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Moderators of Cognitive Therapy and Bright Light Therapy Effects on Depressive Symptoms in Patients with Breast Cancer

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Abstract

Background Cognitive therapy (CT) and bright light therapy (BLT) have been found to be effective to treat depressive symptoms in breast cancer patients. No study has investigated the baseline patients' characteristics that are associated with better outcomes with CT vs. BLT in this population. This study aimed to assess, in breast cancer patients, the moderating role of eight clinical variables on the effects of CT and BLT on depressive symptoms.

Methods This is a secondary analysis of a randomized controlled trial conducted in 59 women who received an 8-week CT or BLT and completed questionnaires evaluating depression and possible moderating variables.

Results Patients benefited more from BLT when they had no prior history of major depressive disorder, higher depression scores on the Hospital Anxiety and Depression Scale (HADS-D) at baseline, a greater initial preference for BLT, and when they received BLT during spring or summer. Patients benefited more from CT when they had a lower initial preference for receiving CT, higher depression scores on the HADS-D, and seasonal depressive symptoms.

Conclusions Although replication is needed, findings of this study suggest the existence of different profiles of patients more likely to benefit from CT and BLT.

Trial registration NCT01637103 https://clinicaltrials.gov/ct2/show/NCT01637103

Keywords Breast cancer · Cognitive therapy · Bright light therapy · Depressive symptoms · Moderator

Introduction

Depressive symptoms are common in breast cancer patients, in whom the prevalence of clinically significant depressive symptoms is up to 46% [1–5]. These rates appear to be at least twice as high as in women of the general population [6]. Depressive symptoms are associated with various negative consequences, such as increased suicide risk [7], lower adherence to cancer treatments [8], and increased healthcare expenditures [9–11]. In order to limit the negative impact of depressive symptoms on patients themselves and society, it is important to offer effective treatments.

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The efficacy of cognitive-behavioral therapy (CBT) in general, and cognitive therapy (CT) in particular, is well established to reduce depressive symptoms in the general population [12–14]. These interventions are the ones most frequently used in oncology [11, 15, 16] and their efficacy has also been demonstrated in this context [17–23]. There is also evidence from randomized controlled trials (RCT) supporting the efficacy of bright light therapy (BLT) to decrease depressive symptoms in the general population [24–27]. BLT typically consists of exposing oneself 30 min every morning to a box that projects a light source of at least 10,000 lux [28, 29]. Because some cancer patients may not have access or may not be willing to get involved in a psychotherapy, BLT appears as a relevant possible alternative. Other well-established treatments for depression in cancer patients exist (e.g., supportive therapy, psychoeducation), but the need to investigate the efficacy of less expensive interventions that require fewer professional resources has been raised [30]. Results of small-scale clinical trials found that BLT was helpful in preventing the deterioration of quality of life [31], fatigue [32], and desynchronization of circadian rhythms in a sample of breast cancer patients [33]. In another preliminary study conducted with cancer survivors, BLT was also found to reduce fatigue

[34] and to improve sleep [35]. However, these studies did not compare BLT effects to those of more established treatments for depression such as CT or CBT.

In the general population, an RCT showed no significant differences at posttreatment between CBT and BLT in reducing seasonal depressive symptoms [36–38]. More recently, our RCT compared the efficacy of CT and BLT to treat depressive symptoms in the context of breast cancer [39]. CT produced the largest reductions of depressive symptoms between pre- and posttreatment (*d*s between − 0.70 and − 1.60 across three depression measures), but BLT also led to moderate to large treatment effects (*d*s between − 0.40 and − 1.20). These results supported CT as the treatment of choice for breast cancer patients with significant depressive symptoms, but they suggested that BLT could be an acceptable alternative.

In order to better guide treatment selection, it would be relevant to identify patients' baseline characteristics that are associated with better outcomes with CBT (or CT) and BLT. In the general population, it has been found that CBT was more effective in reducing depressive symptoms when patients had higher treatment expectancies [40] and a higher preference for CBT [41, 42]. CBT's efficacy in decreasing depressive symptoms has also been found to be associated with the severity and chronicity of depressive symptoms [43–46]. However, the directions of these relationships are inconsistent across studies.

