielded equivocal results, and those treatments need further investigation to explore their effectiveness (Von Ah et al., 2014).

Nursing Implications and Need for Future Research

Oncology nurses are in a prime position to address cognitive changes after cancer and cancer treatment. Nurses need to recognize the cancer- and non-cancer-related factors that may place a survivor at higher risk for cognitive changes. In addition, nurses must fully

TABLE 2. Nonpharmacologic Interventions for Cognitive Impairment for Cancer Survivors

| Study | Intervention | Findings |
|---|---|---|
| Cognitive-Behavioral Training | | |
| Cherrier et al., 2013 | Seven one-hour sessions for seven weeks | Improvement in perceived cognitive function |
| Ferguson, McDonald, et al., 2007 | Memory Attention Adaptation Training (MAAT), 30–50 minutes for four months | Improvement over time in perceived cognitive functioning, verbal memory, attention, and executive psychomotor functioning |
| Ferguson et al., 2012 | MAAT training | Improvement in verbal memory |
| Goedendorp et al., 2014 | Individualized training (5–26 sessions, $\bar{X} = 12.5$, $SD = 4.7$) focused on reducing fatigue | Improvement in perceived concentration; no improvement on neuropsychological assessment |
| Locke et al., 2008 | Six sessions of cognitive rehab and six sessions of problem-solving therapy for two weeks | Improvement in mood; unable to obtain follow-up on objective cognitive functioning |
| McDougall, 2001 | 75 minutes, eight sessions for four weeks with MT and self-efficacy | Improvement in perceived cognitive functioning; memory efficacy, and metamemory; no improvement in memory performance |
| McDougall et al., 2011 | 30 minutes per week for eight weeks of MT with four, two-hour booster sessions | Improvement in perceived cognitive functioning and visual memory |
| Schuurs & Green, 2012 | Two hours per week for four weeks; includes psycho-education and problem-solving approaches | Improvement in immediate (short-term) and delayed memory, visuospatial skills, and language and attention; these were sustained at three months postintervention except for language and attention. |
| Cognitive Training | | |
| Gehring et al., 2009 | Two hours per week for six weeks of cognitive training | Improvement in perceived cognitive function immediately and at six months postintervention; improvement in attention and memory at six months postintervention only |
| Hassler et al., 2010 | 90 minutes per week for 10 weeks of CT | Improvement in learning, perception, concentration, attention, memory, retentiveness, and verbal memory |
| Kesler et al., 2013 | 48 executive function training sessions for 12 weeks | Improvement in cognitive flexibility, verbal fluency, and processing speed |
| Miotto et al., 2013 | Minimum of five 30-minute sessions of semantic organizational strategies | Improvement in verbal recall and increased activation |
| Poppelreuter et al., 2009 | Two intervention groups: four one-hour sessions of (a) attention and memory training in person or (b) attention and memory per computer compared to control | No intervention effects |
| Von Ah et al., 2012 | 10 one-hour sessions for 6–8 weeks; two groups (MT or ST compared to control) | Improvement in perceived cognitive function both groups; MT had improvement in immediate and delayed memory, ST had improvement in immediate and delayed memory as well as processing speed. |
| Zucchella et al., 2013 | 16 one-hour sessions for four weeks | Improvement in visual attention and verbal memory |
| EEG/Neurofeedback | | |
| Alvarez et al., 2013 | 20-session neurofeedback regimen | Improvement in perceived cognitive function |
| Exercise Programs: Combined or Alone | | |
| Baumann et al., 2011 | 60 minutes of resistance training two times per week for 12 weeks | Improvement in attention and working memory; no improvement in verbal memory; no baseline control group |
| Korstjens et al., 2006 | Two-hour sessions two times per week for 12 weeks of physical fitness, plus seven two-hour psycho-education sessions | Improvement in perceived cognitive function |

(Continued on the next page)

^a Interventions that combine pharmacologic and nonpharmacologic approaches
 CT—cognitive training; EEG—electroencephalography; MBSR—mindfulness-based stress reduction; MT—memory training; ST—speed-of-process training

