Light therapy for cancer-related fatigue in (non-)Hodgkin lymphoma survivors

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CHAPTER 4

THE EFFICACY OF LIGHT THERAPY ON COGNITIVE FUNCTIONING OF (NON-)HODGKIN LYMPHOMA SURVIVORS WITH CANCER-RELATED FATIGUE.

Submitted

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ABSTRACT

Objectives

Cancer-related fatigue is associated with cancer-related cognitive impairment. Therefore, this study evaluated short- and long-term effects of light therapy on cognitive complaints and cognitive functioning in fatigued lymphoma survivors.

Methods

Fatigued Hodgkin Lymphoma (HL) and Diffuse Large B-cell Lymphoma (DLBCL) survivors (N = 166; mean survival 13 years) were randomly assigned to receive either bright white light (BWL; intervention) or dim white light (DWL, comparison) therapy for 30 minutes over 25 days. Assessments of fatigue and cognitive complaints (questionnaires) were collected at baseline, post-intervention, and at three and nine months follow-up. Cognitive functioning was assessed with neuropsychological tests at baseline and post-intervention. Differences between groups in changes over time were examined using a mixed-effect modeling approach.

Results

Over one-third of the participants showed cognitive dysfunction at baseline, specifically in verbal memory where deviant scores were observed for immediate recall in 34% and delayed recall in 27% of the participants compared to 16% in the norm population. Neither BWL nor DWL diminished cognitive complaints or improved cognitive functioning (range *p*-values .07 to .80; range effect sizes .04 to .29) in the total group of fatigued survivors nor in the subgroup suffering from cognitive dysfunction.

Conclusion

Approximately one-third of the survivors of HL and DLBCL with cancer-related fatigue experience objectively measured cognitive dysfunctioning. Light therapy does not appear to improve these complaints. Therefore, we suggest that other cognitive rehabilitation interventions should be made available to mitigate cognitive dysfunctioning in these survivors.

INTRODUCTION

Cancer-related cognitive impairment (CRCI) involves cognitive symptoms, such as impairments in short-term and working memory, attention, executive functioning and/or processing speed, reported by patients with non-central nervous system cancers[1]. CRCI includes patient-reported *cognitive complaints* and objectively measured *cognitive decline* assessed by neuropsychological tests. Cognitive complaints are reported by up to 75 percent of cancer survivors that have received chemotherapy[1]. Cognitive decline is shown in 15 to 25 percent of patients treated for breast cancer and in 16 percent of patients treated for lymphoma[2]. As cognitive complaints may also be influenced by additional psychological factors such as fatigue, anxiety, depression, and insomnia[3], this may explain the discrepancy between prevalence rates of subjectively measured cognitive complaints and objectively measured cognitive decline.

Light therapy has been suggested as an effective treatment for cancer-related fatigue. Several studies showed a decline in fatigue after 4 weeks of morning light therapy in survivors of cancer[4, 5]. Moreover, results showed improved sleep quality, sleep-wake cycles, and depression[5-8], which are also associated with CRCI. These effects might be explained by the resynchronizing effect of light on circadian rhythms via stimulation of the suprachiasmatic nucleus (SCN; the biological clock)[9].

Studies on the effect of light on cognitive functioning can be categorized into two groups. First, the effect of short-term exposure to light, i.e. light therapy on 1 or 2 days. Results showed an improvement in alertness and cognitive performance in healthy subjects[10], sleep-deprived healthy subjects[11], and healthy subjects under mental fatigue initiated by demanding tasks[12]. Secondly, a few studies investigated the effect of long-term exposure to light therapy (daily use during at least two consecutive weeks). These studies were limited to patients with dementia and mild traumatic brain injury. Results were inconclusive with some studies showing positive effects on cognitive functioning after light therapy[13-15] and some showing no effects[16, 17].

We recently conducted a double-blind, randomized controlled trial to test the efficacy of light therapy in reducing cancer-related fatigue in chronically fatigued Hodgkin lymphoma (HL) and Diffuse Large B-cell lymphoma (DLBCL) survivors. Results showed that, irrespective of the type of intervention (exposure to bright white light [BWL; intervention group] or dim white light [DWL; comparison group], reduced levels of fatigue were reported. As far as we know, studies measuring the effect of light therapy on cognitive functioning in cancer survivors are lacking. Therefore, the objective of this planned secondary analysis was to evaluate the efficacy of light therapy in diminishing cognitive complaints and improving cognitive functioning in HL and DLBCL survivors with cancer-related fatigue. It was hypothesized that light therapy would diminish cognitive complaints and improve cognitive functioning, especially for survivors who showed cognitive dysfunctioning at baseline.

METHODS

This study was a secondary analysis of a double-blind randomized controlled trial on the efficacy of light therapy on decreasing fatigue in chronically fatigued HL or DLBCL survivors. The study

design and primary results are described in detail elsewhere[18]. The study was executed in accordance with the Declaration of Helsinki and with approval from the institutional review board of the Netherlands Cancer Institute (number NL61017.031.17).

Participants

Survivors were recruited from ten hospitals in the Netherlands between September 2017 and October 2019. Participants were included if they were: (1) aged between 18 and 70 years; (2) diagnosed with HL or DLBCL 2 years before study entry; and (3) experienced moderate to severe fatigue since diagnosis or treatment. Moderate to severe fatigue was defined as a score of the general fatigue subscale of the Multidimensional Fatigue Inventory (MFI)[19] above the 75th percentile compared to age- and sex-matched cancer survivors[20] or a score of 17 or higher on the Work and Social Adjustment Scale[21]. Participants were excluded if there was a somatic cause for fatigue or a (medical) condition that could potentially compromise the effect of light therapy.

Procedure, randomization, and timing of assessments

Survivors were recruited in two separate ways: (1) via referral from their physician, or (2) by showing interest in participating in this clinical study after participation in a survey study on chronotype, sleep quality and fatigue for which they were invited by their treating physician[22]. Eligible survivors received an information brochure and sent a completed screening questionnaire and a response card indicating their interest or reasons for nonparticipation to the research team. Eligibility of interested survivors was confirmed by telephone screening after which eligible survivors received a patient information letter and informed consent.

After signing informed consent, a research assistant not involved in other study procedures randomly assigned participants to the intervention group (BWL) or control group (DWL) at a 1:1 ratio stratified on diagnosis, time since diagnosis, and gender using a minimization technique (randomization software program ALEA; FormVision, Abcoude, the Netherlands). All other members of the research team were blinded to the study arm until the participant completed the final assessment. We told participants that two intensities of light therapy were compared without mentioning the expected absence of an effect of DWL.

Assessments of fatigue and cognitive complaints via questionnaires were at baseline (T0), post-intervention (T1), 3 months post-intervention (T2), and 9 months post-intervention (T3). Neuropsychological tests were completed in person during a visit to the hospital at T0 and T1.

Intervention

Light therapy comprised of exposure to an artificial source of light, which is already widely known for seasonal affective disorder. In line with previous studies on light therapy in cancer survivors[4, 5], the first 37 randomly assigned participants used the Litebook Edge (Litebook, Ltc. Medicine Hat, Canada). This device should have exposed participants in the BWL group to blue-enriched (480 nm) white light of 10.000 lux (app. 1.500 lux at eye level) and the DWL group to blue-enriched (480 nm) white light of 10-20 lux. However, confirmatory spectral measurements indicated that the Litebook Edge exposed participants in the BWL condition to 351 lux at eye level, which is insufficient for light therapy. Therefore, the remaining 127 participants used

Luminette glasses (Lucimed SA, Villers-le-Bouillet, Belgium) for the administration of light therapy, which exposed participants to white light enriched around 468 and 570 nm of 1.500 lux (BWL) or 8 lux (DWL) at eye level. All participants, including Litebook Edge users, were included in the intention-to-treat analyses.