Since its introduction in the 1980s, BLT has been presented as particularly effective for seasonal depression, typically occurring during fall and winter, and atypical depressive symptoms, characterized by symptoms such as hypersomnia and increased appetite [29, 47–50]. However, very few studies have directly compared the efficacy of BLT among patients with or without these characteristics [51–53]. Some studies found that BLT was more effective to decrease seasonal than nonseasonal depressive symptoms [54, 55], while more recent findings suggest that BLT could be equally effective for both types of symptoms [53]. Thus, evidence is lacking to support the assertion that patients with seasonal and atypical depressive symptoms are more responsive to BLT. Nevertheless, in the general population, BLT has been found to be more effective in reducing depressive symptoms when patients had higher treatment expectancies [40], lower levels of depressive symptoms at baseline [52], and a fewer number of past depressive episodes [52, 56].

The goal of this study, conducted in women with nonmetastatic breast cancer, was to explore the moderating role of eight clinical variables on the effects of CT and BLT on depression levels. The moderating variables investigated were initial treatment expectancies (for CT vs. BLT), treatment preference matching, baseline depression severity, current or past history of a depressive disorder, season during treatment phase, and seasonality of depressive symptoms. Based on the available literature in the general population, it was hypothesized that patients would benefit more from CT when having greater preference and expectancies for this intervention. It was also postulated that BLT would be more efficacious in participants who had a lower level of depressive symptoms at baseline, no history of major depressive disorder, and higher expectancies towards BLT. Because of the inconsistencies or the absence of prior data on the possible role of other moderating variables investigated, no a priori hypothesis was stated for these.

Methods

This is a secondary analysis of an RCT conducted in 62 women with breast cancer. More details on the methodology are provided elsewhere [39].

Participants' Recruitment

Inclusion Criteria (1) diagnosis of non-metastatic breast cancer in the past 2 years; (2) score ≥ 7 on the depression subscale of the *Hospital Anxiety and Depression Scale* (HADS-D; [57]) or ≥ 14 on the *Beck Depression Inventory-II* [58]; (3) between 18 and 75 years old; and (4) able to read and understand French.

Exclusion criteria (1) received BLT in the past month or CBT for depression in the past year; (2) severe cognitive impairments (e.g., diagnosis of dementia or a score ≤ 23 on the *Mini-Mental State Examination* (MMSE; [59]); (3) severe psychiatric disorder (e.g., severe major depressive disorder; the exclusion of these patients was a requirement of our ethics' committee given that the RCT had a waiting-list control condition); (4) suicidal ideations with risk of acting out, or suicide attempt in the past 5 years; (5) initiation of a psychotropic medication or dosage change in the past month or expected during the intervention phase; (6) use of a photosensitive medication (e.g., imipramine); and (7) disease contraindicating BLT (e.g., severe cataracts, diabetes).

Recruitment Potential participants were recruited at the CHU de Québec-Université Laval, Quebec city, Canada, between November 2011 and February 2014. Women diagnosed with breast cancer received a letter, signed by their oncologist, inviting them to provide their written consent to be contacted by phone to assess their eligibility and explain the study. The study was approved by the research ethic's committee. Of the 2635 patients solicited to take part in this study, 743 agreed to be screened for depressive symptoms (28.2% of solicited patients), 120 were eligible (16.2% of patients screened), and 62 agreed to participate, thus giving a participation rate of 51.7% among eligible patients.

Study Design and Randomization

This study was a 3-arm RCT with an allocation ratio of 2.5:2.5:1: (1) CT ($n = 25$); (2) BLT ($n = 26$); and (3) waiting-list control group (WLC; $n = 11$). The group allocation was prepared by a statistician prior to study initiation using the SAS PROC PLAN procedure and was contained in individually sealed and opaque envelopes. Participants were stratified according to whether they had seasonal vs. nonseasonal depressive symptoms (see below). The research personnel was blind to the randomization sequence. The treatment phase lasted 8 weeks. WLC participants did not receive any intervention. A post-waiting evaluation was completed after 8 weeks, after which they were randomly reassigned to an 8-week CT or BLT. Study measures were administered again at posttreatment for this group, as well as at 3- and 6-month follow-ups for all groups. For the purpose of this study, only the pre- and posttreatment data of the CT and BLT groups, including data of WLC participants after they were reassigned to CT or BLT, were analyzed. After completing the post-waiting evaluation, 4 participants were reassigned to CT (final $n = 29$), 4 to BLT (final $n = 30$), and 3 dropped out before the second randomization, thus giving a sample size of 59 for this secondary analysis.

