Title: Resetting the late timing of 'night owls' has a positive impact on mental health and performance

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Highlights:

Here we took a group of 'night owls' (i.e. people with extreme late sleeping and waking patterns) and attempted to shift their habitual late timings earlier in a real-world setting using simple, practical non-pharmacological interventions. We show that by using this intervention we can:

- Achieve a phase advance of around two hours
- Decrease self-reported ratings of depression and stress
- Reduce sleepiness in the morning
- Significantly improve simple indices of cognitive and physical performance

Abstract

There is conflict between living according to our endogenous biological rhythms and our external environment, with disruptions resulting in negative consequences to health and performance. This is often documented in shift work and jet lag, but 'societal norms' e.g. typical working hours, can create profound issues for 'night owls', people whose internal biological timing predisposes them to follow an unusually late sleep-wake cycle. Night owls have also been associated with health issues, mood disturbances, poorer performance and increased mortality rates. This study used a randomized control trial design aimed to shift the late timing of night owls to an earlier time (phase advance), using non-pharmacological, practical interventions in a real-world setting. These interventions targeted light exposure (through earlier wake up/sleep times), fixed meals times, caffeine intake and exercise. Overall, participants demonstrated a significant advance of ~2 h in sleep/wake timings as measured by actigraphy and circadian phase markers (dim light melatonin onset and peak time of the cortisol awakening response), whilst having no adverse effect on sleep duration. Importantly, the phase advance was accompanied by significant improvements to self-reported depression and stress, as well as improved cognitive (reaction time) and physical (grip strength) performance measures during the typical 'suboptimal' morning hours. Our findings propose a novel strategy for shifting clock timing towards a pattern that is more aligned to societal demands that could significantly improve elements of performance, mental health and sleep timing in the real world.

Keywords: Late circadian phenotypes; chronotype; actigraphy; dim light melatonin onset; cortisol awakening response; non-pharmacological interventions; phase advancing; depression; stress; performance

Introduction

There is often little regard for the impact of sleep and circadian disruptions in society's attitude towards the organisation of our typical working day. Disturbances to the sleep/wake system that impair daily functioning leading to reduced health are prevalent, with around two thirds of the UK's adult population (67%) reporting some sort of sleep issue [1, 2]. It is well documented that restricted sleep and disrupted circadian rhythmicity result in changes to many physiological processes such as endocrine regulation [3] and core body temperature (CBT) [4], as well as being linked with a variety of health issues, including mood disturbances [5], increased morbidity and mortality rates [6], and declines in cognitive and physical performance [7]. Disruption to circadian and sleep/wake processing represents a substantial economic burden on society, primarily through loss of productivity, absenteeism and poor performance [8], and increases the risk of occupational accidents [9]. A major factor influencing these outcomes is a lack of appreciation for individual differences in vulnerability to sleep disruption and circadian misalignment, and a lack of awareness of the extent to which an individual's circadian timing may not align with the normal 09:00 h - 17:00 h working day.

Individual differences in biological rhythms are influenced by physiological [10, 11], genetic [12] and behavioural [13] factors. These differences allow the categorisation of individuals according to their circadian timing, with particularly early and late timings often referred to as 'larks' and 'night owls' (termed Early and Late circadian phenotypes, ECP/LCP, in this study). At their most extreme these differences can result in clinical diagnoses of the circadian rhythm sleep-wake disorders (CRSWDs), Advanced Sleep-Wake Phase Disorder (ASWPD) and Delayed Sleep-Wake Phase Disorder (DSWPD), which are more prevalent in older and younger subjects, respectively. The extent to which these clinical disorders overlap in terms of mechanisms with extreme circadian phenotypes in the healthy population remains unknown.

DSWPD is often associated with mood disorders such as depression [14], and this group of individuals also tend to be restricted by social factors such as work/school routines which shorten sleep resulting in an accumulation of 'sleep debt'. This causes excessive sleepiness during the day and impairment of cognitive functioning [15]. While clinical assessment is needed to diagnose DSPWD,

many of its symptoms are shared with ‘night owls’ (LCPs). LCPs are categorized based on late sleep/wake timings, a delay in dim light melatonin onset (DLMO) and/or defective sleep homeostasis [16]. LCPs have been associated with higher scores for depression [17], decreased morning cognitive performance, excessive daytime sleepiness [18], as well increased morbidity and mortality risks [6]. Diurnal variations in both cognitive and physical performance measures have also been shown to vary between circadian phenotypes [19], with LCPs often having difficulties fitting into traditional working hours. Since around 50% of a given population would fall into a ‘Late type’ category (waking after 8:18 h) [20], one could propose that these individuals are compromised by having delayed circadian timing and could benefit by being shifted towards an earlier pattern.

Resetting biological clocks can be achieved using behavioural methods, pharmacological methods or a combination of the two. The human circadian system is most responsive to light, which allows sleep/wake activity and physiology to adapt to the 24 h light dark cycle. As a result, light, or lack of light, is a major target to try and reset biological clocks through a process called photic entrainment. Bright light has been shown to shift circadian phase depending on time and duration of light administered (phase response curve) [21, 22]. Exposure in the early morning phase advances the circadian system causing DLMO to peak earlier and sleep onset to become advanced [23]. Conversely, light exposure during the biological night creates a phase delay shown by a later DLMO [24, 25].

Non photic forms of entrainment have also been researched to try and shift circadian phase [26]. These behavioural targets i.e. non-pharmacological interventions, include altering sleep/wake cycles [27], timed physical exercise [28] and timed feeding [29]. Timed feeding has been shown to shift peripheral clocks in mice without affecting the SCN clock [30]. Furthermore, timed feeding has been shown to regulate peripheral metabolic rhythms with a 5-hour delay in meal timings delaying rhythms of plasma glucose and adipose PER2 clock gene expression [29]. An alternative circadian zeitgeber that has been explored is targeted physical exercise. Timed exercise can alter the rhythm of core body temperature [31] and melatonin [32]. A recent paper has further supported these findings, showing

that exercise in the morning and early afternoon elicits a phase advance, whereas scheduled evening exercise causes a phase delay [33].

The majority of our society has stringent work and schooling hours requiring attendance between the hours of 09:00 h and 17:00 h. Despite these traditional imposed social clock requirements, there has been some shift towards understanding biological constraints by allowing flexibility of working hours [34], as well as attempts to move school start times to fit to adolescents' notoriously late running biological clocks [35]. However, despite awareness of the consequences, there is still a long way to go to directly translate research outcomes and affect change in our rapidly evolving 'round the clock' society.

Although attempting a phase advance (shifting the clock earlier) using some of these methods has previously been shown in laboratory studies [28, 36, 37], field studies are lacking. Furthermore, investigating the impact on mental health and diurnal variations in performance have not yet been attempted in real world settings. Here we propose a novel intervention strategy for 'night owls' (LCPs), many of whom suffer from chronic circadian misalignment or disrupted sleep homeostasis. Using simple, practical lifestyle changes, we aimed to phase advance sleep/wake timings, DLMO and time of peak cortisol awakening response. We hypothesised that if a phase advance is achieved this would improve self-rated measures of mental health (depression, anxiety and stress) as well as shift the timing of peak performance earlier, and thus improve simple indices of cognitive (reaction time) and physical (grip strength) performance at non-optimum times of day.

Methods

Participants

The study received a favourable ethical opinion from the University of Birmingham Research Ethics Committee, was performed in accordance with the Declaration of Helsinki and participants gave written informed consent before involvement. A total of 178 individuals completed the Munich ChronoType Questionnaire (MCTQ, paper version [38]) to calculate corrected mid-sleep on free days (MSF_{sc}). Participants classified as Late chronotypes using an age and gender matched MCTQ database were invited to take part in the study (n = 49). Individuals were screened for no diagnoses of sleep or neurological disorders via self-report and were not taking any medications that affected sleep, melatonin and cortisol rhythms. A total of 29 individuals agreed to take part in the study, of which five were excluded based on medical history and two dropped out prior to starting the study.

The final sample consisted of 22 healthy individuals (15 female, aged 21.3 ± 3.3 years, MSF_{sc} 06:52 ± 00:17 h). The study used a randomized control trial design and was conducted over six weeks for each participant which took place between April and June 2016 (sunrise range 06:42 h to 04:40 h, sunset range 19:41 h to 21:32 h, latitude 52° 29' 22.0956" N). Participants were randomly assigned to the experimental (n = 12, 9 female) or control (n = 10, 6 female) groups at the start of the study. Two weeks of acclimatisation was used to assess habitual sleep patterns using actigraphy and gather questionnaire data at baseline (pre-intervention). Following this period, participants were asked to provide saliva samples for melatonin and cortisol in their home environment (details below) before attending the laboratory for testing sessions at 14:00 h, 20:00 h and 08:00 h. To simulate a 'real world' setting, participants were able to leave the laboratory between testing sessions. Participants were then given a schedule to follow for the next three weeks (intervention) before returning to repeat all testing sessions, physiological sampling and questionnaires (Figure 1). Participants completed the test sessions on the same day pre- and post-intervention. Summary details of participants' data pre-intervention for experimental and control groups to confirm accurate matching can be found in Supplemental Table 1.

Non-Pharmacological Interventions

At the final pre-intervention testing session, the experimental group were given an intervention schedule to follow for a period of three weeks. These interventions followed standard sleep hygiene suggestions and targeted appropriately timed light exposure, sleep, meals, caffeine and exercise (summarised in Table 1). The control group were given a placebo single instruction to 'eat lunch at the same time every day' with the assumption that there would be no differences in sleep timings and hence no effect on circadian phase. Adherence to the intervention was monitored through self-report. Meal timings pre- and post-intervention were collected as part of a diet questionnaire which enquired about food intake habits over the prior 2 weeks. Timing of naps were monitored through daily sleep diaries. A feedback questionnaire was administered at the end of the study where participants were asked whether they adhered to the intervention schedule on a scale of 0 (not at all) to 10 (completely). At each testing session participants answered an online questionnaire to record timing of external variables prior to/between sessions such as caffeine intake, exercise and meal times.