Light therapy was completed in the morning within 30 minutes after wakening for the duration of 30 minutes over 3,5 weeks (25 days). Participants were encouraged to engage in other activities like having breakfast or reading while completing light therapy.

Measures

Sociodemographic information was collected with a screening and baseline questionnaire. Clinical information was abstracted from patients' medical records. A *Visual Analogue Scale* (VAS-fatigue) from 0 (no fatigue) to 10 (worst imaginable fatigue) and the general fatigue subscale of the Multidimensional Fatigue Inventory (MFI)[19] were used to describe fatigue.

Cognitive complaints

Self-reported cognitive complaints were assessed with two questionnaires. The *Medical Outcomes Studies cognitive functioning* (MOS-CF6)[23] was used to assess cognitive complaints. This 6-item scale assesses memory, reasoning and thinking during the past week. Responses are given on a 6-point scale from 'always' to 'never'. The total score is the summation of all responses converted to a 0 (worst cognitive functioning) to 100 (best cognitive functioning) scale.

Eight items of the *MD Anderson Symptom Inventory* (MDASI)[24] were included to assess remembering, concentration, and interference caused by cognitive complaints in daily life. These items were rated on an 11-point scale, ranging from 0 (no complaints) to 10 (worst complaints) during the past 24 hours. Memory and concentration were based on the single items 'remembering' and 'concentration'. The interference caused by cognitive complaints was based on the average of the remaining six items.

Cognitive functioning

Objectively measured cognitive functioning was based on three neuropsychological tasks. Attention and vigilance were assessed with the *psychomotor vigilance task* (PVT)[25]. During this task, participants monitor a black computer screen and push a button when a reaction time counter starts to run on the display. A response with feedback on the reaction time appeared on the screen after pressing the button for 1 second. The time counter was presented with a random inter-stimulus interval ranging from 2 to 10 seconds. The total test time was 5 minutes. Derived variables from the PVT were response speed defined as mean 1/reaction times (1/RT; s) and the number of performance lapses (RTs ≥ 500ms).

The *15 words task*[26] was used to assess verbal learning and retention of information. During a learning phase, a list of 15 words was read aloud to the participants after which the participant was asked to recall all the remembered words. After 15 min, participants were asked for delayed recall of all remembered words and for recognition of the presented words in a list of 30 words. Two parallel versions were used in random order to limit practice effects.

Derived variables from the 15 words task were the total number of correct words during the learning phase (5 trials), free recall, and recognition.

Attention and working memory were assessed with the *digit span task*[27]. Participants listened to a sequence of numerical digits and were asked to recall the sequence in the same order (forward) or reverse order (backward). The number of digits increased from 2 to 9 (forward) or 8 (backward) until the participant was no longer able to recall two sequences with the same number of digits correctly. Derived variables from the digit span task were the total number of correctly repeated sequences (forward and backward).

Statistical analysis

Baseline characteristics of the intervention and control group were compared using independent samples t-test, Mann Whitney, Chi-square, or Fisher's Exact tests. Questionnaire scores were calculated according to published scoring algorithms. Missing values were replaced by the average score of the completed items in the same scale for each individual, provided that ≥ 50% of the items in that scale had been completed.

To evaluate the prevalence of cognitive dysfunctioning at baseline, we compared baseline scores of two neuropsychological tests to a Dutch norm population. Specifically, scores on the 15 words task were compared to sex-, age- and education-matched controls[28] and scores on the digit span task were compared to age-matched controls[27] and transformed to t-scores. A score was classified as deviant when it was at least 1 standard deviation (SD) below the mean of the general population. An individual was categorized as showing cognitive dysfunctioning when at least two subtests had a deviant score. Due to the absence of norm data for the PVT, this task was not included in this analysis.

To evaluate differences in the effect of light therapy on cognitive complaints between the intervention and control group over time (T0-T3), we used a mixed effect modelling approach with a random intercept and a restricted maximum likelihood solution. We used baseline to follow-up analysis to evaluate the effect of light therapy on cognitive functioning between groups (T0-T1). Within each mixed-effect model, the control group was the reference category. Models were adjusted for age, education level, and baseline fatigue. Additionally, models were adjusted for possible baseline differences and, in case of non-ignorable drop-out, for different patterns of missing values. Models with and without correction for baseline differences, different missing data patterns, and different covariance structures (UN, AR1, CS) were compared using the Bayesian Information Criterion (BIC)[29] and the Akaike's Information Criterion (AIC)[30]. Models with lower BIC or AIC values are considered to be better fitting models.

Differences in mean change scores over time between the treatment group and the control group were accompanied by standardized effect sizes (ES) calculated based on the mean scores and pooled standard deviation (SD): $(mean_{T1}\text{-}mean_{T0})/pooled\ SD_{T0\text{-}T1}$ or $(mean_{T3}\text{-}mean_{T1})/pooled\ SD_{T1\text{-}T3}$. Effect sizes of 0.2 were considered small, 0.5 moderate, and 0.8 large[31]. An effect size ≥ .50 was considered clinically relevant[32].

All analyses were conducted on an intention-to-treat (ITT) basis. Additionally, we performed a per-protocol analysis on data from participants who adhered to the light therapy on all 25 days; and three sensitivity analyses on data from patients who (1) showed cognitive

dysfunctioning at baseline; (2) used the Luminette glasses; (3) used light therapy during fall or winter (October to March). All statistical analyses were conducted in SPSS version 25.

RESULTS

Participants

In total, 166 participants signed informed consent and were randomly allocated to either BWL (n = 83) or DWL (n = 83). Table 1 summarizes sociodemographic, clinical and fatigue-related characteristics of the study sample. The mean age of the survivors was 45.7 years (SD = 12.2). More than half of the participants were female (60%). Almost half of the group (47%) had completed college or university.

The majority of the participants (83%) was diagnosed with HL and had received chemotherapy (93%). The mean survival was 12.9 years (SD = 9.9). Baseline levels of fatigue were high with a mean VAS-fatigue score of 6.1 (SD = 1.6) and a mean general fatigue score of 15.7 (SD = 2.7). Except for marital status, all baseline characteristics were balanced between groups.

The completion rates of the questionnaires at baseline assessment T0 (n = 165, 99%), and follow-up assessments T1 (n = 157; 95%), T2 (n = 141; 85%), and T3 (n = 142; 86%) differed between groups at T1 (DWL: 90% *v* BWL: 99%; $p = .03$). There were no differences between groups for the completion rates of the PVT at T0 (n = 159; 96%)and T1 (n = 146; 88%) and the 15 words task and digit span task at T0 (n = 164; 99%) and T1 (n = 154; 93).

Baseline cognitive functioning

Fifty-six participants (34%) showed cognitive dysfunctioning in the number of correctly remembered items during the learning phase and 45 participants (27%) during the recall phase of the 15 words task compared to 16% in the norm groups. For the digit span task, deviant scores on the total number of correctly repeated sequences were seen in 27 participants (17%), on the forward digit span task in 25 participants (15%), and on the backward digit span task in 23 participants (14%) compared to 16% in the norm groups. Overall, 53 participants (32%) had a deviant score on two or more subtests. The percentage of cognitive dysfunctioning at baseline did not differ between groups (data not shown).

Efficacy analyses

Figure 1 shows results of the intention-to-treat analyses corrected for age, education, and baseline fatigue (see appendix Table A1 for details). Correction for marital status and missing data patterns did not improve model fit, and both were omitted from the models. For cognitive complaints, results showed no differences between BWL and DWL over time ($p \geq .10$) nor an overall time effect (appendix Table A2) in both groupscombined ($p \geq .62$). Results were similar for cognitive functioning, as there were no differences between groups over time ($p \geq .07$) nor an overall time effect ($p \geq .05$; see appendix Table A2). These results suggest that cognitive complaints and cognitive functioning were unaffected by light therapy.

