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SHORT COMMUNICATION

Does the Modern Urbanized Sleeping Habitat Pose a Breast Cancer Risk?

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Due to its disruptive effects on circadian rhythms and sleep deprivation at night, shiftworking is currently recognized as a risk factor for breast cancer (BC). As revealed by the present analysis based on a comparative case-control study of 1679 women, exposure to light-at-night (LAN) in the "sleeping habitat" is significantly associated with BC risk (odds ratio [OR] = 1.220, 95% confidence interval [CI] = 1.118–1.311; $p < .001$), controlling for education, ethnicity, fertility, and alcohol consumption. The novelty of the present research is that, to the best of the authors' knowledge, it is the first study to have identified an unequivocal positive association between bedroom-light intensity and BC risk. Thus, according to the results of the present study, not only should artificial light exposure in the working environment be considered as a potential risk factor for BC, but also LAN in the "sleeping habitat." (Author correspondence: ahaim@research.haifa.ac.il)

Keywords: Breast cancer, Circadian disruption, Light-at-night, Light pollution, Sleeping habitat

INTRODUCTION

Several possible mechanisms have been suggested in recent years to explain the association between exposure to light pollution, termed "light-at-night" (LAN), and breast cancer (BC). These mechanisms include the suppression of melatonin (MLT) secretion by the pineal gland leading to increased tumor growth (Blask et al., 2005) and the adverse effects of LAN on thermoregulatory (Haim et al., 2005) and immune functions (Nelson, 2004; Stevens et al., 2007). The "LAN-BC" theory is supported by the results of several recent epidemiological studies carried out at various population levels (Kloog et al., 2008, 2009a, 2010) that indicated exposure to LAN was associated with elevated BC rates, whereas no such an association was found for lung cancer. Other studies provided further evidence that women working night shifts are at high risk of developing BC (Davis et al., 2001; Hansen, 2001; Schernhammer et al., 2001), whereas studies on blind women have found BC rates to be lower than those of visually unimpaired women in the same populations (Feychting et al., 1998; Kliukiene et al., 2001; Verkasalo et al., 1999).

With accelerating urbanization worldwide and rising living standards, electricity has become more accessible and affordable for wide segments of the population, resulting in increased LAN exposure in both outdoor, such as public areas and transportation, and indoor spaces, such as workplaces, apartments, and houses. Although several empirical studies have been conducted to evaluate the effects of work-related and outdoor light pollution on hormone-dependent cancers (Davis et al., 2001; Kloog et al., 2008, 2009a, 2009b, 2010; Schernhammer et al., 2006), the association between LAN exposure in the bedroom of apartments and houses (which we term the "sleeping habitat") and cancer has largely escaped investigation, and the existing evidence is essentially scarce. In the framework of their Long Island study, O'Leary and colleagues (2006) conducted personal interviews to trace LAN-exposure histories at work and home. The study cohort included 576 women diagnosed with BC and 585 population-based controls. The questionnaire included questions about the number of sleep hours, frequency of turning lights-on during the night, and the length of time the light was on during the nighttime, but it did not include questions about bedroom-light intensity. The analysis of the data revealed that women who frequently turned on lights during the sleep hours exhibited an increased BC risk (odds ratio

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[OR] = 1.65, 95% confidence interval [CI]: 1.02–2.69). In another study, Davis and colleagues (2001) investigated whether exposure to LAN at home is associated with an increased risk of BC in women. The study included 813 cancer patients aged 20–74 yrs and 793 control subjects of comparable age. Personal interviews were conducted to gather information on sleep habits and the bedroom-light environment 10 yrs before diagnosis and lifetime occupational history. Conditional logistic regression was then used to adjust for other potential risk factors, such as family history of cancer, parity, oral-contraceptive use, and hormone-replacement therapy. Although the analysis revealed that BC risk was significantly higher among subjects with sleep disturbance (OR = 1.14, 95% CI = 1.01–1.28), no clear association between bedroom-light intensity and BC was found (OR = 1.4, 95% CI = 0.8–2.6).

In the past decade, electricity consumption and LAN intensity increased worldwide, and new lighting sources have been introduced, which include the modern outdoor high-intensity discharge (HID) and fluorescent lamps that emit blue wavelengths (Pauley, 2004). These new developments may have presumably strengthened the LAN-BC association. In the present study, we compared light intensities in the "sleeping habitat" of 794 BC patients with light intensities at homes of a control group of 885 women residing in northern Israel. Our working hypothesis was as follows: If exposure to LAN elevates BC risk, then BC patients should have been exposed to higher LAN levels in their "sleeping habitat" than those without BC of the control group, controlling for individual level confounders.

