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Original Article

Dawn simulation light: a potential cardiac events protector

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ABSTRACT

Objective/Background: Major cardiovascular events frequently increase in the morning due to abrupt changes in the sympatho-vagal cardiac control during the transition from sleep to wakefulness. These neural changes are translated into stepwise increases in cardiac functions, resulting in a potential cardiovascular stress. Here, we explored whether light can "optimize" heart rate and its neural control, by actively promoting a less steep transition from sleep to wakefulness, thus minimizing morning cardiovascular vulnerability.
Methods: Seventeen healthy young men were awakened 2-hours before their habitual wake-time. In a counterbalanced within-subject design, we applied a control condition (darkness during sleep and dim light during wakefulness) or dawn-simulation-light (DSL) starting 30-minutes before and ending 30-minutes after scheduled wake-up time.
Results: Our data reveal a significantly gradient reduction in heart rate during the transition from sleep to wakefulness, when applying DSL as compared to a control condition. Likewise, cardiac sympatho-vagal control smoothly increased throughout the 30-min sleep episode preceding scheduled wake-up under DSL and remained stable for the first 30-min of wakefulness. Interestingly, these effects were mostly driven by changes in the parasympathetic cardiac control.
Conclusions: Our data demonstrate for the first time that a non-invasive strategy, as light exposure surrounding the wake-up process, can significantly reduce the deleterious sleep-to-wake evoked cardiac modulation in healthy young men awakened under conditions of increased sleep pressure. A translational approach of this light exposure, which closely resembles natural lighting conditions in the morning, may therefore act as a potential protector for cardiac vulnerability in the critical morning hours.

1. Introduction

Key cardiovascular events are increasingly more intense in the morning hours between 06:00 and 12:00 h [1–3], although they may also occur in the evening (between 18:01 h and midnight) [4], and are associated to higher blood pressure, heart rate (HR), platelet aggregation, vascular resistance and so forth [5]. In particular, sleep–wake transitions in the morning elicit high shifts toward sympathetic activation, in comparison to the remainder of the day, suggesting a key role in increasing cardiac vulnerability after awakening [6,7]. This "morning bias" in major cardiovascular regulatory mechanisms is a salient feature of ischemic diseases, such as brain vascular disease, cerebral infarction, angina and myocardial infarction [5]. Physiological underpinnings for possible adverse cardiovascular events encompass abrupt changes in the autonomic nervous control of the cardiovascular system "around the clock" [8]. The circadian clock impacts on both endothelial and muscle cells [9], as indexed by the 24-h daily fluctuation in nearly 300 genes in the aorta *alone*, most of which directly involved in vascular function [10]. In mouse models deficient for specific "clock genes," blood pressure and heart rate show abnormal timing and amplitude [11]. Conversely, clinical findings also suggest a small 1.28-fold greater incidence of acute MI in a wide window (6 am to noon) compared to other times of day [2], bimodal peaks in morning and evening hours [4], and stress-related contributors to adverse cardiovascular events [3]. Thus, it still remains a matter of debate whether circadian factors play a key role on the onset of long-term cardiovascular events. Nevertheless, a dysfunction of the circadian clock may be one possible risk factor for potential cardiovascular diseases, contributing to some extent to the morning increased rates of HR and heart rate variability (HRV). In this context, strategies allowing for the "optimization" of internal biological

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rhythms regulating cardiovascular events may provide a means to counteract possible adverse events. Quite surprisingly, no non-invasive strategies are known to date.

The present study investigated whether light can "optimize" heart rate and its neural control, by actively promoting a less steep transition from sleep to wakefulness, thus minimizing morning cardiovascular vulnerability. We hypothesized that a "naturalistic" dawn simulation light (DSL) surrounding the wake-up time would result in a smoother increase heart rate and heart rate variability during the transition from sleep to wakefulness, as compared to a control condition. Likewise, we hypothesized that cardiac sympatho-vagal control would smoothly increase during the transition from sleep to wakefulness, as light may minimize the deleterious sleep-to-wake evoked increases in cardiac modulation in the early hours of the morning.

2. Materials and methods

2.1. Participants

Eighteen healthy young men (age range, 20–33 years; mean, 23.1 ± 0.8 years [SD]) participated in a laboratory study on impact of polychromatic light on cognitive performance and sleep–wake regulation [12]. All participants were nonsmokers, drugs and medication free (drug screening prior to the study onset), and devoid of medical, psychiatric, and sleep disorders. Clinical status of all participants was assessed by questionnaires, physical examination, and a polysomnographically recorded adaptation night. This night served as screening night for potential periodic limb movements and sleep apnea, as well as for optimal sleep quality (sleep efficiency >85%). During the baseline week preceding the study, participants were instructed to keep their individual bed- and wake-time within a self-selected range of ±30 min and to sleep for 8 h, as assessed by a wrist activity monitor (Cambridge Neurotechnologies) and sleep logs. Adherence to this individually timed sleep–wake schedule was checked prior to the beginning of the study. Participants were requested to abstain from excessive caffeine and alcohol consumption. The study protocol, the screening questionnaires, and consent form were approved by the Ethical Committee of Basel, Switzerland and were in agreement of the Declaration of Helsinki. All study participants gave their written informed consent.