Measures

Outcome Measure

Depression The *Hospital Anxiety and Depression Scale* (HADS; [60]) is a 14-item questionnaire divided into two subscales of seven items each, assessing depressive (HADS-D) and anxiety symptoms. Only scores on the HADS-D are used in this report. The HADS has the advantage of not containing somatic items that may be confounded with symptoms of medical conditions. The 4-point Likert scale ranges from "0" to "3," and a score ≥ 7 on the HADS-D suggests a clinical level of depressive symptoms [57, 61]. The French-Canadian version has psychometric properties equivalent to those of the original English version [57].

Moderating Variables

Treatment Credibility and Preference Treatment credibility and expectancies for improvement with regard to CT and BLT were assessed using 5 items for each treatment that were adapted from Borkovec and Nau's scale [62]. Items were scored on a Likert scale ranging from "0" (*not at all*) to "10" (*a lot*). Treatment preference was assessed using one item that evaluated to what extent participants preferred receiving CT or BLT. They had to choose one answer between "CT - a lot," "CT – moderately," "CT - a little," "no preference," "BLT - a little," "BLT – moderately," or "BLT - a lot." A score between "3" and "− 3" was calculated according to the match obtained between the patient's treatment preference and the actual treatment randomization. A score of "3" represents the best matching (e.g., being assigned to CT and having responded "CT - a lot") and a score of "− 3" corresponds to the poorest matching (e.g., being assigned to CT and having responded "BLT - a lot"). This questionnaire was administered at the pretreatment evaluation, before opening the randomization envelope. To reduce a possible social desirability bias and to encourage participants to give their real opinion, they were instructed to place their completed questionnaire in a separated sealed envelope and were informed that their answers would not be communicated to people directly involved in the study.

Baseline Depression Severity The baseline HADS-D total score was investigated as a potential moderator of treatment efficacy.

Current Presence and Prior History of a Mood Disorder The *Structured Clinical Interview for DSM-IV* (SCID; [63]) was used to assess the presence and the severity of a current mood disorder (including major depressive disorder and dysthymia) and of a past major depressive disorder.

Season During Treatment Phase The season during which CT or BLT was received (spring or summer vs. fall or winter) was coded.

Seasonality of Depressive Symptoms The *Seasonal Pattern Assessment Questionnaire* (SPAQ; [49]) and the *Structured Interview Guide for the Hamilton Rating Scale for Depression - Seasonal Affective Disorder* (*SAD*) *Version* (SIGH-SAD; [64]) were used to categorize patients' depressive symptoms as seasonal or nonseasonal. Based on previous research [65–67], depressive symptoms were considered to be seasonal when the three SPAQ criteria were met, in combination with a score ≥ 5 on the atypical depressive symptoms subscale of the SIGH-SAD.

The three SPAQ criteria for determining depression seasonality are (1) having a total score of 11 or more on the six items assessing seasonal variations in sleep, social activities, mood, weight, appetite, and energy, which are rated from "0" (*no change*) to "4" (*extremely marked change*), for a total score ranging from 0 to 24; (2) having a score of "2" (*moderate*) or more on the item assessing the impact of seasonal variations on functioning; and (3) depressive symptoms recur approximatively during the same period each year. The SPAQ shows a good internal consistency ($\alpha = 0.81$) and a good concurrent validity with the *Inventory for Seasonal Variation* [68]. The SIGH-SAD is a structured interview that includes items from the *Hamilton Depression Rating Scale*

(HDRS; [69]) and 8 additional items assessing atypical depressive symptoms, such as hypersomnia and increased appetite. These items are rated between "0" and "2," "0" and "3," or "0" and "4," for a maximum total score of 26. All SIGH-SAD interviews were audio recorded and 43.0% of them (98/228) were listened to by a second evaluator for interrater agreement; the interrater agreement was excellent (86.7%). To limit interviewer biases, the evaluator was blind to the participants' experimental condition.

Procedure

Screening and Pretreatment Evaluation

Patients who returned their written consent were contacted for a phone screening, during which a research assistant briefly assessed the main eligibility criteria. The study goals and procedures were explained to potentially eligible patients. Those interested received by mail the pretreatment questionnaires. Within 2 weeks, a face-to-face clinical interview took place at the research center with a Ph.D. student in clinical psychology, during which patients gave their written informed consent to take part in the RCT. Then, missing data on questionnaires and sociodemographic and medical information were completed. Treatment expectancies and preference were then assessed. Finally, the eligibility was confirmed with the administration of the MMSE, the Scale for Suicide Ideation (SSI; [70]) and the SCID, and the assessment of depressive symptoms was completed with the SIGH-SAD. Based on the criteria described above, participants were categorized as having either seasonal or nonseasonal depressive symptoms, and the appropriate randomization envelope was opened to disclose the patients' experimental condition to which she was assigned.