*****INSERT TABLE 1*****

Table 1. Details of intervention schedule given to participants in the experimental group. The control group were given a single instruction (shown in **bold**). Method of monitoring adherence (in addition to a feedback questionnaire administered post-intervention) is given for each intervention target.

Intervention target	**Instructions given**	**How adherence was monitored**
Wake up time	Participants were asked to try and wake up 2-3 hours before habitual wake up time. Participants were asked to maximise outdoor light exposure during the mornings.	Continuous monitoring pre- and post-intervention through actigraphy and sleep diaries.
Sleep/wake timings	Participants were asked to try and keep sleep/wake times fixed (within 15/30mins) between workdays and free days.	Continuous monitoring pre- and post-intervention through actigraphy and sleep diaries.

Sleep onset	Participants were asked to try and go to sleep 2-3 hours before habitual bedtime. Participants were asked to limit light exposure during the evenings.	Continuous monitoring pre- and post-intervention through actigraphy and sleep diaries.
Diet/nutrition	Participants were asked to keep a regular schedule for daily meals. Participants were asked to have breakfast as soon after wake up as possible. **Participants were asked to eat lunch at the same time every day.** Participants were asked not to have dinner after 19:00 h.	A diet questionnaire was administered pre- and post-intervention. An online questionnaire was completed at all testing sessions to record time since last meal.
Caffeine intake	Participants were asked not to drink any caffeine after 15:00 h.	An online questionnaire was completed at all testing sessions to record time since caffeine intake.
Power naps	Participants were asked not to nap after 16:00 h.	Napping was recorded through self-reported daily sleep diaries.
Exercise	If exercise was part of an individual's usual routine they were asked to schedule this during the morning.	An online questionnaire was completed at all testing sessions to record time since exercise.

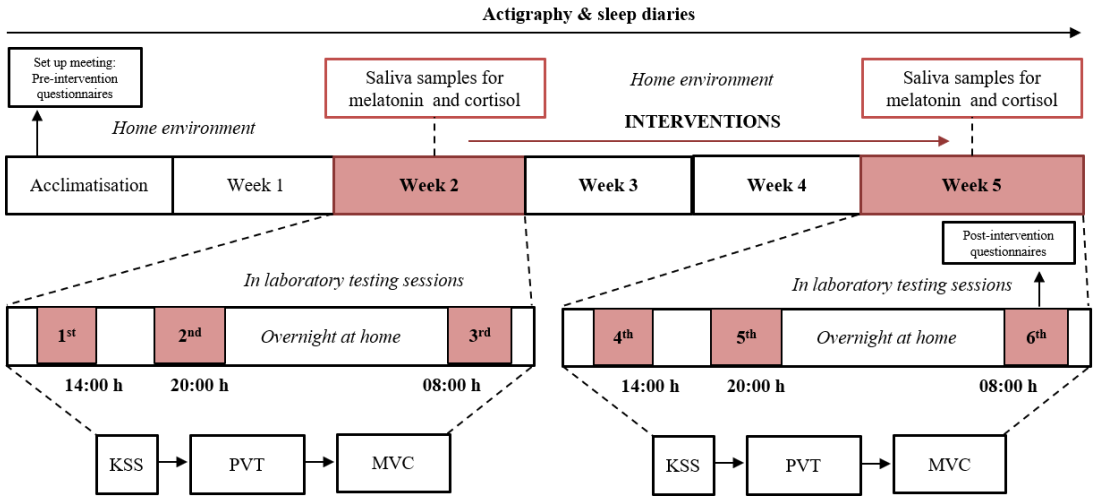

Figure 1. Schematic illustration of experimental protocol. Actigraphy combined with sleep diaries were completed for the duration of the study as well as physiological sampling for melatonin and cortisol measurements prior to attending testing sessions during weeks 2 and 5 (pre- and post-intervention). At each testing session participants completed cognitive (psychomotor vigilance task, PVT) and physical (maximum voluntary contraction, MVC, of isometric grip strength) performance testing coupled with subjective sleepiness ratings using the Karolinska Sleepiness Scale (KSS).

Physiological Data

All participants underwent training in how to collect saliva samples in their home environment following strict protocols. During the sampling period, participants were asked to refrain from cleaning their teeth, drinking caffeinated drinks, alcoholic drinks or any drinks that contained artificial colouring. Each individual was provided with a sample record collection form in order to report the exact times that samples were given and report any factors that could have affected the sampling period e.g. exposure to light, disruption to sampling. Participants provided saliva samples during one morning and one evening during pre-intervention (week 2) and post-intervention (week 5). Samples for melatonin were collected whilst seated in dim lighting conditions i.e. no overhead lights, no electronic devices and curtains closed, every 30 minutes from between three and four hours prior to habitual bedtime until one hour after habitual bedtime. Morning samples for cortisol were collected over a period of 3 hours from wake-up time (the first five samples every 15 minutes and the remaining four samples every 30 minutes). Exact sampling times for each individual were recorded.

Radioimmunoassays (RIA) of melatonin and cortisol in human saliva were performed (Stockgrand Ltd, University of Surrey) using an Iodine^{125} radioactive labelled tracer and solid phase separation [39]. Individual DLMOs were calculated with a linear response function using the mean of the individual pre-intervention concentration values plus two standard deviations of the mean. The time of highest cortisol concentration recorded during the sampling period was used as an indicator of peak cortisol awakening response. Due to insufficient or contaminated samples paired DLMO values (pre- and post-intervention) could not be computed for three subjects in the experimental group and five subjects in the control group.

Behavioural Data

Sleep Analysis*:* Actigraphs (Actiwatch® Light, 2006, Cambridge Neurotechnology Ltd), combined with daily sleep diaries, were worn on the non-dominant wrist for the entire duration of the study (weeks 1-5) to monitor actigraphic sleep and rest-activity patterns (1-minute epochs) in the home environment and analysed with the manufacturer's software (Sleep Analysis 7.23, Cambridge

Neurotechnology Ltd). Due to incorrect wearing of the devices, actigraphic data from two individuals (one in the experimental group and one in the control group) were not usable.

Questionnaires: A set of questionnaires were completed by each participant during a set up meeting pre-intervention and repeated at the end of the final testing session (post-intervention). Questionnaires included the MCTQ, paper version [38], Epworth Sleepiness Scale (ESS) [40], Pittsburgh Sleep Quality Index (PSQI) [41], Profile of Mood States (POMS) [42], Depression, Anxiety and Stress Scale (DASS) [43], and a Diet Questionnaire [29]. Due to insufficient completion of questionnaires, three individuals' results were not recorded for POMS, two for DASS and two for the Diet Questionnaire.

Sleepiness: Daytime subjective sleepiness, measured using the Karolinska Sleepiness Scale (KSS) [44], was assessed at each testing session before the cognitive and physical tasks were performed.

Reaction time: Cognitive testing consisted of a two-minute visual psychomotor vigilance task (PVT) [45]. The PVT was conducted on a desktop computer (DQ67OW, Intel® Core™ i7-2600 processor, 4GB RAM, 32-bit Windows 7) with a standard keyboard and mouse. The same set up was used throughout the study for each participant and each testing session. Participants also performed three trial tests during the acclimatisation phase to familiarise themselves with the set up and minimise learning effects. Milliseconds were recorded for each trial, then a mean response time was taken over the number of trials.

Grip strength: To obtain a simple measure of physical performance an electronic hand dynamometer (EH101, CAMRY) was used to perform a six second maximum voluntary contraction (MVC) test of isometric grip strength [46]. Participants stood with the elbow extended at 180˚ and used their dominant hand in a pronated position to apply as much grip pressure as possible. Raw scores were recorded in kg. Three trials were completed with two minutes rest between each trial and the highest recorded value was used in the subsequent analysis. A set script was used to motivate the participants due to the influence of motivation on performance [47].

Statistical Analysis

Statistical comparisons were performed in GraphPad Prism (version 7.00), using linear regression analysis and two-way repeated measures ANOVA with post hoc tests corrected for multiple comparisons, adding intervention group (experimental/control), assessment period (pre- vs. post-intervention) or time of day (08:00 h, 14:00 h and 20:00 h) as factors. Diurnal variations in performance and sleepiness variables were plotted using second degree polynomial regression curves. Due to data collection occurring at 14:00 h through to 08:00 h, the model is constrained to this time period.

The raw scores for the performance measurements (reaction time in milliseconds from the PVT and grip strength in kilograms from the MVC test) were normalised by converting to percentages relative to each individual's time of peak performance. For example, the testing session where fastest reaction time and strongest grip strength was recorded was designated as 100% for that participant. The subsequent scores were calculated relative to this. Higher percentages always relate to better performance achieved (faster reaction time and stronger grip strength). This was to allow diurnal variations to be quantified in a standardised way across individuals and across different measures of performance (Facer-Childs et al. 2018). These data were normalised relative to each individual in the pre- and post-intervention conditions separately. Test statistics are given to one significant figure. Significance levels are displayed as ns = not significant, $p < 0.05$ = *, $p < 0.01$ = **, $p < 0.001$ = *** and $p < 0.0001$ = ****. Values are represented as the mean ± standard error of the mean (SEM) unless specified otherwise (age and BMI values are given with standard deviations). Exact p values are given to two significant figures, apart from when significance is identified as less than 0.0001, in which case $p < 0.0001$ is reported. The 08:00 h test is described as morning, 14:00 h as afternoon and 20:00 h as evening. Reaction time (measured using the PVT) will be referred to as a simple index of attentional cognitive performance and isometric grip strength (measured using an MVC test) as a simple index of physical performance.

