

**Title:** The acute effects of sleep restriction therapy for insomnia on circadian timing and vigilance

**Running head:** The effects of SRT on circadian timing and vigilance

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## Abstract

Sleep restriction therapy (SRT) has been shown to improve insomnia symptoms by restricting sleep opportunity. Curtailment of time in bed affects the duration and consolidation of sleep, but also its timing. While recent work suggests that people with insomnia are characterised by misalignment between circadian and behavioural timing of sleep, no study has investigated if SRT modifies this relationship. The primary aim of this study was to examine change in phase angle after two weeks of SRT. As a secondary aim, we also sought to assess the effect of SRT on psychomotor vigilance.

Following a one-week baseline phase, participants implemented SRT for two consecutive weeks. Phase angle was derived from the difference between the decimal clock time of dim light melatonin onset (DLMO) and attempted sleep time. Secondary outcomes included vigilance (assessed via hourly measurement during the DLMO laboratory protocol), sleep continuity (assessed via sleep diary and actigraphy), and insomnia severity.

Eighteen participants meeting insomnia criteria (mean age=37.06±8.99) took part in the study. In line with previous research, participants showed robust improvements in subjective and objective sleep continuity, as well as reductions in insomnia severity. The primary outcome (phase angle) was measurable in 15 participants and revealed an increase of 34.8min (~0.58hrs; 95%CI=0.01-1.15) from baseline to post-treatment (2.27±0.94hrs vs 2.85±1.25hrs). DLMO remained relatively stable (20:49hr vs 21:01hr), while attempted sleep was 46.8min later (~0.78hrs; 95%CI=0.41-1.15; 23:05hr vs 23:52hr). With respect to psychomotor vigilance, reaction time was delayed (by 52.71ms, 95%CI=34.44-70.97) and number of lapses increased (by 5.84, 95% CI=3.93-7.75) following SRT.

We show that SRT increases phase angle during treatment, principally by delaying the timing of sleep attempt. Future studies are needed to test if an increase in phase angle is linked to clinical improvement. Finally, reduction in vigilance following SRT appears to be of similar

magnitude to normal sleepers undergoing experimental sleep restriction, reinforcing the importance of appropriate safety advice during implementation.

**Keywords:** Sleep restriction, insomnia, dim light melatonin onset, side effects, vigilance, circadian phase

## Introduction

While insomnia is not considered a circadian rhythm disorder per se, research indicates that it may be characterized by alterations in the alignment between the circadian system and sleep-wake behavior. For example, phase angle between dim light melatonin onset (DLMO) and attempted sleep appears to be shorter in patients with insomnia. Good sleepers went to bed around 3hrs 10min after DLMO, while people with insomnia went to bed 2hrs 13min after DLMO (Flynn-Evans et al., 2017). Additionally, shorter phase angle has been associated with increased actigraphy-defined wake-time after sleep onset (WASO) in both good sleepers and individuals with insomnia (Kim, Lim, Suh, & Lee, 2020). Mismatch between behavioural and circadian timing of sleep could increase the likelihood of an overlap between sleep initiation and the wake maintenance zone (WMZ); consequently leading to sleep disruption (Dijk & Czeisler, 1994). Timing sleep attempt at a more conducive circadian phase, by increasing phase angle, may have therapeutic effects in insomnia.

Insomnia treatment is generally approached from a cognitive-behavioural perspective but manipulation of bed and rise-times through sleep restriction therapy (SRT), a key component of CBT, may also address circadian misalignment. During SRT a 'sleep window' is determined by curtailing the amount of time spent in bed (TIB) to match self-reported total sleep time (TST) (Spielman, Saskin, & Thorpy, 1987). Sleep opportunity is typically reduced by delaying bedtime and fixing rise time, which results in more consolidated sleep but also reduced total sleep time (Kyle et al., 2014; Maurer et al., 2020). The new revised sleep times may directly affect phase angle through delaying sleep attempt but could also act as zeitgebers for the circadian system, potentially shifting phase position. Systematic alteration of bed and rise-time is linked to change in morning and evening light exposure, which in turn has been shown to shift DLMO (Burgess & Eastman, 2004; Burgess & Eastman, 2006). Previous studies in good sleepers have shown that experimental sleep restriction leads to later DLMO (~65min later)

even when bed- and rise times are delayed and advanced, respectively, by 2hrs (Rogers & Dinges, 2008). It is possible therefore that acute SRT may delay DLMO in people with insomnia contributing in part, to deficits in performance (Agostini, Carskadon, Dorrian, Coussens, & Short, 2016; Kyle et al., 2014). On the other hand, insomnia is characterised by more variable rise-times (Buysse et al., 2010) and hence standardising rise-time through implementation of SRT may plausibly have a phase stabilisation effect (Riedel & Lichstein, 2001).

In this first, exploratory study we sought to assess the acute effect of SRT on the relationship between DLMO and attempted sleep (phase angle). While no definite hypothesis was formulated for change in DLMO, we assumed that the delay in attempted sleep would be more pronounced than any potential change in DLMO, consistent with experimental studies in healthy controls (Agostini et al., 2016; Rogers & Dinges, 2008). Consequently, we hypothesised that phase angle would increase owing to the anticipated delaying of bedtime. As a secondary aim, and because SRT has been linked to acute reduction in vigilance and increased sleepiness (Kyle et al., 2014; Kyle, Morgan, Spiegelhalder, & Espie, 2011; Miller, Kyle, & Espie, 2012), we examined for the first time whether SRT is associated with impaired vigilance as measured by repeated hourly assessment of psychomotor speed and state sleepiness. We employed a repeated measures protocol to account for circadian rhythm fluctuations that may mask the true effects of restricted sleep opportunity on vigilance impairment (see Shekleton et al., 2013).

## **Methods**

### **Study design**

The ESPRIT (Effects of Sleep Restriction therapy for Insomnia on circadian Timing) study was a within-subjects assessment of change in circadian phase markers during acute

implementation of SRT. Baseline involved a 7-day assessment of sleep at home and laboratory measurement of circadian phase (DLMO) and vigilance. Following baseline, participants implemented SRT over a 2-week treatment period and were subsequently invited for a second (post-treatment) assessment at the laboratory. The study was conducted in Oxfordshire, UK, approved by CUREC (R60730/RE002) and prospectively registered with ISRCTN (ISRCTN18006597).

