Exploring the relation between Circadian Timing of Morning Bright Light Therapy and the Antidepressant Effect

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Exploring the relation between Circadian Timing of Morning Bright Light Therapy and the Antidepressant Effect

by Kim Wentink

0911080

in partial fulfilment of the requirements for the degree of

Master of Science

in Human Technology Interaction

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Abstract

The circadian timing of morning bright light therapy (BLT) is an important factor to maximize the antidepressant effect in patients diagnosed with a seasonal affective disorder (SAD). Since this factor has – at least to our knowledge – not yet been researched in patients with non-seasonal depressions, this study explores whether there is a relation between the circadian timing of morning BLT and the antidepressant effect in patients with a depression (i.e., with seasonal and non-seasonal mood disorders). In this study, the circadian timing of morning BLT was expressed in terms of the number of hours between the dim-light melatonin onset (DLMO) and the start time of the morning BLT. The DLMO was estimated by means of the Morningness-Eveningness Questionnaire Self-Assessment (MEQ-SA). The antidepressant effect was assessed with the Quick Inventory of Depressive Symptomatology Self Report (QIDS-SR). Participants (n = 47) received morning BLT within the standardized light therapy program of the Geestelijke gezondheidszorg Eindhoven (GGzE) (i.e., 10,000 lux for 30 minutes, start time between 7:30-10:00 AM, during 5 days/week for 1 up to -3 weeks). Morning BLT was highly effective in treating depression and treatment week had a statistically significant influence on the antidepressant effect. The largest antidepressant effect occurred in the first week of treatment. No statistically significant association was found between the circadian timing of morning BLT and its antidepressant effect. However, after the first treatment week, participants reported an earlier habitual sleep onset time within the Pittsburg sleep quality index (PSQI) questionnaire, which correlated statistically significant with the circadian timing of morning BLT. This might be indicative of a circadian phase advancing effect in the first BLT week (inducing an earlier DLMO and thus a later circadian timing of the morning BLT). As the current study had an explorative nature and restricted sample size, more research is needed to establish whether the circadian timing of morning BLT indeed is an effective instrument to optimize bright light treatment of depression. For future studies it is recommended to design studies in which the circadian timing of morning BLT is more precisely controlled and varied than in the current study. Moreover, during such studies it would be useful to account for potential BLT induced circadian phase changes (i.e. changes in DLMO timing of a participant) across the different treatment days and weeks.

Keywords: Depressive disorder, Light therapy, Circadian rhythm, Chronotherapy, Dim Light Melatonin Onset

Acknowledgement

This master thesis was conducted in partial fulfillment of my master's degree Human-Technology Interaction at Eindhoven University of Technology (TU/e). Within this master program, the science of chronobiology and light caught my attention, as a subject to which I would like to contribute. How wonderful is it to be able to improve people's health and well-being with the use of light? A few months later, I was allowed to start my research into bright light therapy in the LichtCafé (of GGzE) in Eindhoven. I am grateful that I got the opportunity to end my study time with combining my knowledge from the bachelor Psychology and the master Human Technology Interaction in this graduation project. Therefore, I would like to use this section to thank all the people who contributed to this project.

First of all, I would like to thank my supervisors, Yvonne de Kort, Karin Smolders and Luc Schlangen, for giving me this opportunity. Besides that, I want to thank them for their close involvement in this project and for sharing their expertise and critical feedback from which I learned a lot. And Luc, in particular, thank you for the excellent guidance, support and for always being available during this process.

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Finally, I would like to thank my family and friends for their unconditional support during this graduation project.

Then all that remains is for me to say, have fun reading!

Kim Wentink,
Eindhoven, August 2021

Table of Contents

1. Introduction

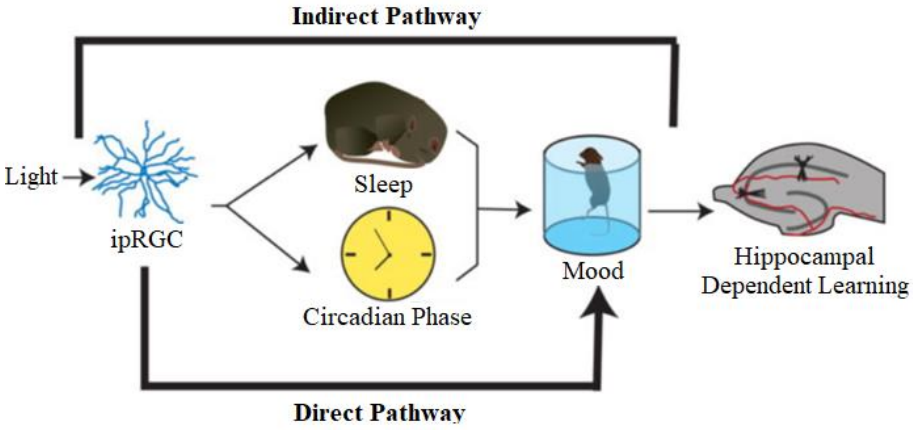
Approximately 649,500 of the Dutch population had a depression in 2011, of which 550,300 were diagnosed with a major depressive disorder, 93,200 with dysthymia and 91,100 with bipolar disorder (de Graaf, ten Have, van Dorsselaer, 2010). Since this population screening, these numbers have only increased (Volksgezondheidenzorg, 2021). Psychoeducation, day structuring, pharmacotherapy or psychotherapy are frequently used methods to treat depression. However, these treatments can be time-consuming (the antidepressant effect is often only visible after multiple weeks) and are not effective for all patients. Nowadays, light therapy has also been listed as a treatment option in the multidisciplinary guideline for depression (Spijker et al., 2013). The advantage of light therapy is that the effect can occur quickly (within 5-7 days), while the treatment has few to no side effects (Campbell et al., 1995; Meesters & Hoofdakker, 1998). In this introduction, it will be discussed how light therapy works and how this therapy can potentially be optimized to improve the quality of life and health of people with depression.

1.1 Pathways of Light

Light has a major influence on our psychological functioning. As well known, light allows us to visually perceive our environment. Via the so called image forming (IF) pathway, light enables visual performance, experience and comfort. Alternatively, light also influences mood, independent of image formation, through its modulating acute and circadian effects (the non-image forming (NIF) pathway) (de Kort & Veitch, 2014). Besides influencing mood via the circadian rhythms and sleep, the so called ‘indirect pathway’ of light, light can also directly affect the mood centers in the brain, via the so-called ‘direct pathway’ (see Figure 1) (LeGates, Fernandez & Hattar, 2014).

Figure 1

The direct and indirect pathway of light's influences on mood centers in the brain



Note. Reprinted from LeGates et al. (2014).

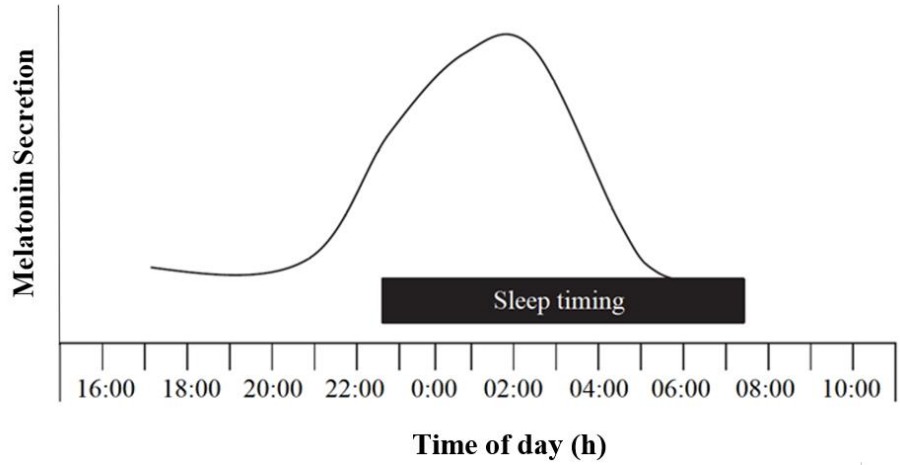
1.1.1 Indirect Pathway of Light. The term circadian is derived from the Latin 'circa diem' to mean 'approximately a day'. As such the circadian rhythm refers to the roughly 24-h rhythm in bodily processes and activities. Various metabolic, chemical, endocrine and behavioral processes in humans show a circadian rhythm, e.g. body temperature, cortisol and melatonin, as well as cognition and mood (Baron & Reid, 2014). All these endogenous rhythms are present independent of external cues and synchronized by a central biological clock, the "master clock", which in humans is located in the suprachiasmatic nucleus (SCN) in the anterior hypothalamus (Baron & Reid, 2014; Gooley, 2017). Most humans have an endogenous circadian period which is slightly longer than 24 hours, for example 24.5 hours, which means that a person delays sleep with almost 30 minutes each day unless synchronized or 'entrained' by sensory inputs (Berson, 2003; Baron & Reid 2014). These sensory inputs are called 'Zeitgebers', 'time cues' or 'time givers'. Light is the most important synchronizer (the strongest 'Zeitgeber') of human circadian rhythms (Berson, 2003; Gooley, 2017). Other Zeitgebers include for example exogenous melatonin, physical and social activity and healthy/structured food intake (Baron & Reid, 2014). Without any external time cues, the

circadian clock will 'free run' at its own period, which is frequently not exactly 24 hours. This process of circadian entrainment, synchronizing the circadian clock to the solar day, ensures a proper timing of physiology and behavior across 24 hours and is critical to maintain a good human performance, sleep behavior, and energy balance (Gooley, 2017).

The gold standard marker of circadian rhythms is the timing of the dim light melatonin-onset (DLMO) (Wirz-Justice & Benedetti, 2020). The DLMO is the timing of the onset of melatonin secretion under low light conditions (Baron & Reid, 2014; Kantermann, Sung & Burgess, 2015). Melatonin secretion has a circadian rhythm that peaks at night and generally begins to rise 2 to 3 hours before the usual onset of nighttime sleep (see Figure 2) (Baron & Reid, 2014; Burgess & Fogg, 2008). The secretion of melatonin from the pineal gland is controlled by the suprachiasmatic nucleus (SCN) (Moore, 1996; Kantermann et al., 2015). When collected over more than 1 cycle, the rhythm of melatonin production has been shown to reflect both the phase and period of the endogenous circadian oscillator (Benloucif et al., 2008).

Figure 2

Illustration of the fluctuation in melatonin levels over a 24-hour period, and the circadian phase between dim light melatonin-onset and habitual sleep timing



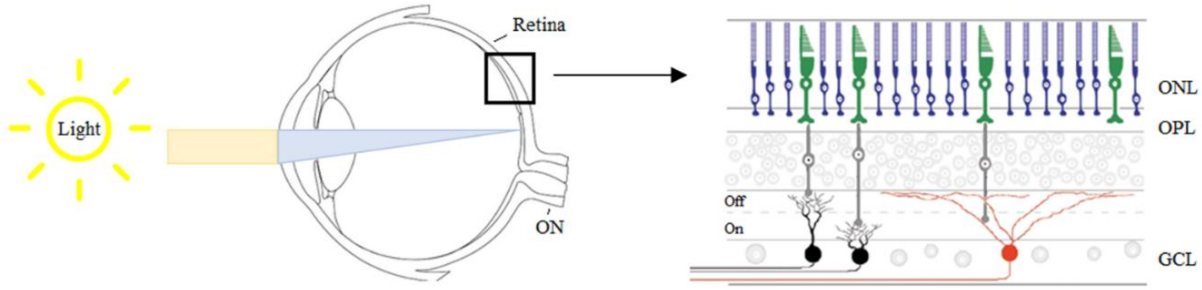
Note. In dim light conditions, the pineal gland begins producing melatonin in the evening (2-3h before habitual bedtime), the melatonin levels peak in the middle of the night and decrease in the early morning (Barrett, Lack & Morris, 1993; Shanahan & Czeisler, 1991). Adapted from Baron & Reid (2014).

1.1.2 Pathways of Light in the Eye. The retinal photoreceptors that mediate pattern-forming vision are distinct from those that mediate light resetting of circadian rhythms (Gooley 2017). These different retinal photoreceptors are connected to the same optic nerve (ON), but have different pathways into the brain. Two pathways can be discriminated: the image forming geniculostriate tract (GLT) and the non-image forming retinohypotalamic tract (RHT). The GLT governs visual perception and visual responses, and feeds the brain with signals from the rods (in blue, Figure 3) and cones (in green, Figure 3) in the outer nuclear layer (ONL). When the light is detected by the rods and cones, it is processed and signalled to retinal ganglion cells (RGCs, in black, Figure 3) through horizontal, amacrine and bipolar cells (in grey, Figure 3) in the outer plexiform layer (OPL) (Berson, 2003; LeGates et al., 2014). These RGCs are the only output neurons from the retina

to the brain and mostly project to the lateral geniculate nucleus (LGN) in the visual cortex (Berson, 2003). The RHT governs circadian, endocrine, and neurobehavioral functions. This pathway enters the brain via the axons of the intrinsically photosensitive retinal ganglion cells (ipRGCs) (in red, Figure 3), which is a small subset of the RGCs (2-5 % of the total number of RCs) in the ganglion cell layer (LeGates et al., 2014; Gooley, 2017). The ipRGCs express the photopigment melanopsin with a peak sensitivity to ~480-nm light (blue wavelength light) and have a lower sensitivity and spatiotemporal resolution than rods or cones (see Figure 4) (Gooley, 2017). However, the dendrites of ipRGCs are spread more widely in the retinal plane (see Figure 3), and thus enabling a greater spatial integration (Berson, 2003).

Figure 3

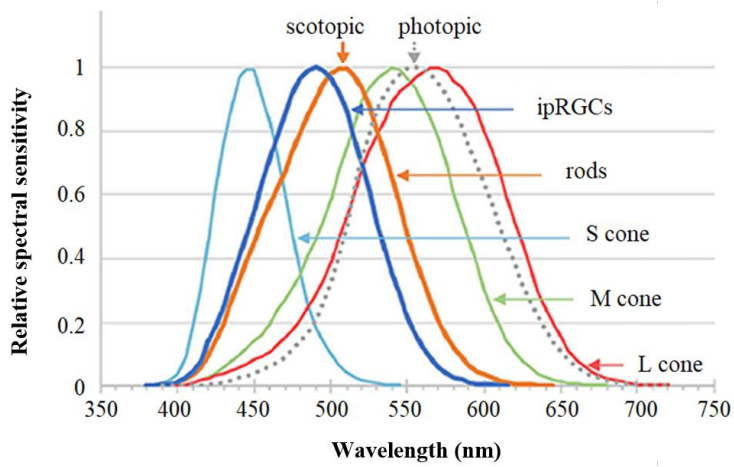
Schematic overview of the retina showing the pathway of light from the photoreceptors to the brain



Note. For clarity, only the cone influenced pathways to the ganglion cell layer (GCL) are shown. Adapted from Berson (2003).

Figure 4

Action spectra for the different photoreceptors of the retina which peak at different wavelengths



Note. Adapted from Schlangen and Price (2021).

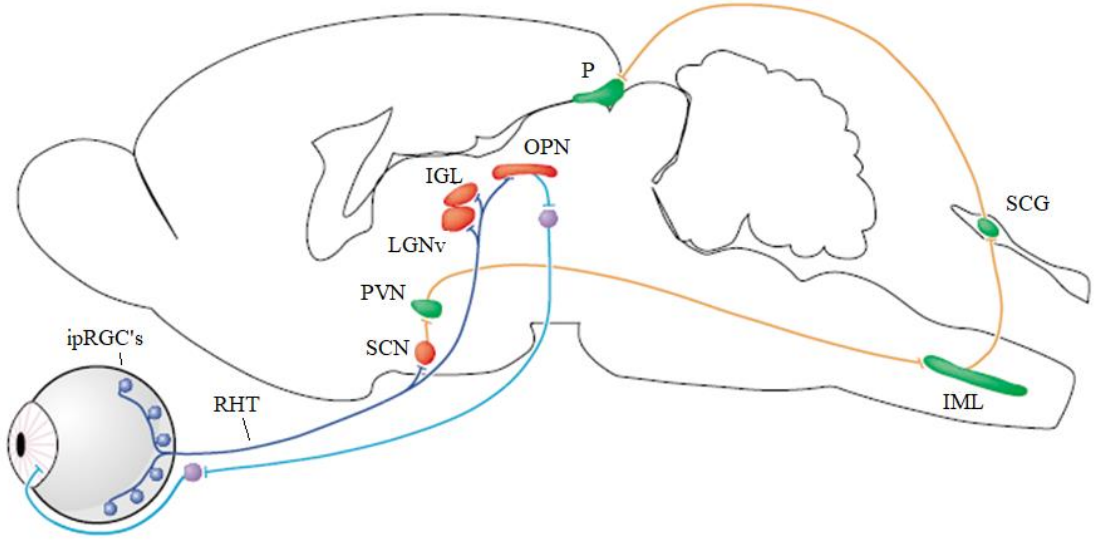
1.1.3 Pathways of Light in the Brain. Like all RGCs, ipRGCs have axons that communicate directly with the brain (in dark blue, Figure 5). Since the ipRGCs have projections to the suprachiasmatic nucleus (SCN) that form the bulk of the RHT and contribute to the entrainment of the circadian clock, this tract is thought to be the sole pathway of light to reset the clock neurons in the SCN (Berson, 2003; Gooley 2017). The orange (Figure 5) polysynaptic pathway originating in the SCN, influences the secretion of melatonin by the pineal gland (P) through the paraventricular nucleus (PVN), the intermediolateral nucleus (IML) and the superior cervical ganglion (SCG) (Berson, 2003; Shankar & Williams, 2021). Also other brain regions that have a role in driving light-mediated processes receive projections from the ipRGCs. For example, the olivary pretectal nucleus (OPN), which has a crucial link to the pupillary light reflex pathway (in light blue and purple, Figure 5), and two components of the lateral geniculate nucleus of the thalamus, the ventral division (LGNv) and the intergeniculate leaflet (IGL) (Berson, 2003). The ipRGCs also influence the orexin system via projections to the lateral hypothalamus (LH),

which for example regulates feeding behavior, arousal and body temperature (LeGates et al., 2014). In summary, the RHT plays a key role in various physiological responses to (day)light, such as (re)setting the biological clock and modulating activity, melatonin levels, and pupil diameter (Berson, 2003).

The two pathways, the GLT and the RHT, are thus very distinct in terms of where they project and how they respond to light (respond to different wavelengths, time length and durations). However, next to their intrinsic (melanopsin-based) light sensitivity, the ipRGCs can also be activated by rod and cone inputs. Therefore, it is likely that both ipRGCs and rod/cone photoreceptors contribute to circadian light resetting in humans (Gooley, 2017). In conclusion, the melanopsin-based photoreception of the ipRGCs has an important role in the non-visual and emotional effects of light as it mediates light resetting of the circadian pacemaker and also directly influences mood centers (An et al., 2020; LeGates, Fernandez & Hattar, 2014; LeGates & Kvarta, 2020; Wirz-Justice & Benedetti, 2020).

Figure 5

Schematic representation of brain regions and circuits that are influenced by ipRGCs



Note. Adapted from Berson (2003).

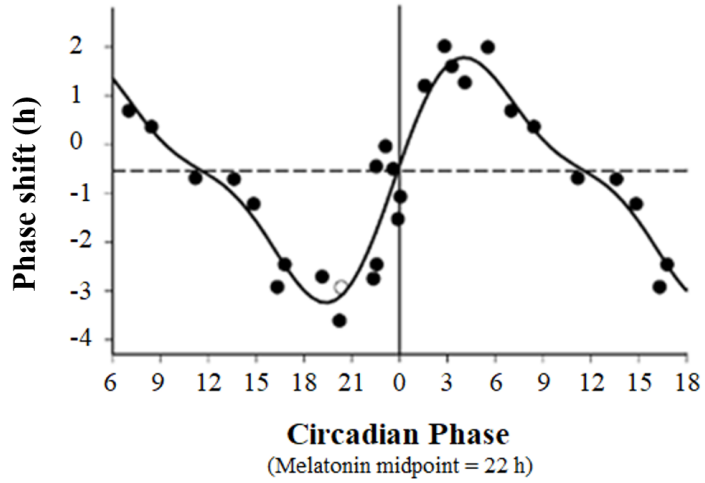
1.2 Circadian Effects of Light

Light exposure can phase shift the internal circadian rhythm. The magnitude and direction of the phase shifting responses to light are determined by characteristics of the light stimulus, such as the timing, intensity, duration, and spectral composition of the light stimulus (Gooley, 2017).

