■ Article

Evidence-Based Interventions for Cancer- and Treatment-Related Cognitive Impairment

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Cancer- and cancer treatment–related cognitive impairment is a common, bothersome, and potentially debilitating symptom incurred by cancer survivors. Cognitive impairment has a significant impact on patients' day-to-day functioning and quality of life, but it remains under-recognized and undertreated. This article, which is an update from the initial Oncology Nursing Society Putting Evidence Into Practice for cancer- and cancer treatment–related cognitive impairment, provides a comprehensive critical review and summary of the evidence regarding interventions addressing cognitive impairment for cancer survivors. This article examines the effectiveness of interventions focused on cancer- and cancer treatment–related cognitive impairment, makes recommendations for practice, and identifies gaps in knowledge and areas for further research.

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Cancer- and cancer treatment–related cognitive impairment is a national research priority (LoBiondo-Wood et al., 2014). As many as 75% of U.S. cancer survivors have reported issues with memory, attention, or feelings of mental slowness (Janelsins et al., 2011). Cognitive deficits in memory, attention, processing speed, and executive functioning have been documented on neuropsychological examination (Falleti, Sanfilippo, Maruff, Weih, & Phillips, 2005; Jansen, Miaskowski, Dodd, Dowling, & Kramer, 2005; Stewart, Bielajew, Collins, Parkinson, & Tomiak, 2006) and functional magnetic resonance imaging (Holohan, Von Ah, McDonald, & Saykin, 2013).

Cognitive impairment is a complex problem that has been associated with other symptoms (e.g., depression, anxiety, fatigue) (Bender & Thelen, 2013), poorer quality of life (Mehnert et al., 2007; Myers, 2013; Von Ah, Russell, Storniolo, & Carpenter, 2009), and poorer perceived work ability (Calvio, Peugeot, Bruns, Todd, & Feuerstein, 2010; Feuerstein, Hansen, Calvio, Johnson, & Ronquillo, 2007; Munir, Burrows, Yarker, Kalawsky, & Bains, 2010). Although cognitive impairment has a significant impact on cancer survivors, it remains under-recognized and undertreated (Vardy, Wefel, Ahles, Tannock, & Schagen, 2008; Von Ah, Jansen, Allen, Schiavone, & Wulff, 2011). As a result, through the Oncology Nursing Society (ONS) Putting Evidence Into Practice (PEP®) initiative, a team of dedicated advanced practice nurses, nurse scientists, and ONS staff have sought to improve patient outcomes by critically examining, synthesizing, and evaluating interventional literature on the treatment and management of cognitive impairment in cancer survivors. This article describes the current evidence for interventions to treat and manage cognitive impairment following cancer and its treatment.

Methods

An extensive review of the literature regarding cognitive impairment was conducted. Search terms, limits, and databases are described in Figure 1. Research studies included in this supplement were retrieved since the initial ONS cognitive impairment PEP review from August 2010 to February 2014. Cognitive impairment was defined as a decline in function in one or more cognitive function domains, including attention and concentration, executive function, information-processing

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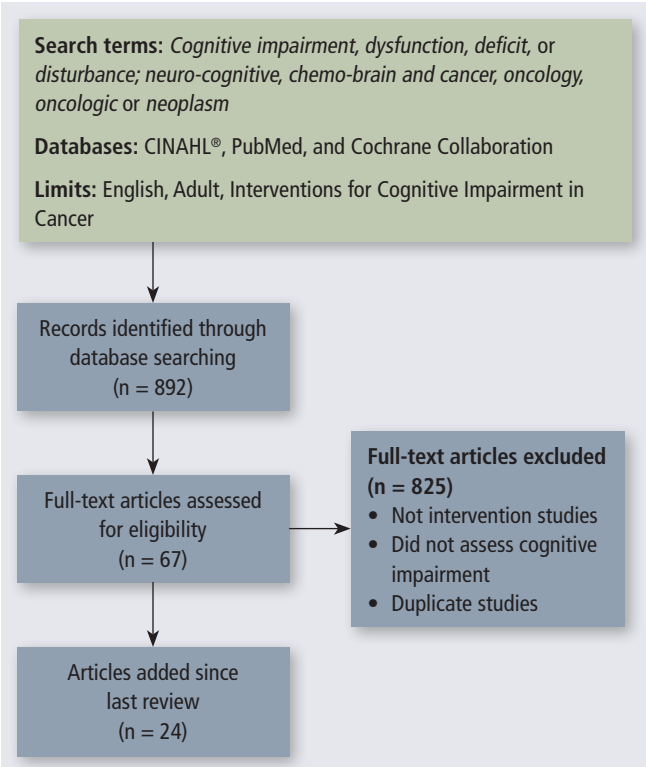