Results

To confirm that the study groups were evenly matched according to the range of variables discussed below, all data were initially compared pre-intervention and no significant differences were found in any of the parameters measured (Supplemental Table 1). Experimental and control groups were of similar age (21.7 ± 2.8 and 20.9 ± 3.9 years), BMI (22.9 ± 3.2 and 22.6 ± 2.1) and MSF_{sc} (07:15 h ± 00:27 and 06:02 h ± 00:14). At baseline (pre-intervention) significant linear relationships were observed between MSF_{sc} and wake up time ($R^2 = 0.53$, $F = 21.21$, $p = 0.0002$), sleep onset ($R^2 = 0.40$, $F = 12.69$, $p = 0.0021$), peak time of the cortisol awakening response ($R^2 = 0.39$, $F = 12.65$, $p = 0.002$), and DLMO ($R^2 = 0.33$, $F = 5.98$, $p = 0.03$) (Figure 2). These results support and validate the classification of participants as LCPs through actigraphic analyses and biological phase markers following the original identification as Late chronotypes from the MCTQ.

*****INSERT FIGURE 2*****

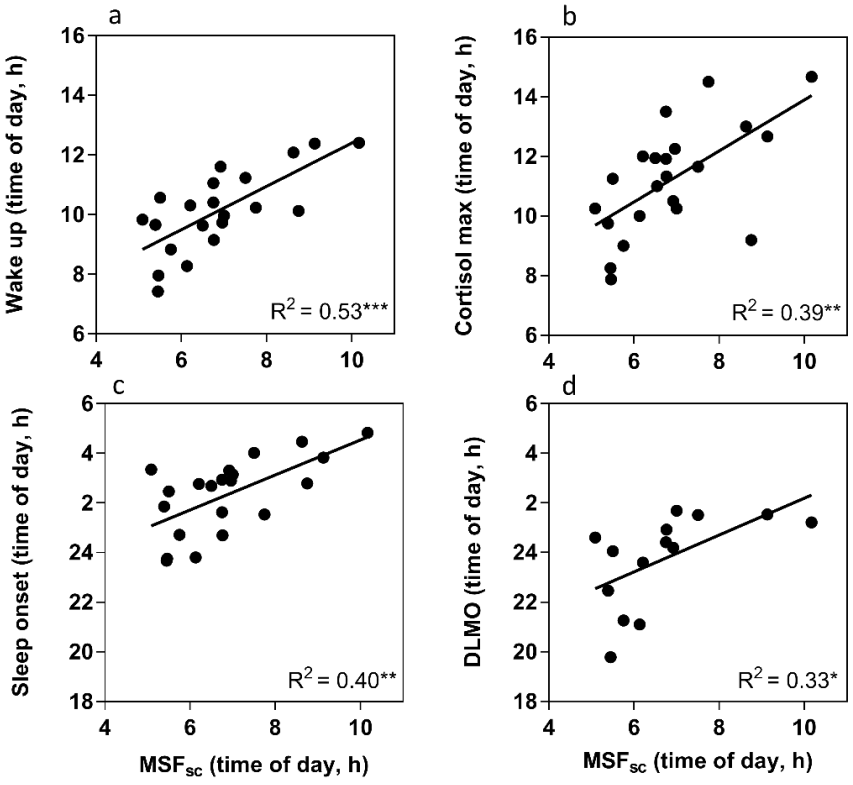

Figure 2. Linear relationships between pre-intervention corrected MSF_{sc} and biological phase markers to validate circadian phenotyping. a) Wake up time (h), b) Time of peak cortisol awakening response (h), c) Sleep onset (h), d) Dim light melatonin onset (DLMO) (h). Corrected mid-sleep on free days (MSF_{sc}) is displayed as time of day (h) on the x axis. Statistical analysis was carried out using linear regression analysis. Asterisks represent significant relationships (* = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$) and R^2 value is shown in the bottom right corner.

Adherence to Interventions

Overall, the experimental group reported on average 7.8 ± 0.7 adherence to the interventions in the feedback questionnaire. Adherence to interventions targeting sleep/wake and dietary variables (monitored through actigraphy and a diet questionnaires) were confirmed with an advance in timings (see below). Avoidance of naps after 16:00 h was confirmed using self-reported sleep diaries. Results from the online questionnaire at the evening testing session confirm an advance in self-reported timing of caffeine intake, exercise and last meal for the experimental group post-intervention. Average self-reported caffeine intake before the 20:00 h testing session was on average 4 hours earlier post-intervention in the experimental group (5.9 ± 1.7 h pre-intervention and 10.3 ± 1.5 h post-intervention), meaning this advanced from 14:00 h to 10:00 h. Average self-reported hours since exercise advanced from 6.8 ± 1.7 h before the evening test session pre-intervention to 7.8 ± 1.8 h before the evening test session post-intervention, as did hours since last meal from 2.4 ± 0.4 h pre-intervention to 3.8 ± 0.8 hrs post intervention. By contrast, the control group had a slight delay in timings of exercise and meal time relative to pre-intervention (6.0 ± 1.9 h to 4.8 ± 1.8 h and 3.5 ± 1.0 h to 2.8 ± 0.8 h respectively) and a slight advance in hours in caffeine from 6.1 ± 2.3 h to 8.7 ± 2.6 h.

Phase Advance

Compared to pre-intervention, a clear phase advance of around 2 h was observed post-intervention in the experimental group, as measured by the MCTQ, actigraphy and circadian phase markers (Figure 3 and Table 2). MSF_{sc} was shifted significantly earlier by 2.57 ± 0.32 h ($p < 0.0001$). This advance was confirmed with actigraphic analysis showing a significant advance of 1.73 ± 0.28 h for sleep onset and 1.92 ± 0.26 h for wake-up time (both $p < 0.0001$), with no significant changes in sleep duration, sleep efficiency or sleep latency. DLMO was advanced by 1.96 ± 0.63 h ($p = 0.018$), and time of peak cortisol awakening response by 2.22 ± 0.50 h ($p = 0.0005$). There were no significant changes in phase angle (time between sleep onset and DLMO). Average self-reported breakfast time in the experimental group shifted significantly earlier by 1.11 ± 0.39 h compared to pre-intervention (p =

0.022). Similarly, average self-reported lunch and dinner times also advanced by 0.75 ± 0.27 h (lunch, $p = 0.023$) and 1.44 ± 0.49 h (dinner, $p = 0.021$). In the control group there was a significant delay of 1.16 ± 0.34 h in sleep onset ($p = 0.0067$) and 1.24 ± 0.32 h in wake-up time ($p = 0.0021$) compared to pre-intervention. By contrast to the experimental group, no other variables were significantly different following the control intervention.

Impact of Interventions on Mental Well-Being

Subjective ratings of depression and stress significantly decreased following the interventions in the experimental group (Figure 4 and Table 2). Overall DASS score decreased by 8.7 ± 2.4 points from 19.8 to 11.2 (pre-intervention). Splitting DASS into depression, anxiety and stress scores separately revealed a significant effect of intervention ($F(1,11) = 13.28$, $p = 0.0039$), and significant decreases in the depression and stress elements but not anxiety ($p = 0.37$). Depression was reduced from 5.5 ± 1.0 to 2.3 ± 1.2 ($p = 0.025$), and stress from 9.5 ± 2.2 to 5.7 ± 1.9 ($p = 0.0061$). There were no significant differences found for the control group in any parameters measured. In both study groups no significant differences were observed for POMS, PSQI or ESS (Figure 4 and Table 2).

380 *****INSERT TABLE 2*****

381 **Table 2.** Summary of main variables and statistical analysis for the experimental group and control
382 group pre- and post-intervention.[1]
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Variable measured	Experimental group		Control group		Interaction (intervention group and assessment period)	Main Effect of Intervention Group (experimental vs. control)	Main Effect of Assessment Period (pre- vs post-intervention)
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention			
MCTQ Score (hh:mm)	07:15 ± 00:27	04:40 ± 00:15	06:02 ± 00:14	07:10 ± 00:18	F (1,20) = 50.8****	F (1, 20) = 3.9^{ns}	F (1, 20) = 14.8**
Nutrition related variables							
Average days per week eating breakfast (days)	4.1 ± 0.6	5.4 ± 0.5	4.7 ± 0.8	4.4 ± 0.8	F (1, 19) = 4.1^{ns}	F (1, 19) = 0.04^{ns}	F (1, 19) = 1.6^{ns}
Average breakfast time (hh:mm)	10:33 ± 00:25	09:24 ± 00:24	10:01 ± 00:34	10:41 ± 00:20	F (1, 18) = 9.2**	F (1, 18) = 0.4^{ns}	F (1, 18) = 0.6^{ns}
Average lunch time (hh:mm)	14:36 ± 00:30	13:51 ± 00:27	13:27 ± 00:17	13:39 ± 00:19	F (1, 18) = 6.4*	F (1, 18) = 1.6^{ns}	F (1, 18) = 2.1^{ns}
Average dinner time (hh:mm)	20:07 ± 00:45	18:41 ± 00:14	18:49 ± 00:17	19:06 ± 00:20	F (1, 15) = 6.5*	F (1, 15) = 0.7^{ns}	F (1, 15) = 3.0^{ns}
Mental well-being variables							
Pittsburgh Sleep Quality Index (PSQI)	4.8 ± 0.7	4.2 ± 0.7	5.3 ± 0.8	4.8 ± 0.5	F (1, 20) = 0.02^{ns}	F (1, 20) = 0.4^{ns}	F (1, 20) = 1.1^{ns}
Profile of Mood States (POMS)	10.3 ± 6.2	-2.9 ± 4.5	8.5 ± 5.7	7.1 ± 6.1	F (1, 17) = 2.2^{ns}	F (1, 17) = 0.3^{ns}	F (1, 17) = 3.4^{ns}
Epworth Sleepiness Scale (ESS)	7.1 ± 1.2	6.3 ± 1.1	9.0 ± 1.0	8.7 ± 0.7	F (1, 20) = 0.2^{ns}	F (1, 20) = 2.8^{ns}	F (1, 20) = 0.7^{ns}
Depression Anxiety and Stress Scale (DASS)	19.8 ± 3.4	11.2 ± 3.1	13.8 ± 3.7	13.6 ± 5.0	F (1, 18) = 2.6^{ns}	F (1, 18) = 2.0^{ns}	F (1, 18) = 5.2*
Actigraphy variables							
Sleep Onset (hh:mm)	02:46 ± 00:26	01:03 ± 00:18	01:37 ± 00:30	02:47 ± 00:27	F (1, 18) = 42.7****	F (1, 18) = 0.3^{ns}	F (1, 18) = 1.7^{ns}
Wake Up Time (hh:mm)	10:31 ± 00:23	08:36 ± 00:15	09:37 ± 00:29	10:51 ± 00:29	F (1, 18) = 59.6****	F (1, 18) = 1.7^{ns}	F (1, 18) = 2.8^{ns}
Sleep Duration (h)	7.75 ± 0.20	7.55 ± 0.20	7.8 ± 0.2	7.9 ± 0.1	F (1, 18) = 0.9^{ns}	F (1, 18) = 0.6^{ns}	F (1, 18) = 0.2^{ns}
Sleep Efficiency (%)	76.80 ± 1.48	75.40 ± 1.25	78.3 ± 1.9	77.2 ± 1.5	F (1, 18) = 0.03^{ns}	F (1, 18) = 0.7^{ns}	F (1, 18) = 1.8^{ns}
Sleep Latency (hh:mm)	00:27 ± 00:04	00:28 ± 00:02	00:21 ± 00:03	00:22 ± 00:03	F (1, 18) = 0.07^{ns}	F (1, 18) = 2.0^{ns}	F (1, 18) = 0.2^{ns}
Physiological variables							
Dim Light Melatonin Onset (hh:mm)	00:02 ± 00:37	22:04 ± 00:21	23:18 ± 00:54	22:54 ± 00:45	F (1, 12) = 2.2^{ns}	F (1, 12) = 0.005^{ns}	F (1, 12) = 5.0*
Cortisol Peak Time (hh:mm)	11:19 ± 00:31	09:06 ± 00:19	11:05 ± 00:36	11:19 ± 00:32	F (1, 20) = 11.1**	F (1, 20) = 2.7^{ns}	F (1, 20) = 7.2*

