Influence of light on exercise performance in athletes and overweight individuals

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List of Abbreviations

95% CI	95% confidence interval
BLUE	blue light group
BRIGHT	bright light group
CONTROL	control light group
C-process	circadian timing process
MSFsc	midpoint of sleep on free days and correcting it for oversleep during the work week
SCN	suprachiasmatic nucleus
S-process	homeostatic (sleep)-process
$\dot{V}O_2max$	maximum oxygen uptake

Summary

Background

Athletes often need to compete at times of the day that do not meet their time of peak performance. To comply with television prime time finals often take place in the late evening, although at this time of the day there seems to be a fast decrease in performance. Bright light exposure increases alertness, reduces sleepiness and suppresses the hormone melatonin. These mechanisms induced by light exposure may prevent the time of the day related decrease in performance.

In contrast to sport competitions, many exercise interventions in clinics or rehabilitation centers often take place in the morning to comply with the staffs working schedules. However, especially in the morning lower exercise intensities are chosen by most people. Light exposure has been show to increase mood and alertness, which may lead to higher training intensity and in mid- and long term to body mass reduction.

Aims:

The aims of this PhD project were: (1) to evaluate a possible positive dose-response relationship between bright light exposure and maximum cycling performance in athletes, (2) to investigate the effects of evening bright and blue light exposures on maximum cycling performance and (3) acoustic reaction time and handgrip strength in elite athletes and (4) to investigate the effect of morning bright light exposure on self-chosen exercise intensity and mood in overweight individuals.

Methods:

During this PhD project three studies were performed. In study 1 data from previous studies conducted by Prof. Schmidt-Trucksäss were analyzed to evaluate a possible dose-response relationship between bright light exposure and maximum cycling performance. In the analyzed studies participants were exposed to bright light and a control light condition in a cross-over design only prior to or prior to and during a 40-minute time trial on a bicycle ergometer. The intensity of bright light and control light was identical in all studies but the studies differed in exposure durations. To compare the differences in the work performed (kJ) during the time trial within one group (i.e. one duration of light exposure) a paired t-test was used. Differences between the groups were tested with analyses of variance with the dose of light exposure (high, medium and low) and the difference in the work performed after bright and control light exposure.

Based on the results of study 1 two further studies (randomized controlled trials) were planned and conducted. In study 2 (first trial; Clinicaltrials.gov ID: NCT02203539) male elite

athletes performed a cardiopulmonary exercise test to assess maximum oxygen uptake ($\dot{V}O_2max$) which determines the level of fitness. One week later participants performed a reaction time task and maximum handgrip strength test before they were exposed to either bright, monochromatic blue or a control light condition in the evening for 60 minutes. The light exposure started 17 hours after each individuals' midpoint of sleep to test all participants at the same internal time. Immediately after the light exposure participants performed the reaction time task and handgrip strength test again and then a 12-minute time trial on a bicycle ergometer. An analysis of covariance with adjustment for $\dot{V}O_2max$ from the baseline test was run to compare the differences in the work performed (kJ) between the three groups. Additionally, linear regression analyses were used to estimate the effect of melanopic light exposure on melatonin suppression and end-spurt performance, which was defined as the ratio of the performance during the first and last minute of the time trial. Analyses of covariance with adjustment for the values before the light exposure were used to compare acoustic reaction time and maximum handgrip strength after the light exposure between the three groups.

In study 3 (second trial; Clinicaltrials.gov ID: NCT02636335) overweight individuals performed a cardiopulmonary exercise test to assess $\dot{V}O_2max$. Two days later participants performed a 30-minute exercise session with self-chosen exercise intensity for familiarization. Three to seven days later participants were exposed to either bright or a control light condition in the morning for 30 minutes prior to and during a 30-minute exercise session with self-chosen exercise intensity on a bicycle ergometer starting at 08:00. Participants also filled out a multidimensional mood questionnaire including the three domains "good-bad", "awake-tired", and "calm-nervous" all of which are bipolar scales. This questionnaire was answered prior to the light exposure, after the light exposure but prior to the exercise session and after the exercise session with persisting light exposure. Analyses of covariance with adjustment for $\dot{V}O_2max$ were used to compare the difference in mean power output (W) during the exercise session between the two groups. Multivariate analyses were used to test for differences in mood before the light exposure, after the light exposure and after the exercise session between the groups.

Results:

Publication 1: Dose-response relationship between light exposure and cycling performance in athletes [1]

In athletes there was no significant difference in the work performed (kJ) during the time trial between bright light and control light in those participants that were exposed to light for only 60 minutes prior to the time trial or those participants exposed to 60 minutes prior to and during the time trial. In contrast athletes exposed to light for 120 minutes prior to and during the time trial performed significantly more work after bright light exposure. Further, there was a significant positive dose-response relationship between the duration of light exposure and the work performed over the three doses.

Publication 2: Effects of bright and blue light exposure on maximum cycling performance in elite athletes [2]
In elite athletes evening bright or blue light exposure for 60 minutes in duration immediately before a 12-minute time trial did not significantly increase the work performed (kJ) compared to a control condition. Athletes exposed to high doses of melanopic light showed a significantly higher performance gain during the time trial, defined as the ratio of the work performed in the first and last minute of the time trial. This was associated with a stronger decrease in melatonin. However, there were no significant changes in sleepiness, motivation or mood through the light exposure between bright or blue light compared to control light. No severe adverse events occurred in any group and minor adverse events (e.g. glare, headache) were reported as often in the bright light group as reported in the control group.

Publication 3: Effects of bright and blue light exposure on simple acoustic reaction time and maximum handgrip strength in elite athletes [3]
In elite athletes evening bright or blue light exposure for 60 minutes in duration immediately before a simple acoustic reaction time task and a maximum handgrip strength test did not significantly reduce reaction time (ms) or increase handgrip strength (kg) compared to a control condition. Further, the actual light intensities reaching the participants' eyes were lower than intended according to the protocol and showed a high variation between participants.

Publication 4: Effect of light exposure on self-chosen exercise intensity and mood in overweight individuals [4]
In overweight individuals morning bright light exposure for 30 minutes in duration prior to and during a 30-minute exercise session did not increase self-chosen exercise intensity (mean power output in Watts) compared to a control condition. None of the three domains of the multidimensional mood questionnaire was significantly altered by light exposure.

Conclusions:

There is a positive dose-response relationship between the duration athletes are exposed to bright light and the maximum cycling performance in a subsequent 40-minute time trial. To increase maximum performance significantly compared to control condition a pre-exercise exposure of 120 minutes seemed to be necessary, because participants with shorter exposure durations showed no higher performance. Exposure to high doses of melanopic light in the evening improved end-spurt performance in elite athletes resulting in a potentially meaningful enhancement of performance. Although bright light did not significantly increase maximum performance further studies are recommended, because the reported difference between bright and control represents a relevant advantage in sports competitions. Acoustic reaction time and maximum handgrip strength were not improved by light exposure in elite athletes. Likewise, in overweight individuals bright light exposure in the morning did neither increase self-chosen exercise intensity in a 30-minute exercise session nor improve mood compared to exposure to control light. Athletes and overweight individuals exposed to bright light showed not more adverse events than participants in the control condition.

Chapter 1

Introduction

Chapter 1 Introduction

Sports competitions take place at different times of the day. Finals are often scheduled around best broadcasting times on television to reach a high audience share, while qualification rounds are often scheduled earlier during the day. Because, physical performance varies over the course of a day [5,6] an athlete`s time of peak performance does consequently not always meet with the time of the competition resulting in disadvantages for some athletes. Training at a specific time of the day can shift the time of peak performance [5,7,8], but because athletes have to compete at different times of the day in a short time frame during sport events methods to shift the time of peak performance need to be applicable much faster. Exposure to light may represent such a method to slow down the decrease of physical performance in the evening. In contrast to sports competitions many exercise interventions in clinics or rehabilitation centers take place in the morning to comply with staffs' working schedules, although this is not an ideal time for exercise for these individuals. At this time of the day, self-chosen exercise intensities are rather low [9] and the subjective rating of perceived exertion in endurance [10] as well as strength exercise [11] is higher than during evening exercise with equal exercise intensity. Light exposure may help to increase exercise intensity in the morning. Especially overweight individuals may benefit from this.
In this PhD thesis data from previous studies were analysed to investigate a possible dose-response relationship between light exposure and physical performance (study 1). In a further step, the possibility of light exposure to improve maximum endurance performance, maximum handgrip strength and simple acoustic reaction time by influencing the time of the day related decrease in physical performance during the evening was investigated. For this, a study was conducted with elite athletes (study 2). Finally, the gained knowledge was transferred into a public health setting by conducting a further study (study 3) which investigated the possible effects of light exposure on self-chosen exercise intensity in overweight individuals in the morning.

1.1 Physiological background

The sleep-wake cycle is regulated by the homeostatic (sleep)-process (S-process) and the circadian timing process (C-process). This two process model was originally introduced 1982 [12] to predict sleep regulation and is today also used to describe neurobehavioral performance [13]. The homeostatic process describes that with elapsed time awake the demand for sleep (i.e. sleep pressure) continuously accumulates asymptotically over time until an individual falls asleep leading to revolving sleep pressure. Especially during non-rapid eye movement or slow-wave sleep, sleep pressure decreases [13,14]. While the S-process can be imagined as an hourglass that only follows one direction until it is turned around the C-process has to be imagined as a clock [15] with a 24-hour oscillation over the day with periodic acrophases (i.e. highest point of the curve) and nadirs (i.e. lowest point of the curve).

1.1.1 Circadian rhythms

The C-process is mainly controlled by the suprachiasmatic nucleus (SCN) which is located in the anterior hypothalamus and referred to as the brain's master clock [14] and has the strongest influence on body functions compared to various smaller body clocks [16]. These body functions show oscillatory patterns over a 24-hour period which appear independently of an individual being awake or asleep. Individuals in a constant routine (room temperature 22°C, humidity 60%, light < 50 lx, no external sound, bed rest in 45° angle) show oscillatory variations in core body and skin temperature, heart rate and urine flow [17]. Metabolic and endocrine systems also underlie the body clock's regulation resulting in diurnal variations in cerebral blood flow, systolic blood pressure, cortisol, growth hormone, thyrotrophin and melatonin [18]. In fact, the phase of the circadian rhythm can be determined by the endogenous melatonin secretion, with lowest secretion appearing during minimal circadian sleep propensity [13]. Because melatonin is a moderator for core body temperature, the variation in core body temperature during the day is vice versa to melatonin [19] and can also be used to describe the circadian phase [20]. If the C-process is imagined as a clock, then the core body temperature and melatonin represent the hands of the clock.

Consequently, not only metabolic functions, but also cognitive performance (e.g. calculation performance or working memory) shows circadian variations [21–23]. Schmidt et al. [13] provide an overview on studies investigating circadian variations in cognitive performance. Because sleepiness and alertness influence cognitive performance [13], even if not systematically, they are of crucial importance. Although alertness shows a diurnal variation during constant routine [23] which consists through sleep deprivation [24], alertness is also affected by the S-process. Subjective alertness is therefore the outcome of the interaction of the C-process and the S-process, which means that alertness and sleepiness are not necessarily reciprocal [13].

Variations in alertness obviously can affect sport performance comprising relatively high cognitive demands like team game sports with complex tactics. But, even simple cognitive tasks relevant to sports like psychomotor vigilance (i.e. reaction time) are influenced by sleep pressure [25]. Further, high levels of subjective sleepiness on the other hand may decrease athletes` and non-athletes` motivation to perform with maximal or even submaximal effort. The previously described circadian variations of metabolic and endocrine systems could influence athletes` performance in different ways. Exercise in high ambient air temperature (and humidity) is tolerated longer after pre-cooling [26]. Starting long duration exercises at the nadir of the core body temperature therefore may be beneficial. In contrast, short duration endurance [27] and strength exercise [28] require warmup for optimal performance and are therefore expected to be higher around the peak of core body temperature, although body temperature alone does not account for the diurnal variation in physical performance [27]. This means, that methods to decelerate or even stop the circadian related drop in core body temperature, the decrease in alertness and increase in sleepiness, which all appear in the late evening may lead to performance enhancement.

1.1.2 Chronotypes

The C-process and therefore the oscillation of different body functions and their patterns are similar in all humans but can be time shifted [29], resulting in some people having their peaks and nadirs of metabolic and endocrine functions earlier during the 24-hour day than others. This means that while external time is the same for all individuals living in the same time zone, by definition internal time strongly differs between chronotypes. While repeated measures of melatonin or core body temperature are necessary to describe the oscillation of the C-process in detail, the chronotype can easily be assessed by questionnaires. Different tools like the Morningness-Eveningness Questionnaire [30] the Circadian Energy Scale [31] or the Munich Chronotype Questionnaire [32] are available to categorize chronotypes. All questionnaires predominantly define chronotypes through the most visible differences in individuals, the sleep-wake patterns. Early chronotypes sleep earlier and wake up earlier, while late chronotypes sleep later and get up later. Due to social duties, individuals have to adapt their sleep-wake pattern on workdays to their working schedule and cannot freely choose sleeping time. On free days, they have to compensate for the sleep deficit accumulated over the working week and sleep longer. The Munich Chronotype Questionnaire can adjust for the accumulated sleep-debt during the work week by calculating the Midpoint of Sleep on Free days and correcting it for oversleep during the work week (MSFsc) [33]. Early and late chronotypes are the extremes. Based on the MSFsc the majority of people are intermediate chronotypes with a near Gaussian distribution, but a slight overrepresentation of late chronotypes [33]. Children are more frequently early chronotypes, but with progressing age the MSFsc gets later until it reaches its peak at an age of around 20 years. With increasing age this effects revolves and MSFsc becomes earlier again. Adult females show earlier MSFsc than males of the same age [34]. This sex difference in chronotypes was also observed in other instruments assessing chronotypes [35]. Unfortunately, these sex and age differences in chronotypes are often ignored when discussing study results regarding diurnal variation in physical performance. Previous studies mainly tested young males which strongly affects the generalizability of the results. However, in competitive long-distance endurance athletes there is a selection bias regarding chronotypes. From South-African runners 65% were early, 32% intermediate and only 3% late chronotypes. In Dutch runners the difference is less pronounced, with 50% early, 44% intermediate and 6% late chronotypes, but still significantly different compared to a control group [36]. In contrast, in team sport athletes (i.e. hockey players) chronotypes are similar to the normative population with 28% being early, 48% intermediate and 24% late chronotypes, respectively [6]. No data is available on short-distance or strength athletes. These differences in time of peak performance lead to clear disadvantages for unfavorable chronotypes. Especially early chronotypes who have to compete in the evening are handicapped most. Changes in competition schedules [37,38] have therefore been claimed by different groups, but were ignored so far. Light exposure is not expected to increase maximum performance, but to reduce the performance decrease in the late evening and therefore may offer an option to equalize chances for athletes without changes in completion schedules. Similar to certain drugs (e.g. asthma inhalers) help athletes to reduce or eliminate disadvantages light exposure does not meet the definition of doping.

1.2 Diurnal variations in performance

A common misconception in sport science is the idea that circadian variations in physical performance have already been investigated. To investigate circadian variations in physical performance the influence of the C-process has to be isolated from the influence of the S-process. In detail, this means that at every measurement point the sleep pressure needs to be at an equal level regardless of the external time. To achieve this, special protocols that include constant routines [39], multiple naps, phase shifts [19], free running or forced desynchronization [40] are required. While a cognitive test can be repeated several times a day, physical performance testing requires up to 48 or 72 hours of regeneration (e.g. maximum strength test) making these protocols partly useless in sport science or so time consuming and costly that they can hardly be applied. By definition constant routine protocols are not applicable to investigate physical performance. Multiple naps are reliable to perform multiple tests at the same day by resetting sleep pressure through short sleep intervals, but since physical performance requires regeneration time this protocol is not applicable in sport science. Light exposure can influence physical performance [41] which makes phase shift protocols (i.e. using light to shift the circadian phase) useless. The remaining two protocols of free running and forced desynchronization require several days of preparation time in a highly controlled environment (e.g. no time clues, constant room temperature, air humidity and light intensity) before the first performance test can be performed and subsequently several more days in the same environment for the remaining test sessions at different times of the day. This high effort was avoided due to cost-benefit reasons in previous studies resulting in the fact that only diurnal variations have been investigated so far. An attempt to indirectly investigate circadian variations in performance is to analyze matches taking place after travels over time zones. These travels result in two teams competing at different internal times and therefore closer or further away from the time of peak performance. An analysis of 40 seasons of the National Football League showed no difference in matches won between west and east coast teams during the day, but a significant advantage for west coast teams during evening matches [37]. This is explained by the time shift of three hours through the travel. When matches take place at the west coast in the evening it is close to the time of peak performance for players from the west coast, but for players arriving from the east coast it is nighttime. For matches taking place at the east coast it is evening for the players from the east coast and late afternoon for the players from the west coast resulting in no disadvantage for the travelling team. Similar conclusions were drawn from the matches of the last five years from the National Basketball Association and the National Hockey League. There was a correlation between the number of time zones traveled and winning percentages. The number of time zones travelled explained 19% of winning percentage in the National Basketball Association and 23% in the National Hockey League [38]. Analyses of five seasons of Australian National Netball competitions also revealed no difference in points scored when players travelled across one time zone or from north to south, but when two time zones were crossed there was a significant difference between points scored by the home and the away team if traveled from east to west [42].

1.2.1 Diurnal variation in endurance performance

Diurnal variations in endurance performance are dependent on fitness level and type of exercise. First studies investigating this innovative approach showed that mean power output in a 30-min time trial was highest around 18:00 [43], with trained athletes showing a higher amplitude in performance than untrained participants. Similarly, power output in a 16.1 km time trial in cyclists [27] and average speed in ultra-distance cyclists [44] showed an acrophase of performance in the late afternoon and early evening. Further, a significant difference of 4% in $\dot{V}O_2$max in adolescent males was reported with higher performance at 12:00 than 16:00 [45]. In contrast, no significant differences in a 15-min time trial were reported in highly-trained competitive cyclists [46]. Time to exhaustion tests at submaximal [47] and maximal exercise [48] also revealed no diurnal variation in endurance performance. Similarly, $\dot{V}O_2$-kinetics and end-exercise $\dot{V}O_2$max in heavy exercise in adults seems to be unaffected by daytime [49]. In general, the studies agree that if there is a peak in performance it appears in the late afternoon or early evening. However, the previously mentioned studies have to be interpreted very carefully, because all studies had low sample sizes (n≤10) and partially measured performance only at two [27,47], three [46] or four times of the day [48] making it likely that the true peak and nadir of performance are missed. Further, recent studies show that the habitual exercise time influences the time of peak performance [8]. In detail, swimmers performing 200-m time trials at 06:30 and 18:30 showed no differences in performance when analyzed as one group, but athletes habitually training in the morning showed significant higher performance in the morning. Additionally, an individual`s chronotype strongly influences not only the time of peak performance but also the difference between the peak and nadir in performance. In detail, early chronotypes reach their peak performance at 12.2 ± 1.4 h with a difference in performance between the peak and lowest performance of 7.6% ± 1.2%. In intermediate chronotypes the corresponding values are 15.8 ± 0.5 h and 10.0% ± 1.6% and in late chronotypes 19.7 ± 0.7 h and 26.2% ± 4.0%, respectively [6]. Although Facer-Childs et al. [6] conducted the study considering the most confounding factors so far, it still shows methodological issues. Habitual training time was not considered as suggested by Rae et al. [8] and no exhaustion criteria were determined. Exhaustion criteria are crucial to identify if the underlying mechanism that causes diurnal variations in performance are physiologically or psychophysiological. If participants were exhausted in all tests the reason for diurnal variations would be physiological, because it would mean that the participants just could not perform better at this time of the day. If participants are not exhausted in all tests diurnal variation could be expected to be limited by psychophysiological factors, for example if an athlete is less motivated to perform maximally in the morning (e.g. low motivation at 07:00 in late chronotypes). Further limitations of previous studies are; that participants were mainly moderately-trained team players raising the question if the results are transferable to elite athletes for whom the diurnal variations in performance are most relevant. Additionally, team players cannot freely choose their training time and therefore not shift their time of peak performance by changing their habitual training time.

