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Conflicted clocks: Social jetlag, entrainment and the role of chronotype

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Chapter 6

Light interventions to decrease social jetlag

Giulia Zerbini, Thomas Kantermann, Till Roenneberg, and Martha Merrow

Abstract

Adequate and efficient sleep is essential for good health and peak performance. The circadian clock is involved in the regulation of sleep timing and efficient sleep is only possible within a certain sleep window. Due to genetic, developmental and environmental differences between individuals, a broad distribution in sleep timing is observed in populations. In contrast to the richness of circadian clock-mediated sleep timing (chronotype), school and working schedules tend to be uniform across social life. Especially late chronotypes - those who sleep late - suffer from a phenomenon called social jetlag (SJL; mismatch between the circadian/biological and social clocks). SJL has been related to several health issues, yet no intervention to decrease it has been tested so far.

If we accept that the major determinants of chronotype are genetics, age and light environment, it is obvious that active modification of chronotype is only possible by using light. Indeed, light is the most important zeitgeber for human behavioral rhythms, keeping the sleep/wake cycle synchronized (entrained) to the external light-dark cycle. Exposure to light (especially blue light) in the early biological night (evening) delays the clock, while exposure to light in the late biological night (morning) advances it. We developed two *in situ* protocols to advance sleep timing and phase of entrainment. In Study 1, evening light exposure was decreased by wearing blue-light-blocking glasses in the evening. In Study 2, morning light exposure was increased by sleeping with open curtains. Our measures were sleep timing (via sleep diaries), activity timing (via actimetry), and entrained phase (via dim-light melatonin onset; DLMO). We found that a decrease in evening light exposure was associated with an advance in sleep onset and in DLMO on workdays (36 and 32 minutes respectively). The increase in morning light exposure did not yield the same results. However, the participants who experienced a greater increase in bedroom light intensities (by sleeping with open curtains) showed the biggest advances in DLMO. In both studies, there was no significant change in SJL. More studies are warranted to determine whether SJL could be decreased by light and whether this would benefit late chronotypes in terms of health and performance.

Introduction

Sleep is a basic human need, important for health and performance. A two process model of sleep regulation suggests a juxtaposed homeostatic (sleep pressure) and circadian process (Borbély, 1982; Daan, Beersma, & Borbély, 1984). The circadian clock actively synchronizes (entrains) to the external light-dark cycle with a specific phase relationship (Duffy & Wright, 2005; Roenneberg & Merrow, 2007; Wright et al., 2013). The variation in genetic background, sex, and age together with the variation in daily light exposure leads to a distribution of entrained phases relative to the light-dark cycle (Hamet & Tremblay, 2006; Roenneberg et al., 2007a; Roenneberg, Kumar, & Merrow, 2007b; Wright et al., 2013). Chronotype is generally measured with questionnaires (e.g Munich ChronoType Questionnaire (MCTQ), Roenneberg, Wirz-Justice, & Merrow, 2003; Morningness-Eveningness Questionnaire (MEQ), Horne & Ostberg, 1976). With the MCTQ, chronotype is assessed as the midpoint of sleep on work-free days (MSF) with a correction for sleep debt accumulated on workdays (MSF_{sc}). We use the MCTQ because we can additionally obtain detailed information about sleep timing (separately for workdays and work-free days).

The substantial individual differences in sleep timing are often neglected in modern society when, for example, standardized social programs are imposed broadly, such as school opening and work times. This leads to a phenomenon named social jetlag (SJL; Wittmann, Dinich, Merrow, & Roenneberg, 2006). SJL represents the mismatch between the circadian and social clocks and is assessed as the absolute difference between the midpoint of sleep on workdays (MSW) and on work-free days (MSF). SJL is usually greater in late chronotypes, with late chronotypes typically being sleep deprived during the school/working week (waking up earlier than the clock would specify and requiring the use of an alarm clock) and sleeping longer and later on work-free days. In most cases of SJL, MSF is later than MSW.

In previous studies, SJL has been significantly associated with several health issues, such as increased nicotine addiction/smoking, alcohol consumption and obesity (Roenneberg, Allebrandt, Merrow, & Vetter, 2012; Wittmann et al., 2006). Here, we aimed to reduce SJL by using light interventions, given that light is the strongest zeitgeber for human behavioral entrainment. Our goal was to advance the sleep timing of late chronotypes and better match it to the demands of early social schedules.

Light intensity, spectral quality and the timing of exposure are utilized by the circadian clock for entrainment (Duffy & Wright, 2005). For instance, when exposed to light pulses at different times of day, humans can respond with advancing or delaying phase shifts (Khalsa, Jewett, Cajochen, & Czeisler, 2003). In particular, light exposure during the beginning of the biological night induces phase delays and light exposure during the end of the biological night induces phase advances (Khalsa et al., 2003). Concerning spectral quality, the circadian response to light is most sensitive to blue light (Brainard et al., 2001). Changing the light intensities in a home setting was shown to influence phase of entrainment (estimated via dim-light melatonin onset; DLMO), with later DLMOs associated with higher evening ambient light intensities (Burgess & Molina, 2014). Another study demonstrated that controlling

morning and evening light exposure was more important than changing sleep timing in influencing DLMO (Appleman, Figueiro, & Rea, 2013). Based on these studies, we developed two *in situ* protocols to advance phase of entrainment in late chronotypes with a relatively high SJL. In Study 1, evening blue light exposure was decreased using orange (blue light blocking) glasses. In Study 2, morning light was increased simply by keeping windows unobstructed. We hypothesized that both protocols (less evening light and more morning light) would advance sleep timing and phase of entrainment, leading to a longer sleep duration on workdays, a consequent reduction of oversleep on work-free days, and a decrease in SJL (Fig. 1). In both studies, we aimed to test the effectiveness of practical interventions in shifting sleep timing and phase of entrainment with the aim of a direct applicability of our findings in real life conditions.