FIGURE 1. PRISMA Diagram of Search Strategy

speed, language, visual-spatial skill, psychomotor ability, learning, and memory (Jansen, 2010). Studies were excluded if they were descriptive only, involved pediatric or adolescent patients with cancer, or evaluated long-term cognitive impairment after a childhood or adolescent cancer or cancer-related treatment.

A systematic approach to reviewing, critiquing, and assigning the level of evidence of the literature was used, as previously reported (Von Ah et al., 2011). Briefly, each article was reviewed by two content experts using a standardized worksheet, assigned an appropriate interventional category, and added to the respective evidence tables. To determine the level of evidence, the team examined the collective strength of each identified intervention and recommended the level of evidence using the ONS PEP weight-of-evidence classification schema (Mitchell & Friese, 2014).

Evidence

Twenty-four studies met inclusion criteria and were added to the level of evidence for each interventional strategy, resulting in 51 empirical studies, one literature review, and one meta-analysis. Although the number of interventional studies has almost doubled since the original review (Von Ah et al., 2011), the research is still limited by small studies with inconsistent findings and often lacking objective evaluations of cognition. The following section provides the literature synthesis under the classification of effectiveness schema categories. Figure 2 depicts a comprehensive list of empirical research by level of evidence and intervention category.

Likely to Be Effective

Cognitive training has been deemed as likely to be effective in addressing cognitive impairment in cancer survivors. Cognitive training programs have been defined as "any intervention aimed at improving, maintaining or restoring mental function through the repeated and structured practice of tasks which pose an inherent problem or mental challenge" (Sitzer, Twamley, & Jeste, 2006, p. 75). Seven trials provided cognitive training; three delivered training in a group format (Hassler et al., 2010; Poppelreuter, Weis, & Bartsch, 2009; Von Ah et al., 2012), and four provided individualized training programs (Gehring et al., 2009; Kesler et al., 2013; Miotto et al., 2013; Zucchella et al., 2013). The studies targeted two patient populations: patients with primary brain tumors and breast cancer survivors. Sample sizes ranged from 11–140 participants, and all but one study employed a randomized, controlled trial study design (Hassler et al., 2010). These programs provided remediation to improve attention and memory performance (Gehring et al., 2009; Hassler et al., 2010; Miotto et al., 2013; Poppelreuter et al., 2009; Von Ah et al., 2012; Zucchella et al., 2013), speed of processing (Von Ah et al., 2012), and/or executive functioning (Gehring et al., 2009; Kesler et al., 2013). Of note, six studies demonstrated statistically significant improvement in cognitive functioning on neuropsychological tests with effects that typically were cognitive domain specific (e.g., training in memory resulted in improved memory performance). For example, Von Ah et al. (2012) noted that memory training improved memory performance ($p = 0.036$, $d = 0.59$) and speed-of-processing training improved processing speed ($p = 0.016$, $d = 0.67$) at a two-month follow-up assessment for breast cancer survivors. Similarly, Miotto et al. (2013) noted significant improvement in verbal memory recall on neuropsychological examination in 21 adult patients with postacute prefrontal cortex lesions. Conversely, Poppelreuter et al. (2009) failed to demonstrate significant improvement in 96 breast cancer survivors in an inpatient rehabilitation center who were divided into two intervention groups receiving attention and memory training. However, Poppelreuter et al. (2009) noted improvement in cognitive functioning in all groups and suggested that improvement may have been caused by unspecified effects of inpatient rehabilitation and/or the timing of the intervention coinciding with the completion of treatment and expected gains by all participants. Overall, the evidence indicates that cognitive training is likely to be effective in improving cognitive performance in cancer survivors, and this finding is supported by a large volume of research in healthy middle-aged and older adults (Ball, Edwards, & Ross, 2007; Ball et al., 2002; Wolinsky et al., 2006; Wolinsky, Vander Weg, Howren, Jones, & Dotson, 2013).