TABLE 2. Nonpharmacologic Interventions for Cognitive Impairment for Cancer Survivors (Continued)

| Study | Intervention | Findings |
|---|---|---|
| Exercise Programs: Combined or Alone (Continued) | | |
| Oh et al., 2011 | 90 minutes per week for 10 weeks of medical qigong | Improvement in perceived cognitive function |
| Reid-Arndt et al., 2012 | 60 minutes of tai chi two times per week for 10 weeks | Improvement in perceived cognitive function, immediate and delayed memory, verbal fluency, attention, and executive functioning; no control |
| Schwartz et al., 2002 ^a | 15–20 minutes of aerobic exercise four days per week with MPH | Improvement in perceived cognitive function (mental health) |
| Ginkgo biloba | | |
| Attia et al., 2012 | 120 mg per day for 24 weeks; six-week washout | Improvement in executive function, nonverbal memory attention, and concentration; no control group for practice effects |
| Barton et al., 2012 | 120 mg per day | No treatment effect |
| Meditation | | |
| Milbury et al., 2013 | Tibetan sound meditation for six weeks | Improvement in perceived cognitive function, verbal memory, and processing speed immediately post-intervention; no improvement six months later |
| MBSR | | |
| Hoffmann et al., 2012 | Eight-week program of MBSR | Improvement in perceived cognitive function—confusion |
| Natural Restorative Environment | | |
| Cimprich, 1993 | 60–90 minutes per week of walking gardening | Improvement in attentional fatigue |
| Cimprich & Ronis, 2003 | 120 minutes per week of exposure to the natural environment | Improvement in capacity to direct attention |
| Structured Rehabilitation | | |
| Rottmann et al., 2012 | Six-day residential course | Improvement in perceived cognitive function |
| Vitamin E | | |
| Chan et al., 2004 | Vitamin E 2,000 IU per day | Improvement in global cognitive functioning, verbal and visual memory, and executive functioning; no improvement in attention |
| Jatoi et al., 2005 ^a | Vitamin E 1,000 IU per day and donepezil for four weeks | No treatment effect |
| ^a Interventions that combine pharmacologic and nonpharmacologic approaches CT—cognitive training; EEG—electroencephalography; MBSR—mindfulness-based stress reduction; MT—memory training; ST—speed-of-process training | | |

assess each survivor for this late and long-term effect of treatment. Survivors often will express concerns regarding memory lapses (remembering names, dates, and places), inability to concentrate, and difficulty following instructions or completing tasks. These concerns should be fully assessed and referred to other healthcare professionals (e.g., neuropsychologist, psychiatrist) for evaluation if they disrupt everyday functioning (Jansen, 2013). At a minimum, nurses should acknowledge the survivors' cognitive concerns because research has suggested that the acknowledgement alone can reduce distress. In addition, nurses should thoroughly assess and treat other symptoms that commonly co-occur with cognitive impairment, such as depression and anxiety. Addressing these other co-related symptoms may also help ameliorate the perception of cognitive

impairment. Nurses should be aware of and refer survivors with concerns to reputable resources, such as the PEP resource for cognitive impairment (www.ons.org/practice-resources/pep/cognitive-impairment). This site is routinely updated with the most relevant empirical research in this area.

Based on the current research, cognitive training has shown to be useful in addressing cognitive impairment and has been identified as likely to be effective in improving cognitive impairment in cancer survivors (Von Ah et al., 2014). More research is needed, however, to fully identify effective interventions that are feasible and cost effective. Much of the current research is still limited by the research design (e.g., lack of randomized, controlled trials; lack of an attention control comparison group; laboratory versus home-based programs), small sample sizes,

Implications for Practice

- ▶ Educate patients that cognitive impairment is a distressing, disruptive, and potentially debilitating symptom that can occur as a direct result of cancer or its treatment.
- ▶ Identify common cognitive changes after treatment, including deficits in attention, memory, speed of processing, language, and executive functioning.
- ▶ Research emerging evidence that nonpharmacologic treatments, such as cognitive training, are likely to be effective.

limited sample diversity (mostly conducted in brain tumor or breast cancer survivors with well-educated and Caucasian participants), and lack of assessment using standardized neuropsychological tests. Research in this area is vital to fully address cancer- and cancer treatment-related cognitive impairment, which has been shown to be a prevalent, bothersome, and potentially debilitating symptom.

