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Daytime bright light exposure, metabolism, and individual differences in wake and sleep energy expenditure during circadian entrainment and misalignment

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ABSTRACT

Daytime light exposure has been reported to impact or have no influence on energy metabolism in humans. Further, whether inter-individual differences in wake, sleep, 24 h energy expenditure, and RQ during circadian entrainment and circadian misalignment are stable across repeated 24 h assessments is largely unknown. We present data from two studies: Study 1 of 15 participants (7 females) exposed to three light exposure conditions: continuous typical room ~100 lx warm white light, continuous ~750 lx warm white light, and alternating hourly ~750 lx warm white and blue-enriched white light on three separate days in a randomized order; and Study 2 of 14 participants (8 females) during circadian misalignment induced by a simulated night shift protocol. Participants were healthy, free of medical disorders, medications, and illicit drugs. Participants maintained a consistent 8 h per night sleep schedule for one week as an outpatient prior to the study verified by wrist actigraphy, sleep diaries, and call-ins to a time stamped recorder. Participants consumed an outpatient energy balance research diet for three days prior to the study. The inpatient protocol for both studies consisted of an initial sleep disorder screening night. For study 1, this was followed by three standard days with 16 h scheduled wakefulness and 8 h scheduled nighttime sleep. For Study 2, it was followed by 16 h scheduled wake and 8 h scheduled sleep at habitual bedtime followed by three night shifts with 8 h scheduled daytime sleep. Energy expenditure was measured using whole-room indirect calorimetry. Constant posture bedrest conditions were maintained to control for energy expenditure associated with activity and the baseline energy balance diet was continued with the same exact meals across days to control for thermic effects of food. No significant impact of light exposure was observed on metabolic outcomes in response to daytime light exposure. Inter-individual variability in energy expenditure was systematic and ranged from substantial to almost perfect consistency during both nighttime sleep and circadian misalignment. Findings show robust and stable trait-like individual differences in whole body 24 h, waking, and sleep energy expenditure, 24 h respiratory quotient—an index of a fat and carbohydrate oxidation—during repeated assessments under entrained conditions, and also in 24 h and sleep energy expenditure during repeated days of circadian misalignment.

1. Introduction

Light exposure has numerous influences on human physiology beyond vision including modulation of sleep and circadian physiology (Czeisler et al., 1989; Duffy and Wright, 2005), alteration of arousal (Altimus et al., 2008; Lupi et al., 2008; Tsai et al., 2009), regulation of the pupillary light reflex,(Hattar et al., 2003; Lucas et al., 2001; Lucas et al., 2003), and alterations in emotion (Iskra-Golec and Smith, 2008;

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Lewy et al., 1980) temperature physiology (Badia et al., 1991; Cajochen et al., 2005; Wright et al., 1997a, 1997b, 2000), and endocrine physiology (Jung et al., 2010; Lewy et al., 1980; Wright et al., 1997a, 1997b, 2000).

Less is known about the influence of light exposure on metabolism. In one study of healthy adults, adverse effects of daytime blue-enriched or evening bright light exposure was observed on insulin sensitivity and insulin responses to a meal (Cheung et al., 2016). In another study, morning bright light exposure had no impact on glucose or insulin in young lean healthy men, but increased fasting and post-prandial glucose in older overweight and obese men with Type-II diabetes (Versteeg et al., 2017). Whether light exposure affects energy expenditure and substrate oxidation is also not clear as inconsistent findings have been reported (Gaist et al., 1990; Pinchasov et al., 2000). (Gaist et al., 1990; Pinchasov et al., 2000) (Ivanova et al., 2017). Understanding whether light exposure influences energy expenditure and substrate oxidation has implications for health.

The effects of sleep loss and circadian disruption on energy expenditure (EE) and substrate oxidation in humans has been the focus of several recent studies (Bandin et al., 2015; Schoffelen and Westerterp, 2008; Van Etten et al., 1995), including studies by our group using whole-room indirect calorimetry. In those studies, we have shown that sleep loss (Jung et al., 2011; Markwald et al., 2013) and circadian misalignment (McHill et al., 2014) alter 24 h EE, sleeping EE, and substrate oxidation. Individual differences in 24 h EE and RQ are well known and are hypothesized to contribute to the risk of obesity (Howard et al., 1991; Ravussin, 1995; Zurlo et al., 1990). There are limited data however, on the stability of individual differences in 24 h, waking, and sleeping EE and RQ measures and contributing mechanisms of such individual differences. It could be hypothesized that individual differences in waking and sleeping EE and RQ are trait-like, and that such stable individual differences and responses to sleep and circadian challenges may be explained by individual factors such as of sex, age, fat mass, and fat free mass.