We found that wearing blue-light-blocking glasses in the evening was effective in advancing sleep timing (on workdays) and phase of entrainment (DLMO), while sleeping with open curtains did not yield similar results. However, the strength of the intervention (amount of increase in morning bedroom light intensities) was correlated with the degree of shift in DLMO in the expected direction (more light was associated with a greater advance).

Figure 1. Decreasing social jetlag (SJL) with light.
The bars represent sleep (red bars on workdays and green bars on work-free days). The vertical black lines represent the midpoint of sleep on workdays (MSW) and on work-free days (MSF). SJL is calculated as the absolute difference between MSW and MSF. The two light interventions to decrease SJL involve wearing blue-light-blocking glasses in the evening (A) and sleeping with open curtains (B). Both interventions are expected to advance sleep timing and phase of entrainment, leading to a reduction of sleep debt accumulated on workdays and, as a consequence, also a reduction of oversleep on work-free days. This should result in a decrease of SJL via a better alignment of MSW and MSF.

Methods

Study 1 – evening (blue) light

Participants

The study was run in February 2015 in Groningen (53°13′ N / 6°33′ E), The Netherlands. Participants were recruited via flyer and online advertisement. A total of 40 participants (24 females) were selected for the study, and 38 (23 females) between the ages of 19 and 47 (mean age 23.7 ± SD 5.5) completed it. Participants were generally healthy, had no sleep complaints, and they did not make use of any medication. Participants had a regular working schedule (at least 4 working days per week), had not performed shift work during the past 5 years, and had not travelled across more than 2 time zones during the month prior to the study. Females were selected only if they made use of hormonal contraceptives (to avoid possible fluctuations in melatonin levels depending on the phase of the menstrual cycle; Lee Barron, 2007). Participants had at least 1.5 hours of SJL assessed via the Munich Chronotype Questionnaire (MCTQ; Roenneberg et al., 2003) as the absolute difference between the midpoint of sleep on work-free days (MSF) and the midpoint of sleep on workdays (MSW) (Wittmann et al., 2006).

Protocol

The study lasted 4 weeks (from 02.02.2015 to 01.03.2015). The participants were randomly assigned to one of two groups: the control group and the intervention group. The groups were matched for age, sex, chronotype (the sleep corrected midpoint of sleep on work-free days; MSF_{sc}) and SJL.

After two weeks of baseline, participants wore a special pair of glasses every evening for the remaining two weeks of the study. The control group wore glasses with clear lenses (no filter of blue light between 400-500 nm, general decrease of light intensity: 8%; for more details see Fig. S1 in the Supplementary Information). The intervention group wore glasses with blue-light-blocking lenses (89-99,9% filter of blue light between 400-500 nm, general decrease of light intensity: 50%; for more details see Fig. S2 in the Supplemental Information). The participants started wearing the glasses 9 hours before their chronotype (MSF_{sc}) until they turned the lights off to sleep. In this way, we aimed to apply the intervention at the same internal time (internal phase) for all participants.

Study 2 - morning (natural) light

Participants

The study was conducted in March 2016 in Groningen (53°13′ N / 6°33′ E), The Netherlands. Participants were recruited via flyers, online advertisements, and internal posting at the University of Groningen. The same inclusion and exclusion criteria (general health, regular working schedule, no shiftwork or travelling across time zones) were applied to select the participants as for Study 1. In addition, only people who habitually slept with dark closed curtains could sign up for the study. The latest 40 chronotypes of the eligible applicants (22

females, mean age 22.6 ± SD 3.1, range 18-35) were selected for the study. 38 participants (20 females, mean age 22.8 ± SD 3.1, range 19-35) completed the study.

Protocol

The study lasted 30 days (from 26.02.16 to 26.03.16). Participants were randomly assigned to the control or the intervention group. The two groups were matched for sex, age, chronotype, and SJL. The control group slept with curtains closed throughout the protocol. The intervention group slept with curtains closed for 10 days (baseline), then for 14 days with curtains open (intervention weeks), and again with curtains closed for 7 days (wash-out week). After baseline and after the intervention weeks the participants filled in the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) to assess whether sleeping with open curtains influenced subjective sleep quality. The two protocols are shown in Figure 2.