Effectiveness Not Established

Cognitive-behavioral training (CBT) has been used in nine studies to address cognitive function in cancer survivors (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, 2013; Sherer, Meyers, & Bergloff, 1997). Generally, CBT programs are designed to change a person's beliefs, expectations, appraisals, and attributions. In the studies reviewed, researchers focused on enhancing self-efficacy (McDougall, 2001; McDougall et al., 2011), self-regulation, and self-awareness (Ferguson et al., 2007, 2012), and provided psychoeducation (Schuurs & Green, 2013), education and counseling about cognitive

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concerns (Sherer et al., 1997) and reducing fatigue (Goedendorp et al., 2014), as well as compensatory strategies for memory, attention (Cherrier et al., 2013; Ferguson et al., 2007, 2012; McDougall, 2001; McDougall et al., 2011), and problem solving (Locke et al., 2008). Most of the programs were delivered using a group format and included mixed samples of cancer survivors, but two focused on breast cancer survivors and two on patients with primary brain tumors. Five studies used random assignment in their design (Cherrier et al., 2013; Ferguson et al., 2007, 2012; Goedendorp et al., 2014; Locke et al., 2008), and six studies had small sample sizes of less than 30 participants (Cherrier et al., 2013; Ferguson et al., 2007; Locke et al., 2008; McDougall, 2001; McDougall et al., 2011; Sherer et al., 1997). Significant improvement in objectively measured cognitive function was noted in only four studies (Ferguson et al., 2007, 2012; McDougall, 2001; Schuurs & Green, 2013); two of the studies did not control for practice effects in their intervention design, which may have accounted for some of the improvement (Ferguson et al., 2007; McDougall, 2001). In addition, one study did not randomly assign participants, which may have introduced bias (Schuurs & Green, 2013). All of the CBT trials noted improvement in perceived functioning (increased productivity, improved memory self-efficacy, less cognitive disability or complaints). Although some improvements were noted in cognitive function across the studies, the work varied in design, content, and duration, and most were limited by small sample sizes or lack of a comparison group to establish effectiveness.

Electroencephalography biofeedback or neurofeedback involves real-time display of brain electrical activity provided to the individual as visual or auditory information. This method was investigated in a small study by Alvarez, Meyer, Granoff, and Lundy (2013) with 23 breast cancer survivors, and improvements were noted in perceived cognitive function. However, objective cognitive performance was not assessed, and further investigation to establish efficacy is needed.

Exercise has been defined as physical activity that is planned or structured and involves repetitive bodily movement to improve or maintain cardiorespiratory endurance, muscular strength, muscular endurance, flexibility, and/or body composition (Centers for Disease Contol and Prevention, 2011). Four studies were conducted using some form of exercise: tai chi (Reid-Arndt, Matsuda, & Cox, 2012), resistance training (60-minute sessions twice weekly for 12 weeks) (Baumann et al., 2011), physical fitness program combined with psychosocial education (Korstjens, Mesters, van der Peet, Gijsen, & van den Borne, 2006), and aerobic exercise (15-minute sessions four days per week) combined with methylphenidate (Schwartz, Thompson, & Masood, 2002). Three of the studies were limited by pre- and postintervention designs, and only one study used a historic nonintervention comparison group (Schwartz et al., 2002). Although some improvements were reported in perceived cognitive function, the difference in the type of exercise intervention programs, small sample sizes, and study designs (combined multiple interventions) make determining the effect of an exercise intervention on cognitive impairment difficult.

