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Via E-mail

December 5, 2005

Dear Mr. Pellatt,

Re: FortisBC Inc. Order No. G-114-05 CPCN Application for Nk'Mip East Osoyoos Substation & Transmission

Please see attached evidence # 8.

Please also a friendly reminder to have the participant distribution list with their address, e-mails, and phone/fax numbers posted in BCUC's web site

http://www.bcuc.com/ApplicationView.aspx?ApplicationId=93

so to better enabling me to CC my submissions to all participants as required in the Commission's hearing guidelines. So far I can't find the list in the web site to download.

Hans Karow

Melatonin Metabolite Levels in Workers Exposed to 60-Hz Magnetic Fields: Work in Substations and with 3-Phase Conductors

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Melatonin suppression by 50/60-Hz magnetic fields represents a plausible biological mechanism for explaining increased health risks in workers. Personal exposure to magnetic fields and ambient light, and excretion of the melatonin metabolite 6-hydroxymelatonin sulfate (6-OHMS), were measured over 3 consecutive workdays in electric utility workers. There was a magnetic feld-dependent reduction in adjusted mean nocturnal and post-work 6-OHMS levels among men working more than 2 hours per day in substation and 3-phase environments and no effect among those working 2 hours or less. No changes were observed among men working in 1-phase environments. The results suggest that circular or elliptical magnetic field polarization, or another factor linked to substations and 3-phase electricity, is associated with magnetic field induced melatonin suppession in humans.

The issue of whether exposure to power frequency (50/60-Hz electric and magnetic fields (EMFs) is associated with health effects in humans remains uncertain in part because human biological responses to EMF exposure have not been reproducibly characterized. The hormone, melatonin, has oncostatic,[1-2] immunological [3-4] and antioxidant properties [5-6]; thus its suppression by EMFs represents a biologically plausible mechanism for increased cancer risks that have been observed in electric utility workers.[7-8]

Melatonin synthesis and secretion follow a diurnal pattern synchronized by ambient light, thereby exerting significant effects on circadian physiology.[9-10] Peak melatonin concentrations occur in the dark phase (0200 to 0400 hours), and lowest concentrations occur during the light phase (1200 to 1800 hours) of the 24-hour light-dark cycle.[9-10] Circulating melatonin levels are age dependent, although only small differences have been reported in subjects between the ages of 20 and 60 years.[11-12] Urinary concentrations of the major metabolite, 6-hydroxymelatonin sulfate (6-OHMS), are well correlated with circulating melatonin, and overnight 6-OHMS excretion represents an integrated measure of nocturnal melatonin production.[13-14]

In experimental animals, exposure to 50/60-Hz magnetic fields has been associated with reduced circulating and pineal melatonin concentrations, although these effects have not been

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observed consistently.15-16 Differences in genetic composition; the timing, duration, or intensity of exposure; field polarization; lighting conditions; or other factors may explain divergent findings among laboratory species. Epidemiological studies of human melatonin levels in response to EMF exposure have been performed in male utility workers, [17-18] healthy women,19 male railway workers20 electric blanket users,21 and workers using video display terminals.22 There was wide variation in the exposure conditions; the duration, precision, and type of measures obtained; the presence of possible confounders (light at night, shift work), and the general characteristics of participants among these studies. Although the response to individual exposure metrics was not always consistent, each study showed some decrement in urinary 6-OHMS excretion.23

Reasons for the inconsistency among the various human and animal studies remain to be elucidated. One potential explanation is that EMFs have no effect on melatonin production and that some unidentified factor produced a number of false positives.16 Alternatively, one or more critical factors that can modify the effects of EMFs on melatonin may not have been carefully considered in all studies.16 Kato and coworkers24-27 reported that circularly polarized fields or elliptical fields with a small axial ratio were most effective at suppressing nocturnal melatonin production in rats, whereas linearly polarized fields or elliptical fields with a large axial ratio had little or no effect. Although numerous investigations of melatonin levels in response to 50/60-Hz EMF exposure have been performed subsequently in rodents, no other studies used circularly or elliptically Polarized magnetic fields. Magnetic fields in close proximity to energized 3-phase conductors (eg, 3-phase distribution lines and substations) have circular or elliptical polarization,28 whereas those associated with single phase conductors are linearly polarized. Exposure monitoring in substations as well as in residential settings has confirmed the presence of elliptically polarized fields.29 The purpose of this analysis was to test the hypothesis that the effect of 60-Hz magnetic field exposure on 6-OHMS excretion was greatest among utility employees working in substations or in the vicinity of energized 3-phase conductors, and that work around l-phase conductors had little or no effect on 6-OHMS excretion.

Methods

The study population was comprised of male workers from six utilities who were engaged in electric power generation (power plant operators, mechanics, electricians), distribution (linemen, meter readers, substation operators), and comparison (utility administrative and maintenance) activities. Data collection was performed between January and September 1997, using procedures similar to those reported previously.17-18 Serial biological monitoring of urinary 6-OHMS excretion was combined with concomitant measurement of personal exposure to 60-Hz magnetic fields and ambient light. Magnetic field and light exposures were recorded at 15-second intervals over the first 3 days of the subjects' workweek using EMDEX II meters (Enertech Consultants, Campbell, CA) worn at the waist. The light sensor was adapted to the EMDEX via the external sensor jack. A custom computer program was developed to calculate magnetic field and light exposure metrics. Work-related activities (work in substations, in the vicinity of 3-phase or l-phase conductors, office, and travel) were recorded in 30-minute increments in a log kept by each participant. Subjects were instructed to log their activities if they had been within approximately 1 meter (arm's length) of an energized conductor (3-phase, l-phase, or within a substation) for at least 30 minutes.

Melatonin production was assessed by radioimmunoassay of urinary 6-OHMS concentrations (CIDtech, Mississagua, Ontario, Canada).30-31 Participants provided overnight urine samples, combining any voids after bedtime with the first morning void on each day of participation. Daily post-work urine samples were also collected. Total overnight 6-OHMS excretion was estimated as the product of the overnight urine volume and the 6-OHMS concentration in each sample. Nocturnal and post-work 6-OHMS concentrations normalized to creatinine (6-OHMS/cr) were also analyzed. The interassay coefficient of variation for 6-OHMS was 8% at 10.5 ng/mL; within-assay variability ranged from 4% to 10% (mean, 6%); and the limit of detection was 0.1 ng/mL.

