AOTA Critically Appraised Papers Series

Evidence Exchange

**A product of the American Occupational Therapy Association's Evidence-Based Literature Review Project*

CRITICALLY APPRAISED PAPER

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,* 299–306. http://dx.doi.org.ezproxy.dominican.edu/10.1016/j.clbc.2013.02.004

CLINICAL BOTTOM LINE:

The present literature regarding patients with breast cancer after chemotherapy treatment indicates increased occurrence of cognitive deficits, particularly in executive function. To explore these deficits, the researchers used an online, computer-based intervention program aimed to improve impaired cognition. The population of this study was a group of female breast cancer survivors who had previously received chemotherapy treatment with or without hormonal therapy. The participants were randomly assigned to the intervention group or the control group. The implemented intervention was a home-based cognitive training computer program accessible through an online subscription to the Lumos Lab, Inc. The intervention group completed the cognitive training computer program, whereas the control group received no treatment. Both the intervention and the control group received pre- and posttests assessing cognition, primarily in the area of executive function.

The components of the computer program were selected to promote improvement in executive function. The program's exercises provided games that focused on memory, spatial sequencing, route planning, and problem solving. Weekly treatments included five exercises per session, for a total of 48 sessions over a duration of 12 weeks. The difficulty level of the sessions was regulated by the computer program and adapted according to each participant's progress. The study found that participants who received the intervention showed significant improvements in executive function, cognitive flexibility, and letter fluency (language), ranging from moderate to large effect sizes.

The results of the study indicate immediate improvement in executive function after the cognitive training computer program. However, the limitations of this study include the small sample size and the lack of practical assessments of executive function. Additionally, long-term effects of the treatment could not be determined because of the lack of follow-up assessments.

Therefore, an online computer-based cognitive training program may not be beneficial as a sole intervention for breast cancer survivors with impaired cognition. Nevertheless, such training could be used as an adjunctive home program in congruence with occupational therapy.

RESEARCH OBJECTIVE

To determine whether a home-based cognitive training computer program could improve the cognition and executive function of breast cancer survivors who had undergone chemotherapy, radiation treatment, or both, with or without hormonal therapy.

DESIGN TYPE AND LEVEL OF EVIDENCE

Level I: Randomized controlled trial

SAMPLE SELECTION

NR

Inclusion Criteria

The women in this study were survivors of Stage I–IIIA breast cancer and had been treated for breast cancer through surgery and chemotherapy, radiation, or both, with or without hormonal therapy. The participants were 40 years of age or older when diagnosed with breast cancer and terminated chemotherapy 18 months before participating in the study. They were required to have a home computer with Internet access and had conveyed interest in the program.

Exclusion Criteria

The research study excluded participants on the basis of the following criteria: previous chemotherapy treatments, sensory deficits, color blindness, neurological and medical conditions that affect cognition, previous psychiatric hospitalization, and a need for central nervous system depressant medication other than common antidepressants.

SAMPLE CHARACTERISTICS

N= (Number of participants taking part in the study)	41		
#/ (%) Male	0 (0%)	#/ (%) Female	41 (100%)
Ethnicity	NR		
Disease/disability diagnosis	Participants were survivors of breast cancer (Stages I–IIIA).		

INTERVENTION(S) AND CONTROL GROUPS

Group 1: Intervention group

Brief description of	Participants completed the Lumos Lab, Inc., home-based cognitive training