However, this means that many endurance athletes, which are mainly early chronotypes [50], are already past their peak performance during competitions that take place in the evening.

Endurance competitions actually often take place in the morning, but not exclusively (e.g. cycling events in a velodrome). Therefore, there is an urgent need for methods to help athletes to remain longer at daytime performance levels and stop the time of the day related decrease in performance in the evening. Based on the data of Facer-Childs et al. [6] early and intermediate chronotypes show the strongest decrease in performance in the late evening.
The main purpose of study 2 therefore was to investigate if endurance athletes can benefit from light exposure in the evening. The light exposure may stop or reduce the decrease in performance which is strongest at this time of the day. With respect to proportion of different chronotypes all participants were supposed to be tested at the same internal time, by starting the light exposure 17 h after each individual's MSFsc.

1.2.2 Diurnal variation in strength performance

Diurnal variations in strength performance are investigated to a much broader extend. A recent review by Chtourou et al. [5] listed 28 studies investigating diurnal variations in strength performance. The limitations of the vast majority of studies are comparable to the studies investigating diurnal variations in endurance performance. Nine-teen studies tested four or less times of the day and in three studies no sufficient time for regeneration was provided for the athletes. In only one study females were tested [51] and in all remaining six studies' sample sizes were small ($n \leq 12$) and neither habitual exercise time nor chronotype were assessed. However, all studies agree that strength performance peaks in the early evening. In detail, peak torque during isometric contraction of knee extensors was highest at 17:06 with an amplitude of 6% in males and 4.7% in females [51], at 18:18 with an amplitude of 3.3% [52] and at 18:20 with an amplitude of 9% in untrained males [53]. Maximum isometric handgrip strength peaked at 18:12 with an amplitude of 5.1% [54]. Peak torque of maximum isometric contraction of elbow flexors was highest at 17:55 with an amplitude of 7.0% [55]. Finally, for isokinetic contractions peaks were between 17:49 and 18:37 depending on the angular velocity (60 to 300 ° x S^{-1}) with amplitudes of 9% to 12% [56]. Similar to the studies presented in the review of Chtourou et al. [5] most recent studies lack the same methodological issues, especially that only two [57–60] or three [61] times of the day were investigated or insufficient time for regeneration was planned in the study design [62]. In total there seems to be striking evidence that strength performance peaks in the late afternoon and early evening.

1.2.3 Mechanisms inducing diurnal variations in physical performance

Studies investigating diurnal variations in endurance performance provide less evidence for the underlying mechanism inducing the variations. In strength performance the diurnal variations are suspected to be caused by variations in the hormone testosterone and core body temperature. The latter is likely to also be responsible for diurnal variations in at least shorter endurance performances.
Testosterone decreases during the day [11,63] which affects strength performance negatively. A short maximum strength training (i.e. 3 repetition maximum bench press and squat) significantly decelerated the reduction of testosterone (-1.2 pg/ml) compared to a control

group (-10.9 pg/ml) between 09:00 and 15:00 and led to higher strength performance in the afternoon. Testosterone therefore decreases performance in the late afternoon. However, peak performance is still mainly reported to occur in the late afternoon, because core body temperature also reaches its peak at this time of the day [19] and has a higher influence on strength. The hypothesis that core body temperature represents the strongest influence on diurnal variation is supported by a study from Robinson et al. [64]. Male participants showed higher performance in grip strength, isometric peak power and peak torque for isokinetic knee extension at different angular velocities at 17:30 compared to 07:30. If rectal temperature was cooled down in a third test session taking place at 17:30 to the levels participants had at 07:30 performance decreased significantly towards morning values [64].
As equal to endurance performance it was hypothesized in this PhD project that a deceleration of the time of the day related decrease in core body temperature in the late evening would reduce the performance decrease in athletes. The proportion of short term and strength competitions taking place in the evening is higher than long endurance competitions. Athletes in such disciplines would therefore strongly benefit.

1.3 Influence of light exposure on the circadian clock

The internal master clock located in the SCN shows an oscillation of approximately 24.18 hours [65] and is partially entrained to the 24-hour day by external factors such as food-uptake or physical activity [66]. However, the most important factor with strongest influence is the light-dark cycle [20,67,68] which resets the inner clock on a daily basis thorough sunrise and sunset. From a physical point of view sunlight or light in general is simply electromagnet radiation (photons) with a specific wavelength. Depending on the spectrum of the light source its color ranges from violet (380 to 450), blue (450 to 495 nm), green (495 to 570 nm), yellow (570 to 590 nm) and orange (590 to 620 nm) to red (620 to 750 nm). Wavelength < 380 nm (ultraviolet) and > 780 nm (infrared) are not visible for humans. Light with a very narrow spectrum is referred to as monochromatic light and appears in the respective color. Natural sunlight and usual indoor illumination contain a broader spectrum (i.e. polychromatic) and therefore appear white. In polychromatic light the peak wavelength defines the wavelength with the highest proportion. The light intensity is described by the illuminance (i.e. luminous flux per unit area) with the SI unit lux (lx) or lm/m^2.
The photons hit the retina at the back of the human eye which contains rod and cone photoreceptors responsible for scotopic (color) and photopic (light/dark) vision [69]. Recently a third kind of photoreceptor was discovered with non-image forming functions. These photoreceptors contain melanopsin [70] and are located in about 1-3% of the cells in the ganglion cell layer [71] and are most sensitive to peak wavelengths of 482 nm (i.e. blue light) [72]. Photons hitting these intrinsic photosensitive retinal ganglion cells are transmitted into an electrical signal [73] through photo transduction by melanopsin [74]. The electrical signals are transmitted to the pretectal area, which regulates the pupillary light reflex [75], the ventrolateral preoptic nucleus, which influences the sleep and wake state [14] and to the SCN [67], entraining the human circadian clock. Via the SCN, the photoreceptors also indirectly affect the sleep/wake rhythm and the circadian regulation of sleep and loco motor activity

[76]. The time of the day that an individual is exposed to light affects the direction of the circadian phase shift induced by light. Exposure to light in the early morning, advances the timing of the circadian phase, while exposure in evening delays it [77] and exposure in the middle of the day causes no or only small shifts [33]. Further, there is dose-response relationship between light exposure and the resetting of the human circadian clock [78], which is non-linear. Exposure to ~100lx for example caused a phase-delaying response of about half that achieved with exposure to ~9000lx [79]. Not only light intensity, but also wavelength is crucial for the resetting of the human circadian clock. Exposure to blue light with 11lx for 6.5h caused a resetting response of the circadian clock of approximately 75% of the exposure to white light with 10`000lx for 6.7h did [80].

Light signals transmitted to the SCN not only shift the circadian rhythm, but also cause a suppression of melatonin. Because the SCN is innervated by the non-visual system this even works in totally blind patients [81] and even through closed eye lids [82]. Equal to the influence on the phase shift there is a positive non-linear dose-response relationship between light exposure and the suppression of melatonin [79,83]. Additionally, exposure to blue light reduces melatonin significantly stronger than white light [77,84] and also leads to significantly lower subjective sleepiness and higher alertness [77]. This increase in alertness may not only be caused by a reduction in melatonin, because light also increases alertness at times of the day when melatonin levels are rather low [85]. These effects of light exposure on alertness and cognition arise eventually, through the stimulation of the cortex [71]. This increase in alertness may be strongest in blue light but even red light induces alertness increase compared to complete darkness [86].

In this PhD thesis it is hypothesized, that the increase in alertness and reduction in sleepiness through bright light exposure will positively affect maximum physical performance. Further, in tests carried out in the late evening athletes will additionally benefit from a suppression of melatonin which will decline the drop in core body temperature in the late evening.

Light also modulates emotional responses in humans [87]. A meta-analysis by Golden et al. [88] provides compelling evidence that bright light therapy trials in seasonal affective disorder and non-seasonal depression show effect sizes as high as most antidepressant pharmacotherapy trials [88]. A combination of bright light and drug treatment showed the highest effect size in treatment of non-seasonal depression [89]. Light therapy is meanwhile a widely used therapy in seasonal affective disorder [90,91] and to reduce negative effects of shift work [92–95]. This positive influence on mood and reduction of sleepiness is hypothesized to improve motivation in overweight individuals and increase self-chosen exercise intensity or reduce subjective effort. Increasing exercise intensity leads to weight reduction in mid- and long term and improves oxidative stress markers [96] which operates protective against risk factors of arteriosclerosis. Both factors are relevant for an individual's health.

1.4 Influence of light exposure on physical performance and weight reduction

The influence of light exposure on physical performance has been investigated to a much smaller extend than the influence on cognitive performance. Two studies [97,98] researched

if a shift of the circadian rhythm through light exposure would increase performance while the remaining studies investigated the acute effects on performance through increase of alertness and reduction of sleepiness induced by light exposure [41,99,100].

Zhang et al. [97] and Thompson et al. [98] exposed untrained participants to bright and control light in a cross-over design for 8 h and 0.5 h, respectively. The aim was to shift the circadian rhythm and induce a lower core body temperature on the subsequent morning acting as pre-cooling mechanism to reduce exhaustion. Both, time to exhaustion in a handgrip strength task [97] and time to finish a 10 km time trial on a bicycle ergometer [98] were significantly improved after bright light exposure. The positive results may have appeared by chance due to the small sample sizes or by a placebo effect, since neither the participants nor the investigators were blinded to the light condition. Further, in both studies participants were low trained and it was not controlled if the phase shift induced any negative effects (e.g. disturbed sleep quality or duration on the subsequent night). Additionally, the time trial in the study by Thompson et al. [98] took place in a humid and high temperature environment which only allows conclusions for this setting. These studies may provide proof of concept that light-induced shifts of the circadian rhythm improve performance, but the results cannot be directly transferred to competitive sports.

O`Brien et al. [100], exposed competitive cyclists to three different light settings (1411lx, 2788lx and 6434lx) during a 20-min time trial. No significant differences appeared between the three light conditions. Ohkuwa et al. [99] exposed athletes to 50 lx or 5000 lx for 90 minutes prior to a 45-sec time trial. Neither maximum power output nor blood lactate concentration differed between the light conditions. Both studies show methodological limitations. O`Brien et al. [100] tested participants between 08:00 and 18:00 and Ohkuwa et al. [99] did not state the time of the day. Regarding diurnal variations in performance this can strongly impact the results. Further, both studies tested low sample sizes of only twelve and ten participants, respectively. Additionally, both studies did not assess chronotype, sleep quality or sleep duration before the time trials. Finally, the lack of pre-exercise exposure in the study of O`Brien et al. [100] may have caused that any effects on alertness through light exposure appeared after the time trial was already finished.

In contrast, Kantermann et al. [41], exposed 34 trained athletes in a randomized order to 230lx and 4420lx for 2 h prior to and during a 40-min time trial. Participants exposed to bright light ~14.8 h after their MSFsc showed significantly higher power output than after exposure to control light. In contrast this affect did not appear in participants exposed to bright light ~11.8 h after their MSFsc. The latter study was the best controlled study so far with a high sample size showing a proof of concept that light can influence maximum performance in trained athletes. However, the exposure duration of two hours prior to and during exercise is not applicable in professional sports. Therefore, the aim of study 2 was to investigate the influence of bright light on cycling performance under realistic conditions (i.e. 1h light exposure exclusively prior to exercise). Further, this was the first study to also investigate the effect of blue light, since striking evidence suggests that the wavelength of light has important influence on mood, alertness, sleepiness and the suppression of melatonin. Additionally, in this study the investigator was fully blinded and a parallel group design was used to blind

participants at least partially by ensuring that they did not know the other light condition. Finally, this study tested only highly trained athletes to make the results transferable into elite sports and performed the tests at the same internal time for all athletes. Light exposure was chosen to start 17 h after the MSFsc for all athletes, because at this time of the day many competitions take place and it was hypothesized that athletes would benefit from the suppression of melatonin additionally to the effects on alertness and sleepiness.

The acute effects of light exposure on self-chosen exercise intensity have not been investigated yet, but studies investigating the influence of light exposure alone [101]; light exposure and exercise [102] and light exposure during exercise [103] have been performed. In detail, three weeks of bright light exposure for 45 minutes per day showed significant reductions in appetite and body fat compared to exposure to control light [101]. In another study, overweight and obese individuals exercised for 30 minutes three times per week for a period of six weeks. One group was additionally exposed to bright light for 60 minutes per day and showed a higher reduction in body fat mass than the control group without light exposure [102]. The only study in which participants exercised while they were simultaneously exposed to bright light was performed in patients with seasonal affective disorder. Exercise under bright light exposure decreased appetite and carbohydrate craving as well as morning fatigue significantly stronger than exercise under normal indoor illumination [103]. Since neither physical activity nor nutrition were controlled in the studies it is uncertain if reported changes in body fat resulted from reduced energy uptake or increased energy expenditure, which are both possible causes. The ventrolateral preoptic nucleus which is influenced by the signals from the non-image forming system is associated with the release of the hormone ghrelin [14]. In sleep restricted adults light exposure showed to influence ghrelin and leptin which are associated with hunger [104]. On the other hand, increases in mood and alertness and reductions in sleepiness may increase exercise intensity additionally. In young adults the nadir of alertness appears in the early morning between 06:00 and 08:00 (i.e. 1 to 2 hours after the nadir of body temperature) [23]. Additionally, at this time of the day sleepiness is also relatively high. Therefore, it was hypothesized that in overweight individuals bright light exposure in the morning would lead to increased alertness, reduced sleepiness and improved mood and that this would increase self-chosen exercise intensity.

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Chapter 2

Aims and Hypotheses

Chapter 2 Aims and Hypotheses

The main aims of this PhD project were:

- Aim 1: To evaluate if there is a positive dose-response relationship between the duration of bright light exposure and maximum cycling performance in athletes.
- Aim 2: To investigate the effects of evening bright and blue light exposures on maximum cycling performance in elite athletes.
- Aim 3: To investigate the effects of evening bright and blue light exposure on acoustic reaction time and maximum handgrip strength in elite athletes.
- Aim 4: To investigate the effect of morning bright light exposure on self-chosen exercise intensity and mood in overweight individuals.

The main hypotheses to be evaluated for this PhD project were:

- Hypothesis 1: In male athletes there is a positive dose-response relationship between the duration of bright light exposure and the total work performed in a 40-minute time trial.
- Hypothesis 2: In elite male athletes an exposure to bright or blue light for 60 minutes prior to a 12-minute time trial in the late evening will increase the total work performed compared to a control condition.
- Hypothesis 3: In elite male athletes an exposure to bright or blue light for 60 minutes prior to a five-minute simple acoustic reaction time task and a maximum handgrip strength test in the late evening will decrease median reaction time and increase maximum handgrip strength compared to a control condition.
- Hypothesis 4: In overweight individuals an exposure to bright light for 30 minutes prior to and during a 30-minute exercise session, taking place at 08:30 a.m., will lead to higher self-chosen mean exercise intensity and improved mood compared to a control condition.

Chapter 3

Publication 1: Dose-response relationship between light exposure and cycling performance

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Chapter 4

Publication 2: Prime time light exposures do not seem to improve maximal physical performance in male elite athletes, but enhance end-spurt performance

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Prime Time Light Exposures Do Not Seem to Improve Maximal Physical Performance in Male Elite Athletes, but Enhance End-Spurt Performance

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Many sports competitions take place during television prime time, a time of the day when many athletes have already exceeded their time of peak performance. We assessed the effect of different light exposure modalities on physical performance and melatonin levels in athletes during prime time. Seventy-two young, male elite athletes with a median (interquartile range) age of 23 (21; 29) years and maximum oxygen uptake (VO2max) of 63 (58; 66) ml/kg/min were randomly assigned to three different light exposure groups: bright light (BRIGHT), blue monochromatic light (BLUE), and control light (CONTROL). Each light exposure lasted 60 min and was scheduled to start 17 h after each individual's midpoint of sleep (median time: 9:17 pm). Immediately after light exposure, a 12-min time trial was performed on a bicycle ergometer. The test supervisor and participants were blinded to the light condition each participant was exposed to. The median received light intensities and peak wavelengths (photopic lx/nm) measured at eye level were 1319/545 in BRIGHT, 203/469 in BLUE, and 115/545 in CONTROL. In a multivariate analysis adjusted for individual VO2max, total work performed in 12 min did not significantly differ between the three groups. The amount of exposure to non-image forming light was positively associated with the performance gain during the time trial, defined as the ratio of the work performed in the first and last minute of the time trial, and with stronger melatonin suppression. Specifically, a tenfold increase in the exposure to melanopic light was associated with a performance gain of 8.0% (95% confidence interval: 2.6, 13.3; $P = 0.004$) and a melatonin decrease of −0.9 pg/ml (95% confidence interval: −1.5, −0.3; $P = 0.006$). Exposure to bright or blue light did not significantly improve maximum cycling performance in a 12-min all-out time trial. However, it is noteworthy that the estimated difference of 4.1 kJ between BRIGHT and CONTROL might represent an important performance advantage justifying further studies. In conclusion, we report novel evidence that evening light exposure, which strongly impacts the human circadian timing system, enables elite athletes to better maintain performance across a 12-min cycling time trial.

Keywords: circadian rhythm, bright light, blue light, melatonin, chronotype

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INTRODUCTION

Many athletes reach their peak endurance performance between the afternoon and the early evening (Reilly and Waterhouse, 2009) depending on their chronotype (Facer-Childs and Brandstaetter, 2015). However, in professional sports, competitions very often take place in the late evening (08:00 p.m.–12:00 a.m.) to comply with prime time on television as just recently shown during the Summer Olympic Games 2016 with many finals taking place between 10:00 p.m. and 00:25 a.m. During this time window, circadian related increases in melatonin levels and sleep propensity are expected, which have detrimental effects on cognitive (Schmidt et al., 2007) and physical performance (Facer-Childs and Brandstaetter, 2015). Exposure to artificial light, however, can shift circadian melatonin rhythms (Gronfier et al., 2004; Wirz-Justice et al., 2004; Revell et al., 2006), acutely lower melatonin levels, increase alertness (Cajochen, 2007), and improve mood (Hoffmann et al., 2008a). The extent of these effects depends on intensity (Zeitzer et al., 2000; Hoffmann et al., 2008a), wavelength (Cajochen et al., 2005; Vandewalle et al., 2007; Hoffmann et al., 2008a,b; Smith et al., 2009; Chellappa et al., 2011; Rüger et al., 2013), individual light-dark history (Hébert et al., 2002), duration (Chang et al., 2012), and time of day of light exposure (Cajochen, 2007). Blue light with a wavelength of 460–480 nm activates the non-image forming system with particularly strong effects on alertness, melatonin, and thermoregulation (Cajochen et al., 2005).

Depending on the type and duration of light exposure as well as the population tested, light exposure studies showed contradictory effects on physical performance in bicycle ergometer time trials. First, there was no statistically significant difference in maximum power output during a 45-s time trial following a 90-min light exposure to 5,000 lx compared to 50 lx in young males (Ohkuwa et al., 2001). Second, exposing young males during a 20-min time trial to either 2,788 lx or 6,434 lx compared to 1,411 lx showed no differences in maximum power output (O'Brien and O'Connor, 2000). Performance-enhancing effects may have been masked by testing long-distance runners in a very short time trial on a bicycle ergometer (Ohkuwa et al., 2001) and by the high-intensity light exposure (1,411 lx) used in the control condition (O'Brien and O'Connor, 2000; i.e., ceiling effect). Third, light exposure to 2,500 lx for 30 min in the evening compared to 0 lx significantly increased power output in a 10-km time trial taking place the next morning (Thompson et al., 2015). None of these studies took time-of-day effects or individual circadian rhythms into account.