1.2.1 Effects of Light Timing. A light pulse can have different effects on the circadian rhythm depending on the (circadian) time of exposure (Baron & Reid, 2014; Khalsa et al**.,** 2003). Morning light, light exposure that occurs after the critical time of the core body temperature minimum (which typically occurs during the melatonin secretion period at about 2 hours prior to the habitual wake up time; by convention the circadian time and phase at this timepoint are set to 0), will advance the circadian rhythm (positive phase shift values), whereas exposure to light in the evening will delay the circadian rhythm (negative phase shift values) (see Figure 6) (Baron & Reid, 2014; Duffy & Wright, 2005; Khalsa et al., 2003).

Figure 6

The Phase Response Curve (PRC): a graphical representation which describes the effects of a light stimulus at different circadian phases

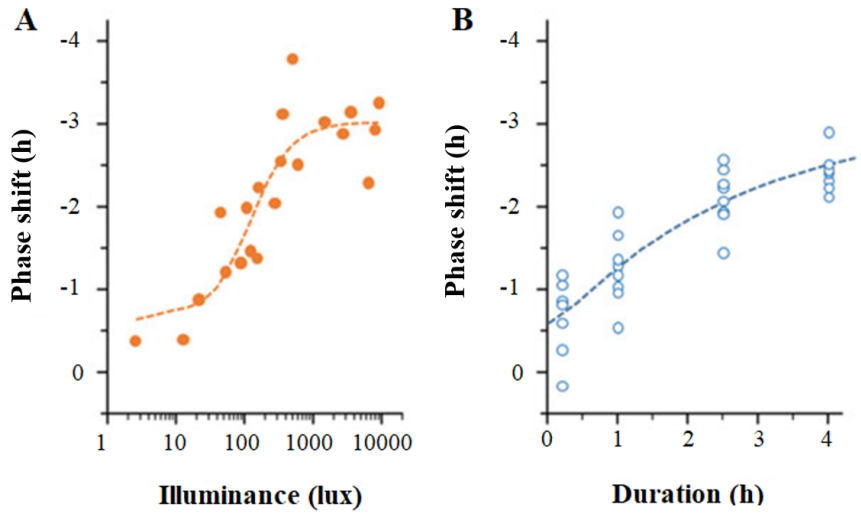


Note. The circadian phase of the midpoint of a 6.5 hour light exposure is plotted relative to the timepoint at which the core body temperature (CBT) rhythm reaches its minimum. At this timepoint the circadian phase equals 0 by definition. By convention, in the PRC phase delays are indicated by negative values on the y-axis and phase advances are indicated by positive values on the y-axis. Adapted from Khalsa et al (2003).

1.2.2 Effects of Light Dose. The magnitude of circadian responses to light can be enhanced by increasing the dose (intensity and duration) of the light pulse. For the intensity, Zeiter et al. (2000) found a nonlinear increase in the phase delay of the circadian rhythm when increasing light intensity (during the biological night), such that ~100 lux of white light elicited a half-maximal and ~10,000 lux a maximal phase shifting response (see Figure 7A) (Gooley, 2017). Duffy, Zeiter and Czeisler (2007) also found a nonlinear increase in the phase shifting when the duration of a light exposure was increased (see Figure 7B) (Gooley, 2017). Furthermore, it was found that the early part of a continuous light stimulus has greater phase shifting effect than the later part of the same light stimulus (Khalsa et al., 2003; Hilaire et al., 2021; Gooley, 2017).

Figure 7

Dose-dependent phase shifting (phase delays) of the circadian rhythm upon light exposure during the early biological night

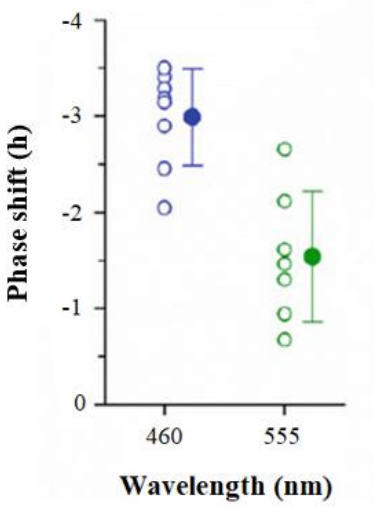


Note. (a) Illuminance-response curve for different intensities of polychromatic white light. (b) Duration-response curve following exposure to bright white light (~10,000 lux for 12 minutes, 1 hour, 2.5 hours and 4 hours). Adapted from Gooley et al. (2017).

1.2.3 Effects of Spectral Composition. The magnitude of the phase shifts to are influenced by the spectral composition of the light stimulus. As mentioned above, the circadian response is strongly mediated by the ipRGCs containing the photopigment melanopsin, which is sensitive to the blue portion of the visual spectrum. Lockley, Brainard and Czeisler (2003) showed twice as great phase shift effects when using 460 nm blue light relative to 555 nm green light (to which the photopic visual system in humans, the IF-pathway, is most sensitive) (see Figure 8). However, it merits to be noted that at lower irradiances, cone receptors might contribute substantially to circadian responses (Gooley, 2017).

Figure 8

Wavelength-dependent phase shifting of the circadian rhythm



Note. Comparing exposure to 6.5 hours of narrow-bandwidth blue light (460 nm) to green light (555 nm) with an average timing of ~6.75 hours before core body temperature minimum. Adapted from Gooley (2017).

1.3 Light and Mood disorders

Mood disorders are often associated with abnormal timing, amplitude or stability of circadian rhythms and sleep-wake patterns (Baron & Reid, 2014; Wirz-Justice & Benedetti, 2020). According to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-V, a distinction can be made between bipolar (and related) disorders and depressive disorders. A depressive disorder is characterized by a bad mood, while a bipolar disorder is diagnosed when this is accompanied by at least one period of (hypo)mania. Various types of bipolar (and related) disorders and depressive disorders can be seen in Table 1. Circadian rhythms are often slowed down and moved back in the case of a depression and accelerated and moved forward in the case of a mania (Eldering et al., 2018). Sometimes, circadian periodicity can also be seen at the symptom level of these mood disorders, such as the diurnal fluctuation of a depressive mood (Eldering et al., 2018). It is therefore important that the

circadian rhythms of depressed persons are properly entrained. This is possible by increasing the Zeitgeber strength, and thus, exposure to well-timed (electric) light (Baron and Reid, 2014; Gooley, 2017; Wirz-Justice & Benedetti, 2020).

Bright light therapy (BLT) is a treatment in which patients diagnosed with a depression are exposed to electrical light. This treatment can be especially useful when it is suspected that a depression has a root cause in a disturbed biological clock or sleep problems. The BLT works according to a few principles: it can activate the biological clock by inhibition of the HPA axis (reduces stress), strengthen the separation between day and night, synchronize the phase relationship of the biological clock and sleep pattern with the light-dark cycle and it can shift the biological clock (advance or delay) (Lieverse et al., 2012). Several studies established BLT to be effective in the treatment of depressions with a seasonal pattern, also called a seasonal affective disorder (SAD) (Golden et al., 2005; Pail et al., 2011; Partonen & Pandi-Perumal, 2010). Both depressive and bipolar disorders can have such a pattern, which applies to the lifetime pattern of mood episodes at particular times of the year. Furthermore, BLT seems also to be effective in mood disorders without seasonal variation (Benedetti, 2018; Dallaspezia & Benedetti, 2020; Even et al., 2007; Golden et al. 2005; Perera et al., 2016, Penders et al., 2016). However, it is important to note that some of these effect sizes were small, and there were also studies in which no effect of light therapy on depressions without a SAD was found.

Table 1

Various types of Bipolar and Related Disorders and Depressive Disorders (DSM-V)

Bipolar and Related Disorders	Depressive Disorders
1. Bipolar I Disorder 2. Bipolar II Disorder 3. Cyclothymic Disorder 4. Substance/Medication-Induced Bipolar and Related Disorder 5. Bipolar and Related Disorder Due to Another Medical Condition 6. Other Specified Bipolar and Related Disorder 7. Unspecified Bipolar and Related Disorder	1. Disruptive Mood Dysregulation Disorder 2. Major Depressive Disorder 3. Persistent Depressive Disorder (Dysthymia) 4. Premenstrual Dysphoric Disorder 5. Substance/Medication-Induced Depressive Disorder 6. Depressive Disorder due to Another Medical Condition 7. Other Specified Depressive Disorder 8. Unspecified Depressive Disorder

1.4 Characteristics of Bright Light Therapy

Using BLT to treat affective disorders, the dose of 10,000 lux at eye-level for 30 minutes appears to be most efficient (Terman & Terman, 2011). Lower intensities can also be effective, but usually they then require a longer exposure duration (Terman & Terman, 2011). Moreover, some patients can be more or less sensitive to light, for these cases shorter (15 minutes) or longer (60 minutes) durations can be applied. In addition, as mentioned earlier, Lockley and colleagues (2003) showed twice as great a phase shifting effect when using 460 nm blue light relative to 555 nm green light. However, bright blue-enriched polychromatic (white) light is found to be no more effective for circadian phase resetting than standard bright (white) light therapy (Hanifin et al., 2019; Smith & Eastman, 2009; Smith, Revell & Eastman, 2009). This applies both for phase advancing or delaying circadian rhythms by means of commonly used therapeutic light levels and for phase delays by nocturnal light with an illuminance of about 130 lux.

To maximize the therapeutic effects of BLT, the timing of the light stimulus appears also to be extremely important. Inappropriately timed BLT can even lead to treatment failure (Terman & Terman, 2005). For example, when morning light is scheduled too early in circadian time, it can result in a phase delay of the circadian rhythm instead of a phase advance (see Figure 6). In this case, a patient can experience insomnia after habitual bedtime and an uncontrollable urge to resume sleep several hours after treatment. In addition, it is possible that a patient suddenly starts waking up hours earlier than expected (Terman & Terman, 2011). When these situations arise, the light therapy sessions needs to be moved to a later timing (Terman & Terman, 2011). Additionally, when evening light is scheduled at a late circadian phase, a patient will experience further delay in circadian rhythm and may develop initial insomnia and hyperactivation (Terman & Terman, 2005). Moreover, if morning light is scheduled too late in circadian time, it is possible that no sign of improvement can be seen in the treatment. It is therefore important to find the optimal combination of dosage and timing to obtain a therapeutic effect (Terman & Terman, 2011).

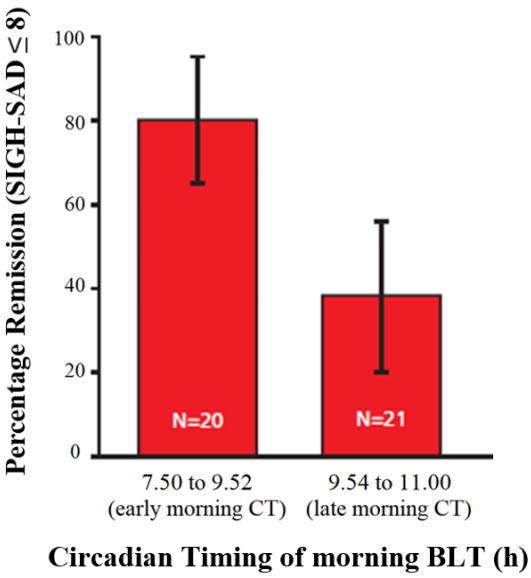
Based on recent clinical studies it, is recommended to expose patients diagnosed with SAD initially to morning light shortly after awakening (Terman and Terman, 2011). However, given the large variations in circadian time across individuals, as the melatonin onset period spans a 5-6 hours range from approximately 19.00-01.00h for the patient population, it is important to assess the internal circadian time of the patient and optimize the timing of the BLT treatment with respect to this internal time of an individual patient (Terman & Terman, 2005; Terman & Terman, 2011; Wirz-Justice & Benedetti, 2020).

1.5 Circadian Timing of Bright Light Therapy

According to Terman et al. (2001) the percentage of change in depression score is negatively correlated ($n = 21$, $r = -0.38$, $p = 0.01$) with the interval between the DLMO and the time of BLT treatment (this interval will be denoted as 'circadian timing of morning BLT' in the report), with preference for therapy 8.5 hours after the DLMO (or 2.5 hours after the sleep midpoint). BLT given 7.5 to 9.5 hours after DLMO produced twice the remission of light given 9.5 to 11.0 hours after DLMO (80% vs 38.1%) (see Figure 9) (Terman & Terman, 2005). These findings were investigated in a protocol with 42 participants (21-56 y/o; 29 woman, 13 men) diagnosed with SAD (based on the DSM-III-R) that received 10 to 14 days of BLT (10,000 lux for 30 minutes at the moment of awakening (median: ~9.53 hours post DLMO)). Based on these results, Terman & Terman (2005) recommend that clinicians start morning BLT no later than 8.5 hours after a patient's DLMO, in order to maximize the likelihood of the antidepressant effect.

Figure 9

Remission rate anchored to the circadian timing (CT) of the treatment session



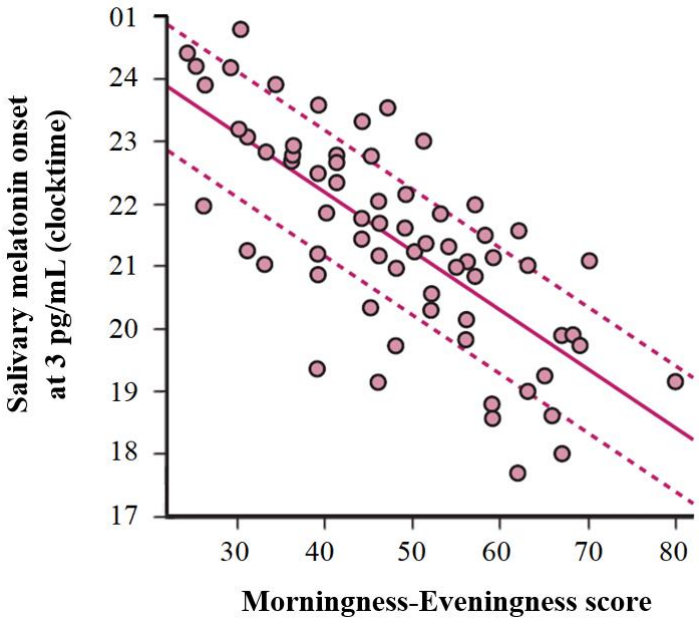
Note. Remission rate (percentage of subjects +/- 95% CI) is measured with the Structured Interview for the Hamilton Depression Rating Scale-Seasonal Affective Disorder Version (SIGH-SAD) to 10,000 lux, 30-minute light exposure in patients with SAD. "Rating scale scores were analyzed as raw data and items in terms of the percentage change from baseline" (Terman, et al., 2001, p. 70). Adjusted from Terman & Terman (2005).

1.5.1 DLMO Measurements. The DLMO can be obtained (non-invasively) from half-hourly or hourly saliva samples collected in the approximately 6 hours before usual sleep begins (Burgess & Fogg, 2008). However, these saliva samples are expensive, have a slow turnaround time and require a lot of effort from staff and patients (Kantermann et al., 2015). An alternative is therefore to estimate the DLMO by asking people about the timing of their sleep (markers) through questionnaires as this also reflects the circadian phase, which is simple, cheaper and location independent (Kantermann et al., 2015; Reiter, Sargent, Roach, 2020). For example, a strong correlation was found between the DLMO and the Morningness-Eveningness Questionnaire (MEQ) score in unmedicated patients with a winter

depression ($r = -0.73$, $p < 0.001$, Figure 10) (Terman and Terman, 2005), in patients with delayed sleep phase disorders ($r = 0.70$, $p < 0.001$) (Kantermann et al., 2015) and in subjects without depression (Burgess & Fogg, 2008). This MEQ was usually used to measure chronotype through questions about preferred timing of sleep and activity planning (Horne & Östberg, 1976). In addition, estimates of DLMO can also be obtained by the 'Mid Sleep time on free days' (MSFsc) variable derived from the Munich ChronoType Questionnaire (MCTQ), the sleep midpoint measured with the Sleep Diary (SD) and the sleep onset measured with the Pittsburg Sleep Quality Index (PSQI) (Kanterman et al., 2015; Reiter, Sargent & Roach, 2020).

Figure 10

Correlation between MEQ and DLMO in a group of 69 patients diagnosed with SAD



Note. Solid line: linear regression, $y = 25.9 – 0.09x$. Dashed lines: "DLMO within 1 hour of the MEQ predictor" (Terman & Terman, 2011, p 1685). Adapted from Terman and Terman (2011).

1.5.2 Recommended Light Exposure Times based on MEQ scores. Based on the relationship that Terman & Terman (2005) found between the DLMO and the MEQ score, they created an algorithm as a "best guess" strategy that could maximize the chance that the patient will receive morning BLT with optimal timing: in the range of 7.5 to 9.5 hours after DLMO. This has resulted in a list of recommended initial light exposure times, which allow the morning BLT session to be planned according to an individual circadian rhythm (see Table 2).

Table 2

Timing of morning bright light therapy based on the MEQ scores

MEQ score	Start time of BLT
23-26	8:15 AM
27-30	8:00 AM
31-34	7:54 AM
35-38	7:30 AM
39-41	7:15 AM
42-45	7:00 AM
46-49	6:45 AM
50-53	6:30 AM
54-57	6:15 AM
58-61	6:00 AM
62-65	5:45 AM
66-68	5:30 AM
69-72	5:15 AM
73-76	5:00 AM
77-80	4:45 AM

Note. MEQ = Morningness-Eveningness Questionnaire; BLT = Bright Light Therapy; Morning BLT (10,000 lux for 30 minutes each session) approximately 8.5 hours after estimated DLMO. Adjusted from Terman & Terman (2005).

1.6 Current study

After the interesting results of the study of Terman et al. (2001) in patients with SAD, the influence of the circadian timing of morning BLT on the treatment response has – at least

to our knowledge - not been researched more extensively. One study of Knapen, Gordijn and Meesters (2016) explored the association between chronotype and the response to light therapy at a fixed time (08.00 AM), but did not find a significant relationship. Furthermore, in their research Terman et al. (2011) and Knapen et al. (2016) only included patients with SAD. Therefore, it is not yet known whether there is an optimal circadian timing (range) that elicits the best clinical response for treatment of mood disorders in general (Wirz-Justice & Benedetti, 2020). It is currently also untested whether chronotype would be an adequate measure to optimize BLT timing on. These aspects are important to improve morning BLT and the health of people with a mood disorder.

This study aims to explore whether there is a relation between the circadian timing of morning BLT and the antidepressant effect in patients with a depression (i.e., with seasonal and non-seasonal mood disorders). The main research question that will be explored is: “To what extent does the circadian timing of morning bright light therapy influence the antidepressant effect?”. Based on the morning BLT results in patients with a SAD as reported by Terman et al. (2001) and Terman and Terman (2005), it is expected that morning BLT administration closer to recommended optimal time of morning BLT (i.e., ~8.5 hours after the estimated dim light melatonin onset) improves the antidepressant effect. Secondary research aims are to explore the antidepressant effect of morning BLT and how this effect is building up across treatment weeks in patients with a depression. In addition, this study will evaluate whether there is a relation between the circadian timing of morning BLT and the resulting phase advance of a patient’s internal time.

2. Method

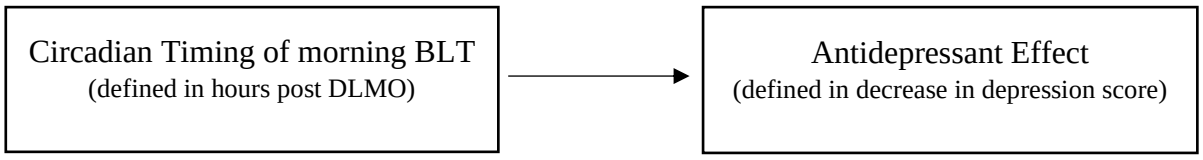
This study was a sub study of a larger randomized controlled trial at the Geestelijke Gezondheidszorg Eindhoven (GGzE) into morning BLT. The larger study started on January 1, 2021 and will last one year. In view of the ongoing research, no further information can be shared about the larger GGzE study. The current (sub)study contains data collected at GGzE from January 11 to July 2 (2021) and was designed within the restrictions of the ongoing morning BLT GGzE study and GGzE's standardized light therapy program. Both studies were approved by the internal research committee of GGzE, and not subject to Central Committee on Human Research approval (assessed by GGzE). The current (sub)study was also approved by the review board of the Human Technology Interaction group in Eindhoven.

2.1 Study Design

The (sub)study had a correlational design and explored the relation between the circadian timing of the morning BLT and the antidepressant effect. The circadian timing of the morning BLT was used as predictor variable and the dependent variable was the antidepressant effect of the BLT treatment (see Figure 11).

Figure 11

Conceptual model of the predictor variable and the dependent variable



Note. BLT = Bright Light Therapy; The circadian timing of the morning BLT (30 minutes, 10,000 lux) was expressed in terms of the number of hours between the DLMO (as derived from the Morningness-Eveningness Questionnaire- Self Assessment (MEQ-SA) score of a participant) and the start time of

the morning BLT. The magnitude of the antidepressant effect of the morning BLT was expressed in the decrease of the depression score over consecutive treatment weeks.