the intervention	computer program, which was designed to improve executive function skills, such as problem solving, working memory, processing speed, and cognitive flexibility. Each participant created her own online account through the cognitive training program to record her progress. The cognitive training program included exercises using games and puzzles that involved visual stimuli, motor responses, and auditory feedback. Depending on the participants' performance, the computer program compensated the difficulty level, and all the exercises began at an easy level. As participants improved, the sessions became more challenging. The training program was divided into two courses, and the courses were completed consecutively. The participants were required to begin the computer training program within 3 days of the initial assessment. The researchers contacted each participant weekly to remind her to complete her sessions. Standardized sets of cognitive tests were given to each participant as a pretest and posttest.
How many participants in the group?	21
Where did the intervention take place?	The participants completed the program from their home computer.
Who Delivered?	A clinical neuropsychologist chose the intervention exercises for the cognitive training computer program. These program sessions were derived from Lumos Lab, Inc., in San Francisco and were drawn directly from the Lumos Lab website. Blinded assessors gave the pretest and posttest.
How often?	Training sessions occurred four times per week. Each session consisted of five exercises, with a total of 48 sessions, each lasting 20–30 min.
For how long?	12 weeks

Group 2: Control group

Brief description of the intervention	Pretest and posttest assessments were administered to the control group. No intervention was administered.
How many participants in the group?	20
Where did the intervention take place?	Participants in the control group did not receive intervention during the study.
Who Delivered?	The researchers who conducted the pre- and posttests were blind to the intervention.

How often?	Cognitive testing was administered twice.
For how long?	There was a 12-week duration between the pretest and posttest.

Intervention Biases:

Contamination:

YES ☐ NO ☐ NR ☒	*Comment:* The researchers did not report whether there was contamination. The cognitive training program was available to the public for purchase. The participants in the control group could have accessed the program online independently.

Co-intervention:

YES ☐ NO ☐ NR ☒	*Comment:* The researchers did not report whether any of the participants were receiving other forms of intervention during the cognitive training program. Participants who were taking common antidepressants at the time of the study were not excluded, but the number of participants using antidepressants was not reported.

Timing:

YES ☒ NO ☐ NR ☐	*Comment:* The timing (12 weeks) was long enough to demonstrate significant changes in some of the measurements of cognition. However, the researchers mentioned that a longer intervention would be beneficial for future studies.

Site:

YES ☒ NO ☐ NR ☐	*Comment:* The intervention occurred in the participants' home, which meant that the researchers had no control over the environment. The home setting for intervention did not allow the researchers to monitor whether the participants were independently completing the program without assistance from others.

Use of different therapists to provide intervention:

YES ☐ NO ☐ NR ☒	*Comment:* Therapists were not present during intervention. However, the researchers made weekly phone calls to remind the participants to adhere to the training sessions throughout the duration of the intervention. The study did not state whether the same researcher contacted the participants each week.

MEASURES AND OUTCOMES

Measure 1:

Name/type of measure used:	Wisconsin Card Sorting Test (WCST)
What outcome was measured?	Cognitive flexibility

Is the measure reliable?	YES ☐ NO ☐ NR ☒
Is the measure valid?	YES ☒ NO ☐ NR ☐
When is the measure used?	Pretest and posttest, 12 weeks apart

Measure 2:

Name/type of measure used:	The Letter Fluency test from the Delis–Kaplan Executive Function System
What outcome was measured?	Executive functions and language
Is the measure reliable?	YES ☐ NO ☐ NR ☒
Is the measure valid?	YES ☒ NO ☐ NR ☐
When is the measure used?	Pretest and posttest, 12 weeks apart

Measure 3:

Name/type of measure used:	Hopkins Verbal Learning Test Revised
What outcome was measured?	Verbal memory and the effects of executive function on verbal declarative memory
Is the measure reliable?	YES ☐ NO ☐ NR ☒
Is the measure valid?	YES ☒ NO ☐ NR ☐
When is the measure used?	Pretest and posttest, 12 weeks apart

Measure 4:

Name/type of measure used:	Digit Span and Symbol Search subtests of the Wechsler Adult Intelligence Scale (fourth edition)
What outcome was measured?	Working memory and processing speed
Is the measure reliable?	YES ☒ NO ☐ NR ☐
Is the measure valid?	YES ☒ NO ☐ NR ☐
When is the measure	Pretest and posttest, 12 weeks apart

used?	