Treatment Phase

Cognitive Therapy Cognitive therapy (CT) was administered individually by Ph.D. students in clinical psychology and involved eight weekly sessions of approximately 60 min. The treatment was manualized and the protocol was based on Beck's cognitive therapy for depression [71], which was slightly adapted to the context of cancer [23]. To ensure treatment integrity, therapists received weekly supervision from the second author, an experienced psychologist specialized in clinical psycho-oncology. Every CT session was prepared and conducted under her supervision, to ensure the respect of the CT protocol. All treatment sessions were audio recorded and 18% of them were rated by an independent licensed psychologist using the *Cognitive Therapy Scale Revised* [72]. All CTS-R scores were above the competence cutoff score of 3, with an average score of 4.4, corresponding to a "proficient" level.

Bright Light Therapy Participants assigned to bright light therapy (BLT) were instructed to expose themselves to a 10,000 lux light box (SADelite®; Northern Light Technologies, Montreal, Canada) 30 min, every morning, before 10:00 A.M. Participants were free to do their usual activities (e.g., reading, eating breakfast) while they were exposing themselves to the lamp, as long as the lamp remained at the height of their eyes, at a distance of 50 cm and at an angle allowing them to see the two fluorescent tubes. The light box was provided by our research team and delivered to the patients' homes, and was then retrieved after 8 weeks. To measure compliance, participants were asked to complete a daily log of start and end times of each exposure session. Participants were contacted by phone every 2 weeks to maximize adherence to the BLT and the daily log, and to track a possible increase in depressive symptoms that would need an immediate clinical attention (i.e., suicidal ideations with a risk of acting out or a HADS-D score ≥ 15; this situation occurred with one participant, who was referred to an appropriate resource). The average percentage of self-reported BLT adherence (number of days of exposure/number of days of exposure expected) was 86.9% and the average daily exposure to BLT was 26.1 min. Only 3 participants had an adherence rate of less than 80%.

Posttreatment Evaluations

After the treatment phase, the same battery of questionnaires was administered. Participants were asked to complete and send back the measures within 2 weeks, after which, a phone call was made to complete missing data and document medical information. Missing data were not frequent, and, when they occurred, the interviewer asked the patient to refer to how they felt at the moment when they initially completed the questionnaire.

Statistical Analyses

Raw data were entered twice by independent research assistants and were compared to ensure maximal integrity. No missing data imputation was performed. Data were analyzed using an intent-to-treat framework. Thus, all participants who completed the pretreatment evaluation were included in the analyses. Because of their robustness to missing data, mixed model analyses were used. SPSS 13.0 [73] was employed to conduct descriptive statistics and SAS 9.3 [74] was used for inferential analyses. The alpha level was set at 5% (two-tailed) for all inferential tests.

To determine the sample size for the main study, sensitivity power analyses were performed with G*Power 3.1 [75] using standard conditions (alpha = 5%, power = 80%), a sample size of $n = 60$, 2 time points (pre- and posttreatment), and an expected dropout rate of 10%. Under these conditions, an effect size of $d = 0.27$ could be detected between CT and BLT. Based on previous findings comparing CBT and BLT in the general population (e.g., [38]), this sample size was expected to be sufficient to detect significant between-group differences.

To investigate the potential moderators of pre- to posttreatment changes on the outcome measure (HADS-D) in CT and BLT patients, a third order condition X moderator X time interaction was added as a fixed effect to the mixed model analyses, which already included the condition, time, and moderator main effects, as well as their second-order interactions, and a random intercept to control for participant variance. The third-order interaction was systematically decomposed using simple effects to estimate temporal change within condition for each moderator level. Given that this measure is independent of the sample size, contrary to *p*-values, the emphasis was put on Cohen's *d* effect sizes calculated for each test. The following variables were analyzed as potential moderators: CT expectancies and credibility, BLT expectancies and credibility, treatment preference matching score, baseline HADS-D score, current depressive disorder, past major depressive disorder, season during which the intervention was received, and seasonality of depressive symptoms. All continuous potential moderating variables were dichotomized to create two distinct and meaningful categories (using published cutoff scores; i.e., baseline HADS-D score) or according to the sampling distribution of the moderating variable (using median split; i.e., CT and BLT expectancies).

