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CLINICAL TRIAL

Advanced cognitive training for breast cancer survivors: a randomized controlled trial

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Abstract The purpose of this study was to evaluate the preliminary efficacy and satisfaction/acceptability of training in memory or speed of processing versus wait-list control for improving cognitive function in breast cancer survivors. 82 breast cancer survivors completed a three-group randomized, controlled trial. Primary outcomes were objective neuropsychological tests of memory and speed of processing. Secondary outcomes were perceived cognitive functioning, symptom distress (mood disturbance, anxiety, and fatigue), quality of life, and intervention satisfaction/acceptability. Data were collected at baseline, post-intervention, and 2-month follow-up. Using repeated-measures mixed-linear ANCOVA models, each intervention was compared to wait-list control while adjusting for age, education, and baseline measures. The effect sizes for differences in means and the reliable improvement percentage were reported. The results show that domain-specific effects were seen for both interventions: memory training improved memory performance at 2-month follow-up ($p = 0.036$, $d = 0.59$); speed of processing training improved processing speed post-intervention ($p = 0.040$, $d = 0.55$) and 2-month follow-up ($p = 0.016$; $d = 0.67$). Transfer effects to non-trained domains were seen for speed of processing training with improved memory post-intervention ($p = 0.007$, $d = 0.75$) and 2-month follow-up ($p = 0.004$, $d = 0.82$). Both interventions were associated with improvements in perceived cognitive functioning, symptom distress, and quality of life. Ratings of satisfaction/acceptability were high for both interventions. It was concluded that while both interventions appeared promising, speed of processing training resulted in immediate and durable improvements in objective measures of processing speed and verbal memory. Speed of processing training may have broader benefits in this clinical population.

Keywords Memory · Speed of processing · Breast cancer survivors · Symptom distress · Quality of life

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Introduction

Breast cancer survivors often report problems with their memory or feelings of mental slowness [1]. Deficits in memory and processing speed have been verified through objective neuropsychological assessments [2–5]. Although subtle, such deficits may have a significant impact on quality of life [6, 7], yet there are very few treatment options for this problem [8, 9].

Behaviorally based cognitive training interventions may be a viable treatment option but, have not been widely tested in individuals with cancer. While memory and speed of processing training have been shown to be effective in

improving memory performance and processing speed in older persons without cancer (≥age 65), [10–13] research in cancer patients has been limited [8, 9]. In long-term breast cancer survivors, only one other small controlled cognitive training trial has been conducted [14] with some positive, but mixed results; compelling the need for further research [8, 9].

The purpose of this pilot study was to evaluate preliminary efficacy and satisfaction/acceptability of memory and speed of processing training in improving cognitive functioning in breast cancer survivors compared to wait-list control group. Primary outcomes were performance on objective neuropsychological tests of memory and speed of processing. Secondary outcomes were perceived cognitive function, symptom distress (mood disturbance, anxiety and fatigue), quality of life, and satisfaction/acceptability. Findings from this study will ultimately lead to a full-scale efficacy trial and our overarching goal of identifying an effective treatment for cognitive impairment in breast cancer survivors.

Patients and methods

Study design

This three-group single-blind, randomized controlled trial compared training in memory and speed of processing to wait-list control among long-term breast cancer survivors. Outcomes were assessed at baseline (prior to randomization), post-intervention, and at 2-month follow-up. The study protocol was approved by the Institutional Review Board.

Recruitment of breast cancer survivors occurred from January 1, 2009 to June 1, 2011 at a Midwestern cancer center and affiliated clinics. Participants were recruited sequentially from clinics and advertisements were mailed to research registry participants (tumor registries, Susan Love/Avon Army of Women). Eligible participants were breast cancer survivors who (1) reported concerns regarding their cognitive functioning (poor memory, feelings of mental slowness, etc.), (2) identified that cognitive concerns negatively impacted their self-esteem and/or interfered with their daily life, and (3) reported that they were interested in and seeking treatment to address their cognitive concerns. Other eligibility criteria included breast cancer survivors who were also post-menopausal, 40 years of age, and older, ≥1-year post-treatment which included chemotherapy for primary non-metastatic breast cancer, disease-free, and able to understand, speak, read, and write English.

Exclusion criteria included substantial cognitive impairment (score < 24 Mini-Mental State Examination, MMSE [15]); history of stroke, encephalitis, traumatic brain injury, brain surgery, dementia, Alzheimer's disease, or Parkinson's disease; history of cranial radiation therapy or intrathecal therapy; current active major depression or substance abuse or history of bipolar disorder, psychosis, schizophrenia, or learning disability; history of or current other cancer except for basal cell skin cancer; history of other cognitive training; or uncorrected vision problems (worse than 20/70).

We planned a priori to enroll 30 per group to achieve 26 per group after attrition to provide 80 % power for two-sided parametric tests to detect large (0.80) effect sizes between each intervention and control group.

