Web-Based Cognitive Rehabilitation for Survivors of Adult Cancer: A Randomised Controlled Trial

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Running Head: WEB-BASED COGNITIVE REHABILITATION FOR CANCER

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Ethical Standards:

This research project complies with the ethical standards of the Human Research Ethics Committee at Griffith University (PSY/F4/14/HREC) and was conducted in accordance with the Helsinki Declaration

Keywords: Cancer, oncology, adult, survivors, cognitive rehabilitation, web-based, online.

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Abstract

Objective: Cognitive dysfunction associated with cancer is frequently reported and can reduce quality of life. This study evaluated a web-based cognitive rehabilitation therapy program (eReCog) in cancer survivors compared to a waitlist control group.

Methods: Adult cancer survivors with self-reported cognitive symptoms who had completed primary treatment at least 6 months prior were recruited. Participants completed telephone screening and were randomly allocated to the 4-week online intervention or waitlist. Primary outcome was perceived cognitive impairment assessed with the Functional Assessment of Cancer Therapy – Cognitive Function version 3. Secondary outcomes were additional measures of subjective cognitive functioning, objective cognitive functioning and psychosocial variables.

Results: 76 women were allocated to the intervention ($n=40$) or waitlist ($n=36$). A significant interaction was found on the instrumental activities of daily living measure of self-reported prospective memory whereby the intervention group reported a greater reduction in prospective memory failures than the waitlist group. Interaction trends were noted on Perceived Cognitive Impairments ($p=.089$) and Executive Functioning ($p=.074$). No significant interactions were observed on other measures of objective cognitive functioning or psychosocial variables.

Conclusions: The web-based intervention shows promise for improving self-reported cognitive functioning in adult cancer survivors. Further research is warranted to better understand the mechanisms by which the intervention might contribute to improved self-reported cognition.

Background

Advances in cancer treatments have led to improved survival rates, but adverse effects of diagnosis and treatment can impact quality of life. Cancer-related cognitive impairment (CRCI) is frequently reported by patients and has been well documented.^{1,2} Up to 30% of cancer patients experience CRCI before beginning treatment; as many as 75% experience cognitive dysfunction during treatment; and up to 35% experience long-term CRCI after treatment completion.^{1,3} CRCI impacts vary from subtle to pronounced, interim to permanent, and stable to progressive⁴ and can involve cognitive domains including memory, attention, processing speed, motor function, and executive functioning.^{3,5}

Many cancer survivors are unprepared for CRCI and coping with poor memory and attention has been identified as a primary “unmet need” in survivorship care.⁶ Research has demonstrated that self-reported cognitive impairment is often associated with increased psychological distress, fatigue, and poorer quality of life (QoL),^{7,8} and this impairment generally correlates poorly with performance on standardised neuropsychological measures.⁹ Therefore, assessing both subjective and objective CRCI is advisable.

Cognitive rehabilitation has the potential to mitigate symptoms of objective and self-reported CRCI. Several randomised controlled trials have been published with reported benefits of such intervention programs for cancer survivors.¹⁰⁻¹³ The terms “cognitive rehabilitation” and “cognitive training” are often used interchangeably, which masks important conceptual differences between them. Cognitive training (CT) is a behavioural method of treatment based on models of neuroplasticity, which suggest that cognitive abilities can be improved by progressive drills that exercise the brain.^{14,15} In contrast, cognitive rehabilitation therapy (CRT) is the process of re-attaining cognitive skills that have been lost or altered due to injury whereby the goal of treatment is to improve functioning on everyday tasks.¹⁶ CRT incorporates psychoeducation, skills training, strategy training, and functional activity training to apply the strategies in everyday life.