Several variables were investigated as possible covariates to include in the mixed models. To be included, a variable had to (1) significantly differ across the three experimental conditions and (2) be significantly correlated with at least two of the three depression scales used in the main RCT [76]. None of the potentially confounding variables tested (i.e., age, marital status, education level, annual income, cancer stage, cancer treatments, medical comorbidity, psychotropic usage, season during therapy, cancer-related life events assessed with the Inventory of Recent Life Experiences for Cancer Patients [77], or general stressful life events assessed with the List of Threatening Experiences [78]) met both criteria. Hence, no covariate was included.

Results

Descriptive Statistics

Table 1 presents the main demographic and clinical characteristics of the study sample at baseline. All patients were white and the mean age was 57.3 years old. Most of them were married or cohabitating (66.1%) and had completed at least a college degree (64.4%). All participants underwent surgery for breast cancer, 81.4% of them had received radiation therapy, 72.9% were currently receiving hormone therapy, and 52.5% of the sample had received chemotherapy. A little more than a half of the participants (52.5%) met criteria for an adjustment disorder (with depressed mood, with anxiety, or with mixed features) and 27.1% had a depressive disorder. The average HADS-D score was 9.0. Despite stratification, which aimed to get a similar proportion of participants with seasonal depressive symptoms in each group, 77.8% of them ($n = 7$) were assigned to BLT (vs. $n = 2$ in CT). This was probably due to the allocation block size of 12 that was too large given the number of participants with seasonal depressive symptoms in the study ($n = 9$) to balance groups on this variable at the end of recruitment. To ensure that this unequal distribution had no confounding effect, the effect sizes of pre- vs. posttreatment changes in BLT participants having seasonal vs. nonseasonal depressive symptoms were compared in the main study. This comparison was done only in the BLT group because of the literature described above suggesting that patients with seasonal depressive symptoms could be more responsive to BLT. The reduction of HADS-D scores was slightly larger for participants having seasonal depressive symptoms ($d = -1.8$) than those with nonseasonal symptoms ($d = -1.4$). Of all demographic and clinical variables presented in Table 1, including the seasonality of depressive symptoms, the only significant between-group differences at pretreatment were on cancer stage and adjuvant treatments received. A greater proportion of CT patients had more advanced cancer stages (65.5% with stages II or III, vs. 30.0% in the BLT condition), X^2 (3) = 8.05, $p = .05$, and more CT patients received chemotherapy (69.0%, vs. 36.7% in BLT) and trastuzumab (an intravenous targeted therapy drug used to treat HER2-positive breast cancer; 29.6%, vs. 0.0% in BLT), X^2 (1) = 6.17, $p = .01$, and X^2 (1) = 9.57, $p = .002$, respectively.

Moderating Variables of Depressive Symptoms Reductions

Table 2 shows the pre- and posttreatment adjusted means, adjusted change scores (deltas), and Cohen's *effect sizes* (*d*) obtained on the HADS-D total score, for each intervention (CT and BLT) and each level of moderating variables (low vs. high or no vs. yes). None of the variables investigated significantly moderated the effect of CT. Large and moderate *d*s were nevertheless found. CT participants with seasonal depressive symptoms experienced a greater reduction of depressive symptoms after receiving that treatment than those with nonseasonal depressive symptoms ($\Delta = -6.50$ vs. -3.81, $d = 0.86$). Participants with a higher HADS-D score at baseline were more responsive to CT than those with lower

Table 1 Participants' characteristics at baseline ($N = 59$)