Meditation has not demonstrated efficacy in addressing post-cancer cognitive impairment. Tibetan sound meditation, which includes breathing awareness, concentration techniques, and visualization and sound exercises, was piloted in a randomized, controlled trial with 47 breast cancer survivors (Milbury et al., 2013). Although improvement was noted in verbal memory, short-term memory, speed of processing, and subjective cognitive function, these results were not statistically significant, and further research is warranted.

Mindfulness-based stress reduction focuses on bringing attention and awareness to each moment in a nonjudgmental way. In a randomized, controlled trial with 229 breast cancer survivors, Hoffman et al. (2012) evaluated an eight-week program. They were primarily interested in effects on mood but noted some improvement on the confusion subscale of the Profile of Mood States. Further research, including objective cognitive performance outcomes, is needed to establish efficacy on mindfulness-based stress reduction in cancer survivors.

Natural restorative environment interventions, based on the attention-restoring theory, indicate that the environment may influence one's ability to concentrate and capacity to direct attention (Cimprich & Ronis, 2003). Two small studies evaluated the impact of natural restorative environmental intervention on cognitive function in patients with breast cancer (Cimprich, 1993; Cimprich & Ronis, 2003). One study used a pre- and

Likely to Be Effective

- Cognitive training: group (Hassler et al., 2010; Poppelreuter et al., 2009; Von Ah et al., 2012)
- Cognitive training: individual (Gehring et al., 2009; Kesler et al., 2013; Miotto et al., 2013; Zucchella et al., 2013)

Effectiveness Not Established

- Cognitive-behavioral training (Cherrier et al., 2013; Ferguson et al., 2007, 2012; Goedendorp et al., 2014; Locke et al., 2008; McDougall et a., 2011; Sherer et al., 1997)
- Electroencephalography or neurofeedback (Alvarez et al., 2013)
- Exercise (Baumann et al., 2011; Korstjens et al., 2006; Reid-Arndt et al., 2012; Schwartz et al., 2002)
- Meditation (Milbury et al., 2013)
- Mindfulness-based stress reduction (Hoffmann et al., 2012)
- Natural restorative environmental (Cimprich, 1993; Cimprich & Ronis, 2003)
- Qigong (Oh et al., 2012)
- Structured rehabilitation (Rottmann et al., 2012)
- Vitamin E (Chan et al., 2004; Jatoi et al., 2005)
- Pharmacologic approaches
  - Methylphenidate (Bruera et al., 1992; Butler et al., 2007; Escalante et al., 2014; Gagnon et al., 2005; Gehring et al., 2012; Gong et al., 2014; Lower et al., 2009; Mar Fan et al., 2008; Meyers et al., 1998; Schwartz et al., 2002; Stone & Minton, 2011)
  - Memantine (Brown et al., 2013)
  - Modafinil (Blackhall et al., 2009; Gehring et al., 2012; Kohli et al., 2009; Lundorff et al., 2009)
  - Donepezil (Jatoi et al., 2005; Shaw et al., 2006)

Effectiveness Unlikely

- Gingko biloba (Attia et al., 2012; Barton et al., 2013)

Not Recommended for Practice

- Erythropoiesis-stimulating agents (Chang et al., 2004; Iconomou et al., 2008; Mancuso et al., 2006; Mar Fan et al., 2009; Massa et al., 2005; O'Shaughnessy, 2002; O'Shaughnessy et al., 2005)

FIGURE 2. Research Addressing Cognitive Impairment Interventions in Cancer Survivors

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postintervention design and the other used a randomized, controlled trial. Both studies noted improvements in the capacity to direct attention for patients prior to adjuvant therapy. Further research is needed to explore its effect on cognitive function after cancer treatment.