Web-based interventions in this area have been scarce. There are no published studies evaluating online CRT in cancer survivors and only three online CT interventions. Kesler and colleagues conducted an RCT with 41 breast cancer survivors, 21 of whom received web-based CT four times per week for 12 weeks. Improved objective executive functioning, processing speed, and verbal fluency; and improved subjective executive functioning skills; were reported in the treatment group post intervention.¹⁴ In another study, Damholdt and colleagues recruited 157 breast cancer survivors and randomly allocated 94 to web-based CT with email support (eCogT) compared to waitlist. They reported no significant group

differences on primary or secondary outcome measures of working memory and perceived cognitive functioning, but found significant improvements for verbal learning and another working memory test in the *eCogT* group at follow-up.¹⁷ Most recently Bray and colleagues conducted an RCT with 242 adult cancer survivors, 121 of whom were assigned to CT with a recommended four 40-minute sessions per week for 15 weeks. They reported significantly less perceived cognitive impairment (PCI), and reduced psychological distress and fatigue at post-intervention and follow-up in the intervention group.¹⁸

The objective of our study was to evaluate the efficacy of a web-based CRT program called *eReCog*. The program was adapted from the face-to-face Responding to Cognitive Concerns (ReCog) intervention and piloted with small samples of cancer survivors and community dwelling adults with beneficial results.¹⁹ The main hypothesis was that participants in *eReCog* would improve more on self-reported cognition compared to a waitlist control group at post-intervention and follow-up. Objective cognition; psychosocial variables of distress, quality of life, illness perception, and fatigue; and program satisfaction were assessed as secondary outcomes relevant to this population.^{12,20,21}

Methods

Intervention

Responding to Cognitive Concerns (ReCog) was developed as a manualised face-to-face, 4-session, group intervention to address cognitive dysfunction in cancer survivors.^{12,21,22} This intervention was adapted into a web-based version (*eReCog*). Its development process and piloting trial are described elsewhere.¹⁹ Based on the principles of cognitive behavioural therapy, the program contains four modules, each including psychoeducation, relaxation, strategy training, discussion questions that allow viewing of others' anonymised responses, and homework.²³ Modules take approximately 30 to 60 minutes and participants are expected to complete one module per week over four weeks. Module topics are (1) Aging, health, cancer and cognitive function, (2) Memory, (3) Attention, and (4) Fatigue, emotions, and cognition.

Participants

Sixty-five participants were sought, based on *a priori* power analysis demonstrating 80% power for detecting small-to-moderate interaction effects^{12,21} at $\alpha=.05$, with an additional 20% (11 participants) added to allow for attrition. Seventy-six participants were eligible and randomly allocated to intervention ($n=40$) or waitlist ($n=36$). Eligibility criteria were: diagnosed with adult-onset cancer excluding central nervous system tumours, aged 18+

years, reported cognitive complaints with memory or concentration, completed primary treatment at least 6 months prior (excluding hormonal treatment, which could be ongoing), were disease-free at the time of enrolment, and able to read and write English fluently. Exclusion criteria were: currently undergoing primary treatment, history of traumatic brain injury or neurological disorder, poorly managed anxiety or depression, or insufficient English skills.

Procedure

The study was approved by Griffith University's ethics committee and preregistered at www.ANZCTR.org.au (ACTRN12615000878572). Individuals were recruited through emails sent to Breast Cancer Network Australia and Griffith University staff and students from March to June 2016. Group allocation was determined via computerised random number generation. Volunteers were allocated to a group upon receiving their initial email expressing interest. During subsequent eligibility screening conducted via telephone by the first author, sociodemographic and medical data were collected. Cognitive complaints were evaluated using the two-item cognitive functioning scale of the European Organisation for Research and Treatment of Cancer – Core Quality of Life Questionnaire (EORTC-QLQ-C30).²⁴ Volunteers answered item #20, “have you had difficulty in concentrating on things, like reading a newspaper or watching television?” and item #25, “have you had difficulty remembering things?” Possible responses were 1=*not at all*, 2=*a little*, 3=*quite a bit*, and 4=*very much*. Eligible volunteers scored 2 or more on either item and believed these impairments were associated with their cancer experience. Volunteers on medication for anxiety or depression were asked whether they believed their symptoms were adequately managed with current treatment.

