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

Tracy A. Bedrosian*, Laura K. Fonken, James C. Walton and Randy J. Nelson

Department of Neuroscience, The Ohio State University Medical Center, Columbus, OH 43210, USA
*Author for correspondence (tracy.bedrosian@osumc.edu).

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 the timing of 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

1. INTRODUCTION

Species have been adapted to specific temporal and spatial niches optimizing survival and reproduction; however, urbanization by humans has dramatically altered habitats. Artificial light at night (LAN), termed ‘light pollution’, is rapidly pervading the environment. For many organisms, this is problematic because it disrupts physiological processes, which rely on precise light information, such as timing of daily rhythms and seasonal adaptations. For example, songbirds living near streetlights have altered mating calls and lay eggs earlier than those living deep in the forest [1], beach mice living near populated coastlines have altered foraging behaviour [2], and bats near streetlights change their commuting patterns, with no evidence of habituation over time [3]. Altering the timing of reproduction and activity exposes these individuals to a greater risk of climatic challenges, predation and disease, which potentially decreases fitness. In a laboratory setting, LAN suppresses cell-mediated and humoral immune function in Japanese quail [4], cockerels [5] and rats [6]. Outside of the laboratory, with the demands of limited resources and other harsh environmental conditions, reduced immune function could seriously impact survival.

In the present study, we exposed Siberian hamsters to dim light throughout the night (5 lux) for four weeks; this level of illumination is approximately five times brighter than maximal moonlight, comparable to the levels of light pollution in areas surrounding urban centres, and is sufficient to suppress melatonin in hamsters [7]. We then assessed immune responses (as a proxy for survival) to three different challenges: (i) delayed-type hypersensitivity (DTH), (ii) lipopolysaccharide-induced fever responses, and (iii) bactericide activity of blood plasma.

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 x 15 x 14 cm) at a constant temperature (22.0 ± 2.0 °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/vol) in 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/vol) 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 anaesthesia 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 ($F_{1,16} = 45.94$, $p < 0.0001$) 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% per cent 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 ($F_{1,19} = 23.42$, $p < 0.0001$; figure 2a); however, LD- versus LdimL-hamsters did not differ in response as there was no effect of lighting condition and no interaction ($p > 0.05$).

(e) Statistical analyses

Repeated-measures ANOVA was used to analyse DTH and fever response data between LD and LdimL groups, with day post-challenge as the repeated measure in both cases. Two-way ANOVA was used to analyse bactericidal, body mass and home-cage activity data with lighting condition (LD versus LdimL) and pre- versus post-LPS, start versus end weight, and light versus dark as the independent variables, respectively. One outlier was removed from analysis of the bactericidal assay and two were removed from activity analyses. All significant main effects were followed up with Fisher’s post hoc comparisons. Statistics were performed using STATVIEW 5.0.1 for Windows PC and mean differences were considered statistically significant when $p < 0.05$.
Suppressed DTH response in LdimL-hamsters in the current study could potentially be a result of dim-light suppression of pineal melatonin synthesis [7]. LdimL-hamsters, in comparison with LD-hamsters, displayed no basal differences in blood bactericidal activity; however, post-LPS plasma from LdimL-hamsters reduced bactericidal capacity. Activation of the immune system appears to be necessary to reveal the effects of LAN on this parameter. LPS-induced fever did not differ between LdimL-compared with LD-hamsters. Consistent with these data, removing melatonin by pinealectomy in Siberian hamsters has no impact on LPS-induced fever [15], which may explain why LAN did not affect a fever response. LPS-treatment did, however, reduce activity levels in LD- but not LdimL-hamsters. Whether this difference represents altered sickness behaviours in LdimL-hamsters, or whether this response is simply masked by the general reduction in activity of LdimL-hamsters remains unspecified.

Taken together, these data suggest that dim light, consistent with typical levels of light pollution from urban development, alters immune function and circadian activity patterns, which could potentially compromise survival. Our study emphasizes the ecological relevance of light pollution on immune function, an important proxy for survival. Under natural conditions, resource limitations 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.

All experiments were approved by the Ohio State University Institutional Animal Care and Use Committee and performed in accordance with NIH guidelines.

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