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Dim Light at Night Increases Body Mass of Female Mice

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Abstract

During the past century the prevalence of light at night has increased in parallel with obesity rates. Dim light at night (dLAN) increases body mass in male mice. However, the effects of light at night on female body mass remain unspecified. Thus, female mice were exposed to a standard light/dark (LD; 16h light at ~150 lux/8h dark at ~0 lux) cycle or to light/dim light at night (dLAN; 16h light at ~150 lux/8h dim light at ~5 lux) cycles for six weeks. Females exposed to dLAN increased the rate of change in body mass compared to LD mice despite reduced total food intake during weeks five and six, suggesting that dLAN disrupted circadian rhythms resulting in deranged metabolism.

Keywords

Circadian disruption; light pollution; light at night; body mass regulation

Introduction

The increase of light at night parallels the increasing rates of obesity and metabolic disorders throughout the world (Fonken & Nelson, 2011; Ogden, Carroll et al., 2014). Circadian regulation of energy homeostasis is controlled by an endogenous biological clock, located in the suprachiasmatic nuclei (SCN) of the hypothalamus. Light information travels directly from light-sensitive ganglion cells in the retina to the SCN which entrains individuals to the external day–night cycle (Hastings, Reddy et al., 2003; Burke, Markwald et al., 2013). Melatonin is produced only during the night in both diurnal and nocturnal animals and its production can be inhibited by exposure to nighttime light (Brainard, Richardson et al., 1982).

People in developed countries are exposed to some environmental light pollution, particularly those who participate in shift work. Shift work disrupts circadian clock function and is linked to circadian and metabolic consequences including sleep disturbances, elevated body mass index, altered plasma lipid metabolism and adiposity, and increased risk for cardiovascular disease (van Amelsvoort, Schouten et al., 1999; Stevens, Blask et al., 2007).

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Declaration of Interest

The authors have no interests to disclose.

Individuals with specific polymorphisms of the *Clock* gene are protected against obesity, suggesting a role for genetic variation in *Clock* in the development of metabolic syndrome, type 2 diabetes, and cardiovascular disease (Scott, Carter et al., 2008). Similarly, mice harboring a mutation in their *Clock* genes are susceptible to obesity and metabolic syndrome (Turek, Joshu et al., 2005). Dim light at night (dLAN) disrupts molecular circadian rhythms and increases body mass in male mice (Fonken, Aubrecht et al., 2013). Considered together, the endogenous biological clocks can be disrupted by light at night exposure and this can have adverse consequences on health. Obesity is more prevalent in women than men (Flegal, Carroll et al., 2010; Ogden, Carroll et al., 2014). Shift work is associated with increased risk for breast cancer and obesity in women (Schernhammer, Laden et al., 2001; Key, Appleby et al., 2003). Most research is focused on male rodents, which potentially misses critical sex differences. Here we expand on our previous work demonstrating that male mice exposed to dim light at night (dLAN) increase body mass (Fonken, Workman et al., 2010). We hypothesized that dLAN exposure in female mice also increases body mass. To assess the link between altered light cycles and metabolic disorder, we placed mice in either a standard light/dark cycle (LD; 16h light at ~150 lux/8h dark at ~0 lux) or exposed to cycles of light/dim light at night (dLAN; 16h light at ~150 lux/8h dim light at ~5 lux and measured weekly body mass, food intake, and home cage activity for 6 weeks.

Materials and Methods

Animals

Twenty female Swiss Webster mice were purchased at eight weeks of age from Charles River laboratories (Wilmington, MA, USA). Mice were individually housed in polypropylene cages (33 cm × 18 cm × 14 cm) at an ambient temperature of 22 ± 2 °C and relative humidity of $40\% \pm 10\%$. Mice were provided Harlan Teklad 8640 food (Madison, WI, USA) and filtered tap water *ad libitum*. Upon arrival mice were housed on a 16:8 light/dark cycle for one week to allow acclimation. After the acclimation period, mice were randomly assigned to exposure to dim light at night (dLAN, 16:8 light/dim light cycle at ~150 lux during the day and ~5 lux during the night; n = 11) or a traditional light:dark cycle (LD 16:8 light/dark cycle; ~150 lux during the day and ~0 lux at night; n=9) for 6 weeks. Food intake was measured daily before the onset of the dark period (15:00 EST). Body mass was measured weekly for the duration of the experiment before the onset of the dark period (15:00 EST). All procedures were approved by the Ohio State University Institutional Animal Care and Use Committee; all experiments conformed to international ethical standards for chronobiology research (Portaluppi, Smolensky et al., 2010).

Locomotor Activity

Home cage locomotor activity was monitored during the fifth and sixth weeks in experimental light conditions; each group was monitored for four consecutive days. Home cage activity was monitored by assessing interruptions of intersecting infrared beams placed around the cage. Activity was tracked in eight mice per group using OPTO M3 animal activity monitors (Columbus Instruments, Columbus, OH, USA) that continuously compiled data using MDI software (Toronto, Ontario, Canada). The total 24 h activity was averaged for the four days of home cage monitoring.