References

- Ahles, T., 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, 30*, 3675-3686.
- Ahles, T.A., Saykin, A.J., Furstenberg, C.T., Cole, B., Mott, L.A., Skalla, K., . . . Silberfarb, P.M. (2002). Neuropsychologic impact of standard-dose systemic chemotherapy in long-term survivors of breast cancer and lymphoma. *Journal of Clinical Oncology, 20*, 485-493.
- Alavinia, S.M., de Boer, A., van Duivenbooden, J.C., Frings-Dresen, M., & Burdorf, A. (2009). Determinants of work ability and its predictive value for disability. *Occupational Medicine (London), 59*, 32-37.
- Alvarez, J., Meyer, F., Granoff, D.L., & Lundy, A. (2013). The effect of EEG biofeedback on reducing postcancer cognitive impairment. *Integrative Cancer Therapies, 12*, 475-487.
- Anderson-Hanley, C., Sherman, M., Riggs, R., Agocha, V., & Compas, B. (2003). Neuropsychological effects of treatments for adults with cancer: A meta-analysis and review of the literature. *Journal of the International Neuropsychological Society, 9*, 967-982.
- Attia, A., Rapp, S.R., Case, L.D., D'Agostino, R.B., Jr., Lesser, G., Naughton, M., . . . Shaw, E.G. (2012). Phase II study of ginkgo biloba in irradiated brain tumor patients: Effect on cognitive function, quality of life and mood. *Journal of Neurooncology, 109*, 357-363.
- Barton, D.L., Burger, K., Novonty, P.J., Fitch, T.R., Kohli, S., Soori, G., . . . Loprinzi, C.L. (2012). The use of ginkgo biloba for the prevention of chemotherapy-related cognitive dysfunction in women receiving adjuvant treatment for cancer. *Supportive Care in Cancer, 21*, 1185-1192. doi:10.1017.s00520-012-1647-9
- Baumann, F.T., Drosselmeyer, N., Leskaroski, A., Knicker, A., Krakowski-Roosen, H., Zopf, E.M., & Bloch, W. (2011). 12-week resistance training with breast cancer patients during chemotherapy: Effects on cognitive abilities. *Breast Care, 6*, 142-143. doi:10.1159/000327505
- Bender, C.M., Ergyn, F.S., Rosenzweig, M.Q., Cohen, S.M., & Sereika, S.M. (2005). Symptom clusters in breast cancer across 3 phases of the disease. *Cancer Nursing, 28*, 219-225.
- Bender, C.M., Sereika, S.M., Berga, S.L., Vogel, V.G., Brufsky, A.M., Paraska, K.K., & Ryan, C.M. (2006). Cognitive impairment associated with adjuvant therapy in breast cancer. *Psycho-Oncology, 15*, 422-430. doi:10.1002/pon.964
- Bender, C.M., & Thelen, B.D. (2013). Cancer and cognitive changes: The complexity of the problem. *Seminars in Oncology Nursing, 29*, 232-237.
- Blackhall, L., Petroni, G., Shu, J., Baum, L., & Farace, E. (2009). A pilot study evaluating the safety and efficacy of modafinil for cancer-related fatigue. *Journal of Palliative Medicine, 12*, 433-439. doi:10.1089/jpm.2008.0230
- Brown, M., Stemmer, S., Simon, J., Stears, J., Jones, R., Cagnoni, P., & Sheeder, J. (1998). White matter disease induced by high-dose chemotherapy: Longitudinal study with MR imaging and proton spectroscopy. *American Journal of Neuroradiology, 19*, 217-221.
- Brown, P.D., Pugh, S., Laack, N.N., Wefel, J.S., Khuntia, D., Meyers, C.A., . . . Radiation Therapy Oncology Group. (2013). Memantine for the prevention of cognitive dysfunction in patients receiving whole-brain radiotherapy: A randomized, double-blind, placebo-controlled trial. *Neuro-Oncology, 10*, 1429-1437. doi:10.1093/neuroc/not114
- Bruera, E.J., Miller, M., Macmillan, K., & Kuehn, N. (1992). Neuropsychological effects of methylphenidate in patients receiving a continuous infusion of narcotics for cancer pain. *Pain, 48*, 163-166.
- Butler, J.M., Jr., Case, L.D., Atkins, J., Frizzell, B., Sanders, G., Griffin, P., . . . Shaw, E.G. (2007). A phase III, double-blind, placebo-controlled prospective randomized clinical trial of d-threo-methylphenidate HCl in brain tumor patients receiving radiation therapy. *International Journal of Radiation Oncology, Biology and Physics, 69*, 1496-1501. doi:10.1016/j.ijrobp.2007.05.076
- Calvio, L., Peugeot, M., Bruns, G.L., Todd, B.L., & Feuerstein, M. (2010). Measures of cognitive function and work in occupationally active breast cancer survivors. *Journal of Occupational and Environmental Medicine, 52*, 219-227. doi:10.1097/JOM.0b013e3181d0bef7
- Castellon, S.A., Silverman, D.H., & Ganz, P.A. (2005). Breast cancer treatment and cognitive functioning: Current status and future challenges in assessment. *Breast Cancer Research and Treatment, 92*, 199-206.
- Chan, A., Cheung, M.C., Law, S.C., & Chan, J.H. (2004). Phase II study of alpha-tocopherol in improving the cognitive function of patients with temporal lobe radionecrosis. *Cancer, 100*, 398-401. doi:10.1002/cncr.11885
- Cherrier, M.M., Anderson, K., David, D., Higano, C.S., Gray, H., Church, A., & Willis, S.L. (2013). A randomized trial of cognitive rehabilitation in cancer survivors. *Life Sciences, 93*, 617-622. doi:10.1016/j.lfs.2013.08.011
- Cimprich, B. (1992). Attentional fatigue following breast cancer surgery. *Research in Nursing and Health, 15*, 199-207.
- Cimprich, B. (1993). Development of an intervention to restore attention in cancer patients. *Cancer Nursing, 16*, 83-92.
- Cimprich, B., & Ronis, D.L. (2003). An environmental intervention to restore attention in women with newly diagnosed breast cancer. *Cancer Nursing, 26*, 284-292.
- de Boer, A., Verbeek, J.H., Spelten, E., Uitterhoeve, A.L., Ansink, A.C., de Reijke, T.M., . . . van dijk, F.J. (2008). Work ability and return-to-work in cancer patients. *British Journal of Cancer, 98*, 1342-1347. doi:10.1038/sj.bjc.6604302
- Escalante, C.P., Meyers, C.A., Reuben, J., Xuemei, W., Qiao, W.,