RESEARCH METHODS

Participants

Data on 1679 women (794 women with BC and 885 controls) were obtained from the "Breast Cancer in Northern Israel" study, initiated in 2000 and which focused on the molecular and environmental etiology of BC in Northern Israel (Rennert et al., 2010). Northern Israel is formed by two administrative districts—the Haifa district and the Northern district—with a combined population of over 2,000,000 residents (ICBS, 2010). In the Haifa district, about 71% of the total population are Jewish, while 29% are Arabs and other ethnic minorities; whereas in the Northern district, 44.2% of the population are Jewish, while the rest (55.8%) are Arab Muslims and other ethnic minorities (ICBS, 2010). All women residing in the region and diagnosed with BC since 2000 were invited to participate in the study. Questions on LAN exposure were added to the general study questionnaire in mid-2006, and the present study covers 1679 women (794 cases and 885 controls) who responded to the "extended" questionnaire between 2006 and 2008.

Frequency matching, which was used in the present study, is a variation of stratified sampling that is commonly used in empirical studies (cf., e.g., Rothman et al., 2008). Instead of predetermining the number of cases and controls to be selected within each population stratum (stratified sampling), frequency matching involves the selection of cases at random, with controls being taken from the corresponding subgroups in proportion to the number of cases (Rothman et al., 2008). Controls were randomly selected from the list of women enrolled in the health-care program provided by the Clalit Health Services, the largest health-care provider in Israel, which covers approximately 60% of the country's adult population. Health-care coverage in Israel is mandatory, and all study participants (both patients and controls) had similar health-insurance coverage and similar access to health services. Cases and controls were matched by age, location of primary clinic, and ethnicity—Jewish versus non-Jewish (Table 1). Respondents reporting any previous BC were excluded. All participants were individually interviewed to obtain data, including reproductive and general medical history, alcohol consumption, LAN exposure, and socioeconomic status in order to include these confounders in our model. The overall study response rate was 85.6% of the approached cases and 51.6% among controls. All participants signed a consent form approved by the Carmel Medical Center's institutional review board committee, and all aspects of the study complied with the ethical standards of the journal (Portaluppi et al., 2010).

Exposure Data

LAN exposure was evaluated from individual interviews regarding exposure to both LAN from outside sources and from sources within the households (bedroom-light levels, light coming from outside the bedroom, availability of shutters in the bedroom, and sleeping with the television on. Nighttime bedroom-light level was evaluated using a 4-point scale: from completely dark (score of 1) to strong light (score of 4). The exact wording of the question was as follows: "How do you define your nighttime bedroom-light level? "1" (completely dark), "2" (low light), "3" (average light), or "4" (very strong light—all lights switched on). Other LAN exposure-related questions included the availability of bedroom shutters and sleeping with the television left on. The answers to these questions were coded dichotomously, that is, yes or no. Other questions in the questionnaire referred to alcohol consumption, number of births, religion, age, and education.

Statistical Analysis

Statistical analysis was performed using SPSS17^{TM} software and the probability $p < .05$ (two-sided) was set as the accepted level of statistical significance. Contingency tables, t tests, and unconditional binary logistic regressions were then used to assess the association between exposure to LAN and BC risk, with adjustment for potential confounders.