Procedure and methods

Eligibility was determined via telephone review of demographic, health, and breast cancer diagnosis and treatment-related information followed by an in-person assessment of cognition (MMSE). If eligible, project staff conducted the baseline neuropsychological assessment and administered the baseline survey questionnaires.

Telephone reminders were made to all participants in advance of their follow-up assessments which occurred post-intervention and 2-month follow-up. All assessments were conducted in the same manner with repeated neuropsychological testing and questionnaires collected by a trained and blinded staff member. Participants received $25 at each data collection visit.

Randomization and interventions

Subjects were randomized using non-stratified blocks of 9. Biostatisticians provided a password protected randomization list to the non-blinded project manager who had primary responsibility for randomization. Participants were notified by telephone of group assignment and intervention dates. Each intervention included ten 1-hour training sessions done in small groups of 3–5 breast cancer survivors over 6–8 weeks and delivered by a separate trained and certified interventionists to avoid diffusion of treatments.

Memory training was adapted from the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) trial [16]. Memory training involved teaching participants strategies for remembering word lists, sequences, and text material by learning how to apply principles of meaningfulness, organization, visualization, and association [16]. Strategies included multiple mnemonic techniques including visual memory support, story mnemonic, and method of loci. Sessions 1–5 focused on strategy instruction and exercises to practice the strategy and Sessions 6–10 provided additional practice exercises to promote self-efficacy with regard to performance.

Speed of processing training utilized the commercially available Insight program (Posit Science®), which was

originally developed as part of the ACTIVE trial and then refined overtime [16]. This program systematically reduces the stimulus duration during a series of progressively more difficult information-processing tasks presented via computer. The exercises automatically adjust to user performance to maintain an 85 % correct rate. The exercises included time-order judgment, discrimination, spatial-match, forward-span, instruction-following, and narrative-memory tasks [17].

The wait-list control group received a letter explaining that they were not selected to receive any study materials but that one of the training programs would be mailed to them at the end of their study participation. All wait-list group participants received the Insight (Posit Science®) program and written instructions after they completed participating in the study.

Outcome measures

Primary outcomes

Objective memory (immediate and delayed) was assessed by composite scores derived from equally weighted average scores from the Rey Auditory Verbal Learning Test (AVLT) a 15 item list learning task including the Sum Recall (trials 1–5), short delay, and recognition score [18] as well as the immediate recall from the Rivermead Behavioral Paragraph Recall Test [19]. Delayed memory was derived from the long-term delay score from the Rey AVLT and long-term delay score from the Rivermead Behavioral Paragraph Recall Test. As in the ACTIVE trial [10, 16], composite scores were used because they measure ability rather than performance on a specific test, are more reliable and reduce the number of outcome analyses needed, thereby reducing inflation of the overall type I error probability [16]. Alternate forms given in fixed order were used to reduce practice effects [16].

Objective speed of processing was measured with the Useful Field of View (UFOV) [20–22], a computer-administered and computer-scored test of visual attention. The assessment requires participants to identify and localize information, with 75 % accuracy, under varying levels of cognitive demand. The results from three subtests measuring divided attention and two levels of selective attention (parts 2–4) were used in combination to determine the composite speed of processing score, with lower scores indicating better speed.

Secondary outcomes

Perceived cognitive functioning was measured with the 48-item Functional Assessment of Cancer Therapy-Cognitive (FACT-Cog) [23] and 18-item Squire Subjective Memory Questionnaire (SSMQ) [24]. Higher scores on both denote better cognitive functioning. *Symptom distress* was measured by three separate measures including the 20-item Center for Epidemiologic Studies Depression Scale (CES-D), the 20-item Spielberger State-Trait Anxiety Inventory-State Subscale (STAI-S) [25] and the 13-item Functional Assessment of Cancer Therapy-Fatigue (FACT-F) [26]. Higher scores on the CES-D and STAI-S indicate worse symptom-specific distress, whereas higher scores on the FACT-F indicate lower symptom-specific distress. *Quality of Life* was measured with the 41-item Quality of Life-Cancer Survivors (QOL-CS) [27] the 66-item quality of life index-cancer version [28] and the 36-Item Short-Form Health Survey (SF-36) [29]. Higher scores on each indicated greater overall life satisfaction. *Satisfaction/acceptability* were assessed post-intervention (3–7 days) with the 8-item, Likert-based Client Satisfaction Questionnaire [30] and the 10-item, Likert-based Acceptability Scale [31]. Higher scores on both scales indicate more positive response.

Demographics and breast cancer disease and treatment variables were assessed to describe the sample. Self-reported disease information was verified with medical records review. There were no adverse events reported.

Statistical analysis

Group equivalence on baseline characteristics was tested using ANOVA and Chi-square tests or the Kruskal–Wallis and two-sided Fisher exact tests when assumptions were violated.

As in ACTIVE [10], neuropsychological tests were standardized by pooling scores at all time points for all subjects using the Blom (rank-based) transformation, producing more normally distributed scores [32]. Standard z scores were computed (person's transformed score minus baseline mean divided by baseline standard deviation) at each time point.