In a recent study (Kantermann et al., 2012) a 120-min light exposure to 4,420 lx, starting ∼14:45 h after the individual midpoint of sleep, significantly increased total work during a 40-min time trial compared to 230 lx. Further, we were able to demonstrate a dose-response relationship between light exposure and physical performance (Knaier et al., 2016), such that longer durations and higher intensities lead to higher power output in a 40-min time trial. However, compared to participants in the control light group, the bright light group only performed significantly more work during the first 24 min of the time trial (Knaier et al., 2016) indicating relatively higher effects for shorter time trials. Thus, for this study time trial duration was set at 12 min, also because this duration is known by most Swiss and German athletes from the Cooper-Test (12 min duration) and represents more competitions (e.g., 5,000 m) than a 40-min time trial. Further, the cardiorespiratory fitness test was expected to last approximately the same duration and served therefore as familiarization.

However, the studies conducted so far still have a number of limitations: assessors were not blinded for type of light exposure (O'Brien and O'Connor, 2000; Ohkuwa et al., 2001; Kantermann et al., 2012; Thompson et al., 2015), melatonin as an accepted marker for circadian phase was not measured (O'Brien and O'Connor, 2000; Ohkuwa et al., 2001; Kantermann et al., 2012), sample size was small (O'Brien and O'Connor, 2000; Ohkuwa et al., 2001; Thompson et al., 2015), examined participants had a relatively low peak aerobic performance (Thompson et al., 2015), and potential confounding factors such as sleep quality and sleep duration or drugs (e.g., caffeine consumption) were not (O'Brien and O'Connor, 2000; Ohkuwa et al., 2001) or only partially monitored (Kantermann et al., 2012; Thompson et al., 2015). Further, the influence of blue light on physical performance has not yet been investigated.

Thus, the aim of this study was to assess the effect of both bright and blue light exposure on physical performance in elite athletes under well controlled conditions to take into account numerous potential confounders. Our primary hypothesis was that exposure to bright (BRIGHT) or blue light (BLUE) prior to a time trial in the late evening would increase work performed in elite endurance athletes compared to a control condition (CONTROL). Secondary aims were to assess the effect of the different light conditions and intensities on melatonin levels, sleepiness, and mood.

MATERIALS AND METHODS

Study Design

This 3-arm parallel group randomized controlled trial was conducted between April 2014 and April 2015 in the laboratories of the Department of Sport, Exercise and Health of the University of Basel, Switzerland (ClinicalTrials.gov Identifier: NCT02203539). The study was approved by the local ethics committee (Ethikkommission Nordwest- und Zentralschweiz 2014-056). Written informed consent was obtained from all study participants before the start of study. We used permuted block randomization with randomly varying block sizes of 3, 6, and 9 to allocate participants at random and in equal numbers to one of the three groups. The randomization list was generated in advance using the online tool available at http://www.randomization.com (accessed April 29, 2014) and transmitted using sequentially numbered, opaque, sealed envelopes. A graphical abstract of the study design is provided (**Figure 1**).

Abbreviations: BRIGHT, bright light; BLUE, blue light; CONTROL, control light; VO2max, maximum oxygen uptake; MSFsc, midpoint of sleep on free days corrected for oversleep due to sleep debt on workdays.

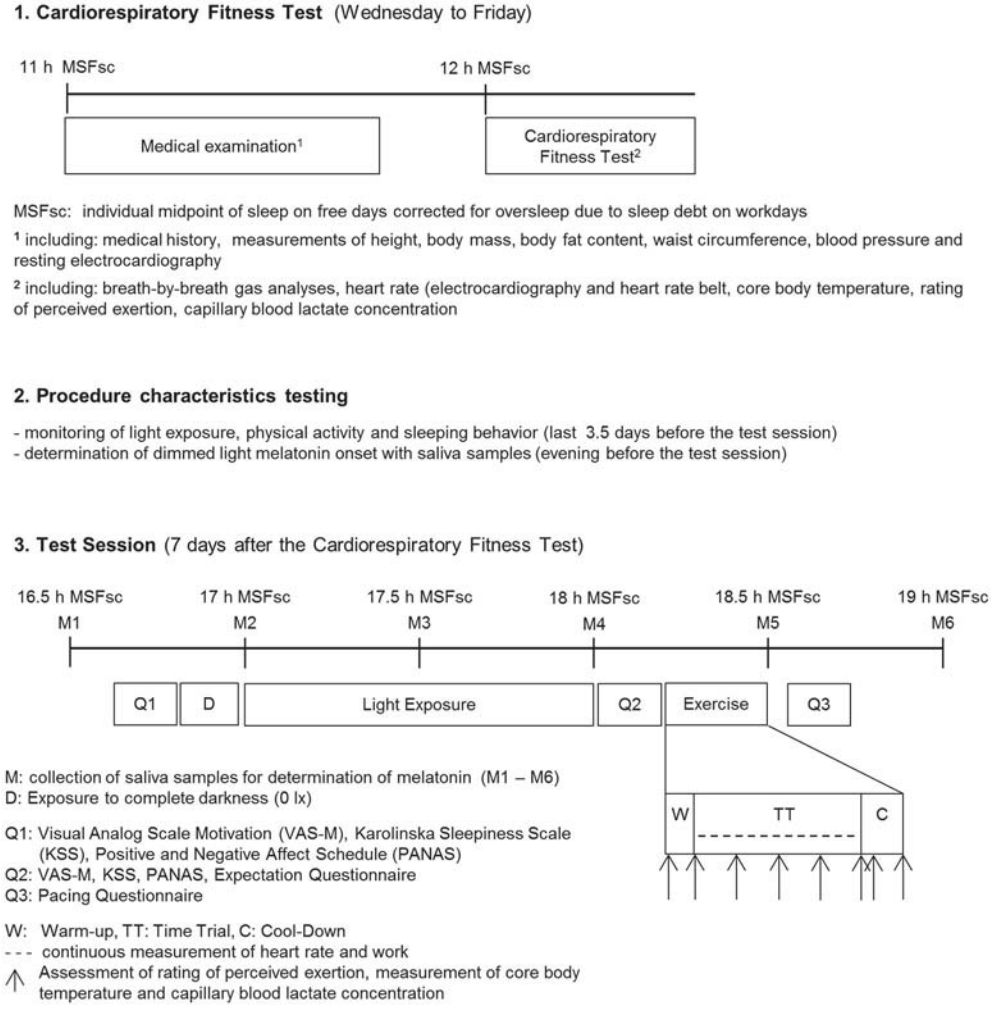

FIGURE 1 | Experimental procedure.

Participants

Physically healthy men between 18 and 35 years of age, with no shift-work in the last 3 months and no travels across time zones in the last 4 weeks before the study, were recruited for a baseline cardiorespiratory fitness test to determine aerobic exercise capacity by measuring maximum oxygen uptake (VO_2max). Only elite endurance athletes with VO_2max $\geq$ 55 ml/kg/min were invited to complete the test session 6–8 days later. Athletes were randomized into the three groups bright light (BRIGHT), blue light (BLUE), and control light (CONTROL). All tests were conducted in the same laboratory by the same test supervisor (R.K.) to guarantee comparability between groups. Further, the tests were only carried out from Wednesday to Friday to ensure that participants had a regular sleeping routine for a minimum of three nights before the test session. To avoid a wide variability in the participants' light-dark history, no tests were carried out for 30 days before and after the 21st of June (longest day of the year). No participants were tested in the week after the change to daylight saving time.

Participant Characteristics Testing

At baseline, a clinical examination was performed, including medical history and a physical examination consisting of measurements of height, body mass, body fat content, waist circumference, blood pressure, and resting electrocardiography. Motivation was measured by a 10 cm visual analog scale and sleep quality was assessed by the Pittsburgh Sleep Quality Index (Buysse et al., 1989). The Munich Chronotype Questionnaire (Roenneberg et al., 2004) was used to determine individuals' midpoint of sleep on free days corrected for oversleep due to sleep debt on workdays (MSFsc). Then a cardiorespiratory fitness test until exhaustion was conducted on a bicycle ergometer (Sport Excalibur, Lode Medical Technology, Groningen, The Netherlands) starting 12 h after the individual MSFsc. After a 5 min warm-up phase at 50 W, workload increased linearly with 25 W/min until exhaustion, followed by a 5 min cool-down phase at 50 W. The protocol is expected to achieve VO_2max according to previous findings (Midgley et al., 2008). Pedaling cadence was chosen by participants but was required

to be over 60 revolutions per minute. Participants were allowed to cycle with their own pedals and shoes. Breath by breath gas analyses (MetaMax 3B, Cortex Biophysik GmbH, Leipzig, Germany) and heart rate (12-channel electrocardiography, Custo med GmbH, Ottobrunn, Germany and additionally a Polar T-34 heart rate belt, Polar Electro Europe AG, Zug, Switzerland) were measured continuously, tympanic temperature and rating of perceived exertion according to the 6–20 Borg scale (Borg, 1982) were assessed at rest, after warm-up and every 3 min until exhaustion. Blood pressure and capillary blood lactate concentration (analyzed by SuperGL Ambulance, Hitado Diagnostic Systems, Moehnesee, Germany) were measured at rest, immediately after exhaustion and during the cool-down phase at 3 min after exhaustion. Exhaustion was only accepted if all of the following four criteria were fulfilled: [1] Respiratory exchange ratio $\geq$1.1; [2] blood lactate concentration >8 mmol/l (Steinacker et al., 2002); [3] rating of perceived exertion $\geq$19; and [4] maximum heart rate >95 % of predicted maximum heart rate [210—age (years)].

Procedure Characteristics Testing

Participants were advised to refrain from alcohol, nicotine, caffeine, chocolate, bananas, sport, and visits to the solarium during the last 2 days before the test session. Further, they were encouraged to keep a constant sleeping routine (i.e., bedtime $\pm$ 1 h) during the 3 days prior to the test session. To monitor compliance regarding sleeping routine and restraint from sport, participants wore two wGT3X+ ActiGraphs (Pensacola, United States, measuring rate of 60 Hz) 24 h per day during the last 3.5 days before the test session. One device was worn on the non-dominant hand above the clothes measuring light exposure and one was worn on the waist measuring physical activity. During this time period participants also kept a diary recording sunlight exposure and physical activity to double-check data from the ActiGraph, sleeping habits during the last 3 days and nutrition during the last 2 days before the test session to monitor if melatonin-affecting substances such as bananas, alcohol etc. were consumed. On the evening before the time trial, participants collected five saliva samples every 60 min, starting 4 h before individual bedtime under dimmed light (i.e., <50 lx) to determine the participants' dim-light melatonin onset with the hockey stick method (Danilenko et al., 2014). Saliva samples were frozen at -24°C until analysis for melatonin (pg/ml) via radioimmunoassay (Bühlmann Laboratory, Schönenbuch, Switzerland).

Test Session

Six to eight days after the baseline test eligible participants were randomly assigned to one of the three different light exposure groups: BRIGHT, BLUE, and CONTROL. All participants were exposed to darkness (0 lx) for 10 min before light exposure to dark adapt the participants' pupils. Light exposure was scheduled to start 17 h after the individual MSFsc and lasted 60 min. The three light conditions were BRIGHT with two Philips Energylight HF3319 devices with ~4,400 lx in total and peak wavelength of 545 nm (range: 400–720 nm; Philips, Eindhoven, The Netherlands), BLUE with two Philips goLITE BLU devices with ~230 lx in total and peak wavelength of 469 nm (range: 440–520 nm; Philips, Eindhoven, The Netherlands) and CONTROL with two Philips Energylight HF3319 devices with ~230 lx in total and peak wavelength of 545 nm (range: 400–720 nm; Philips, Eindhoven, The Netherlands). The lamps were placed on a table at a distance of 60 cm from the participants' eyes.

As different sitting postures and the direction of gaze have influence on the amount of light reaching the eye, individually perceived light intensity was recorded with a sensor (LUXBlick 2.0, Technische Universität Ilmenau, Ilmenau, Germany) with a sampling rate of 1 Hz that was attached to glasses, which participants wore during the light exposure. Participants were not given any information about the alternative study groups and the light sources were only referred to as "Light 1," "Light 2," and "Light 3." Every light setting was arranged in a different room in order to blind the test supervisor (RK) to the light condition each participant was going to be exposed to. The door of each room was labeled with "Light 1," "Light 2," or "Light 3." Participants were allocated at random to one of the three light conditions. Participants were asked to go into the room specified in the envelope. Additionally, two timers were handed out, one indicating when participants had to take the next saliva sample and the other one to show the end of the light exposure. After the end of the light exposure participants immediately returned to the laboratory. From the recorded illuminance levels measured in photometric lux via the "LUXBlick" glasses worn by the participants, the amount of melanopic lux reaching the eye was calculated for each participant (Lucas et al., 2014) to quantify the influence of the non-image forming photoreceptor system on performance. Salivary melatonin was measured 60 min prior to and until 2 h after the start of light exposures at 30 min intervals.

After the light exposure, a questionnaire about the expected effect of the light exposure on the work performed during the time trial was filled out. Sleepiness was assessed with the Karolinska Sleepiness Scale (Kaida et al., 2006), motivation with the visual analog scale, and mood with the Positive And Negative Affect Schedule (Crawford and Henry, 2004) directly before and immediately after light exposure. Following light exposure, athletes performed a 12-min time trial on a bicycle ergometer. The bicycle ergometer test started 18:15 h after MSFsc with a 2-min warm-up phase at 50 W followed by a 12-min time trial and a 3-min cool-down phase at 75 W. At rest, at the end of warm-up, every 3 min during the time trial, and in the first and third minute of the cool-down phase RPE was assessed. Heart rate was measured continuously. Participants were advised to "bike as far (to generate as much work) as possible" during the 12 min. Workload (Power) and cadence were set at 80% of VO_2max as assessed during the baseline cardiorespiratory fitness test. To ensure that participants could pedal with the favored cadence, workload increased quadratically (factor α) with increasing pedaling cadence according to the formula: Power = α (Cadence)^2. The time trial was followed by a questionnaire assessing the participants' pacing strategy during the time trial, on a 10 cm visual analog scale ranging from 0 = "very bad pacing" to 10 = "very good pacing."

Statistical Analysis

The primary outcome of this study was work performed during the 12-min time trial on a bicycle ergometer; secondary outcomes were sleepiness, motivation, and mood after the light exposure. We used analysis of covariance with adjustment for maximum exercise capacity (VO_2max) to compare the work performed during the time trial between elite athletes in BRIGHT, BLUE, and CONTROL groups (Vickers and Altman, 2001). Similarly, we used analysis of covariance to compare the secondary outcomes after the light exposure between athletes in BRIGHT, BLUE, and CONTROL adjusted for the corresponding values before the light exposure. Normality was assessed using normal quantile-quantile plots of the residuals and variance homogeneity was assessed using Tukey-Anscombe Plots. For each analysis, we report the estimated differences (with 95% confidence intervals) in outcome between the three groups. We carried out two additional analyses. First, we used a mixed model for repeated measures to estimate whether the light exposure conferred a differential effect on physical performance at different time points during the time trial. In this analysis, we used a first-order autoregressive structure for the covariances among the 12 min of the time trial for each participant, while different participants were still assumed to be independent. Second, we used linear regression to estimate the effect of the amount of exposure to non-image forming (i.e., melanopic) light on the "performance gain" during the time trial, defined as the ratio of the performance during the first and last minute of the time trial. In this analyses eight participants in group BLUE and one participant in group CONTROL were excluded, because they received considerably lower exposure to melanopic light than planned in the protocol. For our analyses and graphics, we used IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, N.Y., USA) and R version 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria), respectively.

Sample Size

For sample size calculation, we assumed that the work performed in BRIGHT, BLUE, and CONTROL was 228 kJ, 232 kJ, and 220 kJ, respectively, and that the standard deviation was 10 kJ (Díaz et al., 2012; Giles et al., 2012; Kantermann et al., 2012). By adjusting for maximum exercise capacity (VO_2max), we could expect to further reduce error variability and therefore conservatively assumed a correlation of 0.3 between the maximum exercise capacity and work performed during the time trial. With a 2-sided significance level of 0.05, the sample size needed to attain a targeted power of 80% for showing superiority of BRIGHT over CONTROL was 23 participants per group. A total sample size of 3*23 = 69 participants gave a power of 97.5% for the overall comparison between the three groups, a power of 98.8% for the comparison between BLUE and CONTROL and a power of 28.8% for the comparison between BRIGHT and BLUE. We anticipated a drop-out rate of 15% and that 10% of athletes assessed for eligibility would not fulfill the inclusion criteria and therefore aimed at recruiting a total of 90 athletes.

RESULTS

Participant Flow and Characteristics

Eighty-seven participants were assessed for eligibility. Of the 74 participants that met the inclusion criteria and were equally randomized to BRIGHT, BLUE, and CONTROL, two had to be excluded after randomization because it was uncertain if they had reached the inclusion criterion of maximum oxygen uptake (VO_2max) equal or greater than 55 ml/kg/min due to an invalid VO_2max measurement. Further, three participants had to be excluded from the analysis of the primary outcome (total work performed during time trial) due to invalid measurement of VO_2max, no exhaustion during the cardiorespiratory fitness test and premature termination of the time trial, respectively. In the cardiorespiratory fitness test, all included participants showed a VO_2max in the top 10% and the median VO_2max was in the top 1% of the participants' sex and age group (American College of Sports Medicine, 2010). Characteristics of the included participants were balanced between the three groups (**Table 1**).

Procedure Characteristics and Time Trial Performance

Participants were well circadian-entrained as indexed by a normal phase angle between the timing of melatonin onset and habitual bedtime and showed normal sleep quality as well as regular sleep patterns during the last 3 days before the time trial. Motivation was rated rather high (**Table 2**).

Work performed during the time trial was highest in BRIGHT followed by BLUE and CONTROL, with an average (standard deviation) of 229 (23), 218 (34), and 216 (25) kJ, respectively (**Table 3**). In the multivariate analysis adjusted for the pre-specified potential confounder VO_2max, the difference in work performed during the time trial was 4.1 kJ (95% confidence interval [CI] −4.5, 12.7; $P = 0.346$) for participants in BRIGHT and −1.2 kJ (95% CI −9.8, 7.5; $P = 0.787$) for participants in BLUE, both relative to participants in CONTROL (**Table 3**).

In an additional repeated measures analysis adjusted for the individual VO_2max, we added the factor "time on trial" and determined whether there was a statistically significant "group" (BRIGHT, BLUE, CONTROL) x "time on trial" interaction effect on performance ($P = 0.235$).

The median melanopic light exposure (calculated for each participant individually from the photometric light intensity measured on eye level) was 1,153 lx (interquartile range [IQR] 829, 1,390), 2,173 lx (IQR 335, 7,041) and 100 lx (IQR 68, 182) in BRIGHT, BLUE, and CONTROL, respectively. The amount of exposure to non-image forming light (i.e., melanopic light) was positively associated with the "performance gain" during the time trial, defined as the ratio of the performance in the first and last minute of the time trial. A tenfold increase in the exposure to melanopic light was associated with an increase in performance gain of 8.0% (95% CI 2.6, 13.3, $P = 0.004$; **Figure 2**).

Effect of Light Exposure on Melatonin

Immediately after the light exposure melatonin suppression was strongest in BRIGHT followed by BLUE and CONTROL with a median of 0.4, 0.8, and 0.9 pg/ml, respectively (**Figure 3**). When

TABLE 1 | Participant characteristics.