## **Participants**

The study recruited through online and print advertisements, as well as the use of contact lists where adults who had previously volunteered to be involved in research were re-contacted. General inclusion criteria were: willingness to participate; aged 25-55; meeting criteria for DSM-5 chronic insomnia disorder, assessed by items of the Sleep condition indicator (Espie et al., 2014) and structured sleep interview (based on Morin & Espie, 2003); self-reported sleep efficiency <85%; and intermediate chronotype (score between 31 and 69), indicated by the Morningness-Eveningness questionnaire (Horne & Ostberg, 1976). Exclusion criteria were: anxiety or depression ‘caseness’ [scoring >10 on the anxiety/depression subscales of the Hospital anxiety and depression scale (Zigmond & Snaith, 1983)]; current alcohol misuse, assessed by items from the Alcohol use disorders identification test (Bush, Kivlahan, McDonell, Fihn, & Bradley, 1998); additional sleep disorders other than insomnia, assessed via the sleep disorders screen (Wilson et al., 2010); sleep-disruptive medical comorbidity or conditions contraindicated for potential sleep deprivation (e.g. epilepsy); current prescription of CNS or hormonal medication; previous or current engagement with psychological treatment for insomnia; shift work in the last three months; pregnancy or lactation; perimenopausal or menopausal; travelled across more than two time zones in the prior 3 months; smoked >5 cigarettes/week in the previous three months; consumed >300mg of caffeine per day on

average; and history of drug misuse in the past 12 months. Participants were reimbursed £80 for completion of study assessments.

## **Procedures**

People interested in the study completed an online screening questionnaire using the ‘Qualtrics survey tool’ (Qualtrics, Provo, UT), followed by a brief, structured telephone interview with an experienced sleep researcher to confirm inclusion/exclusion criteria. Eligible participants were asked to maintain their habitual sleep-wake patterns for one week. They were further instructed not to modify their caffeine, nicotine, or alcohol intake from the levels reported at screening except for 48 hours prior to their laboratory visit, when participants were instructed to abstain from caffeine and nicotine. Participants were also advised to refrain from eating bananas, chocolate, turkey and tomatoes for the entire day before the laboratory visit. On the day of the laboratory assessment, participants were also asked to refrain from taking aspirin or any medicine that contains ibuprofen. These instructions were given because specific medicines and food items are known to affect salivary melatonin.

Laboratory events were scheduled relative to the onset of each participant’s mean habitual sleep time reported at study induction, and participants were admitted to the laboratory approximately 5.5hrs before that time (see Figure 1). The laboratory assessment ended two hours following habitual sleep time to accommodate completion of DLMO sample collection. Participants remained awake for the entire time, and consequently, were kept awake two hours past their typical bedtime. Upon arrival, participants were asked to fill out questionnaires and remained in a light-controlled room at the Warneford NIHR clinical research facility (Oxford, UK). Ambient light levels remained at a maximum of 10 lux when measured at the eye in the vertical plane. This was verified by light level measurements 10min before the arrival of the participant and 10min before the last computer task. Beclouded goggles (3x0.6 neutral density, LEE Filters, UK) were used when the participant left the room to use the bathroom where



ambient light levels could not be controlled. Saliva samples were collected hourly, whereby a modified constant posture protocol was imposed. Participants were seated for at least 20min prior to each saliva sample, during which a psychomotor vigilance task (PVT) was performed (10min). Participants were not permitted to eat or drink in the 20min before the saliva sample was taken. Food was provided and intake was standardised for timing and content (sandwich after the third saliva sample). Wakefulness was monitored by direct observation from research staff members throughout the laboratory visit. Participants were free to engage in sedentary activities (e.g. listening to the radio, watching movies) at times when they were not required to undertake study procedures.

Two weeks after the start of the intervention, participants returned for their post-treatment laboratory assessment. Participants were admitted to the laboratory at the same clock time as before and followed the same procedures. Consequently, vigilance measures and saliva sampling also occurred at the same clock time as before. When participant bedtime was delayed by more than 30min, participants were asked to stay one hour longer to ensure enough saliva samples were collected to capture melatonin levels.

[INSERT FIGURE 1]

### ***Study intervention***

Sleep restriction therapy was delivered in a 1-hour 1:1 treatment session at the Sleep and Circadian Neuroscience Institute by a researcher trained in behavioural sleep medicine (LFM). The session was guided by a standardised protocol using personalised treatment slides and workbooks; and started with a brief introduction to standard sleep hygiene advice. The key principles of SRT were then explained, and a new sleep window was set to equal the average TST of the previous week with a TIB minimum of 5hrs. The rise time was chosen first according to preference and current working schedule, the bedtime was then set to equal the

new prescribed sleep window. After the initial session, participants received two further sessions (each ~15min), one after the first week of treatment (phone call) and one after the second week of treatment (at the second laboratory visit) to adjust the sleep window according to established sleep efficiency criteria (Spielman et al., 1987). If the sleep efficiency of the previous week was  $\geq 90\%$ , TIB was increased by 15min, if it was  $< 85\%$ , then TIB was decreased by 15min, and if it was between 85 and 89%, then the sleep window was maintained. To support adherence, the PRO-Diary watch was pre-programmed to remind participants of their agreed sleep schedule one hour before bedtime and to prompt sleep diary questions (see below). For the purpose of the study and its focus on acute treatment effects, SRT was implemented for two weeks only. However, all participants were instructed to continue with SRT for at least another two weeks, in line with standard SRT guidelines (Spielman, Yang, & Glovinsky, 2016). To support continuation, participants received workbooks for two more weeks and were given the opportunity to contact the research team if they needed further support.

## **Measures**

*Dim light melatonin onset and phase angle.* Melatonin levels were extracted from saliva samples at baseline and after two weeks of SRT. Saliva samples were collected hourly during each laboratory visit with the first saliva sample being collected 5hrs before habitual sleep time and the last one two to three hours after habitual sleep time, resulting in a total of eight to nine samples (depending on the intervention sleep schedule). Saliva samples were collected with the passive drool method (3.5ml cryovials, Stratech Scientific Ltd.) and were immediately stored at  $-20^{\circ}\text{C}$ . Participants were asked to collect a minimum of 2.5ml at each sample time point within a given time frame of 5min. All samples were shipped to the ARU Biomarker Laboratory (Cambridge, UK), where salivary melatonin concentration was determined using ELISA assays (Bühlmann Direct Saliva Melatonin ELISA, distributed by ALPCO Diagnostics,

Windham, NH, USA) and following a standardised protocol (Salimetrics, LLC, see Middleton, 2013). Each assay was run in duplicate and mean concentration was extracted for analysis. The sensitivity of the assay was 1.37pg/ml and the intraassay coefficient of variation between duplicate repeats was 5.02%.

The times of DLMO-fixed were calculated for each participant as the time at which the concentration of saliva melatonin continuously exceeded 3.5pg/mL, using linear interpolation between the samples immediately prior to and after the threshold (e.g. Van Someren & Nagtegaal, 2007). If DLMO could not be calculated at one time point, the set of paired data was excluded from related analysis (e.g. phase and phase angle). Phase angle was calculated by subtracting the decimal clock time of DLMO from the average decimal clock time of attempted sleep over the past 7 days (phase angle = attempted sleep time – clock time of DLMO). Average attempted sleep time was derived from sleep diary (previous 7 days) and calculated for both time points: baseline and post-treatment.