Separate general linear mixed models were used to test memory and speed of processing treatment effects compared to wait-list control on each outcome. Models included between-subjects treatment and within-subjects time effects along with age and education (known confounding covariates) and the baseline value for the outcome variable. The treatment effect size was computed as the difference between model-based adjusted means at post-intervention or 2-month follow-up divided by the pooled baseline standard deviation.

Reliable improvement was calculated as improvement in performance on a measure by at least 1 standard error of measurement (SEM). The SEM described generally in the study of Dudek [33] was computed as the standard deviation of difference scores (from baseline to either post-

intervention or 2-month follow-up) for the wait-list control group multiplied by the square root of [1 minus test–retest (baseline to immediate post-intervention) reliability] for the wait-list control group.

There was no missing neuropsychological data and less than 0.05 % of questionnaire data. For questionnaires, scale- and person-specific means were computed and substituted for missing items if at least 70 % of items were not missing. Analyses were conducted using SAS 9.3 (SAS Institute Inc, Cary, NC). The significance level was not adjusted for multiple comparisons because this was a pilot study.

Results

Participants

A total of 88 breast cancer survivors consented and were randomized to one of the three groups. Figure 1 shows the accrual flow and reasons for attrition. 208 women were screened for initial eligibility. A total of 91 (43.8 %) participants were eligible upon initial screen, 71 (34.1 %) were ineligible, and 46 (22.1 %) refused (either directly or passively by not responding to follow-up). The top reasons for ineligibility were: no chemotherapy (32.4 %), other cancer (15.5 %), psychiatric diagnosis (14.1 %), and metastatic breast cancer (11.3 %). A total of 91 participants consented and completed the in-person screen; with three breast cancer survivors determined to be ineligible due to no chemotherapy, not 1 year post-adjuvant therapy, or psychiatric diagnosis. Study completion rates by group were 90 % memory training, 90 % speed training, and 100 % wait-list control. Participants that dropped out of the study did so before the start of intervention and they did not differ significantly on demographic, breast cancer variables, or measures of symptom distress than those that completed the study. Because sample sizes slightly exceeded 26 per group, observed power was 81 %.

The overall sample (collapsed across treatment groups) was middle aged (average 56.5 ± 8.5 years old), had early-stage breast cancer (89 % stage II or lower), and were long-term survivors (average of 5.5 years post-treatment (SD = 4.2). All subjects had received surgery (100 %) and chemotherapy (100 %) and 74 % also had radiation therapy. Nearly half the subjects (46 %) were receiving adjuvant endocrine therapy at the time of this study. There were no significant group differences at baseline in age, race, education, cancer severity, cancer treatment (including the use of tamoxifen or aromatase inhibitors), current depressive, anxiety and fatigue symptoms, and cognitive abilities (immediate and delayed memory and processing speed) (see Table 1). In addition, based on published norms of the Rey AVLT [34], clinically significant impairment (defined as 1.0 standard deviations below the norm-based test) was noted for subscales used in the immediate memory composite (the rate ranging from 13 % impaired on the Rey AVLT recognition to 20 % impaired on the Rey AVLT short delay), as well as, measures of delayed memory (23 % impaired on the Rey AVLT delayed recall). These findings are similar to our previous work which found 17 % of breast cancer survivors had clinically significant immediate and delayed memory impairment compared to healthy age- and education-matched controls [35].

Effects on primary outcomes: objective memory and speed of processing performance

Results of the primary outcome measures of objective neuropsychological performance are detailed in Table 2 and Figs. 2, 3. Compared to the wait-list control, the memory training group demonstrated better immediate ($p = 0.036$, $d = 0.59$) and delayed memory performance ($p = 0.013$, $d = 0.70$) at the 2-month follow-up (Table 2; Fig. 2). Differences in post-intervention were not significant. At the 2-month follow-up, the percentage of breast cancer survivors who demonstrated reliable improvement was as follows: Immediate memory—39 % memory training group versus 18 % wait-list control; delayed memory—42 % memory training group versus 11 % wait-list control (see Table 2).

The speed of processing group demonstrated better processing speed compared to the wait-list control group post-intervention ($p = 0.040$, $d = 0.55$) and at the 2-month follow-up ($p = 0.016$, $d = 0.67$) (Table 3; Fig. 3). Post-intervention, the percentage of breast cancer survivors who demonstrated reliable improvement was 68 % for the speed of processing group and 43 % for the wait-list control group. At the 2-month follow-up, the percentage demonstrating reliable improvement was 67 % for the speed of processing compared to 61 % for wait-list control group.

Speed of processing training also improved immediate memory at both post-intervention time points ($p = 0.007$ and $p = 0.004$) and delayed memory at the 2-month follow-up ($p = 0.010$). These effect sizes were moderate to large for immediate memory improvement post-intervention and 2-month follow-up ($d = 0.75$ and $d = 0.82$, respectively) and delayed memory at the 2-month follow-up ($d = 0.72$). For the speed of processing training group, the reliable improvement for immediate memory was 41 and 30 % compared to 10 and 18 % for the wait-list control groups, respectively. For the speed of processing training group, the reliable improvement for delayed memory was 30 and 33 % compared to 24 and 11 % for the wait-list control.