Eligible participants were informed of group allocation and were requested to confirm consent via email. Upon receiving written consent, participants were emailed links to complete the first assessment (baseline). Intervention participants then completed *eReCog* and control participants underwent a 4-week waiting period. Participants were reassessed after the intervention or wait period (post-treatment) and completed a follow-up assessment after a further 3 months. After the 3-month follow-up assessment, participants in the waitlist group could choose to complete the intervention.

Email Delivery and Support

Links to WebNeuro assessment,²⁵ questionnaires via Qualtrics Software (2013; Qualtrics, Provo, UT, USA), and program modules via LessonLAMS (2002; LAMS International) were emailed to participants for online completion. Reminder emails were sent approximately 5 days later if the task was uncompleted. Progression through the modules was tracked to ensure participants completed each module before being sent the next module. After 3 reminder emails with no response, participants were contacted via telephone or assumed to withdraw. Encouragement emails were sent to participants after completing Module 1 with individualised feedback on the goal-setting activity. Additional email support was available for questions regarding content or technical problems.

Measures

Subjective cognitive functioning

Functional Assessment of Cancer Therapy – Cognitive Scale (FACT-Cog-3). This 37-item measure assesses memory, concentration, language, and thinking abilities in cancer patients.²⁶ It contains four subscales: PCI, Perceived Cognitive Abilities (PCA), Comments from Others (OTH), and Impact on Quality of Life (QOL). As recommended, PCI was used as the primary measure of subjective cognitive functioning.²⁶

Brief Assessment of Prospective Memory (BAPM). This 16-item self-report measure was designed to evaluate frequency of prospective memory failures in individuals with brain injury.²⁷ Prospective memory is the ability to remember to complete intended actions in the future despite everyday distractions.²⁸ Eight items comprise the instrumental activities of daily living (IADL) subscale, which assesses common memory lapses such as household and financial management tasks, and 8 items comprise the basic activities of daily living (BADL) subscale assessing uncommon forgetting such as dressing and eating. The mean score for answered items (1 to 5 response scale) is calculated for each subscale. The measure has demonstrated sensitivity in breast cancer survivors.²⁹

Objective cognitive functioning

The online test battery WebNeuro comprises 11 computerised tasks assessing seven cognitive domains: verbal memory, working memory, attention, response speed, information processing efficiency, executive functioning, and impulsivity.²⁵ Online WebNeuro was validated against the computerised IntegNeuro battery,³⁰ which demonstrated convergent and divergent validity with standardised paper-and-pencil neuropsychological tests including

Digit Span (Wechsler Adult Intelligence Scale III), Spatial Span (Wechsler Memory Scale III), California Verbal Learning Test, Trail Making Test, Stroop Test, Finger Tapping Test, Rey Complex Figure Test and others.³¹ For each cognitive domain, individualised Z-scores adjusted for age, sex and education based on the developers' normative sample were calculated. Between 33 and 60 parallel forms are used for each task to reduce practice effects.³² Participants were instructed to complete the WebNeuro assessment in a single sitting of approximately 40 minutes, when unlikely to be interrupted.

Psychosocial variables

Kessler Psychological Distress Scale (K10). This 10-item self-report measure assesses levels of anxiety and depressive symptoms in the past 4 weeks.³³

Brief Illness Perception Questionnaire (BIPQ). Perceived threat of illness was assessed with an 8-item questionnaire. The term "illness" can be substituted with other relevant terms.³⁴ Here, "illness" was substituted with "cognitive difficulties", as previously examined with cancer survivors.¹²

Fatigue. Symptoms of fatigue were assessed with the 3-item EORTC-QLQ-C30 fatigue symptom scale.²⁴

Program satisfaction

Satisfaction was measured by intervention participants' ratings of: (1) satisfaction with the program, (2) change in cognitive functioning, and (3) likelihood of recommending the program to others on a 5-point Likert scale.^{12,21} They provided an overall program rating from 1 (*very poor*) to 10 (*excellent*) and were asked to comment on aspects of the program found most enjoyable, least enjoyable, or otherwise noteworthy.