The per-protocol analysis including participants who adhered to the complete light therapy protocol (Appendix Table A3) and sensitivity analyses including (1) participants with cognitive

Table 1. Baseline sociodemographic, clinical, fatigue, and light therapy characteristics

	All survivors (n=166)	BWL (n=83)	DWL (n=83)	*p*	N
SOCIODEMOGRAPHIC VARIABLES					
Age, *mean years (SD)*	45.7 (12.2)	46.7 (11.9)	44.8 (12.5)	.30	166
Female, *n (%)*	99 (59.6)	50 (60.2)	49 (59.0)	.87	166
Education, *n (%)*				.24	165
None/primary	2 (1.2)	0 (0.0)	2 (2.4)		
High school and vocational	85 (51.5)	43 (51.8)	42 (51.2)		
College or university	78 (47.3)	40 (48.2)	38 (46.3)		
Married or in relationship, *n (%)*	130 (78.8)	71 (85.5)	59 (72.0)	.03*	165
Part- or full-time job, *n (%)*	85 (51.5)	42 (50.6)	43 (52.4)	.81	165
CLINICAL VARIABLES					
Diagnosis, *n (%)*				.68	166
HL	138 (83.1)	70 (84.3)	68 (81.9)		
DLBCL	28 (16.9)	13 (15.7)	15 (18.1)		
Time since diagnosis, *mean years (SD)*[a]	12.9 (9.9)	13.0 (9.6)	12.9 (10.3)	.88	166
Treatments received, *n (%)*					
Radiotherapy	116 (72.0)	56 (69.1)	60 (75.0)	.41	161
Chemotherapy	151 (93.2)	76 (92.7)	75 (93.8)	.79	162
Stem cell transplantation	19 (12.1)	8 (10.1)	11 (14.1)	.45	161
Total body irradiation[b]	2 (1.2)	0 (0.0)	2 (2.5)	.24	162
Surgery (splenectomy)[b]	6 (3.7)	3 (3.7)	3 (3.8)	1.0	162
FATIGUE					
VAS-fatigue, *mean (SD)*[c]	6.1 (1.6)	5.9 (1.8)	6.3 (1.4)	.09	164
General fatigue (MFI), *mean (SD)*[d]	15.7 (2.7)	15.6 (2.9)	15.8 (2.5)	.76	165
LIGHT THERAPY CHARACTERISTICS					
Season start light therapy				.94	164
Autumn	42 (25.6)	23 (27.7)	19 (23.5)		
Winter	47 (28.7)	23 (27.7)	24 (29.6)		
Spring	47 (28.7)	23 (27.7)	24 (29.6)		
Summer	28 (17.1)	14 (16.9)	14 (17.3)		
Light therapy device					
Litebook Edge	37 (22.6)	18 (21.7)	19 (23.5)		164
Luminette	127 (77.4)	65 (78.3)	62 (76.5)		164
Premature stop of light therapy	13 (7.8)	7 (8.4%)	6 (7.2)	.77	166

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Table 1. *(continued)*

	All survivors (n=166)	BWL (n=83)	DWL (n=83)	*p*	N
Days light therapy use, *mean (SD)*	22.7 (4.4)	22.5 (4.6)	22.9 (4.0)	.52	155
> 25 days[b]	3 (1.9)	0 (0.0)	3 (3.9)	.13	155
25 days	58 (37.4)	33 (41.8)	25 (32.9)		
14-24 days	87 (56.1)	41 (51.9)	46 (60.5)		
1-13 days (premature stop)	7 (4.5)	5 (6.3)	2 (2.6)		

BWL bright white light; **DWL** dim white light; **SD** standard deviation; **HL** Hodgkin lymphoma; **DLBCL**: Diffuse large B-cell lymphoma; **MFI** Multidimensional Fatigue inventory; **VAS** visual analogue scale; **WSAS** Work and Social Adjustment Scale

* $p < .05$

[a] Based on Mann-Whitney Test. [b] Based on Fisher's Exact Test. [c] Score range 0 - 10, with higher scores reflecting higher levels of fatigue. [d] Score range 4 - 20, with higher scores reflecting higher levels of general fatigue.

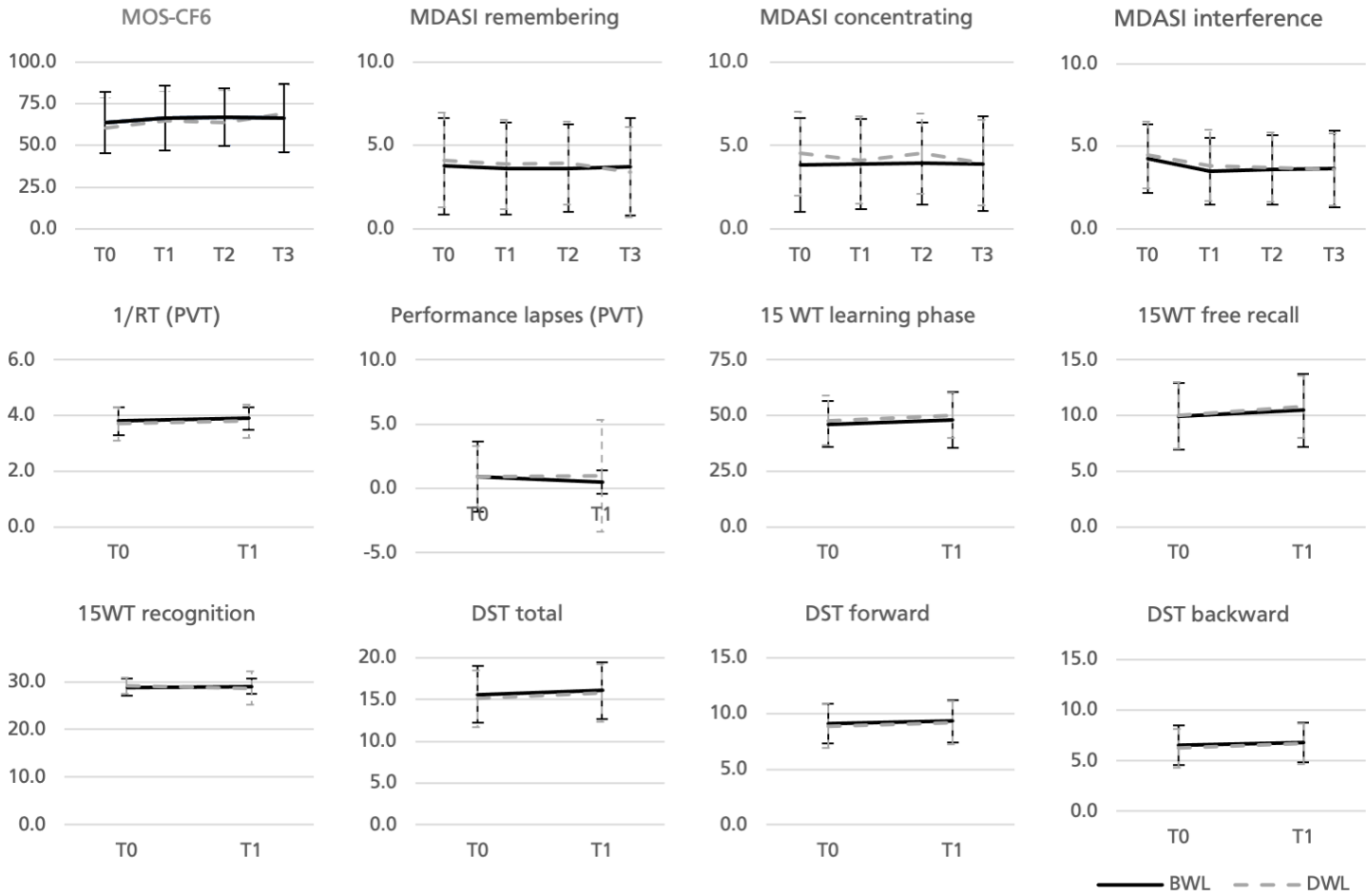
dysfunctioning at baseline (Figure 2 and Appendix Table A4); (2) participants who used the Luminette glasses (appendix Table A5), and (3) participants who used light therapy during fall or winter (appendix Table A6) did not change the conclusions from the intention-to-treat analysis.