Qigong incorporates the practice of coordinated gentle exercise and relaxation through meditation and breathing. One study examined the effects of a 10-week medical qigong program in 81 patients with cancer (Oh et al., 2012). Although the researchers found significant improvement in perceived cognitive function, further testing using objective cognitive function tests is warranted to determine efficacy.

Structured rehabilitation was not found to be effective in one trial. A total of 394 breast, prostate, and colon cancer survivors were randomly assigned to a six-day residential psychosocial rehabilitation program that included education, supportive discussions, physical activity, relaxation, massage, social activities, and dietary counseling or to a control group (Rottmann et al., 2012). Objective cognitive performance was not assessed and perceived cognitive function (a one-item measure) significantly improved in the control group when compared to those in the structured rehabilitation intervention group.

Vitamin E, or alpha-tocopherol, is a fat-soluble antioxidant and has been proposed to prevent the production of reactive oxygen (Ahles & Saykin, 2007). Two studies examined the effect of vitamin E on cognitive function (Chan, Cheung, Law, & Chan, 2004; Jatoi et al., 2005). Chan et al. (2004) demonstrated improvements in domains of executive function, verbal memory, and visual memory for patients who received 1,000 IU of vitamin E twice daily for one year. However, Jatoi et al. (2005) closed their randomized, double-blind placebo controlled study early because of poor accrual and thus failed to demonstrate a significant effect of vitamin E on cognitive impairment. In addition, two meta-analyses suggest that vitamin E doses of 400 IU per day or more are associated with a higher mortality risk (Bjelakovic, Nikolova, Gluud, Simonetti, & Gluud, 2007; Miller et al., 2005). Further research is needed to establish effectiveness of vitamin E (Bjelokovic et al., 2007); however, high doses of vitamin E (400 IU per day or greater) should be avoided (Miller et al., 2005).

Dexmethylphenidate and methylphenidate are stimulants commonly used in the treatment of attention deficit hyperactivity disorder for children. Nine empirical studies (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 et al., 2002), one literature review that focused on methylphenidate in palliative care (Stone & Minton, 2011), and one meta-analysis that included two empirical studies (Gong et al., 2014) have been conducted with equivocal results as to whether the stimulants improve cognitive impairment in cancer survivors. Three studies examined the use of methylphenidate in patients with advanced cancer and demonstrated improvement in subjective reports of alertness and objective measures of attention, memory, executive functioning, and psychomotor function; however, only one (Bruera et al., 1992) of the studies was a randomized, controlled trial, and all had small sample sizes ranging from 14–30 (Gagnon et al., 2005; Meyers et al., 1998). In addition, as part of a comprehensive literature review to address central side effects of opioid use, the European Palliative Care Research found that evidence is limited regarding the use of methylphenidate to counteract sedation or cognitive dysfunction (Stone & Minton, 2011). Similarly, trials among

Patient Education: Cognitive Impairment

Cognitive impairment describes problems with the ability to think, learn, remember, and make decisions. This may occur in as many as 80% of patients with cancer.

Cognitive impairment can be caused or worsened by one or more of these factors.

- Cancer
- Cancer treatments
  - Radiation to the brain
  - Chemotherapy
  - Hormone therapy
- Other medications
- Anxiety
- Stress
- Depression
- Difficulty sleeping
- Feeling tired

Studies show that cognitive training is likely to help cognitive function. This involves doing tasks that can help improve attention, thinking, and remembering. Training can be done one-on-one or in a group.

Other approaches have been tried to prevent or treat thinking or memory problems. However, there is not enough research to recommend using them.

Note. Full Oncology Nursing Society Putting Evidence Into Practice information for this topic and description of the categories of evidence are located at www.ons.org/practice-resources/pep/cognitive-impairment. Users should refer to this resource for full dosages, references, and other essential information about the evidence.

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other cancer survivors did not demonstrate any improvement in cognitive function (Butler et al., 2007; Lower et al., 2009; Mar Fan et al., 2008), reported mixed results (Escalante et al., 2014; Gehring et al., 2012), or noted that results were confounded by the receipt of other interventions (e.g., exercise) (Schwartz et al., 2002). Overall, studies evaluating the impact of the stimulants on cognitive function in cancer survivors produced mixed results and were significantly limited by small sample sizes, failure to recruit participants, and high attrition rates.