2.2 Participants

The participants were people aged 18 years or older (m/f) diagnosed with an unipolar or bipolar depression (either seasonal or non-seasonal) as described in the DSM-V and verified by the Quick Inventory of Depressive Symptomatology Self-Report (QIDS-SR) (score > 5) prior to the BLT. The exclusion criteria are described in Table 3. In addition, there were a number of contraindications that the patient was asked to assess with his/her own practitioner to decide whether the morning BLT could be applied safely. These contraindications are described in Table 4. Finally, there were some drug-related contraindications to morning BLT (see Table 5).

Table 3

Exclusion criteria

	Exclusion Criteria
1	A current (hypo)manic episode or a mixed episode
2	Diagnosed dementia
3	Prominent active suicidality
4	A current psychotic episode
5	Patients younger than 18 years old
6	QIDS-SR score ≤ 5
7	Not able to give an informed consent
8	Dose adjustment or switch of antidepressants 3 weeks before and/or during light therapy
9	Long-term use of agomelatine (as it is ethically irresponsible to temporarily discontinue long-term use of this drug)
10	Insufficient knowledge of the Dutch or English language to be able to complete the (Dutch or English) questionnaires

Table 4

Contraindications

	Relative Contraindications
1	Pregnancy in the first 12 weeks
2	Diabetes or other systemic diseased related to problems with the vascular system
3	Eye diseases in which the sensitivity to light is increased
4	Epilepsy

Table 5

Drug related contraindications

	Drug Relative Contraindications
1	Use of antibiotics during the light therapy
2	Use of medication or creams that can cause photosensitivity (only apply creams after the light therapy)
3	Use of melatonin (after discontinuation a washout period of 1 month is maintained before starting the light therapy)
4	Use of agomelatine. In the case of short-term use, which is less than 3 weeks, this may be discontinued after discussing this with the practitioner (after discontinuation a washout period of 1 month is maintained before starting the light therapy)

2.3 Setting and Materials

2.3.1 Setting. The morning BLT was given in the LichtCafé, which is located at the Grand Café Het Ketelhuis on De Grote Beek estate in Eindhoven (Dr. Poletlaan 45) (see Figure 12). The LichtCafé is part of GGzE and offers an expert supervised and accessible form of morning BLT. It is a healing and inspiring environment where, in addition to morning BLT, other "Zeitgebers" are also involved in the treatment. This concerns nutrition, exercise, balance between activities and relaxation, social interaction and sleep. There are, for example, exercise bikes in front of various light boxes, walking groups, other people with whom the patients can meet and coffee or tea with a piece of fruit. Experts from GGzE are always present in the LichtCafé to guide the morning BLT and give lifestyle advice. In addition to this guidance, patients can also make use of the online coaching that is offered. Besides, the LichtCafé aims

to have a destigmatizing effect as it is in the middle of society. These aspects were also offered to the participants in this (sub)study. An overview of some aspects the participants made use, is given in Appendix A. The four pillars that the LichtCafé strives for are shown in Table 6.

Figure 12

The LichtCafé

Table 6

Four pillars of the LichtCafé

	Pillars
1	Expert and accessible form of light therapy in a healing and inspiring environment (in society)
2	Light therapy with integrated lifestyle advice
3	Scientific research
4	Knowledge platform concerns chronobiology (aimed at improving treatment and prevention by sharing knowledge)

2.3.2 Materials. During therapy, participants were seated in front of a BLT lamp (Innosol Lucia 2x55W with dimmer, Figure 13) as to receive 10,000 lux on the eye position (established using a Voltcraft MS-1300 lux meter). In addition, a timer was available for the participant to time a duration of 30 minutes per treatment session (see Figure 13).

Figure 13

Materials of the morning BLT

2.4 Procedure

2.4.1 Intake procedure. Prior to the start of the treatment, the participants were asked for permission by means of an information letter and an informed consent as used in the ongoing morning BLT GGzE study. Furthermore, the participants were asked to complete the QIDS-SR independently. When this QIDS-SR score was higher than 5 (higher than the cut-off point of 'no depression'), there was an indication for morning BLT (see Table 10). This QIDS-SR score was also the baseline depression score of the participant in this study (denoted in this report as 'QIDS-SR baseline'). This was followed by an intake interview with an expert from the LichtCafé in which the inclusion and exclusion criteria were checked, the relative contraindications were discussed and the following questions from the intake questionnaire in USER (a program that is used by the employees of GGzE) were posed: age, sex, somatic

history, current medication use, previous depressive episodes, previous received BLT, and criteria of SAD (see Table 7). In addition, permission was asked to extract their diagnosis and QIDS-SR questionnaires from their file. However, in the current (sub) study the researcher had no access to the somatic history, current medication use, previous depressive episodes and previous received BLT of the participants.

When participants were eligible for morning BLT, participants received an online information module about morning BLT in the LichtCafé via the treatment platform Minddistrict. This module (named 'Prefer Light - Light Therapy in the Light Café') provided information about the procedure and operation of the BLT (Appendix B). A schematic overview of the intake procedure can be seen in Figure 14.

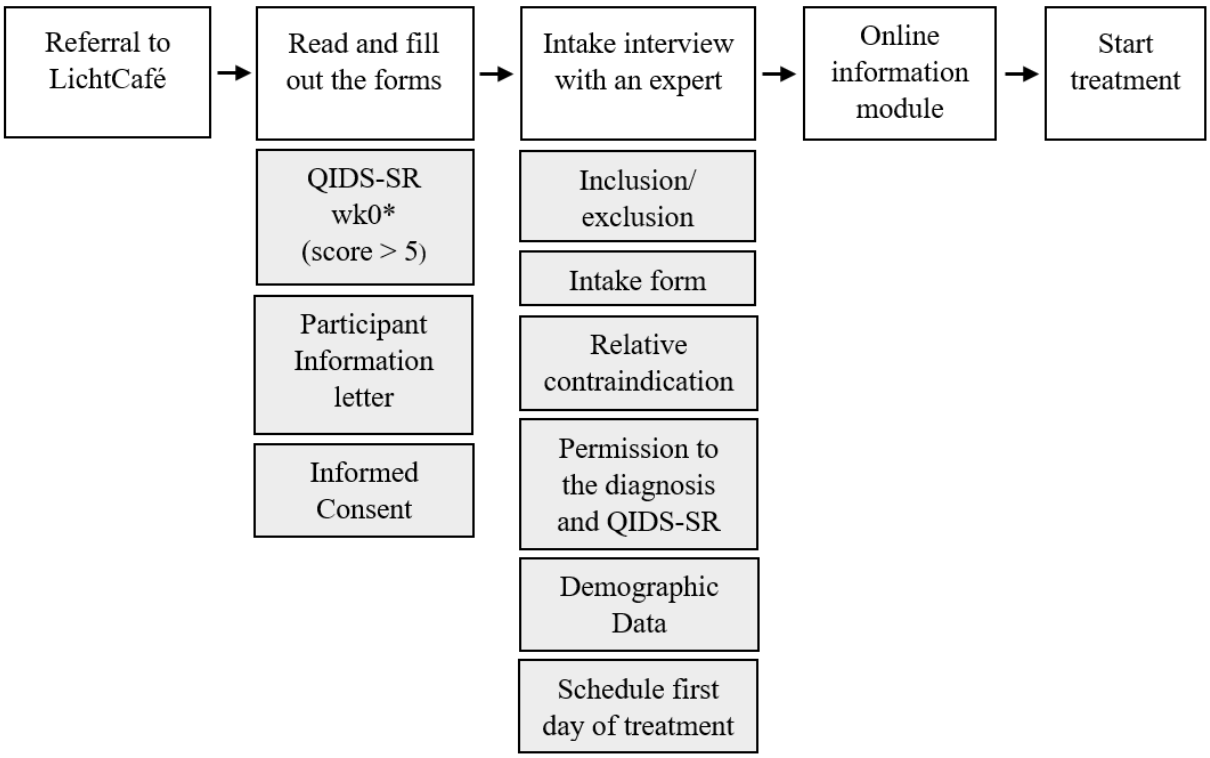
Table 7

Seasonal Affective Disorder criteria

	Criteria
A	Frequent depression in autumn/winter
B	Gloom clears up completely in spring and summer
C	Had depression in autumn/winter for ≥ 2 years
D	More frequent depression in autumn/winter than in spring/summer

Figure 14

Schematic overview of the intake procedure of an participant



Note. *Timing of completion varied from 1 to 7 days before the start of the morning BLT.

2.4.2 Treatment procedure. The morning BLT consisted of an exposure to 10,000 lux measured at the eye position of the participant, with a duration of 30 minutes (daily) and with a timing between 7.30 am and 10 am during weekdays (Monday – Friday) (Terman & Terman, 2005). The timing of the morning BLT was scheduled according to the social schedule of the participant and was kept constant across the treatment days and weeks. However, in practice, sometimes the timing of the morning BLT was adjusted. Participants with an adjustment of more than 30 minutes across the different treatment days/weeks were excluded from the current (sub)study. After one week of treatment, on the fifth treatment day (Friday), the QIDS-SR score was measured again. Under guidance of an expert at the LichtCafé, it was determined during the Friday LichtCafé visit of each treatment week whether the morning BLT was to be

terminated (QIDS-SR score ≤ 5, or when a special situation required the light therapy to be terminated) or extended by one more week. The BLT was given in blocks of five consecutive days and after the first week the treatment could be extended by maximally 2 x 5 consecutive days (i.e., 2 extra treatment weeks), with a maximum of three treatment weeks. Thus, the QIDS-SR score was measured the first (baseline), fifth, 10th and 15th day of morning BLT. The number of assessments was dependent on the duration of the therapy, with a minimum of 2 and a maximum of 4 assessments (see Table 8). When people ended light therapy earlier with a QIDS-SR score > 5 (the 'premature quitters'), the reason was documented.

At the start of the first session, participants were guided by an expert from the LichtCafé. An explanation about the correct use of the BLT lamp was given, the possible side effects were mentioned, and the distance from the BLT lamp as to receive 10,000 lux on the eye level was checked with the lux meter. In practice, the distance between the patient's eyes and the lamp was approximately 30-45 cm. During this first session, the participant filled in the MEQ-SA once. Furthermore on every first day of the treatment week, the PSQI (modified to probe the past week instead of the past 4 weeks) and the Sleep Diary-Monday-version (SD-M) were taken. On every fifth day of BLT, simultaneously with the administration of the QIDS-SR, the Extra Activities Questionnaire (EAQ) and the Sleep Diary-Friday-version (SD-F) were conducted. These questionnaires were mostly filled in during the 30 minutes of a morning BLT session (see section 2.6.1 'Time Load'). An schematic overview of the treatment procedure can be seen in Table 8. The measurements will be explained in section 2.5 'Measures'.

Table 8

Overview of the treatment procedure and questionnaires during the various treatment weeks

	BLT day 1 Monday	**BLT day 2** Tuesday	**BLT day 3** Wednesday	**BLT day 4** Thursday	**BLT day 5** Friday	
Treatment week 1	Explanation MEQ-SA ~10 min PSQI week 1 ~10 min SD-M** week 1 ~5 min				QIDS-SR week 1 SD-F** week 1 ~5 min	QIDS-SR ≤ 5 or special situation*: END therapy QIDS-SR > 5: Go to treatment week 2
Treatment week 2	PSQI*** week 2 ~10 min SD-M** week 2 ~5 min				QIDS-SR week 2 SD-F** week 2 ~5 min	QIDS-SR ≤ 5 or special situation*: END therapy QIDS-SR > 5: Go to treatment week 3
Treatment week 3	PSQI*** week 3 ~10 min SD-M** week 3 ~5 min				QIDS-SR week 3 SD-F** week 3 ~5 min	END therapy (irrespective of QIDS-SR week 3 score)

Note. MEQ-SA = Morning-Eveningness Questionnaire – Self Assessment; PSQI = Pittsburg sleep Quality Index; QIDS-SR = Quick inventory of depression – self report; SD-M = Sleep Diary Monday version; SD-F = Sleep Diary Friday version; The treatment consisted of minimally 1 week and maximally 3 weeks, pending the QIDS-SR score on Friday. The explanation on LT day 1/week 1 and the QIDS-SR week 1, week 2 and week 3 are already included in the standardized light therapy program of the LichtCafé (no extra time load). *The 'premature quitters' with QIDS-SR > 5. **Added to the research procedure since the 24th of May (see Appendix B for SD-M and SD-F). ***Removed from the research procedure since the 16th of April.

2.5 Measures

Different methods and questionnaires were used to measure the variables of interest in this (sub) study.

2.5.1 Circadian Timing of morning BLT. The circadian timing of the morning BLT variable was expressed in terms of the number of hours between the DLMO (denoted in this report as 'DLMOmeq') and the start time of the morning BLT (denoted in this report as 'BLT start time'). The DLMOmeq was estimated by subtracting 8.5h from the recommended start times (as these times were ~8.5h post DLMO) assessed with Terman and Termans' (2005) algorithm (see section 1.5.2 'Recommended Light Exposure Times based on the MEQ scores' and Table 2). This algorithm was based on the MEQ-SA, that consisted 19 questions in which each item is scored on a scale of 0-6 points (Horne & Östberg, 1976). The total score on the MEQ-SA could range from 16-86, with lower scores reflecting an later recommended (circadian) start timing and higher scores reflecting an earlier recommended (circadian) start timing. The questionnaire was completed on paper in the LichtCafé (see Appendix D for an English and Dutch version of the MEQ-SA, see Appendix D and F for the scoring).

2.5.2 Antidepressant Effect. The magnitude of the antidepressant effect was measured by the difference between the depression scores on BLT day 1 (Monday) and on BLT day 5 (Friday) per treatment week (see Table 9). The depression scores were assessed with the QIDS-SR (Rush, Trivedi, Ibrahim et al., 2003) (see Appendix C). This questionnaire was used because of its good psychometric properties (e.g. Cronbach's alpha = 0.86) and was completed digitally by the Dutch participants. For the English participants, the QIDS-SR was completed on paper in the LichtCafé as no English version was available in the online program of GGzE

(see Appendix C). The questionnaire consisted of 16 questions aimed at mapping out depressive symptoms over the past seven days. The nine symptoms of the DSM-V criteria (depressed mood, anhedonia, difficulty concentrating/decision making, self-image, suicidal thoughts/plans, energy level, sleeping problems, weight/appetite and psychomotor changes) were scored. Of the 16 items, four were about sleep, two about psychomotor imbalance and four about weight/appetite. The other domains were probed using one question. Each item was scored on a scale of 0-3 points (see Appendix C and F for the scoring). The total score on the QIDS-SR ranged from 0 to 27, which indicated the severity of the depression (see Table 10).

Table 9

Antidepressant effect variables

Variable	Measure
Antidepressant effect week 1	$QIDS\text{-}SR_{baseline}$ - $QIDS\text{-}SR_{week1}$
Antidepressant effect week 2	$QIDS\text{-}SR_{week1}$ - $QIDS\text{-}SR_{week2}$
Antidepressant effect week 3	$QIDS\text{-}SR_{week2}$ - $QIDS\text{-}SR_{week3}$

Table 10

Classification of depression severity based on the QIDS-SR scores

Score	Severity of depression
0-5	No
6-10	Mild
11-15	Moderate
16-20	Severe
21-27	Very severe

2.5.3 Phase advance. The phase advance variables were estimated by the difference between the Sleep onsets (SO) on BLT day 1 (Monday) and on BLT day 5 (Friday) per treatment week (see Table 11). The sleep onset (SO) strongly associates with the DLMO, and thus could be used as another indicator of the participants internal time (Reiter et al., 2020). The SO was measured by adding the usual sleep latency (S_{lat}) to the usual bedtime (BT) of

the participants ($SO = BT + S_{lat}$). The S_{lat} and BT could be estimated by the first two questions of the PSQI. The PSQI is a self-report questionnaire to measure sleep quality and consists of 19 questions divided into 7 domains about the sleep quality of the participants in the past week (Buysse, et al., 1989) (see Appendix E). This questionnaire showed a high degree of internal consistency (Cronbach's alpha = 0.83).

Table 11

Phase advance variables

Variable	Measure
Phase advance week 1	$(SO_{week2} - SO_{week1}) * 60$
Phase advance week 2	$(SO_{week2} - SO_{week1}) * 60$
Phase advance week 3	$(SO_{week2} - SO_{week1}) * 60$

Note. The difference in SO was multiplied with 60 to estimate the phase advance in minutes. Positive values indicated a phase advance and negative values indicated a phase delay (see Figure 6).

2.5.4 Chronotype. The MEQ-SA score was also used to determine the participants chronotype, with lower scores reflecting an evening type and higher scores reflecting a morning type (see Table 12).

Table 12

Classification of chronotypes based on the MEQ-SA scores

Score	Chronotype
16-30	Definite Evening
31-41	Moderate Evening
42-58	Intermediate
59-69	Moderate Morning
70-86	Definite Morning

2.5.5 Treatment Attendance and Duration. Finally, the attendance (in morning BLT sessions) during the first, second and/or third treatment week and the duration (in weeks) of each treatment were registered.

2.6 Ethical Aspects

During the entire period, participants were able to decide whether they wanted to continue with the study or not. If not, they still received the BLT treatment as regular care. All the participants gave written informed consent prior to the study.

2.6.1 Time Load. On the first day of therapy, it took the participants 25 minutes to complete the MEQ, PSQI and SD-M. On Fridays, it took another 5 minutes to complete the EAQ and the SD-F, which added together resulted in 30 minutes of extra time load compared to the regular morning BLT (see Table 8). When the morning BLT was maximally extended (by two more weeks), the PSQI (10 minutes), the SD-M (5 minutes), and the SD-F (5 minutes) were completed two more times, which resulted in a total of 40 more minutes of time load. Thus, the total extra load of the entire study compared to the regular morning BLT amounted to a maximum of 70 minutes. However, (a large part of) the questionnaires were completed during the morning BLT sessions. Therefore, the actual extra burden of this study was much lower.

2.6.2 Side Effects. Possible side effects experienced by the participants were constantly monitored by the employees of the LichtCafé. When serious side effects occurred, a psychiatrist was consulted about prematurely discontinuing the BLT or adjusting the treatment procedure. This approach corresponded to the regular treatment at GGzE.

2.6.3 Data Storage. The data was encrypted and stored for a period of 15 years in a database in the secure digital environment of GGzE, to which only the researchers had access. According to the privacy of the participants, the data was linked to the participant via a code key only known by the researchers.

2.7 Analyses

2.7.1 Data preparation. The measurements were coded in Excel files according to the codebook of the ongoing morning BLT GGzE study (see Appendix F). To perform the statistical analyses using the software IBM SPSS 26, the datasets were exported from Excel, structured, merged and cleaned up. After organizing and uncluttering this dataset, the data was checked for abnormalities or missing values. Data with missing MEQ-SA- and QIDS-$SR_{baseline}$ values were excluded from the dataset. No abnormalities were found. Variables expressed in time were recoded to a continuous variable reflecting the number of hours since midnight to allow calculations with these variables. For example, a 'BLT start time' of 9.30 a.m. was converted to 9.50 hours after midnight (0.00). The predictor (see section 2.5.1 'Circadian Timing of morning BLT') and dependent variables (see section 2.5.2 'Antidepressant Effect' and Table 9) were calculated, and these new variables were added to the dataset. A circadian timing of morning BLT-value of 8.5 indicates an optimal morning BLT timing and a circadian timing of morning BLT-value > 8.5 indicate a (too) late-timed morning BLT (no participants with a circadian timing of morning BLT-value < 8.5 were included in this dataset).

2.7.2 Statistical analyses. All variables of interest were checked for normality, linearity, homoscedasticity and influential outliers. The standardized residuals of the dependent (antidepressant effect- and phase advance) variables were saved as new variables. Normality tests using the Shapiro-Wilk test and the Skewness/Kurtosis tests and histograms (see Appendix G) were conducted for all these standardized residual variables. When considered not normally distributed, possible transformations of the dependent variables were checked. However, no transformation resulted in a more normal distribution. Moreover, homoscedasticity and linearity were checked by ZPRED* ZRESID scatterplots for all standardized residual variables (see Appendix H). Finally, outliers were checked by means of z-scores. No variables with a z-score of more than ± 3 were found.