- Manzullo, E., . . . Cleeland, C. (2014). A randomized, double-blind, 2-period, placebo-controlled crossover trial of a sustained-release methylphenidate in the treatment of fatigue in cancer patients. *Cancer, 20*, 8-14.
- Falletti, M.G., Sanfilippo, A., Maruff, P., Weih, L., & Phillips, K.A. (2005). The nature and severity of cognitive impairment associated with adjuvant chemotherapy in women with breast cancer: A meta-analysis of the current literature. *Brain and Cognition, 59*, 60-70.
- Ferguson, R.J., Ahles, T.A., Saykin, A.J., McDonald, B.C., Furstenberg, C.T., Cole, B.F., & Mott, L.A. (2007). Cognitive-behavioral management of chemotherapy-related cognitive change. *Psycho-Oncology, 16*, 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*, 176-186. doi:10.1002/pon.1878
- Ferguson, R.J., McDonald, B.C., Saykin, A.J., & Ahles, T.A. (2007). Brain structure and function differences in monozygotic twins: Possible effects of breast cancer chemotherapy. *Journal of Clinical Oncology, 25*, 3866-3870. doi:10.1200/jco.2007.10.8639
- Feuerstein, M., Hansen, J.A., Calvio, L.C., Johnson, L., & Ronquillo, J.G. (2007). Work productivity in brain tumor survivors. *Journal of Occupational and Environmental Medicine, 49*, 803-811. doi:10.1097/JOM.0b013e318095a458
- Gagnon, B., Low, G., & Schreier, G. (2005). Methylphenidate hydrochloride improves cognitive function in patients with advanced cancer and hypoactive delirium: A prospective clinical study. *Journal of Psychiatry and Neuroscience, 30*, 100-107.
- Gehring, K., Patwardhan, S.Y., Collins, R., Groves, M.D., Etzel, C.J., Meyers, C.A., & Wefel, J.S. (2012). A randomized trial of efficacy of methylphenidate and modafinil for improving cognitive functioning and symptoms in patients with primary brain tumor. *Journal of Neurooncology, 107*, 165-174.
- 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, 27*, 3712-3722. doi:10.1200/jco.2008.20.5765
- Goedendorp, M.M., Knoop, H., Gielissen, M., Verhagen, C., & Bleijenberg, G. (2014). The effects of cognitive behavioral therapy for postcancer fatigue on perceived cognitive disabilities and neuropsychological test performance. *Journal of Pain and Symptom Management, 47*, 35-44.
- Hansen, J.A., Feuerstein, M., Calvio, L.C., & Olsen, C.H. (2008). Breast cancer survivors at work. *Journal of Occupational and Environmental Medicine, 50*, 777-784. doi:10.1097/JOM.0b013e318165159e
- Hassler, M.R., Elandt, K., Preusser, M., Lehrner, J., Binder, P., Dieckmann, K., . . . Marosi, C. (2010). Neurocognitive training in patients with high-grade glioma: A pilot study. *Journal of Neurooncology, 97*, 109-115. doi:10.1007/s11060-009-0006-2
- Hede, K. (2008). Chemobrain is real but may need new name. *Journal of the National Cancer Institute, 100*, 162-169.
- Hess, L.M., & Insel, K.C. (2007). Chemotherapy-related change in cognitive function: A conceptual model. *Oncology Nursing Forum, 34*, 981-994.
- Hewitt, M., Greenfield, S., & Stovall, E. (2005). *From cancer patient to cancer survivor: Lost in transition*. Washington, DC: National Academies Press.