DISCUSSION

The results of this double blind, randomized controlled trial, showed that over one-third of long-term HL and DLBCL survivors presenting with chronic cancer-related fatigue experience (objectively assessed) cognitive dysfunctioning. We previously showed that light therapy, irrespective of light intensity, improved fatigue in long-term chronically fatigued lymphoma survivors. The results of the current analyses suggest that light therapy has no effect on cognitive complaints or cognitive functioning in this group. There was no superiority for the effect of exposure to morning BWL compared to DWL on cognitive complaints or cognitive functioning, nor was there an overall improvement irrespective of exposure to BWL or DWL.

Cognitive dysfunctioning was predominantly seen for verbal memory; the prevalence was twice as high in the study population compared to the norm population. The prevalence of problems with attention and working memory was comparable to the norm population. These prevalence rates are in line with previous studies on survivors of different types of cancer[33]. Although normative data for the PVT is lacking, the PVT scores in our sample were comparable to that of the community-based sample of the Wisconsin Sleep Cohort study[34] and are therefore, likely within the normative range.

The finding that light therapy was not effective in our sample as a treatment for CRCI is in line with a previous study on light therapy in individuals with dementia[16] and a Cochrane review[17]. This Cochrane review included 11 trials comprising 499 participants. The pooled data of these studies showed no effect of light therapy on cognitive functioning assessed with a Mini-Mental State Examination. However, our findings contradict studies (not included in the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Left page
Figure 1. Effects of light therapy on cognitive complaints and cognitive functioning in participants exposed to BWL (n=83) and dim white light DWL(n=82). Exact values, p-values, and effect sizes are available in Appendix Table A1.
15WT 15 words task; **BWL** bright white light; **DST** Digit Span Task; **DWL** dim white light; **MDASI** MD Anderson Symptom Inventory; **MOS-CF6** Medical Outcomes Studies – Cognitions; **PVT** Psychomotor Vigilance Task; **T0** baseline; **T1** post intervention; **T2** 3 months after light therapy; **T3** 9 months after light therapy.

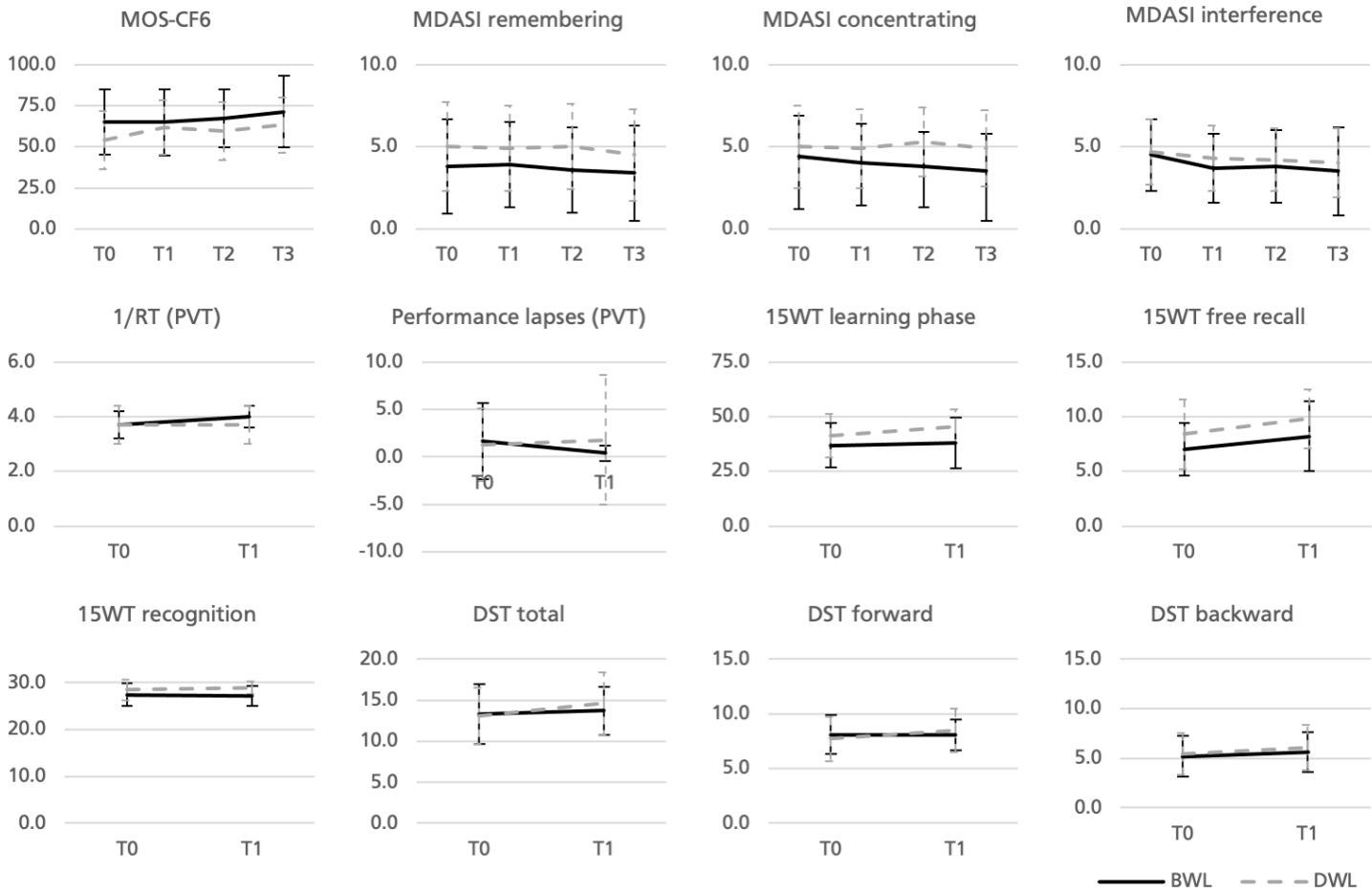
Cochrane review) that show an effect of light therapy on cognitive functioning in seniors[14] and individuals with mild traumatic brain injury[15]. These studies tested comparable light therapy protocols but used monochromatic blue light instead of the polychromatic white light used in the current study. This might explain the differences in results, as blue wavelengths are assumed responsible for the restoring effect of light therapy on the circadian rhythm[9]. However, it is reasonable to expect similar results as the light used in our study was enriched in this blue spectrum. Another study that tested light therapy in individuals with dementia[13] showed a positive effect on cognitive functioning. However, this study included a comparison between whole day bright and dim light in group care facilities for a duration of multiple years and is therefore less comparable to our study design.

Another reason for the contradicting results of the current study compared to previous studies might be related to the characteristics of our study population. The studies showing an effect of light therapy recruited seniors with or without dementia and individuals with brain traumatic brain injury[13-15]. These populations showed cognitive decline in multiple domains, while the cognitive decline in the current sample was limited to a verbal memory. Therefore, the overall cognitive decline in these populations might not be comparable.