To explore the main research question, first a visual inspection of the association between circadian timing of morning BLT and the antidepressant effect was done for every treatment week by means of a scatter plot (see Appendix I, Figure I1). Moreover, a Linear Mixed Model (LMM) analysis was performed to explore the relation between circadian timing of morning BLT and the antidepressant effect across the three treatment weeks. To enable the analysis, the variables of interest were restructured into a long format and stored in a new SPSS data file. A null model with participant ID included as random intercept was performed and the intraclass correlation between the QIDS-SR scores was analyzed. Based on these results, it was decided to run the analysis further with a 'hierarchical model' (a LMM with participant ID included as random intercept and the predictors). The antidepressant effect was added as dependent variable, treatment week as a fixed effect, and the circadian timing of morning BLT as covariate. The main effects of treatment week and circadian timing of morning BLT were analyzed. It was explored whether adding the interaction effect between treatment week and the circadian timing of morning BLT and/or random slopes did improve the model. A Chi-square test was performed to test whether there

was a significant difference between the -2 log-likelihood (-2LL) statistics of these different models and thus, to test which model explained the data best. Finally, visualizations of the estimated marginal means and the standard errors conducted from the LMM using post-hoc analysis with Bonferroni correction, were created to gain more insight about the buildup of the QIDS-SR scores and the antidepressant effect across the treatment weeks.

Additional to the main research question, a visual inspection of the associations between the circadian timing of morning BLT and the phase advance per treatment week was done by means of scatter plots (see Appendix I, Figure I2). Thereafter, Spearman Correlation tests for the visually observed associations were conducted.

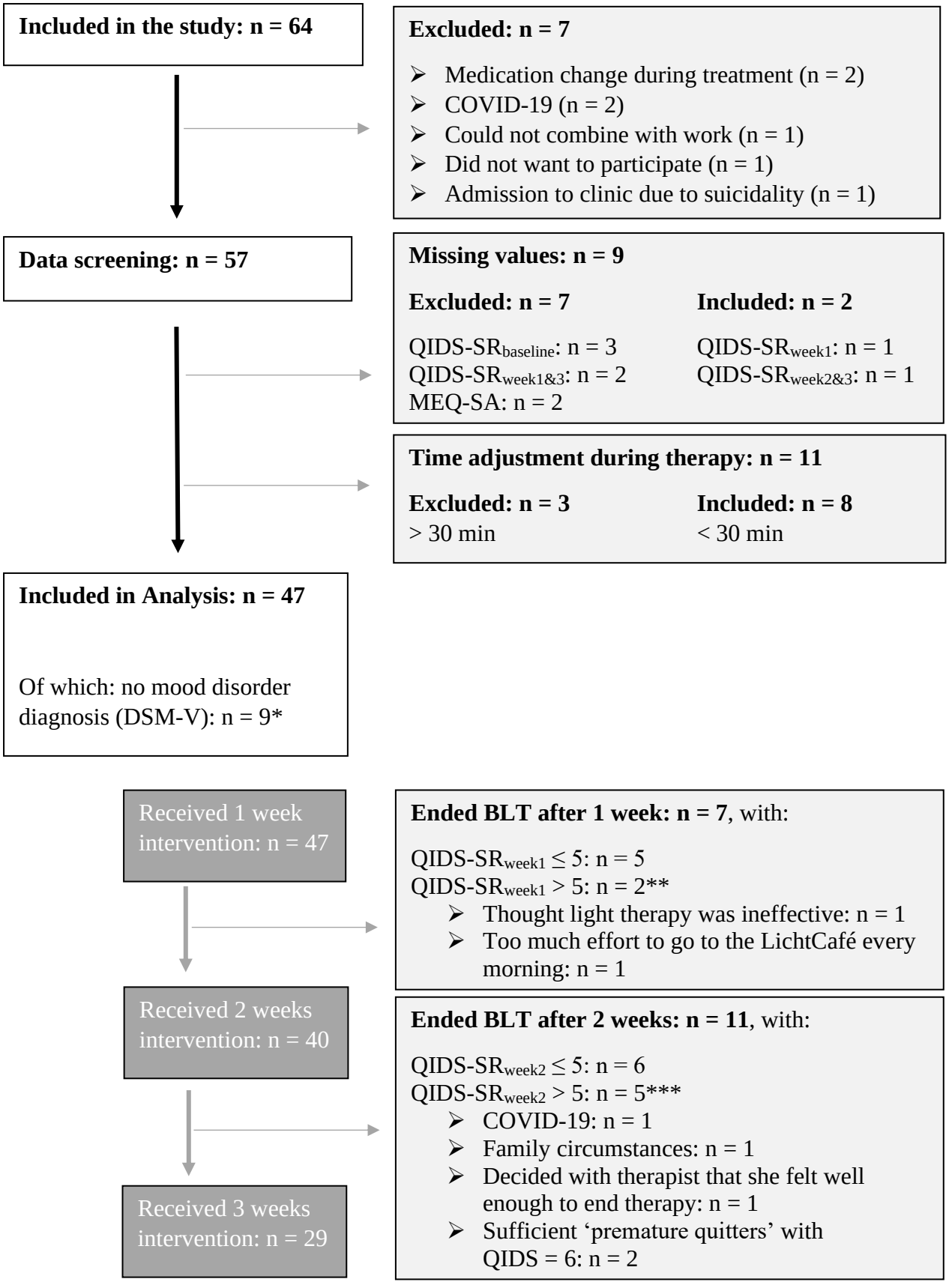
3. Results

3.1 Participant Flow and Missing Data

Of the 64 participants who indicated to participate in the study, 7 were excluded for various reasons at the start or during the BLT (see Figure 15). After the BLT, another 10 participants were excluded, 7 due to missing data and 3 participants due to start time adjustment of the BLT during the treatment weeks with more than 30 minutes. Finally, 47 participants were included in the analysis. However, 9 of these participants were not diagnosed with a depressive disorder according to the DSM-V but did show depressive symptoms (QIDS > 5) and 7 participants were ‘premature quitters’ (QIDS-SR-score > 5). In Figure 15, the participant flow for the current study can be seen.

Figure 15

Participant flow and missing data



Note. *Were included in the current study as they had depressive symptoms (QIDS-SR > 5) and their $QIDS\text{-}SR_{baseline}$ did not differ statistically significant from the $QIDS\text{-}SR_{baseline}$ of the diagnosed group ($F(1, 45) = 0.579$, $p = 0.451$). **Were included in the treatment week 1 analysis as their antidepressant effect did not differ statistically significant from the QIDS-SR-score ≤ 5 group ($F(1, 5) = 0.001$, $p = 0.981$). ***Were included in the treatment week 2 analysis as their antidepressant effect did not differ statistically significant from the QIDS-SR-score ≤ 5 group ($F(1, 9) = 3.895$, $p = a0.080$).

3.2 Participants characteristics

The 47 participants included in the analysis, were on average 45.02 (SD = 14.03) years old with a range from 19 to 74 years old. Of these participants, 9 were categorized with a depression type ‘Others’, which meant that they were not diagnosed with a depressive disorder, however they had depressive complaints as their QIDS-SR-score was > 5. Diagnoses that were included in the ‘Other’ category were Autism Spectrum Disorder (ASD) Schizophrenia, Unspecified Schizophrenia Spectrum Disorder, Post-Traumatic Stress Disorder (PTSD), Brief Psychotic Disorder, Borderline Personality Disorder, Unspecified Personality Disorder and ADHD. Further descriptions of these participants are given in Table 13.

Table 13

Participant characteristics

Variable	Category	Frequency	Percent
Gender	Man	16	34.0
	Woman	31	36.0
Season	Winter*	22	46.8
	Spring**	25	53.2
Chronotype	Definite Evening	1	2.1
	Moderate Evening	9	19.1
	Intermediate	28	59.6
	Moderate Morning	7	14.9
	Definite Morning	2	4.3
Depression Type	Dysthymia	8	17.0
	Major Depressive Disorder	18	38.3
	Bipolar I Disorder	3	6.4
	Bipolar II Disorder	6	12.8
	Other Specified Depressive Disorder	1	2.1
	Unspecified Depressive Disorder	2	4.3
	Unspecified Bipolar Disorder	1	2.1
	Other	8	17.0
Bipolar Disorder	Yes	37	78.7
	No	10	21.3
SAD	0 criteria	11	23.4
	1 criteria	10	21.3
	2 criteria	3	6.4
	3 criteria	16	34.0
	4 criteria	7	14.9
BLT Before	Yes	18	61.7
	No	29	38.3
Duration BLT	1 week	7	14.9
	2 weeks	11	23.4
	3 weeks	29	61.7

Note. SAD = Seasonal Affective Disorder; BLT = Bright Light Therapy; *December 21st – March 20th; **March 21st – June 20th.

3.3 Descriptive Statistics

The descriptive statistics of the attendance of week 1, 2 and 3, the circadian timing of morning BLT, the antidepressant effect of week 1, 2 and 3, the phase advance of week 1, 2 and 3 are given in Table 14. The statistics of the the Shapiro-Wilk- and the Skewness/Kurtosis tests are shown in Table 15.

Table 14

Descriptive statistics

Variable	n	Mean	SD	Min.	Max.
Attendance week 1 (in days)	47	4.77	0.48	3	5
Attendance week 2 (in days)	40	4.47	0.91	0	5
Attendance week 3 (in days)	29	4.55	0.63	3	5
Circadian timing of morning BLT (h)	47	10.71	0.89	8.75	12.25
Antidepressant effect week 1	46*	4.02	4.79	-4.00	16.00
Antidepressant effect week 2	38**	1.32	3.59	-8.00	8.00
Antidepressant effect week 3	28*	2.07	2.96	-3.00	9.00
Phase advance week 1 (minutes)	26	30.19	41.19	-60	125
Phase advance week 2 (minutes)	22	15.82	35.64	-60	78
Phase advance week 3 (minutes)	15	-6.53	35.62	-60	80

Note. *One missing value; **Two missing values.

Table 15

Shapiro-Wilk, Skewness and Kurtosis tests

Standardized residuals	Shapiro-Wilk*			Skewness**		Kurtosis**	
	Statistic	df	Sig.	Statistic	SE	Statistic	SE
Antidepressant effect week 1	**.934**	46	**.012**	.708	.350	-.163	.688
Antidepressant effect week 2	.984	38	.848	-.352	.383	.209	.750
Antidepressant effect week 3	**.955**	28	.270	.310	.441	-.291	.858
Phase advance week 1	**.949**	26	.224	.665	.456	.341	.887
Phase advance week 2	**.917**	22	.065	.194	.491	-.158	.953
Phase advance week 3	**.939**	15	.376	.678	.580	**1.118**	1.121

Note. Bold when not considered normally distributed; *Considered normal distributed when $W \geq .97$ and $p > 0.05$; **Considered normally distributed for statistic values between -1 and 1.

3.4 Linear Mixed Model analysis

A LMM analysis was performed to explore the relation between the circadian timing and the antidepressant effect across the three treatment weeks. From the ICC analyzed with the null model (in which the participant ID was included as random intercept), it resulted that 88.6% (95% CI: 0.80 - 0.94) of the variance in the QIDS-SR score could be explained by the variance on participant level. A statistically significant main effect of treatment week on the antidepressant effect was found ($F(2,120) = 5.39$, $p < 0.01$). The main effect of treatment week on the antidepressant effect did statistically significantly differ from treatment week 1, both for treatment week 2 and treatment week 3 (see Table 16). However, results showed no statistically significant main effect of circadian timing on the antidepressant effect ($F(1,120) = 0.68$, $p = 0.41$). Since the -2LL statistics of the LMM with interaction effect and the LMM with random slopes, did both not differ statistically significant from the 'hierarchical model' (with only the 'main effects' included, see Table 17), the interaction effects and the random slopes were not included in the LMM analysis. Furthermore, the standardized residuals of the antidepressant effect variables did not all met the normality assumption (see Table 15). In view of the small deviation from $W \geq 0.97$, the histograms of the standardized residuals of the variables and the Skewness/Kurtosis tests which indicated all to be normally distributed, the results were not expected to be (strongly) affected by this violation.

Visualizations of the buildup of the QIDS-SR scores (Figure 16) and the antidepressant effect (Figure 17) across the treatment weeks, conducted from the LMM using post-hoc analysis with Bonferroni correction, were created.

Table 16

Estimated model fixed effects of the linear mixed model

Effect	Estimate	SE	df	t	p	95% CI
Intercept	0.64	4.19	120	0.152	0.88	-7.66 – 8.93
Circadian timing of morning BLT	0.32	0.39	120	0.83	0.411	-0.45 – 1.09
Treatment week 2	-2.54	0.82	120	-3.09	**0.00**	-4.17 – -0.92
Treatment week 3	-2.06	0.90	120	-2.29	**0.02**	-3.85 – -0.28

Note. Dependent variable: Antidepressant effect; Bold when considered statistically significant ($p < 0.05$); Treatment week 1 was used as reference.

Table 17

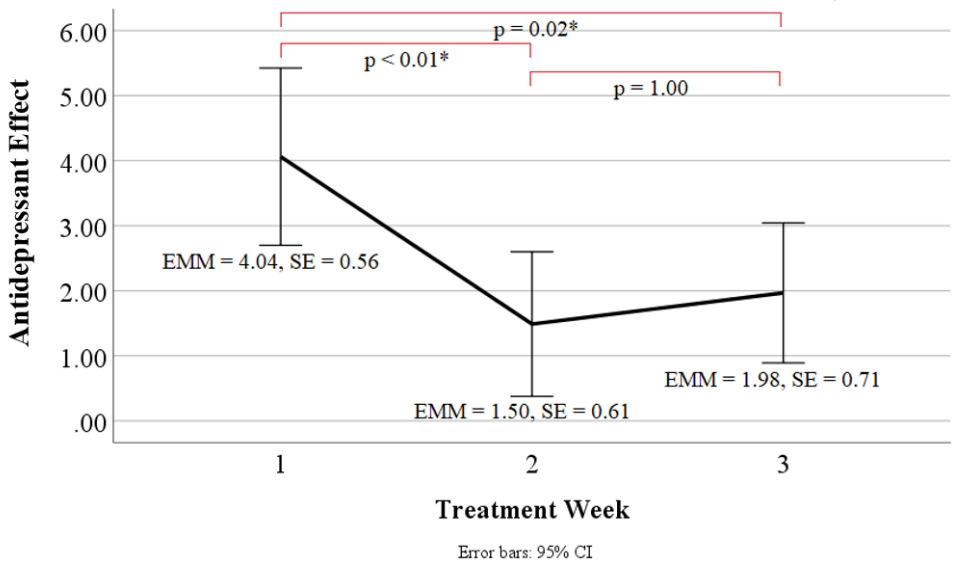
Degrees of freedom and -2 Likelihood Statistics of the Linear Mixed Model and the X^2-test

Model	Included	df	-2LL	X^2	X^2df	p
Hierarchical model	Treatment week Circadian timing of morning BLT	5	666.029			
Hierarchical model with interaction effect*	Treatment week Circadian timing of morning BLT Treatment week*****Circadian timing of morning BLT	7	665.572	0.457	2	0.80
Hierarchical model with random slopes*	Treatment week Circadian timing of morning BLT	11	665.572	0	4	1.00

Note. Bold when considered statistically significant ($p < 0.05$); *Compared with hierarchical model

Figure 16

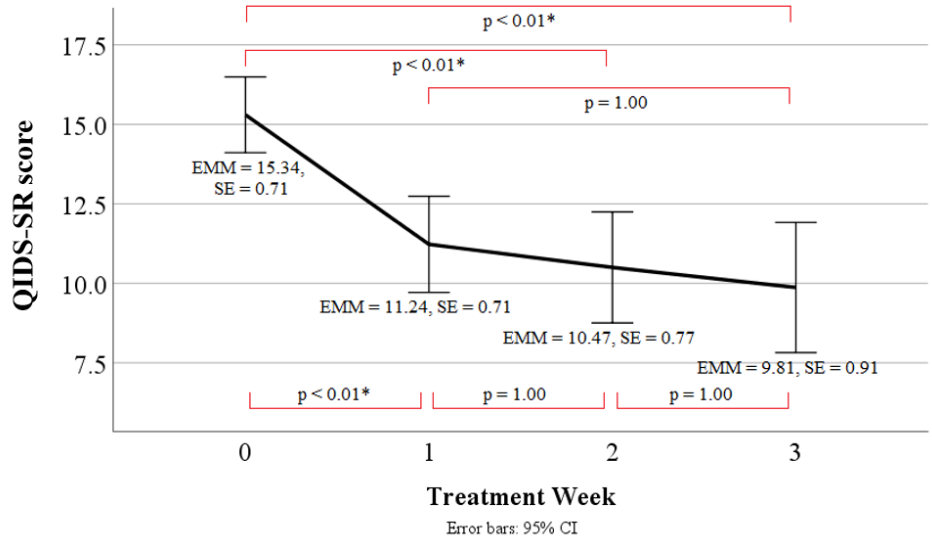
Comparison of the estimated marginal means of antidepressant effect across treatment weeks



Note. EMM = estimated marginal mean; SE = standard error; Antidepressant effect is assessed by the difference between QIDS-SR scores across treatment weeks; *Indicates a statistically significant contrast.

Figure 17

Comparison of the estimated marginal means of QIDS-SR scores across treatment weeks



Note. EMM = estimated marginal mean; SE = standard error; *Indicates a statistically significant contrast.

3.5 Spearman Correlation tests

Between the circadian timing of morning BLT treatment and the phase advance in the first week of treatment, a statistically significant negative correlation was found (see Table 18). However, since the standardized residuals of the phase advance variables had some difficulties in the normality assumption (see Table 15), and there was worked within a restricted sample size, drawing conclusions from these results should be done with caution. A visualization of this association is shown in Figure 18.

Table 18

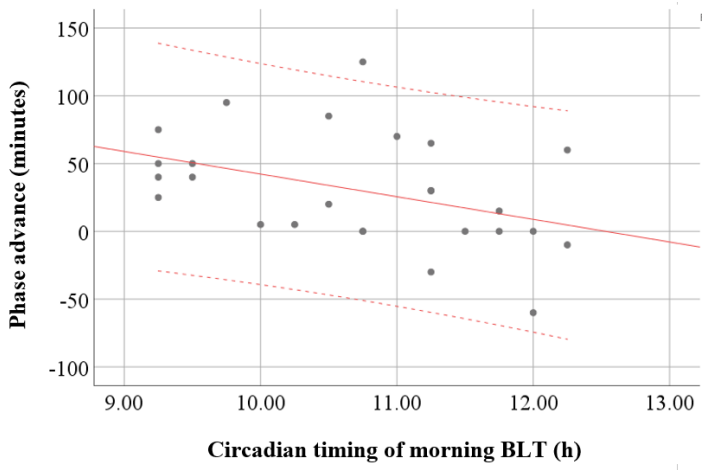
Spearman correlation between the circadian timing of morning BLT and the phase advance per treatment week

Circadian timing of morning BLT	r	p	n
Phase advance week 1	-0.40	**0.04**	26
Phase advance week 2	0.00	0.99	22
Phase advance week 3	-0.03	0.88	15

Note. Bold when considered statistically significant ($p < 0.05$).

Figure 18

Association of the circadian timing of morning and the phase advance in treatment week 1



Note. Solid line, linear regression; dashed lines: 95% interval.

4. Discussion

In earlier studies, adjusting the timing of light exposure to a patient's internal time, appeared to increase the therapeutic effect in patients with a SAD (Terman & Terman, 2011): BLT given between 7.5 and 9.5 hours post DLMO of a depressed patient that is diagnosed with SAD produced twice the remission as compared to BLT given between 9.5 and 11.0 hours post DLMO (80% vs 38.1%) (Terman et al., 2001). The current study explored more broadly whether the circadian timing of the morning BLT influences its antidepressant effect within patients with a depression in general.

4.1 Interpretation and implications of the results

Results indicate that morning BLT in the LichtCafé was effective in reducing the depression score: the depression scores in the first, second and third treatment week were statistically significant lower than the baseline depression score. Furthermore, the treatment week had a statistically significant influence on the antidepressant effect: the morning BLT was most effective in the first week of treatment, as the antidepressant effect in the first treatment week was statistically significant higher compared to the antidepressant effect in the second and third week of treatment. The antidepressant effect obtained in the second and third treatment week were not statistically significant different from each other, implicating no further improvement of the morning BLT (in terms of depression score) in the second and third treatment week. No statistically significant association between the circadian timing and the antidepressant effect was found, which was in contrast with the significant correlation between circadian timing and the percentage change in the depression score ($n = 21$, $r = -0.38$, $p = 0.01$) reported by Terman and colleagues (2001).