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[1] Statistical analysis was done with two-way repeated measures ANOVA with Sidak's post hoc tests corrected for multiple comparisons. Intervention group (experimental/control) and assessment period (pre- and post-intervention) are used as factors in the statistical analysis. Ns = not significant, *= $p < 0.05$, **= $p < 0.01$, ****= $p < 0.0001$. Values are shown as mean ± SEM unless specified.

*****INSERT FIGURE 3*****

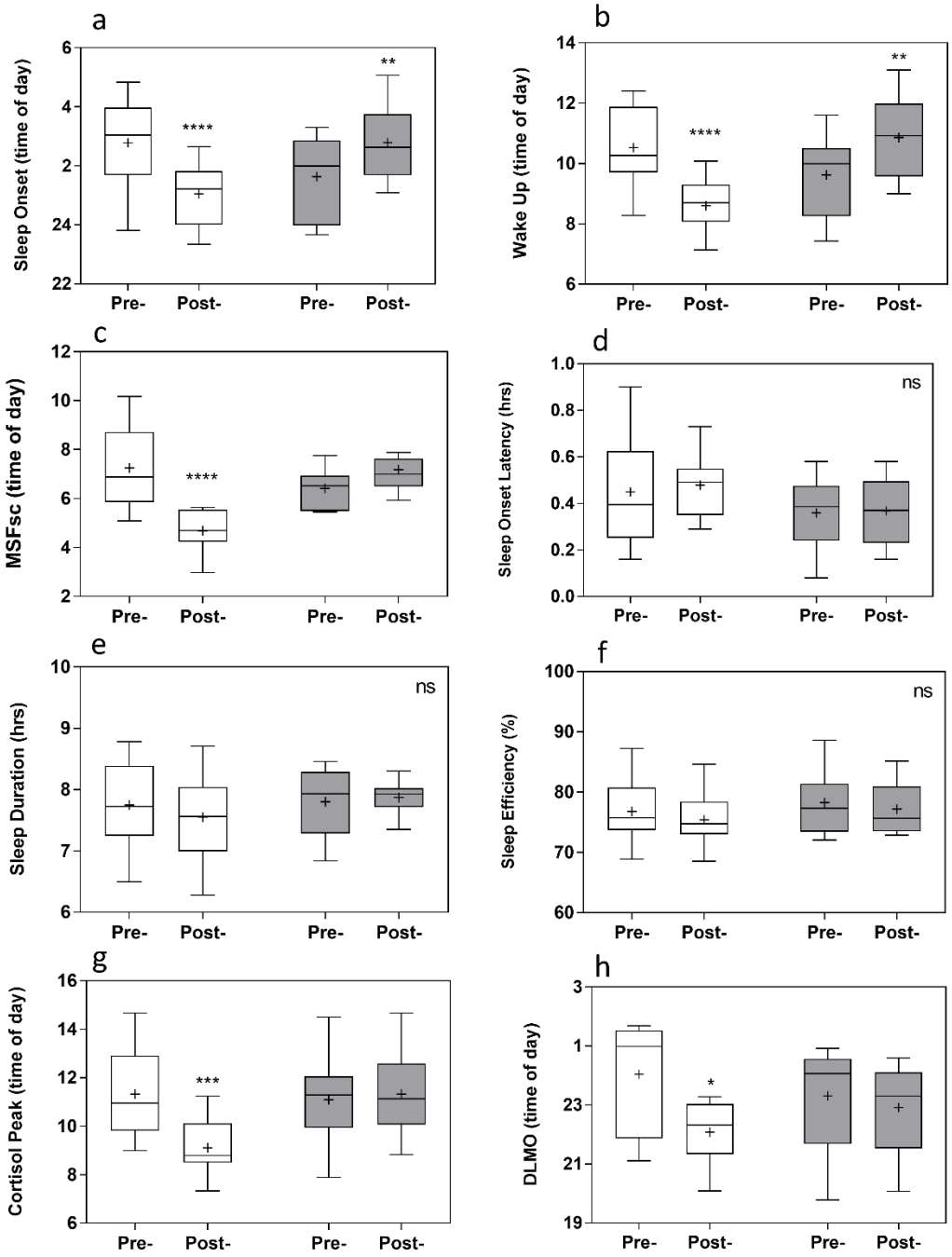
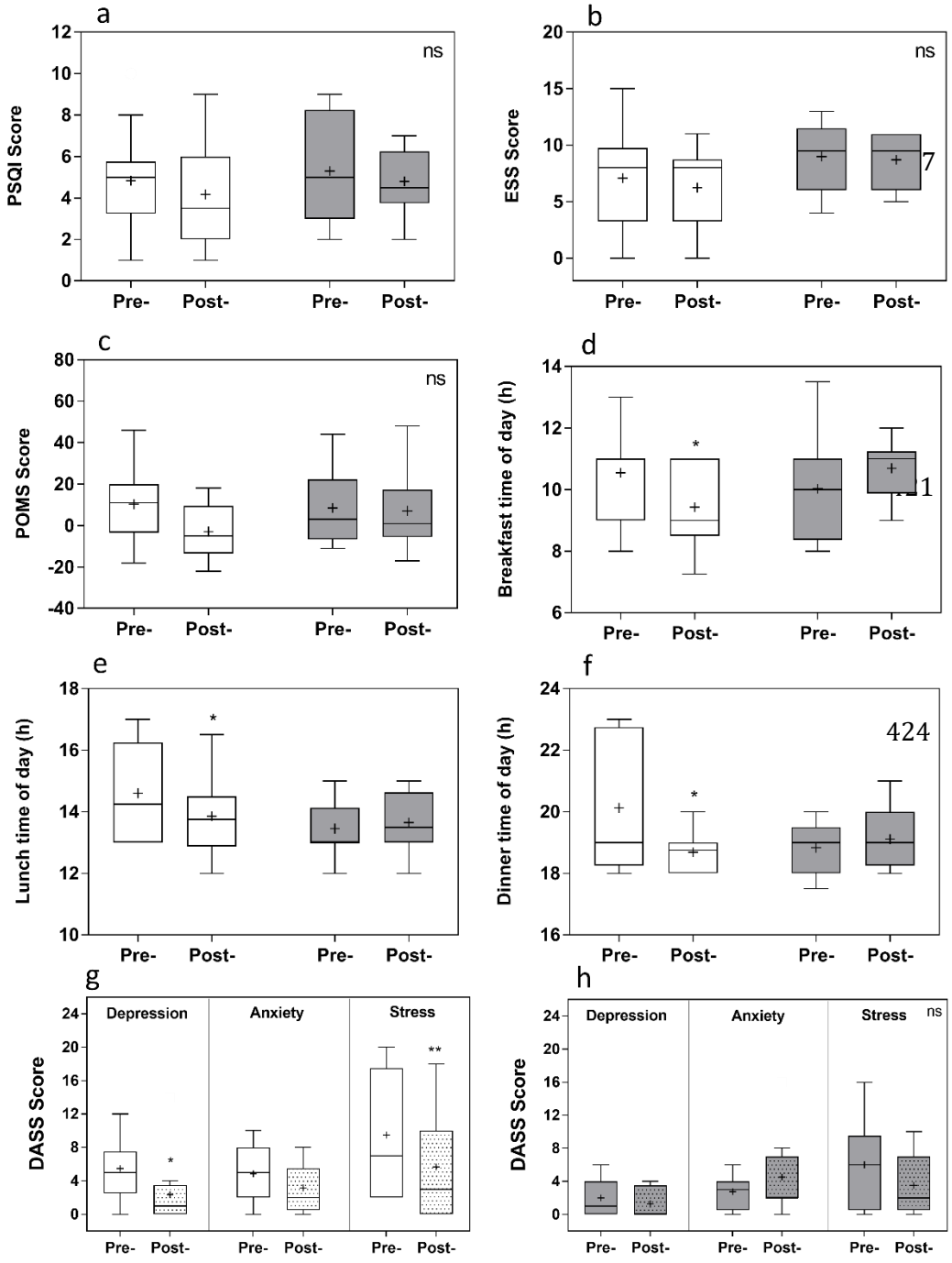


Figure 3. Actigraphy, MCTQ and physiological data pre-intervention (pre-) and post-intervention (post-) for experimental (white) and control (light grey) groups. a) Sleep onset, b) Wake up time, c) Corrected mid-sleep on free days (MSF_{sc}), d) Sleep onset latency, e) Sleep duration, f) Sleep efficiency, g) Time of cortisol maximum during the cortisol awakening response, H) Dim light melatonin onset (DLMO). Data are shown as Tukey box-plots; the line in the box indicates the median, the mean value is shown by the + symbol. Asterisks represent significant differences pre- and post-intervention. Ns = not significant, *= $p < 0.05$, ***= $p < 0.001$, ****= $p < 0.0001$.