Characteristic	BRIGHT ($n = 24$)	BLUE ($n = 24$)	CONTROL ($n = 24$)
Age (years)	23 (22; 30)	23 (21; 26)	24 (23; 30)
Height (cm)	181 (178; 183)	179 (172; 184)	180 (176; 186)
Body mass (kg)	74 (70; 78)	75 (66; 80)	72 (69; 76)
BMI (kg/m^2)	22 (21; 24)	23 (22; 24)	22 (21; 24)
Body fat (%)	10 (8; 13)	11 (10; 14)	10 (8; 12)
Waist circumference (cm)	79 (75; 82)	78 (74; 81)	78 (75; 82)
Heart rate at rest (bpm)	63 (58; 73)	54 (50; 66)	59 (54; 67)
Pmax (W)	418 (401; 439)	393 (366; 454)	398 (375; 420)
VO_2max[1] (ml/kg/min)	64 (61; 66)	60 (57; 66)	62 (59; 65)
VO_2max[1] (l/min)	4.83 (4.30; 5.04)	4.55 (4.24; 5.14)	4.48 (4.34; 4.68)
BLOOD PRESSURE (mmHg)			
Systolic	130 (125; 135)	130 (122; 134)	125 (120; 130)
Diastolic	80 (75; 89)	80 (76; 85)	78 (75; 85)
CHRONOTYPE			
MSFsc (hh:mm)	3:54 (3:24; 5:00)	4:30 (3:54; 5:18)	4:12 (3:42; 4:36)
DLMO[2] (hh:mm)	20:30 (19:48; 21:36)	21:18 (20:24; 22:00)	20:54 (20:30; 21:42)
SMOKING (%)			
Never smoker	92	92	92
Former smoker	8	8	8
Current smoker	0	0	0
MAIN SPORT (%)			
Bike / Triathlon	58	42	50
Other endurance	9	25	13
Game	25	33	21
Other	8	0	16

BRIGHT, bright light; BLUE, blue light; CONTROL, control light; BMI, body mass index; Pmax, maximum power output during cardiorespiratory fitness test; VO_2max, maximum oxygen uptake; MSFsc, mid-sleep on free days corrected for "oversleep" due to the sleep debt accumulated over the workweek; DLMO, dim light melatonin onset.
[1]Available in 23 (96%) and 23 (96%) participants in BRIGHT and BLUE, respectively.
[2]Available in 21 (88%), 19 (79%) and 18 (75%) participants in BRIGHT, BLUE and CONTROL, respectively. Data are median (interquartile range) if not stated otherwise.

adjusting for melatonin levels before the light exposure, the difference in melatonin levels after the light exposure, but before the time trial, was −1.1 pg/ml (95%CI −2.2, 0.0) for participants in BRIGHT and −0.5 pg/ml (95%CI −1.6, 0.6) for participants in BLUE, both relative to participants in CONTROL. Similarly, when adjusting for melatonin levels before the light exposure, the amount of exposure to melanopic light was negatively associated with melatonin levels after the light exposure. A tenfold increase in the exposure to melanopic light was associated with a decrease in melatonin by −0.9 pg/ml (95% CI −1.5, −0.3; $P = 0.006$).

TABLE 2 | Procedure characteristics.

Characteristic	BRIGHT ($n = 24$)	BLUE ($n = 24$)	CONTROL ($n = 24$)
CARDIORESPIRATORY FITNESS TEST			
Start (hh:mm after MSFsc)	11:48 (11:30; 12:30)	12:00 (11:30; 12:42)	11:36 (11:00; 11:54)
VAS-M (cm)	9.4 (8.5; 10)	9.5 (8.6; 10)	9.4 (8.5; 10)
PSQI	3 (2.8; 4)	3 (1.8; 4)	3 (1; 3.2)
EXHAUSTION CRITERIA			
HRmax[1] (bpm)	193 (186; 200)	192 (185; 196)	192 (188; 200)
RER[2]	1.16 (1.14; 1.2)	1.19 (1.16; 1.21)	1.21 (1.17; 1.22)
RPE[3]	20 (20; 20)	20 (20; 20)	20 (20; 20)
Blood lactate[3] (mmol/l)	13.2 (12.1; 15)	15.7 (13.7; 16.6)	14.9 (12.9; 15.7)
LIGHT EXPOSURE			
Photopic (lx)	1326 (960; 1591)	202 (29; 598)	115 (78; 208)
Melanopic (lx)	1159 (839; 1390)	2173 (319; 6414)	100 (68; 182)
TIME TRIAL			
Start (hh:mm after MSFsc)	18:16 (18:15; 18:18)	18:16 (18:14; 18:18)	18:16 (18:15; 18:18)
PSQI	2.5 (2; 4.2)	3 (2; 4.2)	2.5 (1; 4)
SLEEP (hh:mm)			
Mid-sleep TT-3	3:30 (2:42; 4:42)	3:30 (3:00; 4:06)	3:18 (2:54; 4:00)
Mid-sleep TT-2	3:12 (2:30; 4:06)	3:42 (3:00; 4:12)	3:24 (2:54; 4:00)
Mid-sleep TT-1	3:24 (3:00; 4:06)	3:42 (3:12; 4:24)	3:30 (3:00; 4:18)
Sleep duration TT-3	7:48 (7:24; 8:36)	7:30 (6:48; 8:48)	7:42 (6:42; 8:18)
Sleep duration TT-2	7:30 (6:36; 8:00)	7:24 (6:54; 8:48)	7:30 (7:00; 8:00)
Sleep duration TT-1	7:36 (6:42; 8:18)	7:36 (7:00; 8:24)	7:42 (7:06; 8:24)

BRIGHT, bright light; BLUE, blue light; CONTROL, control light; MSFsc, mid-sleep on free days corrected for "oversleep" due to the sleep debt accumulated over the workweek; VAS-M, Visual Analog Scale Motivation; PSQI, Pittsburgh Sleep Quality Index; HRmax, maximum heart rate; RER, respiratory exchange ratio; RPE, rate of perceived exertion; TT-3, three nights before the time trial; TT-2, two nights before the time trial; TT-1, one night before the time trial.
[1]Available in 22 (92%) participants in BLUE.
[2]Available in 23 (96%) and 23 (96%) participants in BRIGHT and BLUE, respectively.
[3]Available in 23 (96%) participants in BLUE.
Data are median (interquartile range).

Effect of Light Exposure on Sleepiness, Motivation, and Mood

The difference in sleepiness between participants in BRIGHT and BLUE was −1.2 points on the Karolinska Sleepiness Scale (95% CI −1.9; −0.4), indicating higher alertness effects by bright rather than blue light at the beginning of the time trial. There was no statistically significant effect of light exposure on motivation or the positive or negative domain of the positive and negative affect schedule (**Table 4**).

Adverse Effects and Expectations About Light Exposure

Only minor adverse effects due to the light exposure, such as slight headaches or getting tired, were reported (BRIGHT: $n = 4$; BLUE: $n = 2$; CONTROL: $n = 4$). Expectations about the

TABLE 3 | Analysis of covariance to determine the effects of light exposure on physical performance.

Characteristic	BRIGHT ($n = 24$)	BLUE ($n = 23$)	CONTROL ($n = 24$)	BRIGHT vs. CONTROL	BLUE vs. CONTROL	BRIGHT vs. BLUE
	Time trial [mean (*SD*)]	Time trial [mean (*SD*)]	Time trial [mean (*SD*)]	Adjusted difference[2,3] (95% CI)	Adjusted difference[2,3] (95% CI)	Adjusted difference[2,3] (95% CI)
Work[1] (kJ)	229 (23)	218 (34)	216 (25)	4.1 (−4.5; 12.7)	−1.2 (−9.8; 7.5)	5.3 (−3.4; 14)

BRIGHT, bright light; BLUE, blue light; CONTROL, control light; SD, standard deviation; CI confidence interval.

[1]*Available in 23 (96%) participants in BLUE—one participant terminated the time trial prematurely.*

[2]*Work (kJ) adjusted for maximum oxygen uptake (VO_2max, l/min).*

[3]*Analysis based on 69 (96%) participants—one participant in BLUE terminated the time trial prematurely and two participants in BRIGHT and BLUE had invalid VO_2max measurements in the cardiorespiratory fitness test [definitely above 55 ml/kg/min (inclusion criterion)].*

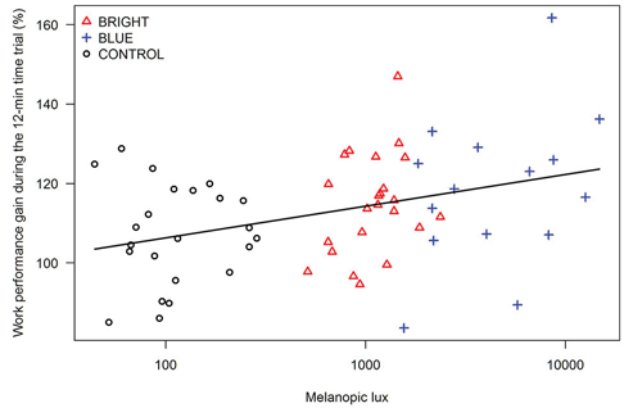

FIGURE 2 | Correlation between the amount of exposure to non-image forming light (i.e., melanopic lx) and the "performance gain" (in %) during the time trial, defined as the ratio of the performance in the first and last minute of the time trial (BRIGHT = bright light, BLUE = blue light, and CONTROL = control light).

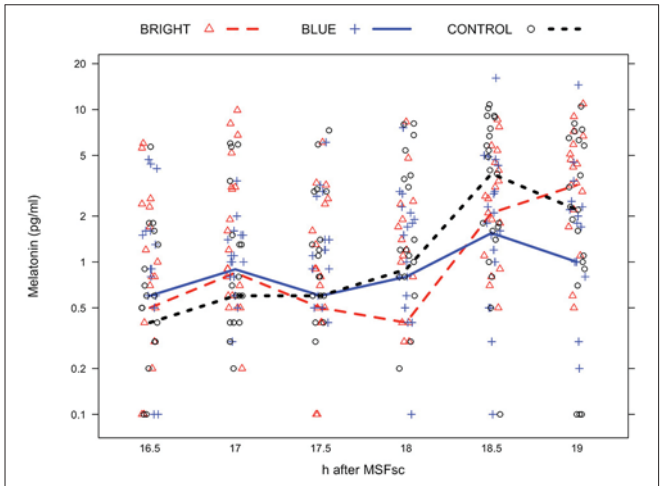

FIGURE 3 | Median saliva melatonin concentration (in pg/ml) in each group (BRIGHT = bright light, BLUE = blue light, and CONTROL = control light) at 16.5 h (i.e., 30 min before the light exposure), 17 h (i.e., immediately before the light exposure), 17.5 h (i.e., 30 min after the start of the light exposure), 18 h (i.e., immediately after the light exposure), 18.5 h (i.e., immediately after the time trial), and 19.0 h (i.e., 30 minutes after the time trial) after MSFsc (mid-sleep on free days corrected for "oversleep" due to the sleep debt accumulated over the workweek). The maximum number of missing melatonin samples per time point and light exposure group was 3/24 (12%), with a total of 16/360 (4%) samples missing.

impact of the light exposure on performance during the time trial differed between the three groups, with 38% of participants in BLUE expecting a decrease in performance and 13% in BRIGHT and 21% in CONTROL. Participants in all three groups generally rated their pacing strategy as very good.

DISCUSSION

Effect of Light Exposure on Performance, Melatonin, and Sleepiness

In this randomized controlled trial, exposure to bright light before a 12-min time trial on a bicycle ergometer induced a stronger though statistically non-significant performance enhancement as well as greater reductions in sleepiness and melatonin levels in elite athletes than exposure to blue or control light. However, BRIGHT showed the highest performance in the second half of the time trial compared to BLUE and CONTROL. Competitions at this duration e.g., 5,000 m running or 4 km cycling do markedly benefit from the ability to conduct a strong second half, and exercise science has demonstrated this as the preferred pacing strategy (Tucker et al., 2006; Corbett, 2009).

In our study all three groups showed a favorable pattern of the pacing strategy in the 12-min time trial, but group BLUE had the strongest gain in performance compared to CONTROL and BRIGHT, respectively. This finding is further supported by a statistically significant correlation between the amount of exposure to melanopic light and the performance gain during the time trial (**Figure 2**). A tenfold increase in exposure to melanopic light was associated with 8.0% increase in performance gain across the 12 min time trial. The amount of evening exposure to melanopic light correlates well with the degree of melatonin suppression and light's alerting action (Cajochen et al., 2005). This reduction in melatonin may have caused a delay of the opening of the sleep gate, which usually takes place around the onset of melatonin secretion in the evening (i.e., 08:00 p.m.–00:00 a.m., depending on chronotype) and enables athletes to prevent the time-of-day-related drop in performance. Thus,

TABLE 4 | Analysis of covariance to determine the effects of light exposure on sleepiness, motivation and mood.

	BRIGHT ($n = 24$)		BLUE ($n = 24$)		CONTROL ($n = 24$)		BRIGHT vs. CONTROL	BLUE vs. CONTROL	BRIGHT vs BLUE
Characteristic	Before [mean (*SD*)]	After [mean (*SD*)]	Before [mean (*SD*)]	After [mean (*SD*)]	Before [mean (*SD*)]	After [mean (*SD*)]	Adjusted difference[1] (95% CI)	Adjusted difference[1] (95% CI)	Adjusted difference[1] (95% CI)
KSS	3.2	3.1	2.9	4	3	3.5	−0.6	0.6	−1.2
	(1)	(1.2)	(1.2)	(1.7)	(0.8)	(1.4)	(-1.3; 0.2)	(−0.2; 1.4)	(−1.9; −0.4)
VAS-M	8.9	8.7	8.7	8.6	9.3	9.2	−0.2	−0.1	−0.1
(cm)	(1)	(1.4)	(1.7)	(1.6)	(0.8)	(0.7)	(-0.6; 0.2)	(−0.5; 0.3)	(−0.5; 0.3)
PANAS	3.6	3.6	3.7	3.4	3.7	3.5	0.1	−0.1	0.3
−(pos)	(0.4)	(0.6)	(0.5)	(0.7)	(0.4)	(0.6)	(-0.1; 0.4)	(−0.4; 0.1)	(0; 0.5)
PANAS	1.5	1.4	1.4	1.2	1.5	1.3	0.1	0	0.1
−(neg)	(0.5)	(0.4)	(0.4)	(0.2)	(0.5)	(0.3)	(0; 0.2)	(−0.2; 0.1)	(0; 0.2)

BRIGHT, bright light; BLUE, blue light; CONTROL, control light; KSS, Karolinska Sleepiness Scale; VAS-M, Visual Analog Scale Motivation; PANAS, Positive and Negative Affect Schedule; SD, standard deviation; CI confidence interval.
[1]*Scale after the light exposure adjusted for the corresponding value before the light exposure.*

we have first evidence that late-evening melanopic light exposure allows athletes to perform an enhanced end-spurt compared to moderate light conditions, most likely by a strong activation of the human circadian timing system. Although pacing was positively influenced in BLUE, no superiority over CONTROL in the total work performed during the time trial was observed. This may result from the smaller light emitting device used in BLUE compared to the ones used in CONTROL and BRIGHT going along with a higher likelihood to look past the light source leading to higher variations in the received amount of light within this group.

Yet even though our findings are "small" the reported difference of 4.1 kJ between control and bright light are relevant in competitive sport: a cyclist exposed to control light with a VO_2max of 4.5 l/min, 180 cm height, 73 kg body mass would be expected to perform 214 kJ in a 12-min time trial, equivalent to a mean velocity of 41.1 km/h and a total distance covered of 8,220 m. If exposed to bright light the expected work performed would be 218 kJ (+1.9%), resulting in a total distance of 8,280 m, thus 60 m more in 12:00 min. The distance of 8,220 m would be covered in 11:54.8 min and thus 5.2 s faster which represents a substantial improvement in a competitive sport environment.

In BRIGHT, participants showed a higher reduction of melatonin than in BLUE and CONTROL. This reduction was also reflected in a lower subjective sleepiness ratings indicating higher alerting effects of bright light compared to blue light exposure. In contrast, many previous studies reported a superiority of blue light over bright light on various physiological parameters (e.g., alertness, melatonin reduction, mood), even at lower doses than those used in this study (Zeitzer et al., 2000; Cajochen et al., 2005; Smith et al., 2009; Chellappa et al., 2011; Rüger et al., 2013). In a previous study from our laboratory (Knaier et al., 2016), participants were exposed to the same intensity and duration of bright and control light as in the current study, but at an earlier time point in respect to the participants' MSFsc (14:30 h), thus 3:45 h earlier. Those participants showed a small positive effect on physical performance during the first 12 min of the time trial [plus 2 kJ (95% CI −4, 8)]. Compared to those results, the effect of bright light on work performed in the present study is higher [plus 4 kJ (95% CI −5, 13)], which is remarkable because the level of cardiorespiratory fitness of the current study population was considerably higher (median VO_2max = 63 ml/kg/min vs. 56 ml/kg/min). This higher level of fitness is important, since effects of performance enhancement often get smaller with higher athletic level of the examined participant (Wenger and Bell, 1986). A possible reason for the higher effect through bright light despite a higher level of cardiorespiratory fitness may be the longer time interval between the MSFsc and the start of the time trial in the current study (18:15 vs. 14:30 h) meaning that athletes were closer to bed rest at the time of testing.

Interestingly in CONTROL adverse events were reported as often as in BRIGHT. While getting tired ($n = 2$ in CONTROL) could be expected due to the low light intensity the reported slight headaches ($n = 2$ in CONTROL) have not been reported in previous studies and are not explainable. However, since all reported adverse effects of light exposure were only minor, this indicates that bright as well as blue light exposure is safe to use

in this population. After the light exposure more participants in group BLUE (38%) expected the light to decrease performance than in CONTROL (21%), although there were no significant differences in subjective sleepiness between the groups. This may be explained by the smaller light device used in BLUE compared to CONTROL or that the participants were irritated by the color of the light.

Strengths and Limitations

To our knowledge this is the largest trial on light exposure and aerobic exercise performance in elite athletes. Light exposure was monitored by objective means for the 3 days prior to the time trial. Further, actual light exposure in the laboratory was measured at the eye level, which has never been done before. Sleep quality and physical activity as potential confounders were also controlled in parallel with light exposure prior to the time trial. MSFsc was assessed with an established questionnaire, melatonin was measured to determine the dimmed-light melatonin onset and to assess the melatonin suppressing effects of light to objectively control for the chronotype of the study participants. Additionally, mood, sleepiness, and expectations associated with the light exposure were assessed with standardized questionnaires. However, since 36 out of 72 participants were not cyclists, they could have benefited from a familiarization trial. Further, we are aware that a realistic competitive situation cannot be reproduced in a laboratory study since e.g., nervousness and anxious arousal may override the effects of light exposure on performance. Thus, our results should be interpreted with care before the background of the transfer to competitive sports.

CONCLUSIONS

Our study provides novel evidence that exposure to non-image forming light can provide elite athletes with a potentially meaningful enhancement of performance in short duration competitions taking place late at night. Our data indicate reduced sleepiness and suppressed melatonin levels as underlying mechanisms. High doses of melanopic light may activate the circadian system and thus compensate for an unfavorable chronotype. The findings from this trial may have a strong impact on the usage of bright light with respect to time of competition, but also clearly show that more data are needed to obtain more precise estimates of the performance-enhancing effect of bright light exposure.