Several factors may have contributed to the difference in outcomes between the current study and that of Terman et al. (2001): 1) Terman and colleagues (2001) only

included patients diagnosed with SAD, compared to all types of depressions in the current (sub)study, possibly implying that the circadian timing of the morning BLT and the antidepressant effect are only related to each other in patients with a SAD. 2) The current study and the study of Terman et al. (2001) differed in the instruments used to assess the circadian timing- and depression score variables, which might have led to different values of these variables. In the current study, the depression score was measured with the QIDS-SR (16) (range depression score = 0 – 27), while Terman and colleagues (2001) measured the depression score with the SIGH-SAD (29) (range depression score = 0 – 90) which is a questionnaire specific for patients with a SAD. Also, the two questionnaires differed in the (amount of) questions from the QIDS-SR. Furthermore, in earlier studies (Terman et al., 2001; Terman & Terman, 2005) the DLMO was measured by means of plasma melatonin samples, while in the current study the DLMO was estimated by means of a MEQ-SA questionnaire, producing a rough DLMO estimate within a range of around 4 hours (observed by Kantermann, et al. 2015). Moreover, the diagnosis in the study of Terman and colleagues (2001) was based on the DSM-III-R, while the current study is based on the DSM-V. However, this is not expected to have a major influence on the outcome differences between the studies. 3) There were some differences in the experimental design of the two studies, which made it hard to compare the results. In the study protocol of Terman et al. (2001) (n = 42, 21-56 y/o, 29 women, 13 men), the participants received 10 to 14 days morning BLT with a measurement of depression score on the first and last day of treatment, while in the current study the participants received 5, 10 or 15 days morning BLT with a measurement of depression score on the first and every last day of the treatment week (n = 47, 19-74 y/o, 31 women, 16 men). The dose of light to which the participants were exposed during the treatment sessions was the same (~10,000 lux for 30 minutes), however the (circadian) timing (interval) of morning BLT differed between the two studies. The participants in Terman and

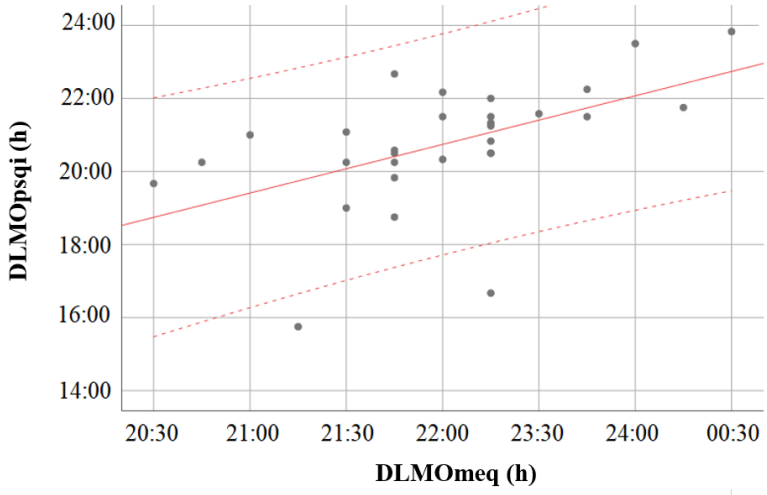
colleagues' (2001) study received morning BLT soon after their habitual wake-up time (6.32 AM ± 56 minutes), while in the current study the patients received morning BLT according to their social schedule (8.47 AM ± 50 minutes), and thus were exposed to the morning BLT later in time. The habitual time of 'going-out-of-bed' of the participants in this study was 8:18 AM ± 119 minutes (derived with the $PSQI_{week1}$). This difference in start time of morning BLT resulted also in a difference in the circadian timings of morning BLT (i.e. in terms of hours post DLMO): a circadian timing of morning BLT median of 10.75 (range = 8.75 – 12.25) in the current study, compared to a circadian timing of morning BLT median of 9.53 (range = 7.5 – 11.0) in the study of Terman et al. (2001). 4) There may have been a phase advance of the patients circadian rhythm during the first treatment week of the morning BLT (on average a phase advance of 30.19 ± 41.19 minutes, ranging from -60 to 125 minutes was observed). Since this phase shift was measured with the patients' sleep onset (as derived from the PSQI), a marker for circadian time that correlated in this study with the DLMO (estimated with the MEQ) ($r = 0.532$, $p < 0.01$, see Figure 19), this would suggest that the DLMO likely also shifted during the first week of treatment. This phase advance in the first treatment week was associated with the circadian timing of morning BLT ($r = -0.40$, $p < 0.05$), indicating an earlier circadian timing of morning BLT inducing a greater magnitude of the phase advance of the patients internal time (see Figure 18). The potential phase shift in the first week suggests that we are not dealing with a circadian timing of morning BLT that remains fixed per participant across the treatment days and/or weeks, as considered in this study (providing only one estimate of the circadian timing of morning BLT on the first day of treatment), but with a DLMO (and circadian timing of morning BLT) that might shift across therapy weeks.

Observing a potential phase advance in the first week of treatment while having a fixed timing of the morning BLT (per participant) across all the treatment days and weeks, could result in an even later circadian timed morning BLT in the second and third treatment

week than illustrated in this study. This firstly might be an explanation, when considering the finding of Terman and Terman (2005) to be true (morning BLT later than 9.53 hours post DLMO leads to a less effective treatment in terms of remission rate), for the morning BLT to be less effective in the second and third week of treatment. Moreover, it might also be an explanation for not finding an association between the circadian timing of morning BLT and phase advance in the second and third treatment week (when taking into account the phase response curve (Figure 6)).

Figure 19

Correlation of the DLMOmeq and the DLMOpsqi



Note. DLMO = Dim Light Melatonin Onset; PSQI = Pittsburgh Sleep Quality Index; MEQ = Morningenss-Eveningness Questionnaire; Both measured on the first day of morning BLT (baseline score); DLMOpsqi was derived by subtracting 2.5 from the SO measured with the PSQI (DLMOpsqi = SO – 2.5), as the DLMO was approximately around 2.5 hours before the SO (Baron & Reid, 2014; see section 2.5.3 ‘Phase Advance’); Solid line, linear regression; dashed lines: 95% interval.

4.2 Limitations of the current study

The current study, as part of a larger GGzE study, obtained a relatively small sample size (n = 47), which had implications on the statistical power of this (sub)study. The current

results are therefore preliminary (based on an initial exploration) and should be interpreted with caution. Continuation of the morning BLT GGzE study will hopefully result in a doubling of the sample size in the future. Furthermore, the DLMO estimation in the current study was made according to the "best guess" strategy of Terman and Terman (2005), which is based on a correlation between the MEQ score and DLMO tested in a group of 69 patients with a winter depression. However, this correlation was never replicated or tested within a larger group (with and without SAD) and seemed to be not that accurate (Kantermann, et al. (2015) observed range in the DLMO estimation of ~4 hours).

Moreover, some limitations of the current (sub) study were caused by the fact that the current (sub)study had the be executed within the standardized light therapy program of the LichtCafé. 1) In this program, the participants choose, based on their social schedule, the timeslot (between 7.30 and 10.30 AM) in which they preferred to receive morning BLT. This meant that the current study followed a correlational design in which the circadian timing of morning BLT could not be controlled. Since the timing of morning BLT in the current study was based on the preference of the participants, this resulted in a possible suboptimal (too) late circadian timing (range) (Terman and Terman, 2005). 2) The baseline depression score (QIDS-$SR_{baseline}$) was not always measured on the same day before treatment. 3) Only one putative baseline DLMO value could be estimated per participant (it appears to shift over time). 4) Besides the morning BLT, the LichtCafé focuses on various lifestyle components and environmental factors. Daily lifestyle advices were given by the therapist (e.g. about rhythms, diet, feeding patters, movement, activities and sleep), social contact was stimulated and the patients were activated by getting ready and going to the LichtCafé every morning. Since this study was designed within this standardized light therapy program of the LichtCafé, these possible confounding factors (i.e., activation, social interaction, exercise and lifestyle changes) on the antidepressant effect could not be controlled and might influenced

the explored relation between the circadian timing of the morning BLT and the antidepressant effect.

4.3 Recommendations for future research

In the current study, no patients with an early circadian timing (i.e., between 7.5 – 8.75 hours post DLMO according to Terman and Terman (2005)) were included. To explore whether the findings of Terman and colleagues (2001) and Terman and Terman (2005) could be replicated for patients with all types of depressions, earlier circadian timings of morning BLT had to be included in the study. For future research it is recommended to design studies in which the circadian timing of morning BLT is more precisely controlled and varied than in the current (sub) study. Furthermore, in future studies, it is recommended to control for the potential confounding variables (e.g., activation, social interaction, exercise, nutrition, and lifestyle changes). Another recommendation is to estimate a more precise circadian timing of morning BLT value and to assess the DLMO (and thus internal time) of a participant on a weekly, or even daily, basis. As mentioned before, the 7-day sleep diary midpoint was the sleep marker which was most strongly associated with DLMO (Reiter et al., 2020). Therefore, during the current (sub)study it was decided to add a sleep diary (SD) questionnaire to the ongoing morning BLT GGzE study protocol, to potentially improve the DLMO estimation on which to determine the circadian timing of BLT (as compared to the currently used MEQ-based DLMO estimate) (Appendix B). The SD inclusion was approved on May 18th. Therefore, there was insufficient data of the SD available to use this in the current analysis. However, the SD can be used in future research. Finally, it would be recommended to adjust the timing of the BLT treatment with respect to the internal time of a participant across the treatment days/weeks (as this appeared to shift).

5. Conclusion

In the current study, morning BLT was more effective (in terms of antidepressant effect) in the first week of treatment as compared to the second and third treatment week. The first week of morning BLT resulted in a putative circadian phase advance (as estimated based on the PSQI derived sleep timing) of the patient's internal time. An earlier circadian timing of morning BLT was related to a greater magnitude of this phase advance. However, to answer the research question "To what extent does the circadian timing of morning bright light therapy influence the antidepressant effect?", no statistically significant relation between the circadian timing of morning BLT and the antidepressant effect was found. However, this might be due to the explorative nature and restricted sample size of this study. Moreover, the negative result in the current study might be due to (i) the inaccuracy in the DLMO estimate on which the circadian timing of the morning BLT is based, (ii) the limited number of observations for a relatively early circadian timing of the morning BLT, or (iii) the inclusion of patients diagnosed with various types of depressions (not only patients with a SAD). Further research into the relation between the circadian timing of the morning BLT and the antidepressant effect is needed to establish whether this circadian timing is an effective instrument to optimize bright light treatment. For future research, it is recommended to design studies in which the circadian timing of morning BLT is more precisely controlled and varied and in which potential confounding variables are controlled. Moreover, it would be useful to estimate a more accurate DLMO value and to account for potential morning BLT induced circadian phase changes across the treatment days and/or weeks (for example with the use of the SD). Finally, if allowed by the sample size, it would be interesting to evaluate whether the relation between the circadian timing of morning BLT and the antidepressant effect differs between patients with a SAD and patients with no SAD.

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Appendices

Appendix A. Overview of extra activities

Treatment week 1:

- 4 participants changed their diet
- 10 participants changed their lifestyle
- 8 participants changed their movement
- 2 participants made use of the home trainer
- 2 participants made use of the walking group

Treatment week 2:

- 3 participants changed their diet
- 5 participants changed their lifestyle
- 7 participants changed their movement
- 4 participants made use of the home trainer
- 0 participants made use of the walking group

Treatment week 3

- 2 participants changed their diet
- 5 participants changed their lifestyle
- 5 participants changed their movement
- 0 participants made use of the home trainer
- 3 participants made use of the walking group

Appendix B. Sleep diary

The Sleep Diary (SD) is a self-report questionnaire based on an abbreviate of the Consensus Sleep Diary (Carney, et al., 2012). It required about 5 minutes to complete and was only administered twice a week ("Sleep Diary Monday" and "Sleep Diary Friday"), as to limit the extra burden on the participants of the morning BLT GGzE study. According to Reiter, et al. (2020) the 7-day sleep diary midpoint is the sleep marker which is most strongly associated with DLMO. To measure this midsleep point (MS) the local time of preparing to sleep (Sprep), the sleep latency (Slat) and the sleep end (SE) were needed (Table B1). These sleep markers were measured in the first three questions of the SD. Besides the sleep markers, to estimate the DLMO, there were some control questions included to check whether the morning BLT was scheduled too early in circadian time (Terman and Terman, 2011). In addition, the morning BLT might be scheduled too late in circadian time if 5 days of treatment shows no sign of improvement (Terman & Terman, 2011), which could be checked by their QIDS-SR scores. Besides these control questions, it has space to write down the scheduled start time of the morning BLT, which was now gathered from de timetable of the LichtCafé. Finally, questions were included about the total time the participant was awake during the night, how they woke up (by an alarm, themselves or different), how they would rate their sleep quality, whether they worked irregular/night shifts and on which days they worked in the previous seven days. It also contains a question about daylight (Roenneberg, Wirz-Justice & Merrow, 2003). These questions can be used in future research to, for example, investigate the sleep quality in patients with a depression, their internal rhythm, and the potential influence of exposure to daylight.

Table B1

Calculation of the Midsleep Point measured with the Sleep Diary

Sleep marker	Calculation
Sleep onset (SO)	Sprep + Slat
Sleep duration (SD)	SE – SO
Mid-sleep (MS)	SO + SD/2

SLAAPLOGBOEK MAANDAG

STUDIE: Lichttherapie

Geboortejaar

Usernummer: ……..

|_|__|__|__|

Datum

Meetmoment

|__|__|-|__|__|-| 2 | 0 |__|__|

Behandelweek: … | dag: …

Tijdstip Lichttherapie: … : …

De volgende vragen gaan over uw slaap gedurende de afgelopen nachten en hoeveel tijd u de afgelopen dagen buiten was. Gebruik bij het invullen van tijdstippen de 24-uurs klok (dus van 0:00 tot 23:59 uur, bijvoorbeeld 22:15 uur).

	1	**2**	**3**	**4**	**5**	**6**	**7**
Avond - ochtend	Hoe laat probeerde u te gaan slapen? *Niet het tijdstip dat in bed ging liggen, maar vanaf wanneer u daadwerkelijk probeerde te slapen*	Hoe lang kostte het u om in slaap te vallen?	Hoe laat was uw laatste moment van wakker worden? *Hoe laat werd u wakker?*	Hoeveel minuten was u wakker vannacht? *Tussen de eerste keer in slaap vallen en de laatste keer wakker worden*	Waardoor werd u wakker?	Hoe zou u uw slaapkwaliteit beoordelen? *"Slaapkwaliteit" is uw beleving van of uw slaap goed of slecht was*	Hoeveel minuten was u buiten in daglicht? *Zonder een dak boven uw hoofd*
VR- ZA	… : …	… minuten	… : …	… minuten	o Wekker o Uit mezelf o Anders	o Erg slecht o Slecht o Redelijk o Goed o Erg goed	… minuten *op vrijdag*
ZA - ZO	… : …	… minuten	… : …	… minuten	o Wekker o Uit mezelf o Anders	o Erg slecht o Slecht o Redelijk o Goed o Erg goed	… minuten *op zaterdag*
ZO - MA	… : …	… minuten	… : …	… minuten	o Wekker o Uit mezelf o Anders	o Erg slecht o Slecht o Redelijk o Goed o Erg goed	… minuten *op zondag*

SLEEP DIARY MONDAY

STUDY: Lichttherapie

Year of Birth

Usernummer: .....

|_|__|__|__|

Date

Measurement moment

|__|__|-|__|__|-| 2 | 0 |__|__|

Treatment week: … | day: …

Time of Light therapy: … : …

The following questions are about your sleep during the previous nights and how much time you were outside in the past few days. When entering times, use the 24-hour clock (so from 00:00 to 23:59, for example 22:15).

	1	**2**	**3**	**4**	**5**	**6**	**7**
Evening - morning	What time did you try to go to sleep? *Not when you went to bed, but when you actually began "trying" to sleep.*	How long did it take you to fall asleep? *Beginning at the time you answered for question 1 how long did it take you to fall asleep?*	What time was your final awakening ? *What time did you wake up?*	What was the total time you were awake between the time you first fell asleep and your final awakening?	How did you wake up?	How would you rate the quality of your sleep? *"Sleep quality" is your perception of whether your sleep was good or poor.*	In total, how many minutes were you outside in daylight? *Without a roof over your head*
FR-SA	… : …	… minutes	… : …	… minutes	o By an alarm o By myself o Different	o Very poor o Poor o Fair o Good o Very good	… minutes *on Friday*
SA – SU	… : …	… minutes	… : …	… minutes	o By an alarm o By myself o Different	o Very poor o Poor o Fair o Good o Very good	… minutes *on Saturday*
SU - MO	… : …	… minutes	… : …	… minutes	o By an alarm o By myself o Different	o Very poor o Poor o Fair o Good o Very good	… minutes *on Sunday*

SLAAPLOGBOEK VRIJDAG

STUDIE: Lichttherapie

Geboortejaar

Usernummer: ……..

|_|__|__|__|

Datum

Meetmoment

|__|__|-|__|__|-| 2 | 0 |__|__|

Behandelweek: … | dag: …

Tijdstip Lichttherapie: … : …

De volgende vragen gaan over uw slaap gedurende de afgelopen nachten en hoeveel tijd u de afgelopen dagen buiten was. Gebruik bij het invullen van tijdstippen de 24-uurs klok (dus van 0:00 tot 23:59 uur, bijvoorbeeld 22:15 uur).

	1	**2**	**3**	**4**	**5**	**6**	**7**
Avond - ochtend	Hoe laat probeerde u te gaan slapen? *Niet het tijdstip dat in bed ging liggen, maar vanaf wanneer u daadwerkelijk probeerde te slapen*	Hoe lang kostte het u om in slaap te vallen?	Hoe laat was uw laatste moment van wakker worden? *Hoe laat werd u wakker?*	Hoeveel minuten was u wakker vannacht? *Tussen de eerste keer in slaap vallen en de laatste keer wakker worden*	Waardoor werd u wakker?	Hoe zou u uw slaapkwaliteit beoordelen? *"Slaapkwaliteit" is uw beleving van of uw slaap goed of slecht was*	Hoeveel minuten was u buiten in daglicht? *Zonder een dak boven uw hoofd*
MA- DI	… : …	… minuten	… : …	… minuten	o Wekker o Uit mezelf o Anders	o Erg slecht o Slecht o Redelijk o Goed o Erg goed	… minuten *op maandag*
DI - WO	… : …	… minuten	… : …	… minuten	o Wekker o Uit mezelf o Anders	o Erg slecht o Slecht o Redelijk o Goed o Erg goed	… minuten *op dinsdag*
WO – DO	… : …	… minuten	… : …	… minuten	o Wekker o Uit mezelf o Anders	o Erg slecht o Slecht o Redelijk o Goed o Erg goed	… minuten *op woensdag*
DO – VR	… : …	… minuten	… : …	… minuten	o Wekker o Uit mezelf o Anders	o Erg slecht o Slecht o Redelijk o Goed o Erg goed	… minuten *op donderdag*

1. Heeft u door de behandeling de afgelopen week het volgende ervaren?
   Wanneer u de vraag met "Ja" beantwoord, geef dan aan hoeveel dagen u dit heeft ervaren.

a.	Een oncontroleerbare drang om enkele uren na de behandeling mijn slaap te hervatten	Nee	Ja, ___ dagen
b.	Slapeloosheid na mijn gebruikelijke bedtijd *U heeft wakker gelegen na uw gebruikelijke bedtijd*	Nee	Ja, ___ nachten
c.	Plotseling (uren) eerder wakker geworden dan ik had verwacht en ik kon daarna niet meer in slaap vallen	Nee	Ja, ___ ochtenden

2. Hebt u de afgelopen week in ploegendienst/ onregelmatige dienst/nachtdienst gewerkt? Nee Ja

Beantwoord de volgende vraag wanneer u vraag 2 met "Nee" heeft beantwoord:

3. Op de volgende dagen heb ik (de afgelopen week) **gewerkt:**
   Met werkdagen bedoelen we dagen waarop u werkt, studeert of vaste afspraken hebt

   ma di wo do vr za zo

Overige opmerkingen?

SLEEP DIARY FRIDAY

STUDY: Lichttherapie

Year of Birth

Usernummer: ……..

|_|_|__|__|

Date

Measurement moment

|__|__|-|__|__|-|2|0|__|__|

Treatment week: … | day: …

Time of light therapy: … : …

The following questions are about your sleep during the previous nights and how much time you were outside in the past few days. When entering times, use the 24-hour clock (so from 00:00 to 23:59, for example 22:15).