414 ***INSERT FIGURE 4***

415



431

432 **Figure 4.** Sleep and mental well-being data pre-intervention (pre-) and post-intervention (post-) for
433 experimental (white) and control (light grey) groups. a) Pittsburgh Sleep Quality Index (PSQI), b) Epworth
434 Sleepiness Scale (ESS), c) Profile of Mood States (POMS), d) Breakfast time of day (h), e) Lunch time of
435 day (h), f) Dinner time of day (h). Depression, Anxiety and Stress Scale (DASS) data for experimental (g)
436 and control (h) groups and shown with a clear pattern (pre-interventions) and a dotted fill pattern (post-
437 intervention). Data are shown as Tukey box-plots; the line in the box indicates the median, the mean value
438 is shown by the + symbol. Asterisks represent significant differences pre- and post-intervention. Ns = not
439 significant, *= $p < 0.05$, **= $p < 0.01$.

Impact of Interventions on Performance and Sleepiness

Using second order polynomial regression analysis, peak performance and sleepiness times were identified from best fit diurnal variation curves (Figure 5). Within the constraints of the model (08:00 h to 20:00 h), sleepiness was highest at 08:00 h for both the experimental and control groups pre- and post-intervention. At the pre-intervention testing, strongest grip strength in the experimental group occurred at the 20:00 h testing session which advanced to 15:21 h post-intervention. In the control group, timing of peak grip strength was delayed from 17:12 h to 20:00 h post-intervention. The same was seen for the PVT with fastest reaction time advancing in the experimental group from 20:00 h to 12:30 h and delaying in the control group from 15:48 h to 19:48 h.

There was a significant reduction in inter-individual variation of performance in the experimental group but no significant changes in the control group. During pre-intervention testing, average grip strength varied by 14.2% in the experimental group, which was reduced to 7.2% post-intervention ($p = 0.0024$). The same was seen for reaction time with average inter-individual differences reduced from 13.0% pre-intervention to 4.4% post-intervention ($p = 0.028$).

A significant interaction of time of day and intervention was found for sleepiness in the experimental group ($F(2,22) = 3.44$, $p = 0.049$) as well as main effects of time of day ($F(2,22) = 11.41$, $p = 0.0004$) and interventions ($F(2,11) = 5.36$, $p = 0.041$). Following interventions, sleepiness was lower at 08:00 h (4.6 ± 0.6 vs 6.3 ± 0.3) and 14:00 h (3.6 ± 0.5 vs 4.7 ± 0.5) but these differences were only significant at 08:00 h ($p = 0.0061$). The experimental group also showed a significant main effect of time of day on grip strength performance ($F(2,22) = 21.73$, $p < 0.0001$), as well as a significant main effect of interventions ($F(1,11) = 4.94$, $p = 0.048$) and an interaction effect ($F(2,22) = 9.19$, $p = 0.0013$). Post hoc tests revealed that grip strength at both 08:00 h and 14:00 h significantly improved following interventions ($p = 0.015$ and $p = 0.0075$ respectively). For PVT performance, there was a main effect of time of day ($F(2,22) = 3.85$, $p = 0.037$) but not interventions. The interaction was found to be significant, however ($F(2,22) = 7.93$, $p = 0.0026$). Reaction time at 08:00 h was significantly faster after interventions ($p = 0.017$) but there was no change at 14:00 h or 20:00 h.

In the control group, a significant main effect of time of day was found for sleepiness ($F(2,18) = 8.86$, $p = 0.0021$), MVC ($F(2,18) = 14.73$, $p = 0.0002$) and PVT ($F(2,18) = 3.63$), $p = 0.048$) performance, but not for interventions or the interaction. Post hoc tests did not show any significant changes from pre- to post-intervention in the control group for any parameters.

*****INSERT FIGURE 5*****

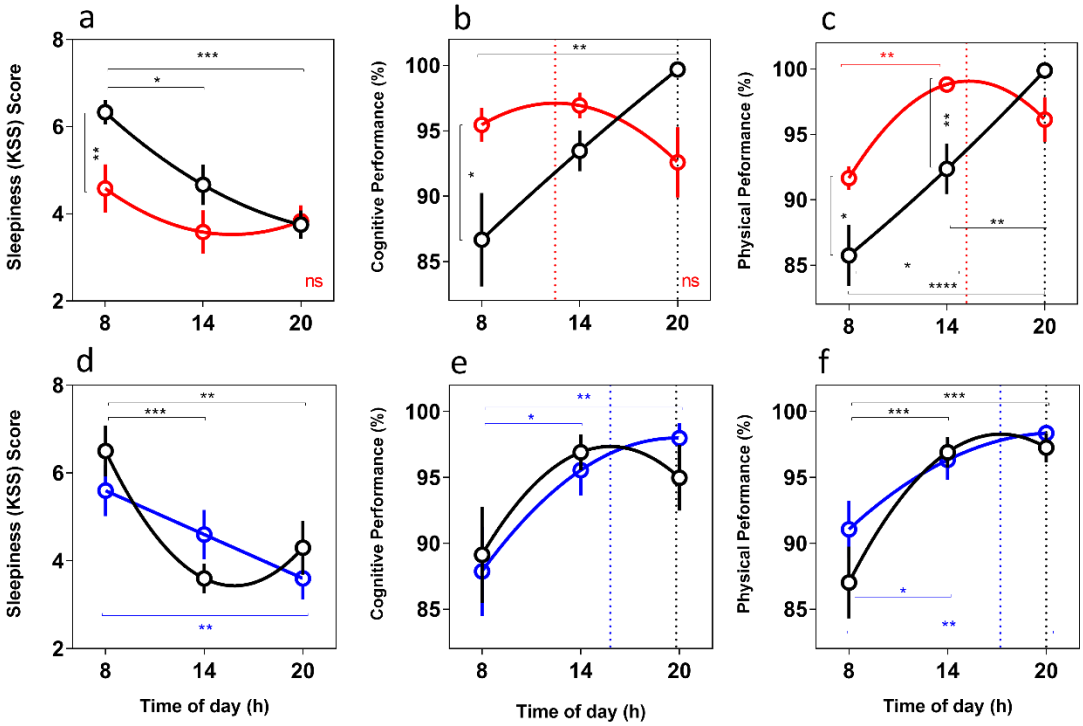


Figure 5. Nonlinear regression curves to show diurnal variations in sleepiness, cognitive and physical performance pre-intervention (black) and post-intervention in experimental (red) and control (blue) groups. (a,d) Subjective sleepiness measured with the Karolinska Sleepiness Scale (KSS). (b,e) Psychomotor vigilance task (PVT) performance (average percentage of individual maximum), (c,f) Grip strength performance (average percentage of individual maximum). Higher percentages relate to better performance e.g. 100% is fastest reaction time and strongest grip strength. Dashed lines represent the time of peak performance in each condition (pre-intervention is black in both groups and post-intervention is shown in red for the experimental group and blue for the control group). Clock time of test (h) is shown on the x-axis for each parameter. Ns = not significant, *= $p < 0.05$, **= $p < 0.01$, ***= $p < 0.001$.

Discussion

Researchers, clinicians and industry experts are constantly seeking ways to better understand how we can improve mental health, well-being and performance. One factor that seems constantly overlooked is the timing of behaviour e.g. sleeping, eating and working. Here we took a group of 'night owls' and attempted to reset their habitual late timings in behaviour in a real-world setting using simple, practical, non-pharmacological interventions. We show that a phase advance of around two hours can be achieved which was accompanied by significant reductions in subjective ratings of depression and stress. In addition, elements of cognitive (reaction time) and physical (grip strength) performance significantly improved during 'non optimal' times, and diurnal peaks in performance occurred earlier in the day.

Phase Advance

Actigraphy analysis revealed a significant advance in both actigraphic sleep onset and wake up time pre- to post-intervention in the experimental group. Sleep duration, latency and efficiency all remained similar pre- and post-intervention confirming that the earlier sleep onset was not associated with increased sleep latency and hence a curtailment of sleep duration. The behavioural impact of the intervention can therefore be attributed specifically to the shifting of sleep timing and not to an alteration of sleep homeostasis. In support of the actigraphy data, we also found a significant phase advance in melatonin onset (DLMO) of nearly 2 h (00:02 to 22:04 h). This was coupled with a similar advance in peak timing of the cortisol awakening response that shifted from 11:19 to 09:06 h. Phase angle, measured as the time between DLMO and sleep onset, was also consistent pre- and post-intervention. By using a gold standard circadian phase marker, in addition to objective actigraphy, these results suggest a true circadian phase advance was observed in the experimental group following the interventions.