Memantine, an N-methyl-D-aspartate receptor antagonist, has been shown to have a neuroprotective effect in preclinical models and has been effective in treating patients with vascular disease (Orgogozo, Rigaud, Stöffler, Möbius, & Forette, 2002; Wilcock, Mobius, Stoffler, & MMM 500 Group, 2002). Memantine was used in one randomized, double-blind, placebo-controlled trial to address radiation-induced injury in 508 patients receiving whole brain radiation therapy (Brown et al., 2013). Although patients in the memantine arm demonstrated longer time to clinical decline and reduced rates of decline in memory, executive function, and processing speed, the study failed to find a significant difference in delayed recall, which was its primary endpoint. Brown et al. (2013) suggested that they were underpowered to see a significant effect because only 149 participants remained in the study at 24 weeks. More research is needed to determine the effectiveness of memantine for cognitive impairment in patients with cancer.

Modafinil, a psychostimulant used in the treatment of patients with narcolepsy, has been used in four small trials among cancer survivors with equivocal results (Blackhall, Petroni, Shu, Baum, & Farace, 2009; Gehring et al., 2012; Kohli et al., 2009; Lundorff, Jonsson, & Sjogren, 2009). Lundorff et al. (2009) noted improvements in attention and psychomotor speed but not in the working memories of 28 patients with advanced cancer. Similarly, Kohli et al. (2009) reported improvement in speed of memory and episodic memory but not in working memory in 68 breast cancer survivors. In contrast, Blackhall et al. (2009) noted improvement in cognitive flexibility but failed to find significant improvement in cognitive performance on neuropsychological examination with escalating doses of modafinil (100–200 mg) among 27 patients with all stages of cancer. Most recently, Gehring et al. (2012) noted as much as a 50% improvement on a test of executive functioning, which required divided attention in 24 patients with a primary brain tumor; however, no placebo control group was used in the study, raising concerns of practice effects. Conflicting results may be related to the varying study methodologies employed in the studies: variations of the dose and duration of modafinil, population of the patients examined, small sample sizes, and lack of control groups. Thus, the effectiveness of modafinil is difficult to determine without further research.

Donepezil, an acetylcholinesterase inhibitor that is used to treat mild to moderate Alzheimer dementia, has been used with mixed results in two small trials (Jatoi et al., 2005; Shaw et al., 2006). Shaw et al. (2006) administered 5–10 mg per day of donepezil and noted significant improvement in attention, concentration, and verbal and figural memory in 35 patients with a brain tumor. Jatoi et al. (2005) attempted to evaluate the effect of donepezil 5 mg daily in combination with vitamin E 1,000 IU daily on cognition in patients with lung cancer, but no conclusions regarding efficacy could be determined because the study closed early as a result of poor accrual. Therefore, further clinical testing is warranted to establish the effectiveness of donepezil in cancer survivors.

Implications for Practice

- Incorporate the evaluation of cognitive concerns in nursing assessment, acknowledging any issues reported and educating patients and their families about the possibility of cancer- and cancer treatment–related cognitive impairment.
- Acknowledge patient reports of cognitive concerns and collaborate with the multidisciplinary team to provide referral for neuropsychological testing if warranted.
- Discuss use of cognitive training exercises as an intervention likely to be effective in improving cancer- and cancer treatment–related cognitive impairment.

Effectiveness Unlikely

Gingko biloba, an antioxidant believed to possess neuroprotective effects (Nada & Shah, 2012; Smith & Luo, 2004), failed to demonstrate effectiveness in two randomized, controlled trials (Attia et al., 2012; Barton et al., 2013). Barton et al. (2013) investigated 120 mg per day of gingko biloba to prevent cognitive decline in 210 women with breast cancer receiving adjuvant chemotherapy and did not find therapeutic benefit. Similarly, in a smaller trial, Attia et al. (2012) found no therapeutic benefit in 34 patients with an irradiated brain.