	1	**2**	**3**	**4**	**5**	**6**	**7**
Evening - morning	What time did you try to go to sleep? *Not when you went to bed, but when you actually began "trying" to sleep.*	How long did it take you to fall asleep? *Beginning at the time you answered for question 1 how long did it take you to fall asleep?*	What time was your final awakening ? *What time did you wake up?*	What was the total time you were awake between the time you first fell asleep and your final awakening?	How did you wake up?	How would you rate the quality of your sleep? *"Sleep quality" is your perception of whether your sleep was good or poor.*	In total, how many minutes were you outside in daylight? *Without a roof over your head*
MO- TU	… : …	… minutes	… : …	… minutes	o By an alarm o By myself o Different	o Very poor o Poor o Fair o Good o Very good	… minutes *on Monday*
TU - WE	… : …	… minutes	… : …	… minutes	o By an alarm o By myself o Different	o Very poor o Poor o Fair o Good o Very good	… minutes *on Tuesday*
WE – TH	… : …	… minutes	… : …	… minutes	o By an alarm o By myself o Different	o Very poor o Poor o Fair o Good o Very good	… minutes *on Wednesday*
TH – FR	… : …	… minutes	… : …	… minutes	o By an alarm o By myself o Different	o Very poor o Poor o Fair o Good o Very good	… minutes *on Thursday*

1. Have you experienced the following as a result of the treatment in the past week?
   If you answer the question with "Yes", please indicate how many days you have experienced this.

b. An uncontrollable urge to return to sleep a few hours after the treatment — No — Yes, ___ days

c. Insomnia after my usual bedtime — No — Yes, ___ nights
   You have been awake after your usual bedtime

d. Suddenly woke up (hours) earlier than I expected and I couldn't fall asleep after that — No, — Yes, ___ mornings

2. Have you worked shifts / irregular shifts / night shifts in the past week? — No — Yes

Answer the following question if you answered question 2 with "No":

3. I worked on the following days (in the preceding seven days):
   By working days we mean days on which you work, study or have fixed appointments.

fr sa su mo tu we th

Other comments?

Appendix C. Quick Inventory of Depressive Symptomatology – Self Report

QIDS-SR (Dutch Version)

Kruis bij elke vraag het antwoord aan dat de afgelopen 7 dagen het meest op u van toepassing was.

1. In slaap vallen
0. Ik word 's nachts niet wakker
1. Ik slaap onrustig en licht en word een aantal keren per nacht even wakker
2. Ik ben tenminste 1 keer per nacht klaar wakker, maar val weer gemakkelijk in slaap
3. Ik word vaker dan 1 keer per nacht wakker en blijf dan 20 minuten of langer wakker, meer dan de helft van de week

2. Slaap gedurende de nacht
0. Meestal word ik niet eerder dan 30 minuten voordat ik op moet staan, wakker
1. Ik word meer dan 30 minuten voordat ik op moet staan wakker, meer dan de helft van de tijd
2. Ik word tenminste 1 uur voordat ik op moet staan wakker, meer dan de helft van de tijd
3. Ik word tenminste 2 uur voordat ik op moet staan wakker, meer dan de helft van de tijd

3. Te vroeg wakker worden
0. Ik slaap niet langer dan 7-8 uur per nacht, zonder overdag een dutje te doen
1. Ik slaap niet langer dan 10 uur binnen 1 etmaal (inclusief dutten)
2. Ik slaap niet langer dan 12 uur binnen 1 etmaal (inclusief dutten)
3. Ik slaap langer dan 12 uur binnen 1 etmaal (inclusief dutten)

4. Te veel slapen
0. Ik slaap niet langer dan 7-8 uur per nacht, zonder overdag een dutje te doen
1. Ik slaap niet langer dan 10 uur binnen 1 etmaal (inclusief dutten)
2. Ik slaap niet langer dan 12 uur binnen 1 etmaal (inclusief dutten)
3. Ik slaap langer dan 12 uur binnen 1 etmaal (inclusief dutten)

Kruis bij elke vraag het antwoord aan dat de afgelopen 7 dagen het meest op u van toepassing was.

5. Somber voelen
0. Ik ben niet somber
1. Ik ben minder dan de helft van de tijd somber
2. Ik ben meer dan de helft van de tijd somber
3. Ik ben bijna altijd somber

6. Verminderde eetlust
0. Mijn eetlust is niet anders dan gewoonlijk
1. Ik eet wat minder vaak of minder grote hoeveelheden dan gewoonlijk
2. Ik eet veel minder dan gewoonlijk en alleen met inspanning
3. Ik eet nauwelijks binnen een etmaal en alleen met extreme inspanning of op aandringen van anderen

7. Toegenomen eetlust
0. Mijn eetlust is niet anders dan gewoonlijk
1. Ik voel vaker dan gewoonlijk de behoefte om te eten
2. Ik eet regelmatig vaker en grotere hoeveelheden dan gewoonlijk
3. Ik voel een sterke neiging om zowel tijdens de maaltijden als tussendoor te veel te eten

8. Gewichtsafname gedurende de afgelopen 2 weken
0. Geen gewichtsverandering
1. Ik heb het gevoel dat ik wat ben afgevallen
2. Ik ben 1 kg of meer afgevallen
3. Ik ben 2,5 kg of meer afgevallen

9. Gewichtstoename gedurende de afgelopen 2 weken
1. Ik heb het gevoel dat ik wat ben aangekomen
2. Ik ben 1 kg of meer aangekomen
3. Ik ben 2,5 kg of meer aangekomen

10. Concentratie/ besluitvaardigheid
0. Er is geen verandering in gebruikelijke concentratievermogen of in besluitvaardigheid
1. Ik voel mij nu en dan besluiteloos of merk dat ik mijn aandacht er niet bij kan houden
2. Ik heb bijna altijd grote moeite om mijn aandacht vast te houden en om beslissingen te nemen
3. Ik kan mij niet goed genoeg concentreren om te lezen of kan zelfs niet de kleinste beslissingen nemen

Kruis bij elke vraag het antwoord aan dat de afgelopen 7 dagen het meest op u van toepassing was.

11. Zelfbeeld
0. Ik vind mijzelf even waardevol en nuttig als een ander
1. Ik maak mijzelf meer verwijten dan gewoonlijk
2. Ik heb sterk de indruk dat ik anderen in moeilijkheden breng
3. Ik denk voortdurend aan mijn grotere en kleinere tekortkomingen

12. Gedachten aan dood en zelfmoord
0. Ik denk niet aan zelfmoord of aan dood
1. Ik heb het gevoel dat mijn leven leeg is en vraag me af of het nog wel de moeite waard is
2. Ik denk enkele malen per week wel even aan zelfmoord of aan de dood
3. Ik denk een aantal keren per dag serieus na over zelfmoord of dood, óf ik heb zelfmoordplannen gemaakt, óf ik heb al een poging gedaan om mijn leven te beëindigen

13. Algemene interesse
0. Geen verandering van mijn normale interesse in andere mensen en activiteiten.
1. Ik merk dat ik minder geïnteresseerd ben in anderen en in activiteiten.
2. Ik heb alleen nog interesse in een of twee dingen die ik voorheen deed.
3. Ik heb vrijwel geen interesse meer in dingen die ik voorheen deed.

14. Energie
0. Geen verandering in mijn gebruikelijke energie.
1. Ik word sneller moe dan gewoonlijk.
2. Ik heb grote moeite met het beginnen aan of volhouden van gebruikelijke dagelijkse activiteiten. (bijvoorbeeld boodschappen doen, huiswerk, koken, of naar het werk gaan).
3. Ik ben niet in staat om mijn normale dagelijkse activiteiten uit te voeren vanwege een gebrek aan energie.

15. Gevoel van traagheid
0. Ik denk, spreek en beweeg in mijn normale tempo.
1. Mijn denken is vertraagd en mijn stem klinkt vlak en saai
2. Ik heb meer tijd nodig om te antwoorden op vragen, en mijn denken is zeker vertraagd.
3. Het kost me zeker veel moeite om te reageren op vragen.

16. Rusteloos gevoel
0. Ik voel mij niet rusteloos
1. Ik ben vaak zenuwachtig, ik wring met mijn handen en ik kan niet rustig op een stoel zitten.
2. Ik heb de neiging te bewegen en ben nogal rusteloos
3. Ik kan vaak niet stilzitten en loop dan te ijsberen

QIDS-SR (English version)

The Quick Inventory of Depressive Symptomatology (16-Item) (Self-Report) (QIDS-SR16)

Name or ID: _____ Date: _____

CHECK THE ONE RESPONSE TO EACH ITEM THAT BEST DESCRIBES YOU FOR THE PAST SEVEN DAYS.

During the past seven days....

1. Falling Asleep:

- ☐ 0 I never take longer than 30 minutes to fall asleep.
- ☐ 1 I take at least 30 minutes to fall asleep, less than half the time.
- ☐ 2 I take at least 30 minutes to fall asleep, more than half the time.
- ☐ 3 I take more than 60 minutes to fall asleep, more than half the time.

2. Sleep During the Night

- ☐ 0 I do not wake up at night.
- ☐ 1 I have a restless, light sleep with a few brief awakenings each night.
- ☐ 2 I wake up at least once a night, but I go back to sleep easily.
- ☐ 3 I awaken more than once a night and stay awake for 20 minutes or more, more than half the time.

3. Waking Up Too Early:

- ☐ 0 Most of the time, I awaken no more than 30 minutes before I need to get up.
- ☐ 1 More than half the time, I awaken more than 30 minutes before I need to get up.
- ☐ 2 I almost always awaken at least one hour or so before I need to, but I go back to sleep eventually.
- ☐ 3 I awaken at least one hour before I need to, and can't go back to sleep.

4. Sleeping Too Much:

- ☐ 0 I sleep no longer than 7-8 hours/night, without napping during the day.
- ☐ 1 I sleep no longer than 10 hours in a 24-hour period including naps.
- ☐ 2 I sleep no longer than 12 hours in a 24-hour period including naps.
- ☐ 3 I sleep longer than 12 hours in a 24-hour period including naps.

During the past seven days....

5. Feeling Sad:

- ☐ 0 I do not feel sad.
- ☐ 1 I feel sad less than half the time.
- ☐ 2 I feel sad more than half the time.
- ☐ 3 I feel sad nearly all of the time.

Please complete either 6 or 7 (not both)

6. Decreased Appetite:

- ☐ 0 There is no change in my usual appetite.
- ☐ 1 I eat somewhat less often or lesser amounts of food than usual.
- ☐ 2 I eat much less than usual and only with personal effort.
- ☐ 3 I rarely eat within a 24-hour period, and only with extreme personal effort or when others persuade me to eat.

- OR -

7. Increased Appetite:

- ☐ 0 There is no change from my usual appetite.
- ☐ 1 I feel a need to eat more frequently than usual.
- ☐ 2 I regularly eat more often and/or greater amounts of food than usual.
- ☐ 3 I feel driven to overeat both at mealtime and between meals.

Please complete either 8 or 9 (not both)

8. Decreased Weight (Within the Last Two Weeks):

- ☐ 0 I have not had a change in my weight.
- ☐ 1 I feel as if I have had a slight weight loss.
- ☐ 2 I have lost 2 pounds or more.
- ☐ 3 I have lost 5 pounds or more.

- OR -

9. Increased Weight (Within the Last Two Weeks):

- ☐ 0 I have not had a change in my weight.
- ☐ 1 I feel as if I have had a slight weight gain.
- ☐ 2 I have gained 2 pounds or more.
- ☐ 3 I have gained 5 pounds or more.

Pg. 1 of 2

The Quick Inventory of Depressive Symptomatology (16-Item) (Self-Report) (QIDS-SR16)

During the past seven days...

10. Concentration / Decision Making:

- ☐ 0 There is no change in my usual capacity to concentrate or make decisions.
- ☐ 1 I occasionally feel indecisive or find that my attention wanders.
- ☐ 2 Most of the time, I struggle to focus my attention or to make decisions.
- ☐ 3 I cannot concentrate well enough to read or cannot make even minor decisions.

11. View of Myself:

- ☐ 0 I see myself as equally worthwhile and deserving as other people.
- ☐ 1 I am more self-blaming than usual.
- ☐ 2 I largely believe that I cause problems for others.
- ☐ 3 I think almost constantly about major and minor defects in myself.

12. Thoughts of Death or Suicide:

- ☐ 0 I do not think of suicide or death.
- ☐ 1 I feel that life is empty or wonder if it's worth living.
- ☐ 2 I think of suicide or death several times a week for several minutes.
- ☐ 3 I think of suicide or death several times a day in some detail, or I have made specific plans for suicide or have actually tried to take my life.

13. General Interest

- ☐ 0 There is no change from usual in how interested I am in other people or activities.
- ☐ 1 I notice that I am less interested in people or activities.
- ☐ 2 I find I have interest in only one or two of my formerly pursued activities.
- ☐ 3 I have virtually no interest in formerly pursued activities.

During the past seven days...

14. Energy Level:

- ☐ 0 There is no change in my usual level of energy.
- ☐ 1 I get tired more easily than usual.
- ☐ 2 I have to make a big effort to start or finish my usual daily activities (for example, shopping, homework, cooking, or going to work).
- ☐ 3 I really cannot carry out most of my usual daily activities because I just don't have the energy.

15. Feeling Slowed Down:

- ☐ 0 I think, speak, and move at my usual rate of speed.
- ☐ 1 I find that my thinking is slowed down or my voice sounds dull or flat.
- ☐ 2 It takes me several seconds to respond to most questions and I'm sure my thinking is slowed.
- ☐ 3 I am often unable to respond to questions without extreme effort.

16. Feeling Restless:

- ☐ 0 I do not feel restless.
- ☐ 1 I'm often fidgety, wringing my hands, or need to shift how I am sitting.
- ☐ 2 I have impulses to move about and am quite restless.
- ☐ 3 At times, I am unable to stay seated and need to pace around.

Pg. 2 of 2

Appendix D. Morningness-Eveningness Questionnaire Self-Assesment

OCHTEND-AVONDTYPE VRAGENLIJST (MEQ-SA)

Kies bij iedere vraag het antwoord dat het beste bij u past. Zet een cirkeltje om het antwoord dat het beste aangeeft hoe u zich in de afgelopen weken hebt gevoeld.

1. Hoe laat zou u *ongeveer* opstaan, als u volledig vrij was in uw dagindeling?

[5] 05:00–06:30 u
[4] 06:30–07:45 u
[3] 07:45–09:45 u
[2] 09:45–11:00 u
[1] 11:00–12:00 u

2. Hoe laat zou u *ongeveer* naar bed gaan als u volledig vrij was in het indelen van uw avond?
[5] 20:00–21:00 u
[4] 21:00–22:15 u
[3] 22:15–00:30 u
[2] 00:30–01:45 u
[1] 01:45–03:00 u

3. Als u ’s morgens op een voor u gebruikelijke tijd op moet staan, hoe sterk afhankelijk bent u dan van een wekker?

[4] Helemaal niet afhankelijk
[3] Enigszins afhankelijk
[2] Nogal afhankelijk
[1] Erg afhankelijk

4. Hoe gemakkelijk vindt u het om ’s morgens op te staan (als u niet onverwachts gewekt wordt)

[1] Erg moeilijk
[2] Nogal moeilijk
[3] Nogal gemakkelijk
[4] Erg gemakkelijk

5. Hoe wakker voelt u zich ‘s morgens gedurende het eerste half uur nadat u wakker bent geworden?

[1] Helemaal niet wakker
[2] Een beetje wakker
[3] Behoorlijk wakker
[4] Klaarwakker

6. Hoe hongerig voelt u zich ‘s morgens gedurende het eerste half uur nadat u wakker bent geworden?

[1] Helemaal niet hongerig
[2] Een beetje hongerig
[3] Behoorlijk hongerig
[4] Erg hongerig

7. Hoe voelt u zich ‘s morgens gedurende het eerste half uur nadat u wakker bent geworden?

[1] Erg moe
[2] Behoorlijk moe
[3] Behoorlijk uitgerust
[4] Erg uitgerust

8. Als u de volgende dag geen verplichtingen hebt, hoe laat zou u dan naar bed gaan in vergelijking tot uw gebruikelijk bedtijd?

[4] Zelden of nooit later
[3] Minder dan 1 uur later
[2] 1 à 2 uur later
[1] meer dan 2 uur later

9. U heeft besloten om te gaan trainen. Een vriend stelt voor dit twee keer per week één uur te doen en de tijd die hem het beste past is tussen 7-8 u ‘s morgens. Als u even alleen aan uw eigen “interne klok” denkt, hoe verwacht u dan dat u zal presteren?

[4] Ik zou in goede vorm zijn
[3] Ik zou in redelijke vorm zijn
[2] Ik zou het moeilijk vinden
[1] Ik zou het erg moeilijk vinden

10. Om ongeveer hoe laat bent u ’s avonds zo moe dat u wel moet gaan slapen?

[5] 20:00–21:00 u
[4] 21:00–22:15 u
[3] 22:15–00:45 u
[2] 00:45–02:00 u
[1] 02:00–03:00 u

11. U wilt zo goed mogelijk presteren op een test die u geestelijk erg zal inspannen en twee uur zal duren. U bent volledig vrij in uw dagindeling. Als u even alleen aan uw eigen “interne klok” denkt, welke van de vier volgende test-tijdstippen zou u dan kiezen?

[6] 08–10 u
[4] 11–13 u
[2] 15–17 u
[0] 19–21 u

12. Als u ‘s avonds om 23:00 uur naar bed zou gaan, hoe moe zou u dan zijn?

[0] Helemaal niet moe
[2] Een beetje moe
[3] Behoorlijk moe
[5] Erg moe

13. Om de één of andere reden bent u enkele uren later naar bed gegaan dan voor u gebruikelijk is. De volgende ochtend bent u vrij om op te staan wanneer u wilt. Welke van de hieronder genoemde antwoorden is het beste op u van toepassing?

[4] Ik word op de gewone tijd wakker en slaap niet meer in
[3] Ik word op de gewone tijd wakker en doezel daarna nog wat
[2] Ik word op de gewone tijd wakker, maar slaap ook weer in
[1] Ik word later dan gewoonlijk wakker

14. Gedurende één nacht moet u van 04-06 u wakker blijven om de wacht te houden. De volgende dag hebt u geen verplichtingen. Welke van de volgende keuzes zou het beste bij u passen?

[1] Zou pas naar bed gaan als mijn wacht voorbij was
[2] Zou van te voren een dutje doen en na de wacht gaan slapen
[3] Zou van te voren goed slapen en na de wacht een dutje doen
[4] Zou alleen voorafgaand aan de wacht slapen

15. U moet twee uur zware lichamelijke arbeid verrichten. U bent volledig vrij in uw dagindeling. Als u even alleen aan uw eigen “interne klok” denkt, welke van de volgende tijden zou u dan kiezen?

[4] 08–10 u
[3] 11–13 u
[2] 15–17 u
[1] 19–21 u

16. U heeft besloten om te gaan trainen. Een vriendin stelt voor dit twee keer per week één uur te doen en de tijd die haar het beste past is van 22-23u. Als u even alleen aan uw eigen “interne klok” denkt, hoe verwacht u dan dat u zal presteren?

[4] Ik zou in goede vorm zijn
[3] Ik zou in redelijke vorm zijn
[2] Ik zou het moeilijk vinden
[1] Ik zou het erg moeilijk vinden

17. Stelt u zich voor dat u uw eigen werktijden kan kiezen en dat u een vijf-urige werkdag heeft (inclusief pauzes). Uw werk is uitdagend en uw salaris is afhankelijk van uw prestaties. Hoe laat zou u uw vijf-urige werkdag *ongeveer* laten beginnen?

[5] 5 uren te beginnen tussen 04–08 u
[4] 5 uren te beginnen tussen 08–09 u
[3] 5 uren te beginnen tussen 09–14 u
[2] 5 uren te beginnen tussen 14–17 u
[1] 5 uren te beginnen tussen 17–04 u

18. Op *ongeveer* welke tijd van de dag voelt u zich over het algemeen het best?

[5] 05–08 u
[4] 08–10 u
[3] 10–17 u
[2] 17–22 u
[1] 22–05 u

19. Er wordt wel eens gesproken over ochtendtypes en avondtypes. Wat voor type denkt u dat u bent?

[6] een uitgesproken ochtendtype
[4] meer een ochtendtype dan een avondtype
[2] meer een avondtype dan een ochtendtype
[1] een uitgesproken avondtype

Morningness-Eveningness Questionnaire (MEQ-SA)

Choose at every question the answer that is most fitting for you. Circle the answer that most is most fitting for your situation pas weeks.

1. What time would you get up if you were entirely free to plan your day?

[5] 05:00–06:30 u
[4] 06:30–07:45 u
[3] 07:45–09:45 u
[2] 09:45–11:00 u
[1] 11:00–12:00 u

2. What time would you go to bed if you were entirely free to plan your evening?

[5] 20:00–21:00 u
[4] 21:00–22:15 u
[3] 22:15–00:30 u
[2] 00:30–01:45 u
[1] 01:45–03:00 u

3. If there is a specific time at which you have to get up in the morning, to what extent do you depend on being woken up by an alarm clock?