- 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-III breast cancer: A randomized, controlled trial. *Journal of Clinical Oncology, 30*, 1335-1342. doi:10.1200/JCO.2010.34.0331
- Holohan, K., Von Ah, D., McDonald, B.C., & Saykin, A. (2013). Neuroimaging, cancer and cognition: State of the knowledge brief. *Seminars in Oncology Nursing, 29*, 280-287.
- Ilmarinen, J., & Tuomi, K. (2004). Past, present and future work ability. *People and Work: Research Reports, 65*, 1-25.
- Inagaki, M., Yoshikawa, E., Matsuoka, Y., Sugawara, Y., Nakano, T., Akechi, T., . . . Uchitomi, Y. (2007). Smaller regional volumes of brain gray and white matter demonstrated in breast cancer survivors exposed to adjuvant chemotherapy. *Cancer, 109*, 146-156. doi:10.1002/cncr.22368
- Jansen, C. (2013). Cognitive changes associated with cancer and cancer therapy: Patient assessment and education. *Seminars in Oncology Nursing, 4*, 270-279.
- Jansen, C.E., Miaskowski, C., Dodd, M., Dowling, G., & Kramer, J. (2005). A metaanalysis of studies of the effects of cancer chemotherapy on various domains of cognitive function. *Cancer, 104*, 2222-2233. doi:10.1002/cncr.21469
- 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, 13*, 66-69. doi:10.1007/s00520-004-0696-0
- Jenkins, V., Shilling, V., Deutsch, G., Bloomfield, D., Morris, R., Allan, S., . . . Winstanley, J. (2006). A 3-year prospective study of the effects of adjuvant treatments on cognition in women with early stage breast cancer. *British Journal of Cancer, 94*, 828-834.
- Jim, H.S.L., Phillips, K.M., Chait, S., Faul, L.A., Popa, M.A., Lee, Y.H., . . . Small, B.J. (2012). Meta-analysis of cognitive functioning in breast cancer survivors previously treated with standard-dose chemotherapy. *Journal of Clinical Oncology, 30*, 3578-3587. doi:10.1200/JCO.2011.39.5640
- Kesler, S.R., Hadi Hosseini, S.M., Heckler, C., Janelsins, M., Palesh, O., Mustian, K., & Morrow, G.R. (2013). Cognitive training for improving executive function in chemotherapy-treated breast cancer survivors. *Clinical Breast Cancer, 13*, 299-306. doi:10.1016/j.clbc.2013.02.004
- Kinnunen, U., Parkatti, T., & Rasku, A. (1994). Occupational well-being among aging teachers in Finland. *Scandinavian Journal of Education Research, 38*, 315-332.
- 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*, 2605-2616. doi:10.1002/cncr.24287
- Koppelmans, V., Breteler, M.M., Boogerd, W., Seynaeve, C., Gundy, C., & Schagen, S.B. (2012). Neuropsychological performance in survivors of breast cancer more than 20 years after adjuvant chemotherapy. *Journal of Clinical Oncology*. Retrieved from <http://jco.ascopubs.org/content/30/10/1080.short>
- Korstjens, I., Mesters, I., van der Peet, E., Gijsen, B., & van den Borne, B. (2006). Quality of life of cancer survivors after physical and psychosocial rehabilitation. *European Journal of Cancer Prevention, 15*, 541-547. doi:10.1097/01.cj.0000220625.77857.95
- Kreukels, B.P., Schagen, S.B., Ridderinkhof, K.R., Boogerd, W., Hamburger, H.L., & van Dam, F.S. (2005). Electrophysiological