Not Recommended for Practice

Erythropoiesis-stimulating agents are not recommended for practice to address cognitive impairment following cancer and cancer treatment. Erythropoietin-stimulating agents, which stimulate the production of red blood cells in the bone marrow, have been evaluated in seven studies addressing anemia, a potential underlying mechanism of cancer- and cancer treatment–related cognitive impairment (Chang, Couture, Young, Lau, & McWatters, 2004; Iconomou et al., 2008; Mancuso, Migliorino, De Santis, Saponiero, & De Marinis, 2006; Mar Fan et al., 2009; Massa, Madeddu, Lusso, Gramignano, & Mantovani, 2006; O'Shaughnessy, 2002; O'Shaughnessy et al., 2005). Although conclusions from the studies were inconsistent and ranged from no therapeutic benefit (Iconomou et al., 2008; Mancuso et al., 2006; Mar Fan et al., 2009; O'Shaughnessy, 2002; O'Shaughnessy et al., 2005) to significant improvements in cognitive functioning (Chang et al., 2004; Massa et al., 2006), the U.S. Food and Drug Administration (2011) issued a black box warning regarding the increased risk of serious cardiovascular and thrombovascular events and their potential to shorten overall survival in patients with cancer. As a result, the use of erythropoietin-stimulating agents is not recommended to address cognitive impairment in cancer survivors.

Implications for Nursing and Conclusion

Oncology nurses may play an integral role in identifying cancer survivors with clinically significant cognitive impairment.

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Nurses need to listen carefully to their patients and recognize common descriptions (e.g., expressions of difficulty concentrating, trouble following directions, memory lapses, decreased awareness, inability to plan or problem solve) as potential indicators of clinically significant cognitive impairment (Jansen, 2013). Nurses should use readily available and reputable resources such as ONS (2014), the American Society of Clinical Oncology (2013), or Livestrong Foundation (2014) to provide support to survivors with cognitive concerns. In addition, after careful assessment to address and eliminate other correlated symptoms (Bender & Thelen, 2013), nurses may need to refer survivors with significant cognitive impairment that affects everyday functioning to a specialist for a comprehensive neuropsychological evaluation (Jansen, 2013).

With regard to evidence-based interventions, this review demonstrated that cognitive training provided in a group or individual format seems to provide the most improvement in cognitive function for cancer survivors. Although other interventions, such as CBT, exercise, and mediation or mindfulness-based stress reduction, may be beneficial to improve cognitive function, empirical data are limited in their support of these approaches in cancer survivors. Gingko biloba was not found to be effective in a large randomized trial and, therefore, is unlikely to have a positive impact to prevent or treat cognitive impairment after cancer. Nurses also should warn their patients that erythropoietin is not recommended for practice to address cognitive impairment.

Future research is needed and must explore the underlying physiologic mechanisms associated with cognitive impairment and potential genetic polymorphisms that may predispose patients to cognitive impairment after cancer and its treatment. To date, most of the cognitive intervention research has been primarily explored in small samples of patients with brain tumors and breast cancer survivors. Large randomized, controlled trials in multiple centers accessing a diverse population of cancer survivors, including survivors with various types of cancer, of various ages, and from differing ethnicities, are warranted to further test the effectiveness of the pharmacologic and nonpharmacologic interventions for cancer- and cancer treatment–related cognitive impairment.

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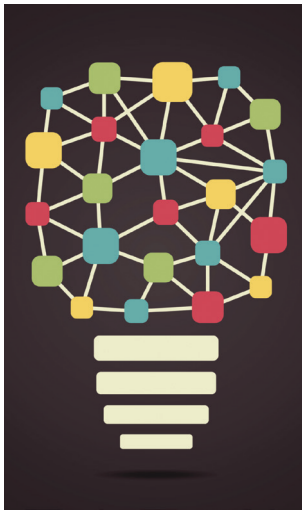

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