Chronic exposure to dim light at night suppresses immune responses in Siberian hamsters

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1. INTRODUCTION
Species have been adapted to specific niches optimizing survival and reproduction; however, urbanization by humans has dramatically altered natural habitats. Artificial light at night (LAN), termed ‘light pollution’, is an often overlooked, yet increasing disruptor of habitats, which perturbs physiological processes that rely on precise light information. For example, LAN alters reproduction and activity in some species, which decreases the odds of successful breeding and increases the threat of predation for these individuals, leading to reduced fitness. LAN also suppresses immune function, an important proxy for survival. To investigate the impact of LAN in a species naive to light pollution in its native habitat, immune function was examined in Siberian hamsters derived from wild-caught stock. After four weeks exposure to dim LAN, immune responses to three different challenges were assessed: (i) delayed-type hypersensitivity (DTH), (ii) lipopolysaccharide-induced fever, and (iii) bactericide activity of blood. LAN suppressed DTH response and reduced bactericide activity of blood after lipopolysaccharide treatment, in addition to altering daily patterns of locomotor activity, suggesting that human encroachment on habitats via night-time lighting may inadvertently compromise immune function and ultimately fitness.

Keywords: light pollution; delayed-type hypersensitivity; bactericide; lipopolysaccharide; Phodopus sungorus

2. MATERIAL AND METHODS
(a) Animals
Eighteen individually-housed adult (greater than eight weeks of age) male Siberian hamsters (Phodopus sungorus) were obtained from our breeding colony at The Ohio State University and maintained in polypropylene cages (30 × 15 × 14 cm) at a constant temperature (22 ± 2 °C) and relative humidity (50 ± 5%). Food (Harlan Teklad 8640, Indianapolis, IN, USA) and filtered tap water were available ad libitum. Hamsters were exposed to either a standard 16 L : 8 D cycle (LD; 150 lux : 0 lux) or a 16 : 8 light-dim light cycle (LdimL; 150 lux : 5 lux), with bright lights illuminated from 23.00 to 15.00 h eastern standard time (BST). Both the bright and dim lights were standard fluorescent bulbs emitting ‘cool white’ light composed of wavelengths distributed across the visible spectrum, and light intensity was measured at cage level. The same individuals were used for each test procedure. All experiments were approved by The Ohio State University Institutional Animal Care and Use Committee and performed in accordance with NIH guidelines.

(b) Delayed-type hypersensitivity
After four weeks of housing in either an LD or LdimL condition, DTH, an ecologically valid in vivo assay of cell-mediated immune function [8] was assessed as previously described [9]. Briefly, DTH was induced by sensitization to, and later challenge with, the antigen 2,4-dinitro-1-fluorobenzene (DNFB; Sigma). Responses to this challenge reflect cell-mediated immune function, including T-cell-mediated inflammation and antigen processing and presentation [8]. On days 1 and 2, hamsters were sensitized by applying 25 μl of DNFB (0.5% wt/volume in 4 : 1 acetone to olive oil vehicle) to the dorsum. Seven days later baseline pinnae thickness was measured with a constant loading dial micrometer (Mitutoyo, Tokyo), and then hamsters were challenged on the right pinna with 20 μl of 0.2% (wt/volume) DNFB in vehicle, while the left pinna was treated with the vehicle solution alone. The thicknesses of both pinnae were measured every 24 h for the next 5 days by the same investigator (T.A.B.). All measurements were made between 07.00 and 08.30 h EST and animals were brought into the procedure room individually to minimize potential stressors.

(c) Lipopolysaccharide-induced fever
Procedures were performed as previously described [10] approximately eight weeks following DTH measurements. Briefly, hamsters were implanted intraperitoneally with radiotelemetric transmitters (Mini-Mitter, Sunriver, OR, USA) under isoflurane anesthesia and allowed to recover for 5 days. Homecages were placed on TR-3000 receiver boards and connected to DP-24 Data-Ports (Mini-Mitter), which continuously collected activity and temperature data in 15 min bins. At the beginning of the dark/dim phase (15:00 h), each hamster was given an intraperitoneal (IP) injection of saline to establish the baseline activity and temperature information. Twenty-four hours after saline injection, lipopolysaccharide (LPS; 400 μg kg−1), a component of Gram-negative bacteria cell walls, was administered IP to induce fever. Temperature and activity data were collected through to 19 h post-LPS.
3. RESULTS

(a) Immune responses

(i) DTH
DNFB challenge-induced swelling in the right pinnae of both groups ($F_{1,16} = 3.27, p < 0.05$); however, exposure to dim LAN impaired the inflammatory response ($F_{1,16} = 10.88, p < 0.01$; figure 1a). Post hoc comparisons of individual days revealed LdimL-hamsters significantly reduced swelling compared with LD-hamsters on day 2 ($p < 0.05$).

(ii) Blood plasma bactericidal capacity
Both groups had greater blood bactericidal activity post-LPS compared with baseline ($F_{1,16} = 45.29, p < 0.0001$) and there was a significant lighting treatment by baseline versus post-LPS interaction effect ($F_{1,16} = 5.77, p < 0.05$). Plasma from LD hamsters post-LPS killed more than twice as many CFUs as pre-LPS, with a similar induction (143%) in the LdimL group post-LPS. This induction in the LdimL group, however, was only 71% of that in the LD group. Post hoc comparisons confirmed post-LPS LdimL-hamsters killed significantly fewer CFUs compared with LD-hamsters ($p < 0.05$; figure 1b).

(b) Response to LPS

(i) LPS-induced fever
All hamsters showed a distinct peak in core body temperature shortly after LPS injection ($F_{1,16} = 23.42, p < 0.0001$; figure 2a); however, LD- versus LdimL-hamsters did not differ in response as there was no effect of lighting condition and no interaction ($p > 0.05$).

4. DISCUSSION

Chronic exposure to ambient light levels found in urban environments at night disrupts circadian activity patterns and alters immune function in Siberian hamsters derived from wild-caught stock. Four weeks of 5 lux LAN was sufficient to alter both cell-mediated immunity and bactericidal capacity, without affecting febrile response to LPS. Alteration of circadian activity patterns demonstrates that a single environmental factor, chronic dim light exposure at night, is sufficient to alter physiology and behaviour in this species.
In vivo T-cell-mediated immune responses, as assayed by DTH [9], are sensitive to melatonin concentrations, as melatonin enhances antigen presentation and amplifies T-cell proliferation [12]. Suppressed DTH response in LdimL-hamsters in the current study could potentially be a result of dim-light suppression of pineal melatonin synthesis [7]. Results of this assay reflect altered immune function, an effect that may have fitness consequences by either damaging host defence or shunting energy towards other processes. It must be noted that DTH responses may change over the course of a day owing to many factors, but we restricted our assay to one morning timepoint, at the nadir of the cortisol and thermoregulatory demands can interact to compromise immune function. Further alterations in immune function by exposure to LAN could potentially reduce the odds of survival. Thus, night-time light exposure should be considered an important contributing factor in species decline. Future studies should address the mechanisms underlying these phenomena and the ultimate consequences of artificial light on ecosystem stability.

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