- correlates of information processing in breast-cancer patients treated with adjuvant chemotherapy. *Breast Cancer Research and Treatment*, *94*, 53–61.
- Kuoppala, J., Lamminpaa, A., Vaananen-Tomppo, I., & Hinkka, K. (2011). Employee well-being and sick leave, occupational accident, and disability pension: A cohort study of civil servants. *Journal of Occupational and Environmental Medicine*, *53*, 633–640.
- Lindbohm, M.L., Taskila, T., Kuosma, E., Hietanen, P., Carlsen, K., Gudbergsson, S., & Gunnarsdottir, H. (2012). Work ability of survivors of breast, prostate, and testicular cancer in Nordic countries: A NOCWO study. *Journal of Cancer Survivorship*, *6*, 72–81. doi:10.1007/s11764-011-0200-z
- LoBiondo-Wood, G., Brown, C.G., Knobf, M.T., Lyon, D.E., Mallory, G., Mitchell, S.A., . . . Fellman, B. (2014). Priorities for oncology nursing: The 2013 National Survey. *Oncology Nursing Forum*, *42*, 67–76.
- Locke, D.E., Cerhan, J.H., Wu, W., Malec, J.F., Clark, M.M., Rumans, 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*, 383–91.
- Lower, E.E., Fleishman, S., Cooper, A., Zeldis, J., Faleck, H., Yu, Z., & Manning, D. (2009). Efficacy of dexamethylphenidate for the treatment of fatigue after cancer chemotherapy: A randomized clinical trial. *Journal of Pain and Symptom Management*, *38*, 650–662.
- Lundorff, L.E., Jonsson, B.H., & Sjogren, P. (2009). Modafinil for attentional and psychomotor dysfunction in advanced cancer: A double-blind, randomised, cross-over trial. *Palliative Medicine*, *23*, 731–738. doi:10.1177/0269216309106872
- Mandelblatt, J.S., Hurria, A., McDonald, B.C., Saykin, A., Stern, R.A., Van Meter, J.W., . . . Ahles, T. (2013). Cognitive effects of cancer and its treatments at the intersection of aging: What do we know, what do we need to know? *Seminars in Oncology Nursing*, *40*, 709–725.
- Mar Fan, H., Clemons, M., Xu, W., Chemerynsky, I., Breunis, H., Braganza, S., & Tannock, I. (2008). A randomised, placebo-controlled, double-blind trial of the effects of d-methylphenidate on fatigue and cognitive dysfunction in women undergoing adjuvant chemotherapy for breast cancer. *Supportive Care in Cancer*, *16*, 577–583.
- McDougall, G.J. (2001). Memory improvement program for elderly cancer survivors. *Geriatric Nursing*, *22*, 185–190.
- McDougall, G.J., Becker, H., Acee, T.W., Vaughan, P.W., & Delville, C.L. (2011). Symptom management of affective and cognitive disturbance with a group of cancer survivors. *Archives of Psychiatric Nursing*, *25*, 24–35. doi:10.1016/j.apnu.2010.05.004
- Mehnert, A., Scherwath, A., Schirmer, L., Schleimer, B., Petersen, C., Schultz-Kindermann, F., . . . Koch, U. (2007). The association between neuropsychological impairment, self-perceived cognitive deficits, fatigue, and quality of life in breast cancer survivors following standard adjuvant versus high-dose chemotherapy. *Patient Education and Counseling*, *66*, 108–118.
- Merriman, J., Von Ah, D., Miaskowski, C., & Auouzerat, B.E. (2013). Proposed mechanisms for cancer- and treatment-related cognitive changes. *Seminars in Oncology Nursing*, *29*, 260–269.
- Meyers, C.A., Weitzner, M.A., Valentine, A.D., & Levin, V.A. (1998). Methylphenidate therapy improves cognition, mood, and function of brain tumor patients. *Journal of Clinical Oncology*, *16*, 2522–2527.