AUTHOR CONTRIBUTIONS

Conceptualization: AS and CC: Methodology: RK, JS, AS, and CC; Formal Analysis: RK, JS, and CC; Investigation: RK, AR, CK, HH, and AS; Writing original draft: RK, JS, AS, CC, and CH; Writing–Review and Editing: AR, CK, and HH; Visualization: JS, RK, CH, and CC; Supervision: AS

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JS has been an employee of F. Hoffmann-La Roche Ltd since December 1, 2016. The present study was conducted before JS joined F. Hoffmann-La Roche Ltd and has no connection to her employment by the company.

Chapter 5

Publication 3: Effects of bright and blue light on acoustic reaction time and maximum handgrip strength in male athletes: a randomized controlled trial

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Chapter 6

Publication 4: Influence of morning bright light exposure on self-chosen exercise intensity and mood in individuals with overweight

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Abstract

Objective: To assess the influence of bright light exposure on self-chosen exercise intensity and mood.

Methods: In this randomized controlled single-blind parallel group design, 26 individuals with overweight (11 males, 15 females; age 25 ±5.7 years; body mass index 28.9 ±2.1 kg/m2) performed a cardiopulmonary exercise test to measure maximum oxygen uptake (V̇O2max). Two days later a 30-minute exercise session with self-chosen exercise intensity was performed for familiarization. Then participants were randomly allocated to bright light or a control light condition. Three to seven days later, participants were exposed to light for 30 minutes starting at 8:00 am, immediately followed by a 30-minute exercise session with persisting light exposure. Multidimensional mood questionnaires were filled out before and after the light exposure and after the exercise session.

Results: In the multivariate analysis adjusted for V̇O2max, the mean power output during the exercise session was 8.5 W higher (95% confidence interval -12.7, 29.7; P=0.416) for participants in bright light compared to control light. There were no significant differences between the groups for any of the three domains of the questionnaire.

Conclusions: Bright light exposure does not increase self-chosen exercise intensity or improve mood in a 30-minute exercise session starting at 08:30.

Introduction

Overweight and obesity are globally one of the leading causes of death and are associated with a decrease in life expectancy of up to 20 years [1]. The recommended amounts of physical activity get updated regularly [2], but it is still unclear if these amounts are sufficient to prevent overweight [3]. However, the main challenge actually is to keep people with overweight and obesity motivated to exercise. Especially high training intensities have further beneficial health effects compared to lower intensities like a higher reduction in total cholesterol or triglycerides [4] and higher energy expenditure. But those intensities are likely to be avoided due to higher subjective effort. Particularly in the morning, lower exercise intensities are chosen than in the afternoon [5]. Methods to increase self-chosen exercise intensity or to reduce subjective effort during physical activity would therefore be highly beneficial to keep individuals with overweight motivated to exercise.

Light has positive effects on human health. It positively influences circadian rhythms of shift workers [6], can be used in the treatment of seasonal affective disorder [7, 8] and showed reductions in carbohydrate craving, appetite and morning fatigue [9]. Yet so far, the influence of light on physical performance has only been examined regarding maximum performance [10–13]. If light exposure can reduce subjective effort through increased vitality [14] while self-chosen exercise intensity remains the same, people with overweight might continue with their exercise programs.

Furthermore, light exposure might increase self-chosen exercise intensity by raising alertness and reducing sleepiness [15]. This would be very beneficial because even small increases in exercise intensity can reduce the risk of arteriosclerosis. Training at 55% compared to 40% of maximum performance for example can lead to significant improvements in levels of oxidative stress markers [16]. In addition, the small imbalance in daily energy consumption and expenditure of only 100 kcal/day or less causes probably 90% of overweight in the US population [17]. This demonstrates that an even slightly higher energy expenditure through increased exercise intensity could be relevant. Thus, we hypothesized that an exposure to bright light during exercise in the morning may increase participants' motivation and reduce sleepiness and therefore lead to higher training intensity at lower or similar subjective effort.

Methods

This randomized controlled parallel group design study was approved by the local ethics committee (Ethikkommission Nordwest- und Zentralschweiz, Reg.-No. 2015-365) and complied with the declaration of Helsinki. Written informed consent was signed by all participants. The study was conducted from January 2016 to April 2016 and from September 2016 to June 2017 at the Department of Sport Exercise and Health of the University of Basel, Switzerland (ClinicalTrial.gov Identifier: NCT02636335). This study was originally registered on ClinicalTrial.gov with five appointments (cardiopulmonary exercise test, familiarization trial and three identical exercise sessions). Three exercise sessions (on every other day; i.e. 6 study days) were originally intended to be performed in order to examine if possible effects of bright

light on self-chosen exercise intensity or mood hold true for repetitive exercise sessions as well as to investigate the usability of light exposure in interventional studies. During the study the protocol was reduced from three to a single exercise session after 15 participants completed all three test sessions, because – despite enormous efforts – not enough participants could be recruited to meet the pre-specified sample size. This change in the protocol does not affect the pre-specified primary outcome (i.e. mean power in the first exercise session) of the study. All analyses were performed regarding the first exercise session, with exception of the physical activity which was analyzed for the subgroup that performed all three exercise sessions. Males and females with overweight and obesity (body mass index [BMI] > 25 kg/m2 and ≤ 35 kg/m2) between 18 and 40 years of age were invited to participate in the study. Exclusion criteria were depression, uncontrolled hypertension, shift-work in the last three months or travels across more than one time zone in the last four weeks before the study.

Clinical examination and cardiopulmonary exercise test

The clinical examination started with computer based questionnaires (Munich Chronotype Questionnaire [18], 13-item Functional Assessment of Chronic Illness Therapy Fatigue Scale [19] and Pittsburgh Sleep Quality Index [20]). This was followed by the measurement of anthropometric data including, body height, body mass and body fat content with bioelectrical impedance analyses (Inbody 720, Biospace, Seoul, South Korea). Medical examination comprised measurement of resting blood pressure, a 12-channel resting electrocardiography and a physical examination by a physician. To measure the maximum oxygen uptake ($\dot{V}O_2max$) a cardiopulmonary exercise test was performed on a bicycle ergometer (ergoselect 200 P, ergoline GmbH, Bitz, Germany), starting with a three-minute warm-up phase at 25 W, followed by a linear increasing workload of 15 W/min until participants' exhaustion, followed by a five-minute cool-down phase at 25 W. Pedaling cadence was chosen by participants but had to be over 60 revolutions per minute. Breath by breath gas analyses (MetaLyzer 3B, Cortex Biophysik GmbH, Leipzig, Germany) and heart rate (Custo med GmbH, Ottobrunn, Germany) were measured continuously, rating of perceived exertion (Borg Scale 6-20) [21] was asked every three minutes during the increasing workload phase and concentration of blood lactate was measured at rest, at exhaustion and three minutes after exhaustion from capillary blood samples from the earlobe (analyzed by SuperGL Ambulance, Hitado Diagnostic Systems, Moehnesee, Germany). Exhaustion was only accepted if three of the following four criteria were fulfilled: (1) maximum respiratory exchange ratio ≥ 1.10, (2) maximum heart rate ≥ 95% of age predicted heart rate (i.e. [210 – age in years] bpm), (3) rating of perceived exertion ≥ 19 and (4) maximum concentration of blood lactate > 8 mmol/l.

Familiarization trial and activity monitoring

Two days after the cardiopulmonary exercise test, participants performed a 30 min exercise session on a bicycle ergometer (ergobike 8008 TRS, Daum electronic GmbH, Fürth, Germany) for familiarization. The exercise session started with a three-minute warm-up phase at 25 W,

followed by 30 minutes with self-chosen exercise intensity, followed by a five-minute cool-down phase at 25 W. Participants could change the workload through the exercise session, but cadence had to be over 60 revolutions per minute. Minimum and maximum possible workloads were 25 W and 800 W. Workload and heart rate (Polar T-34 heart rate belt, Polar Electro Europe AG, Zug, Switzerland) were measured continuously during the exercise session by the ergometer and stored on a secure digital memory card. Participants could not see the current workload or their heart rate, but the elapsed time. Rating of perceived exertion was assessed every six minutes during the exercise session. During the study period physical activity was objectively controlled with an accelerometer wGT3X+ActiGraphs (ActiGraph, Pensacola, United States). The device was worn on the non-dominant hand, measuring rate was 60 Hz and recording started at 12 am on the day before exercise session 1 and ended at 8 am on the day of exercise session 3 (i.e. 128 hours in total).

Light exposure

Light was administered by two lights (HF3309 PL-L 36 W Philips EnergyLights) with a light intensity of ~4400 lx under bright light and ~230 lx under control light. The light devices were built up on a table at a distance of 60 cm from the participants' eyes. Light exposure started at 8 am (i.e. 30 minutes prior to the exercise session) and went on until the end of the exercise session.

Exercise session and mood assessment

At 07:45 am participants arrived in the laboratory and answered the multidimensional mood questionnaire [22]. The light exposure started at 08:00 am and the participants received a standardized breakfast including 30g muesli, 200g yoghurt, 20g jam, 200ml orange juice and water (i.e. 325 kcal, 6g fat, 50g carbohydrate, 16g protein). At 08:25 am participants answered the multidimensional mood questionnaire for the second time and at 08:30 am the exercise session started. Immediately after the exercise session participants filled out the multidimensional mood questionnaire again and a questionnaire asking about participants` pacing strategy.

Randomization, allocation and blinding

Participants were randomized to bright light or control light group after successfully completing the familiarization trial. We used permuted block randomization with randomly varying block sizes of 1, 2 and 3 to randomly allocate participants in equal numbers to one of the two groups. The randomization list was generated in advance using the online tool available at http://www.randomization.com (accessed December 8, 2015) and transmitted using sequentially numbered, opaque, sealed envelopes by a person otherwise not involved in the study. Participants were blinded to the light condition they were allocated to. The control light was equipped with four additional red light emitting diodes in the center of the light to look special and avoid that participants could expect that they were allocated to the control condition. The red lights have no physiological effect and the blinding purpose worked

successfully in a previous study [13]. Test supervisors were not blinded to the light condition but were instructed not to motivate the participants at any time during the exercise session.

Statistics

The primary outcome of this study was the average power output during the 30-minute exercise session on a bicycle ergometer with self-chosen exercise intensity during the first exercise session. We used analysis of covariance with adjustment for $\dot{V}O_2max$ from the cardiopulmonary exercise test to compare the power output during the exercise session between the participants in bright light and control light [23]. We used linear mixed effects models to compare the values of the three domains of the multidimensional mood questionnaire (good-bad; awake-tired; calm-nervous) after the light exposure but before the exercise and after the exercise between bright light and control light. Specifically, we included fixed effects for the time and the group indicators. A random intercept for the participants was included to take into account the fact that each participant was measured at each time point (pre light exposure; post light exposure; post exercise). Similarly, we analyzed the steps per day in the subgroup that performed all three exercise sessions. For each analysis, we report the estimated differences (with 95% confidence intervals [95% CI]) in outcome between the two groups. We used IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, N.Y., USA) for our analyses. All significance tests were two-sided and P-Values <0.05 were considered statistically significant.

Sample size calculation

We assumed a mean maximum performance of 210 ± 40 Watt in the cardiopulmonary exercise test and that participants in control would choose mean exercise intensities during the exercise session of 42.5% ± 9% of their maximum performance (i.e. 89 ± 25 W). Bright light improved maximum physical performance in well-trained athletes by 4.5%. [12] Bearing in mind possible ceiling effects in the performance of well-trained athletes and that it is easier to improve submaximal performance than maximum performance, we expect the participants in the bright light group to choose exercise intensities at 52.5% of maximum performance (i.e. 110 ± 25 W). To achieve a power of 80%, with an alpha 0.05, an expected correlation between the maximum performance from the baseline test and the self-chosen exercise intensity in the test session of 0.7, we planned to test 13 participants per group.

Results

Participants

The flow of participants through the trial is presented in Figure 1 and participants characteristics are presented in Table 1. Three participants showed sleeping disturbances and none of the participants showed fatigue (Table 1). As stated above, a subgroup of 15 participants (bright light n=8; control light n=7) performed three exercise sessions and was analyzed for physical activity (not shown in Figure 1).

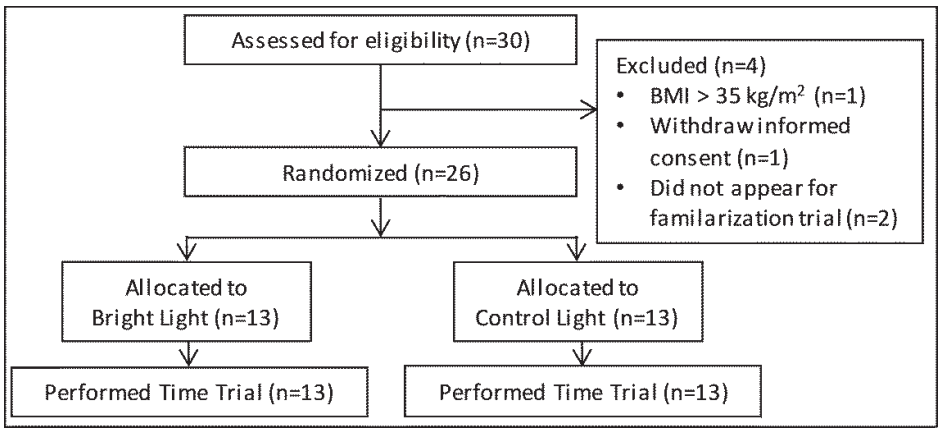

Figure 1: Flow of participants through the trial

Table 1: Participant characteristics – median (interquartile range) or quantity.

Characteristic	**Bright light (n=13)**	**Control light (n=13)**
Sex (male / female)	5 / 8	6 / 7
Age (years)	25 (22; 31)	24 (21; 30)
Height (cm)	170 (164; 181)	176 (167; 180)
Body mass (kg)	82 (76; 99)	86 (80; 94)
BMI (kg/m^2)	29.1 (27.5; 30.5)	29.7 (27.0; 30.1)
Body fat (%)	32 (26; 39)	33 (29; 40)
Blood pressure (mmHg)		
Systolic	120 (110; 127)	121 (110; 137)
Diastolic	75 (72; 82)	80 (70; 85)
MSFsc (hh:mm)	04:10 (03:34; 5:07)	05:04 (4:11; 05:43)
$\dot{V}O_2$max (l/min)	3.03 (2.72; 3.14)	2.85 (2.41; 3.29)
$\dot{V}O_2$max (ml/kg/min)	37 (32; 39)	33 (29; 37)
Pmax (W)	217 (206; 248)	211 (176; 252)
Maximum heart rate (bpm)	193 (185; 196)	185 (183; 190)
Fatigue Score	48 (45; 50)	49 (47; 50)
PSQI (n)		
≤ 5	13	10
> 5	0	3
Smoking (n)		
Never smoker	10	10
Former smoker	2	2
Current smoker	1	1

Abbreviations: BMI, body mass index; MSFsc, mid-sleep on free days corrected for "oversleep" due to the sleep debt accumulated over the workweek; $\dot{V}O_2$max, maximum oxygen uptake; Pmax, maximum power output during cardiorespiratory fitness test; PSQI, Pittsburgh Sleep Quality Index.

Effect of light exposure on self-chosen exercise intensity and subjective effort

The mean (standard deviation [SD]) of average power output during the exercise session was 92 (19) Watts in bright light and 80 (37) watts in control light, respectively. This were 40.4% (6.8) of the maximum power output from the cardiopulmonary exercise test in bright light and 36.9% (17.1) in control light, respectively. The difference in the mean power output during the first exercise session adjusted for $\dot{V}O_2max$ from the cardiopulmonary exercise test was 8.5 W (95% CI -12.7; 29.7; P=0.416) for participants in bright light relative to participants in control light (Figure 2A). No significant differences could be seen in objective effort (i.e. heart rate, Figure 2B), subjective effort (i.e. rating of perceived exertion, Figure 2C) or in the exercise intensity relative to maximum power from the cardiopulmonary exercise test (Figure 2D). Mean (SD) of average heart rate during the exercise session as percent of maximum heart rate from the cardiopulmonary exercise test was 71.9% (5.9%) in bright and 67.9% (8.3%) in control, respectively.

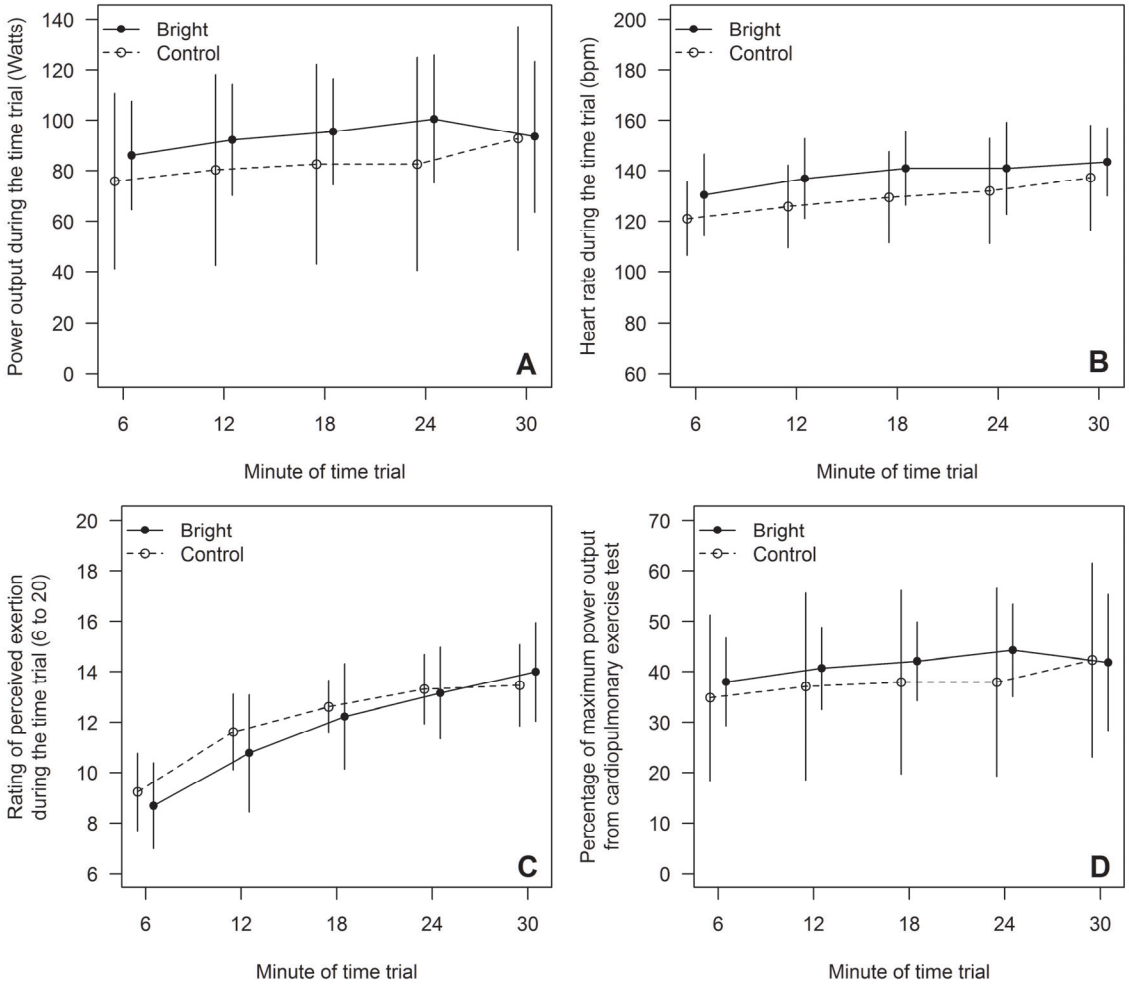

Figure 2: Participants power output (A), heart rate (B), rating of perceived exertion (C) and power output in percentage of peak power output from the cardiorespiratory fitness test (D) during the exercise session in each group.