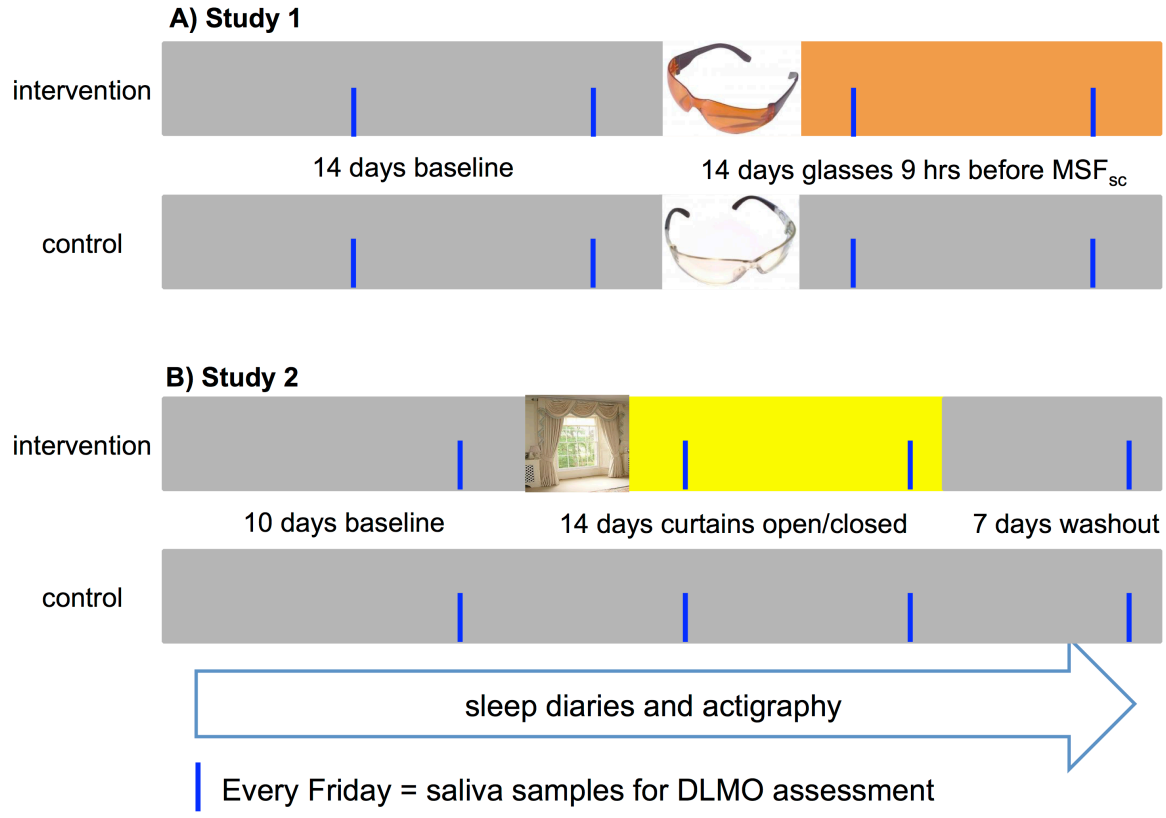

Figure 2. Experimental design.

A) Protocol used in Study 1. After 2 weeks of baseline (grey blocks), the intervention group started wearing the orange (blue-light-blocking) glasses and the control group the glasses with clear lenses for 2 weeks. B) Protocol used in Study 2. After 10 days of baseline (grey blocks), the intervention group slept with bedroom curtains open for 2 weeks and after that with bedroom curtains closed for 1 week. The control group slept with bedroom curtains closed throughout the study.

In both studies, participants collected saliva samples every Friday of the protocol (4 times), filled in a sleep diary, and wore continuously an actiwatch (for light and activity measurements). The evenings of saliva sample collection are indicated with vertical blue lines.

Study 1 and 2

Sleep, activity, and light assessment

During both protocols, the participants filled in a daily sleep diary and continuously wore an actiwatch (Study 1: Daqtometer Version 2.3, Daxtix GbR, Suettorf, DE; Study 2: MotionWatch 8, CamNtech, Cambridge, UK). The actiwatches recorded both activity and light intensity levels. Actigraphy data were analyzed with ChronoSapiens (version 9). In Study 2, participants also used a light sensor (HOBO pendant temperature/light 64K data logger, Onset, Bourne, MA, US) in the bedroom to assess light intensities throughout the study.

Circadian phase assessment (DLMO)

Circadian phase was estimated by assessing dim-light melatonin onset (DLMO) from saliva samples. The participants collected 7-hourly saliva samples every Friday evening (if Friday was not possible, either Thursday or Saturday were allowed for the saliva sample collection). The saliva sample collection was individually timed, starting 5 hours before and finishing 1 hour after habitual sleep onset (weighted average sleep onset on workdays and on work-free days, based on the participants' answers to the MCTQ). The saliva sample collection took place at the participants' home. Participants were requested to dim their home lighting as much as possible, and to start wearing a pair of blue-light blocking glasses half an hour before the collection of the first sample until the collection of the last sample. During each evening of saliva samples collection, the use of toothpaste and the ingestion of coffee, tea, alcohol, chocolate, banana, and food with artificial additives were not allowed. The saliva samples were collected using Salivettes (Sarstedt, Nümbrecht, DE). The samples were kept in the fridge and sent per mail to the lab within 3 days. Upon arrival, the samples were frozen at –80 °C and subsequently analyzed using direct saliva melatonin radioimmunoassay (RIA) test kits (Bühlmann, Schönenbuch, CH). DLMO was calculated by linear interpolation between the time points before and after melatonin concentrations crossed and stayed above the threshold of 3 pg/mL. The lower limit detection of the kit was below 0.5 pg/mL. In study 1, the intra-assay variability was 19.81% (low melatonin) and 22.13% (high melatonin), while the inter-assay variability was 14.67% (low melatonin) and 16.54% (high melatonin). In study 2, the intra-assay variability was 12.60% (low melatonin) and 16.18% (high melatonin), while the inter-assay variability was 14.72% (low melatonin) and 13.25% (high melatonin).