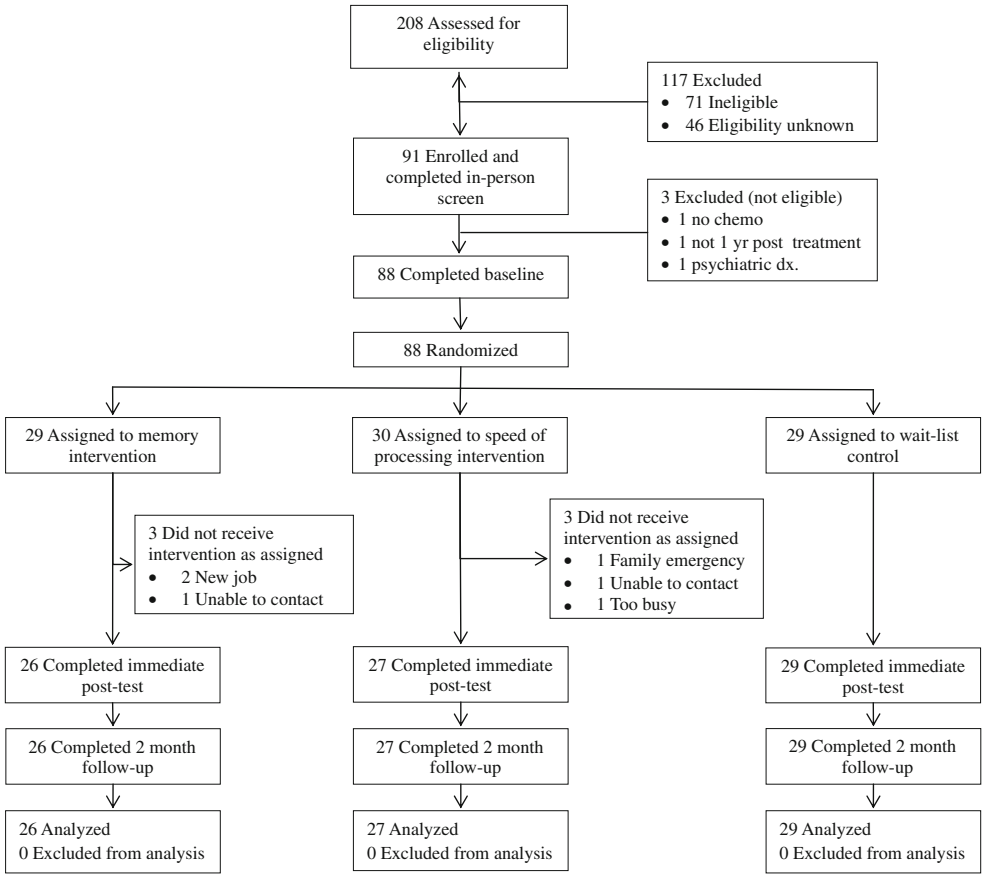

Fig. 1 Consort diagram. Participant flow diagram

Secondary outcomes: perceived cognitive function, symptom distress, and quality of life

Table 3 and Figs. 2, 3 display the effects of memory and speed of processing training on secondary outcomes. Memory training had a positive effect on perceived cognitive functioning on both the FACT-Cog ($p = 0.036$ and $p = 0.021$) and SSMQ ($p = 0.012$ and $p = 0.003$) at both post-intervention time points. In addition, memory training had a positive effect on one measure of symptom distress (STAI-S) at the 2-month follow-up ($p = 0.017$) and a marginally significant effect on the SF-36-mental health outcome scale ($p = 0.078$).

Compared to wait-list control, speed of processing training improved perceived cognitive functioning on the FACT-Cog post-intervention ($p = 0.042$) and had marginal significant effect on the SSQM at the 2-month follow-up ($p = 0.065$). Compared to controls, breast cancer survivors who received the speed of processing training also had significantly lower symptom distress on the CES-D and FACT-F at both post-intervention time points and lower symptom distress on the STAI-S at the 2-month follow-up. In addition, compared to the wait-list control, the speed of processing training group had better mental health outcomes (SF-36) post ($p = 0.010$) and at the 2-month follow-up ($p = 0.031$).

Acceptability/satisfaction

There were no differences in satisfaction/acceptability between the memory and speed of processing groups. The majority in both the memory and speed of processing groups found the training to be highly satisfactory at 73 and 89 %, respectively. Similarly, participants in both intervention groups (memory, speed) agreed or strongly agreed that the program was understandable (96, 89 %) and enjoyable (81, 73 %). Most disagreed or strongly disagreed that they would have preferred something else (80, 81 %), wanted a different format (100, 96 %), was too difficult (77, 89 %), took too much time (92, 100 %), or that the training was boring (96, 100 %).