TABLE 1. Descriptive statistics of the research variables

Variable	Cases	Controls	OR (95% CI)
Age (yrs)	58.89 (13.69)*	60.86 (13.51)*	0.127†
Alcohol consumption			
Yes	143 (13%)	142 (16%)	
No	691 (87%)	743 (84%)	
Total	794 (100%)	885 (100%)	0.780 (0.593–1.026)
Bedroom light			
None (0)	369 (46.5%)	479 (54.1%)	
Low (1)	106 (13.4%)	112 (12.7%)	
Average (2)	85 (10.7%)	94 (10.6%)	
High (3)	234 (29.5%)	200 (22.6%)	
Total	794 (100%)	885 (100%)	1.359 (1.121–1.647)
Bedroom shutters			
Open	527 (66.4%)	629 (71.1%)	
Closed	267 (33.6%)	256 (28.9%)	
Total	794 (100%)	885 (100%)	0.803 (0.653–0.988)
Education (yrs)			
>12 yrs	223 (29.3%)	223 (25.2%)	
<12 yrs	561 (70.7%)	662 (74.8%)	
Total	794 (100%)	885 (100%)	1.233 (0.994–1.529)
No. births by religion	2.83 (2.02)*	3.17 (2.16)*	<0.01†
Jewish	609 (76.7%)	668 (75.5%)	
Non-Jewish	185 (23.3%)	217 (24.5%)	
Total	794 (100%)	885 (100%)	1.069 (0.854–1.339)
TV on while sleeping			
Yes	180 (22.7 %)	216 (24.4%)	
No	614 (77.3%)	669 (75.6%)	
Total	794 (100%)	885 (100%)	0.908 (0.724–1.138)

*Mean value and standard deviation in the parentheses, number of cases (percent of total) for all other cases.
†Statistically significant differences between groups by *t* test.

RESULTS

Table 1 presents the descriptive statistics of the research variables. Table 2 reports the results of the binary logistic regressions run for the whole sample, and Table 3 reports the results of the binary logistic regressions run for the Jewish women separately to allow for more homogeneity in the analyses.

As Table 2 shows, the intensity of bedroom light emerged as the strongest predictor of BC, which appears to increase its risk significantly (OR = 1.220, 95% CI = 1.118–1.311; $p < .001$). Religion (Jews versus non-Jews) and number of births also emerged as statistically significant (OR = 0.737, 95% CI = 0.556–0.977, $p < .05$, and OR = 0.932, 95% CI = 0.886–0.979, $p < .01$, respectively), implying that Jewish women (who exhibit much lower birth rates—2.72 births for Jews versus 4.07 for Arabs) are at higher risk of developing BC than non-Jewish survey participants. Other variables, e.g., alcohol consumption, education, etc., did not emerge as being significant determinants ($p > .05$).

The results of the regression analysis run for Jewish women separately (Table 3) were essentially similar to the results obtained for the entire sample (Table 2), with the exception of one variable—alcohol consumption, which emerged as statistically significant ($p < .05$).

TABLE 2. Factors affecting BC incidence (method: binary logistic regression)*

Variable	*p* value	OR (95% CI)
Age (yrs)	.300	0.996 (0.988–1.004)
Alcohol consumption (yes)	.097	0.787 (0.593–1.004)
Bedroom light (scoring 1 to 4)	<.001	1.220 (1.118–1.311)
Bedroom shutters (open)	.060	0.818 (0.663–1.008)
Education (>12 yrs)	.187	0.857 (0.861–1.078)
Number of births	.005	0.932 (0.886–0.979)
Religion (non-Jewish)	.034	0.737 (0.556–0.977)
TV on while sleeping (yes)	.443	0.914 (0.725–1.151)

*Total number of observations = 1679 (794 cases/885 controls).

TABLE 3. Factors affecting BC incidence (method: binary logistic regression; Jewish population only)*

Variable	*p* value	OR (95% CI)
Age (yrs)	.163	0.994 (0.985–1.003)
Alcohol consumption (yes)	.017	0.688 (0.507–0.935)
Bedroom light (scoring 1 to 4)	<.001	1.278 (1.115–1.414)
Bedroom shutters (open)	.220	0.859 (0.673–1.096)
Education (>12 yrs)	.232	0.857 (0.666–1.103)
Number of births	.015	0.917 (0.855–0.984)
TV on while sleeping (yes)	.215	0.846 (0.649–1.102)

*Total number of observations = 1277 (609 cases/668 controls).

The protective effect of this factor (OR = 0.688, 95% CI = 0.507–0.935) may be attributed to the fact that alcohol consumption in Israel, in general, is low, especially among women, and is mostly limited to red wine, as common for most non-Muslim countries of the Mediterranean (Kesteloot, 2004). Several studies have shown that red-wine consumption in small quantities can exert a protective effect against the development of BC (Damianaki et al., 2000; Soleas et al., 2002).