Statistical analysis

Statistical analyses were done using R software (R version 3.3.0; The R Core team, 2013). Data about sleep timing, activity and DLMO were analyzed with a mixed within-between model with simple planned comparisons (to baseline). A 2 (group: control vs intervention) x 3 (time: baseline vs first intervention week vs second intervention week) design was used for the analyses in Study 1. A 2 (group: control vs intervention) x 4 (time: baseline vs first intervention week vs second intervention week vs wash-out week) design was used for the analyses in Study 2. In Study 1, morning light (from 6:00 h till 12:00h) was analyzed as a covariate to control for the advancing effects that also morning light potentially has on sleep and phase of entrainment. In Study 2, evening light (from 18:00 till 0:00) was analyzed as a

covariate to control for the delaying effects that evening light potentially has on sleep and phase of entrainment.

If the interaction effect between group and time was significant, the change in the variables of interest during the first intervention week and the second intervention week (and the wash-out week in Study 2) relative to baseline was analyzed comparing the two groups (control vs intervention) with one-tailed independent t tests (Bonferroni correction was applied for multiple comparisons). In addition, in Study 2 the changes in bedroom light intensities and in sleep quality (PSQI) between baseline and during/after the intervention were compared between the two groups with a Mann-Whitney-Wilcoxon test.

The study was conducted according to the principles of the Medical Research Involving Human Subjects Act (WMO, 2012), and the Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil, October 2013). The Medical Ethical Committee of the University Medical Center Groningen approved both studies. The participants signed a written informed consent and received financial compensation for taking part in the studies.

Results

Study 1 – evening (blue) light

The demographics of the participants are reported in Table 1. The two groups had the same ratio of female and male participants. Independent t tests were run to confirm that control and intervention groups did not differ at baseline in terms of age, chronotype, and SJL (age: $t(36) = -0.116$, $p > .05$; chronotype: $t(36) = -1.312$, $p > .05$; SJL: $t(36) = -0.334$, $p > .05$).

In Figure 3 the light profiles for the two groups during baseline, and during first and second intervention weeks are shown. Overall, participants were exposed to comparable light levels, and therefore any change observed in the variables of interest is likely to be related to wearing the blue-light-blocking glasses and not to differences in light exposure between groups and across the protocol.

The analysis of the variables assessed with the daily sleep diaries revealed significant changes in sleep on workdays but not on work-free days. In all analyses morning light (between 6:00 h and 12:00 h) was analyzed as a covariate. In particular, we found a significant interaction effect between group and time on sleep onset on workdays ($F_{2,39.14} = 3.653$, $p = 0.0351$), indicating differences between the control and the intervention groups across the protocol. To explore in which weeks of the protocol the two groups differed, we compared the change in sleep onset on workdays during the first and the second intervention week (relative to baseline) between the groups (Fig. 4). The intervention group showed an advance in the sleep onset on workdays (on average 36 minutes) during the first intervention week relative to baseline. This advance was significant compared to the control group ($t(36) = -2.606$, $p = 0.0133$). The effect size was large (eta squared = 0.16) according to Cohen's guidelines (0.01

= small effect; 0.06 = medium effect; 0.14 = large effect). Although the intervention group showed an earlier sleep onset also during the second intervention week relative to baseline (on average 18 minutes), the effect was not significant anymore when compared to the control group ($t(35) = -1.136$, $p > .05$).

Table 1. Demographics of 38 (23 females) participants (Study 1) randomly assigned to the control and the intervention group (data from the Munich ChronoType Questionnaire).

	Control group		Intervention group	
Parameter	Average (SD)	Range	Average (SD)	Range
Age	23.63 (7.00)	19 - 47	23.84 (3.72)	19 - 33
Chronotype (MSF_{sc}, h)	5.02 (1.04)	3.17 - 7.20	5.49 (1.15)	3.51 - 8.40
Social Jetlag (h)	2.07 (0.51)	1.46 - 3.46	2.12 (0.47)	1.58 - 3.46
Sleep onset on workdays (h)	-0.29 (0.84)	-1.58 - 1.25	-0.13 (1.14)	-1.83 - 2.67
Sleep end on workdays (h)	7.19 (0.80)	5.75 - 8.50	7.62 (1.21)	5.17 - 9.42
Sleep duration on workdays (h)	7.48 (0.87)	5.17 - 9.42	7.75 (0.88)	5.25 - 9.33
Sleep onset on work-free days (h)	1.05 (1.09)	-1.08 - 3.25	1.45 (1.25)	-0.33 - 4.17
Sleep end on work-free days (h)	9.97 (0.92)	8.00 - 12.00	10.28 (1.28)	8.25 - 13.00
Sleep duration on work-free days (h)	8.92 (0.67)	7.42 - 10.08	8.82 (0.90)	7.17 - 10.5

The two groups did not significantly differ in relation to their demographic and sleep characteristics at baseline. Data concerning chronotype, sleep onset and sleep end refer to external clock time and are reported in decimals (clock times before midnight are expressed with negative numbers).