Data analyses were performed by using the Proc Mixed procedure for repeated measures in version 6.12 of the Statistical Analysis Software computer package (SAS Institute Inc, Cary, NC). Workplace exposure metrics based on either field intensity (time-weighted geometric mean) or temporal stability (standardized rate of change metric [RCMS]) were calculated for each workday of participation. 17-18 The RCMS estimates first-lag serial autocorrelation of personal magnetic field exposures; low values of RCMS represent temporally stable exposures.32 Ambient light exposure was summarized using the workshift arithmetic time-weighted average. Analyses were performed using log-transformed values of overnight 6-OHMS, 6-OHMS/cr, ambient light, and geometric mean magnetic field exposures (RCMS was untransformed). Mean values were back-transformed for presentation in the tables.

Subjects were first grouped into tertiles of workplace magnetic field exposure and then into groups who spent more than 2 hours, or 2 hours or less, per day in substations or 3-phase environments. Because substation and 3-phase environments

TABLE1
Magnetic Field Exposures for Work Activities

Time Spent Performing Activity	Workplace Exposure Tertiles: Substation and 3-PhaseActivities			Workplace Exposure Tertiles: l-Phase Activities		
	1	2	3	1	2	3
Geometric mean (μT)						
< 2 hours	0.04 ± 0.10 (142)	0.08 ± O.lO(133)	0.20 ± 0.10 (96)	0.04± 0.10 (137)	0.08 ± O.lO(146)	0.22 ± 0.10 (133)
>2 hours	0.03 ± 0.12(6)	0.09 ± 0.11 (18)	0.27 ± 0.11 (52)†	0.04 ± 0.11 (11)	0.10 ± 0.12 (5)	0.20 ± 0.11 (15)
RCMS exposures(per15 sec)						
<2 hours	1.04 ± 0.01 (140)	0.74 ± 0.01 (125)	0.46 ± 0.01 (106)	1.03 ± 0.01 (142)	0.73 ± 0.01 (135)	0.42 ± 0.01 (139)
>2 hours	0.95 ± 0.04 (9)*	0.88 ± 0.02 (22)‡	0.36 ± 0.02 (45)†	1.05 ± 0.04 (7)	0.70 ± 0.03 (12)	0.48 ± 0.03 (12)

* RCMS, standardized rate of change metric.
. Mean ± standard error of the mean (worker-days of exposure in parentheses).
† $P < 0.01$ vs ≤2 hour group.
‡ $P < 0.05$ vs ≤2 hour group.

were both expected to have circularly or elliptically polarized magnetic fields, these activities were combined. Mean magnetic field exposures among subjects with more than 2 hours, or 2 hours or less, of work in substation or 3-phase environments were compared statistically within each tertile by using the least significant differences method in SAS. Least-squares means of 6-OHMS excretion (adjusted for the effects of age, ambient light exposure, and month of participation) were then calculated by exposure tertile in groups with more than 2 hours, or 2 hours or less, of work in substations and in 3-phase environments. Adjusted mean 6-OHMS levels in the high and low exposure tertiles were compared statistically for each group. The study population was then reclassified on the basis of work in the vicinity of l-phase conductors, and analyses of mean 6-OHMS excretion in groups with more than 2 hours, or 2 hours or less, per day of l-phase work were performed in the same manner. Additional analyses were performed using 0.5-,1.0-, and 1.5-hour periods to assess cut point bias. There were insufficient worker-days of exposure to assess outcomes using cut points above 2 hours. Results of separate analyses incorporating potential confounding variables obtained from questionnaires, including personal, occupational, medical, and lifestyle factors, were consistent with those presented below.

Results

Complete data were available for 149 of 161 subjects; the mean age was 44 ± 9 years; and approximately 91% were Caucasian and non-Hispanic. There were 60 (40%) electric power distribution, 50 (33%) generation, and 39 (26%) comparison workers. Geometric mean magnetic field exposures for subjects working in substations and in the vicinity of 3-phase conductors were similar among subjects in the first and second exposure tertiles (Table 1). For subjects in the highest exposure tertile, geometric mean magnetic field exposures were greater for those with more than 2 hours of work in substations and in 3-phase environments (Table 1). Magnetic field exposures among men working more than 2 hours in substation/3-phase environments were more temporally stable than those with 2 hours or less (Table 1). For those working in l-phase environments, there were no statistically significant differences in geometric mean or RCMS magnetic field exposures among those with more than 2 hours, or 2 hours or less, of work (Table 1).

A diurnal variation in mean urinary 6-OHMS excretion was observed among all subjects; mean concentrations were 3.0 ng/mg creatinine in the post-work and 18.2 ng/mg creatinine in the overnight samples. Results summarizing 6-OHMS excretion in response to occupational magnetic field exposure and substation/3-phase work activities are presented in Table 2. In workers with more than 2 hours of substation or 3-phase work, there was a clear trend of decreasing nocturnal 6-OHMS/cr excretion with increasing magnetic field exposure using either the geometric mean ($P = 0.03$) or the temporal stability metric ($P = 0.01$). Adjusted mean overnight 6-OHMS levels and post-work 6-OHM/cr concentrations also exhibited a decreasing trend across tertiles of magnetic field exposure for those participating in more than 2 hours of substation and 3-phase activities, although statistically significant differences between the upper and lower tertiles were observed only for the temporal stability metric (Table 2). In contrast, no decrease in 6-OHMS excretion was observed among those with 2 hours or less of substation/3-phase work (Table 2). An increase in overnight 6-OHMS excretion was observed with increasing exposure to temporally stable magnetic fields among those with 2 hours or less of substation/3-phase work. However, statistically significant increases were not observed in this group for any of the other 6-OHMS variables

TABLE 2
Melatonin Metabolite Excretion* in Electric Utility Workers with Substation and s-phase Activities

Substation and J-Phase	1	2	3	Difference: Tertile 1 vs 3	P-value: Tertile 1 vs 3
Workplace geometric mean exposure tertiles					
Nocturnal 6-OHMS/cr concentration (ng/mg cr)					
≤2 hours	15.0	14.9	14.7	-2%	0.84
>2 hours	23.5	18.0	13.5	-43%	0.03
Overnight 6-OHMS excretion (µg)					
< 2 hours	7.9	7.9	8.2	+4%	0.81
>2 hours	13.1	8.8	8.0	-39%	0.11
Post-work 6-OHMS/cr concentration (ng/mg cr)					
< 2 hours	2.1	2.4	2.5	+19%	0.19
>2 hours	3.5	1.8	2.3	-34%	0.21
Workplace temporal stability exposure tertiles					
Nocturnal 6-OHMS/cr concentration (µg/mg cr)					
< 2 hours	13.7	15.2	15.7	+13%	0.11
>2 hours	23.6	16.1	13.8	-42%	0.01
Overnight 6-OHMS excretion (µg)					
< 2 hours	7.2	8.1	8.8	+22%	0.05
>2 hours	13.5	8.9	7.8	-42%	0.03
Post-work 6-OHMS/cr concentration (µg/mg cr)					
< 2 hours	2.2	2.3	2.3	+5%	0.87
>2 hours	3.5	2.7	1.8	-49%	0.02

• Least squares means adjusted for the effects of age, average workplace light exposure, and month of participation.