Statistical Analyses

The main analyses used 2(Group) x 3(Time) repeated measures analyses of variance. No statistically significant differences between groups were present on outcome variables at baseline; therefore baseline scores were not used as a covariate. Imputation of missing 3-month follow-up scores was performed for 3 participants (2 waitlist; 1 intervention) by carrying forward their post-treatment scores. Since results did not differ with and without imputation, results included this imputed data. Where Mauchly's Test indicated violations to the sphericity assumption, the Huynh-Feldt correction was used. Within-group planned comparisons across time were computed. Within-group effect sizes (Cohen's *d*) were

calculated controlling for the correlation between the two means from baseline to post-treatment, and from baseline to 3-month follow-up.³⁵

Results

Descriptive Statistics

Seventy-one women enrolled and completed baseline assessments, including 37 assigned to *eReCog* and 34 assigned to waitlist (Figure 1). Thirty-one women in each group completed the 3-month follow-up assessments, indicating 16.2% attrition from intervention and 8.8% attrition from waitlist. Participants who withdrew were less likely to have had hormonal treatment, more likely to be unpartnered, and completed primary treatment longer ago on average ($M=97.78$, $SD=44.14$) than completers ($M=42.97$, $SD=37.79$).

Several of the demographic and outcome variables had skewed distributions. Variable transformations made no difference to the results, so analyses using raw data are reported. Intervention and waitlist groups did not differ at baseline on demographic and medical characteristics, which are presented in Table 1.

Insert Figure 1 about here.

Insert Table 1 about here.

Subjective Cognitive Functioning

Descriptive statistics for self-report measures are presented in Table 2. A significant interaction occurred on the prospective memory IADL subscale, $F(2,126)=3.80$, $p=.025$, $\eta^2=0.045$, because the intervention group reported a reduction in prospective memory failures at post-treatment, $F(1,31)=9.11$, $p=.005$, and 3-month follow-up, $F(1,31)=33.00$, $p<.001$, and the waitlist group a reduction at 3-month follow-up only, $F(1,32)=5.99$, $p=.020$.

An interaction trend was noted on the PCI, $F(2,109)=2.57$, $p=.089$. Mean improvements from baseline to follow-up were 8.9 for intervention and 5.6 for waitlist participants, compared to an estimated minimally important difference of 6.5 for this measure.¹⁸

Within-group comparisons found the intervention group reported an improvement in their perceived cognitive abilities post-intervention, $F(1,31)=11.79$, $p=.002$, $d=0.30$, and at 3-

month follow-up, $F(1,31)=8.24, p=.007, d=0.42$. The waitlist group reported improvement at 3-month follow-up only, $F(1,32)=5.00, p=.032, d=0.22$). Additionally, the intervention group reported their cognitive problems had less impact on their quality of life at post-treatment, $F(1,31)=8.39, p=.007, d=0.26$, and 3-month follow-up, $F(1,31)=9.37, p=.005, d=0.56$. The Waitlist group reported less impact on quality of life at 3-month follow-up only, $F(1,32)=4.59, p=.040, d=0.24$.

Insert Table 2 about here.

Objective Cognitive Functioning

No significant Group x Time interactions were found on domains of neuropsychological testing. A trend towards an interaction was noted for Executive Functioning, $F(2,112)=2.83, p=.063$. Within-group effects and effect sizes for each cognitive domain are shown in Table 3.

Insert Table 3 about here.

Psychosocial Variables

No interactions were found on psychosocial variables (Table 2). Intervention participants reported reduced fatigue at post-treatment, $F(1,31)=4.32, p=.046, d=-.27$, but this effect was not maintained at 3-month follow-up, $F(1,31)=0.19, p=.670, d=-.08$. No significant effects were found on measures of distress or illness perceptions.

Participant Satisfaction

Among intervention participants, 94% were “satisfied” or “very satisfied” and 6% were “neither satisfied nor dissatisfied”; 84% were “likely” or “very likely” to recommend the program; 68% reported their cognitive functioning had improved “a little” or “a lot”, whereas 32% reported “no change”. The mean rating of the program was 7.7/10 ranging from 5 (*average*) to 10 (*excellent*).