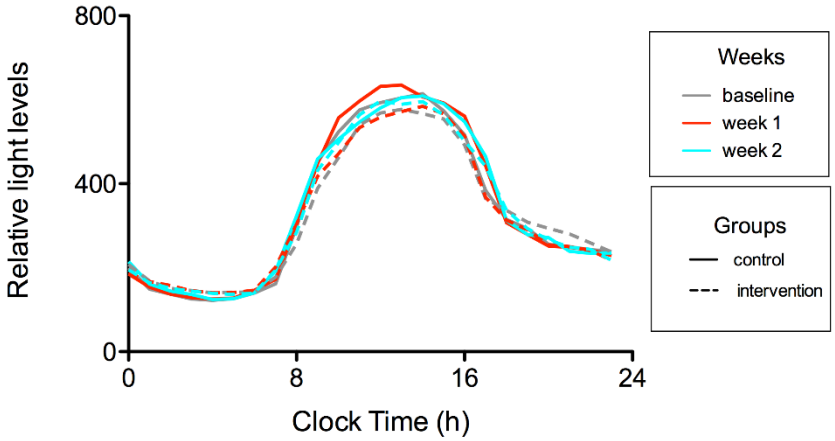

Figure 3. Light profiles of the control and intervention groups across the weeks of the protocol.
The average light intensities (relative light levels) in bins of 1 hour were calculated during the two weeks of baseline (grey), the first (red) and second (light blue) intervention week, separately for the control (solid line) and intervention (dashed line) groups. The data do not show evident differences in light exposure between the groups across the weeks of the protocol.

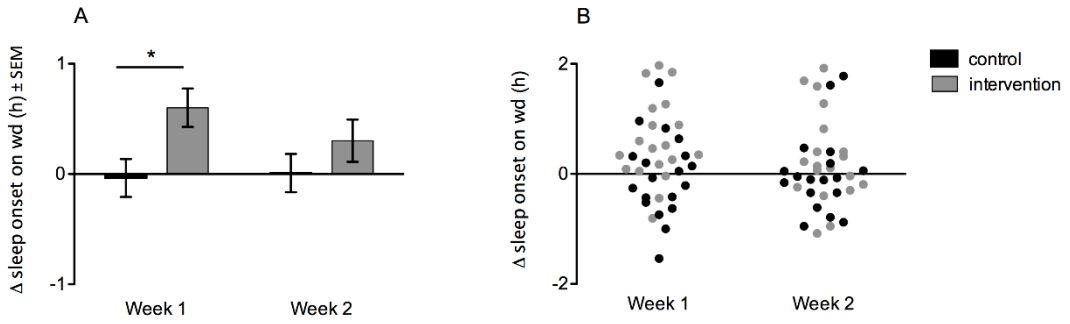

Figure 4. Shift in sleep onset on workdays relative to baseline.
Both group averages with standard error of the mean (A) and individual data points (B) are plotted separately for the control (black) and the intervention (grey) groups. The changes in sleep onset during the first and second intervention weeks are plotted relative to baseline. Positive values represent phase advances and negative values phase delays. During the first intervention week (relative to baseline), the intervention group significantly advanced the sleep onset on workdays (on average 36 minutes) compared to the control group (*p < .05 with Bonferroni correction).

There was a trend for an interaction effect between group and time on DLMO ($F_{2,25.447}$ = 3.001, p = 0.0676). As for sleep onset on workdays, we compared the shift in DLMO during first and second intervention week (relative to baseline) between the two groups (Fig. 5). Compared to the control group, the intervention group showed a significant advance in DLMO (on average 32 minutes) during the first intervention week (t (24) = -2.402, p = 0.0244), but not during the second intervention week (t (22) = -0.388, p > .05). As for sleep onset, the effect size during the first intervention week was large (eta squared = 0.22).

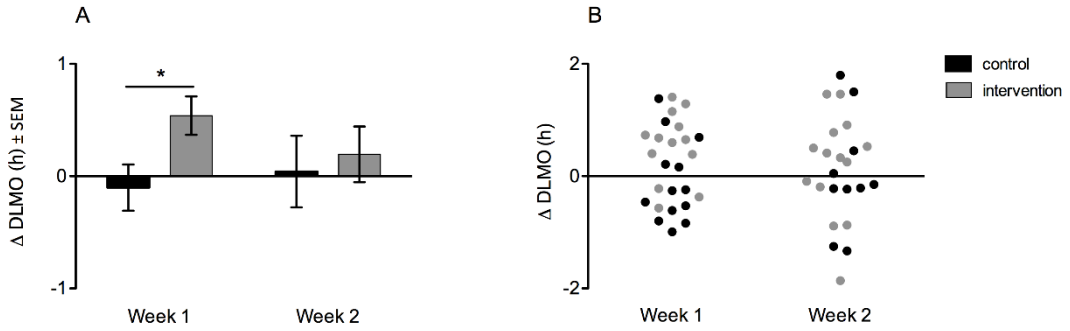

Figure 5. Shift in dim-light melatonin onset (DLMO) relative to baseline.
Both group averages with standard error of the mean (A) and individual data points (B) are plotted separately for the control (black) and the intervention (grey) groups. The changes in DLMO during the first and second intervention weeks are plotted relative to baseline. Positive values represent phase advances and negative values phase delays. During the first intervention week (relative to baseline), the intervention group significantly advanced DLMO (on average 32 minutes) compared to the control group (*p < .05 with Bonferroni correction).