*Sleep continuity.* Participants were instructed to complete a sleep diary that was based on the consensus sleep diary (Carney et al., 2012) in the morning (just after waking up) and in the evening (just before switching off the light) for 7 days during baseline and for 14 days during the treatment phase using the time-stamped monitoring system of the PRO-Diary (Camntech Ltd.). During the baseline phase, sleep-diary questions could be accessed up to 3hrs after habitual rise time and up to 3hrs before habitual bedtime. During the treatment phase, sleep diary questions were prompted by audible tone 30min after scheduled rise time and 30min before scheduled bedtime. Participants provided subjective estimates for sleep onset latency (SOL), WASO, and TST. The PRO-Diary watch was further set to record activity in 30 second epochs, comparable to recording settings in other sleep studies (Ancoli-Israel et al., 2003). Sleep continuity outcomes of interest were SOL, WASO and sleep efficiency ( $SE = TST/TIB$ ),

whereby TIB was defined as the time between sleep attempt and rise from bed), which were averaged across 7-day periods (baseline, week-1 and week-2). We also performed analysis on TST to evaluate the extent of sleep restriction during the acute period of the treatment. Actigraphy data were analysed using MotionWare Software 1.1.26 (Camntech Ltd.).

*Insomnia severity.* Insomnia severity was measured by the Insomnia severity index (ISI; Morin, 1993) at baseline and after 2 weeks of treatment (post-treatment). The ISI comprises 7 items that are rated on a 0–4 scale with a higher total score (range 0-28) indicating more severe insomnia and a cut-off score of >10 for detecting insomnia cases. The ISI has good internal consistency ( $\alpha \geq 0.90$ ) (Morin, Belleville, B  langer, & Ivers, 2011).

*Psychomotor vigilance task and subjective sleepiness.* We performed hourly psychomotor vigilance tasks using the PC-PVT 2.0 software (Khitrov et al., 2014). Task duration was 10 min and inter stimulus interval varied from 2-10sec. The task was conducted on a Dell laptop computer (32cm screen) set up on a desk in the laboratory room of the participant. The viewing distance was kept constant at about 45cm. Upon starting and finishing the task, a sleepiness question appeared asking ‘*How sleepy are you?*’. The answer scale ranged 1-10 (1=not at all, 10=extremely). Reaction times <100ms and > 3000ms were excluded from analysis. Reaction times >500ms were considered attentional lapses. Subjective sleepiness scores were derived by calculating the average of the pre- and post-PVT-session answer.

*TIB manipulation check and adverse events.* To investigate if participants followed their new sleep schedule as prescribed, we compared self-reported and actigraphy-derived TIB between the intervention and baseline. Serious adverse events were recorded when a member of the research team was made aware of their occurrence and were defined as: (a) death, (b) suicide attempt, (c) admission to hospital, and (d) formal complaints about the behavioural intervention.

## **Statistical analyses**

### ***Power analysis***

Based on previously reported between-group effects for phase angle differences in people with insomnia versus good sleeper controls (Cohen's  $d=0.65$ ) (Flynn-Evans et al., 2017), the study was powered to detect a minimum standardised effect size of 0.65 for pre-to-post change at 5% level of significance with 80% power. Accounting for 10% attrition, we sought to recruit 22 participants.

### ***Analysis plan***

Summary statistics (means and standard deviations for continuous variables, frequencies and percentages for binary and categorical variables) are presented for demographics and outcomes. All analyses were conducted using SPSS.25 (IBM). Given the exploratory nature of the study, no adjustments were made for multiple testing; however, effect sizes and 95% confidence intervals are presented for all outcomes. To assess the efficacy of SRT over two weeks, we first analysed sleep continuity. Linear-mixed effect models (LMMs) were fitted for daily sleep diary and actigraphy data with fixed effects for time point (baseline, week-1, week-2). A participant-specific random intercept was embedded to account for repeated measures and their non-independence. After testing for normality and homogeneity of variances, two-sided paired t-tests were applied to test the null hypothesis that there is no difference between baseline and post-treatment on the primary outcome, phase angle. Secondary outcomes, such as insomnia severity and DLMO were analysed in the same way. T- and p-values are presented. For repeated measurements of sleepiness and vigilance data, LMMs were fitted with fixed effects for time point (baseline, week-2), session number (1-8), and time point x session number interaction. Between-time point comparisons (baseline vs post-treatment) were also conducted for each session number (1-8) to investigate differences specific to the time of each scheduled

measure in relation to habitual bedtime. Cohen's  $d$  statistics were calculated as the within-subject treatment effect divided by the standard deviation of the change score.

## **Results**

### **Participant characteristics**

All participants were recruited during British summer time between March and July 2019. Three hundred and thirty individuals were screened online, 24 of whom were deemed eligible. The main reason for exclusion was a mixture of not meeting age/consent/shift-work/travel/medication or menopause criteria. Eighteen participants completed baseline assessments and the two-week SRT phase. All participants completed all post-treatment assessments. See Figure 2 for the CONSORT flow diagram.

[INSERT FIGURE 2]

Table 1 provides the baseline characteristics. The sample had a mean age of  $37.06 \pm 8.99$  (range 25-54 years), the majority were male (61.1%), and reported a BMI of  $26.01 (\pm 3.94)$ . Consistent with inclusion criteria, ISI scores were in the clinical range (mean =  $17.78 \pm 2.76$ ) and self-reported SE was below 85% as indicated by sleep diary (mean SE =  $75.32 \pm 14.15\%$ ; see Table 2).

[ INSERT TABLE 1]

### **SRT implementation: TIB manipulation check and sleep outcomes**

Before considering the primary circadian outcomes we first summarise data on SRT implementation and efficacy. In relation to the prescribed sleep window, 12/18 participants curtailed their sleep window from both sides (delaying bedtime and advancing rise time); five delayed their bedtime only; and one advanced rise time only. From week-1 to week-2, 8/18 participants increased their sleep window by 15min, 7/18 kept the same sleep window and 3/18

decreased it by 15min in accordance with SE criteria. In line with prescribed TIB restriction, self-reported average TIB was significantly lower during treatment week-1 and week-2 when compared to baseline (see Table 2; TIB decrease=102-112min). Consistent with this, actigraphy-derived TIB similarly revealed a significant reduction of TIB in the SRT group during week-1 and week-2 (see Table 2; TIB decrease=101-114min). Together, these results indicate that participants adhered to their new sleep schedule.

*Self-reported sleep.* Within-group comparisons revealed differences for SOL, WASO and SE during weeks 1 and 2 (see Table 2; SOL decrease=13-22min, WASO decrease=34-44min, SE increase=8-12%). To assess the extent to which sleep time was restricted, we further analysed TST. Results showed that participants reported sleeping 41min less during week-1 and 30min less during week-2 (see Table 2).

*Actigraphy.* Similar to diary data, actigraphy sleep parameters decreased during weeks 1 and 2 (see Table 2; SOL decrease=5-6min, WASO decrease=18-19min, SE increase=2%). TST also decreased by 75min at both time points relative to baseline ( $p < .001$ ).

*Insomnia severity.* Results from paired t-tests revealed a significant reduction of -6.61 on the ISI between baseline and post-treatment (95% CI=-8.56 to -4.66;  $t_{1,17} = -7.14$ ;  $p < .001$ ; see Table 2).