Measure 5:

Name/type of measure used:	Behavioral Rating Inventory of Executive Function (BRIEF)
What outcome was measured?	Self-report measure of executive function
Is the measure reliable?	YES ☐ NO ☐ NR ☒
Is the measure valid?	YES ☒ NO ☐ NR ☐
When is the measure used?	Pretest and posttest, 12 weeks apart

Measurement Biases

Were the evaluators blind to treatment status?

YES ☒ NO ☐ NR ☐	*Comment:*

Recall or memory bias.

YES ☒ NO ☐ NR ☐	*Comment:* The BRIEF is a subjective assessment relying on participants' self-rating of executive function and therefore may be subject to recall bias.

Others (list and explain):

Sampling procedure bias may exist because the procedure was not listed.

RESULTS

Participants completed an average of four sessions each week. They took an average of 13 ± 0.92 weeks to complete the program. There was 95% compliance with program completion in the intervention group. Compliance also correlated with high positive performance across weekly sessions and exercises (mean correlation = .72 ±. 13). The intervention group demonstrated improvement in the WCST scores compared with the control group. The effect size was 0.58 (p = .008). The intervention group showed improvement on the Letter Fluency test, with an effect size of 0.82 (p = .003). Intervention group scores for the symbol search activity included an effect size of 0.87 (p = .009). A trending improvement on the Hopkins Verbal Learning Test Revised had an effect size of 0.56 (p = .07). The Wechsler Adult Intelligence Scale Digit Span subscale scores

were not significantly improved, with an effect size of 0.14 (p = .75). Although global BRIEF scores were reduced, they were not significant, with an effect size of 0.26 (p = .22). Through an exploratory analysis, significant improvements were shown in the BRIEF Planning and Organization subscales, with an effect size of 0.44 (p = .02).

Was this study adequately powered (large enough to show a difference)?

YES ☐ NO ☒ NR ☐	*Comment:* Two participants from the intervention group and 1 participant from the control group dropped out, which made the study inadequately powered.

Were appropriate analytic methods used?

YES ☒ NO ☐ NR ☐	*Comment:*

Were statistics appropriately reported (in written or table format)?

YES ☒ NO ☐	*Comment:*

Was the percent/number of subjects/participants who dropped out of the study reported?

YES ☒ NO ☐

Limitations:

A limitation of this study was the small sample size, which made generalization to the greater population of women who have had breast cancer and been treated with chemotherapy difficult. Variables such as treatment history and disease history were not the same for all participants. Influence of these variables on the intervention could not be determined, given the absence of statistical power. Additionally, the researchers were not able to include a follow-up to indicate whether the cognitive training had consistent effects over a period of time. The study also reported that cognitive changes related to chemotherapy may not be observed through standardized scores. Another limitation of the study was that the cognitive training only included visual stimuli, not auditory stimuli. Using both visual and auditory stimuli might have led to a larger effect on the intervention. Similarities between the online cognitive training program and the WCST and Letter Fluency tests are another limitation, because significant scores on these tests might have been the result of practice rather than cognitive improvement. The study was also limited because of the lack of evidence on generalizability to daily functions.

CONCLUSIONS

Cognitive impairments are a common deficit in breast cancer survivors. Through the use of an online cognitive training program, the study established improvements in cognitive flexibility, executive function, verbal memory, verbal fluency, and processing speed in breast cancer survivors. With the increasing survival rates of breast cancer patients comes an increase in the need for an intervention that will improve cognition. The authors stated that the intervention administered may be feasible for breast cancers survivors over the long term. However, long-term effects on executive function were not determined in the study. Additional research that may be beneficial to female breast cancer survivors could include an intervention with an emphasis on metacognition, a longer intervention duration, and more focus on generalizability to real-life functions.

This work is based on the evidence-based literature review completed by Kaitlyn Williams, OTS; Morgan Mousley, OTS; Katie Blank, OTS; Jocelle Flores, OTS; and Kitsum Li, OTD, OTR/L, Faculty Advisor, Dominican University of California.