We did not find any significant interaction effect for sleep end and sleep duration on workdays (sleep end: $F_{2,42.23} = 0.669$, $p > .05$; sleep duration: $F_{2,27.11} = 1.049$, $p > .05$). Still, there was a trend indicating that the intervention group slept longer (on average 17 minutes) compared to the control group during the first intervention week relative to baseline ($t(36) = 1.873$, $p = 0.0692$). SJL did not significantly change between groups and across the protocol ($F_{2,26.79} = 0.689$, $p >. 05$). Finally, center of gravity (a phase marker that can be derived from actigraphy data) also did not significantly change both on workdays and on work-free days (workdays: $F_{2,32.70} = 0.221$, $p > .05$; work-free days: $F_{2,153.69} = 0.802$, $p > .05$).

Study 2 - morning (natural) light

The demographics of the participants are reported in Table 2. In the control group there were 11 females and 9 males, while in the intervention group there were 9 females and 9 males (2 dropouts in the intervention group). Independent t tests were run to confirm that control and intervention groups did not differ at baseline in terms of age, chronotype, and SJL (age: $t(36) = -0.130$, $p > .05$; chronotype: $t(36) = -1.076$, $p > .05$; SJL: $t(36) = 0.047$, $p > .05$).

Table 2. Demographics of 38 (20 females) participants (Study 2) randomly assigned to the control and the intervention group (data from the Munich ChronoType Questionnaire).

	Control group		Intervention group	
Parameter	Average (SD)	Range	Average (SD)	Range
Age	22.70 (3.45)	19 - 35	22.83 (2.81)	19 – 29
Chronotype (MSF_{sc}, h)	5.37 (0.53)	4.70 – 6.40	5.59 (0.73)	4.71 – 7.80
Social Jetlag (h)	1.67 (0.66)	0.63 – 2.96	1.66 (0.67)	0.71 – 2.92
Sleep onset on workdays (h)	-0.21 (0.62)	-1.42 – 0.71	0.25 (0.68)	-0.92 – 1.75
Sleep end on workdays (h)	8.00 (0.86)	7.00 – 10.00	8.20 (0.55)	7.50 – 9.00
Sleep duration on workdays (h)	8.21 (0.84)	6.29 – 9.75	7.95 (0.71)	7.15 – 9.92
Sleep onset on work-free days (h)	1.22 (0.55)	0.50 – 2.30	1.51 (0.91)	0.08 – 4.00
Sleep end on work-free days (h)	9.91 (0.83)	9.00 – 12.00	10.26 (0.90)	9.00 – 12.50
Sleep duration on work-free days (h)	8.69 (0.83)	7.33 – 10.50	8.76 (0.72)	7.25 – 9.98

The two groups did not significantly differ in relation to their demographic and sleep characteristics at baseline. Data concerning chronotype, sleep onset and sleep end refer to external clock time and are reported in decimals (clock times before midnight are expressed with negative numbers).

We first compared the light intensities in the bedrooms during the intervention weeks (relative to baseline) between the two groups. Sleeping with open curtains significantly increased the morning light levels (first 2 hours after dawn) in the bedrooms of the intervention group compared to the control group ($U = 42$, $z = -3.664$, $p = 0.0001$; Fig. 6). The intervention did not negatively affect subjective sleep quality ($U = 106.5$, $z = 0.420$, $p > .05$).

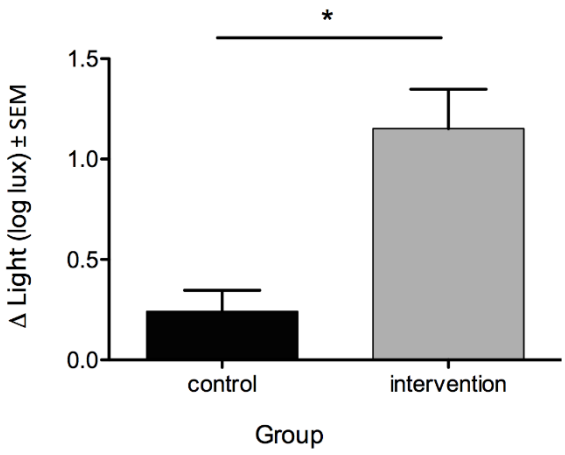

Figure 6. Change in bedroom light intensities relative to baseline.
The bars represent the average light intensities with standard error of the mean (log lux) recorded in the bedrooms during the intervention weeks relative to baseline for the control (black) and the intervention (grey) groups. Light intensities during the 2 hours after dawn are plotted. During the intervention weeks, for the participants who slept with open curtains (intervention group), a significant increase in morning bedroom light intensities was observed as compared to the control group. (* $p < .05$).

Although the intervention was effective in increasing the morning bedroom light intensity, the two groups did not differ in terms of morning light exposure (between 6:00 h and 12:00 h) across the weeks ($F_{3,34.036} = 1.208$, $p > .05$; Fig. 7). Similarly, we did not find any significant change between groups in all the variables assessed with the sleep diaries and actigraphy both on workdays and on work-free days. SJL and DLMO also did not significantly change between groups across the study (SJL: $F_{3,59.736} = 1.991$, $p > .05$; DLMO: $F_{3,53.016} = 0.856$, $p > .05$). However, the interaction effect between the change in bedroom light intensities and time (week of protocol) on DLMO was significant ($F_{3,37.929} = 3.2410$, $p = 0.0326$). The shift in DLMO during the first intervention week (relative to baseline) was significantly correlated to the change in bedroom light intensity in the intervention group ($b = 0.832$, $t(13) = 2.711$, $p = 0.0178$, $R^2 = 0.36$; Fig. 8A). In other words, the strength of the intervention (increase in morning bedroom light intensity) was associated with the change in DLMO, with greater advances in the participants whose bedrooms received more morning light during the intervention. A similar correlation was found during the second intervention week, but this was not significant ($b = 0.557$, $t(13) = 1.635$, $p = 0.126$; Fig. 8B).