[INSERT TABLE 2]

### **Phase angle**

Three participants were excluded from the analysis because DLMO could not be detected for both time points (all melatonin concentrations were greater than 3.5pg/mL threshold). Pairwise comparisons of the remaining 15 participants indicated an average increase in phase angle of 0.58hrs (95% CI=0.01 to 1.15;  $t_{1,14} = 2.17$ ,  $p = .048$ ) from baseline to post-treatment (see Figure 3 and Table 3; see Figure S1).

[INSERT FIGURE 3]

### **DLMO and sleep timing**

To further elucidate the effects of SRT on phase angle, we performed analysis on its composite components, DLMO and attempted sleep time in the same 15 participants. A paired t-test revealed no effect for time point on DLMO, indicating that the average rise-time of melatonin did not change from baseline to post-treatment ( $t_{1,14}=0.62$ ,  $p=.543$ ; see Table 3). Paired t-test of attempted sleep time revealed that after two weeks of SRT participants attempted sleep on average 0.78hrs later (95%CI=0.41 to 1.15;  $t_{1,14}=4.51$ ,  $p<.001$ ; see Table 3). Consistent with delayed sleep attempt, additional exploratory analysis of the positioning of the sleep window showed that participants went to bed on average 0.97hrs later (95%CI=0.54 to 1.40;  $t_{1,14}=4.79$ ,  $p<.001$ ), but also got out of bed 0.95hrs earlier (95%CI=0.61 to 1.30;  $t_{1,14}=-5.96$ ,  $p<.001$ ) relative to baseline.

[INSERT TABLE 3]

### **Vigilance and subjective sleepiness**

*PVT Reaction time.* Baseline data (RT and lapses) from one participant at session 1 was excluded due to lack of sufficient valid trials (only one valid trial). As shown in Figure 4 and Table 4, there were significant main effects for time point (baseline vs post-treatment;  $F_{1,253}=32.29$ ,  $p<.001$ ) and session number (1-8;  $F_{7,253}=4.55$ ,  $p<.001$ ). Participants responded on average 52.71ms slower (95%CI=34.44 to 70.97) to the stimulus at post-treatment when compared to baseline. There was no significant time point x session number interaction ( $F_{7,253}=.80$ ,  $p=.587$ ) but exploratory pairwise comparisons for each session (baseline vs post-treatment) revealed that reaction time was significantly slower at sessions 5-8 ( $p\leq.029$ ; session 6=habitual sleep time at baseline; see Figure 4 and supplementary Table S1).



*Attentional Lapses (RTs >500ms).* Analysis of attentional lapses similarly revealed significant main effects for time point (baseline vs post-treatment;  $F_{1,253}=36.16$ ,  $p<.001$ ) and session number (1-8;  $F_{7,253}=5.71$ ,  $p<.001$ ). On average, participants had 5.84 more lapses (95% CI=3.93 to 7.75) when compared to baseline (see Table 4). Again, there was no significant time point x session number interaction ( $F_{7,253}=0.74$ ,  $p=.64$ ) but exploratory pairwise comparisons for each session (baseline vs. post-treatment) revealed more lapses at session 3, 5, 6, and 7 ( $ps\leq.032$ ; see supplementary Table S1).

[INSERT TABLE 4]

*Subjective sleepiness.* There was a significant main effect for time point (baseline vs post-treatment,  $F_{1,254}=4.20$ ,  $p=.042$ ) and session number (1-8;  $F_{7,254}=47.37$ ,  $p<.001$ ). On average, participants rated their sleepiness 0.31 points higher (95% CI=0.01 to 0.61) at post-treatment when compared to baseline (see Table 4 and Figure 4). There was no significant time point x session interaction ( $F_{7,254}=.202$ ,  $p=.985$ ) and exploratory pairwise comparisons for each session between baseline and post-treatment did not reveal any significant differences ( $ps>.141$ ; see supplementary Table S1).

[INSERT FIGURE 4]

### **Adverse events**

No serious adverse events were reported.

### **Discussion**

We designed this study to examine the acute effects of SRT on (a) the relationship between circadian phase and sleep-wake behaviour, and (b) repeated measures of vigilance. Reduction in TIB and improvements in self-reported and actigraphy-derived sleep variables indicate that SRT was implemented as instructed, and effective as expected.

Consistent with our hypothesis the primary outcome, phase angle, demonstrated an average increase of 35min following SRT. In our sample, the average phase angle at baseline was 2hrs and 16min, which is comparable to the phase angle duration of 2hrs and 13min reported by Flynn-Evans and colleagues (2017). Intriguingly, after two weeks of SRT, average phase angle was 2hrs and 51min, which is more comparable to healthy controls (3 hrs 10 min; Flynn-Evans et al., 2017), and suggests that SRT may work, at least in part, through timing sleep attempt at a more conducive circadian phase.

Further analysis of sleep-wake behaviour revealed that change in phase angle was principally explained by a delay of attempted sleep time, which was approximately 47min later during the second week of treatment compared to baseline. In contrast, the average time for DLMO shifted later by just 12min and hence was similar to baseline. The absence of a marked change in DLMO between baseline and post-treatment may be explained by the shift in rise time we observed and/or reduction in bed- and rise time variability (see supplementary Figure S1) (Maurer et al., 2020). After two weeks of SRT, participants got out of bed approximately 57min earlier than at baseline. Hence, bed- and rise time were curtailed by a comparable amount, potentially leading to greater and more standardised light exposure in the evening and morning and, consequently, no change in melatonin onset. Indeed, the relative stability of DLMO is in line with results from Miller and colleagues (2015) who reported no change in the phase of core body temperature after five weeks of SRT.

Although phase angle increased, the delay of bedtime and advancement of rise-time indicates that timing of the entire sleep period did not shift. This was confirmed by follow-up analysis of sleep mid-point (baseline=03:11hr vs post-treatment=03:09hr;  $t_{1,14}=0.216$ ,  $p=0.831$ ), and reinforces the absence of change in circadian phase indexed by DLMO. It suggests that, in addition to increasing phase angle, SRT may stabilise sleep at its centre, potentially re-aligning circadian and homeostatic drives for sleep. The relative contribution of change in phase angle

and the consolidation of sleep anchored around its pre-treatment mid-point could be investigated in a prospective study wherein participants are randomised to one of three groups: a restricted sleep opportunity that centres sleep around its midpoint (e.g. delaying bed-time and advancing rise time in equal measure), a group that is prescribed only a delayed bed-time (with no change in rise-time), or a group that is prescribed only an advanced rise-time (with no change in bed-time). ).