TABLE 3
Melatonin Metabolite Excretion* in Electric Utility Workers with 1 -Phase Activities

1 -Phase Activities	1	2	3	Difference: Tertile 1 vs 3	P-value: Tertile 1 vs 3
Workplace geometric mean exposure tertiles					
Nocturnal 6-OHMS/cr concentration (ng/mg cr)					
≤2 hours	15.4	15.2	14.1	-8%	0.37
>2 hours	13.5	16.9	15.1	+12%	0.66
Overnight 6-OHMS excretion (µg)					
≤2 hours	8.1	8.0	8.1	**0%**	**0.99**
>2 hours	8.4	7.8	8.4	**0%**	**0.98**
Post-work 6-OHMS/cr concentration (ng/mg cr)					
≤2 hours	2.1	2.3	2.4	+14%	0.30
>2 hours	2.3	2.7	2.3	0%	0.96
Workplace temporal stability exposure tertiles					
Nocturnal 6-OHMS/cr concentration (ng/mg cr)					
≤2 hours	14.3	14.9	15.4	+8%	0.35
>2 hours	13.4	20.0	12.7	-5%	0.84
Overnight B-OHMS excretion (µg)					
≤2 hours	7.5	8.0	8.5	+13%	0.20
>2 hours	7.4	9.5	7.9	+7%	0.82
Post-work 6-OHMS/cr concentration (ng/mg cr)					
≤2 hours	2.3	2.4	2.1	**-9%**	0.38
>2 hours	2.3	2.2	2.4	+4%	0.78

• Least squares means adjusted for the effects of age, average workplace light exposure, and month of participation.

or for magnetic field intensity. When the same analysis was performed for work in l-phase environments, there were no statistically significant differences in mean 6-OHMS excretion for those with or without 2 hours of l-phase work when using either the metric mean or the temporal stability metric (Table 3).

Results obtained among workers with more than 1.0 or 1.5 hours of substation/3-phase work (Table 4) were very similar to those obtained using the 2-hour cut point (Table 3). Differences between the upper and lower tertiles were progressively greater as the duration of time spent in substation/3-phase environments increased. There were no statistically significant differences in mean 6-OHMS excretion among subjects below the chosen cut points for substation/3-phase activities or among those with l-phase work activities above or below the cut points (results not shown).

Discussion

Decreased nocturnal or post-work urinary 6-OHMS excretion have been associated with magnetic field exposures in studies of electric railway workers20 and in our earlier studies of electric utility workers. 17-18 In the present study, another population of male electric utility workers had decreased overnight 6-OHMS levels as well as lower nocturnal and post-work 6-OHMS/cr concentrations with increasing exposure to 60-Hz magnetic fields in substations or near energized 3-phase conductors. Differences in mean 6-OHMS excretion between the upper and lower exposure tertiles became progressively greater as the cut point for the amount of time spent in substations and in 3-phase environments increased from 0.5 to 2 hours. These findings are consistent with the hypothesis that magnetic fields with circular or elliptical polarization are more effective at suppressing melatonin production than linearly polarized fields.24-27 The lack of effects observed in those with 2 hours or less of substation/3-phase work or among those with l-phase exposures further supports the hypothesis. Alternatively, this classification scheme may have simply selected those with more intense and temporally stable exposures. How-

TABLE 4
Melatonin Metabolite Excretion*: Cut Point Analysis

Melatonin Metabolite	Above Cut Point for Substation and 3-Phase Activities		
	0.5 hours	1.0 hours	1.5 hours
Workplace geometric mean			
Nocturnal 6-OHMS/cr	-14% (P = 0.42)	-40% (P = 0.02)	-42% (P = 0.02)
Overnight 6-OHMS	*-5% (P = 0.82)*	-34% (P = 0.12)	-37% (P = 0.09)
Post-work 6-OHMS/cr	-12% (P = 0.55)	-33% (P = 0.21)	-32% (P = 0.23)
Workplace temporal stability			
Nocturnal 6-OHMS/cr	-26% (P = 0.11)	-37% (P = 0.02)	*-39% (P = 0.02)*
Overnight 6-OHMS	-22% (P = 0.23)	-36% *(P = 0.06)*	-38% (P = 0.04)
Post-work 6-OHMS/cr	-37% (P = 0.04)	-44% (P = 0.02)	-44% (P = 0.02)

• Difference in adjusted mean melatonin metabolite levels between the upper and lower magnetic field exposure tertiles.

ever, if intensity or temporal stability was the critical parameter, then one might also expect to observe a trend of decreasing mean 6-OHMS excretion among those with 2 hours or less of substation/3-phase work or among those with l-phase exposures. A trend of decreasing mean 6-OHMS excretion was observed only among those with more than 2 hours of substation/3-phase work, even though a gradient of exposure across tertiles and similar magnitudes of magnetic field intensity or temporal stability were observed among subjects in each group of substation/3-phase and l-phase activity. Clearly, further investigation of magnetic field exposures in substations and in the vicinity of 3-phase and l-phase conductors is needed. The intensity, temporal stability, and degree of magnetic field polarization in each environment should be quantitatively assessed along with other potentially relevant magnetic field parameters, such as high frequency transients and harmonic content.

Temporally stable magnetic field exposures that occurred in substation/3-phase environments were more strongly associated with decreased mean 6-OHMS excretion than magnetic field intensity, as measured by the geometric mean. These findings are consistent with previous studies in electric utility workers that indicated decreased 6-OHMS excretion in response to temporally stable magnetic field exposures.17-18 The importance of temporally stable magnetic field exposures in eliciting biological effects was originally described by Litovitz and coworkers.33 The basis for the biological activity of temporally stable exposures remains unexplained but may provide a clue as to the fundamental mechanism of interaction between 60-Hz magnetic fields and melatonin production. Kruglikov and Dertinger34 indicate that a highly correlated exposure is required for stochastic resonance at a cellular level. However, further work is required to determine whether such a mechanism might mediate the effects of temporally stable magnetic field exposures on 6-OHMS excretion in humans.