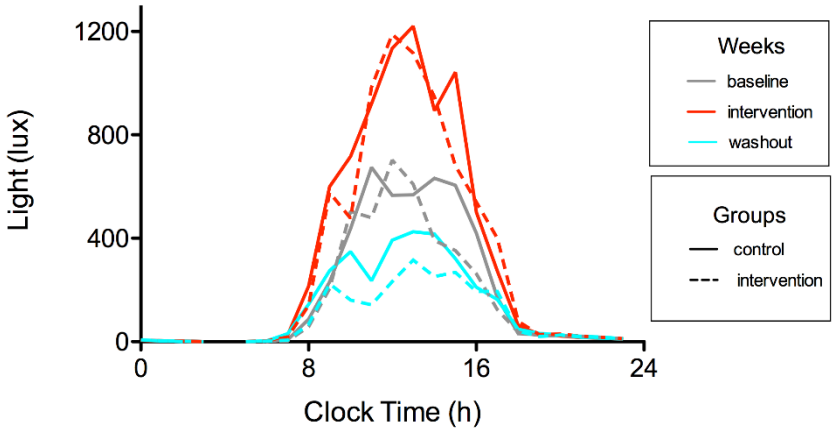

Figure 7. Light profiles of the control and intervention groups across the weeks of the protocol.
The average light intensities (lux) in bins of 1 hour were calculated during the baseline (grey), the two intervention weeks (red), and the washout (light blue), separately for the control (solid line) and intervention (dashed line) groups. The data do not show evident differences in light exposure between the groups. Both groups were exposed to more light throughout the day during the intervention weeks.

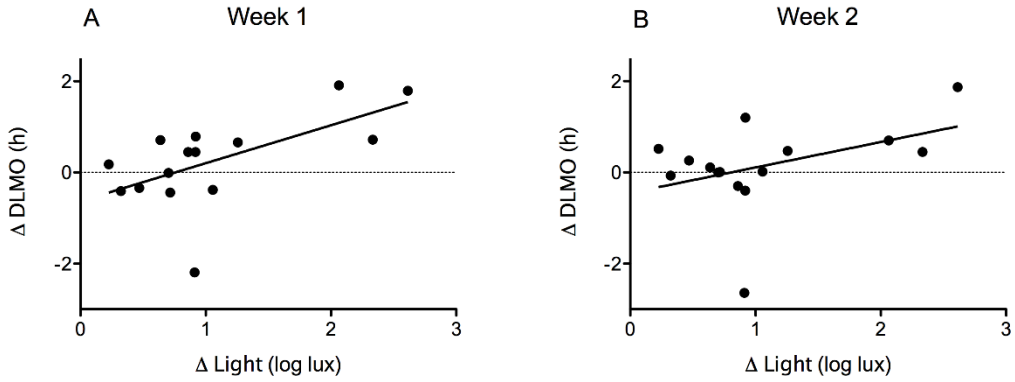

Figure 8. Correlation between change in dim-light melatonin onset (DLMO) and in bedroom light intensities.
The correlation between the shift in DLMO and the change in morning bedroom light intensities during the first (A) and the second (B) intervention weeks relative to baseline is plotted for the intervention group only. There was a positive significant (only during the first intervention week) correlation, indicating that the participants who experienced a greater increase in morning bedroom light intensities showed a greater advance (positive values) in their DLMO ($p < .05$, $R^2 = 0.36$).

Discussion

We used the timing of light interventions with the aim of modifying sleep timing and phase of entrainment. Our goal was to develop protocols to reduce SJL. Wearing blue-light-blocking glasses in the evening was effective in advancing both sleep timing (on workdays) and phase

of entrainment (estimated via DLMO, measured only on workdays). In contrast, the intervention involving sleeping with open curtains did not significantly change the same parameters. In both conditions, a reduction of SJL was not observed. The most obvious explanation for this is that the significant changes in sleep timing were observed only on workdays (Study 1). With no appreciable change on work-free days, the SJL would actually increase rather than decrease.