Alternatively, the lack of an effect of light therapy on cognitive functioning in HL and DLBCL survivors might be explained by the suggested absence of a disturbed circadian rhythm in our sample. Therefore, we hypothesize that there is no causal relationship between a disturbed circadian rhythm and CRCI in long-term lymphoma survivors. Previous studies found some indications for such an association in advanced cancer patients[35] but also showed indications for different biological mechanisms, for example skeletal muscular and mitochondrial dysfunction, inflammation dysfunction, a dysregulation of cytokine activity, and central nervous system disorders[36]. Light therapy is known for its restorative effect on circadian rhythm. Consequently, a lack of an association between disturbed circadian rhythms and CRCI may explain why light therapy had no effect on cognitive complaints or cognitive functioning. It should be mentioned that alternative mechanism of action, for example stimulation of mood regulation areas, have also been reported for light therapy.

Study limitations

The current study had several strengths, including a randomized controlled double-blind design with a large sample size. However, there are also some limitations. First, as this study described a secondary analysis, participants were not recruited based on cognitive dysfunctioning. Whereas all suffered from cancer related fatigue, only over one-third of the current sample experienced cognitive dysfunctioning. Therefore, we cannot rule out that there was insufficient room for improvement in the total group. However, the sensitivity analysis in survivors who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BWL
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Figure 2. Effects of light therapy on cognitive complaints and cognitive functioning in participants who showed cognitive dysfunctioning at baseline exposed to BWL (n=25) or DWL (n=28). Exact values, p-values, and effect sizes are available in Appendix Table A4.
15WT 15 words task; **BWL** bright white light; **DST** Digit Span Task; **DWL** dim white light; **MDASI** MD Anderson Symptom Inventory; **MOS-CF6** Medical Outcomes Studies – Cognitions; **PVT** Psychomotor Vigilance Task; **T0** baseline; **T1** post intervention; **T2** 3 months after light therapy; **T3** 9 months after light therapy.

experienced cognitive dysfunctioning showed similar results to the complete sample but suffered from insufficient power to detect significant effects. Second, the PVT was originally developed for studies investigating the influence of sleep deprivation or circadian rhythms on sustained attention[25]. Sustained attention shows a circadian rhythm with the highest level of alertness between 10:00 and 14:00 hour[37]. To account for this rhythm, the PVT is normally assessed on multiple time points during the day. We assessed the PVT only once at both measurements points. To limit the effect of the circadian rhythm on cognitive functioning, the neuropsychological tasks were completed at similar times at pre- and post-intervention. A third possible limitation of the study is that the sample was highly educated.

Clinical implications

Over one-third of the survivors of HL and DLBCL showed cognitive dysfunctioning, predominantly in verbal memory. The experience of cognitive dysfunctioning can be very disturbing for survivors and can lead to problems in daily life, for example in people's professional life. Therefore, early identification of those at risk, for example via the Amsterdam Cognition Scan[38], is advised and rehabilitation interventions (e.g. internet-based cognitive rehabilitation[39]) should be available for these survivors.

Conclusions

This study showed that approximately one third of the HL and DLBCL survivors, with an average time since diagnosis of 13 years, experience objectively defined cognitive dysfunctioning. This was specifically seen for the verbal memory domain. Cognitive functioning on attention and working memory was comparable to the norm population. Although previous studies suggested that light therapy improved cognitive functioning in senior individuals, and individuals with dementia and mild traumatic brain injury, the current results suggest that light therapy does not improve cognitive functioning in survivors of HL and DLBCL. Sufficiently powered studies in survivors with confirmed cognitive dysfunctioning are necessary to support our conclusions.

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APPENDIX

Table A1. Mean values and standard deviations per time-point and between-group differences for the mixed-effects models of the outcome measurements.

	T0[a]		T1[a]	
	n	M [SD]	n	M [SD]
COGNITIVE COMPLAINTS				
MOS-CF6				
BWL	83	63.8 [18.2]	82	66.4 [19.5]
DWL[c]	82	60.5 [17.9]	75	64.7 [17.7]
MDASI remembering				
BWL	83	3.8 [2.9]	82	3.6 [2.8]
DWL[c]	82	4.1 [2.8]	75	3.9 [2.7]
MDASI concentrating				
BWL	83	3.8 [2.8]	82	3.9 [2.7]
DWL[c]	82	4.5 [2.5]	75	4.1 [2.6]
MDASI interference				
BWL	83	4.3 [2.1]	82	3.5 [2.0]
DWL[c]	82	4.5 [2.0]	74	3.8 [2.2]
COGNITIVE FUNCTIONING				
1/RT (PVT)[d]				
BWL	80	3.8 [0.5]	74	3.9 [0.4]
DWL[c]	78	3.7 [0.6]	71	3.8 [0.6]
Performance lapses (PVT)[d]				
BWL	80	0.9 [2.7]	74	0.5 [0.9]
DWL[c]	78	0.9 [2.4]	71	1.0 [4.3]
No. correct items learning phase (15WT)				
BWL	83	46.2 [10.4]	79	48.1 [12.6]
DWL[c]	81	47.7 [11.1]	75	50.0 [10.0]
No. correct items free recall (15WT)				
BWL	83	10.0 [3.0]	79	10.5 [3.3]
DWL[c]	81	10.0 [3.0]	75	10.8 [2.8]
No. correct items recognition (15WT)				
BWL	83	28.8 [1.8]	79	29.0 [1.6]
DWL[c]	80	29.1 [1.7]	75	28.7 [3.5]

T2[a]		T3[a]		Linear time effect T0-T3			ES[b]	
n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
72	66.9 [17.2]	73	66.4 [20.4]	-0.41	0.26	.12	0.06	0.19
68	63.8 [18.9]	69	69.3 [16.7]					
72	3.6 [2.6]	73	3.7 [2.9]	0.06	0.04	.10	0.03	0.18
69	4.0 [2.5]	69	3.4 [2.7]					
72	3.9 [2.5]	73	3.9 [2.8]	0.03	0.04	.39	0.17	0.02
69	4.5 [2.4]	69	4.0 [2.6]					
72	3.6 [2.1]	73	3.7 [2.3]	0.03	0.03	.29	0.08	0.19
69	3.7 [2.1]	69	3.6 [2.2]					
				Between-group difference T0-T1				
	N/A		N/A	0.06	0.08	.48	0.10	N/A
	N/A		N/A					
	N/A		N/A	-0.65	0.49	.19	0.18	N/A
	N/A		N/A					
	N/A		N/A	-0.69	1.25	.58	0.06	N/A
	N/A		N/A					
	N/A		N/A	-0.32	0.37	.39	0.10	N/A
	N/A		N/A					
	N/A		N/A	0.83	0.46	.07	0.27	N/A
	N/A		N/A					

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Table A1. *(continued)*

	T0[a]		T1[a]	
	n	**M [SD]**	**n**	**M [SD]**
No. correct items digit span task				
BWL	83	15.6 [3.4]	79	16.1 [3.4]
DWL[c]	81	15.1 [3.4]	75	15.8 [3.5]
Forward digit span task				
BWL	83	9.1 [1.8]	79	9.3 [1.9]
DWL[c]	81	8.9 [2.0]	75	9.2 [1.9]
Backward digit span task				
BWL	83	6.5 [1.9]	79	6.8 [2.0]
DWL[c]	81	6.2 [1.9]	75	6.7 [2.0]

Raw means and standard deviations are reported.
BWL Bright white light; **DWL** Dim white light; **MDASI** MD Anderson Symptom Inventory; **MOS-CF6** Medical Outcomes Studies – Cognitions.
[a] **T0** baseline; **T1** post intervention; **T2** 3 months after light therapy; **T3** 9 months after light therapy.
[b] The effect size was calculated based on the mean scores and pooled standard deviation (SD): ($mean_{T1}$-$mean_{T0}$)/pooled $SD_{T0\text{-}T1}$ or ($mean_{T3}$-$mean_{T1}$)/pooled $SD_{T1\text{-}T3}$; small 0.2, moderate 0.5, large 0.8. [c] DWL is the reference group. [d] 1 case excluded because of influential outlier.