Studies performed in rats by Kato and coworkers indicated that circularly polarized magnetic fields were more effective at inducing melatonin suppression than linearly polarized fields.24-27 They observed decreased circulating melatonin concentrations in rats when using 1.4 μT circularly polarized magnetic fields.24,25,27 The same group reported that chronic exposure to a horizontally polarized magnetic field was effective at a higher intensity of 5 μT but not at 1 μT.26-27 Linearly polarized 50/60-Hz magnetic fields have been effective at reducing circulating melatonin levels in other rodent studies,35-38 although results have been inconsistent.39-42 Sheep penned under a 3-phase transmission line had no noticeable changes in circulating melatonin levels after 6 to 10 months of exposure.42a Field polarization at ground level under the power lines was not reported, although a large axial ratio (ie, close to linear polarization) would have been expected.27-28 Inasmuch as no other laboratory has attempted to evaluate the effects of field polarization on magnetic field induced melatonin suppression in experimental animals, the role of this parameter remains undefined.

Human laboratory-based studies, performed using either circularly43-44 or linearly polarized45 magnetic fields, have generally yielded negative results. However, it is difficult to draw conclusions regarding the effectiveness of circular polarization from these studies owing to questions concerning the timing of exposure. Magnetic field induced delays in human melatonin secretion were observed by using circularly polarized fields when 20-μT exposures of 1.5 to 4.0 hours duration commenced before the nocturnal melatonin onset.46 Similarly, decreased nocturnal 6-OHMS excretion in utility workers occurred in response to magnetic field exposures occurring at home, or for work and home exposures combined, but not during sleep. 17 Repeated short-term exposure (20 minutes per day for 3 weeks) to a high-intensity, 2900~μT magnetic field delivered before the nocturnal melatonin onset (1000 or 1800 hours) was also associated with reduced nocturnal melatonin production in humans.47

Kato and Shigemitsu27 presented theoretical calculations to explain why circularly or elliptically polarized fields would be more effective at suppressing melatonin than linearly polarized fields. These authors indicate that magnetic fields with circular or elliptical polarization are expected to more effectively induce electrical currents in the rat pineal gland. Recent estimates suggest that occupationally relevant electric field exposures (10 kV/m) in humans may result in average induced current densities of 1451 μA/m*in the pineal gland compared with average current densities of 6 μA/m* attained owing to endogenous electrical activity.48 However, differences due to field polarization were not addressed.

The characterization of human biological responses to 60-Hz magnetic fields is critical for determining whether concern over potential health effects is warranted. Melatonin suppression is a plausible link to increased cancer risks that have been associated with such exposures. Results from the present analysis suggest that magnetic field induced melatonin suppression seems to be enhanced by work in substations and with energized 3-phase conductors. Failure to characterize magnetic field polarization or other potentially important modifying factors18.49 may partially explain the inconsistent findings reported to date. Recently developed personal exposure devices are now available to evaluate the role of field polarization and other biologically based exposure parameters on human 6-OHMS excretion.50 Reduced melatonin secretion may serve as an important model for understanding human biological responses to magnetic field exposures.

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References

1. Panzer A, Viljoen M. The validity of melatonin as an oncostatic agent. J *Pineal Res.* 1997;22: 184-202.
2. Blask DE. Melatonin in oncology. In: Yu H, Reiter RJ, eds. Melatonin Biosynfhesis, *Physiological Effects, and Clinical Applications.* Boca Raton: CRC Press; 1993:447-475.
3. Fraschini F, Demartini G, Esposti D, Scaglione F. Melatonin involvement in immunity and cancer. *Biol Signals Recept.* 1998;7:61-72.
4. Conti A, Maestroni GJM. The clinical neuro-immunotherapeutic role of melatonin in oncology. *J Pineal Res.* 1995;19: 103-1 10.
3. Reiter RJ, Melchiorri D, Sewerynek E, et al. A review of the evidence supporting melatonin's role as an antioxidant. J *Pineal Res.* 1995;18:1-11.
6. Reiter RJ. Oxidative damage in the central nervous system: protection by melatonin. *Prog Neurobiol.* 1998;56:359-38.
7. Savitz DA. Overview of epidemiological research on electric and magnetic fields and cancer. *Am Ind Hyg Assoc J. 1993;* 54: 197-204.
8. Kheiffets LI, Abdelmonem AA, Buffler PA, Zhang ZW. Occupational electric and magnetic field exposure and brain cancer: a meta-analysis. *J Occ Environ Med.* 1995;37:1327-1341.
9 Brezinski A. Melatonin in humans. New *Engl J Med.* 1997;336:186-195.
10. Reiter RJ. Alterations of the circadian melatonin rhythm by the electromagnetic spectrum: a study in environmental toxi*cology. Reg Toxic01 Pharmacol. 1992;* 151226-244.
11. Waldhauser F, Weizenbacher G, Tatzer E, et al. Alterations in nocturnal serum melatonin levels in humans with growth and aging. *J Clin Endocr Metab. 1988;* 66:648-652.
12. Touitou Y, Fevre M, Lagoguey M, et al. Age- and mental health-related circadian rhythms of plasma levels of melatonin, prolactin, luteinizing hormone and follicle-stimulating hormone in man. J *Endoer.* 1981;91:467-475.
13. Bojkowski CJ, Arendt JA, Shih MC, Markey SP. Melatonin secretion in humans assessed by measuring its metabolite, 6-sulfatoxymelatonin. *Clin Chem.* 1987;33: 1343-1348.
14. Bartsch C, Bartsch H, Schmidt A, Ilg S, Bichler KH, Fluechter SH. Melatonin and 6-sulfatoxymelatonin circadian rhythms in serum and urine of primary prostate cancer patients: evidence for reduced pineal activity and relevance of urinary determinations. *Clin Chim Acta.* 1992; 209: 153-167.
15. Reiter RJ. Melatonin in the context of the reported bioeffects of environmental electromagnetic fields. *Bioelectrochem Bioenergetics.* 1998;47:135-142.
16. Brainard GC, Kavet R, Kheifets LI. The relationship between electromagnetic field and light exposures to melatonin and breast cancer risk: a review of the relevant literature. *J Pineal Res. 1999;26:* 65-100.
17. Burch JB, Reif JS, Yost MG, Keefe TJ, Pitrat CA. Nocturnal excretion of a urinary melatonin metabolite in electric utility workers. *Scand J* Work *Environ Health.* 1998;24:183-189.
18. Burch JB, Reif JS, Yost MG, Keefe TJ, Pitrat CA. Reduced excretion of a melatonin metabolite in workers exposed to 60 Hz magnetic fields. *Am J Epidemiol.* 1999; 150:27-36.
19. Kaune W, Davis *S,* Stevens R *Relafion Between Residential Magnetic Fields, Light-at-Night, and Nocturnal Urine Melatonin Levels in Women.* Palo Alto, CA: Electric Power Research Institute; 1997. TR- 107242-V 1, EPRI Report.
20. Pfluger DH, Minder CE. Effects of exposure to 16.7 Hz magnetic fields on urinary 6-hydroxymelatonin sulfate excretion of Swiss railway workers. *J Pineal Res.* 1996:21:91-100.
21. Wilson BW, Wright CW, Morris JE, et al. Evidence for an effect of ELF electromagnetic fields on human pineal gland function. *J Pineal Res.* 1990;9:259-269.
22. Ametz BB, Berg M. Melatonin and adrenocorticotropic hormone levels in video display unit workers during work and leisure. J *Occup Med.* 1996;38:

23. National Institute of Environmental Health Sciences. *Assessment of Health Effects from Exposure to Power-Line Frequency Electric and Magnetic Fields.* Portier CJ, Wolfe MS, eds. Research Triangle Park, NC: US Dept. Health and Human Services; 19983 11-3 13. Pub *No.* 98 -398 1.
24. Kato M, Honma K, Shigemitsu T, Shiga Y. Effects of circularly polarized 50-Hz magnetic field on plasma and pineal melatonin levels in rats. *Bioelectromagnetits.* 1993;14:97-106.
25. Kato M, Honma K, Shigemitsu T, Shiga Y. Circularly polarized 50-Hz magnetic field exposure reduces pineal gland and blood melatonin concentrations in Long-Evans rats. *Neurosci Lett.* 1994;166:59-62.
26. Kato M, Honma K, Shigemitsu T, Shiga Y. Horizontal or vertical 50-Hz I-μT magnetic fields have no effect on pineal gland or plasma melatonin concentration of albino rats. *Neurosci Lett.* 1994;168: 205-208.
27. Kato M, Shigemitsu T. Effects of 50-Hz magnetic fields on pineal function in the rat. In: Stevens RG, Wilson BW, Anderson LE, eds. *The Melatonin Hypothesis.* Columbus, OH: Batelle Press; 1997:337-316.
28. Deno DW. Transmission line fields. *IEEE Trans Power Appar Sys.* 1976;95: 1600-1611.
29. Dietrich FM, Feero WE, Robertson DC, Sicree RM. *Measurement of Power System Magnetic Fields by Waveform Capture.* Palo Alto, CA: Electric Power Research Institute; 1992. TR-100061 EPRI Report.
30. Arendt J, Bojkowski C, Franey C, Wright J, Marks V. Immunoassay of 6-hydroxymelatonin sulfate in human plasma and urine: abolition of the urinary 24-hour rhythm with atenolol. *J Clin Endocr Metab.* 1985;60:1166-1173.
31 Aldous ME, Arendt J. Radioimmunoassay for 6-sulphatoxymelatonin in urine using an iodinated tracer. *Ann Clin Biothem. 1988;25:298-303.*
32. Yost MG. Alternative magnetic field exposure metrics: occupational measurements in trolley workers. *Radiation Protection and Dosimetty.* 1999;83:99-106.
33. Litovitz TA, Penafiel M, Krause D, Zhang D, Mullins JM. The role of temporal sensing in bioelectromagnetic effects. *Bioelectromagnetics.* 1997;18: 388-395.
34. Kruglikov IL, Dertinger H. Stochastic resonance as a possible mechanism of amplification of weak electric signals in living *cells. Bioelectromagnetics.* 1994; 15:539-547.
35. Selmaoui B, Touitou Y. Sinusoidal 50 Hz magnetic fields depress rat pineal NAT activity and serum melatonin. Role of duration and intensity of exposure. *Life Sci.* 1995;57:1351-1358.
36. Loescher W, Wahnschaffe U, Mevissen M, Lerchl A, Stamm A. Effects of weak alternating magnetic fields on nocturnal melatonin production and mammary carcinogenesis in rats. Oncology. 1994;51: 288-295.
37. Mevissen M, Lerchl A, Loescher W. Study of pineal function and DMBA-induced breast cancer formation in rats during exposure to a lOO-mG, 50 Hz magnetic field. *J Toxico1 Environ Health.* 1996;48:169-185.
38. Yellon SM. Acute 60 Hz magnetic field exposure effects on the melatonin rhythm in the pineal and circulation of the adult Djungarian hamster. *J Pineal Res. 1994;* 16:136-144.
39. Loescher W, Mevissen M, Lerchl A. Exposure of female rats to a 100-μT 50 Hz magnetic field does not induce consistent changes in nocturnal levels of melatonin. *Radiat Res.* 1998;150:557-567.
40. John TM, Liu GY, Brown GM. 60 Hz magnetic field exposure and urinary 6-sulfatoxymelatonin levels in the rat. *Bioelectromognetics.* 1998;19: 172-l 80.
41. Heikkinen P, Kumlin T, Laitinen JT, Komulainen H, Juutilainen J. Chronic exposure to 50-Hz magnetic fields or 900-MHz electromagnetic fields does not alter nocturnal 6-hydroxymelatonin sulfate secretion in CBA/S mice. Elec*tro- and Magnetobiology.* 1999;18:33-42.
42 Truong H, **Yellon** SM. Effect of various acute 60 Hz magnetic field exposures on the nocturnal melatonin rise in the adult Djungarian hamster. *J Pineal Res. 1997;* 22: 177-183.
42a. Lee JM, Stormshak F, Thompson JM, Hess DL, Foster DL. Melatonm and puberty in female lambs exposed to EMF: a replicate study. *Bioelectromagnetics* 1995;16:119-23.
43. Graham C, Cook MR. Riffle DW, Gerkovich MM, Cohen HD. Nocturnal melatonin levels in human volunteers exposed to intermittent 60 Hz magnetic fields. *Bioelectromagnetics.* 1996; 17:263-273.
44. Graham C, Cook MR, Riffle DW. Human melatonin during continuous magnetic field exposure. *Bioelectromagnetics.* 1996;18:166-171.
45. Selmaoui B, Lambrozo J, Touitou Y. Magnetic fields and pineal function in humans: evaluation of nocturnal exposure to extremely low frequency magnetic fields on serum melatonin and unnary 6-sulfatoxymelatonin circadian rhythms. *Life Sci. 1996;58:* 1539-1549.
46 Wood AW, Armstrong SM, Sait ML, Devine L, Martin MJ. Changes in human plasma melatonin profiles in response to 50 Hz magnetic field exposure. J *Pineal Res.* 1998;25:116-127.
47. Karasek M, Woldanska-Okonska M, Czemicki J, Zylinska K, Swietoslawski J. Chronic exposure to 2.9 mT, 40 Hz magnetic field reduces melatonin concentrations in humans. *J Pineal Res.* 1998; 251240-244.
48. Furse CM, Gandhi OP. Calculation of electric fields and currents induced in a millimeter-resolution human model at 60 Hz using the FDTD method. *Bioelectromagnetics.* 1998; 19:293-299.
49. Burch JB, Reif JS, Yost MG. Geomagnetic disturbances are associated with reduced nocturnal excretion of a melatonin metabolite in humans. *Neurosci Lett.* 1999;266:209-212.
50. Bowman JD, Methner MM. *Hazard Surveillance for Workplace Magnetic Fields: Field Characteristics from Waveform Measurements.* Cinncinati, OH: National Institute of Occupational Safety and Health; 1998. Report to the U S Dept. of Energy for Interagency Agreement No. DE-AIOl-94CE34008.