While sleep became more efficient with SRT, actigraphy-defined sleep time decreased by approximately 75min. Previous work has linked SRT-related sleep loss to vigilance impairment, but no study has assessed vigilance over an extended testing protocol involving hourly measurements. We found slower reaction times and increased lapses at week-2 of SRT. Indeed, the magnitude of impairment ( $ES=0.62-0.64$ ) is comparable to healthy controls when undergoing experimental chronic sleep restriction (Lowe, Safati, & Hall, 2017). While these effects may be interpreted as side effects, they also represent a manifestation of increased sleep drive, a proposed mechanism of SRT that serves to decrease arousal and facilitate sleep onset (Maurer, Espie, & Kyle, 2018). Indeed, exploratory testing principally localised differences to the hours proximal to habitual sleep time at baseline, suggesting a greater presence of sleep pressure close to sleep attempt. On average, state sleepiness during testing also increased following treatment but to a smaller degree ( $ES=0.21$ ) than performance impairment. Studies investigating sleep loss in healthy controls have similarly reported that deterioration of reaction time is often more pronounced than deterioration of subjective state sleepiness (Leproult et al., 2003). In the context of SRT, discrepancy in magnitude of vigilance impairment between subjective and objective measures might represent a potential safety risk (e.g. participants might not be aware of their attentional deficits), reinforcing the importance of safety guidelines when delivering SRT in clinical practice (e.g. avoid driving).

The main strength of this study lies in the highly standardised and controlled measurement of salivary melatonin and repeated measurements of vigilance. Furthermore, delivery of digital prompts close to bedtime enabled us to support adherence. Nonetheless, results of this study must be considered preliminary since we recruited a small sample size ( $n=18$  [ $n=15$  with useable DLMO data]) and did not include a control group. We also focused on the first two weeks of treatment, when restriction is most pronounced; we consider that measurement *during* treatment will help advance understanding of SRT mechanisms. Long-term changes in circadian phase and phase angle should be investigated in future studies. A related point is that the present study cannot disentangle the mechanistic effects of circadian (re)alignment vs. increased homeostatic sleep drive. Given the interdependence between the two processes it is likely that SRT instructions – altered timing, duration, and regularity of sleep opportunity - act on both circadian and sleep homeostatic mechanisms (Maurer et al., 2018). Moreover, this study did not assess or control for light exposure outside of the laboratory environment, which is strongly linked to melatonin levels and should therefore be considered in future research designs.

Furthermore, we did not correct for multiple testing and were only powered for the detection of medium to large effects on our primary outcomes. Consequently, the risk for both type I and type II error is evident (Lieber, 1990). To allow the reader to judge, we report exact values, confidence intervals, and effect sizes.

The generalisability of our results is also limited by the characteristics of our study sample: mainly young and male. All participants had to undergo a thorough screening process where we excluded for comorbid mental health problems, extreme chronotype, use of medication and menopause. These characteristics, however, are over-represented in the insomnia population (Sarsour, Morin, Foley, Kalsekar, & Walsh, 2010). Strict criteria were considered necessary to remove confounding variables.

While we implemented SRT consistent with Spielman and colleagues (1987; 2016), poor reporting in our field (cf. Kyle et al., 2015) precludes us from concluding that our approach is representative of research or clinical practice. Here, bed- and rise times were chosen according to feasibility and participant preference and emphasis was placed on delaying bedtimes to (a) accommodate the reduced sleep opportunity and (b) optimise adherence (Spielman et al., 2016). Despite this, most participants ended up curtailing TIB equally from both sides, resulting in similar shifts in bed- and rise time during the acute treatment phase. Comparability to other research is hindered because SRT studies, and indeed CBT-I studies more generally, do not report on changes in bed- and rise times (Kyle et al., 2015; Schwartz & Carney, 2012). We hope that our work will stimulate the field to focus and report on such information i.e. specific details of the SRT protocol used, positioning/titration of the sleep window, and corresponding bed and rise times.

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## Tables

**Table 1.** Baseline characteristics

Baseline characteristics	N=18	
Demographics		
Age, years; M (SD)	37.06	8.99
Male (n; %)	11	61.1
<i>Marital status (n; %)</i>		
Married/domestic partnership	10	55.6
Single	8	44.4
<i>Employment status (n; %)</i>		
Employed for wages	15	83.3
Student	3	16.7
<i>Highest level of qualification (n; %)</i>		
A-Levels, diploma or the equivalent	1	5.6
Some college credit, no degree	1	5.6
Trade/technical/vocational training	1	5.6
Bachelor's degree	3	16.7
Master's degree	6	33.3
Professional degree	3	16.7
Doctoral degree	3	16.7
Health characteristics		
BMI, M (SD)	26.01	3.94
Sleep problem duration, years, M (SD)	9.21	7.08

Notes: BMI=Body mass index (weight/height<sup>2</sup>)

**Table 2.** Means and standard deviations for sleep outcomes and insomnia severity

Sleep diary (N=18)		<i>M</i>	<i>SD</i>	<i>Diff<sub>adj</sub></i>	95% CI		<i>p</i>	<i>ES</i>
TIB	Baseline	517.28	88.10					
	Week1	414.82	56.43	-101.96	-117.05	-86.87	<.001	-1.70
	Week 2	404.14	68.83	-112.40	-127.78	-97.01	<.001	-1.84
SOL	Baseline	33.09	37.42					
	Week 1	20.48	31.74	-12.98	-19.73	-6.23	<.001	-0.60
	Week 2	11.88	10.83	-21.96	-28.41	-15.17	<.001	-1.03
WASO	Baseline	76.62	79.71					
	Week 1	42.22	57.53	-34.15	-46.33	-21.96	<.001	-0.92
	Week 2	35.03	48.84	-43.72	-55.97	-31.47	<.001	-0.74
SE	Baseline	75.32	14.15					
	Week 1	84.06	15.29	8.42	5.54	11.31	<.001	0.82
	Week 2	87.40	13.09	12.29	9.35	15.24	<.001	1.06
TST	Baseline	388.29	74.67					
	Week 1	348.34	68.76	-40.93	-53.36	-28.50	<.001	-1.45
	Week 2	356.67	60.48	-29.87	-42.58	-17.17	<.001	-1.00
<b>Actigraphy (N=18)</b>								
TIB	Baseline	502.20	73.21					
	Week 1	399.91	49.10	-99.37	-111.74	-87.00	<.001	-1.87
	Week 2	399.22	43.15	-101.34	-113.85	-88.84	<.001	-1.72
SOL	Baseline	10.82	17.13					
	Week 1	5.32	7.29	-4.91	-7.67	-2.15	.001	-0.71
	Week 2	4.50	7.07	-5.93	-8.71	-3.14	<.001	-0.87
WASO	Baseline	57.62	29.31					
	Week 1	39.62	18.65	-19.10	-22.86	-15.33	<.001	-1.27
	Week 2	39.92	18.72	-18.33	-22.63	-15.02	<.001	-1.03
SE	Baseline	85.92	6.25					
	Week 1	87.82	5.85	2.07	1.18	2.97	<.001	1.18
	Week 2	88.17	5.62	2.49	1.59	3.40	<.001	1.08
TST	Baseline	429.70	60.34					
	Week 1	351.16	50.13	-74.94	-85.47	-64.40	<.001	-1.92
	Week 2	352.54	49.80	-74.57	-85.22	-63.93	<.001	-1.75
<b>Insomnia severity (N=18)</b>								
ISI*	Baseline	17.78	2.76					
	Week 2	11.17	4.27	-6.61	-8.56	-4.66	<.001	-1.68