	CT ($n = 29$)		BLT ($n = 30$)		Total ($N = 59$)		Between-group differences
Variables	*M*	*SD*	*M*	*SD*	*M*	*SD*	*p*
Age (years; range = 34–75)	55.3	10.2	59.2	9.6	57.3	10.0	.13
	n	%	*n*	%	*n*	%	
Marital status							.22
Married/cohabitating	20	69.0	19	63.3	39	66.1	
Separated/divorced	6	20.7	4	13.3	10	17.0	
Single	3	10.3	3	10.0	6	10.2	
Widow	0	0.0	4	13.3	4	6.8	
Education							.35
High school	12	41.4	11	36.7	23	39.0	
College	5	17.2	10	33.3	15	25.4	
University	12	41.4	9	30.0	21	35.6	
Occupation							.13
Retired	7	24.1	15	50.0	22	37.3	
Full-time work	10	34.5	8	26.7	18	30.5	
Sick leave	5	17.2	3	10.0	8	13.6	
Part-time work	5	17.2	1	3.3	6	10.2	
Unemployed	2	6.9	1	3.3	3	5.1	
Other	0	0.0	2	6.7	2	3.4	
Family income (Canadian dollars)							.58
40,000 and less	9	31.0	9	30.0	18	30.5	
40,001–80,000	10	34.5	15	50.0	25	42.4	
80,001 and more	8	27.6	4	13.3	12	20.3	
Do not know/refuse to answer	2	6.9	2	6.7	4	6.8	
	M	*SD*	*M*	*SD*	*M*	*SD*	
Time since cancer diagnosis (months; range = 7–22)	14.4	4.3	15.0	3.7	14.7	4.0	.55
	n	%	*n*	%	*n*	%	
Cancer stages							.05
0	1	3.5	4	13.3	5	8.5	
I	9	31.0	17	56.7	26	44.1	
II	13	44.8	7	23.3	20	33.9	
III	6	20.7	2	6.7	8	13.6	
Adjuvant treatments received*							
Surgery	29	100.0	30	100.0	59	100.0	N/A
Chemotherapy	20	69.0	11	36.7	31	52.5	.01
Radiation therapy	25	86.2	23	76.6	48	81.4	.35
Hormone therapy	20	69.0	23	76.6	43	72.9	.51
Trastuzumab	8	29.6	0	0.0	8	13.6	.002
Psychiatric disorders*							
Adjustment disorder	17	58.6	14	46.7	31	52.5	.36
Depressive disorder	6	29.7	10	33.3	16	27.1	.28
Anxiety disorder	4	13.8	4	13.3	8	13.6	.96
None	5	17.2	4	13.3	9	15.3	.68
Major depressive disorder in the past	12	41.4	12	40.0	24	40.7	.91
Seasonal depressive symptoms	2	6.9	7	23.3	9	15.3	.08
Psychotropic medication	18	62.1	16	53.3	34	57.6	.50
	M	*SD*	*M*	*SD*	*M*	*SD*	
HADS-D score (range = 2–15)	8.48	2.8	9.53	3.1	9.02	3.0	.18

CT, cognitive therapy; *BLT*, bright light therapy; *Sum of percentages exceeds 100% because of overlapping categories

Table 2 Pre- and posttreatment adjusted means and differences (deltas) on the HADS-D total score for each level of moderating variable

Variable	CT ($n = 29$)								BLT ($n = 30$)							
	Low or no			High or yes					Low or no			High or yes				
	Pre (M)	Post (M)	Δ	Pre (M)	Post (M)	Δ	F^1	d	Pre (M)	Post (M)	Δ	Pre (M)	Post (M)	Δ	F^1	d
CT expectancies	7.79	4.36	− 3.43	9.13	4.60	− 4.53	0.75, $p = .39$	− 0.34	10.00	5.00	− 5.00	9.13	5.98	− 3.15	2.27, $p = .14$	0.58
BLT expectancies	8.33	4.48	− 3.86	8.88	4.50	− 4.38	0.11, $p = .74$	− 0.16	9.05	5.32	− 3.72	10.67	5.81	− 4.86	0.57, $p = .45$	− 0.36
Treatment preference matching	8.00	2.50	− 5.50	8.50	5.06	− 3.44	1.27, $p = .27$	0.64	7.50	5.47	− 2.03	10.69	5.46	− 5.23	7.42, $p = .009$	− 1.00
Baseline HADS-D score	6.36	3.43	− 2.93	10.47	5.47	− 5.00	2.74, $p = .10$	− 0.77	6.36	4.34	− 2.02	11.37	6.13	− 5.23	8.15, $p = .006$	− 1.20
Current depressive disorder	8.20	4.32	− 3.88	10.25	5.50	− 4.75	0.32, $p = .57$	− 0.28	9.09	4.63	− 4.46	11.00	7.86	− 3.14	1.18, $p = .28$	0.43
Past major depressive disorder	7.82	3.71	− 4.12	9.42	5.58	− 3.83	0.04, $p = .83$	0.10	9.22	3.80	− 5.42	10.00	8.14	− 1.86	12.74, $p = .00$	1.19
Fall or winter during CT/BLT	8.07	3.60	− 4.47	8.93	5.43	− 3.50	0.54, $p = .47$	0.30	10.42	4.58	− 5.83	8.71	6.21	− 2.50	8.55, $p = .005$	1.04
Seasonal depressive symptoms	8.41	4.59	− 3.81	9.50	3.00	− 6.50	1.10, $p = .30$	− 0.86	8.91	4.99	− 3.92	11.57	7.07	− 4.50	0.22, $p = .64$	− 0.18