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Circularly polarized 50-Hz magnetic field exposure reduces pineal gland and blood melatonin concentrations of Long-Evans rats

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In order to determine if pigmented rats also exhibit melatonin suppression like that described for albino rats exposed to circularly polarized, 50-Hz, 1-μT magnetic fields for 6 weeks, two experiments were conducted with male Long-Evans rats. The field-exposed experimental group received circularly polarized, 50-Hz, 1-μT magnetic fields for 6 weeks, the concurrent sham-exposed control group was exposed to the stray field of 0.02 μT. In addition, prior to the exposure experiment, two cage-control groups were placed in the facility for 6 weeks without activation of the 50-Hz magnetic field generation apparatus, Rats were sacrificed at 12.00 and at 24.00 h for collection of plasma and pineal gland: melatonin was determined by radioimmunoassay. Significant reductions of plasma and pineal gland melatonin contents were observed at 0.02 μT as compared to the control values, and a further reduction was observed at 1 μT. As do albino rats, pigmented rats also exhibit melatonin suppression when exposed to time-varying magnetic fields.

There are two 'hypotheses' concerning the mechanisms of 'magnetosensitivity'. One assumes a direct effect of magnetic field upon the pineal gland because of the electric (eddy) current induced inside the body [3]. The other hypothesis stresses the importance of the retina in the perception of the geomagnetic field [5,6,11]. Olcese et al. [8] reported that acute transection of the optic nerves in rats abolished the inhibition of pineal melatonin synthesis produced by magnetic stimulation, and Reuss and Olcese [10] reported that pineal responses to a magnetic -field stimulus was absent in intact rats housed in total darkness. From these results, the authors hypothesized that retinal photoreceptors might also be capable of responding to a magnetic field,

Because ocular pigmentation diminishes the proportion of incident light reaching retinal photoreceptive cells, Olcese and Reuss [7] compared the inhibition of pineal melatonin synthesis of albino Sprague-Dawley and pigmented Long-Evans rats following a single, 30-min rotation of the earth's horizontal magnetic field component by 50°. Finding similar sensitivity to magnetic field disruption of melatonin synthesis in the two strains, they concluded . . . 'rats regardless of their pigmentation are still capable to responding to an artificial magnetic field suggests that pigmentation - or lack thereof - may not be a significant factor in the mediation of magnetic field information to other components of the magnetosensitivity system, e.g. the pineal organs', However, in his later paper, Olcese [5] described that 'it would seem that pigmentation is in fact an important factor determining pineal sensitivity to magnetic field' after they demonstrated that magnetic field stimulation did not depress melatonin in ACI rats, a fully pigmented strain.

Olcese and his colleague's investigation was focused on pineal responses to acute manipulation of the ambient magnetic field inversion by 5° to 70° of the horizontal component of the earth strength, quasi-static geomagnetic field for periods of 15 to 30 min. Kato et al. [2] reported that circularly polarized, 50-Hz sinusoidal magnetic field exposure for 6 weeks significantly suppressed melatonin concentration in albino Wistar-King rats. In the present experiments, we investigated whether such a time-varying magnetic field exposure for 6 weeks has similar effects on pigmented Long-Evans rats,

The experimental subjects were male Long-Evans (hooded) rats. At the beginning of the exposure, they were 11-18 weeks of age and had an average body weight of 330 g. Body weight was measured and the subjects were examined at intervals of 10-15 days during the ex-

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periment: all subjects showed reasonable gains in body weight, and none displayed any pathological signs.

The magnetic and sham-exposure facility are described by Shigemitsu et al. [12]. Briefly, sets of rectangular coils in horizontal and vertical planes enclose a volume of approximately 1 m^3 of isofield in which the subjects are housed. This apparatus is located in the northwest corner of the animal room. A similar apparatus, but without field-generation circuitry, is located in the southeastern corner of the same room to house the sham-exposed control group. Because the two sets of animals are located 4.5 m apart, the control group receives 'stray' magnetic field exposure from the exposure coils exposing the experimental group. When the exposure coils were energized to produce 1 μT, the stray 50-Hz magnetic field in the sham-exposure volume was less than 0.02 μT. When the magnetic field coils were not energized, the 50-Hz magnetic field intensity in the room was 0.014 μT [12]. The experimental group was exposed to a circularly polarized, 5 0 - Hz. 1-μT magnetic field for 6 weeks continuously, except for twice a week break on Monday and Thursday for cleaning the cages and feeding and for evaluation of the subject's health, The exposure period was from December 4, 1991 through January 15, 1992. Forty-eight rats were housed in the exposure facility, and another 48 rats were housed in the sham-exposure facility. In addition, a control experiment was conducted from September 30 through November 9, 1991. Thirty rats were housed in each of the two facilities without turning on the power supply; the other conditions'were the same as the exposure experiments. The temperature of the room was maintained at 21 ± 2°C. Relative humidity varied from 40 to 60%. The rats were housed in standard cages, 2 rats per cage, under a 12-12 h light-dark photoperiod (light on 06.00 h). The room was constantly illuminated with 4 small, dim red lights (< 0.07 lux measured in the dark period). The rats were provided with food and water ad libitum.