Effect of light exposure on mood

Participants showed normal values for all three domains (good-bad; awake-tired; calm-nervous) of the multidimensional mood questionnaire for this population [24]. We found little evidence that the groups differed at any time point with regards to the three domains good-bad, awake-tired or calm-nervous. In addition, there were no significant differences between the time points (i.e. before and after the light exposure and after the exercise session) within the groups with regards to the three domains (Table 2).

Table 2: Participants' mood rating – median (interquartile range) if not stated otherwise.

Characteristic	Bright light (n=13)	Control light (n=13)	Mean difference (95% confidence interval) Bright light vs. Control light
Good – Bad Mood Scale			
Pre Light Exposure	18 (18; 20)	18 (14; 20)	1.2 (-0.9, 3.3)
Post Light Exposure	19 (18; 20)	18 (16; 20)	1.0 (-1.0, 3.1)
Post Exercise	20 (17; 20)	18 (16; 20)	1.0 (-1.0, 3.1)
Wakefulness – Tiredness Scale			
Pre Light Exposure	16 (12; 19)	13 (11; 18)	1.9 (-0.7, 4.4)
Post Light Exposure	17 (13; 19)	14 (12; 19)	1.5 (-1.0, 4.1)
Post Exercise	17 (15; 18)	15 (14; 16)	1.8 (-0.8, 4.3)
Calm – Nervous Scale			
Pre Light Exposure	17 (15; 20)	16 (13; 18)	1.7 (-0.6, 4.0)
Post Light Exposure	19 (16; 20)	16 (13; 20)	1.6 (-0.6, 3.9)
Post Exercise	16 (15; 19)	17 (14; 19)	-0.2 (-2.4, 2.1)

Participnats' pacing and physical activity

Participants mean (SD) self-rated pacing on a visual analog scale with 10 cm from 0 (very bad) to 10 (very good) was 7.7 (1.7) for participants in bright light and 6.6 (1.5) for participants in control light, respectively.

Participants in bright light and control light showed no significant differences in physical activity (i.e. steps per day) throughout the entire study period (Table 3). In bright light and control light the exercise sessions in the morning did neither increase nor decrease objectively monitored physical activity significantly on the same (days 2, 4) or subsequent day (days 1, 3, 5).

Success of blinding

In group bright light eight participants expected to be in the intervention group and five to be in the control group. In group control light six participants expected to be in the intervention group and seven in the control group.

Table 3: Participants´ physical activity – median (interquartile range). Physical activity was assessed in a subgroup of participants (see methods).

Characteristic	Bright light (n=8)	Control light (n=7)
	Steps per day	**Steps per day**
Day 1	10,062 (101; 12,111)	7,948 (404; 11,331)
Day 2 (Exercise Session 1)	13,108 (11,817; 17,106)	11,244 (9,488; 15,224)
Day 3	10,396 (6,890; 16,460)	9,019 (7,198; 10,595)
Day 4 (Exercise Session 2)	9,103 (7,157; 15,594)	9,403 (8,685; 16,276)
Day 5	11,179 (8357; 12,530)	9,861 (5,980; 17,792)
Day 6 (Exercise Session 3)	1,718 (1,187; 2,608)	2,892 (1,620; 5860)

Discussion

The main finding of the present study suggests that exposure to bright light for 30 minutes prior to and during a 30-minute exercise session with self-chosen exercise intensity starting at 08:30 does not improve mean power output, reduce subjective effort or positively influence mood in participants with overweight. This is the first study investigating the acute influence of light exposure on self-chosen exercise intensity. Previous studies exclusively focused on the effects of light exposure on maximum performance in male athletes and partially found positive effects of light on maximum performance [10–13]. However, those results do not support any conclusions regarding self-chosen submaximal exercise intensity. In our study population, we expected significant positive effects on mean power output, because submaximal performance can be increased more easily. Yet, in contrast to previous studies with evening light exposure, the participants in our study were exposed to light in the morning. At 08:30 melatonin levels may already have been relatively low reducing the chance of positive effects of light exposure on alertness or reduction in sleepiness. This is supported by the relatively normal values on the wakefulness/tiredness domain of the multidimensional mood questionnaire before the light exposure despite the early time of the day. Therefore, exposure to bright light at an earlier time of the day when melatonin levels are higher may lead to a stronger increase in exercise intensity. 08:30 was chosen, because at this time of the day exercise sessions often take place in fitness and health facilities. Terman et al. (2005) suggested to expose patients with seasonal and non-seasonal depression not later than 8.5 h after the dim light melatonin onset to bright light to induce an antidepressant effect [25]. Analog to that, participants in future studies are to be exposed to bright light at 06:00. This exposure time would best be applied in a home-based setting as “Prior Work Exercise”, which would open a perspective for broader dissemination.

Although participants were allocated randomly to the groups, participants in the bright light group had an earlier MSFsc than participants in control light (Table 1). They therefore performed the exercise session at a later time regarding usual wake up times, which may have partially masked the effect of bright light, because performance increases rapidly in the first hours after usual wake up times [26]. Further, participants had to come to the laboratory and

were therefore already awake for 2.2 h (1.8, 2.7) in bright light and 1.8 h (1.6, 2.4) in control light before the exercise session started. On their way to the laboratory participants were exposed to several different light sources (e.g. sunlight or indoor illumination). Bearing in mind that light intensities of just 100 lx already induces 50% of the alerting response that light intensities of 10000 lx does [15] participants in both groups are likely to be influenced by showing a higher alertness when arriving in the laboratory. This influence is higher in bright light, due to the longer time since awakening. Previous studies [9, 27] reported significant changes in mood after three and four weeks of daily use of bright light. In participants in our study mood was not altered after 60 minutes of bright light exposure combined with exercise. This indicates that bright light treatment may only change mood in mid- and long-term treatment.

Changes in mood might also be the reason for previously examined effects of light exposure on changes in body fat mass over longer lasting periods [27, 28]. In a six-week intervention trial by Dunai et al., [28] participants were allocated to bright light or a control group. Both groups exercised for 30 minutes three times per week at 65% of heart rate reserve, while the bright light group additionally had 60 minutes of bright light exposure per day. The bright light group showed a significantly higher reduction in body fat mass than the control group. A cross-over trial with three weeks bright light versus three weeks room light exposure for 45 minutes per day without exercise conducted by Danilenko et al. [27] in females with overweight showed significant reductions in appetite and body fat content in the bright light group. Unfortunately, neither physical activity nor nutrition was recorded during the intervention period. Objectively monitored physical activity data from our study suggests that exposure to high doses of light in the morning does not increase physical activity on the same or on the subsequent days. At the same time, our results show that the changes in body fat are also not due to increased energy expenditure during exercise.

Vetter et al. (2017) reported that the effect of training intensity on endurance performance is linear [29]. It can be assumed that in low trained individuals even a small increase in training intensity would be beneficial to increase fitness. Because overweight is spreading rapidly worldwide in all age groups [30] even small effects should be considered as relevant. Since the influence of bright light on mean power output only points in the direction of a superiority of bright light, but is not significantly this needs to be investigated in a larger scale study.

Conclusions

Bright light exposure prior and during exercise session starting at 08:30 in condition of normal vigilance may not increase self-chosen exercise intensity or decrease subjective effort in a 30-minute endurance exercise session. Mood was not altered after a single bright light exposure session. However, exposure to bright light at a time of the day when participants are sleepier may increase exercise intensity acutely.

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Chapter 7

Synthesis, Discussion and Perspectives

Chapter 7 Synthesis, Discussion and Perspectives

This chapter summarizes and discusses the main results of the three publications [1–3] and the manuscript submitted [4] in the framework of this PhD project.

7.1 Synthesis

Table 1 summarizes the main effects of the different light exposure modalities in studies 1 – 3 compared to a control light conditions.

Table 1: Effects of different light exposure modalities on physical performance, sleepiness, motivation, and mood compared to a control light condition.

	Study 1			Study 2		Study 3
Light factors						
Exposure prior to exercise (min)	120	60	60	60	60	30
Exposure during exercise (min)	40	40	no	no	no	30
Peak wavelength (nm) (color)	545 (white)	545 (white)	545 (white)	545 (white)	469 (blue)	545 (white)
Intensity (lx)*	4400	4400	4400	4400	230	4400
Start time of exposure (h after MSFsc / am)	12.3 h	13.5 h	13.5 h	17 h	17 h	08:00 am
Task factors						
Duration/kind of task	40 min all-out time trial	40 min all-out time trial	40 min all-out time trial	12 min all-out time trial	12 min all-out time trial	30 min exercise session
Individual performance factors						
Fitness/Skill Level	athletes	athletes	athletes	elite athletes	elite athletes	overweight individuals
Outcomes						
Work performed (kJ) / power output (W)	23 kJ (10; 36)	-2 kJ (-20; 16)	-4 kJ (-17; 9)	4.1 kJ (-4.5; 12.7)	-1.2 kJ (-9.8; 7.5)	8.5 W (-12.7; 29.7)
Sleepiness	n. s. (KSS)	n. s. (KSS)	n. s. (KSS)	n. s. (KSS)	n. s. (KSS)	n. s. (MDMQ)
Motivation	not assessed			n. s. (VAS-M)	n. s. (VAS-M)	not assessed
Mood	not assessed			n. s. (PANAS)	n. s. (PANAS)	n. s. (MDMQ)

Abbreviations: n.s., no significant difference; MSFsc, mid-sleep on free days corrected for "oversleep" due to the sleep debt accumulated over the workweek; KSS, Karolinska Sleepiness Scale; MDMQ, Multidimensional Mood Questionnaire; VAS-M, Visual Analog Scale Motivation; PANAS, Positive and Negative Affect Schedule.

*: Intended light intensity according to the study protocol.

Study 1: Knaier et al. (2016). Dose–response relationship between light exposure and cycling performance. Scand. J. Med. Sci. Sports 26, 794–801.

Study 2: Knaier et al. (2017). Prime time light exposures do not seem to improve maximal physical performance in male elite athletes, but enhance end-spurt performance. Front. Physiol. 8:264.

Study 3: Knaier et al. (2017). Influence of morning bright light exposure on self-chosen exercise intensity and mood in individuals with overweight individuals. Submitted to: Obesity.

Control condition: Equal exposure duration and same start time of light exposure as in each group, peak wavelength 545 nm, light intensity 230 lx.

7.1.1 Aim 1: Evaluating the dose-response relationship between light exposure and cycling performance in athletes.

The aim of the first publication was to evaluate a possible positive dose-response relationship between the duration of light exposure and a following cycling performance. In the group that was exposed to light only 60 minutes prior to the time trial (i.e. short), the median (interquartile range) total work performed during the 40-minute time trial after bright light exposure was 520 kJ (443; 594) and after control light exposure 514 kJ (449; 595), respectively. In the group exposed to light for the 60 minutes prior to as well as during the time trial (i.e. medium), the total work performed was 485 kJ (463; 590) vs. 498 kJ (458; 574) and in the group exposed for 120 minutes prior to as well as during the time trial (i.e. long) 527 kJ (492; 573) vs. 512 kJ (468; 544), respectively. Only the latter group showed a significant (P=0.002) difference between bright and control light exposure. The estimated mean difference (95% confidence interval [95% CI]) in the effect between bright light exposure and control light exposure on total work performed for the three doses were: between long and medium exposure duration 26 kJ (1; 51), between long and short exposure duration 28 kJ (6, 50) and between medium and short exposure duration 2 kJ (-23, 27). The analyses of covariance showed a significant (P=0.006) positive dose-response relationship between the work performed and the exposure duration. This was also the case when the effect was adjusted for the maximum oxygen uptake from the baseline test (P=0.012). An explorative analysis for the effect over time during the time trial showed high differences in the work performed between bright light and control light for the initial 12 minutes of the time trial. In detail, the mean (95% CI) differences were 2 kJ (-4; 8) for the short, 4 kJ (-5; 13) for the medium and 10 kJ (5; 15) for the long exposure duration, respectively.

7.1.2 Aim 2: Effect of light exposure on maximum cycling performance in elite athletes

Study 2 was conducted to investigate the influence of bright and blue light exposure on cycling performance in elite athletes (N=69). The mean (standard deviation) of total work performed during the 12-minute time trial was 229 kJ (23) in bright light group (BRIGHT) (N=23), 218 kJ (34) in blue light group (BLUE) (N=22) and 216 kJ (25) in control light group (CONTROL) (N=24). If adjusted for the maximum oxygen uptake from the baseline test the estimated differences (95% confidence interval) in the work performed were 4.1 kJ (-4.5; 12.7; P=0.346) in BRIGHT and -1.2 kJ (-9.8; 7.5; P=0.787) in BLUE, both relative to CONTROL. There was a positive association between the amount of exposure to melanopic light and the performance gain during the time trial, defined as the ratio of the work performed in the first and last minute of the time trial. In detail, a tenfold increase in melanopic light was associated with an increase in performance gain of 8.0% (95% CI 2.6; 13.3; P=0.004). This tenfold increase in exposure to melanopic light also went along with a significant decrease in melatonin of -0.9 pg/ml (95% CI -1.5; -0.3; P=0.006). Compared to CONTROL, neither BRIGHT nor BLUE showed any significant effects on motivation, sleepiness or mood. The factors were assessed with a visual analog scale, the Karolinska Sleepiness Scale [5] and the positive and negative affect

schedule [6]. Only minor adverse events were reported, with no relevant differences in frequency between the groups.

7.1.3 Aim 3: Effect of light exposure on acoustic reaction time and handgrip strength in elite athletes

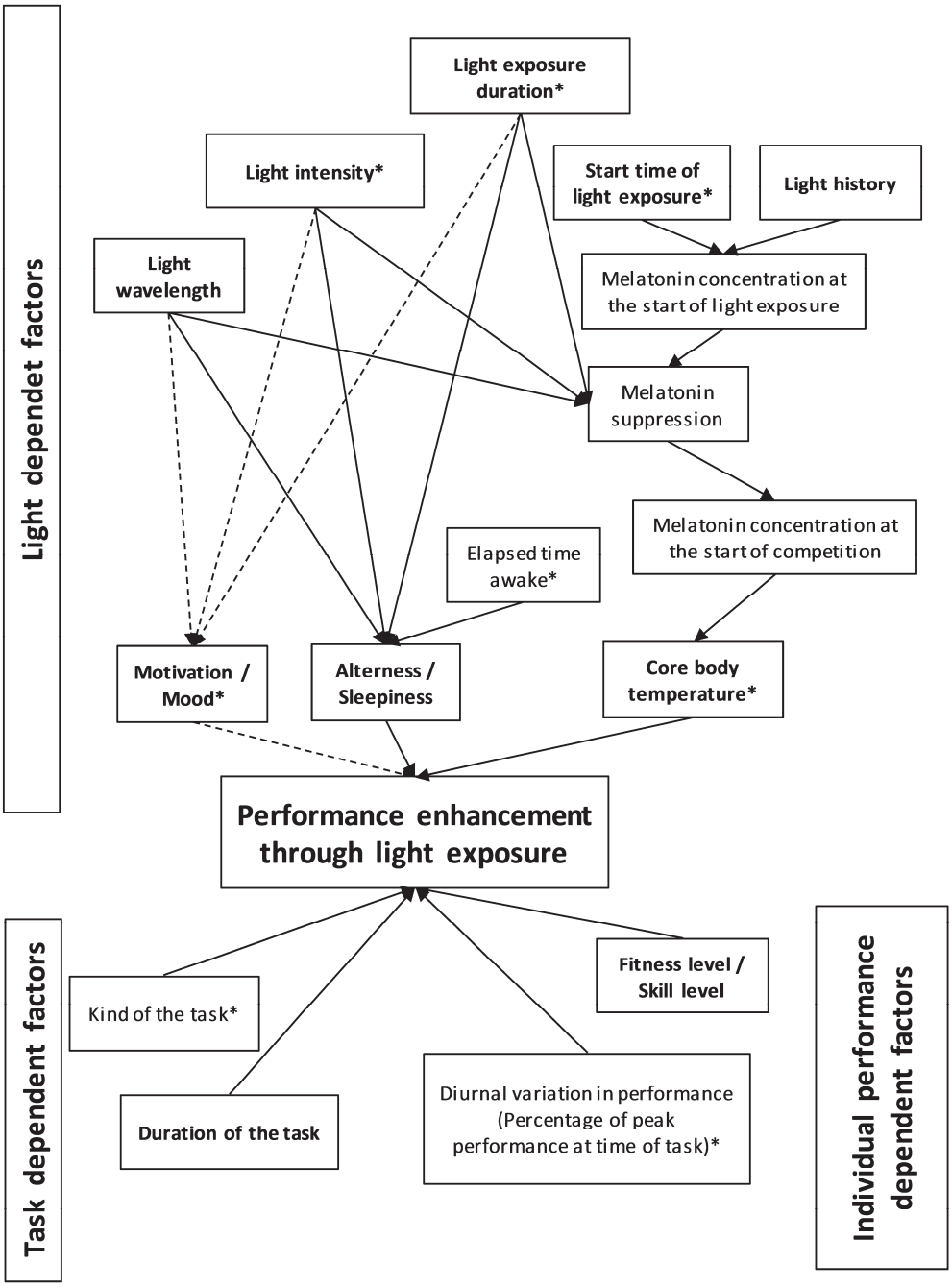
The secondary outcomes of study 2 were analyzed to investigate the effect of bright and blue light on simple acoustic reaction time and maximum handgrip strength in elite athletes (N=72, N=24 per group). Relative to CONTROL the estimated differences (95% CI) in reaction time after the light exposures, adjusted for the values before light exposure, were -1 ms (-8, 6) in BRIGHT and 2 ms (-5, 9) in BLUE. The differences in handgrip strength relative to CONTROL were 0.9 kg (-1.5, 3.3) for BRIGHT and -0.3 kg (-2.7, 2.0) for BLUE. After light exposure, the melatonin concentration threshold of 2 pg/ml was reached by 17% of participants in BRIGHT, 22% of participants in BLUE and 29% of participants in CONTROL, respectively. The median (interquartile range) light intensities (lx) actually reaching the participants' eyes were much lower than specified by the manufacturer and thus intended according to the protocol. These light intensities were 1326 lx (961; 1591) vs. ~4400 lx in BRIGHT, 203 lx (30; 598) vs ~230 lx in BLUE and 115 lx (78; 208) vs ~230 lx in CONTROL, respectively. In an explorative analysis, with adjustment for the reaction time before the light exposure, every increase in 100 lx of light exposure was associated with an estimated change in reaction time of 0.1 ms (95% CI -0.3; 0.6). The change in handgrip strength was 0.0 kg (95% CI -0.3, 0.3) per 100 lx increase in light intensity after adjustment for the baseline values.

7.1.4 Aim 4: Effect of light exposure on self-chosen exercise intensity and mood in overweight individuals

The aim of study 3 was to investigate the influence of bright light on self-chosen exercise intensity and mood in overweight individuals (N=26, N=13 per group). The mean (standard deviation) power output performed during the 30-minute exercise session was 92 Watts (19) in BRIGHT and 80 Watts (37) in CONTROL. The estimated difference (95% confidence Interval) was 8.5 Watts (-12.7; 29.7; P=0.416) for participants in BRIGHT compared to CONTROL. Rating of perceived exertion and heart rate during the exercise session did not differ significantly between the groups at any time during the exercise session. Further, there were no significant differences in any of the three domains (i.e. good-bad mood, awake-tired, calm-nervous) of the multidimensional mood questionnaire [7] between the groups at any point in time. Participants' mean (standard deviation) rating of their pacing during the exercise session was 7.7 (1.7) in BRIGHT and 6.6 (1.5) in CONTROL (scale: "0=bad pacing" to "10=good pacing"). Eight participants in BRIGHT and six in CONTROL expected to be in the intervention group, while five participants in BRIGHT and seven in CONTROL expected to be in the control group. There were no significant changes in steps per day between the groups or between days during the intervention period in the subgroup that performed all three exercise sessions.