Statistics

Main effect of lighting (LD vs dLAN) was assessed in all analyses. Repeated measures ANOVA were used to analyze food intake, body mass, and change in body mass across weeks. A Greenhouse-Geisser correction was applied to body mass and change in body mass data because the assumption of sphericity was violated; only adjusted results are reported (Vasey & Thayer, 1987). A multivariate ANOVA was used to analyze food intake, body mass, and change in body mass differences for weeks one-six. A Univariate ANOVA was used to analyze average total activity. Due to unequal variance total food intake for the entire 6 weeks period was analyzed with a Kruskal-Wallis test. Statistics were performed using SPSS 22 for Windows (IBM, New York, NY, USA). Outliers determined by Z score (± 2 SEM from mean) were removed from subsequent analysis. Mean differences were considered statistically significant when p was <0.05 .

Results

Body Mass

Body mass ($F_{2,3,36,5}=65.1$, $p<0.01$; Fig 1A) and change in body mass ($F_{2,7,46,6}=33.2$, $p<0.01$; Fig 1B) significantly increased across weeks in both groups. Lighting and body mass interacted across weeks ($F_{2,3,36,5}=5.5$, $p<0.01$; Fig 1A) such that mice in dLAN gained more body mass than mice LD across the weeks of the experiment. dLAN mice and LD had similar body mass at baseline, week 1 and 6 ($p>0.05$ in each case; Fig 1B), dLAN mice increased body mass weeks 2-5 (week 2 $F_{1,16}=4.6$, $p<0.05$; week 3 $F_{1,16}=6.1$, $p<0.05$; week 4 $F_{1,16}=8.2$, $p<0.05$; week 5 $F_{1,16}=6.4$, $p<0.05$; Fig 1A). One mouse in LD and one mouse in dLAN were removed from body mass analysis because they were outliers based on Z score analyses. Lighting and change in body mass did not interact across weeks ($p>0.05$), however, mice in dLAN had increased change in body mass compared to LD mice every week of the experiment (week 1 $F_{1,17}=7.17$, $p<0.05$; week 2 $F_{1,17}=9.22$, $p<0.01$; week 3 $F_{1,17}=11.8$, $p<0.01$; week 4 $F_{1,17}=9.7$, $p<0.01$; week 5 $F_{1,17}=6.09$, $p<0.05$; week 6 $F_{1,17}=4.9$, $p<0.05$; Fig 1B).

Food Intake

Food intake and lighting interacted across weeks ($F_{5,85}=3.74$, $p<0.01$; Fig 1C) such that mice in the LD condition consumed more food than mice in dLAN during the fifth and sixth weeks (week 5 $F_{1,17}=12.1$, $p<0.01$; week 6 $F_{1,17}=6.7$, $p<0.05$; Fig 1C).

Locomotor Activity

Average total locomotor activity was similar between LD and dLAN mice ($p>0.05$; Fig 1D).

Discussion

Our previous work established that exposure to dLAN increased body mass and disrupted molecular circadian rhythms in males (Fonken, Aubrecht et al., 2013). We hypothesized that dLAN also elevates body mass in female mice. Female Swiss-Webster mice exposed to ~5 lux of nightly illumination increased body mass and rates of body mass change compared to mice exposed to dark nights despite reduced food intake. Increased food intake without

increased change in body mass in female mice maintained under dark nights suggests a role for dLAN to dysregulate metabolic processes. Similarly, exposure of male mice to 5 lux of dLAN increased body mass and impaired glucose regulation (Fonken, Workman et al., 2010); LD and dLAN exposed mice had similar average total activity counts, suggesting that body mass differences are not due to lack of locomotion.

Removal of dLAN exposure can reverse metabolic disruption (Fonken, Weil et al., 2013). Dark nights restore nightly melatonin secretion (Brainard, Richardson et al., 1982). However, because the nightly melatonin signal is faint in this mouse strain, it seems more likely that the metabolic effects of dLAN are mediated via changes in core clock gene expression and protein production. For example, changes in phase and amplitude of several core clock genes occurred in response to dLAN in male mice that gained body mass (Fonken, Aubrecht et al., 2013). It appears from our data that no strong sex differences in the metabolic effects of dLAN exist in mice.

Light at night is increasingly pervasive in developed countries. Light at night disrupts regular circadian patterns communicated via the SCN (Brainard, Richardson et al., 1982; Hastings, Reddy et al., 2003). The consequences of light at night have profound implications for the population at large, but particularly shift workers. Shift work has been linked to increased body mass, as well as elevated rates of heart disease and cancer (van Amelsvoort, Schouten et al., 1999; Stevens, Blask et al., 2007). Collectively, our results suggest that dLAN has effects on body mass and likely metabolic function in both male and female mice that mimic health problems associated with shift work. Light at night appears to affect the health of shift workers which might be minimized by the use of long wavelength lighting that does not impair melatonin secretion (Lockley, Brainard et al., 2003).

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Figure 1. Female mice exposed to dim light at night (dLAN) had a greater change in body mass than mice exposed to dark nights (LD), despite decreased food intake in dLAN mice compared to LD mice in weeks five and six

Body mass interacted with lighting across the six weeks of the experiment such that mice in dLAN (n=11) had a greater gain in body mass than mice in LD (n=9) (A). Change in body mass was increased in dLAN (n=11) mice compared to LD (n=9) mice across the six weeks of the experiment (B). Food intake across the six weeks of the experiment, LD (n=8) mice had increased food intake on weeks five and six compared to dLAN (n=11) exposed mice (C). Mice in LD (n=7) and dLAN (n=8) had similar amounts of 24 hour (h) activity averaged for the four days of home cage monitoring (D). Significant mean differences $p < 0.05$ indicated by asterisk (*).