DISCUSSION

The present analysis is based on a comparative case-control study of 1679 women (794 cases and 885 controls) who were individually interviewed about their lifestyle and LAN exposure. The study revealed that exposure to LAN in the "sleeping habitat" was significantly associated with BC, controlling for education, ethnicity, fertility, and alcohol consumption. Our results are thus consistent with those of previous studies that revealed a significant LAN-BC association (Kloog et al., 2008, 2009a, 2009b, 2010; Schernhammer et al., 2001). Our results also correspond with those of the case-control studies conducted by O'Leary and colleagues (2006) and Davis and colleagues (2001). However, in the research reported here, the association between bedroom-light intensity and BC ($p < .001$) was stronger than it was in the study by Davis and colleagues (2001), thus supporting our working hypothesis of a linkage between LAN exposure and BC.

This difference in results may have several explanations. First, our study population was relatively homogenous, with a separate analysis performed for Jewish women, whereas the study by Davis and colleagues (2001) involved a more heterogeneous general population of diverse ethnic background. Second, it should be borne in mind that the study by Davis and colleagues (2001) was conducted some 15 yrs ago (in 1992–1995). Since then, light pollution has increased, and women are currently exposed to higher light-intensity levels. Lastly, in the past decade, light bulbs emitting bluer light waves (~460 nm) have been widely introduced to save energy consumption and reduce CO_2 emission. The results of a study carried out by Cajochen and colleagues (2005) revealed that short-wavelength light (460 nm) given for 2 h in the late evening decreased MLT production while increasing alertness, body temperature, and heart rate. Concurrently, exposure to a wavelength of 550 nm for the same duration of time did not cause such effects.

Better understanding in the last decades of the way by which light is transferred from the retina to different areas of the brain has opened new areas for research. The discovery of the non–image-forming photoreceptors (NIFPs) and the non-vision pigment melanopsin (Berson et al., 2002) enhanced chronobiological research, showing that even a subterranean rodent, such as the "blind" mole rat *Spalax ehernbergi*, is photosensitive to different photoperiod regimes (Haim et al., 1983), light intensities, and wavelengths (Zubidat et al., 2009, 2010). Therefore, our vision system, which evolved from a mammalian system that entailed a subterranean stage in evolution (Vaughan, 1972), became more complex as it includes more types of functional photoreceptors whereby the NIFPs seem to play a major role in regulating circadian systems.

It is interesting to note that recent reviews on MLT, LAN, and BC (Haus, 2009; Srinivasan et al., 2008) report that nighttime MLT treatment in physiological concentrations acts like an endogenous antiestrogen that can decrease the formation of estrogens from androgens through inhibition of the aromatase enzyme. This finding suggests the importance of MLT in modulating estrogen levels in relation to BC risk.

The International Agency for Research on Cancer (IARC) recently recognized shiftworking as a 2A probable human carcinogen risk factor (Straif et al., 2007). Shiftworkers are exposed to high LAN intensity in their work environment during the dark period of the 24-h cycle, when pineal MLT should be produced and secreted into the plasma, thus causing circadian rhythm disruption. This suppression of pineal MLT production may lead to increased tumor growth of hormone-dependent cancers (Blask et al., 2005).

The novelty of the present research lies in the fact that to the best of our knowledge, this is the first large-scale case-control study of the general population that has identified a significant positive association between bedroom light ("sleeping habitat") and ambient nighttime light (light pollution) levels with BC risk, providing evidence that the relative risk of BC appears to increase in more illuminated sleeping environments. Our main conclusion is that not only should LAN in the working environment be considered a potential BC risk factor, as noted in shiftworker studies (Hansen, 2001), but also the modern human "sleeping habitat" with high LAN levels.

The main limitation of the present study is that we were unable to measure precise light levels in the "sleeping habitat," which would have been a more accurate way of measuring LAN in the bedroom compared to the limits of a questionnaire-based method. We attempted to compensate for this limitation, at least in part, by the application of a well-designed questionnaire and through study of a relatively large number of participants (n = 1679), thereby resulting in good statistical power. Nevertheless, more precise measurements of light levels in the "sleeping habitat" should be investigated in follow-up studies. Moreover, the fact that the response rate of the invited participants was not 100% may also be viewed as an additional limitation of the study.

Beyond doubts, LAN is an integral part of our lifestyle and that in the future LAN levels may increase. Fortunately, this is an environmental variable that can easily be controlled, thus reducing its health risk. Simple solutions exist to avoid the penetration of street illumination

into the "sleeping habitat," such as by the installation of window blinds in the bedroom, and also by the use of eye covers while sleeping.

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