Notes: SOL=Sleep onset latency; WASO=Wake after sleep onset; SE=Sleep efficiency, TST=Total sleep time; ISI=Insomnia severity index; *Diff<sub>adj</sub>*=Mean difference derived from linear mixed models

and adjusted for missing values; 95%CI=95% Confidence interval of the mean difference; ES=Effect size (Cohen's d). Significant p-values are displayed in bold.\*derived from paired t-tests

**Table 3.** Overview of changes in phase angle, DLMO and timing of sleep

N=15		M	SD	Diff	95% CI		t	p	ES
Phase angle	Baseline	2.27	0.94						
<i>in dec hrs</i>	Week 2	2.85	1.25	0.58	0.01	1.15	2.17	<b>0.048</b>	0.56
DLMO	Baseline	20.82	1.33						
<i>in dec clock time</i>	Week 2	21.02	0.93	0.20	-0.49	0.90	0.62	0.543	0.16
Bedtime	Baseline	22.70	0.67						
<i>in dec clock time</i>	Week 2	23.67	0.71	0.97	0.54	1.40	4.79	<b>&lt;.001</b>	1.24
Attempted sleep time	Baseline	23.09	0.67						
<i>in dec clock time</i>	Week 2	23.87	0.60	0.78	0.41	1.15	4.51	<b>&lt;.001</b>	1.16
Risetime	Baseline	7.41	1.00						
<i>in dec clock time</i>	Week 2	6.45	0.69	-0.95	-1.30	-0.61	5.96	<b>&lt;.001</b>	-1.54

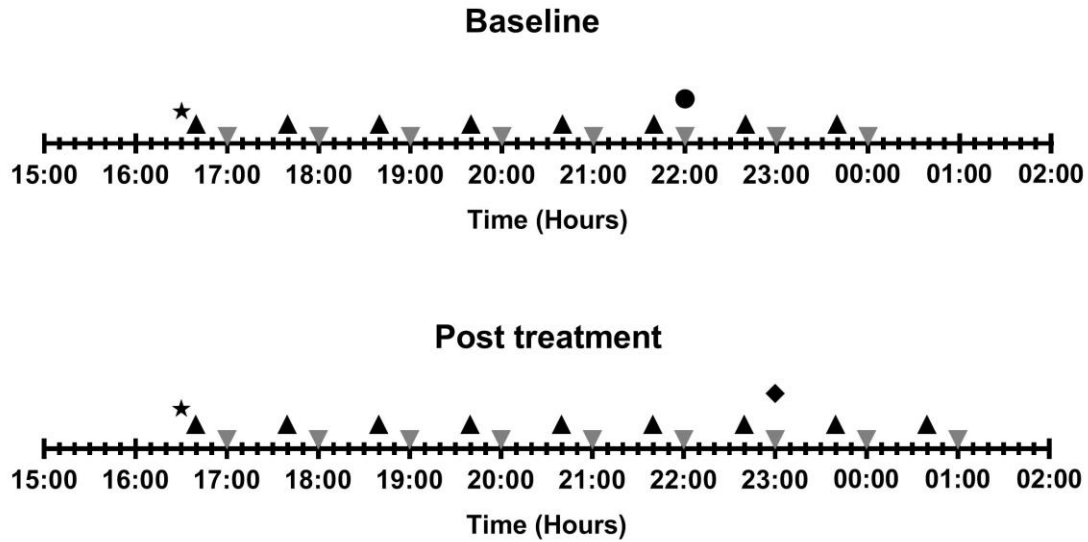
*Notes:* DLMO=Dim light melatonin onset determined at the average decimal clock time of melatonin levels crossing the threshold of 3.5pg/ml; Diff=Mean difference between baseline and intervention; ES=Effect size; 95% CI, 95% Confidence Intervals. Attempted sleep time, bedtime and rise time were derived from sleep diaries and presented in decimal clock time. Significant p-values are displayed in bold.

**Table 4.** Overview of main effects on vigilance and sleepiness

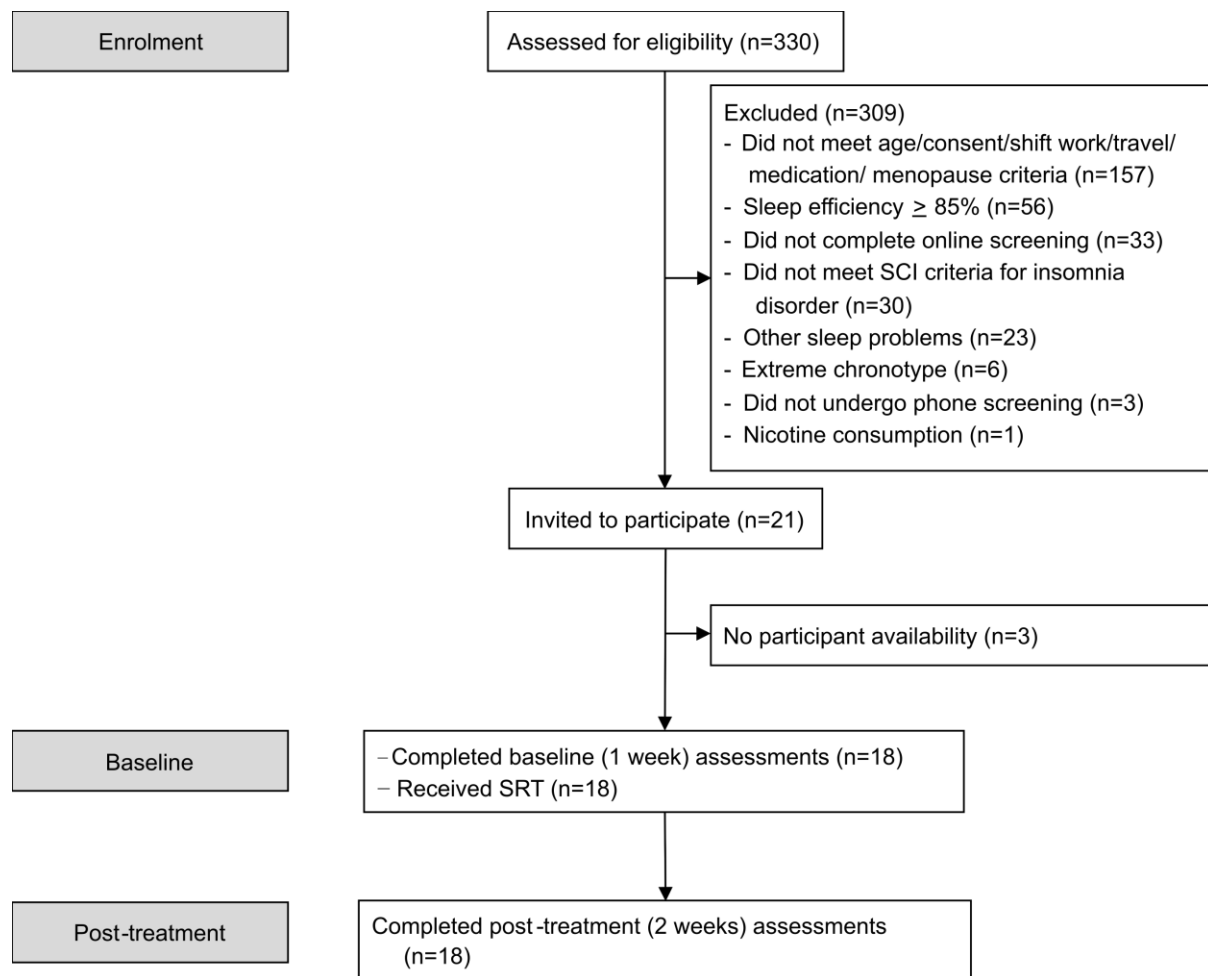
<b>Vigilance</b>		<b>M</b>	<b>SD</b>	<b>Diff<sub>adj</sub></b>	<b>95% CI</b>		<b>p</b>	<b>ES</b>
Reaction time	Baseline	335.46	68.31					
	Week 2	388.70	139.96	52.71	34.44	70.97	<b>&lt;.001</b>	0.62
Lapses	Baseline	5.82	8.75					
	Week 2	11.79	16.05	5.84	3.93	7.75	<b>&lt;.001</b>	0.64
Sleepiness rating	Baseline	5.79	2.20					
	Week 2	6.08	2.08	0.31	0.01	0.61	<b>0.042</b>	0.21