CT, cognitive therapy; *BLT*, bright light therapy; *Pre*, pretreatment; *Post*, posttreatment; $d = 0.20$ = small effect; $d = 0.50$ = moderate effect; $d = 0.80$ = large effect. [1] $df = 51$

scores (Δ = − 5.00 vs. − 2.93, $d = 0.77$). Participants with a lower pretreatment preference for receiving CT showed larger treatment effects than those with a higher preference (Δ = − 5.50 vs. − 3.44, $d = 0.64$).

Four variables significantly moderated the effect of BLT, with large *d*s ranging from 1.00 to 1.20. Specifically, a greater reduction of HADS-D scores was found in BLT patients who had a higher preference for BLT at baseline (Δ = − 5.23 vs. − 2.03 for those with a lower preference), who had a greater HADS-D score at baseline (Δ = − 5.23 vs. − 2.02 for those with a lower score), who had no prior history of major depressive disorder (Δ = − 5.42 vs. − 1.86 for those with such antecedents), and who completed BLT during spring or summer (Δ = − 5.83 vs. − 2.50 during fall or winter). Although this difference was not statistically significant, a moderate effect size was also found for treatment expectancies, that is, participants with lower treatment expectancies towards CT at baseline were more responsive to BLT than those with higher levels ($d = 0.58$).

Discussion

The goal of this exploratory study, conducted in women with non-metastatic breast cancer, was to assess the moderating role of 8 clinical variables on the pre- vs. posttreatment effects of CT and BLT on depressive symptoms. This was a secondary analysis of an RCT comparing the efficacy of these two interventions to a waiting-list control condition. Our initial hypotheses, based on the existing evidence of studies conducted in non-cancer populations, were only partially supported. As hypothesized, a past history of depression was a predictor of lower BLT effects on depressive symptoms. However, contrary to what was expected, higher treatment expectancies towards CT and preference for CT at baseline did not predict CT response, and BLT response was not predicted by higher treatment expectancies towards BLT. Some unexpected results also emerged from the analyses. Both BLT and CT patients with more severe HADS-D scores at baseline benefited more from the treatment they received. Participants with a stronger preference for receiving BLT at baseline benefited more from this intervention. Conversely, a lower preference for CT was associated with better CT response, and lower expectancies towards CT were related to a better BLT response. Participants with seasonal depressive symptoms benefited more from CT than those with nonseasonal depressive symptoms, a difference that was not found in the BLT condition. Finally, participants were more responsive to BLT when they received the intervention during spring or summer, in comparison to fall or winter.

As expected, a past history of depression was associated with smaller BLT effects. This finding is consistent with those of a few previous studies suggesting that BLT was more effective for patients with a lower number of past depressive

episodes [52, 56]. More surprisingly, patients responded better to BLT when they had a higher HADS-D score at baseline. Although the effect size was lower (but nevertheless of a moderate magnitude), the same pattern was observed in the CT condition. This could be explained by the regression to the mean phenomenon (i.e., the tendency for a higher score at pretreatment to get closer to the mean at posttreatment) and because having higher scores at baseline leave more room for improvement.

Patients with a stronger preference for receiving BLT benefited more from this intervention, while those with a lower preference for CT benefited more from CT. This result contradicts prior results showing that CBT was more effective in reducing depressive symptoms when patients had higher initial treatment expectancies [40] and a higher preference for CBT [41, 42]. Results found in BLT patients could suggest that those having a greater preference for BLT are more likely to adhere to this home-based intervention, and hence more likely to experience its therapeutic effects. In CT, the therapist support may possibly help patients to get more involved in the treatment, even when they are less motivated initially, explaining why it is not necessary to prefer CT in order to benefit from it. Although this observation needs to be replicated in further studies, it suggests that CT is effective independently of patients' baseline preference, and is therefore a suitable treatment for a wide range of patients when available.