7.2 General discussion

Figure 1 shows factors influencing the possibility of light exposure to enhance performance. Bold print highlights the factors that were considered in the conducted studies of this PhD project. Asterisks indicate factors that need to be considered more carefully in upcoming studies and are discussed in more detail in Table 2 (see Chapter "7.4 Perspectives").



Bold print (**A**): Factors that were considered in the previous study designs.
Asterisk (*): Factors that need to be considered to a higher extent in future studies.
Dotted arrows: Unclear pathway/relationship.

Figure 1: Factors influencing the possibility of light exposure to enhance performance.

7.2.1 Influence of light exposure on cycling performance and melatonin suppression

The data analysis of study 1 [1] showed a dose-response relationship between the exposure duration to light and the total work performed during a 40-minute time trial. Only the participants exposed to bright light for two hours prior to and during the time trial performed significantly more work during the time trial compared to control light. The lack of an effect of bright light exposure in the groups with medium and short exposure duration suggests a non-linear dose-response relationship and that a certain threshold of exposure duration needs to be reached. The dose-response relationships between light exposure intensity and melatonin suppression [8], light exposure duration and melatonin suppression [9] as well as light exposure intensity and subjective sleepiness [10] are all also known to be non-linear. However, the three latter relationships show an asymptotic slope, without a certain threshold that needs to be exceeded.

In contrast to study 1 [1], participants in study 2 [2] did not show a significant dose-response relationship between the light intensity a person was exposed to and the work performed in the time trial. In both studies the same light devices were used. In study 2 the light exposure intensity actually reaching the participants' eyes was remarkably lower than intended in the study protocol. This lower intensity results from different directions of gaze and sitting postures. In study 1 the actual light intensity was not measured on eye level but it is expected to be comparably to study 2 since the same light devices were used. The differences in the effect on performance seen in the group exposed to light for 120 minutes prior to and during the time trial in study 1 and participants in study 2 suggests, that exposure duration was too short in study 2. For two different reasons 60 minutes of light exposure only prior to the time trial were chosen for study 2 – despite the fact that in study 1 no effects on performance were seen in the group exposed to light for the same duration. Firstly, the time trial in study 2 was of shorter duration (12 minutes versus 60 minutes). All groups in study 1 showed the highest effects of light exposure on performance in the first 12 to 24 minutes of the time trial depending on the exposure duration prior to the time trial. Secondly, in study 2 the time trial started at a later time of the day. This results in athletes having higher melatonin levels, whereby they additionally benefit from melatonin suppression through light exposure and not only from the alerting effects of light as in study 1. However, the later time of the day and the shorter time trial chosen in study 2 seem to be not effective to compensate for the shorter exposure duration compared to study 1.

The hypothesized underlying mechanisms for the improvement in physical performance in the evening through light exposure were mainly a reduction of melatonin levels going along with changes in core body temperature, apart from improvement in motivation and mood and reduction of sleepiness and increase in alertness (see Figure 1). As previously reported [11,12], blue light was expected to show the strongest decrease in melatonin. In contrast to previous studies, however, the highest suppression in melatonin was seen in group BRIGHT. This may be explained by the high variations in received light intensity caused through the small light device. This variation made it harder to compare participants in BRIGHT and BLUE

on group level. Another explanation for the lower melatonin suppression in group BLUE may be the amount of melanopsin containing photoreceptors that varies from human to human [13]. A high variation in the suppression of melatonin between subjects has been reported previously by Lockley et al. [12]. In the latter study the range of melatonin suppression in participants exposed to blue light was 65-96% and 0-88% in subjects exposed to white light, respectively. Similarly, Thompson et al. [14] reported high variations in the effects of light exposure on phase shifts between subjects. The suppression of melatonin is one of the expected underlying mechanisms through which maximum performance or self-chosen exercise intensity is likely to be influenced. Therefore, testing if a person shows a high or low melatonin suppression through light exposure could help to identify subjects with more melanopsin containing photoreceptors and help to predict in whom light exposure may be an effective tool to influence performance.

However, group BRIGHT which showed the strongest decrease in melatonin also showed the highest positive influence on maximum performance. Similarly, the significantly higher performance gain caused by melanopic light in group BLUE was also associated with a significantly higher reduction in melatonin. Melatonin reduction in the evening therefore seems to be an important factor to improve performance and enhance end-spurt performance. The reason for the importance of melatonin is likely because it is a mediator for core body temperature. The ideal exposure duration still needs to be found. To suppress melatonin to a relevant extend through bright or blue light in comparison to dim light a minimum duration of 30 minutes is necessary [10], while 60 minutes are necessary to show an effect compared to normal room light conditions [2]. The duration of 60 minutes necessary to reach relevant differences between bright and control light may partially explain why self-chosen exercise intensity in study 3 was not increased. In study 3 thirty minutes of light exposure prior to the exercise session were chosen to simulate a realistic setting in sports therapy. In daily practice individuals do not wait 60 minutes before they start with their training. Thirty minutes seemed more realistic in regard to the time people need to change clothes and perform a warm-up before exercise. Further, the effect on self-chosen exercise intensity was also hypothesized to result from increased mood through the bright light exposure.

In study 2 [2], we expected higher effects of bright light exposure on maximum performance compared to the group with equal exposure duration and intensity from study 1 [1]. Light exposure was scheduled later and athletes would therefore benefit from melatonin suppression in contrast to the latter group. Indeed, the effect of bright light on the work performed during the 12-minute time trial was higher (+4 kJ) than the work performed in the initial twelve minutes of the 40-minute time trial (+2 kJ), although the level of fitness was higher in the group performing the 12-minute time trial.

Kantermann et al. [15] showed that maximum performance was improved at a time of the day when melatonin concentrations are low [16]. This indicates that other underlying mechanisms activated by light exposure such as increased alertness or differences in the

study design or participant characteristics had an influence. Vandewalle et al. [17] showed that light also increases alertness at times of the day when melatonin levels are low. The different levels of fitness of participants between the studies may partially explain the higher effects reported by Kantermann et al. [15]. Further, exposure duration differed between the studies with longer exposure duration in Kantermann et al. [15] prior to the time trial and an additional exposure during the time trial. However, since alertness increases and sleepiness decreases rather quickly after the start of light exposure, the differences in the exposure duration to light may not be the only reason. In contrast to participants in Kantermann et al. [15], median start of exposure time in study 2 was later and around 21:17 which may have appeared to be in the wake maintenance zone for some participants. Alertness is rather high during this time of the day, which may explain the smaller effects. In the last Summer Olympic Games 2016 in Rio de Janeiro many finals took place between 20:00 and 00:25. Individuals with an early chronotype that are exposed to light around 22:00 or later would most likely be outside of their wake maintenance zone and may benefit from a suppression of melatonin and an increase of alertness. In regard to the high percentage of early chronotypes in endurance competitions [18] this is of relevance to many athletes. Further, longer exposure durations in all participants would presumably lead to stronger suppression of melatonin.

Participants performing the 40-minute time trial showed close to equal pacing strategies in all groups, with relatively constant speed during the first 32 minutes and a higher speed in the last eight minutes [1]. Similarly, in the 12-minute time trial all groups showed equal pacing strategies, with a faster second half than first half. For competitions of this duration this has been proven to be the preferred pacing strategy [19,20]. However, those participants exposed to higher intensities of melanopic light showed a significantly higher performance gain, resulting in an improved end-spurt performance. This positive effect on the pacing strategy is likely to be caused by the associated stronger decrease in melatonin, which may have caused a delay of the opening of the sleep gate, enabling athletes to prevent the time-of-day-related drop in performance. Total work performed during the time trial was not increased in BLUE compared to CONTROL. This may be explained by the higher variation in the actual amount of received light in BLUE.

In summary, high doses of melanopic light are beneficial to reduce melatonin, but this requires an exposure prior to the time trial. Longer exposure duration and higher exposure intensity are expected to induce stronger melatonin suppression. Suppression of melatonin can vary strongly between subjects that are exposed to the same light intensity [12]. Especially subjects who show high reductions in melatonin levels through light exposure may benefit most from evening light exposure. Bright light exposure did not significantly reduce sleepiness in athletes if exposed 17 hours after the MSFsc. This time is around the wake maintenance phase. Therefore, exposure to bright light after this phase may induce beneficial effects on performance through increase of alertness, reduction in sleepiness and suppression of melatonin. In total, rather longer exposure durations, specific wavelength and

ideal timing of light exposure seem to be important to improve physical performance than solely light intensity.

Self-chosen exercise intensity was not significantly increased in the morning in overweight individuals. This may have been influenced by several confounders. Although the participants were randomly allocated to one of the two light conditions, participants in bright light group had an one hour earlier MSFsc. Performance increases rapidly after usual wake-up times. Therefore, participants in the bright light group were tested at a later internal time, a time when performance is already higher and melatonin levels are likely to be already lower, thus leaving less room for improvement through light exposure. Additionally, participants in the bright light group were exposed longer to ambivalent light before the exercise session started and therefore had a different light history. Bearing in mind that light intensities of just 100 lx already induce 50% of the alerting response of bright light with 10'000 lx [12] the longer time awake may have masked the effect of the light intervention. Further, in study 2 the light exposure prior to exercise was chosen to be relatively short to make a practical daily use as easy as possible. In study 1 persisting light exposure during exercise showed higher effects on maximum performance than light exposure solely prior to exercise. However, the persisting light exposure during exercise in study 2 seems not to be sufficient to compensate the shorter exposure prior to exercise. Longer exposure duration prior to exercise, higher light intensities or a start time of light exposure earlier during the day may increase the effect of light exposure on self-chosen exercise intensity.

In all studies of this project the control light condition was equipped with four red light emitting diodes to avoid that participants would assume that they are allocated to the control group. In the study conducted with elite athletes (i.e. study 2) the participants were asked if they expected that the light they had been exposed to would either increase performance, not affect performance or decrease performance. There were no significant differences between the groups, but those participants exposed to blue light more frequently expected blue light to have a negative effect on their performance in the upcoming time trial. This may be explained by the unusual color of light irritating the participants or the small light device. Similarly, in study 3 [4] participants were directly asked if they expected to be allocated to the control or the intervention group. Eight participants in bright and six participants in control expected to be allocated to the intervention group. This small difference suggests that the installation of the four red light emitting diodes was relatively successful to reduce the chance of participants guessing correctly the group they were allocated to.

7.2.2 Influence of light exposure on motivation, sleepiness and mood

Elite athletes' showed already very high motivation to perform the time trial with maximum effort before the light exposure started. This ceiling effect explains why light exposure did not significantly improve motivation in those participants.

The athletes showed relatively normal values for sleepiness on the Karolinska Sleepiness Scale for this time of the day. Sleepiness increased by 0.5 points in CONTROL. The control light

condition with an intended light intensity of ~230 lx is relatively high compared to other studies [10,21] investigating the influence of light on sleepiness. Light intensities of just 100 lx already induce 50% of light's maximum alerting response [10]. The actual median light intensity reaching the participants' eyes was 115 lx in the athletes allocated to CONTROL. Therefore, the control light condition may have already worked as an intervention and explains why no significant differences were seen between BRIGHT and CONTROL. In BLUE sleepiness increased by 1.1 points on the Karolinska Sleepiness Scale but this was not significantly different from CONTROL. This stronger increase in sleepiness in blue light is in contrast to previous findings [11,22], but may be explained by the high variation in actual received light intensity in this group.

In athletes mood was assessed with the positive and negative affect schedule [6] before and after the light exposure. In overweight individuals mood was assessed with the multidimensional mood questionnaire [23] before the light exposure, after the light exposure but before the exercise session and after the exercise session with persisting light exposure. In both populations there were no significant differences between any light condition, at any point in time on any domain of mood (i.e. positive mood/negative mood; good-bad mood, awake-tired, calm-nervous). Athletes showed high positive mood and low negative mood in the positive and negative affect schedule, explaining why similarly to their motivation improvement through light exposure was unlikely. Overweight individuals showed, despite the early time during the day, mood levels in all three domains that are comparable with normative values in this age group [23], also suggesting a ceiling effect. This means that there was no room for improvement of vigilance through bright light because participants already had high vigilance. In the study by Dunai et al. [24] mood was positively influenced through the combination of bright light and exercise after 3 weeks of intervention. This indicates that repeated light exposure over mid- and long term is necessary to improve mood in overweight individuals. Similarly, in patients with seasonal affective disorder and non-seasonal depression mood is altered in longer lasting intervention studies [25]. Since the two latter patient groups show less positive mood compared to a normative population, light exposure might improve mood in a short intervention period or even acutely. The hypothesis put forward in this project, that mood elevations may improve self-chosen exercise intensity therefore may be more effective in participants with seasonal and non-seasonal depression. Another field of application would be to expose participants at an earlier time of the day when they have lower vigilance. Light exposure in a home-based setting immediately after wake-up and before work is likely to show higher effects. Furthermore, this setting would make visits to the laboratory obsolete and would allow a broader dissemination.

7.2.3 Influence of light exposure on reaction time and handgrip strength

Beaven et al. [26] showed a positive influence of blue light on acoustic choice reaction time in young adults. In contrast, in this project blue light did not improve simple acoustic reaction time in athletes. Differences in the studies that might explain the conflictive results are discussed in detail in the third publication of this project [3] (see chapter 5). A recent study in

healthy adults showed that exposure to blue light for 30 minutes before a working memory task significantly improved response time in the N-back task [27]. This was associated with increased activation of the dorsolateral and ventrolateral prefrontal cortex visible in the functional magnetic resonance imaging [28]. Interestingly, total reaction time and reaction time for correct responses was improved through blue light in the one-back and two-back task, but not in the zero-back task. These results indicate that blue light exposure may only improve performance in more cognitive tasks but not in simple tasks. This lack of effect in simple tasks could explain the difference seen between the results by Beaven et al. [26] using a complex task and the participants in this project [3] using a simple task. In the latter study reaction time was changed by -1 ms (95% CI: -8, 6) in BRIGHT compared to CONTROL. The mean difference in reaction times between elite 100 meters sprinter athletes reaching the finals and those reaching the second round of world championships is 13 ms. Therefore, even the highest assumable improvement of 8 ms through bright light exposure would not be relevant in most competitions. In regard to the results by Alkozei et al. [28] and Beaven et al. [26] further studies may focus on the influence of light exposure on complex tasks like choice reaction time, which is of importance in game sports.

Maximum handgrip strength was not improved by either bright or blue light in athletes investigated in this project [3]. In contrast, Zhang et al. [29] showed a positive influence of bright light exposure on time to exhaustion in a handgrip strength test in untrained individuals. The study design, light exposure and investigated population differed strongly between the studies and are discussed in detail in the third publication [3].

The primary outcome in the study investigating elite athletes (i.e. study 2) was the work performed during the time trial. A handgrip strength test was chosen because strength tests involving higher muscle mass are more likely to have caused fatigue and impact the primary outcome. In normally-trained older adults [30] handgrip strength correlates with upper body strength and leg extensor strength. In young athletes comparable data is missing. Upcoming studies should involve strength tests with higher muscle mass that represent overall strength better.

7.3 Strengths and limitations

The data analyzed (i.e. publication one) [1] and the studies conducted (i.e. publications two, three and four) [2–4] in the framework of this PhD project showed several strengths compared to previous studies, but also some limitations. In contrast to previous studies by other groups all studies in this project provided a sample size calculation and investigated homogenous samples. Further, sleep quality, physical activity and light exposure duration were recorded with diaries and in study 2 additionally objectively measured. Furthermore, study 2 [2] was the first study on physical activity and light exposure to investigate the influence of different wavelengths (i.e. blue light [469 nm] versus bright white light [545 nm]) and to collect melatonin samples to measure the melatonin suppressing effects of the different light exposures and to assess the dimmed-light melatonin onset. It was also the first

study to measure the light intensity actually reaching the participants' eyes. This measurement of actual individual light exposure revealed a limitation that has not been reported before. Participants showed much lower mean light intensities as originally planned and additionally showed high variations within the groups. Bearing in mind the dose-response relationship between bright light exposure durations and maximum cycling performance [1] it is possible that higher light intensities may have induced a stronger performance increase. The high variations in received light intensity result in the problem of per protocol analyses vs. analyses according to the intention to treat principle. This needs to be avoided in future studies by achieving an almost equal illumination level for all participants.

A limitation affecting all studies involving light exposure is that there is no placebo to light. Blinding of study participants according to the definition of CONSORT Statement is therefore impossible and will always remain a problem [31,32]. Both, study 2 and study 3, used a parallel group design which at least ensured that the participants did not know the other light conditions and could therefore hardly anticipate if they had been allocated to the control or an intervention group. The choice of a parallel group design appears to be the best method to "blind" participants to the light exposure they received. Further, the control light was equipped with four red light emitting diodes to look special and decrease the chance of this light device to be spotted as control light. Moreover, this was the first study to blind the investigator and therefore at least fulfilled the criteria for single-blind.

In study 3 a familiarization trial was performed before the exercise session with self-chosen exercise intensity. Some participants still rated their pacing below 7 on a scale from 0 to 10. However, because this was still the case in some participants after the fourth exercise session (familiarization trial plus three exercise sessions [in a subgroup] after light exposure) it is unclear if participants may have benefited from a second familiarization trial. In the remaining studies no familiarization trial was performed, because in cycling trained athletes hardly benefit from them. In detail, the coefficient of variation from time trial 1 to time trial 2 was 2.1% and from time trial 2 to time trial 3 was 1.9% in highly trained athletes [33]. However, since not all participants were cyclists some may have benefited from a familiarization trial.

In study 3 the standard deviation of the work performed assumed in the sample size calculation was much lower than in the subsequent study. The higher standard deviation caused a broader 95% confidence interval and may explain the inconclusive results. However, sample size calculations are always a priori assumptions based on previous findings. The standard deviation assumed for the sample size calculation was double-checked with two previously and independently conducted studies by other groups [34,35].

The strongest limitation that concerns all studies is the measurement of core body temperature. The gold standard is the measurement of core body temperature in the pulmonary artery [36] which is strongly invasive. In sport science the measurement of rectal temperature is an accepted procedure, because it is stable in steady state conditions, although the response to changes in blood temperature is slow [37] and there is a higher chance of data loss during running trials [38]. Measurement of rectal temperature was

avoided for the studies conducted in this project, because it was expected to strongly decrease compliance. Core body temperature was therefore measured with a hand-held tympanic ear thermometer. Unfortunately, several values for core body temperature were below physiologically reasonable values and in several participants there were very high variations during the time trial that can only be explained by measurement errors. Therefore, the collected data on core body temperature were not analyzed. Another method to measure core body temperature is via telemetric pills that are swallowed several hours before the time frame of interest. These pills show high limits of agreement with +0.35°C under rest [39], +0.22°C under exercise [40] and +0.04°C under exercise in heat condition [38]. This method was avoided due to the high variability in patients' transit time making it hard to time the moment the pill needs to be swallowed [41]. Further reasons were the high price of around 35 US-Dollar per pill and the high time effort for the calibration. For the calibration each pill needs to be placed in a water bath with a constant temperature of 35°C until the temperature of the pill stabilizes, followed by the same procedure in a 45°C and a verification test in a 40°C water bath. If accuracy is outside the accepted range of ±0.1°C the procedure needs to be repeated [42]. However, measuring core body temperature, as a marker of circadian phase, with sufficient rigor is highly relevant. Future studies need to use methods with higher accuracy then tympanic ear temperature, such as rectal or telemetric pill measurement despite the chance of lower compliance.