Plasma and pineal gland melatonin were assayed by radioimmunoassay (RIA) as described earlier [2]. Rats were euthanized by decapitation at 12.00 h or at 24.00 h, and trunk blood and the pineal gland were collected immediately. All the procedures following thereafter are the same as described in a previous paper [2]. The Student's t-test was used for comparison between two mean values after discarding of extreme values, if any, by the Smir-

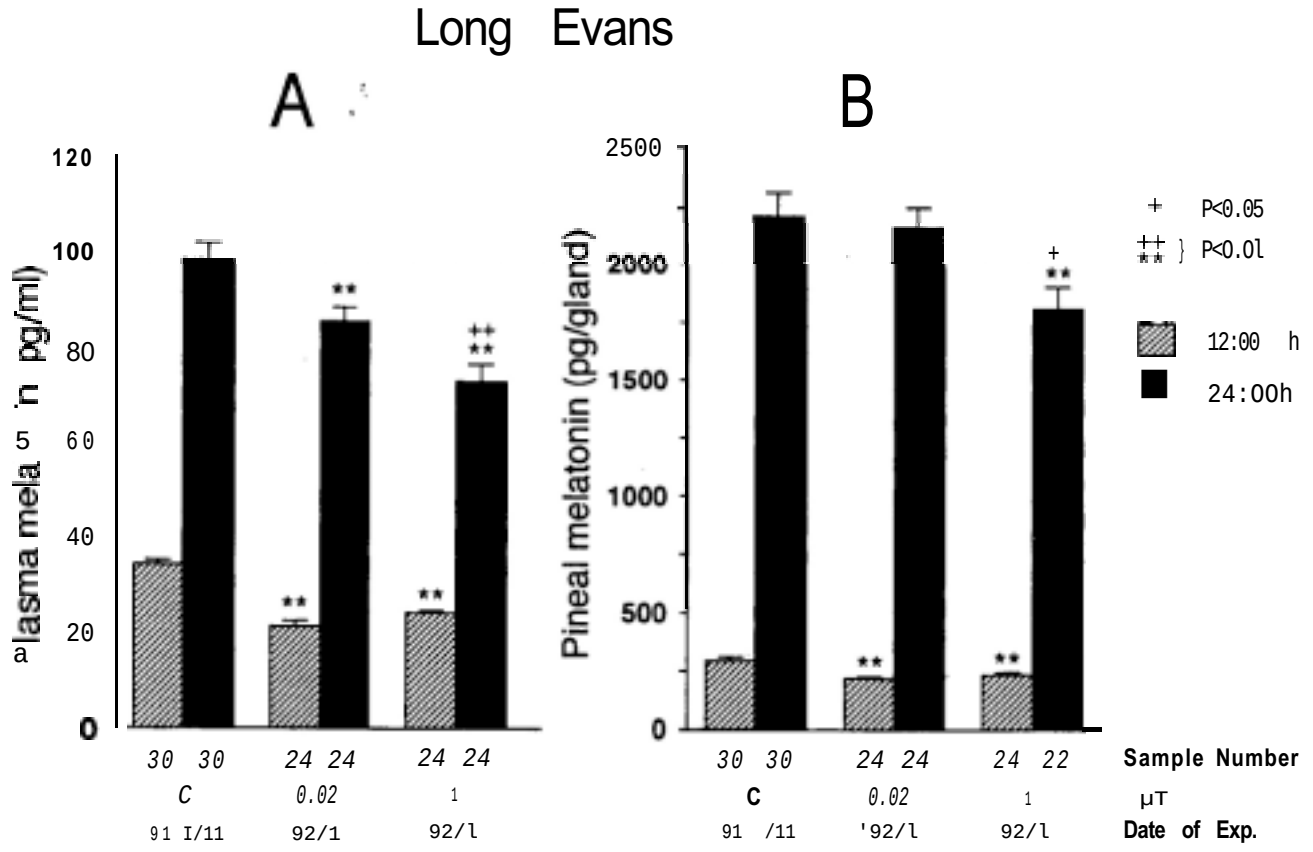

Fig. 1. Concentration of melatonin in plasma (A) and in pineal gland (B) at 12.00 and 24.00 h at different strength of the magnetic fields across time. Sample numbers of the rats, magnetic flux density in microteslas and date of experimentation are indicated at the bottom of the figure. C: control, 0.02-μT sham-exposure rats, and 1 μT is the exposed group. **, indicates the statistical difference between control values and the exposed or sham-exposed groups at the level of $P < 0.01$. + and ++ show the statistical difference between the sham-exposed and exposed groups at the levels of $P < 0.05$ and $P < 0.01$, respectively.

noff test. A value of $P < 0.05$ was considered to be significant.

Plasma melatonin contents in the control group were 34.4 ± 1.0 pg/ml (mean ± standard error) at 12.00 h and 98.3 ± 3.3 pg/ml at 24.00 h, respectively. In the exposure group (1 μT), the values were significantly ($P < 0.01$) depressed to 24.0 ± 0.8 pg/ml at 12.00 h and to 72.7 ± 3.5 pg/rnl at 24.00 h. The 0.02-μT sham-exposure group also showed significant ($P < 0.01$) decrease of melatonin concentration at 12.00 h (21.4 ± 1.1 pg/ml) as well as at 24.00 h (85.3 ± 3.0 pg/ml), respectively. The values of 1-μT exposure and 0.02-μT sham-exposure groups showed no significant difference at 12.00 h. At 24.00 h, however, the melatonin concentration was further suppressed significantly ($P < 0.01$) from 0.02-μT sham-exposure rats to 1-μT exposed group. These results are illustrated in Fig. 1A.

Melatonin concentration in the pineal gland of the control group was 291.7 ± 17.2 pg/gland at 12.00 h and 2212.9 ± 99.0 pg/gland at 24.00 h, respectively. There is a significant ($P < 0.01$) decrease of the content in the 0.02-μT sham-exposed group at 12.00 h (215.0 ± 8.8 pg/gland), although there is no significant decrease at 24.00 h (2152.1 ± 94.0 pg/gland). There is a significant ($P < 0.01$) decrease of melatonin content in the 1-μT exposed group both at 12.00 h (232.2 ± 12.6 pg/gland) and at 24.00 h (1806.5 ± 96.2 pg/gland) as compared with the control group. At 24.00 h, the value of 1-μT exposed rats was significantly ($P < 0.05$) lower than that of 0.02-μT sham-exposed rats. These results are illustrated in Fig. 1B.