As light is the dominant zeitgeber of the circadian system it has been one of the main treatment options of CRSWDs such as DSWPD [48], and mood disorders e.g. seasonal affective disorder [49]. Although controlled light exposure was not specifically administered in this study, participants were

asked to wake up earlier and maximise exposure to morning light, thereby contributing to a phase advance in the circadian system. Simultaneously, the earlier sleep onset times observed combined with the instructions to decrease evening light exposure e.g. from room lighting and electronic devices, could have contributed to the delay in DLMO and sleep onset [50] [51]. Timing of food intake could also be a factor influencing the phase advance. Meal timing has been suggested to have an entraining effect on the circadian system, in particular the peripheral clocks involved in metabolism [29] . Along with the importance of sleep for appetite regulation, studies have found that a morning carbohydrate rich meal can phase advance CBT [52]. There was a significant advance in average self-reported breakfast time (10:33 to 09:25 h) and an increase in the number of days/week breakfast was eaten, although this did not quite reach significance. The same was seen with average self-reported timing of lunch and dinner, which occurred significantly earlier post-intervention, allowing us to confirm adherence to the intervention requirement of not eating dinner after 19:00. These advances in meal times, which were observed in the experimental group but not the control group, could potentially be contributing to the advance in circadian timing, however, as the phase shifting effects of food were not measured directly in this study it remains speculative.

Impact of interventions on mental well-being and performance

The association of a delayed sleep phase with reduced mental health e.g. depression, has been shown in a number of independent studies [17, 53, 54]. Targeting sleep and circadian phase has also become a focus in the development of novel treatments in neuropsychological disorders. Following the interventions, we found a significant decrease in depression and stress score in the experimental group, indicative of better mental health. This was coupled with a similar trend in mood disturbances, with POMS score reducing from 10.33 to -2.89, although this did not quite reach statistical significance. Interestingly, it was the depression and stress elements of the DASS scale that were reduced significantly, with anxiety score not being affected. Although anxiety and depression are two separate conditions with different diagnostic criteria, they are often comorbid. These results, however, suggest each factor is affected independently, indicating separable relationships with sleep timing.

548 This is consistent with the literature suggesting that the temporal relationship between
549 anxiety/depression and reductions in sleep quality or quantity is also different (i.e. anxiety generally
550 preceding sleep issues, depression generally following sleep issues [55]). Being able to objectively
551 explore these factors separately and identify the direction of causality would be an important future
552 step within this work to determine the potential clinical usefulness of the approach for improving
553 mental health.

554 Daytime sleepiness, measured here using the KSS, is one of the key factors associated with poor
555 performance [56] and higher risk of errors [57]. Increased sleepiness, leading to lapses of
556 concentration and even micro sleeps, has been proposed as a main influence in many of the vehicle-
557 related incidents recorded annually [58]. Being able to reduce daytime sleepiness remains a leading
558 motivation in both clinical settings and when considering performance/productivity in the real world
559 [59-61]. Here we show that the experimental intervention significantly decreased daytime sleepiness
560 at 08:00 h and at 14:00 h. Sleepiness was still at its highest in the morning, although significantly
561 lower than pre-intervention. This near two-point difference in the morning means a change from
562 'some signs of sleepiness' to 'rather alert' (score of 6 to 4 on the KSS). There was a loss of significant
563 diurnal variations in KSS score, similar to what was observed for reaction time and grip strength
564 measures. The KSS score has previously been shown to correlate significantly with performance
565 variables such as the PVT [62], as well as objective drowsiness [63]. Therefore, this intervention
566 could prove useful to those professions that are generally more affected by sleepiness and require high
567 vigilance such as air traffic control, lorry driving and aviation [64], especially since the risk of
568 accidents has been shown to exhibit diurnal variation [65].

569 Understanding diurnal variations in performance has allowed some studies to shed light on the reason
570 behind the high risk of motor accidents at non-optimal times of day [66], whilst others have examined
571 the effect on performance in athletes [67, 68]. In line with these suggestions, we now show the
572 potential of manipulating these diurnal variations in night owls (LCPs), producing a phase advance, to
573 create a profile with peak performance occurring earlier in the day. There were significant
574 improvements in reaction time (measured using a PVT) and isometric grip strength (measured using

an MVC test) at 'non-optimal' morning times in the experimental group but not in the control group. The experimental group also showed a significant decrease in diurnal variations of sleepiness and performance variables. This reduction in amplitude is in line with previous research which showed a much larger range in performance differences for night owls (LCPs) compared with morning larks (ECPs) [67, 69]. The diurnal curves of reaction time and grip strength mirror the advance in sleep and circadian timings, with peak grip strength being shifted from 20:00 h to 15:21 h, and fastest reaction time occurring at 12:30 h instead of 20:00 h post-intervention.

Limitations

It is important to recognise that since we investigated relatively simple measures of cognitive (reaction time) and physical (grip strength) performance we should be cautious in over generalising how this intervention would impact more complex measures. Sleep deprivation studies [70, 71] would suggest that more complex cognitive processes are likely to be affected, although the impact tends to be smaller. The PVT is a standard tool used in clinical and research settings to measure sustained attention, and has been shown to be sensitive to sleep loss and time of day [72], with minimal practice effects. Here we used a shortened version of the PVT (2-minute vs 10 minute) which could have reduced the sensitivity to time of day effects, as pointed out by Basner, Mollicone [73]. An investigation into the validity of a 2 minute and 5 minute PVT, however, showed similar time of day relationships compared to the 10 minute PVT, although overall reaction times were increased with task duration, as expected [45]. This can give us confidence that the time of day effects we observed in our study are reliable. Grip strength is a simple measure of muscle strength, which is frequently used as an evaluation of muscle function in exercise and clinical settings. MVC of isometric grip strength offers a robust approach to investigating contributions from central and peripheral mechanisms because the ability to produce maximal force relies on the capability of the muscle as well as the activation from the central nervous system [69]. Using isometric grip strength allows us to provide an insight into how this intervention can impact a simple index of physical performance. Previous research has correlated measures of muscle strength with sprint and jump performance [74].

However, performance itself is multifaceted and cannot be defined by one measure alone, so future work will need to explore how diurnal variations in different cognitive and physical performance tasks are influenced by this intervention.

We have relatively small sample sizes so further studies will be required to investigate how this intervention could impact larger cohorts and different populations. This also limits our ability to perform higher order analysis due to low power, which should be incorporated in future research in line with the discussion from Bland and Altman [75].

Although we were able to partially monitor adherence to the interventions, with the experimental group reporting 78% adherence (7.8 ± 0.7 out of 10), this was mostly done by self-report. Since the control group were only asked to eat lunch at the same time each day, this was confirmed with no significant changes in timing of lunch reported in the diet questionnaire. A more tightly controlled experiment would have perhaps allowed more detailed assessment of each individual's behaviour and adherence to the protocol, however a strength of this study is that we were investigating individuals in a more realistic setting as opposed to artificial laboratory conditions.

Despite the value in using a real-world protocol due to its relative ease of implementation and less disruption to individuals' daily lives, it does limit the ability to control the many environmental and social influences that can have an impact. In addition, care should be taken when using these interventions to ensure that the timings do not risk overlapping with the delay period of the human phase response curve to light [21, 22]. Constant routine and forced desynchrony protocols allow the characterisation of a truly endogenous rhythm through removing/minimising the influence of external cues. The present study, however, was not aimed at finding endogenous components to performance and mental health measures but looked at the integrated system as a whole. The combination of endogenous circadian rhythms, sleep homeostasis, environmental cues and social schedules is what affects daily functioning and diurnal variations in the real world. Therefore, although we cannot attribute the changes we see strictly to one or other of these influences, we provide evidence that a practical intervention can phase advance night owls in a real life setting with positive outcomes on self-reported depression and stress, reaction time and grip strength.

Conclusions

Here we show the ability of a simple non-pharmacological intervention to phase advance night owls, reduce negative elements of mental health and sleepiness as well as manipulate peak performance times in the real world. These findings could yield considerable benefits in a number of different settings. Within the general population, of which a large proportion are night owls, these findings could offer a simple strategy to improve mental well-being and performance. Within clinical settings, further treatments for mental health in depression and stress could be explored specifically targeting circadian disruption without the need for pharmacological agents. This intervention could also be applied within more niche settings e.g. industry or sporting sectors, who have a key focus on developing strategies to maximise productivity and optimise performance. Despite the need for further research, this remains an exciting prospect for a society that is increasingly suffering from poor health, reduced mental well-being and under continuous pressure to achieve personal best performance.

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Author Contributions

E.F.C. and A.P.B. conceived of and designed the study with contributions from D.J.S. E.F.C collected and analysed the data. RIA analyses was performed by B.M. E.F.C wrote the manuscript with contributions from A.P.B and D.J.S. All other authors commented on the manuscript.

Competing Interests

B.M. and D.J.S. are co-directors of Stockgrand Ltd. The authors declare no other competing financial interests.

List of abbreviations

ECP: Early circadian phenotype

LCP: Late circadian phenotype

CBT: Core body temperature

CRSWDs: Circadian rhythm sleep-wake disorders

MSF_{sc}: Corrected mid-sleep on free days

DLMO: Dim light melatonin onset

KSS: Karolinska Sleepiness Scale

PVT: Psychomotor vigilance task

MVC: Maximum voluntary contraction

References

[1] Altevogt BM, Colten HR. Sleep disorders and sleep deprivation: an unmet public health problem: National Academies Press; 2006.

[2] Aviva. Sleepless cities revealed as one in three adults suffer from insomnia. In: Aviva, editor. Aviva Wellbeing Report: Aviva Wellbeing Report; 2017.

[3] Robertson MD, Russell-Jones D, Umpleby AM, Dijk D-J. Effects of three weeks of mild sleep restriction implemented in the home environment on multiple metabolic and endocrine markers in healthy young men. Metabolism. 2013;62:204-11.