Discussion

To our knowledge, this was the largest cognitive training study in long-term breast cancer survivors to date. The main study findings were that both memory and speed of

Table 1 Description of the sample and equivalence across groups

	Memory training ($n = 26$) Mean (SD)	Speed of processing ($n = 27$) Mean (SD)	Wait-list control ($n = 29$) Mean (SD)	p
Age (years)	55.19 (7.58)	56.93 (7.83)	57.21 (9.80)	0.645
Education (years)	15.96 (1.87)	15.63 (2.50)	15.43 (2.27)	0.678
Months post-treatment	59.50 (46.12)	78.00 (60.53)	59.00 (41.42)	0.665
Cognitive status (MMSE)	29.15 (1.16)	29.33 (0.78)	29.00 (1.13)	0.553
Depressive symptoms (CES-D)	8.98 (5.17)	13.04 (11.03)	13.69 (10.05)	0.374
Anxiety (STAI-state score)	32.87 (7.26)	36.15 (9.02)	36.48 (10.13)	0.269
Fatigue (FACT-F)	39.15 (10.34)	35.91 (11.11)	36.62 (10.88)	0.314
Immediate memory				
Rey AVLT (sum recall)	50.65 (8.28)	51.70 (7.57)	48.34 (5.83)	0.270
Rey AVLT (short delay)	11.00 (2.70)	11.19 (2.45)	10.55 (2.50)	0.633
Rey AVLT (recognition)	14.00 (1.60)	13.67 (1.44)	13.93 (1.85)	0.737
Rivermead	11.29 (2.87)	11.50 (2.09)	10.62 (2.70)	0.413
Delayed memory				
Rey AVLT (delay)	10.62 (2.99)	11.37 (2.73)	10.24 (3.01)	0.345
Rivermead (delay)	10.54 (3.44)	11.11 (2.03)	9.81 (2.74)	0.223
Information-processing speed				
Divided attention	52.81 (94.43)	31.63 (30.52)	49.71 (28.56)	0.409
Selective attention 1	132.50 (93.59)	113.26 (51.87)	140.68 (73.77)	0.384
Selective attention 2	281.46 (113.55)	246.15 (107.55)	267.21 (158.77)	0.607
	n (%)	n (%)	n (%)	
Race				0.198
White, non-hispanic	21 (81)	26 (96)	26 (90)	
Non-white, non-hispanic	5 (19)	1 (4)	3 (10)	
Marital status				0.463
Married/partnered	14 (54)	19 (70)	18 (62)	
Single/divorced/widow	12 (46)	8 (30)	11 (38)	
Tamoxifen user				0.273
No, never used	12 (46)	6 (23)	10 (37)	
Yes, but not in the last month	4 (15)	5 (19)	8 (30)	
Yes, used in the last month	10 (38)	15 (58)	9 (33)	
Aromatase inhibitor user				0.827
No, never used	19 (73)	21 (78)	18 (62)	
Yes, but not in the last month	5 (19)	5 (18)	7 (24)	
Yes, used in the last month	2 (8)	1 (4)	4 (14)	

MMSE Mini-Mental State Examination, *CES-D* Center for Epidemiological Studies Scale, *STAI-S* State-Trait Anxiety Inventory-State Subscale, *FACT-F* Functional Assessment of Cancer Therapy-Fatigue, *Rey AVLT* Rey Auditory Verbal Learning Test, *Rivermead* Rivermead Behavioral Paragraph Recall test

processing training improved objective measures of cognitive performance. Importantly, we also noted significant improvements in perceived cognitive function, symptom distress (mood disturbance, anxiety, and fatigue) and quality of life of breast cancer survivors in the cognitive training groups compared to wait-list control. Similar findings were noted by Ferguson et al. [14], who tested the efficacy of an attention and memory program ($n = 19$) against wait-list control ($n = 21$) in long-term breast cancer survivors, and found statistically significant improvements in memory and some quality of life indicators (spirituality). Taken together, findings suggest that cognitive training may be a promising intervention for treating cognitive deficits in breast cancer survivors.

As predicted, we noted cognitive domain-specific intervention effects; that is memory training improved

Table 2 Training effects on primary outcomes post and 2-month follow-up ($n = 82$)

Measure	Memory training ($n = 26$)		Speed of processing training ($n = 27$)		Wait-list control ($n = 29$)
	Net effect size (p value)*	Reliable improvement (%)‡	Net effect size (p value)*	Reliable improvement (%)‡	Reliable improvement (%)‡
Immediate memory					
Post	−0.26	23	0.75 ($p = 0.007$)	41	10
2-month	0.59 ($p = 0.036$)	39	0.82 ($p = 0.004$)	30	18
Delayed memory					
Post	−0.07	19	0.19	30	24
2-month	0.70 ($p = 0.013$)	42	0.72 ($p = 0.010$)	33	11
Speed of processing					
Post	0.11	65	0.55 ($p = 0.040$)	68	43
2-month	0.31	73	0.67 ($p = 0.016$)	67	61