[4] Not at all dependent
[3] Slightly dependent
[2] Fairly dependent
[1] Very dependent

4. How easy do you find it to get up in the morning (when you are not woken up unexpectedly)?

[1] Not at all easy
[2] Not very easy
[3] Fairly easy
[4] Very easy

5. How alert do you feel during the first half hour after you wake up in the morning?

[1] Not at all alert
[2] Slightly alert
[3] Fairly alert
[4] Very alert

6. How hungry do you feel during the first half-hour after you wake up in the morning?

[1] Not at all hungry
[2] Slightly hungry
[3] Fairly hungry
[4] Very hungry

7. During the first half-hour after you wake up in the morning, how tired do you feel?

[1] Very tired
[2] Fairly tired
[3] Fairly refreshed
[4] Very refreshed

8. If you have no commitment the next day, what time would you go to bed compared to your usual bedtime?

[4] Seldom or never later
[3] Less than one hour later
[2] 1-2 hours later
[1] More than two hours later

9. You have decided to engage in some physical exercise. A friend suggests that you do this for one hour twice a week and the best time for him/her is between 7:00 – 8:00 am. Bearing in mind nothing but your own internal "clock", how do you think you would perform?

[4] Would be in good form
[3] Would be in reasonable form
[2] Would find it difficult
[1] Would find it very difficult

10. At what time of day do you feel you become tired as a result of need for sleep?

[5] 20:00–21:00 u
[4] 21:00–22:15 u
[3] 22:15–00:45 u
[2] 00:45–02:00 u
[1] 02:00–03:00 u

11. You want to be at your peak performance for a test that you know is going to be mentally exhausting and will last for two hours. You are entirely free to plan your day. Considering only your own internal "clock", which ONE of the four testing times would you choose?

[6] 08–10 u
[4] 11–13 u
[2] 15–17 u
[0] 19–21 u

12. If you got into bed at 11:00 pm, how tired would you be?

[0] Not at all tired
[2] A little tired
[3] Fairly tired
[5] Very tired

13. For some reason, you have gone to bed several hours later than usual, but there is no need to get up at any particular time the next morning. Which ONE of the following are you most likely to do?

[4] Will wake up at usual time, but will NOT fall back asleep
[3] Will wake up at usual time and will doze thereafter
[2] Will wake up at usual time but will fall asleep again
[1] Will NOT wake up until later than usual

14. One night you have to remain awake between 4:00 – 6:00 am in order to carry out a night watch. You have no commitments the next day. Which ONE of the alternatives will suite you best?

[1] Would NOT go to bed until watch was over
[2] Would take a nap before and sleep after
[3] Would take a good sleep before and nap after
[4] Would sleep only before watch

15. You have to do two hours of hard physical work. You are entirely free to plan your day and considering only your own internal "clock" which ONE of the following times would you choose?

[4] 08–10 u
[3] 11–13 u
[2] 15–17 u
[1] 19–21 u

16. You have decided to engage in hard physical exercise. A friend suggests that you do this for one hour twice a week and the best time for him/her is between 10:00 – 11:00 pm. Bearing in mind nothing else but your own internal "clock", how well do you think you would perform?

[4] Would be in good form
[3] Would be in reasonable form
[2] Would find it difficult
[1] Would find it very difficult

17. Suppose that you can choose your school hours. Assume that you went to school for five hours per day and that school was interesting and enjoyable. Which five consecutive hours would you select?

[5] 5 hours starting between 4:00 – 7:59 am
[4] 5 hours starting between 8:00 – 8:59 am
[3] 5 hours starting between 9:00 am – 1:59 pm
[2] 5 hours starting between 2:00 – 4:59 pm
[1] 5 hours starting between 5:00 pm – 3:59 am

18. At what time of the day do you think that you reach your “feeling best” peak?

[5] 05–08 u
[4] 08–10 u
[3] 10–17 u
[2] 17–22 u
[1] 22–05 u

19. One hears about “morning” and “evening” types of people. Which ONE of these types do you consider yourself to be?

[6] Definitely a “morning” type
[4] Rather more a “morning” type than an “evening” type
[2] Rather more an “evening” type than a “morning” type
[1] Definitely an “evening” type

Appendix E. Pittsburg Sleep Quality Index

Slaap vragenlijst (PSQI)

De volgende vragen hebben betrekking op uw slaap gedurende de afgelopen week. Uw antwoorden zouden een zo nauwkeurig mogelijke weergave moeten zijn van de meerderheid van de dagen en nachten gedurende deze periode. Vul het best passende antwoord in de kaders in.

1. Hoe laat ging u 's avond meestal naar bed gedurende de afgelopen week? Gebruikelijke bedtijd: |__|__|:|__|__|
2. Hoeveel minuten duurde het de afgelopen week gewoonlijk elke nacht vooraleer u in slaap viel? Aantal minuten: |__|__|__|
3. Hoe laat stond u tijdens de afgelopen week 's morgens op? Gebruikelijk tijdstip van opstaan: |__|__|:|__|__|
4. Aan hoeveel uren SLAAP kwam u gemiddeld per nacht tijdens de afgelopen week? (Dat kan verschillen van het aantal uren dat u in bed doorbracht) Aantal uren per nacht: |__|__|

Zet bij de volgende vragen een kruisje in het vakje onder het antwoord dat op u van toepassing is. Sla geen vragen over.

5. Hoe vaak had u tijdens de afgelopen week moeilijkheden met slapen, omdat u …

	NIET TIJDENS DE AFGELOPEN WEEK	ÉÉN MAAL PER WEEK	TWEEMAAL PER WEEK	DRIE – OF MEERMAALS PER WEEK
a) niet binnen 30 minuten in slaap viel?	0	1	2	3
b) midden in de nacht of in de vroege morgen wakker werd?	0	1	2	3
c) naar het toilet moest gaan?	0	1	2	3
d) niet makkelijk kon ademhalen?	0	1	2	3
e) luid hoestte of snurkte?	0	1	2	3
f) het te koud had?	0	1	2	3
g) het te warm had?	0	1	2	3
h) nachtmerries had?	0	1	2	3
i) Pijn had?	0	1	2	3
j) (een) andere reden (en) had? OMSCHRIJF: …… ……	0	1	2	3

	NIET TIJDENS DE AFGELOPEN WEEK	ÉÉN MAAL PER WEEK	TWEEMAAL PER WEEK	DRIE – OF MEERMAALS PER WEEK
6. Hoe vaak nam u gedurende de afgelopen week geneesmiddelen in (al dan niet voorgeschreven) als hulp bij het slapen?	0	1	2	3
7. Hoe vaak had u het de afgelopen week moeilijk om wakker te blijven tijdens het autorijden, het eten of deelname aan een sociale activiteit?	0	1	2	3

	GEEN ENKEL PROBLEEM	SLECHTS EEN KLEIN PROBLEEM	ENIGSZINS EEN PROBLEEM	EEN HEEL GROOT PROBLEEM
8. In welke mate was het de afgelopen week voor u een probleem om met voldoende enthousiasme uw dagelijkse activiteiten uit te voeren?	0	1	2	3

	ZEER GOED	REDELIJK GOED	EERDER SLECHT	ZEER SLECHT
9. Hoe zou u uw globale slaapkwaliteit tijdens de afgelopen week beoordelen?	0	1	2	3

10.1. Ik heb op dit ogenblik geen kamergenoot of bedpartner (op regelmatige basis) 1☐ geen kamergenoot of bedpartner

10.2. Indien u een kamergenoot of bedpartner hebt, vraag hem/haar hoe vaak u tijdens de afgelopen week:

	NIET TIJDENS DE AFGELOPEN WEEK	ÉÉN MAAL PER WEEK	TWEEMAAL PER WEEK	DRIE – OF MEERMAALS PER WEEK
a) Luid snurkte.	0	1	2	3
b) Lange ademhalingspauzes had tijdens het slapen.	0	1	2	3
c) Trekkende of schoppende benen had tijdens het slapen.	0	1	2	3
d) Periodes van verwardheid had tijdens het slapen.	0	1	2	3
e) Een andere rusteloosheid had tijdens het slapen. OMSCHRIJF: …… ……	0	1	2	3

Sleep questionnaire (PSQI)

The following questions relate to your usual sleep habits during the past week only. Your answers should indicate the most accurate reply for the majority of days and nights in the past week. Please answer all questions

1. During the past week, when have you usually gone to bed at night? — Usual bed time: |__|__|:|__|__|
2. During the past week, how long (in minutes has it usually take you to fall asleep each night? — Number of minutes: |__|__|__|
3. During the past week, when have you usually gotten up in the morning? — Usual getting up time: |__|__|:|__|__|
4. During the past week, how many hours of actual sleep did you get at night? (this may be different than the number of hours you spend in bed.) — Hours of sleep per night |__|__|

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past week, how often have you had trouble sleeping because you

	NOT DURING THE PAST WEEKT	ONCE A WEEK	TWICE A WEEK	THREE OR MORE TIMES A WEEK
a) cannot get to sleep within 30 minutes?	0	1	2	3
b) wake up in the middle of the night or early morning?	0	1	2	3
c) have to get up to use the bathroom?	0	1	2	3
d) cannot breathe comfortably	0	1	2	3
e) cough or snore loudly?	0	1	2	3
f) feel too cold ?	0	1	2	3
g) feel too hot?	0	1	2	3
h) had bad dreams?	0	1	2	3
i) have pain?	0	1	2	3
j) other reasons(s)? Please dscribe:	0	1	2	3

	NOT DURING THE PAST WEEK	ONCE A WEEK	TWICE A WEEK	THREE OR MORE TIMES A WEEK
6. During thepast week, how often have you taken medicine (prescribed of "over the counter" to help you sleep?	0	1	2	3
7. During the past week, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?	0	1	2	3

	NOT A PROBLEM AT ALL	ONLY A VERY SLIGHT PROBLEM	SOMEWHAT OF A PROBLEM	A VERY BIG PROBLEM
8. During the past week, how much of a problem has it been for you to keep up enough enthusiasm to get things done?	0	1	2	3

	VERY GOOD	FAIRLY GOOD	FAIRLY BAD	VERY BAD
9. During the past week, how would you rate your sleep quality overall	0	1	2	3

10.1. I have a roommate or bed partner on a regular basis ☐ No roommate or bed partner

10.2. If you have a roommate or bed partner, ask him/her how often in the past week you have had

	NOT DURING THE PAST WEEK	ONCE A WEEK	TWICE A WEEK	THREE OR MORE TIMES A WEEK
a) Loud snoring.	0	1	2	3
b) Long pauses between breaths while asleep.	0	1	2	3
c) Legs twitching or jerking while you sleep.	0	1	2	3
d) episodes of disorientation of confusion during sleep.	0	1	2	3
e) Other restlessness while you sleep. Please describe	0	1	2	3

Appendix F. Code Book

Meetinstrumenten

Instrument
Intakevragenlijst
Infomatie uit EPD
QIDS-SR
MEQ
PSQI
Slaapdagboek

Intakevragenlijst

Variabelnaam	Variabellabel	Waardes
subjno	Subjectidentificatienummer (USER nummer)	
leeftijd	Leeftijd (in jaren)	
geslacht	Geslacht	0 = man 1 = vrouw
intake_sad_a	SAD criterium A (Regelmatig depressie in herfst/winter)	0 = nee 1 = ja
intake_sad_b	SAD criterium B (Somberheid klaart volledig op in lente en zomer)	0 = nee 1 = ja
intake_sad_c	SAD criterium C (Voorafgaande 2 jaar depressie in herfst/winter of LT gehad)	0 = nee 1 = ja
intake_sad_d	SAD criterium D (Vaker depressie in herfst winter dan in lente/zomer)	0 = nee 1 = ja

Elektronisch patiëntendossier (EPD)

Variabelnaam	Variabellabel	Waardes
Subjno	Subjectidentificatienummer (USER nummer)	
dsm_diagnose	DSM-V diagnose	

QIDS-SR

Variabelnaam	Variabellabel	Waardes
subjno	Subjectidentificatienummer (USER nummer)	
meetmoment	Meetmoment	0=intake 1= Extra voormeting groep 2 2 =dag 5 week 1 lichttherapie 3 =dag 5 week 2 lichttherapie 4 =dag 5 week 3 lichttherapie
qids_datum	Datum afname QIDS	
qids_sr_01	Duur tot in slaap vallen	0 = <30min 1 = tenminste 30min, < helft van de keren 2 = teminste 30min, > helft van de keren 3 = >60min, > helft van de keren
qids_sr_02	Nachtrust	0 = wordt niet wakker 1 = rusteloze, lichte slaap met enkele keren kort ontwaken 2 = Wordt tenminste 1keer wakker, slaap makkelijk weer in 3 = >1 keer ontwaken, blijf >20min wakker, > helft van de keren.
qids_sr_03	Te vroeg wakker worden	0 = meestal niet meer dan 30min voortijdig wakker 1 = > helft van de keren >30min voortijdig wakker 2 = Structureel >1 uur voortijdig wakker, val uiteindelijk weer in slaap 3 = >1 uur voortijdig wakker, val niet meer in slaap
qids_sr_04	Te veel slapen	0 = 7-8u slaap, geen dagdutjes 1 = 10u slaap in 24u, inclusief dagdutjes 2 = 12u slaap in 24u inclusief dagdutjes 3 = >12u slaap in 24u inclusief dagdutjes
qids_sr_05	Verdrietig voelen	0 = niet verdrietig 1 = verdrietig < helft van de keren 2 = verdrietig > helft van de keren 3 = bijna altijd verdrietig

qids_sr_06	Verminderde eetlust	0 = geen verandering eetlust 1 = eet minder vaak of minder veel 2 = eet veel minder, eten kost veel moeite 3 = eet gedurende 24u nauwelijks, enkel met grote moeite
qids_sr_07	Toegenomen eetlust	0 = geen verandering eetlust 1 = behoefte aan meer eten 2 = eet vaker of meer 3 = neiging tot overeten tijdens maaltijden en ertussen in
qids_sr_08	Gewichtsverlies	0 = geen verandering gewicht 1 = denk iets te zijn afgevallen 2 = 2+ kg afgevallen 3 = 5+ kg afgevallen
qids_sr_09	Gewichtstoename	0 = geen verandering gewicht 1 = denk iets te zijn aangekomen 2 = 2+ kg aangekomen 3 = 5+ kg aangekomen
qids_sr_10	Concentratie/ besluitvaardigheid	0 = ongestoord 1 = soms besluiteloos, aandacht kan afdwalen 2 = meestal besluiteloos en aandachtsproblemen 3 = Kan niet lezen door concentratieproblemen, kan minimale keuzes niet maken
qids_sr_11	Zelfbeeld	0 = zelf even waardevol als anderen 1 = ik geef mezelf vaak de schuld 2 = ik denk problemen te veroorzaken voor anderen 3 = ik denk continue aan grote en kleine zelfdefecten
qids_sr_12	Suïcidaliteit	0 = denk niet aan suïcide/ dood 1 = vraag me af of het leven nog de moeite waard is 2 = denk meerdere keren per week aan dood/ suïcide 3 = Meermaals per dag denk ik aan dood/ suïcide of heb zelfmoordplannen
qids_sr_13	Algemente interesse	0 = geen verandering in mijn interesses 1 = minder interesse in anderen/ activiteiten 2 = slechts nog zin in 1 of 2 gebruikelijke dingen

		3 = vrijwel in alles interesse verloren
qids_sr_14	Energieniveau	0 = geen verandering energieniveau 1 = sneller moe 2 = dagelijkse activiteiten kosten veel moeite 3 = geen energie voor dagelijkse activiteiten
qids_sr_15	Vertraagd voelen	0 = ik spreek, denk en beweeg zoals gebruikelijk 1 = ik denk trager of stem klinkt zachter/platter 2 = ik antwoord en denk erg traag 3 = ik kan enkel met grote moeite antwoorden op vragen
qids_sr_16	Rusteloosheid	0 = geen rusteloosheid 1 = ik ben wat onrustig, in handen wrijvend en in stoel verzittend 2 = ik heb impulsen om te bewegen en ben vrij onrustig 3 = kan soms niet stilzitten en moet rondlopen

MEQ-SA

Variabelnaam	Variabellabel	Waardes
subjno	Subjectidentificatienummer (USER nummer)	
meetmoment	Meetmoment	0=intake
meq_datum	Datum afname MEQ	
meq_01	Hoe laat zou u ongeveer opstaan, als u volledig vrij was in uw dagindeling?	5 = 05:00–06:30 u 4 = 06:30–07:45 u 3 = 07:45–09:45 u 2 = 09:45–11:00 u 1 = 11:00–12:00 u
meq_02	Hoe laat zou u ongeveer naar bed gaan als u volledig vrij was in het indelen van uw avond?	5 = 20:00–21:00 u 4 = 21:00–22:15 u 3 = 22:15–00:30 u 2 = 00:30–01:45 u 1 = 01:45–03:00 u
meq_03	Als u ’s morgens op een voor u gebruikelijke tijd op moet staan, hoe sterk afhankelijk bent u dan van een wekker?	4 = Helemaal niet afhankelijk 3 = Enigszins afhankelijk 2 = Nogal afhankelijk 1 = Erg afhankelijk

meq_04	Hoe gemakkelijk vindt u het om ’s morgens op te staan (als u niet onverwachts gewekt wordt)	1 = Erg moeilijk 2 = Nogal moeilijk 3 = Nogal gemakkelijk 4 = Erg gemakkelijk
meq_05	Hoe wakker voelt u zich ‘s morgens gedurende het eerste half uur nadat u wakker bent geworden?	1 = Helemaal niet wakker 2 = Een beetje wakker 3 = Behoorlijk wakker 4 = Klaarwakker
meq_06	Hoe hongerig voelt u zich ‘s morgens gedurende het eerste half uur nadat u wakker bent geworden?	1 = Helemaal niet hongerig 2 = Een beetje hongerig 3 = Behoorlijk hongerig 4 = Erg hongerig
meq_07	Hoe voelt u zich ‘s morgens gedurende het eerste half uur nadat u wakker bent geworden?	1 = Erg moe 2 = Behoorlijk moe 3 = Behoorlijk uitgerust 4 = Erg uitgerust
meq_08	Als u de volgende dag geen verplichtingen hebt, hoe laat zou u dan naar bed gaan in vergelijking tot uw gebruikelijk bedtijd?	4 = Zelden of nooit later 3 = Minder dan 1 uur later 2 = 1 à 2 uur later 1 = meer dan 2 uur later
meq_09	U heeft besloten om te gaan trainen. Een vriend stelt voor dit twee keer per week één uur te doen en de tijd die hem het beste past is tussen 7-8 u ‘s morgens. Als u even alleen aan uw eigen “interne klok” denkt, hoe verwacht u dan dat u zal presteren?	4 = Ik zou in goede vorm zijn 3 = Ik zou in redelijke vorm zijn 2 = Ik zou het moeilijk vinden 1 = Ik zou het erg moeilijk vinden
meq_10	Om ongeveer hoe laat bent u ’s avonds zo moe dat u wel moet gaan slapen?	5 = 20:00–21:00 u 4 = 21:00–22:15 u 3 = 22:15–00:45 u 2 = 00:45–02:00 u 1 = 02:00–03:00 u
meq_11	U wilt zo goed mogelijk presteren op een test die u geestelijk erg zal inspannen en twee uur zal duren. U bent volledig vrij in uw dagindeling. Als u even alleen aan uw eigen “interne klok” denkt, welke van de vier volgende test-tijdstippen zou u dan kiezen?	6 = 08–10 u 4 = 11–13 u 2 = 15–17 u 0 = 19–21 u
meq_12	Als u ‘s avonds om 23:00 uur naar bed zou gaan, hoe moe zou u dan zijn?	0 = Helemaal niet moe 2 = Een beetje moe 3 = Behoorlijk moe 5 = Erg moe
meq_13	Om de één of andere reden bent u enkele uren later naar bed gegaan dan voor u gebruikelijk is. De volgende ochtend bent u vrij om op te staan wanneer u wilt.	4 = Ik word op de gewone tijd wakker en slaap niet meer in 3 = Ik word op de gewone tijd wakker en doezel daarna nog wat

	Welke van de hieronder genoemde antwoorden is het beste op u van toepassing?	2 = Ik word op de gewone tijd wakker, maar slaap ook weer in 1 = Ik word later dan gewoonlijk wakker
meq_14	Gedurende één nacht moet u van 04-06 u wakker blijven om de wacht te houden. De volgende dag hebt u geen verplichtingen. Welke van de volgende keuzes zou het beste bij u passen?	1 = Zou pas naar bed gaan als mijn wacht voorbij was 2 = Zou van te voren een dutje doen en na de wacht gaan slapen 3 = Zou van te voren goed slapen en na de wacht een dutje doen 4 = Zou alleen voorafgaand aan de wacht slapen
meq_15	U moet twee uur zware lichamelijke arbeid verrichten. U bent volledig vrij in uw dagindeling. Als u even alleen aan uw eigen “interne klok” denkt, welke van de volgende tijden zou u dan kiezen?	4 = 08–10 u 3 = 11–13 u 2 = 15–17 u 1 = 19–21 u
meq_16	U heeft besloten om te gaan trainen. Een vriendin stelt voor dit twee keer per week één uur te doen en de tijd die haar het beste past is van 22-23u. Als u even alleen aan uw eigen “interne klok” denkt, hoe verwacht u dan dat u zal presteren?	4 = Ik zou in goede vorm zijn 3 = Ik zou in redelijke vorm zijn 2 = Ik zou het moeilijk vinden 1 = Ik zou het erg moeilijk vinden
meq_17	Stelt u zich voor dat u uw eigen werktijden kan kiezen en dat u een vijf-urige werkdag heeft (inclusief pauzes). Uw werk is uitdagend en uw salaris is afhankelijk van uw prestaties. Hoe laat zou u uw vijf-urige werkdag ongeveer laten beginnen?	5 = 5 uren te beginnen tussen 04–08 u 4 = 5 uren te beginnen tussen 08–09 u 3 = 5 uren te beginnen tussen 09–14 u 2 = 5 uren te beginnen tussen 14–17 u 1 = 5 uren te beginnen tussen 17–04 u
meq_18	Op ongeveer welke tijd van de dag voelt u zich over het algemeen het best?	5 = 05–08 u 4 = 08–10 u 3 = 10–17 u 2 = 17–22 u 1 = 22–05 u
meq_19	Er wordt wel eens gesproken over ochtendtypes en avondtypes. Wat voor type denkt u dat u bent?	6 = een uitgesproken ochtendtype 4 = meer een ochtendtype dan een avondtype 2 = meer een avondtype dan een ochtendtype

		1 = een uitgesproken avondtype

PSQI

Variabelnaam	Variabellabel	Waardes
subjno	Subjectidentificatienummer (USER nummer)	
meetmoment	Meetmoment	
psqi_datum	Datum afname PSQI	
psqi_01	Hoe laat ging u ’s avond meestal naar bed gedurende de afgelopen maand?	
psqi_02	Hoeveel minuten duurde het de afgelopen maand gewoonlijk elke nacht vooraleer u in slaap viel?	
psqi_03	Hoe laat stond u tijdens de afgelopen maand ’s morgens op?	
psqi_04	Aan hoeveel uren SLAAP kwam u gemiddeld per nacht tijdens de afgelopen maand?	