[4] Refinetti R, Menaker M. The circadian rhythm of body temperature. Physiology & behavior. 1992;51:613-37.

[5] Dickinson DL, Wolkow AP, Rajaratnam SMW, Drummond SPA. Personal sleep debt and daytime sleepiness mediate the relationship between sleep and mental health outcomes in young adults. Depress Anxiety. 2018.

[6] Knutson KL, von Schantz M. Associations between chronotype, morbidity and mortality in the UK Biobank cohort. Chronobiology international. 2018:1-9.

[7] Smith RS, Efron B, Mah CD, Malhotra A. The impact of circadian misalignment on athletic performance in professional football players. Sleep. 2013;36:1999-2001.

[8] Schaefer EW, Williams MV, Zee PC. Sleep and circadian misalignment for the hospitalist: a review. J Hosp Med. 2012;7:489-96.

690 [9] Akerstedt T, Fredlund P, Gillberg M, Jansson B. A prospective study of fatal occupational
691 accidents -- relationship to sleeping difficulties and occupational factors. J Sleep Res. 2002;11:69-71.
692 [10] Burgess HJ, Fogg LF. Individual differences in the amount and timing of salivary melatonin
693 secretion. PloS one. 2008;3:e3055.
694 [11] Kudielka BM, Federenko IS, Hellhammer DH, Wüst S. Morningness and eveningness: the free
695 cortisol rise after awakening in "early birds" and "night owls". Biological Psychology. 2006;72:141-6.
696 [12] Archer SN, Viola AU, Kyriakopoulou V, von Schantz M, Dijk D-J. Inter-individual differences
697 in habitual sleep timing and entrained phase of endogenous circadian rhythms of BMAL1, PER2 and
698 PER3 mRNA in human leukocytes. Sleep. 2008;31:608-17.
699 [13] Roenneberg T, Kuehnle T, Juda M, Kantermann T, Allebrandt K, Gordijn M, et al. Epidemiology
700 of the human circadian clock. Sleep Med Rev. 2007;11:429-38.
701 [14] Shirayama M, Shirayama Y, Iida H, Kato M, Kajimura N, Watanabe T, et al. The psychological
702 aspects of patients with delayed sleep phase syndrome (DSPS). Sleep Med. 2003;4:427-33.
703 [15] Zhu L, Zee PC. Circadian Rhythm Sleep Disorders. Neurologic clinics. 2012;30:1167-91.
704 [16] Mongrain V, Carrier J, Dumont M. Circadian and homeostatic sleep regulation in morningness-
705 eveningness. J Sleep Res. 2006;15:162-6.
706 [17] Merikanto I, Lahti T, Kronholm E, Peltonen M, Laatikainen T, Vartiainen E, et al. Evening types
707 are prone to depression. Chronobiology international. 2013;30:719-25.
708 [18] Giannotti F, Cortesi F, Sebastiani T, Ottaviano S. Circadian preference, sleep and daytime
709 behaviour in adolescence. Journal of sleep research. 2002;11:191-9.
710 [19] Facer-Childs ER, Boiling S, Balanos GM. The effects of time of day and chronotype on cognitive
711 and physical performance in healthy volunteers. Sports medicine - open. 2018;4:47.
712 [20] Roenneberg T, Merrow M. Entrainment of the human circadian clock. Cold Spring Harb Sym.
713 2007;72:293-9.
714 [21] Khalsa SB, Jewett ME, Cajochen C, Czeisler CA. A phase response curve to single bright light
715 pulses in human subjects. J Physiol. 2003;549:945-52.
716 [22] St Hilaire MA, Gooley JJ, Khalsa SB, Kronauer RE, Czeisler CA, Lockley SW. Human phase
717 response curve to a 1 h pulse of bright white light. J Physiol. 2012;590:3035-45.
718 [23] Crowley SJ, Eastman CI. Phase advancing human circadian rhythms with morning bright light,
719 afternoon melatonin, and gradually shifted sleep: can we reduce morning bright-light duration? Sleep
720 Medicine. 2015;16:288-97.
721 [24] Kelly TL, Kripke DF, Hayduk R, Ryman D, Pasche B, Barbault A. Bright light and LEET effects
722 on circadian rhythms, sleep and cognitive performance. Stress Medicine. 1997;13:251-8.
723 [25] Zeitzer JM, Fisicaro RA, Ruby NF, Heller HC. Millisecond Flashes of Light Phase Delay the
724 Human Circadian Clock during Sleep. Journal of Biological Rhythms. 2014;29:370-6.
725 [26] Mistlberger RE, Skene DJ. Nonphotic Entrainment in Humans? Journal of Biological Rhythms.
726 2005;20:339-52.
727 [27] Wehr TA, Wirz-Justice A, Goodwin FK, Duncan W, Gillin JC. Phase advance of the circadian
728 sleep-wake cycle as an antidepressant. Science. 1979;206:710-3.
729 [28] Miyazaki T, Hashimoto S, Masubuchi S, Honma S, Honma K-I. Phase-advance shifts of human
730 circadian pacemaker are accelerated by daytime physical exercise. American Journal of Physiology-
731 Regulatory, Integrative and Comparative Physiology. 2001;281:R197-R205.
732 [29] Wehrens SMT, Christou S, Isherwood C, Middleton B, Gibbs MA, Archer SN, et al. Meal
733 Timing Regulates the Human Circadian System. Curr Biol. 2017;27:1768-75 e3.
734 [30] Damiola F, Le Minh N, Preitner N, Kornmann B, Fleury-Olela F, Schibler U. Restricted feeding
735 uncouples circadian oscillators in peripheral tissues from the central pacemaker in the suprachiasmatic
736 nucleus. Genes Dev. 2000;14:2950-61.
737 [31] Eastman CI, Hoese EK, Youngstedt SD, Liu LW. Phase-Shifting Human Circadian-Rhythms
738 with Exercise during the Night-Shift. Physiology & Behavior. 1995;58:1287-91.
739 [32] Buxton OM, Lee CW, L'Hermite-Balériaux M, Turek FW, Van Cauter E. Exercise elicits phase
740 shifts and acute alterations of melatonin that vary with circadian phase. American Journal of
741 Physiology-Regulatory, Integrative and Comparative Physiology. 2003;284:R714-R24.
742 [33] Youngstedt SD, Elliott JA, Kripke DF. Human Circadian Phase-Response Curves for Exercise. J
743 Physiol. 2019.

744 [34] Joyce K, Pabayo R, Critchley J, Bambra C. Flexible working conditions and their effects on
745 employee health and wellbeing. Cochrane Database Syst Rev. 2009;2.
746 [35] Lo JC, Lee SM, Lee XK, Sasmita K, Chee N, Tandi J, et al. Sustained benefits of delaying school
747 start time on adolescent sleep and well-being. Sleep. 2018;41.
748 [36] Paul MA, Gray GW, Lieberman HR, Love RJ, Miller JC, Trouborst M, et al. Phase advance with
749 separate and combined melatonin and light treatment. Psychopharmacology. 2011;214:515-23.
750 [37] Petit E, Mougin F, Bourdin H, Tio G, Haffen E. Impact of 5-h phase advance on sleep
751 architecture and physical performance in athletes. Applied physiology, nutrition, and metabolism =
752 Physiologie appliquee, nutrition et metabolisme. 2014;39:1230-6.
753 [38] Roenneberg T, Wirz-Justice A, Merrow M. Life between clocks: daily temporal patterns of
754 human chronotypes. J Biol Rhythms. 2003;18:80-90.
755 [39] Moreno C, Vasconcelos S, Marqueze E, Lowden A, Middleton B, Fischer F, et al. Sleep patterns
756 in Amazon rubber tappers with and without electric light at home. Sci Rep-Uk. 2015;5:14074.
757 [40] Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale.
758 Sleep. 1991;14:540-5.
759 [41] Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality
760 Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28:193-213.
761 [42] McNair D M LMDLF. Manual for the profile of mood states. Educational and Industrial Testing
762 Service, San Diego, CA. 1971;27:p.
763 [43] Lovibond PF, Lovibond SH. The Structure of Negative Emotional States - Comparison of the
764 Depression Anxiety Stress Scales (Dass) with the Beck Depression and Anxiety Inventories. Behav
765 Res Ther. 1995;33:335-43.
766 [44] Åkerstedt T, Gillberg M. Subjective and objective sleepiness in the active individual. Int J
767 Neurosci. 1990;52:29-37.
768 [45] Loh S, Lamond N, Dorrian J, Roach G, Dawson D. The validity of psychomotor vigilance tasks
769 of less than 10-minute duration. Behav Res Methods Instrum Comput. 2004;36:339-46.
770 [46] Bohannon RW. Dynamometer measurements of hand-grip strength predict multiple outcomes.
771 Perceptual and motor skills. 2001;93:323-8.
772 [47] Marcora SM. Do we really need a central governor to explain brain regulation of exercise
773 performance? European Journal of Applied Physiology. 2008;104:929-31.
774 [48] Rosenthal NE, Joseph-Vanderpool JR, Levendosky AA, Johnston SH, Allen R, Kelly KA, et al.
775 Phase-shifting effects of bright morning light as treatment for delayed sleep phase syndrome. Sleep.
776 1990;13:354-61.
777 [49] Rosenthal NE, Sack DA, Gillin JC, Lewy AJ, Goodwin FK, Davenport Y, et al. Seasonal
778 affective disorder: a description of the syndrome and preliminary findings with light therapy. Arch
779 Gen Psychiat. 1984;41:72-80.
780 [50] Chang A-M, Aeschbach D, Duffy JF, Czeisler CA. Evening use of light-emitting eReaders
781 negatively affects sleep, circadian timing, and next-morning alertness. Proceedings of the National
782 Academy of Sciences. 2015;112:1232-7.
783 [51] Santhi N, Thorne HC, van der Veen DR, Johnsen S, Mills SL, Hommes V, et al. The spectral
784 composition of evening light and individual differences in the suppression of melatonin and delay of
785 sleep in humans. Journal of pineal research. 2012;53:47-59.
786 [52] Krauchi K, Cajochen C, Werth E, Wirz-Justice A. Alteration of internal circadian phase
787 relationships after morning versus evening carbohydrate-rich meals in humans. Journal of Biological
788 Rhythms. 2002;17:364-76.
789 [53] Alvaro PK, Roberts RM, Harris JK. The independent relationships between insomnia,
790 depression, subtypes of anxiety, and chronotype during adolescence. Sleep medicine. 2014;15:934-41.
791 [54] Levandovski R, Dantas G, Fernandes LC, Caumo W, Torres I, Roenneberg T, et al. Depression
792 scores associate with chronotype and social jetlag in a rural population. Chronobiology international.
793 2011;28:771-8.
794 [55] Krystal AD. PSYCHIATRIC DISORDERS AND SLEEP. Neurologic clinics. 2012;30:1389-413.
795 [56] Dinges DF, Pack F, Williams K, Gillen KA, Powell JW, Ott GE, et al. Cumulative sleepiness,
796 mood disturbance, and psychomotor vigilance performance decrements during a week of sleep
797 restricted to 4-5 hours per night. Sleep. 1997;20:267-77.
798 [57] Dinges DF. An overview of sleepiness and accidents. Journal of sleep research. 1995;4:4-14.