Discussion

This RCT aimed to evaluate the efficacy of eReCog in adult cancer survivors. We hypothesised that intervention participants would report improved subjective cognition compared to waitlist participants, a hypothesis that was partially supported. A significant Group x Time interaction and two trends towards interactions were found, all representing greater improvements in the intervention than the waitlist group.

The primary outcome measure PCI demonstrated a trend towards an interaction ($p=.089$). The intervention group surpassed the minimally important difference of 6.5 points on this measure from baseline to 3-month follow-up, indicating clinically relevant reductions in their perceived cognitive impairment, whereas the waitlist group did not. Participants in this study reported fewer problems with their PCI at baseline than previous cancer cognitive rehabilitation studies.^{12,18,21,36,37} Having more stringent inclusion criteria (e.g., reporting “quite a bit” of difficulty with memory or concentration) might have resulted in a more impaired sample allowing for greater improvement. Notwithstanding, baseline PCI scores in this study were still lower than non-cancer comparison groups, and their follow-up scores, although improved, remained below baseline scores for healthy individuals.^{12,19}

Improved PCI on the FACT-Cog-3 was observed in both groups, similar to previous research with cancer survivors. King and Green’s RCT utilising the ReCog intervention¹² showed 73% of intervention and 50% of waitlist participants demonstrated clinically significant improvement on PCI at follow-up. The authors suggested the improvements in the waitlist group might have resulted from increased awareness and improved perceptions of their cognitive functioning due to assessment sessions. These researchers also reported similar improvements on other FACT-Cog-3 subscales for both intervention and waitlist groups, which was seen in the current study on both PCA and QOL subscales.

The interaction on the IADL subscale assessing prospective memory failures was significant. In general terms, it is believed that when people refer to “poor memory” they are referring to prospective memory failures³⁸. Only one other published cognitive rehabilitation study with cancer survivors has assessed prospective remembering,¹² although failures in this cognitive domain have been reported in chemotherapy-treated breast cancer survivors compared to healthy participants.²⁹ This type of impairment is likely to be noticed on everyday activities and potentially provides an acceptable measure of memory functioning on daily tasks. Despite both groups reporting reduced prospective memory failures, the effect size was larger for intervention than waitlist participants at the 3-month follow-up (difference

in $d=.36$). This effect may be due to the successful implementation of memory strategies learnt in *eReCog*, which is designed to help improve daily functioning on everyday tasks.

Improved self-reported cognitive functioning in this study may also be explained by the similarity of the computerised WebNeuro assessment to typical cognitive training programs. Although no significant interaction effects were observed on objective cognitive functioning domains, participants reported that WebNeuro was comparable to other “brain training” programs trialled. Evidence suggests placebo effects can occur in cognitive interventions when participants know the intended outcome.³⁹ For example, Foroughi and colleagues³⁹ intentionally created a placebo effect by using suggestive flyers advertising “Brain Training and Cognitive Enhancement” versus a control flyer “Email Today and Participate in a Study”. The placebo participants showed improvements after a single 1-hour cognitive training session whereas the nonsuggestive flyer group showed no improvements. Recruitment materials for the current study advised prospective participants they would have the opportunity to participate in “a 4-week online interactive program, which aims to improve cancer-related cognitive issues such as memory and concentration”. Participant expectations to receive an intervention coupled with the similarity of WebNeuro assessments to cognitive training may have influenced self-report measures of cognition in both groups.

Strengths and limitations

Strengths in the study include that it is the first known RCT to evaluate an online CRT program (*eReCog*) in cancer survivors. The intervention was adapted from its face-to-face counterpart (*ReCog*), and the results presented here provide preliminary evidence that online cognitive rehabilitation interventions translated from face-to-face format can be effective. Another strength to our study was the utilisation of a comprehensive assessment battery to evaluate subjective and objective cognitive function, as well as psychosocial variables typically reported as problematic in this clinical group.