*Notes:* Diff<sub>adj</sub>= Mean difference between baseline and intervention, derived from linear mixed models and adjusted for missing values; 95%CI= 95% confidence interval of the mean difference; ES=Effect size (Cohen's d). Significant p-values are displayed in bold.

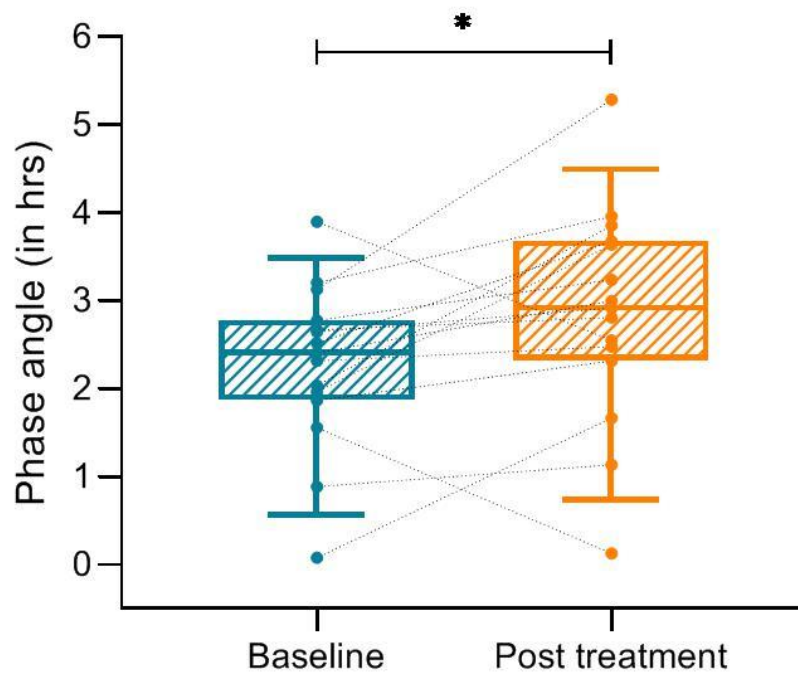
- ★ Arrival in dim light room (<10 lux) & Questionnaires
- ▲ PVT+Sleepiness assessment; start modified constant posture
- ▼ Saliva samples
- Habitual sleep time
- ◆ Scheduled sleep time



**Figure 1.** Schematic exemplary study protocol of the laboratory assessments at baseline and post-treatment. Participants arrived at the same clock time for both assessments (indicated by the star symbol) and remained in dim light until completion of the last saliva sample. Saliva samples took place hourly (grey triangle) and were scheduled 20 min after hourly measures of vigilance and sleepiness (black triangles). In this example, sleep time was delayed by 1 hr during the treatment phase (baseline = black filled circle; post-treatment = black filled diamond). Consequently, the laboratory assessment was extended to ensure enough saliva samples were collected to capture melatonin onset.

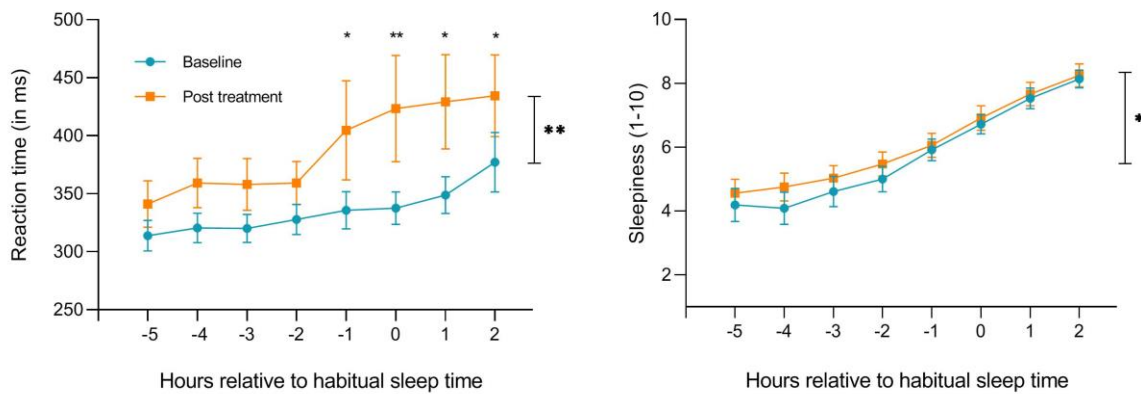


**Figure 2.** Participant recruitment Consolidated Standards of Reporting Trials (CONSORT)-style flow diagram. SCI, sleep condition indicator; SRT, sleep restriction therapy.



**Figure 3.** Changes in phase angle from baseline to posttreatment. Dots represent individual measurements at baseline (blue) and post-treatment (orange). Solid lines present the median with the box extending from the 25th to the 75th percentile and whiskers from the 10th to the 90th percentile. Dotted lines represent the individual phase angle change from baseline to posttreatment.