[58] Connor J, Whitlock G, Norton R, Jackson R. The role of driver sleepiness in car crashes: a systematic review of epidemiological studies. Accident Analysis & Prevention. 2001;33:31-41.
[59] Chong MS, Ayalon L, Marler M, Loredo JS, Corey-Bloom J, Palmer BW, et al. Continuous positive airway pressure reduces subjective daytime sleepiness in patients with mild to moderate Alzheimer's disease with sleep disordered breathing. J Am Geriatr Soc. 2006;54:777-81.
[60] Phipps-Nelson J, Redman JR, Dijk D-J, Rajaratnam SM. Daytime exposure to bright light, as compared to dim light, decreases sleepiness and improves psychomotor vigilance performance. Sleep. 2003;26:695-700.
[61] Rogers AE, Aldrich MS, Lin X. A comparison of three different sleep schedules for reducing daytime sleepiness in narcolepsy. Sleep. 2001;24:385-91.
[62] Kaida K, Takahashi M, Akerstedt T, Nakata A, Otsuka Y, Haratani T, et al. Validation of the Karolinska sleepiness scale against performance and EEG variables. Clin Neurophysiol. 2006;117:1574-81.
[63] Anderson C, Chang AM, Sullivan JP, Ronda JM, Czeisler CA. Assessment of Drowsiness Based on Ocular Parameters Detected by Infrared Reflectance Oculography. J Clin Sleep Med. 2013;9:907-20.
[64] Borghini G, Astolfi L, Vecchiato G, Mattia D, Babiloni F. Measuring neurophysiological signals in aircraft pilots and car drivers for the assessment of mental workload, fatigue and drowsiness. Neuroscience & Biobehavioral Reviews. 2014;44:58-75.
[65] George C. Sleep· 5: Driving and automobile crashes in patients with obstructive sleep apnoea/hypopnoea syndrome. Thorax. 2004;59:804-7.
[66] Lenné MG, Triggs TJ, Redman JR. Time of day variations in driving performance. Accident Analysis & Prevention. 1997;29:431-7.
[67] Facer-Childs E, Brandstaetter R. The Impact of Circadian Phenotype and Time since Awakening on Diurnal Performance in Athletes. Curr Biol. 2015;25:518-22.
[68] Rae DE, Stephenson KJ, Roden LC. Factors to consider when assessing diurnal variation in sports performance: the influence of chronotype and habitual training time-of-day. Eur J Appl Physiol. 2015;115:1339-49.
[69] Tamm AS, Lagerquist O, Ley AL, Collins DF. Chronotype Influences Diurnal Variations in the Excitability of the Human Motor Cortex and the Ability to Generate Torque during a Maximum Voluntary Contraction. Journal of Biological Rhythms. 2009;24:211-24.
[70] Banks S, Dinges DF. Behavioral and physiological consequences of sleep restriction. J Clin Sleep Med. 2007;3:519-28.
[71] Lim J, Dinges DF. A meta-analysis of the impact of short-term sleep deprivation on cognitive variables. Psychol Bull. 2010;136:375-89.
[72] Kline CE, Durstine JL, Davis JM, Moore TA, Devlin TM, Youngstedt SD. Circadian Rhythms of Psychomotor Vigilance, Mood, and Sleepiness in the Ultra-Short Sleep/Wake Protocol. Chronobiology International. 2010;27:161-80.
[73] Basner M, Mollicone D, Dinges DF. Validity and Sensitivity of a Brief Psychomotor Vigilance Test (PVT-B) to Total and Partial Sleep Deprivation. Acta Astronaut. 2011;69:949-59.
[74] Wisløff U, Castagna C, Helgerud J, Jones R, Hoff J. Strong correlation of maximal squat strength with sprint performance and vertical jump height in elite soccer players. Brit J Sport Med. 2004;38:285-8.
[75] Bland JM, Altman DG. Comparisons against baseline within randomised groups are often used and can be highly misleading. Trials. 2011;12:264.

Supplemental Information

Supplemental Table 1 (S1). Summary of demographic, mental well-being, nutrition related, actigraphic and physiological details pre-intervention for experimental and control groups. [2]

Variable Measured (mean ± SEM)	Experimental Group	Control Group (Con)	Significance
Sample Size	N = 12	N = 10	n/a
Demographic variables			
Age (years, mean ± SD)	21.7 ± 2.8	20.9 ± 3.9	p = 0.60[b]
Percentage of Males/Females (%)	M: 25	M: 40	p = 0.65[c]
	F: 75	F: 60	
BMI (mean ± SD)	22.9 ± 3.2	22.6 ± 2.1	p = 0.81[a]
MCTQ Score (hh:mm)	07:15 ± 00:27	06:24 ± 00:14	p = 0.12[a]
Nutrition related variables			
Average days per week eating breakfast (days)	4.09 ± 0.62	4.70 ± 0.84	p = 0.38[a]
Average breakfast time (hh:mm)	10:33 ± 00:25	10:01 ± 00:34	p = 0.47[a]
Average lunch time (hh:mm)	14:36 ± 00:30	13:27 ± 00:17	p = 0.10[b]
Average dinner time (hh:mm)	20:07 ± 00:45	18:49 ± 00:17	p = 0.34[b]
Mental Well-Being Variables			
Pittsburgh Sleep Quality Index (PSQI)	4.83 ± 0.71	5.30 ± 0.80	p = 0.67[a]
Profile of Mood States (POMS)	10.33 ± 6.15	8.50 ± 5.74	p = 0.54[a]
Epworth Sleepiness Scale (ESS)	7.08 ± 1.16	9.00 ± 0.99	p = 0.24[a]
Depression Anxiety and Stress Scale (DASS)	19.83 ± 3.36	13.78 ± 3.66	p = 0.24[a]
Actigraphy Variables and Non-Parametric Circadian Rhythm Analysis (NPCRA)			
Bed Time (hh:mm)	02:19 ± 00:25	01:16 ± 00:30	p = 0.15[a]
Get Up Time (hh:mm)	10:46 ± 00:23	09:54 ± 00:31	p = 0.17[a]
Sleep Onset (hh:mm)	02:46 ± 00:26	01:37 ± 00:30	p = 0.13[a]
Wake Up Time (hh:mm)	10:31 ± 00:23	09:37 ± 00:29	p = 0.14[a]
Sleep Duration (h)	7.75 ± 0.20	7.81 ± 0.20	p = 0.91[a]
Sleep Efficiency (%)	76.80 ± 1.48	78.26 ± 1.91	p = 0.55[a]
Sleep Latency (hh:mm)	00:27 ± 00:04	00:21 ± 00:03	p = 0.34[a]
Fragmentation Index	34.86 ± 3.63	30.47 ± 2.27	p = 0.48[b]
Inter-daily Stability	0.38 ± 0.03	0.38 ± 0.05	p = 0.26[b]
Intra-daily Variability	0.85 ± 0.05	0.79 ± 0.06	p = 0.25[a]
L5 Onset (hh:mm)	03:57 ± 00:27	03:03 ± 00:34	p = 0.40[a]

[2] Values are shown as mean ± SEM unless specified. Significance is shown with [a]unpaired two sample t-tests, [b]non-parametric Mann-Whitney or [c]Fisher's exact test. Phase angle is calculated by the interval time between dim light melatonin onset and sleep onset.

M10 Onset (hh:mm)	12:43 ± 00:37	12:14 ± 00:36	p = 0.96[a]
Relative Amplitude	0.83 ± 0.03	0.82 ± 0.03	p = 0.26[b]
Physiological Variables			
Dim Light Melatonin Onset (DLMO) (hh:mm)	00:02 ± 00:34	23:18 ± 00:54	p = 0.97[a]
Phase Angle (h)	2.94 ± 0.29	2.47 ± 0.72	p = 0.30[b]
Peak Melatonin Concentration (pg/nl)	26.89 ± 3.98	21.02 ± 5.85	p = 0.22[a]
Peak Time of Melatonin (hh:mm)	02:06 ± 00:28	02:01 ± 00:33	p = 0.73[a]
Cortisol Peak Time (hh:mm)	11:19 ± 00:31	11:05 ± 00:36	p = 0.78[a]
Peak Cortisol Concentration (nmol/l)	23.31 ± 2.39	22.64 ± 3.57	p = 0.79[b]
Cortisol Awakening Response (%)	113.16 ± 33.71	112.37 ± 45.28	p = 0.64[b]
Area Under the Curve (total time)	98.83 ± 10.47	104.41 ± 14.01	p = 0.75[a]

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