There are some limitations to note. No published studies have used WebNeuro to measure cognitive functioning in adult cancer survivors and further investigation into its appropriateness for this purpose seems warranted. Participants completed the WebNeuro assessments in an uncontrolled environment (e.g., home); therefore performance on tasks is susceptible to unknown influences (e.g., telephone interruptions). In addition, recruitment predominantly occurring through a breast cancer organisation resulted in a sample that was 100% female and 98.5% survivors of breast cancer, limiting the generalisation of findings to males and survivors of other types of cancer. Statistical significance and trends should be

interpreted with caution as multiple comparisons were conducted in this study; descriptive statistics and effect sizes provide further interpretative information.

Clinical implications

The web-based cognitive rehabilitation program *eReCog* shows some promise for improving subjective cognitive functioning and possibly objective cognitive functioning in female adult cancer survivors. Many improvements were found in the waitlist group also, but effect sizes tended to be larger for intervention than waitlist. Development of online cognitive remediation interventions has the potential to provide accessible supportive care to alleviate cognitive symptoms in cancer survivors, particularly those living in smaller communities or with limited mobility.

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Table 1. Baseline demographic and medical characteristics.

Variables	Intervention (n=32)	Waitlist (n=33)
Demographic		
Age [Mean(SD)]	55.1 (9.2)	56.9 (9.2)
Education [Mean(SD)]	15.3 (2.6)	15.1 (2.9)
Female	100.0%	100.0%
Born in Australia	81.3%	81.8%
First Language English	93.8%	97.0%
Living with partner	65.6%	81.8%
State or Territory		
New South Wales	43.8%	42.4%
Other	56.2%	57.6%
Medical		
Cancer Type		
Breast	96.9%	100.0%
Leukaemia	3.1%	0.0%
Treatment		
Surgery	100.0%	100.0%
Chemotherapy	87.5%	81.8%
Radiotherapy	68.8%	66.7%
Hormone Therapy	84.4%	93.9%
Current Hormone Therapy	68.8%	63.6%
Years since primary treatment [Mean(SD)]	3.4 (2.7)	4.1 (3.7)

Table 2. Descriptive statistics and effect sizes for self-report measures.

Measure (Range)	Intervention (n=32)					Waitlist (n=33)					Interaction	
	T1	T2	T3	T2 <i>d</i>	T3 <i>d</i>	T1	T2	T3	T2 <i>d</i>	T3 <i>d</i>		(<i>p</i>)
<i>FACT-Cog-3</i>												
PCI (0-72)	41.6(15.4)	44.1(14.8)	50.5(12.7)***	0.17	0.62	42.5(16.0)	46.2(14.1)**	48.2(15.0)**	0.24	0.37		.089
PCA (0-28)	15.6(5.4)	17.2(4.9)**	18.0(5.7)**	0.30	0.42	17.3(5.9)	17.8(6.4)	18.5(5.5)*	0.09	0.22		.369
OTH (0-16)	14.9(1.9)	14.6(2.4)	15.6(1.7)	0.11	0.21	14.1(3.0)	14.2(2.9)	14.7(1.8)	0.02	0.21		.775
QOL (0-16)	11.9(4.4)	13.1(3.0)**	14.1(2.6)**	0.26	0.56	11.5(3.6)	12.1(3.4)	12.3(3.6)*	0.18	0.24		.170
<i>Prospective Memory</i>												
IADL (0-5)	2.05(0.58)	1.78(0.46)**	1.67(0.52)***	-0.52	-0.68	1.83(0.52)	1.79(0.53)	1.66(0.50)*	-0.07	-0.32		.025
BADL (0-5)	1.28(0.26)	1.19(0.34)*	1.18(0.29)*	-0.29	-0.36	1.33(0.34)	1.31(0.39)	1.25(0.25)	-0.05	-0.26		.450
<i>EORTC-QLQ</i>												
Cog Scale (0-100)	64.1(23.6)	70.8(18.0)*	71.9(20.9)	0.31	0.35	65.7(23.9)	73.2(21.1)**	73.2(19.5)**	0.33	0.34		.964
<i>Psychosocial</i>												
Fatigue (0-100)	31.9(19.5)	27.1(15.7)*	30.6(17.4)	-0.27	-0.08	39.4(20.0)	35.7(18.0)	35.7(21.1)	-0.19	-0.18		.532
Distress (10-50)	16.3(6.1)	16.3(6.5)	16.4(6.6)	-0.01	0.02	18.0(6.4)	18.1(6.1)	17.5(5.2)	0.02	-0.07		.738
BIPQ (0-80)	39.0(11.9)	39.7(11.4)	36.8(10.7)	0.06	-0.19	39.8(12.2)	41.7(12.1)	39.5(10.7)	0.16	-0.02		.631