Post represents immediate post-intervention, 2-month represents 2-month follow-up

* Only significant p values reported

‡ Calculated as the percentage of participants in each group who were ≥ 1 SEM above baseline

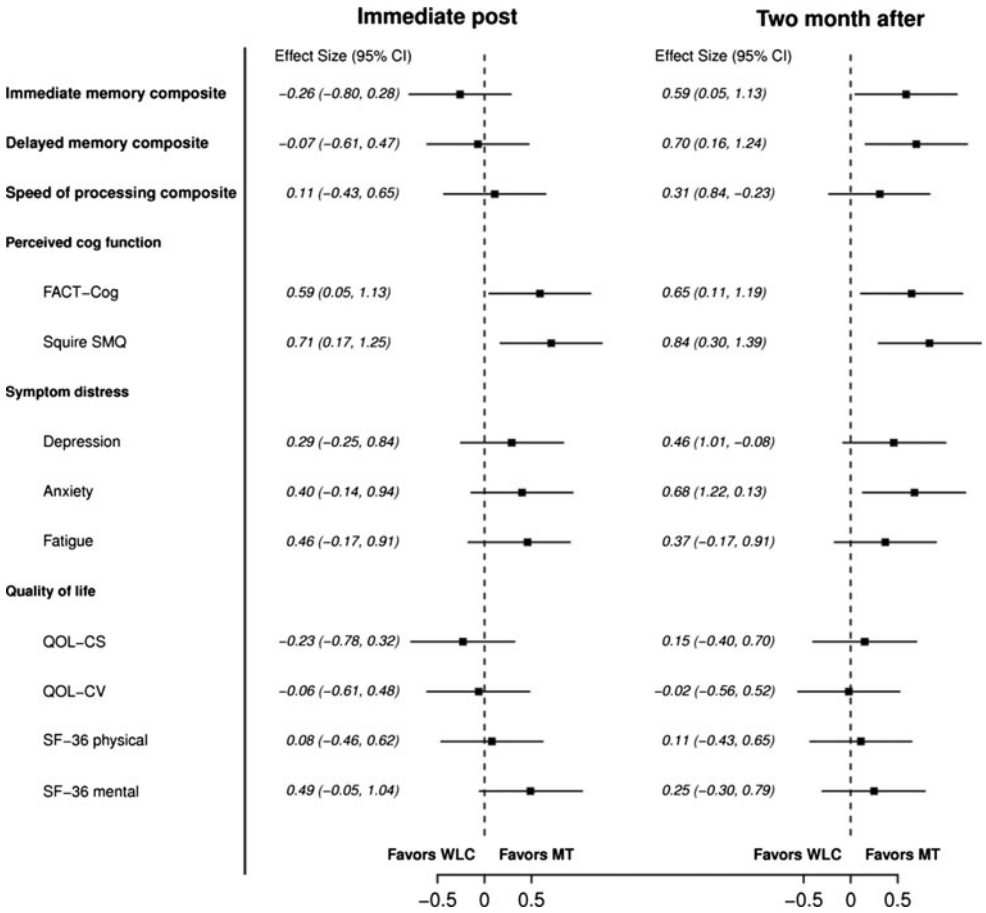

Fig. 2 Forest plot of effect sizes and confidence intervals for memory training compared to wait-list control at both time points

memory performance and speed of processing improved processing speed. There was significant improvement in immediate and delayed memory in the memory training group at the 2-month follow-up. Unlike other cognitive studies [10, 11], the memory training intervention did not demonstrate significant effects post-intervention. However,