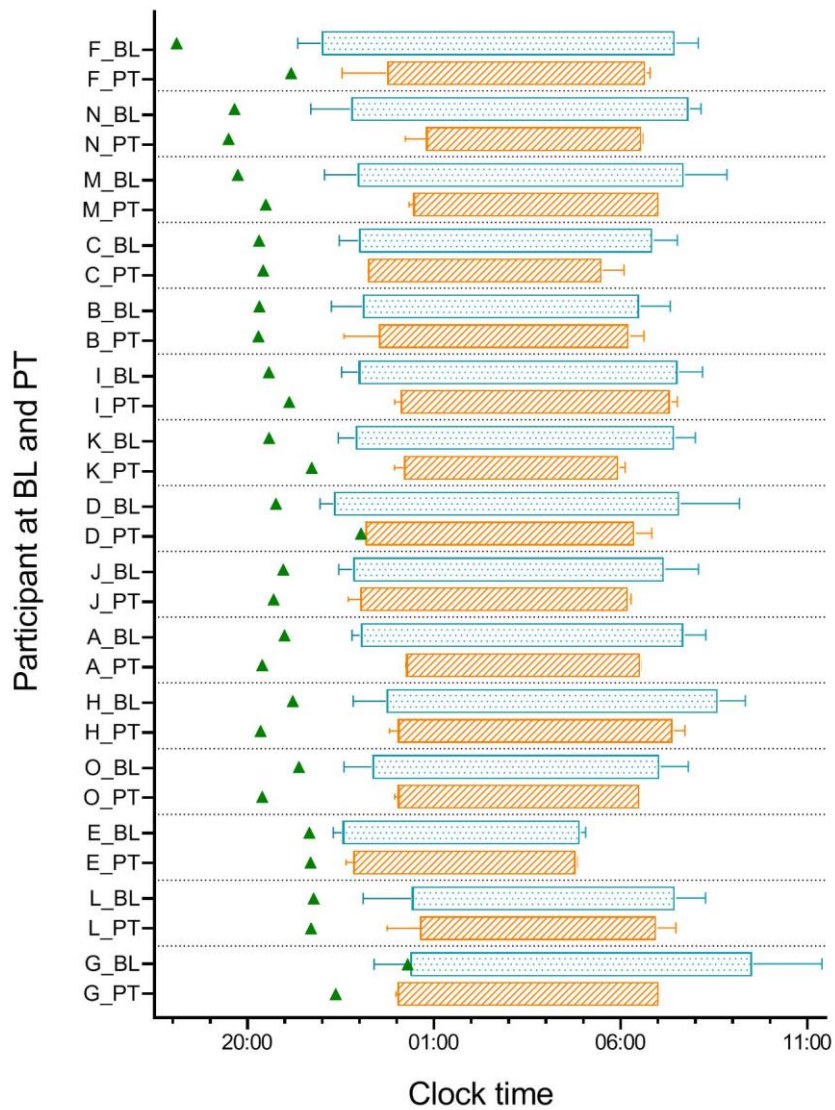
**Figure 4.** Repeated measures of reaction times (RTs) and sleepiness at baseline and after 2 weeks of SRT (post-treatment). Raw means  $\pm$  SEM are presented for each session at each time point with orange squares representing means at baseline and blue circles at posttreatment. Here, session number six refers to the time participants reported attempting sleep at baseline. The graph on the left shows RTs derived from hourly scheduled psychomotor vigilance tasks (PVTs). The graph on the right displays average subjective sleepiness ratings. Both measures were scheduled relative to habitual sleep time (0 on x-axis), starting the first task  $\sim 5$  hr before ( $-5$  on x-axis). Statistical effects are derived from linear mixed models and represented by a single or double asterisk (\* $p < .05$ ; \*\* $p < .01$ ). Main effects for time point (baseline versus post-treatment) are presented on the right-hand of the graphs and session specific effects are presented between the SEM bars.

## Supplement

**Table S1.** Overview of vigilance and sleepiness measures per session number at baseline and post-treatment

Session number (relative to ST*)	Baseline		Post-treatment		Diff <sub>adj</sub>	95% CI	<i>p</i>	
	M	SD	M	SD				
<i>Reaction time</i>								
1 (-5)	313.82	54.45	341.12	85.39	-28.04	-80.30	24.21	.292
2 (-4)	320.60	52.85	359.34	90.11	-31.68	-83.93	20.58	.234
3 (-3)	320.05	51.20	357.96	94.67	-37.91	-89.36	13.55	.148
4 (-2)	327.81	54.50	359.35	79.06	-31.91	-83.00	19.91	.228
5 (-1)	335.71	68.28	404.78	181.83	-69.07	-120.53	-17.608	<b>.009</b>
6 (0)	337.60	59.47	423.38	195.12	-85.78	-137.23	-34.32	<b>.001</b>
7 (+1)	348.91	67.70	429.18	172.67	-80.27	-131.73	-28.81	<b>.002</b>
8 (+2)	377.14	108.94	434.50	149.89	-57.36	-108.82	-5.903	<b>.029</b>
<i>Lapses</i>								
1 (-5)	2.94	5.02	6.11	10.21	-3.31	-8.78	2.17	.235
2 (-4)	4.18	5.66	9.39	14.27	-3.81	-9.28	1.66	.172
3 (-3)	3.44	4.02	9.33	15.45	-5.89	-11.28	-0.50	<b>.032</b>
4 (-2)	4.44	6.20	8.22	12.79	-3.78	-9.17	1.61	.169
5 (-1)	6.67	10.17	12.89	18.60	-6.22	-11.61	-0.83	<b>.024</b>
6 (0)	5.72	7.17	15.28	20.07	-9.56	-14.95	-4.17	<b>.001</b>
7 (+1)	7.06	8.92	16.06	16.93	-9.00	-14.39	-3.61	<b>.001</b>
8 (+2)	11.83	15.25	17.00	17.26	-5.17	-10.56	0.22	.060
<i>Sleepiness</i>								
1 (-5)	4.19	2.20	4.56	1.85	-0.36	-1.20	0.48	0.397
2 (-4)	4.09	2.08	4.75	1.86	-0.64	-1.49	0.21	0.141
3 (-3)	4.61	2.00	5.03	1.68	-0.42	-1.25	0.42	0.328
4 (-2)	5.00	1.71	5.47	1.59	-0.47	-1.31	0.37	0.268
5 (-1)	5.92	1.43	6.06	1.61	-0.14	-0.98	0.70	0.744
6 (0)	6.72	1.30	6.92	1.62	-0.19	-1.03	0.64	0.648
7 (+1)	7.53	1.38	7.67	1.57	-0.14	-0.98	0.70	0.744
8 (+2)	8.14	1.17	8.25	1.53	-0.11	-0.95	0.73	0.794

Notes: Diff<sub>adj</sub>= Mean difference between baseline and intervention, derived from linear mixed models and adjusted for missing values; 95% CI= 95% confidence interval of the mean difference; Significant p-values are displayed in bold.\*ST=habitual sleep time at baseline



**Figure S1.** Sleep and circadian phase shift between baseline (X\_BL) and post-treatment (X\_PT) assessments. Each row represents the data of a single participant at baseline or post-treatment. Green triangles represent DLMO. Boxplots (mean/SD) are positioned for sleep diary derived attempted sleep time (from sleep attempt in the evening to rise time the next day), averaged for the previous 7 days at baseline (blue) and post-treatment (orange) for every participant.