Note: * $p < .05$, ** $p < .01$, *** $p < .001$ for within group comparisons to Time 1. Mean(SD) and possible ranges are shown. T1=Baseline; T2=Post-treatment; T3=3-month follow-up. FACT-Cog-3=Functional Assessment of Cancer Therapy-Cognitive Scale; PCI=Perceived Cognitive Impairment; PCA=Perceived Cognitive Abilities; OTH=Comments from Others; QOL=Impact on Quality of Life; IADL=Instrumental Activities of Daily Living; BADL=Basic Activities of Daily Living; EORTC-QLQ=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; BIPQ=Brief Illness Perceptions Questionnaire. Lower scores indicate better functioning on IADL, BADL, fatigue, distress, and BIPQ. T2 *d*=within-group effect sizes from baseline to post-treatment. T3 *d*= within-group effect sizes from baseline to follow-up.

Table 3. Descriptive statistics and effect sizes for neuropsychological tests.

Domain	Intervention (<i>n</i> =32)					Waitlist (<i>n</i> =33)					Interaction (<i>p</i>)
	T1	T2	T3	T2 <i>d</i>	T3 <i>d</i>	T1	T2	T3	T2 <i>d</i>	T3 <i>d</i>	
Verbal Memory	0.07(0.71)	0.02(0.66)	-0.38(1.17)*	-0.08	-0.45	-0.07(0.73)	-0.51(1.48)	-0.83(1.44)***	-0.35	-0.61	.309
Working Memory	-0.34(1.04)	-0.35(1.08)	-0.37(1.15)	-0.01	-0.03	-0.60(1.10)	-0.51(0.70)	-0.35(1.08)	0.09	0.23	.704
Attention	-0.24(0.80)	-0.15(0.85)	-0.19(0.73)	0.11	0.07	-0.15(0.80)	-0.19(0.63)	-0.21(0.73)	-0.05	-0.07	.341
InfoProcessing	0.09(0.55)	-0.09(0.66)*	0.02(0.58)	-0.29	-0.12	0.01(0.62)	-0.11(0.81)	-0.26(0.58)**	-0.15	-0.45	.139
Executive Function	-0.20(0.66)	0.54(0.69)***	0.43(0.73)***	1.09	0.90	0.04(0.63)	0.36(0.68)**	0.45(0.90)**	0.49	0.51	.074
Response Speed	-0.03(1.12)	-0.19(1.20)	-0.12(0.85)	-0.13	-0.08	-0.37(1.46)	-0.05(1.12)	-0.03(1.02)	0.24	0.26	.247
Impulsivity	-0.46(0.41)	-0.23(0.41)*	-0.24(0.29)*	0.56	0.61	-0.29(0.42)	-0.23(0.49)	-0.25(0.47)	0.13	0.08	.211

Note: **p*<.05, ***p*<.01, ****p*<.001 for within group comparisons to Time 1. Mean(SD) of Z-scores based on the developers' normative sample are reported. T1=Baseline; T2=Post-treatment; T3=3-month follow-up. T2 *d*=within-group effect sizes from baseline to post-treatment. T3 *d* = within-group effect sizes from baseline to follow-up.

Figure 1. Participant CONSORT flowchart.