	T2[a]		T3[a]		Between-group difference T0-T1			ES[b]	
	n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
		N/A		N/A	-0.38	0.43	.38	0.12	N/A
		N/A		N/A					
		N/A		N/A	-0.08	0.31	.80	0.07	N/A
		N/A		N/A					
		N/A		N/A	-0.27	0.24	.26	0.14	N/A
		N/A		N/A					

Table A2. Mean values and standard deviations per time-point and linear time effects of the outcome measurements for all participants.

	T0[a]		T1[a]	
	n	M [SD]	n	M [SD]
COGNITIVE COMPLAINTS				
MOS-CF6	165	62.2 [18.1]	157	65.6 [18.6]
MDASI remembering	165	4.0 [2.9]	157	3.7 [2.7]
MDASI concentrating	165	4.2 [2.7]	157	4.0 [2.7]
MDASI interference	165	4.4 [2.0]	156	3.7 [2.1]
COGNITIVE FUNCTIONING				
Reaction time (PVT)[c]	158	3.8 [0.5]	145	3.9 [0.5]
Performance lapses (PVT)[c]	158	0.9 [2.6]	145	0.7 [3.1]
No. correct items learning phase (15WT)	164	46.9 [10.7]	154	49.0 [11.4]
No. correct items free recall (15WT)	164	10.0 [3.0]	165	10.6 [3.1]
No. correct items recognition (15WT)	163	29.0 [1.7]	154	28.9 [2.7]
No. correct items digit span task	164	15.3 [3.4]	154	15.9 [3.4]
Forward digit span task	164	9.0 [1.9]	154	9.2 [1.9]
Backward digit span task	164	6.4 [1.9]	154	6.7 [2.0]

Raw means and standard deviations are reported.
15WT 15 words task; **MDASI** MD Anderson Symptom Inventory; **MOS-CF6** Medical Outcomes Studies – Cognitions; **PVT** Psychomotor Vigilance Task.
[a] **T0** baseline; **T1** post intervention; **T2** 3 months after light therapy; **T3** 9 months after light therapy.
[b] The effect size was calculated based on the mean scores and pooled standard deviation (SD): ($mean_{T1}$-$mean_{T0}$)/pooled $SD_{T0\text{-}T1}$ or ($mean_{T3}$-$mean_{T1}$)/pooled $SD_{T1\text{-}T3}$; small 0.2, moderate 0.5, large 0.8. [c] One case excluded because of influential outlier.

	T2[a]		T3[a]		Linear time effect			ES[b]	
	n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
	140	65.4 [18.0]	142	67.8 [18.7]	0.09	0.72	.90	0.18	0.10
	141	3.8 [2.6]	142	3.6 [2.8]	-0.05	0.11	.66	0.08	0.06
	141	4.2 [2.5]	142	3.9 [2.7]	0.03	0.10	.77	0.07	0.01
	141	3.7 [2.1]	142	3.6 [2.2]	0.04	0.07	.62	0.34	0.01
		N/A		N/A	-0.42	0.22	.06	0.14	N/A
		N/A		N/A	0.43	1.33	.74	0.06	N/A
		N/A		N/A	4.86	3.41	.16	0.19	N/A
		N/A		N/A	-0.27	1.00	.79	0.20	N/A
		N/A		N/A	0.19	1.26	.88	0.05	N/A
		N/A		N/A	1.39	1.16	.23	0.20	N/A
		N/A		N/A	0.07	0.85	.93	0.14	N/A
		N/A		N/A	1.32	0.67	.05	0.20	N/A

Table A3. Mean values and standard deviations per time-point and between-group differences for the mixed-effects models of the outcome measurements for participants who used light therapy on at least 25 days.

	T0[a]		T1[a]	
	n	M [SD]	n	M [SD]
COGNITIVE COMPLAINTS				
MOS-CF6				
BWL	33	62.4 [17.5]	33	68.2 [19.6]
DWL[c]	28	61.5 [15.6]	28	64.6 [19.2]
MDASI remembering				
BWL	33	4.3 [3.0]	33	3.7 [3.0]
DWL[c]	28	3.8 [3.0]	28	3.6 [3.0]
MDASI concentrating				
BWL	33	4.3 [2.8]	33	3.7 [2.9]
DWL[c]	28	4.3 [2.7]	28	3.9 [2.8]
MDASI interference				
BWL	33	4.5 [1.9]	33	3.8 [1.9]
DWL[c]	28	4.7 [1.8]	27	4.1 [2.1]
COGNITIVE FUNCTIONING				
1/RT (PVT)[d]				
BWL	32	3.7 [0.5]	30	3.9 [0.4]
DWL[c]	28	3.8 [0.6]	28	3.8 [0.7]
Performance lapses (PVT)[d]				
BWL	32	1.4 [3.5]	30	0.4 [0.8]
DWL[c]	28	1.1 [3.0]	28	1.9 [6.8]
No. correct items learning phase (15WT)				
BWL	33	42.6 [11.0]	33	43.7 [11.9]
DWL[c]	28	46.2 [13.7]	28	50.0 [12.2]
No. correct items free recall (15WT)				
BWL	33	8.8 [3.1]	33	9.2 [3.3]
DWL[c]	28	9.5 [3.5]	28	10.3 [3.0]
No. correct items recognition (15WT)				
BWL	33	28.4 [2.0]	33	28.4 [2.0]
DWL[c]	28	29.2 [1.4]	28	29.4 [1.2]

T2[a]		T3[a]		Linear time effect T0-T3			ES[b]	
n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
31	66.2 [17.7]	31	64.9 [22.2]	-0.37	0.46	.42	0.14	0.30
26	63.8 [21.4]	27	68.0 [19.6]					
31	3.5 [2.7]	31	3.9 [3.0]	-0.04	0.05	.47	0.16	0.04
28	4.0 [3.2]	27	3.7 [3.1]					
31	4.1 [2.5]	31	4.1 [2.8]	-0.02	0.06	.69	0.10	0.04
26	4.3 [2.8]	27	4.0 [3.0]					
31	4.0 [2.2]	31	3.8 [2.3]	0.02	0.05	.64	0.06	0.11
26	3.5 [2.1]	27	3.8 [2.3]					
				Between-group difference T0-T1				
	N/A		N/A	0.23	0.16	.14	0.42	N/A
	N/A		N/A					
	N/A		N/A	-1.72	1.10	.12	0.43	N/A
	N/A		N/A					
	N/A		N/A	-2.65	2.09	.21	0.22	N/A
	N/A		N/A					
	N/A		N/A	-0.54	0.63	.40	0.12	N/A
	N/A		N/A					
	N/A		N/A	-0.11	0.48	.82	0.12	N/A
	N/A		N/A					

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Table A3. *(continued)*

	T0[a]		T1[a]	
	n	**M [SD]**	**n**	**M [SD]**
No. correct items digit span task				
BWL	33	14.8 [3.6]	33	15.7 [3.1]
DWL[c]	28	14.9 [4.1]	28	15.1 [3.9]
Forward digit span task				
BWL	33	8.7 [1.8]	33	9.0 [1.7]
DWL[c]	28	8.6 [2.4]	28	8.7 [2.1]
Backward digit span task				
BWL	33	6.2 [2.0]	33	6.6 [2.0]
DWL[c]	28	6.2 [2.2]	28	6.4 [2.2]

Raw means and standard deviations are reported.
BWL Bright white light; **DWL** Dim white light; **MDASI** MD Anderson Symptom Inventory; **MOS-CF6** Medical Outcomes Studies – Cognitions.
[a] **T0** baseline; **T1** post intervention; **T2** 3 months after light therapy; **T3** 9 months after light therapy.
[b] The effect size was calculated based on the mean scores and pooled standard deviation (SD): $(mean_{T1}-mean_{T0})$/pooled SD_{T0-T1} or $(mean_{T3}-mean_{T1})$/pooled SD_{T1-T3}; small 0.2, moderate 0.5, large 0.8. [c] DWL is the reference group. [d] 1 case excluded because of influential outlier.