Also intriguing are the results indicating that patients derived a stronger therapeutic effect from BLT when they used it during spring or summer, and the finding showing that BLT was not differently effective for patients with seasonal vs. nonseasonal depressive symptoms. This last result is inconsistent with most of the BLT literature [51, 52], but is in line with a more recent trial conducted in depressed patients of the general population [53]. Concerning the better BLT outcomes when administered during spring and summer, a possible explanation is that BLT encouraged participants to also expose themselves more to natural daylight. In Canada, where the study was conducted, spring and summer seasons are indeed much more conducive to outside activities, and the greater amount of brightness during these seasons may have an additional positive effect on mood. This hypothesis is consistent with a study that revealed that a greater number of minutes of light exposure of 1000 lux or greater (without necessarily using BLT) and a higher intensity of light exposure were correlated with lower levels of depressive symptoms in cancer patients [79]. Future studies should measure light exposure throughout the day using a light sensor device to verify this hypothesis. An even more surprising result is the greater response to CT observed for patients with seasonal depressive symptoms. However, given that the number of participants categorized as having seasonal depressive symptoms was very low and that, to our knowledge, the efficacy of CT for decreasing seasonal vs. nonseasonal depressive symptoms has never been investigated, this result should be interpreted carefully. A potential explanation could be that CT participants with seasonal depressive symptoms were aware that the level of light exposure influenced their depressive symptoms and they may have incorporated more outdoor activities when they were applying behavioral activation strategies as part of CT.

To our knowledge, this study was the first to investigate the moderating role of clinical variables on the effects of CT and BLT on depressive symptoms in the context of cancer. Identifying variables that are predictive of treatment response is important to eventually be able to better orient the provision of care. The strengths of the current study include the random assignment to CT and BLT, which maximized the study's internal validity. Also, several measures were taken to ensure treatment integrity and adherence (e.g., use of a manualized CT protocol, assessment of CT sessions by an independent psychologist, completion of a daily log of adherence to BLT sessions).

However, many limitations need to be acknowledged as well. The main limitation is the small sample size that impacted the statistical power to detect significant effects and which also limits the representativeness of the sample. Also, the sample was fairly homogeneous in terms of demographic and clinical characteristics, and the participation rate was relatively low. Hence, the results may not generalize to women who are less educated, with more advanced cancer or patients with other types of cancer. Also, many other variables than the ones investigated in this study may have influenced CT and BLT effects (e.g., level of motivation, social support, treatment side effects, differences in treatment modalities; e.g., CT delivered at the research center vs. BLT delivered at home). For these reasons, and because of its exploratory nature, the results obtained in this study should be replicated and interpreted very cautiously.

There are also limitations that are more specific to the BLT condition. Despite the clear instructions systematically given at the beginning of treatment and phone calls made every 2 weeks to promote treatment adherence, it remains possible that the light box was not always positioned correctly or that the information indicated in the daily log was overestimated because of a social desirability bias. It is also possible that the posttreatment phase, occurring up to 2 weeks between the end of the intervention phase, may have underestimated BLT effects. Indeed, although mixed findings have been found [37, 80–83], it is generally believed that BLT effects are short-lived after the light exposure is ceased. However, although these three factors may have reduced BLT effects overall, they are unlikely to have affected the moderating analyses. It is also relevant to discuss the failure to stratify patients on the presence of seasonal depressive symptoms. However, since the research question in the current study was to explore if patients with seasonal depressive symptoms were more responsive to BLT, it was somehow a good thing to have more of

these patients in this group. Nonetheless, it remains important to continue studying this question using a greater sample size and a higher proportion of patients having seasonal depressive symptoms.

In sum, this secondary analysis of an RCT of women with breast cancer suggests that CT is effective to reduce depressive symptoms, especially when patients have a lower initial preference for receiving CT, higher depression scores on the HADS-D, and seasonal depressive symptoms, while patients benefited more from BLT when they had no prior history of a major depressive disorder, higher depression scores on the HADS-D at baseline, a greater initial preference for BLT, and when they received BLT during spring or summer. It is important to keep in mind that findings of the main study indicated that CT produced larger treatment effects than BLT [39]. Hence, it would be important to make this intervention more accessible in routine cancer care and to emphasize prioritizing this therapeutic option when available. For patients not interested in receiving CT or for whom this intervention is not accessible, BLT could be a valuable alternative, especially for those interested in this approach and who do not have a past history of major depressive disorder. It could be interesting in future studies to investigate the feasibility and the cost-effectiveness of a stepped care approach using BLT. Patients with a strong preference for BLT and having no history of depression could be first oriented to BLT, with the possibility of receiving CT subsequently if the patient is still symptomatic. The efficacy of an approach combining CT and BLT is also an interesting area for future research.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Informed Consent Informed consent was obtained from all individual participants included in the study.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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