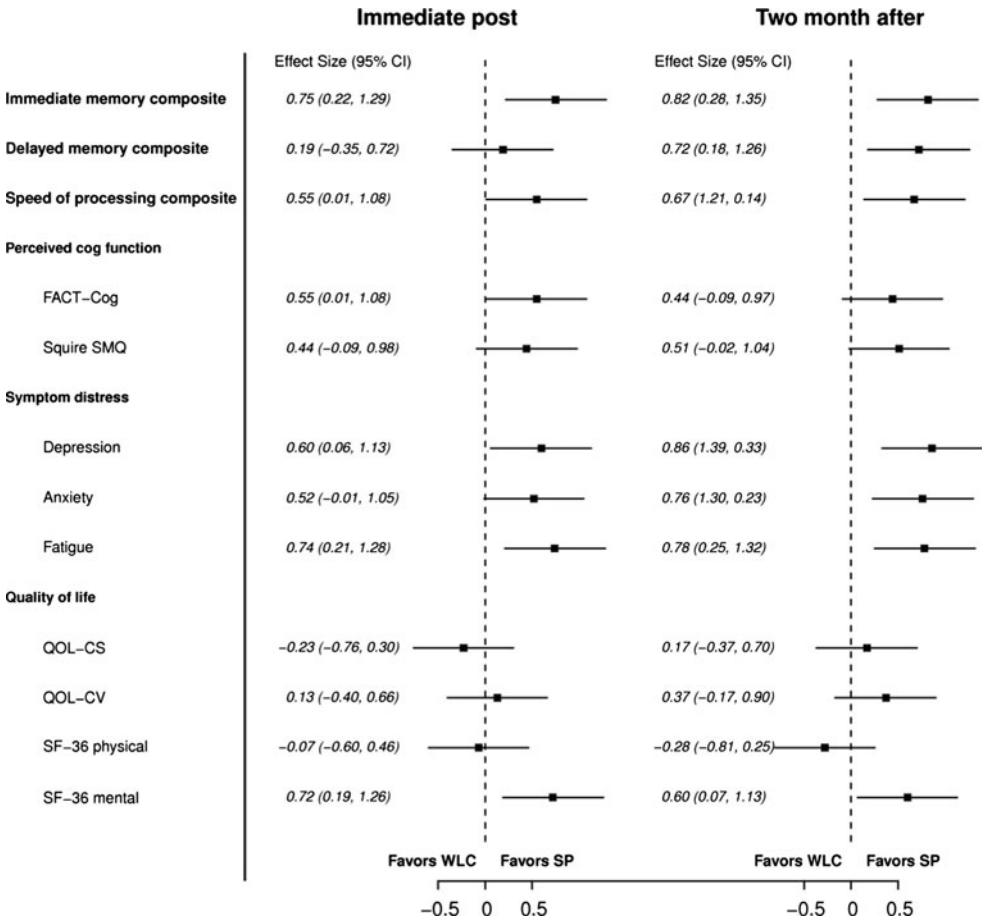

Fig. 3 Forest plot of effect sizes and confidence intervals for speed of processing training compared to wait-list control at both time points

the percentage of participants demonstrating reliable improvement in immediate memory was comparable to the ACTIVE trial (23 vs. 26 %) [10].

Speed of processing training had significant positive effects on processing speed at both post-intervention time points. In addition, the speed of processing training improved immediate memory performance at both time points and delayed memory at the 2-month follow-up. The InSight program (Posit Science®), originally developed as part of the ACTIVE trial, was revised to include tasks which appear to have resulted in benefits in memory performance. The revised program includes enhanced gaming elements and four additional programs designed to not only improve visual processing speed but also improve attention, learning and memory. In addition, this program now includes game elements that are specifically designed to enhance the level of enjoyment and maximize usage and engagement of the program. Based on the results from the ACTIVE trial, we predicted that this program would significantly improve processing speed and are now encouraged by the significant improvement noted in memory performance. These findings suggest that the InSight program may have broader cognitive benefits in this clinical population.

Notably, for both intervention groups, training effects on objective tests did not wane between the immediate and 2-month post-intervention testing. In fact, training effects actually improved in the memory training group, with increases in number of participants demonstrating reliable improvement (23–39 %). One explanation may be that the participants continued to engage in study-related training and improved their skills over time. For the speed of processing group, who did not have access to the training materials, this finding indicates that the training effect was durable over this period, negating the need for booster training prior to 2-month follow-up. Similar findings were noted in a recent meta-analysis of cognitive training interventions, which found that 4 of 7 studies demonstrated significant positive training effects with follow-up periods ranging from 3 months to 5 years [36].

Importantly, intervention effects transferred to clinically significant improvements in perceived cognitive function, symptom distress (mood disturbance, anxiety, and fatigue), and quality of life. Transfer effects to measures of improved perceived cognitive performance and health is of great importance in this younger, active population of breast cancer survivor. Findings from our previous work and others indicate the detrimental impact of perceived