While the negative effects of evening (blue) light exposure on sleep timing and alertness have been widely described (Chang, Aeschbach, Duffy, & Czeisler, 2015; Chellappa et al., 2013; Wahnschaffe et al., 2013; Wood, Rea, Plitnick, & Figueiro, 2013), little research has been done on interventions that decrease evening light exposure. Wearing blue-light-blocking glasses has been shown to significantly reduce both the suppression of melatonin by light and subjective alertness before bedtime (Sasseville, Paquet, Sevigny, & Hebert, 2006; van der Lely et al., 2015). To the best of our knowledge, this is the first study showing that wearing blue-light-blocking glasses in the evening is related to an advance in sleep onset and DLMO (on workdays). Both have large effect sizes.
Surprisingly, the effect was not maintained during the second intervention week. An adaptation to the new light regime and therefore a decrease in responsiveness to the intervention could explain the lack of a sustained effect related to wearing the orange glasses. Continuously wearing orange contact lenses for two weeks was found to decrease the sensitivity to light (reduced melatonin suppression; Giménez, Beersma, Bollen, van der Linden, & Gordijn, 2014). Our participants did not wear the blue-light-blocking glasses continuously, rather only in the evening. A study where participants wore glasses with yellow-tinted lenses for 8 hours a day found no evidence of adaptation in terms of color perception, suggesting that the sensitivity of the visual photoreceptors quickly renormalized once the glasses were removed (Tregillus, Werner, & Webster, 2016). Likely, the circadian system becomes less sensitive during reduced exposure to light but normalizes with increased light levels. We also cannot exclude a more trivial explanation for this finding, such as a reduction in compliance during the second intervention week. Although we have no indication for this, there was no sensor on the glasses to objectively measure when they were worn.

Study 2 did not show a significant change in sleep timing or in entrained phase following the light intervention (increased morning light). The beneficial effects of morning light in relation to sleep and depressive disorders have been described (Rosenthal et al., 1990; J. S. Terman, Terman, Lo, & Cooper, 2001), but there is a lack of (field) studies on the effects of morning light on the sleep-wake cycle in healthy individuals. A study run during winter in the Antarctic found that an hour of morning bright light advanced both sleep and melatonin rhythms (Corbett, Middleton, & Arendt, 2012). In our experiment, the light could not be described as ‘bright’; the participants who slept with open curtains were in fact not directly exposed to a light source. However, they received earlier light in their bedrooms during the intervention since twilight occurred earlier than their usual (baseline workdays) wake-up time (twilight time: 6:15 h; average wake-up time: 8:15 h). Similar to our findings, studies investigating the effects of artificial dawn on sleep have not found significant advances in sleep timing or DLMO (Giménez et al., 2010; Tonetti et al., 2015).

Additionally, there was great variation in the amount of increase of morning bedroom light during the intervention. Interestingly, the participants who experienced a larger increase in morning bedroom light levels experienced a larger advance in their DLMO. This significant correlation supports the idea that a stronger intervention would lead to advancing circadian phase. An alternative explanation is that there is heterogeneity in which individuals respond to light. This has been already described in some studies (Dijk et al., 2012; Santhi et al., 2011). Whether these individual differences in response to light are more pronounced in the morning compared to the evening needs further elucidation. Another point is that our study occurred in March when photoperiod changes rapidly (advance in dawn of 1 hour across the month) in The Netherlands. There is evidence that humans track dawn and advance their sleep timing especially in March (Kantermann, Juda, Merrow, & Roenneberg, 2007). This means that observing an additional advance in the intervention group could have been difficult. We also did not restrict our participants' behavior (e.g. light exposure in the evening), but it was shown that the advancing effects of morning light are counteracted by evening light exposure (Burgess, 2012).
Finally, we did not assess subjective parameters such as sleep inertia after waking in our study. Interestingly, Giménez and colleagues found that using a wake-up lamp (artificial dawn) decreased sleep inertia, which suggests that sleeping with open curtains could have the same beneficial effect (Giménez et al., 2010).

Based on the tools used in this study, the most effective way to advance sleep timing and phase of entrainment in late chronotypes would probably involve a combination of increased morning light exposure and decreased evening light exposure (Appleman et al., 2013). Alternatively, studies investigating individual differences in response to light at different times of day could determine whether for some individuals or chronotypes a light intervention in the morning is more effective than in the evening and whether for others the opposite is true.

Future studies should also investigate more long-term effects of such interventions to explore how the circadian system adapts to new light regimes and whether late chronotypes could find a stable, earlier phase of entrainment. Similar studies should be also repeated in participants suffering from extreme SJL to assess whether SJL can be decreased with light and whether this would lead to better health outcomes.

Acknowledgments

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Supplementary Information

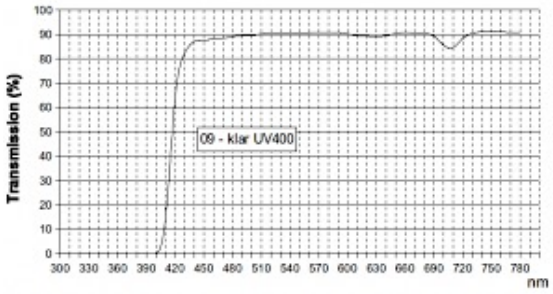

Figure S1. Transmission curve of the glasses with clear lenses

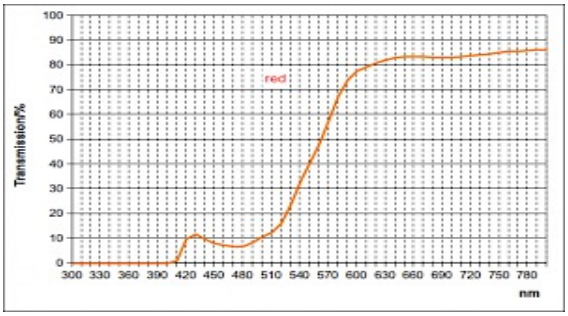

Figure S2. Transmission curve of the glasses with orange (blue-light-blocking) lenses