7.4 Perspectives

This chapter illustrates perspectives for further research that can be realized in a short time frame and perspectives that may be realized in a medium to long term. Table 2 shows factors that appeared to be problematic in the studies performed in this project and indicates approaches how these problems may be dealt with in subsequent studies to increase the possibility of light exposure to enhance performance.

Table 2: Factors that need to be considered to a higher extent in future study designs.

Factor	Problems/difficulties	Approaches
Light intensity	- There were high variations in the actual light intensity between individuals. - The actual light intensities were lower than planned per protocol.	- Pursue equal illumination of the entire room. - Use of light visors. - Use of light devices with higher light intensities.
Light exposure duration	Exposure duration of 30 to 60 minutes prior to exercise seems insufficient to improve performance, but longer durations are unpractical.	- Use of higher light intensities to compensate for shorter exposure durations. - Set exposure time later in the evening or earlier in the morning when melatonin levels are higher. - In athletes: use of light visors, which are wearable during warm-up, not disturbing the warm-up procedure.
Start time of light exposure	In study 2 start time of light exposure was set at a time when participants already showed high wakefulness.	Set start time of exposure in the morning to maximum 8.5 hours after the dim light melatonin onset (i.e. around 06:00).
Elapsed time awake	At the start time of light exposure in the morning participants already were already exposed to ambivalent light sources.	Set start time of light exposure immediately after wake-up (e.g. “Pre-Work” exercise).
Motivation/ Mood	A single light exposure session did not positively affect mood.	Use of light therapy over longer lasting periods (i.e. minimum three weeks).
Core body temperature	Core body temperature, as an expected underlying mechanism, could not be measured with sufficient rigor.	Use of telemetric pills.
Kind of task	- Simple reaction time was not altered. - Handgrip strength does not represent overall strength in trained people.	- Use of more complex tasks, because studies suggest that light may improve performance only in more complex tasks. - Use of strength tests involving higher muscle mass (e.g. leg extensor).
Diurnal variation in performance	Light exposure is not expected to improve performance at the time of peak performance, but to slow down the time of the day related decrease in performance. It is unclear how far away each participant was from his individual time of peak performance.	Use of light exposure at those times of the day when athletes show rapid decreases in performance. More research is necessary to identify these times of the day.

Short-term perspectives

The first studies investigating the influence of light exposure on physical performance simply applied light of different intensities regardless of confounding factors. The study by

Kantermann et al. [15] showed that the time at which light exposure is applied is of high importance and the study by Knaier et al. [1] pointed out that not only the dose in the sense of intensity, but also in the sense of exposure duration is relevant. In medicine, physicians do not only prescribe a drug to a patient. They also provide information to the patient in what form (e.g. injection or pill), in which dose and at what time of the day the drug has to be taken. Further, the goal of the drug administration (e.g. palliation or therapy), pharmacokinetics and the current health status of a patient (e.g. hormone levels, blood pressure etc.) are taken into consideration when prescribing the drug. Similarly, the application of light has to be managed in future research and in the field. Relevant factors are equal to those of drugs: The form (i.e. transcranial or via the eyes) [2,15,43], the dose (i.e. light intensity, peak wavelength and exposure duration) [1,2,15] and the timing of application (i.e. internal time and external time) [15] have to be considered. Especially, the timing seems to be relevant in two different ways. Firstly, the effects of light exposure on mood, alertness, sleepiness and melatonin suppression can all appear temporally delayed, making it necessary to expose patients prior to exercise. Secondly, the timing of the application has to be set in accordance to the goal that is aimed to be accomplished by the light exposure. Long lasting exposure durations on the day before a competition for example may be used to shift the circadian rhythm. This shift leads to a lower core body temperature on the subsequent morning which may be an advantage for exercises in humid or hot environments [44]. In contrast, shorter exposure durations that are applied immediately before a competition in the evening may prevent the time of the day related decrease in body temperature resulting in higher maximum performance [15]. Similarly, to pharmacokinetics in drugs, before light exposure is applied it has to be considered if other interventions are in place to influence the circadian rhythm like changes in timing of exercise, food uptake or sleep. Like in the prescription of drugs an individual's physical status has to be considered in the administration of light. In high trained athletes the effects of interventions on maximum performance can be assumed to be smaller than in non-trained athletes [45]. Further, older people also show reduced effects through light exposure, at least on cognitive performance [46]. Finally, genetic factors such as an individual's chronotype have to be considered, because the chronotype influences the external time of the day at which light is supposed to be applied. Many of the mentioned factors that are relevant for the application of light exposure are well-known and could already easily be considered in future studies and practice. Most factors regard athletes as well as patients.

To gain a better understanding of the physiological influence of light on physical performance melatonin and core body temperature as markers of the circadian phase need to be determined with sufficient rigor. The high variations in light intensities during the exposure need to be eliminated. Possible solutions may be an equal illumination of the entire room or the use of light visors. Light visors are glasses or baseball caps with integrated light emitting diodes that apply light exposure to the individual wearing them. An additional benefit of these devices is that it would allow longer exposure durations than classical light devices like those used in this project. The exposure duration of 60 minutes was chosen, because this duration seems to be realistic in a competition setting without disturbing an athlete's preparation.

Light visors would hardly disturb the preparation procedure of an athlete and therefore allow longer exposure durations, which may result in higher performance enhancing effects.

Further goals that may be targeted in the near future are the use of light exposure to reduce negative effects of travels across time zones before competitions. This approach has already been investigated outside athletics [47]. Although the problem of jet lag is well known in sport science [48] rather few research has been done on light exposure as a method to reduce jetlag. Thompson et al. [14] allocated 22 elite female athletes randomly to either bright light or control light exposure for 4 days for 45 to 60 minutes per day. Sleep symptoms showed high variations between- and within individuals but where not altered to a relevant extend [14]. The lack of studies investigating light as a method to reduce jet lag symptoms is surprising regarding to the previously reported strong disadvantages in sports [49-51].

Another field of research is the use of light reduction to improve sleep or regeneration after competitions. Many athletes use tablets and computers nowadays before sleep. The use of these devices reduces melatonin [52,53] and could therefore negatively impact sleep quality and athletes' regeneration. Glasses blocking mainly short wavelengths may improve sleep quality. Regeneration of athletes plays an increasing role, since methods to improve maximum performance become less efficient, because elite athletes are already close to their maximum possible performance.

The data presented in this project suggest that light exposure may improve self-chosen exercise intensity in overweight individuals to a small extent. However, even small increases in exercise intensity should be considered relevant, bearing in mind the worldwide fast increase in overweight and obesity. Light exposure may be used in a home-based setting immediately after wake-up times combined with an early exercise session. Home-based light exposure would allow a daily use, since no visits to laboratories are necessary. The effect of light exposure on self-chosen exercise intensity at an earlier time of the day yet still needs to be investigated. Furthermore, the absence of high acute effects does not necessarily mean that there are no highly positive long-term effects of light exposure in overweight individuals. One study showed a significantly stronger reduction in fat mass in participants exercising for three weeks under bright light compared to exercise under control light [24]. In the latter study a given exercise intensity was compulsory in both groups suggesting other mechanism than increased exercise intensity. Future studies therefore may focus especially on the underlying physiological mechanisms that led to long-term reductions in body mass through light exposure. In upcoming intervention studies sufficient methods need to be used to control for known confounding factors during the intervention time frame. These methods include at least monitoring of light exposure and physical activity with objective methods and detailed documentation of subjective mood, fatigue, sleeping and eating behavior.

Bright light therapy has been successfully used in several studies in patients with seasonal affective disorder and non-seasonal depression to improve mood [25]. In those patients, the chances to increase physical activity through improved mood may be higher than in

overweight individuals without depressive symptoms. However, previous studies did not yet investigate if physical activity is increased through light exposure therapy. This would be relevant with regard to two recent meta-analyses that showed that overweight and obesity are associated with higher depression prevalence in children and adolescents [54] as well as in adults [55]. Because women with depression are at a higher risk to become overweight or obese future studies should primarily investigate female participants.

Long-term perspectives

In the study by Kantermann et al. [15] the effect of light exposure on performance did not only vary depending on the time of exposure, but also in-between participants that were exposed to light at the same internal time. This was independent of different fitness levels. This variation suggests that people benefit to different extends from light exposure. A long-term goal should be to develop methods that identify groups or individuals who will benefit from light exposure and those who will not, due to a missing possible predisposition for example people who show low reduction of melatonin through light exposure. For the studies in this project a parallel group design was chosen for several reasons (i.e. variable of interest is unstable, blinding purpose, increase of participants' compliance). The downside of this design is that it was not possible to identify certain groups of individuals in which light exposure positively affected performance. To investigate this aspect, future studies may prefer to use a cross-over design, which allows to identify which participant profited from the light exposure and which one did not.

As described previously the timing of light exposure plays a key role. Many previous studies showed a decrease in physical performance in the late evening. The aim of study 2 was to prevent this decrease in performance through light exposure. Therefore, the light exposure was scheduled to start 17 h after each individual's MSFsc. This time was expected to be around the time of the day when performance decreases rapidly but many competitions take place. However, recent studies show that not only external time of peak performance is shifted in different chronotypes but also internal time. In detail, early chronotypes showed their time of peak performance on average 05:36 h and late chronotypes 11:11 h after entrained awakening. Further, the decrease of performance in the evening shows different slopes between the chronotypes. The methodological problems regarding most studies investigating diurnal variations have been discussed in Chapter 1.2. A more holistic understanding of diurnal variations in physical performance is of urgent need. Especially, the time frame at which performance shows the fastest decrease needs to be identified, because light exposure at this time of the day is assumed to lead to the highest effects. Studies investigating diurnal variations in endurance and strength performance, especially around times when performance decreases rapidly need to be conducted.

Of upmost important is the transfer of previous findings from sports physiology to a public health setting as done with the conduction of study 3 in this project. Both, chronobiology [56] and physical activity have high impact on human health. An increase of just 10% in physical

activity could prevent half a million deaths [57] and individuals reaching the recommended 150 minutes of moderate physical activity per week [58] would show a 25% reduced mortality rate [59]. On the other side even small losses of sleep can impair cognitive performance [60] and increase cardiovascular risk [61] and demonstrate that not only physical activity but also a sufficient amount of sleep is necessary for health. Further, circadian variations can also trigger the onset of acute cardiovascular diseases [62]. Shift work is further associated with diabetes, obesity and cardiovascular diseases [63], against which physical activity works protectively. The prevalence of overweight is increasing and one of the leading causes of death. Reid et al. [64] for example recently showed that the time an individual is exposed to high doses of light influences the body mass index independently of sleep timing and duration. These results open an interesting research field, since the underlying physiological mechanism could not be explained by the authors. Further, possible effects of light exposure on body mass or physical activity may be especially relevant in working spaces. Previous studies mainly investigated influences of light on cognitive performance [65] or circadian entrainment [66] in shift workers, but not if light exposure can help prevent overweight in this population. Seasonal affective disorder and non-seasonal depression are also associated with overweight [54,55]. Light therapy already shows promising effects in mood enhancement in this population [25] and should also be investigated in regard to changes in body weight to a higher extend.

7.5 Conclusions

In trained athletes, bright light exposure is an effective tool to increase total work performed during a 40-minute time trial on a bicycle ergometer if the exposure lasts for 120 min prior to and during the time trial. Exposure to bright light for durations of 60 minutes prior to and during the time trial or only 60 minutes prior to the time trial did not significantly improve physical performance compared to a control light condition. There is a dose-response relationship between the exposure duration to bright light and the work performed in a time trial. It seems that this dose-response relationship is nonlinear and a certain threshold of exposure duration and intensity needs to be exceeded to positively affect physical performance in athletes.

In elite endurance trained athletes bright light exposure for 60 minutes prior to exercise increased the total work performed during a 12-minute time trial to an extend that may be relevant in competitive sports, but this difference was not significant. Blue light exposure did not improve maximum performance compared to control light. However, end-spurt performance, defined as the ratio of the work performed in the first and last minute of the time trial, was improved through melanopic light. In detail, a tenfold increase in exposure to melanopic light was associated with a significant performance gain of 8.0% which was associated with a significant reduction in melatonin concentration of -0.9 pg/ml. No significant differences were observed through bright or blue light exposure compared to control light regarding participants' motivation, sleepiness or mood. Simple acoustic reaction time and maximum handgrip strength were not altered by either bright or blue light exposure

compared to the control light condition. Participants reported only minor adverse events through light exposure like slight headaches. The frequency of adverse events was equal in bright and control light and lowest in blue light suggesting that light exposure is a method that is safe to use in athletes. However, in all three groups the actual light intensities reaching the participants' eyes were much lower than intended in the protocol and showed high variations between the participants.

In overweight individuals, an exposure to bright light for 30 minutes prior to and during a 30-minute exercise session with self-chosen exercise intensity did not increase mean power output during the exercise session compared to a control light condition. The light exposure prior to exercise was chosen to be relatively short to make a practical daily use as easy as possible. Therefore, light exposure persisted during exercise. In study 1 this persisting light exposure during exercise showed higher effects on maximum performance. However, longer exposure duration prior to exercise, higher light intensities and a start time of light exposure earlier during the day are likely to increase the effect of light exposure on self-chosen exercise intensity. The three domains of the multidimensional mood questionnaire (i.e. good-bad mood, awake-tired, calm-nervous) did not differ between the groups. Participants' steps per day during the study period were neither altered by the exercise in the exercise session nor by the light exposure. Similarly, to the studies in athletes only minor adverse events (e.g. glare, slight headaches) were reported indicating light exposure to be safe to use in overweight individuals.

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ACADEMIC EXPERIENCE

since 02/2014 — Doctoral candidate, University of Basel, Switzerland

- Research fields: - light exposure and exercise
  - physical performance and chronobiology
  - physical exercise testing

10/2013 – 01/2014 — Project assistant, University of Basel, Switzerland

EDUCATION

10/2010 – 03/2013 — University of Leipzig, Germany, Master of Science in Sport Science "Diagnostics and Intervention", Grade: 1.6, Master thesis: Grade: 1.0

10/2006 – 09/2009 — University of Bremen, Germany, Bachelor of Arts in Sport Science and Public Health. Grade: 1.7, Bachelor thesis: Grade: 1.3

PROFESSIONAL EXPERIENCE

04/2012 – 05/2012 — Internship at the Olympic Training Center Berlin, Germany

- Assisting performance diagnostics with professional athletes

02/2009 – 06/2009 — Student research assistant, Bremen Institute for Prevention Research and Epidemiology, Germany

- Cardiopulmonary exercise testing with ~100 adults and children

MEMBERSHIPS

since 2016 — Member of European College of Sport Science (ECSS)

since 2014 — Swiss School of Public Health (SSPH+)

TEACHING EXPERIENCE

Courses: Measurement and Evaluation I & II
Presentation and Communication Skills I & II

Supervision: 3 Master theses and 4 Bachelor theses

GRANTS/ STIPENDS

PhD Program Health Sciences (PPHS) Extension Stipend 2017

PUBLICATION LIST

Knaier, R; Schäfer, J; Anja Rossmeissl, A; Klenk, C; Hanssen, H; Höchsmann, C; Cajochen, C; Schmidt-Trucksäss, A. (2017). Effects of bright and blue light on acoustic reaction time and maximum handgrip strength in male athletes: a randomized controlled trial. *European Journal of Applied Physiology*. IF: 2.130

Knaier, R; Schäfer, J; Anja Rossmeissl, A; Klenk, C; Hanssen, H; Höchsmann, C; Cajochen, C; Schmidt-Trucksäss, A. (2017). Prime time light exposures do not seem to improve maximal physical performance in male elite athletes, but enhance end-spurt performance. *Frontiers in Physiology*. IF: 4.134

Knaier, R; Meister, S; Aeschbacher, T; Gemperle, D; Rossmeissl, A; Cajochen, C; Schmidt-Trucksäss, A. (2016). Dose-response relationship between light exposure and cycling performance. *Scandinavian Journal of Medicine & Science in Sports*; 26(7):794-801. IF: 3.331

Falz, R; **Knaier, R**; Hoppe, S; Busse, M. (2014). The influence of cardiac and hematological parameters on the maximal Oxygen uptake in healthy and athletic male adults. *Clinical Sports Medicine International*, 7(1), 1-8.

Submitted manuscripts:

Knaier, R; Klenk, C; Königstein, K; Hinrichs, T; Rossmeissl, A; Infanger, D; Cajochen, C; Schmidt-Trucksäss, A. (submitted). Influence of morning bright light exposure on self-chosen exercise intensity and mood in individuals with overweight. Submitted to: Obesity (July 2017)

Höchsmann, C; **Knaier, R**; Eymann, J; Hintermann, J; Infanger, D; Schmidt-Trucksäss, A. (submitted). Smartphones are excellent tools for step counting in various walking conditions. Submitted to: Medicine & Science in Sports & Exercise (July 2017)

REVIEWER WORK

Reviews for the Journal of Sport and Health Science and Journal of Sleep Research

CONFERENCE PARTICIPATIONS

2017 Oral presentation at "*22nd Annual Congress of the European College of Sport Science*", Essen, Germany.

2017 Oral presentation at "*9. Jahrestagung der Sportwissenschaftlichen Gesellschaft der Schweiz*", Zurich, Switzerland.

2016 Poster presentation at "*21st Annual Congress of the European College of Sport Science*", Vienna, Austria.

2016 Oral presentation at "*8. Jahrestagung der Sportwissenschaftlichen Gesellschaft der Schweiz*", Bern, Switzerland.

GRADUATE EDUCATION

Course	ECTS
Forschungsergebnisse visualisieren – Statistische Diagramme, Schematische Darsellungen und Fotos; University of Basel, Philipp Mayer	0
The messenger is the message; University of Basel, Sibylle Sommerer	1
Successful fund acquisition; University of Basel, Andrea Degen	1
Start your PhD successfully; University of Basel, Tanja Treschan	1
Mündliche Präsentationen, Methoden und Selbstvertrauen; University of Basel, Susanne Matuschek	1
Summer School 2014 Measurement of Physical Activity; Swiss School of Public Health, Arno Schmidt-Trucksäss	2
Open Access – neues Modell für das wissenschaftliche Publizieren; University of Basel, Nicolas Sartori)	0
Project Management in Clinical Drug Development: Theory and Practice; European Center of Pharmaceutical Medicine and Clinical Trial Unit of the University of Basel, Alexander Gissler	4
Winter School 2014 Writing a Journal Article … and Getting it Published; Swiss School of Public Health, Kali Tal	1
Introduction to the statistical software R; Swiss School of Public Health, Jan Hattendorf	0
Peer Review – From Submission to Retraction; University of Basel, Markus Geisler	1
Creating the Job Hunting Package; University of Basel, Verity Elston	1
Good Clinical Practice; University of Basel, Clinical Trial Unit	0
Wissenschaftliche Poster kreativ entwerfen und gestalten; University of Basel, Martina Schradi	0
Self-Branding and Self-Promotion; University of Basel, Petra Wüst	0
Introduction to Endnote; University of Basel, Cornelia Eitel	0
Systematic Reviews and Meta-Analysis: a practical Approach; Swiss School of Public Health, Matthias Egger	1
Team based health care models – barriers and facilitators; University of Lucerne, Anneke van Vught	0
Fragebogen: Konstruktion – Auswertung – Interpretation; Swiss School of Public Health, Thomas Kohlmann, Thomas Abel	1
Effective ways of investing in health – from concepts to policy; University of Lucerne, Jan de Maeseneer	0
Evidence-based Public Health, Swiss School of Public Health, Matthias Egger	1
How to Improve Your Negotiation Skills; University of Basel, Melissa Davies	1
Get Your Video Abstract; University of Basel, Judith König, Tilman Hassenstein	2
Medical Decision Making; University of Lucerne, Brendan Delaney, Olga Kostopoulou	1