- Milbury, K., Chaoul, A., Biegler, K.A., Wangyal, T., Spelman, A., Meyers, C.A., . . . Cohan, L. (2013). Tibetan sound meditation for cognitive dysfunction: Results of a randomized controlled pilot trial. *Psycho-Oncology*, *22*, 2354–2363.
- Miotto, E.C., Savage, C.R., Evans, J.J., Wilson, B.A., Morton, M.G., Balardin, J.B., . . . Amaro Junior, E. (2013). Semantic strategy training increases memory performance and brain activity in patients with prefrontal cortex lesions. *Clinical Neurology and Neurosurgery*, *115*, 309–316. doi:10.1016/j.clineuro.2012.05.024
- Myers, J.S. (2013). Cancer- and chemotherapy-related cognitive changes: The patient experience. *Seminars in Oncology Nursing*, *29*, 300–307.
- National Comprehensive Cancer Network. (2013). Survivorship http://www.nccn.org/professionals/physician_gls/pdf/survivorship.pdf
- Oh, B., Butow, P.N., Mullan, B.A., Clarke, S.J., Beale, P.J., Pavlakis, N., . . . Vardy, J. (2011). Effect of medical qigong on cognitive function, quality of life, and a biomarker of inflammation in cancer patients: A randomized controlled trial. *Supportive Care Cancer*, *20*, 1235–1242. doi:10.1007/s00520-011-1209-6
- 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*, 274–296. doi:10.1080/07347330902776044
- Pryce, J. (2007). Cancer survivorship and work: Symptoms, supervisor response, co-worker disclosure and work adjustment. *Journal of Occupational Rehabilitation*, *17*, 83–92.
- Reid-Arndt, S.A., Matsuda, S., & Cox, C.R. (2012). Tai chi effects on neuropsychological, emotional, and physical functioning: A pilot study. *Contemporary Therapies in Clinical Practice*, *18*, 26–30. doi:10.1016/j.ctcp.2011.02.005
- Rottmann, N., Dalton, S.O., Bidstrup, P.E., Wurtzen, H., Hoybye, M.T., Ross, L., . . . Johansen, C. (2012). No improvement in distress and quality of life following psychosocial cancer rehabilitation. *Psycho-Oncology*, *21*, 505–514.
- Salonen, P., Arola, H., Nygard, C. H., Huhtala, H.S., & Koivisto, A.M. (2003). Factors associated with premature departure from working life among ageing food industry employees. *Occupational Medicine (London)*, *53*, 65–68.
- 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*, 201–216.
- Schagen, S.B., Hamburger, H.L., Muller, M.J., Boogerd, W., & van Dam, F.S. (2001). Neuropsychological evaluation of late effects of adjuvant high-dose chemotherapy on cognitive function. *Journal of Neuro-Oncology*, *51*, 159–165.
- Schuurs, A., & Green, H.J. (2012). A feasibility study of group cognitive rehabilitation for cancer survivors: Enhancing cognitive function and quality of life. *Psycho-Oncology*, *22*, 1043–1049. doi:10.1002/pon.3102
- Schwartz, A.L., Thompson, J.A., & Masood, N. (2002). Interferon-induced fatigue in patients with melanoma: A pilot study of exercise and methylphenidate [Online exclusive]. *Oncology Nursing Forum*, *29*, E85–E90. doi:10.1188/02.ONF.E85-E90
- Sell, L., Bultmann, U., Rugulies, R., Villadsen, E., Faber, A., & Sogaard, K. (2009). Predicting long-term sickness absence and early retirement pension from self-reported work ability. *International Archives of Occupational and Environmental Health*, *82*, 1133–1138.
- Shaw, E.G., Rosdhal, R., D'Agostino, R.B., Jr., Lovato, J., Naughton,