With regards to metabolism, the aim of study 1 in this report was to determine the effects of exposure to different levels of light (dim light, continuous bright warm light, and intermittent exposure to blue-enriched white light) on EE, substrate utilization (i.e., RQ), and glucose metabolism. We hypothesized that intermittent exposure blue-enriched white light would acutely increase EE relative to room-light control during the daytime hours. We focused on blue-enriched white light since non-image forming responses are most robust in response to light in the blue-green spectrum (Lucas et al., 2001). We also assessed whether light exposure influenced macronutrient oxidation as well as post meal glucose and insulin levels. Because we saw no effects of the different light exposure conditions tested on EE and 24 h RQ, this provided an opportunity to determine the repeatability of these measures under highly-controlled circadian entrained conditions. In addition to quantifying the repeatability of EE and RQ, we used data from a previously reported study from our group, here referred to study 2, to determine how the stability of individual differences in these measures is affected by circadian misalignment.(McHill et al., 2014). We hypothesized that individual differences in EE and RQ would be stable and trait-like during circadian entrained (study 1) and circadian misaligned (study 2) conditions.

2. Materials methods

2.1. Institutional approval and ethics

Procedures followed were in accordance with the ethical standards of the Helsinki Declaration of 1975 as revised in 1983. Studies were approved by the scientific and advisory review committee of the Colorado Clinical and Translational Sciences Institute and the Colorado Multiple Institutional Review Board.

Study 1 – daytime light exposure, energy and glucose metabolism, and stability of 24 h, scheduled wake and sleep EE.

2.2. Participants and screening procedures

15 healthy adults (7 females) aged 23.3 ± 3.4 y, weight 65.3 ± 6.3 kg, body mass index (BMI) 22.4 ± 2.0 kg/m^2 (± SD) participated. After providing written informed consent, participants underwent health screening consisting of medical, psychological, and sleep history, semi-structured clinical psychiatric interview, physical examination, complete blood count, comprehensive metabolic panel, urine toxicology, 12-lead electrocardiogram, and a polysomnographic sleep disorders screen. Inclusion criteria were age of 18–40 years old; BMI of 18.5–24.9 kg/m^2; habitual nightly sleep duration > 7 h and < 9.25 h (based on self-report); and low to moderate caffeine use (< 500 mg/day). Exclusion criteria included self-reported smoking or nicotine use; current or chronic medical/psychiatric/sleep conditions; shift work or dwelling below Denver altitude (1600 m) in the year prior to study; travel across more than one time zone in the 3 weeks prior to study; recent self-reported weight loss; and positive urine toxicology screen.

After confirming inclusion criteria, RMR was assessed on a separate day. RMR was measured in the morning, following an overnight fast and 24 h abstention from exercise, using standard indirect calorimetry with the ventilated hood technique (TrueOne® 2400, ParvoMedics, Sandy, UT). Prior to the measurement, participants rested quietly for 30 min in a dimly lit, thermoneutral room. Respiratory gas exchange was measured for 30 min, and values from the last 20 min were used to determine RMR.

2.3. Experimental design and study procedures

The in-laboratory portion of the study was performed in the University of Colorado Hospital Clinical and Translational Research Center (CTRC) at the University of Colorado Anschutz Medical Campus. For one week prior to the laboratory study, participants were instructed to discontinue the use of caffeine, alcohol, nicotine, and over-the-counter medication and to maintain a consistent ~8 h per night sleep schedule based on habitual sleep and circadian timing. Sleep timing was verified via wrist actigraphy with light-exposure monitoring (Actiwatch-Spectrum; Philips Respironics Inc.), sleep logs, and call-ins to a time-stamped voice recorder to report sleep and wake times. Three days prior to admission, participants were provided a 3-day outpatient diet estimated to meet individual daily energy needs determined from RMR with an activity factor of 1.5. Participants were also instructed to refrain from planned exercise during these 3 days.

Upon admission for the laboratory portion of the study, verification of drug- and alcohol-free status was confirmed using urine toxicology screen and breath alcohol assessments (Lifeloc Technologies; model FC10). Participants were admitted ~8 h prior to their habitual bedtime and placed into room light (~100 lx in the angle of gaze; IL-1400 photometer, International Light) to begin the 4 day study period. Day 1 of the laboratory visit included an 8 h sleep opportunity to habituate participants to recordings as well as to serve as a sleep disorders screen. Days 2–4 were experimental days that consisted of 16 h of scheduled wakefulness followed by an 8 h sleep opportunity. Wakefulness and sleep opportunities were scheduled relative to each subject's habitual bed and wake times based on the week of pre-study monitoring. A modified constant routine (Broussard et al., 2018; Duffy and Wright, 2005) was employed to control for the influence of environmental and behavioral factors on our primary outcome measures. Specifically, during scheduled wakefulness participants were studied in a semi-recumbent posture with the head of the bed raised to ~35 degrees, ambient temperature was maintained in the thermoneutral range (22.3–22.9 °C). Wakefulness and compliance with modified constant routine procedures were verified via monitoring by research staff and continuous monitoring of electroencephalographic (EEG) activity.