These results clearly show that 50-Hz, circularly polarized magnetic fields reduce blood and pineal gland melatonin concentrations in pigmented rats, as they also do in albino rats. Furthermore, these results also indicate that the 'threshold' magnetic field strength required for melatonin reduction is lower in pigmented rats. Kato et al. [2] demonstrated that for albino (Wistar-King) rats, the threshold was something less than 1 μT: they also determined that 0.1-μT fields did not affect melatonin in albino rats. However, in this experiment with pigmented (Long-Evans) rats, a field of 0.02 μT was capable of producing suppression of both pineal gland and blood melatonin concentrations. These results suggest that even strain difference should be considered when biological effects of magnetic field exposure are assessed.

The observation of reductions in day-time melatonin concentrations of pineal gland and blood is noteworthy. This effect was reported for the first time by Kato et al. [2], and these experiments confirm it. Most investigators have examined the effects of magnetic fields on melatonin at night, when the gland is actively synthesizing and releasing melatonin. Thus little consideration has been given to relationships between day and/or night exposure to magnetic fields and mechanisms regulating melatonin.

The 0.02-μT magnetic field did suppress the plasma melatonin level at 24.00 h significantly, but did not the pineal melatonin at the same time of day. We do not know the reason for this discrepancy, but there are reports in which a similar discrepancy is described between the pineal and serum melatonin [1,13,14].

Olcese and Reuss [7] showed that 30-min magnetic field exposure similarly inhibited the N-acetyltransferase (NAT) activity and the melatonin content of the pineal gland in both albino Sprague-Dawley and pigmented Long-Evans (black-hooded) rats strains, Because they apparently did not study the effects of different magnetic field parameters, it is hard to say which one is more sensitive to magnetic field stimulation.

Lynch, Deng and Wurtman [4] compared thresholds of light intensity required to suppress melatonin contents of pineal gland as well as plasma for Sprague-Dawley and Long-Evans strains, anticipating that 'the albino's inability to attenuate light impinging on its retinae would increase its sensitivity to the photic suppression of pineal melatonin content and of circulating melatonin levels'. They found, however, that the pigmented Long-Evans strain is more sensitive to light; threshold intensities were 0.022 ,μw/cm* in the Long-Evans vs 0.110 $\mu w/cm^2$ in the Sprague-Dawley strain.

Taking into account our own results of the present (Long-Evans) and previous (Wistar-King) magnetic field exposure experiments, and those of Lynch, Deng and Wurtman on light stimulation, it would be reasonable to say that some common or similar mechanisms exist between photosensitivity and magnetosensitivity, and the inhibition of melatonin synthesis exists in both albino and pigmented rat strains. On this point, Phillips and Borland [9] suggest that, based on behavioral experiments conducted with newts showing that magnetic compass orientation is affected by the wavelength of light, photoreceptors are responsible for picking up magnetic field information. However, it also is possible that pigmented and non-pigmented rat strains differ in other important respects besides pigmentation which complicate elucidation of photo-receptor and magneto-receptor inter-relationships.

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1 Brown, G.M., Chik, C.L., Ho, A.K., Kennedy, S. and Garfinkel, P., Effects of food restriction on pineal function. In R.J. Reiter and S.F. Pang (Eds.), Advance in Pineal Research, Vol. 3, John Lobbey, London, 1989, pp. 87-92.

2 Kato, M., Honma, K., Shigemitsu, T. and Shiga, Y., Effects of exposure to a circularly polarized 50-Hz magnetic field on plasma and pineal melatonin levels in rats, Bioelectromagnetics, 14 (1993) 97-106.

3 Lerchl, A., Nonaka, K.O. and Reiter, R.J., Pineal gland 'magnetosensitivity' to static magnetic fields is a consequence of induced electric currents (eddy currents), J. Pineal Res., 10 (1991) 109-116.

4 Lynch, H.L., Deng, W.H. and Wurtman, R.J., Light intensities required to suppress nocturnal melatonin secretion in albino and pigmented rats, Life Sci., 35 (1984) 841-847.

5 Olcese, J.M., The neurobiology of magnetic field detection in rodents, Prog. Neurobiol., 35 (1990) 325-330.

6 Olcese, J. and Hurlbut, E., Comparative studies on the retinal dopamine response to altered magnetic fields in rodents, Brain Res., 498 (1989) 145-148.

7 Olcese, J. and Reuss, S., Magnetic field effects on pineal gland melatonin synthesis: comparative studies on albino and pigmented rodents, Brain Res., 369 (1986) 365-368.

8 Olcese, J., Reuss, S. and Vollrath, L., Evidence for the involvement of the visual system in mediating magnetic field effects on pineal function in the rat, Brain Res., 333 (1985) 382-384.

9 Phillips, J.B. and Borland, S.C., Behavioural evidence for use of a light-dependent magnetoreception mechanism by a vertebrate, Nature, 359 (1992) 142-144.

10 Reuss, S. and Olcese, J., Magnetic field effects on the rat pineal gland: role of retina1 activation by light, Neurosci. Lett., 64 (1986) 97-101.

11 Schneider, T. and Semm, P., The biological and possible clinical significance of magnetic influences on the pineal m elatonin synthesis, Exp. Clin. Endocrinol., 11 (1992) 251-258.

12 Shigemitsu, T., Takeshita, K., Shiga, Y. and Kato, M., A 50 Hz magnetic field exposure system for small animals, Bioelectromagnetics, 14 (1993) 107-116.

13 Wilkinson, M., Arendt, J. Bradtke, J. and Ziegler, D., Determination of a dark-induced increase of pineal N-acetyl-transferase activity and simultaneous radioimmunoassay of melatonin in pineal, serum and pituitary tissue of the male rat, J. Endocrinol., 72 (1977) 243-244.

14 Yellon, SM. and Gottfried, L., An acute 60 Hz magnetic field exposure suppresses the nighttime melatonin rhythm in the adult Djungarian hamster in short days, Proc. 1992 Annual Rev. Bioeffects Res., U.S. Department Energy and EPRI, A-22.