- M.J., Robbins, M.E., & Rapp, S.R. (2006). Phase II study of donepezil in irradiated brain tumor patients: Effect on cognitive function, mood, and quality of life. *Journal of Clinical Oncology*, *24*, 1415-1420. doi:10.1200/JCO.2005.03.3001
- Sherer, M., Meyers, C.A., & Bergloff, P. (1997). Efficacy of postacute brain injury rehabilitation for patients with primary malignant brain tumors. *Cancer*, *80*, 250-257.
- Silverman, D., Dy, C., Castellon, S., Lai, J., Pio, B., Abraham, L., . . . Ganz, P. (2007). Altered frontocortical, cerebellar, and basal ganglia activity in adjuvant-treated breast cancer survivors 5-10 years after chemotherapy. *Breast Cancer Research and Treatment*, *103*, 303-311. doi:10.1007/s10549-006-9380-z
- 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. *Clinical Neuropsychology*, *20*, 76-89.
- Stewart, A., Collins, B., Mackenzie, J., Tomiak, E., Verma, S., & Bielajew, C. (2008). The cognitive effects of adjuvant chemotherapy in early stage breast cancer: A prospective study. *Psycho-Oncology*, *17*, 122-130. doi:10.1002/pon.1210
- Taskila, T., Martikainen, R., Hietanen, P., & Lindbohm, M.L. (2007). Comparative study of work ability between cancer survivors and their referents. *European Journal of Cancer*, *43*, 914-920. doi:10.1016/j.ejca.2007.01.012
- Tchen, N., Juffs, H.G., Downie, F.P., Yi, Q.L., Hu, H., Chemerynsky, I., . . . Tannock, I.F. (2003). Cognitive function, fatigue, and menopausal symptoms in women receiving adjuvant chemotherapy for breast cancer. *Journal of Clinical Oncology*, *21*, 4175-4183.
- van Dam, F.S., Schagen, S.B., Muller, M.J., Boogerd, W., Wall, E., Droogleeve Fortuyn, M.E., & Rodenhuis, S. (1998). Impairment of cognitive function in women receiving adjuvant treatment for high-risk breast cancer: High-dose versus standard-dose chemotherapy. *Journal of the National Cancer Institute*, *90*, 210-218.
- Vardy, J., Wefel, J.S., Ahles, T.A., Tannock, I.F., & Schagen, S.B. (2008). Cancer and cancer-therapy related cognitive dysfunction: An international perspective from the Venice cognitive workshop. *Annals of Oncology*, *19*, 623-629. doi:10.1093/annonc/mdm500
- Von Ah, D., Carpenter, J.S., Saykin, A., Monahan, P.O., Wu, J., Yu, M., . . . Unverzagt, F. (2012). Advanced cognitive training for breast cancer survivors: A randomized controlled trial. *Breast Cancer Research and Treatment*, *135*, 799-809. doi:10.1007/s10549-012-2210-6
- Von Ah, D., Champion, V.L., Sledge, G.W., Monahan, P.O., Stornilo, A.M., Miller, K., . . . Unverzagt, F.W. (2010). *Effect of cognitive impairment on quality of life among breast cancer survivors*. Paper presented at the 38th Annual Meeting of the International Neuropsychological Society, Acapulco, Mexico. Retrieved from <http://www.nursinglibrary.org/Portal/main.aspx?pageid=4024&pid=24179>
- Von Ah, D., Habermann, B., Carpenter, J., & Schneider, B. (2013). Impact of perceived cognitive impairment in breast cancer survivors. *European Journal of Oncology Nursing*, *17*, 236-241.
- Von Ah, D., Harvison, K., Monahan, P., Moser, L., Zhao, Q., Carpenter, J., . . . Unverzagt, F. (2009). Cognitive function in breast cancer survivors compared to healthy age- and education-matched women. *Clinical Neuropsychologist*, *23*, 661-674.
- Von Ah, D., Jansen, C., & Allen, D. (2014). Evidence-based interventions for cancer- and cancer treatment-related cognitive impairment. *Clinical Journal of Oncology Nursing*, *18*(Suppl. 3), 17-25. doi:10.1188/14.CJON.S3.17-25
- 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*, 607-615.
- Von Ah, D., Russell, K.M., Stornilo, A.M., & Carpenter, J.S. (2009). Cognitive dysfunction and its relationship to quality of life in breast cancer survivors. *Oncology Nursing Forum*, *36*, 326-336.
- Von Ah, D., Storey, S., Jansen, C., & Allen, D. (2013). Coping strategies and interventions for cognitive changes associated with cancer and cancer therapy. *Seminars in Oncology Nursing*, *29*, 288-299.
- 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*, 2292-2299.
- Wieneke, M.H., & Dienst, E.R. (1995). Neuropsychological assessment of cognitive functioning following chemotherapy for breast cancer. *Psycho-Oncology*, *4*, 61-66. doi:10.1002/pon.2960040108
- Zucchella, C., Capone, A., Dodella, V., DeNunzio, A.M., Vecchione, C., Sandrini, G., . . . Bartolo, M. (2013). Cognitive rehabilitation for early post-surgery in patients affected by primary brain tumor: A randomized controlled trial. *Journal of Neurooncology*, *4*, 93-100. doi:10.1007/s11060-013011530-z