Slaapdagboek maandag

Variabelnaam	Variabeltabel	Waardes
Subjno	Subjectidentificatienummer	
Meetmoment	Meetmoment	W1D1 = week 1 dag 1 W2D1 = week 2 dag 1 W3D1 = week 3 dag 1
Datum	Datum afname Slaaplogboek maandag	
Tijdstip LT	Tijdstip ontvangen Licht Therapie	
Vr-za-1	Hoe laat probeerde u te gaan slapen?	
Vr-za-2	Hoe lang kostte het u om in slaap te vallen?	
Vr-za-3	Hoe laat was uw laatste moment van wakker worden?	
Vr-za-4	Hoeveel minuten was u wakker vannacht?	
Vr-za-5	Waardoor werd u wakker?	0 = Wekker 1 = Uit mezelf 2 = Anders
Vr-za-6	Hoe zou u uw slaapkwaliteit beoordelen?	0 = Erg slecht 1 = Slecht 2 = Redelijk

		3 = Goed 4 = Erg goed
Vr-za-7	Hoeveel minuten was u buiten in daglicht?	
Za-zo-1	Hoe laat probeerde u te gaan slapen?	
Za-zo-2	Hoe lang kostte het u om in slaap te vallen?	
Za-zo-3	Hoe laat was uw laatste moment van wakker worden?	
Za-zo-4	Hoeveel minuten was u wakker vannacht?	
Za-zo-5	Waardoor werd u wakker?	0 = Wekker 1 = Uit mezelf 2 = Anders
Za-zo-6	Hoe zou u uw slaapkwaliteit beoordelen?	0 = Erg slecht 1 = Slecht 2 = Redelijk 3 = Goed 4 = Erg goed
Za-zo-7	Hoeveel minuten was u buiten in daglicht?	
Zo-ma-1	Hoe laat probeerde u te gaan slapen?	
Zo-ma-2	Hoe lang kostte het u om in slaap te vallen?	
Zo-ma-3	Hoe laat was uw laatste moment van wakker worden?	
Zo-ma-4	Hoeveel minuten was u wakker vannacht?	
Zo-ma-5	Waardoor werd u wakker?	0 = Wekker 1 = Uit mezelf 2 = Anders
Zo-ma-6	Hoe zou u uw slaapkwaliteit beoordelen?	0 = Erg slecht 1 = Slecht 2 = Redelijk 3 = Goed 4 = Erg goed
Zo-ma-7	Hoeveel minuten was u buiten in daglicht?	

Slaapdagboek vrijdag

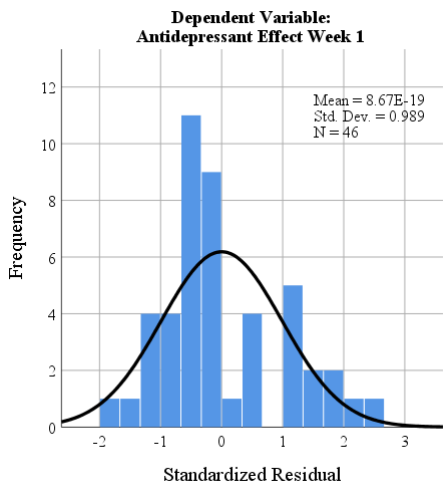
Variabelnaam	Variabeltabel	Waardes
Subjno	Subjectidentificatienummer	
Meetmoment	Meetmoment	W1D5 = week 1 dag 5 W2D5 = week 2 dag 5 W3D5 = week 3 dag 5
Datum	Datum afname Slaaplogboek vrijdag	

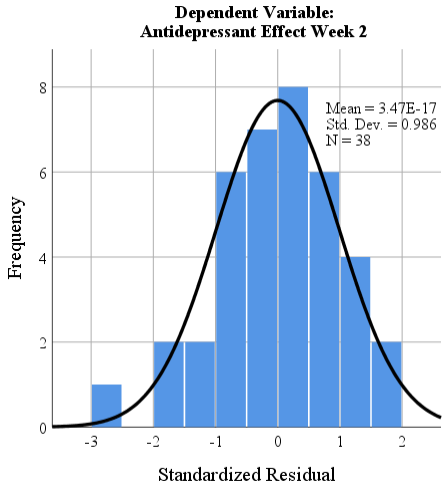
Tijdstip LT	Tijdstip ontvangen Licht Therapie	
ma-di-1	Hoe laat probeerde u te gaan slapen?	
ma-di-2	Hoe lang kostte het u om in slaap te vallen?	
ma-di-3	Hoe laat was uw laatste moment van wakker worden?	
ma-di-4	Hoeveel minuten was u wakker vannacht?	
ma-di-5	Waardoor werd u wakker?	0 = Wekker 1 = Uit mezelf 2 = Anders
ma-di-6	Hoe zou u uw slaapkwaliteit beoordelen?	0 = Erg slecht 1 = Slecht 2 = Redelijk 3 = Goed 4 = Erg goed
ma-di-7	Hoeveel minuten was u buiten in daglicht?	
di-wo-1	Hoe laat probeerde u te gaan slapen?	
di-wo-2	Hoe lang kostte het u om in slaap te vallen?	
di-wo-3	Hoe laat was uw laatste moment van wakker worden?	
di-wo-4	Hoeveel minuten was u wakker vannacht?	
di-wo-5	Waardoor werd u wakker?	0 = Wekker 1 = Uit mezelf 2 = Anders
di-wo-6	Hoe zou u uw slaapkwaliteit beoordelen?	0 = Erg slecht 1 = Slecht 2 = Redelijk 3 = Goed 4 = Erg goed
di-wo-7	Hoeveel minuten was u buiten in daglicht?	
wo-do-1	Hoe laat probeerde u te gaan slapen?	
wo-do-2	Hoe lang kostte het u om in slaap te vallen?	
wo-do-3	Hoe laat was uw laatste moment van wakker worden?	
wo-do-4	Hoeveel minuten was u wakker vannacht?	
wo-do-5	Waardoor werd u wakker?	0 = Wekker 1 = Uit mezelf 2 = Anders
wo-do-6	Hoe zou u uw slaapkwaliteit beoordelen?	0 = Erg slecht 1 = Slecht 2 = Redelijk 3 = Goed 4 = Erg goed

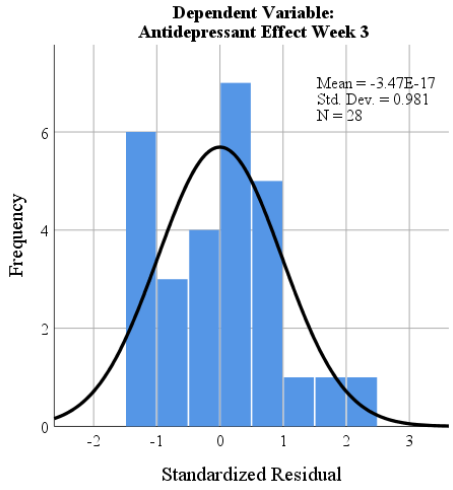
wo-do-7	Hoeveel minuten was u buiten in daglicht?	
do-vr-1	Hoe laat probeerde u te gaan slapen?	
do-vr-2	Hoe lang kostte het u om in slaap te vallen?	
do-vr-3	Hoe laat was uw laatste moment van wakker worden?	
do-vr-4	Hoeveel minuten was u wakker vannacht?	
do-vr-5	Waardoor werd u wakker?	0 = Wekker 1 = Uit mezelf 2 = Anders
do-vr-6	Hoe zou u uw slaapkwaliteit beoordelen?	0 = Erg slecht 1 = Slecht 2 = Redelijk 3 = Goed 4 = Erg goed
do-vr-7	Hoeveel minuten was u buiten in daglicht?	
sd-1a	Heeft u door de behandeling de afgelopen week het volgende ervaren? Een oncontroleerbare drang om enkele uren na de behandeling mijn slaap te hervatten	0 = Nee 1 = Ja, 1 dag 2 = Ja, 2 dagen 3 = Ja, 3 dagen 4 = Ja, 4 dagen 5 = Ja, 5 dagen 6 = Ja, 6 dagen 7 = Ja, 7 dagen
sd-1b	Heeft u door de behandeling de afgelopen week het volgende ervaren? Slapeloosheid na mijn gebruikelijke bedtijd	0 = Nee 1 = Ja, 1 nacht 2 = Ja, 2 nachten 3 = Ja, 3 nachten 4 = Ja, 4 nachten 5 = Ja, 5 nachten 6 = Ja, 6 nachten 7 = Ja, 7 nachten
sd-1c	Heeft u door de behandeling de afgelopen week het volgende ervaren? Plotseling (uren) eerder wakker geworden dan ik had verwacht en ik kon daarna niet meer in slaap vallen	0 = Nee 1 = Ja, 1 ochtend 2 = Ja, 2 ochtenden 3 = Ja, 3 ochtenden 4 = Ja, 4 ochtenden 5 = Ja, 5 ochtenden 6 = Ja, 6 ochtenden 7 = Ja, 7 ochtenden
sd-2	Hebt u de afgelopen week in ploegendiens/onregelmatige diens/nachtdienst gewerkt?	0 = Nee 1 = Ja
sd-3	Op de volgende dagen heb ik (de afgelopen week) gewerkt	0 = zondag 1 = maandag 2 = dinsdag 3 = woensdag 4 = donderdag 5 = vrijdag 6 = zaterdag

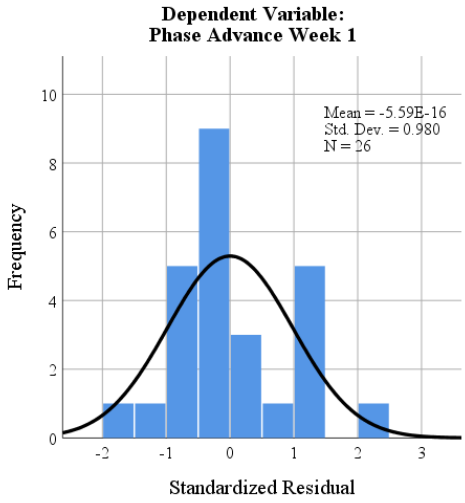
Appendix G. Histograms of Standardized Residuals of the Dependent Variables

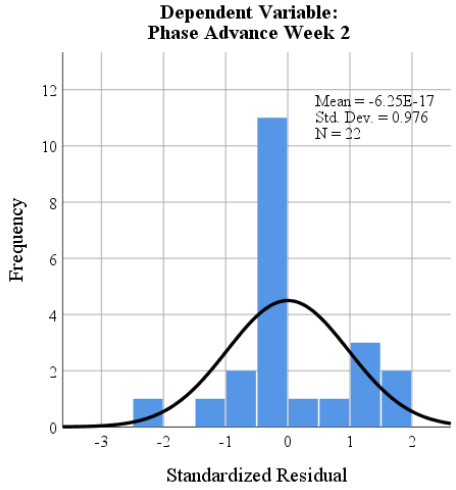
Independent variable: circadian timing of morning BLT

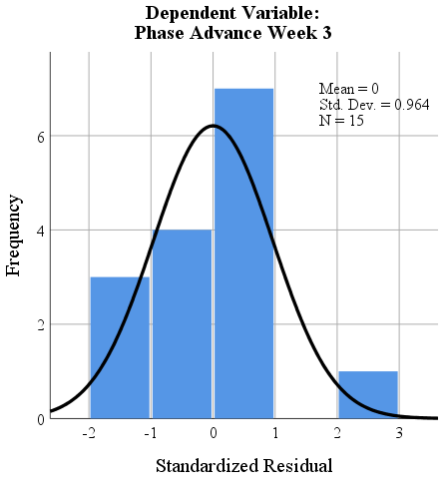






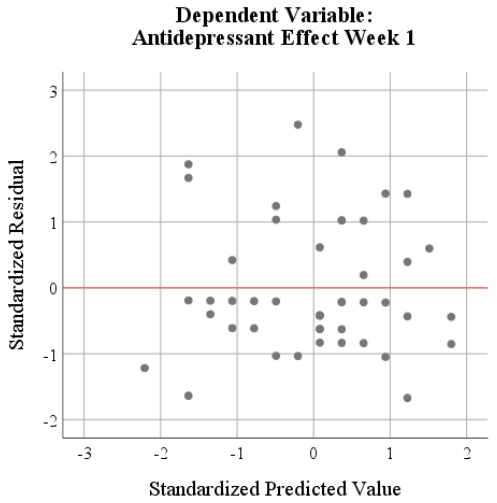


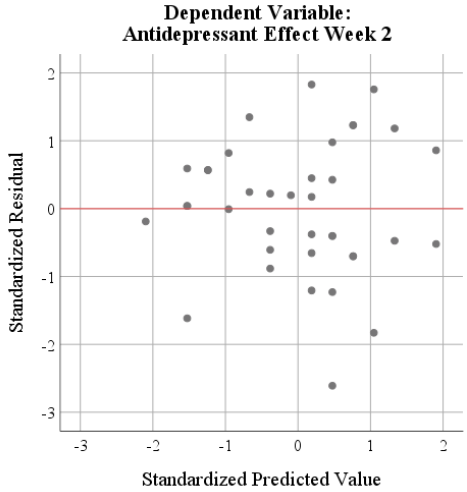


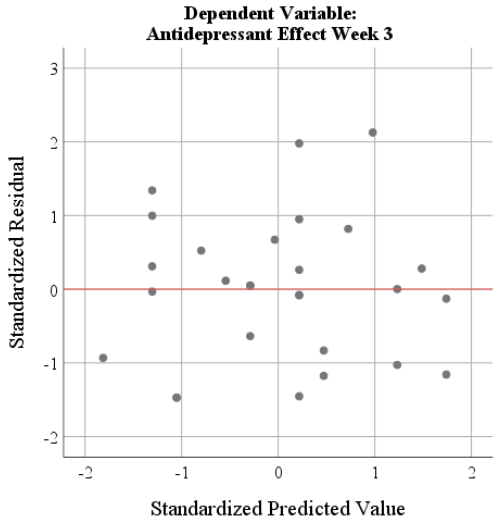


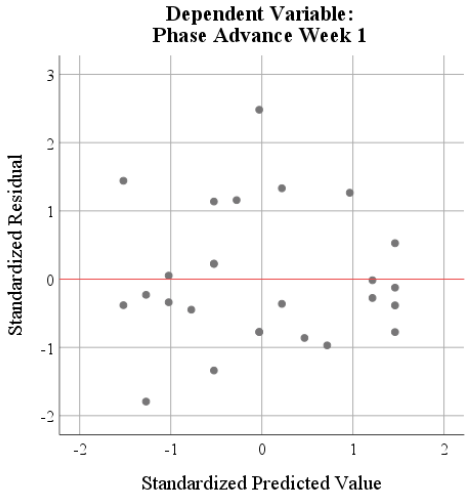
Appendix H. Scatterplots of Standardized Residuals

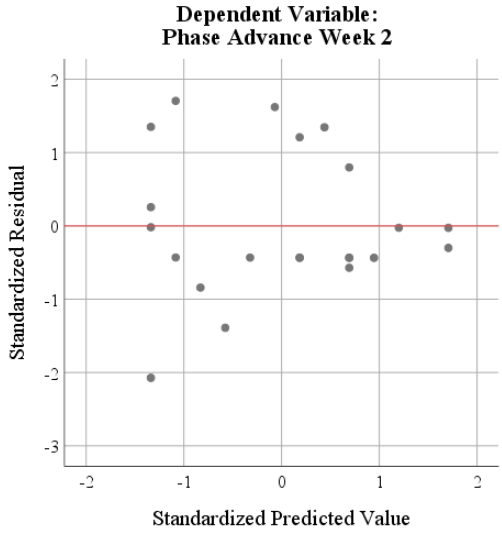
Independent variable: circadian timing of morning BLT

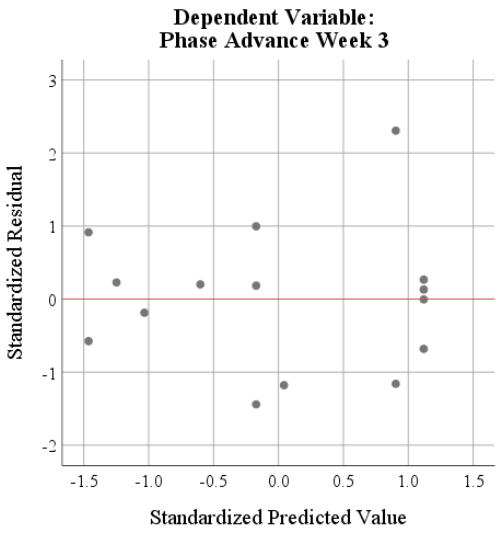












Appendix I. Visual Inspection of Associations

Figure I1

Scatterplot of the circadian timing of morning BLT and the antidepressant effect (per treatment week)

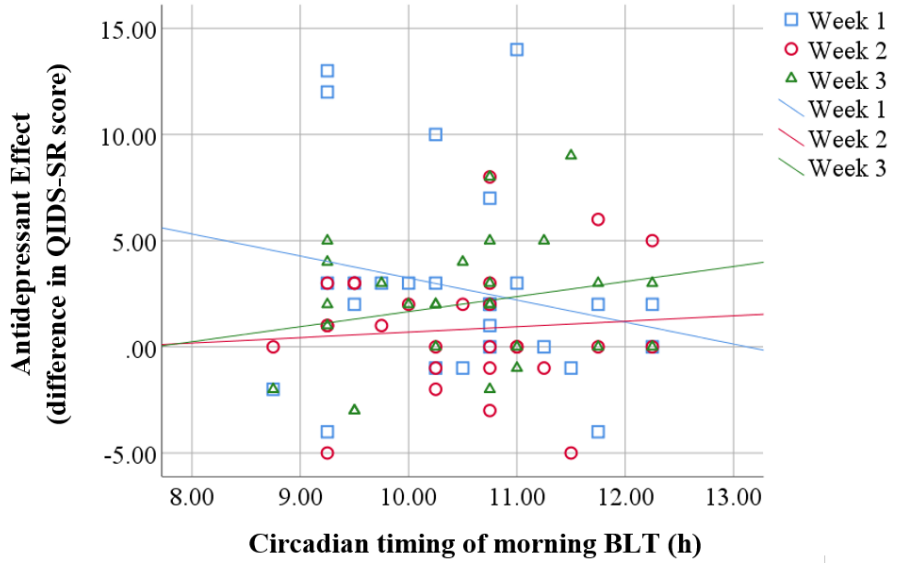


Figure I2

Scatterplot of the phase advance and the circadian timing of morning BLT (per treatment week)