	T2[a]		T3[a]		Between-group difference T0-T1			ES[b]	
	n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
		N/A		N/A	0.41	0.68	.55	0.17	N/A
		N/A		N/A					
		N/A		N/A	0.22	0.54	.69	0.15	N/A
		N/A		N/A					
		N/A		N/A	0.19	0.34	.58	0.15	N/A
		N/A		N/A					

Table A4: Mean values and standard deviations per time-point and between-group differences for the mixed-effects models of the outcome measurements for participants showed deviant cognitive functioning on baseline.

	T0[a]		T1[a]	
	n	M [SD]	n	M [SD]
COGNITIVE COMPLAINTS				
MOS-CF6				
BWL	25	65.0 [19.9]	24	65.0 [20.1]
DWL[c]	28	54.0 [17.6]	27	61.9 [16.5]
MDASI remembering				
BWL	25	3.8 [2.9]	24	3.9 [2.6]
DWL[c]	28	5.0 [2.7]	27	4.9 [2.6]
MDASI concentrating				
BWL	25	4.4 [3.2]	24	4.0 [2.6]
DWL[c]	28	5.0 [2.5]	27	4.9 [2.4]
MDASI interference				
BWL	25	4.5 [2.2]	24	3.7 [2.1]
DWL[c]	28	4.7 [2.0]	27	4.3 [2.0]
COGNITIVE FUNCTIONING				
1/RT (PVT)[d]				
BWL	25	3.7 [0.5]	23	4.0 [0.4]
DWL[c]	28	3.7 [0.7]	28	3.7 [0.7]
Performance lapses (PVT)[d]				
BWL	25	1.7 [4.0]	23	0.4 [0.8]
DWL[c]	28	1.3 [3.8]	28	1.8 [6.8]
No. correct items learning phase (15WT)				
BWL	25	36.8 [10.1]	24	37.9 [11.5]
DWL[c]	28	41.3 [10.1]	28	45.6 [7.7]
No. correct items free recall (15WT)				
BWL	25	7.0 [2.4]	24	8.2 [3.2]
DWL[c]	28	8.4 [3.2]	28	9.8 [2.7]
No. correct items recognition (15WT)				
BWL	25	27.4 [2.4]	24	27.1 [2.1]
DWL[c]	28	28.4 [2.3]	28	28.9 [1.4]

	T2[a]		T3[a]		Linear time effect T0-T3			ES[b]	
	n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
	20	67.3 [17.5]	21	71.3 [21.9]	0.46	0.41	.27	0.39	0.33
	25	59.6 [17.5]	26	63.2 [16.7]					
	20	3.6 [2.6]	21	3.4 [2.9]	-0.03	0.07	.65	0.04	0.07
	25	5.0 [2.6]	26	4.5 [2.8]					
	20	3.8 [2.5]	21	3.5 [3.0]	-0.14	0.07	.05	0.15	0.24
	25	5.3 [2.1]	26	4.9 [2.3]					
	20	3.8 [2.2]	21	3.5 [2.7]	-0.07	0.06	.20	0.28	0.04
	25	4.2 [1.9]	26	4.0 [2.1]					
					Between-group difference T0-T1				
		N/A		N/A	0.25	0.20	.20	0.43	N/A
		N/A		N/A					
		N/A		N/A	-2.26	1.28	.09	0.41	N/A
		N/A		N/A					
		N/A		N/A	-3.28	2.42	.18	0.32	N/A
		N/A		N/A					
		N/A		N/A	-0.20	0.70	.78	0.09	N/A
		N/A		N/A					
		N/A		N/A	0.27	0.55	.62	0.11	N/A
		N/A		N/A					

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Table A4. *(continued)*

	T0[a]		T1[a]	
	n	**M [SD]**	**n**	**M [SD]**
No. correct items digit span task				
BWL	25	13.3 [3.7]	24	13.7 [2.9]
DWL[c]	28	13.1 [3.4]	28	14.6 [3.8]
Forward digit span task				
BWL	25	8.1 [1.8]	24	8.1 [1.4]
DWL[c]	28	7.7 [2.0]	28	8.5 [2.0]
Backward digit span task				
BWL	25	5.2 [2.1]	24	5.6 [2.0]
DWL[c]	28	5.4 [2.1]	28	6.1 [2.3]

Raw means and standard deviations are reported.
BWL Bright white light; **DWL** Dim white light; **MDASI** MD Anderson Symptom Inventory; **MOS-CF6** Medical Outcomes Studies – Cognitions.
[a] **T0** baseline; **T1** post intervention; **T2** 3 months after light therapy; **T3** 9 months after light therapy.
[b] The effect size was calculated based on the mean scores and pooled standard deviation (SD): $(mean_{T1}-mean_{T0})/pooled\ SD_{T0\text{-}T1}$ or $(mean_{T3}-mean_{T1})/pooled\ SD_{T1\text{-}T3}$; small 0.2, moderate 0.5, large 0.8. [c] DWL is the reference group. [d] 1 case excluded because of influential outlier.

	T2[a]		T3[a]		Between-group difference T0-T1			ES[b]	
	n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
		N/A		N/A	-0.93	0.76	.22	0.30	N/A
		N/A		N/A					
		N/A		N/A	-0.72	0.57	.22	0.40	N/A
		N/A		N/A					
		N/A		N/A	-0.21	0.40	.60	0.15	N/A
		N/A		N/A					

Table A5. Mean values and standard deviations per time-point and between-group differences for the mixed-effects models of the outcome measurements for Luminette Glasses users only.

	T0[a]		T1[a]	
	n	M [SD]	n	M [SD]
COGNITIVE COMPLAINTS				
MOS-CF6				
BWL	65	62.9 [17.8]	64	65.9 [19.4]
DWL[c]	62	60.6 [16.1]	58	64.0 [16.3]
MDASI remembering				
BWL	65	3.9 [2.8]	64	3.8 [2.7]
DWL[c]	62	4.3 [2.8]	58	3.8 [2.6]
MDASI concentrating				
BWL	65	4.0 [2.7]	64	4.1 [2.7]
DWL[c]	62	4.6 [2.4]	58	4.2 [2.5]
MDASI interference				
BWL	65	4.4 [1.9]	64	3.6 [1.9]
DWL[c]	62	4.5 [1.9]	57	3.9 [2.0]
COGNITIVE FUNCTIONING				
1/RT (PVT)[d]				
BWL	62	3.8 [0.5]	57	3.9 [0.4]
DWL[c]	59	3.7 [0.5]	54	3.8 [0.6]
Performance lapses (PVT)[d]				
BWL	62	1.1 [3.0]	57	0.5 [0.9]
DWL[c]	59	0.8 [2.2]	54	1.0 [4.9]
No. correct items learning phase (15WT)				
BWL	65	46.6 [10.3]	61	48.7 [11.9]
DWL[c]	62	48.6 [11.1]	57	49.8 [10.4]
No. correct items free recall (15WT)				
BWL	65	10.2 [2.9]	61	10.7 [3.0]
DWL[c]	62	10.3 [3.0]	57	11.0 [2.7]
No. correct items recognition (15WT)				
BWL	65	29.0 [1.7]	61	29.1 [1.6]
DWL[c]	61	29.3 [1.1]	57	28.7 [4.0]
No. correct items digit span task				
BWL	65	15.5 [3.5]	61	16.2 [3.6]
DWL[c]	62	15.1 [3.6]	57	15.9 [3.7]