Table 3 Training effects on secondary outcomes post and 2-month follow-up

Measure	Memory training			Speed of processing training			Wait-list control
	Mean (SD)	Net effect size (p value)*	95 % Confidence interval	Mean (SD)	Net effect size (p value)*	95 % Confidence interval	Mean (SD)
FACT-COG							
Post	93.86 (15.54)	0.59 ($p = 0.036$)	0.05, 1.13	93.21 (15.50)	0.55 ($p = 0.042$)	0.01, 1.08	84.82 (15.80)
2-month	98.17 (15.34)	0.65 ($p = 0.021$)	0.11, 1.19	94.98 (15.29)	0.44	−0.09, 0.97	88.32 (15.59)
Squire							
Post	83.58 (15.59)	0.71 ($p = 0.012$)	0.17, 1.25	79.51 (15.54)	0.44	−0.09, 0.98	72.69 (15.83)
2-month	86.47 (13.54)	0.84 ($p = 0.003$)	0.30, 1.39	81.95 (13.48)	0.51($p = 0.065$)	−0.02, 1.04	75.15 (13.74)
CES-D							
Post	9.69 (7.47)	−0.29	−0.25, 0.84	10.39 (8.56)	−0.60 ($p = 0.031$)	0.06, 1.13	15.00 (12.37)
2-month	7.88 (5.40)	−0.46	1.01,−0.08	7.85 (7.16)	−0.86 ($p = 0.002$)	1.39, 0.33	13.79 (11.60)
STAI-S							
Post	31.96 (8.10)	−0.40	−0.14, 0.94	33.78 (8.32)	−0.52 ($p = 0.059$)	−0.01, 1.05	37.07 (11.09)
2-month	30.15 (6.97)	−0.68 ($p = 0.017$)	1.22, 0.13	32.15 (7.46)	−0.76 ($p = 0.006$)	1.30, 0.23	36.97 (11.01)
FACT-F							
Post	40.20 (9.22)	0.46	−0.17, 0.91	39.26 (8.90)	0.74 ($p = 0.008$)	0.21, 1.26	35.07 (12.07)
2-month	40.06 (9.93)	0.37	−0.17, 0.91	39.56 (8.96)	0.78 ($p = 0.005$)	0.25, 1.32	35.55 (12.56)
QOL-CS							
Post	6.54 (1.29)	−0.23	−0.78, 0.32	6.55 (0.61)	−0.23	−0.76, 0.30	6.73 (0.59)
2-month	6.02 (1.32)	0.15	−0.40, 0.70	6.69 (0.63)	0.17	−0.37, 0.70	6.88 (1.12)
QOL-CV							
Post	22.06 (3.44)	−0.06	−0.61, 0.48	22.98 (2.08)	0.13	−0.40, 0.66	23.38 (2.24)
2-month	22.15 (4.45)	−0.02	−0.56, 0.52	22.71 (2.08)	0.37	−0.17, 0.90	22.58 (2.24)
SF-36-physical							
Post	45.71 (5.98)	0.08	−0.46, 0.62	44.69 (4.40)	−0.07	−0.60, 0.46	43.18 (4.72)
2-month	45.03 (6.17)	0.11	−0.43, 0.65	45.00 (4.48)	−0.28	−0.81, 0.25	44.49 (4.81)
SF-36-Mental							
Post	45.33 (5.98)	0.49 ($p = 0.078$)	−0.05, 1.04	47.33 (5.10)	0.72 ($p = 0.010$)	0.19, 1.26	48.09 (5.03)
2-month	44.91 (6.82)	0.25	−0.30, 0.79	43.67 (5.21)	0.60 ($p = 0.031$)	0.07, 1.13	45.11 (5.13)

Post-test represents immediate post-intervention, 2-month represents 2-month follow-up

FACT-C Functional Assessment of Cancer Therapy-Cognitive, *SSMQ* Squire Subjective Memory Questionnaire, *CES-D* Center for Epidemiological Studies Scale, *STAI-S* State-Trait Anxiety Inventory-State Subscale, *FACT-F* Functional Assessment of Cancer Therapy-Fatigue, *QOL-CS* Quality of Life-Cancer Survivors, *QOL-CV* Quality of Life Index-Cancer Version, *SF-36* Short-Form Health Survey

* Only p values <0.08 reported

cognitive impairment on quality of life [6, 7] and work ability [37–39]; thus, development and validation of effective interventions are paramount.

Methodological strengths of the study include the blinding of participants and cognitive testers, use of alternate forms, and composite test scores to measure overall ability versus scores on individual tests [16] and examination of those demonstrating reliable improvement. The attrition rate was equivalent across intervention groups and comparable to other cognitive training studies in breast cancer survivor [14]. Both interventions were also rated as highly satisfactory/acceptable.

Limitations of the study include lack of a demographically more diverse population for generalizability and lack of a longer follow-up period to determine the need for or possible timing of booster training. In addition, positive outcomes may be due in part to social contact contributions such as support received within the training groups from the interventionist and/or other breast cancer survivors. While the threat of social contact contributions on objectively measured cognitive abilities is unlikely and was not demonstrated in the original ACTIVE trial [10, 11], future planned research will include an active attention control condition to address this concern.

Conclusion

Memory training and speed of processing training are promising treatment options for breast cancer survivors with self-reported cognitive concerns. The interventions tested here showed preliminary efficacy on primary domain-specific tests. Speed of processing training also had positive effects on memory performance which warrant further study. Importantly, both interventions also had transfer effects on specific self-reported measures of cognitive function, symptom distress, and quality of life which impact individual functioning and well-being. In addition, both interventions were highly satisfactory/acceptable to breast cancer survivors. These pilot study findings point to the importance of full-scale efficacy testing of these interventions in a larger, more diverse sample of breast cancer survivors, and possibly other cancer survivors.

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Conflict of interest The authors declare that they have no conflict of interest. Posit Science Corporation is the developer of the speed of processing (Insight®) program used in this study. Posit Science Corporation holds the patent for and a proprietary interest in this software. The software was provided at cost of the CD by Posit Science. Dr. Karlene Ball is on the Board of Directors of Posit Science and has stock in the company. Dr. Unverzagt has received support for training for an investigator initiated research from Posit Science.

Ethical approval This study was conducted in accordance with all laws of the United States and the study was approved by the Indiana University Simon Cancer Center Scientific Review Group and Institutional Review Board in which was conducted.

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