2.2. Protocol

The study was carried out during the winter season (January to March) in Basel, Switzerland, and comprised two segments in a balanced cross-over design, separated by at least 1-week intervening period. No order effects were observed due to this cross-over design. Participants remained in individual bedrooms with no information about time of day. All rooms were completely dark, without windows. The experiment lasted 48 h, including 2 days and two sleep restriction nights (6 h) following the habitual subject sleep time. The rationale for including a study protocol with two sleep restriction nights was due to two major reasons: (1) chronic sleep restriction (CSR) is increasingly usual in contemporary society, negatively impacting on numerous aspects of human physiology [13]. However, CSR impact on cardiac physiology is virtually unknown; (2) light dynamically promotes increased alertness and cognitive performance, and has been shown to ameliorate the deleterious effects of CSR on subjective alertness and performance [12]. However, it remains completely unknown if light can act as an adjuvant on minimizing potentially deleterious cardiovascular events, under increased sleep pressure. During the day, participants were exposed to dim light (<8 lux) during 2 h after wake-up and to 40 lux until they went to bed. Blood pressure measurements were performed after wake-up times on both days of the study protocol, and no significant differences were observed between DSL and control conditions. The light treatment was administered after the sleep restriction night either with no additional light for the control condition or with a DSL. Polychromatic DSL light gradually increasing from 0 to 250 lux during 30 minutes before wake-up time; the light remained around 250 lux for 20 minutes after wake-up time, placed near the bed at eye level. DSL illuminance, photon density, and correlated color temperature, at 45 cm from the device, were: (1) 5 min after light onset: 1.2 lux, 1.9E±16/m2 s, 1090 K; (2) 15 min after light onset: 13 lux, 1.4E±17/m2 s, 1500 K; (3) 30 min after light onset: 250 lux, 2.4E±18/m2 s, 2750 K. The control "wake-up technique" (non-DSL condition) was with a technician's voice.

2.3. Salivary cortisol

Saliva cortisol samples were scheduled during wakefulness every 30 min during the first 4 h after wake-up time and followed by hourly intervals thereof. Samples were frozen and kept at –20 °C until the cortisol assays were conducted. Cortisol was measured by ALPCO (ALPCO Diagnostics, Salem, NH, USA), using a direct salivary enzyme-linked immunosorbent assay (ELISA) for quantitative determination of cortisol. The sensitivity was 1.0 ng/mL and intra-assay coefficient of variances amounts to 10.3% for baseline values 6.6 ng/mL.

2.4. Electrocardiographic (ECG) recordings and analysis

A two-derivation ECG system was recorded throughout the laboratory study. R–R intervals, ie, time length between the R peaks of consecutive QRS complexes, were calculated, and all traces were visually checked for artifacts by an investigator. The R wave peak detection and R–R signal were analyzed by HeartScope software (AMPS, Inc, NY, USA). Occasional ectopic beats were identified and replaced with interpolated R–R interval data. All data acquisition and post-acquisition analyses were carried out in accordance with established standards, including those put forth by the Task Force on HRV Interpretation [14]. To avoid excluding large sections of the recording contaminated by movement artifacts during wakefulness, we used a sampling period of 2.5 min for HRV estimation [15], in accordance with the recommendations of the Task Force on HRV Interpretation [14]. Power densities in the low-frequency (LF) band (0.04–0.15 Hz) and in the high-frequency (HF) band (0.15–0.50 Hz) were calculated for each 2.5-min segment using autoregressive algorithms. Moreover, the LF-to-(LF + HF) ratio [LF/(LF + HF) ratio] was used as an index of sympatho-vagal balance. The indexes selected are those most commonly used in the analysis of HRV [16,17]. Furthermore, we also performed symbolic analyses to quantify different aspects of cardiac control related to the organization of different autonomic subsystems. Symbolic analysis is a non-linear method based on the conversion of the series into a sequence of symbols [17–19]. The full dynamic of the series (the min–max range) is spread over six bins, each of which is identified by a number (symbol) from 0 to 5. Original values inside each bin are substituted by the symbol defining the specific bin, thus obtaining a symbolic series. The symbolic series is converted into a series of patterns of three symbols. Four different families of patterns can be identified [17–19]: 0V (patterns with no variation, all symbols are equal), 1V (patterns with one variation, two consecutive symbols are equal and the remaining one is different), 2LV (patterns with two like variations, the second and the third symbol change with respect to the previous one and the changes have the same sign), and 2UV (patterns with two unlike variations, the second and the third symbol change with respect to the previous one and the changes have opposite sign) [19]. This method has been applied to evaluate cardiac autonomic control from HRV [18]. It has been demonstrated that 0V% is a marker of