	T2[a]		T3[a]		Linear time effect T0-T3			ES[b]	
	n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
	55	65.5 [16.6]	57	65.2 [20.5]	-0.49	0.30	.11	0.02	0.29
	52	61.9 [17.3]	54	69.6 [15.7]					
	55	3.6 [2.5]	57	3.8 [2.9]	0.05	0.04	.30	0.08	0.09
	53	4.0 [2.3]	54	3.6 [2.6]					
	55	4.0 [2.3]	57	4.1 [2.7]	0.04	0.04	.42	0.19	0.02
	53	4.5 [2.2]	54	4.0 [2.5]					
	55	3.7 [1.9]	57	3.7 [2.1]	0.03	0.03	.28	0.11	0.25
	53	3.8 [1.9]	54	3.5 [2.0]					
					Between-group difference T0-T1				
		N/A		N/A	0.06	0.09	.49	0.15	N/A
		N/A		N/A					
		N/A		N/A	-0.84	0.61	.17	0.29	N/A
		N/A		N/A					
		N/A		N/A	-0.83	1.33	.54	0.07	N/A
		N/A		N/A					
		N/A		N/A	-0.23	0.41	.57	0.09	N/A
		N/A		N/A					
		N/A		N/A	1.05	0.55	.06	0.33	N/A
		N/A		N/A					
		N/A		N/A	-0.40	0.45	.37	0.07	N/A
		N/A		N/A					

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Table A5. *(continued)*

	T0[a]		T1[a]	
	n	M [SD]	n	M [SD]
Forward digit span task				
BWL	65	8.9 [1.8]	61	9.4 [2.0]
DWL[c]	62	8.9 [2.1]	57	9.2 [2.0]
Backward digit span task				
BWL	65	6.6 [2.0]	61	6.8 [2.1]
DWL[c]	62	6.2 [2.0]	57	6.8 [2.2]

Raw means and standard deviations are reported.
BWL Bright white light; **DWL** Dim white light; **MDASI** MD Anderson Symptom Inventory; **MOS-CF6** Medical Outcomes Studies – Cognitions.
[a] **T0** baseline; **T1** post intervention; **T2** 3 months after light therapy; **T3** 9 months after light therapy.
[b] The effect size was calculated based on the mean scores and pooled standard deviation (SD): ($mean_{T1}$-$mean_{T0}$)/pooled $SD_{T0\text{-}T1}$ or ($mean_{T3}$-$mean_{T1}$)/pooled $SD_{T1\text{-}T3}$; small 0.2, moderate 0.5, large 0.8. [c] DWL is the reference group. [d] 1 case excluded because of influential outlier.

	T2[a]		T3[a]		Between-group difference T0-T1			ES[b]	
	n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
		N/A		N/A	0.02	0.35	.95	0.08	N/A
		N/A		N/A					
		N/A		N/A	-0.40	0.26	.12	0.19	N/A
		N/A		N/A					

Table A6. Mean values and standard deviations per time-point and between-group differences for the mixed-effects models of the outcome measurements for participants who used light therapy during fall or winter.

	T0[a]		T1[a]	
	n	M [SD]	n	M [SD]
COGNITIVE COMPLAINTS				
MOS-CF6				
BWL	46	62.4 [16.7]	46	65.9 [18.0]
DWL[c]	43	57.1 [18.6]	41	62.4 [19.0]
MDASI remembering				
BWL	46	4.0 [2.9]	46	3.8 [2.7]
DWL[c]	43	4.2 [2.8]	41	4.0 [2.6]
MDASI concentrating				
BWL	46	3.8 [2.6]	46	3.9 [2.5]
DWL[c]	43	5.0 [2.5]	43	4.5 [2.6]
MDASI interference				
BWL	46	3.9 [1.9]	46	3.1 [2.0]
DWL[c]	43	5.0 [2.0]	40	4.1 [2.1]
COGNITIVE FUNCTIONING				
1/RT (PVT)[d]				
BWL	43	3.9 [0.4]	39	3.9 [0.4]
DWL[c]	42	3.7 [0.6]	38	3.7 [0.6]
Performance lapses (PVT)[d]				
BWL	43	0.8 [2.1]	39	0.5 [1.0]
DWL[c]	42	1.0 [2.6]	38	1.5 [5.8]
No. correct items learning phase (15WT)				
BWL	46	45.7 [10.0]	44	49.2 [12.5]
DWL[c]	43	48.8 [11.3]	42	50.6 [10.4]
No. correct items free recall (15WT)				
BWL	46	9.9 [2.9]	44	10.6 [3.5]
DWL[c]	43	10.3 [3.1]	42	11.0 [2.6]
No. correct items recognition (15WT)				
BWL	46	28.6 [2.0]	44	29.1 [1.5]
DWL[c]	43	29.2 [1.1]	42	28.6 [4.2]

	T2[a]		T3[a]		Linear time effect T0-T3			ES[b]	
	n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
	39	66.4 [17.1]	41	68.8 [16.6]	-0.22	0.35	.54	0.06	0.04
	39	58.9 [20.7]	38	66.1 [18.6]					
	39	3.7 [2.8]	41	3.6 [2.9]	0.08	0.06	.14	0.03	0.20
	39	4.1 [2.7]	38	3.3 [3.1]					
	39	3.9 [2.5]	41	3.7 [2.8]	0.02	0.05	.74	0.22	0.09
	39	5.1 [2.4]	38	4.5 [2.6]					
	39	3.3 [1.8]	41	3.1 [2.1]	-0.01	0.04	.89	0.06	0.09
	39	4.2 [2.1]	38	4.0 [2.2]					
					Between-group difference T0-T1				
		N/A		N/A	0.03	0.10	.78	0.05	N/A
		N/A		N/A					
		N/A		N/A	-0.70	1.08	.52	0.28	N/A
		N/A		N/A					
		N/A		N/A	1.51	1.72	.38	0.16	N/A
		N/A		N/A					
		N/A		N/A	-0.09	0.49	.85	0.00	N/A
		N/A		N/A					
		N/A		N/A	1.46	0.74	.05	0.43	N/A
		N/A		N/A					

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Table A6. *(continued)*

	T0[a]		T1[a]	
	n	**M [SD]**	**n**	**M [SD]**
No. correct items digit span task				
BWL	46	15.8 [3.1]	44	16.2 [3.3]
DWL[c]	43	14.9 [3.6]	42	15.9 [3.7]
Forward digit span task				
BWL	46	9.3 [1.6]	44	9.3 [1.9]
DWL[c]	43	8.8 [2.1]	42	9.2 [2.0]
Backward digit span task				
BWL	46	6.5 [1.8]	44	6.9 [1.8]
DWL[c]	43	6.2 [2.1]	42	6.6 [2.1]

Raw means and standard deviations are reported.
BWL Bright white light; **DWL** Dim white light; **MDASI** MD Anderson Symptom Inventory; **MOS-CF6** Medical Outcomes Studies – Cognitions.
[a] **T0** baseline; **T1** post intervention; **T2** 3 months after light therapy; **T3** 9 months after light therapy.
[b] The effect size was calculated based on the mean scores and pooled standard deviation (SD): $(mean_{T1}-mean_{T0})$/pooled SD_{T0-T1} or $(mean_{T3}-mean_{T1})$/pooled SD_{T1-T3}; small 0.2, moderate 0.5, large 0.8. [c] DWL is the reference group. [d] One case excluded because of influential outlier. For 1/RT. no random intercept was included in the model because convergence could not be reached for the model including a random intercept.

	T2[a]		T3[a]		Between-group difference T0-T1			ES[b]	
	n	M [SD]	n	M [SD]	B	SE	*p*	T0-T1	T1-T3
		N/A		N/A	-0.61	0.57	.28	0.20	N/A
		N/A		N/A					
		N/A		N/A	-0.62	0.43	.15	0.27	N/A
		N/A		N/A					
		N/A		N/A	0.02	0.29	.95	0.08	N/A
		N/A		N/A