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ENDOCRINE FUNCTIONS IN YOUNG MEN EXPOSED FOR ONE NIGHT TO A 50-HZ MAGNETIC FIELD. A CIRCADIAN STUDY OF PITUITARY, THYROID AND ADRENOCORTICAL HORMONES

Brahim Selmaoui*, Jacques Lambrozo and Yvan Touitou***

*Faculté de Médecine Pitié-Salpêtrière, Service de Biochimie Médicale,
91 boulevard de l'Hôpital 75634 Paris Cedex 13, France
**EDF-Service des Etudes Médicales,
22-30 Avenue de Wagram 75382 Paris Cedex 08, France

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Summary

In recent years, some epidemiologic studies have suggested that extremely low frequency magnetic and electric fields might affect human health, and, in particular, that the incidence of certain types of cancer, depression, and miscarriage might increase among individuals living or working in environments exposed to such fields. Work in our laboratory studies whether and how changes in the electromagnetic environment might affect human health. The study presented here was designed to look for possible effects of acute exposure to 50-Hz linearly polarized magnetic fields (10 μT) on the hormones of the hypothalamic-pituitary-thyroid and hypothalamic-pituitary-adrenal axes. Thirty-two young men (20-30 years old) were divided into two groups (sham-exposed or control group, and exposed group) of 16 subjects each. All subjects participated in two 24-hour experiments to evaluate the effects of both continuous and intermittent (one hour "off" and one hour "on" with the field switched "on" and "off" every 15 seconds) exposure to linearly polarized magnetic fields. The subjects were exposed to the magnetic field (generated by three Helmholtz coils per bed) from 2300 to 0800 while recumbent. Blood samples were collected during each session at 3 hour intervals from 1100 to 2000 and hourly from 2200 to 0800. Total urine was collected every 3 hours from 0800 to 2300 and then again at 0800. No significant differences were observed between sham-exposed and exposed men for any of the parameters measured: thyroid-stimulating hormone, follicle-stimulating hormone, luteinizing hormone, triiodothyronine, thyroxine, free triiodothyronine, free thyroxine, thyroxine-binding globulin, cortisol, 17-hydroxycorticosteroids (17-OH-CS) and TBK. These results suggest that acute exposure to either continuous or intermittent 50-Hz linearly polarized magnetic fields of 10 μT does not affect, at least under our experimental conditions, these endocrine functions or their circadian rhythmicity in healthy young men.

Key Words: **50-Hz magnetic field, hypothalamic-pituitary-thyroid axis, hypothalamic-pituitary-adrenal axis, circadian rhythm**

Corresponding author: Pr Y. Touitou, Faculté de Médecine Pitié-Salpêtrière, Service de Biochimie, 91 boulevard de l'Hôpital 75634 Paris Cedex 13, France. Fax (33) 1 40 77 96 65, phone (33) 1 40 77 96 63

Biological effects of electromagnetic fields and their consequences on human health are receiving increasing scientific interest and have become the subject of great public debate. The controversy has been stimulated by some epidemiologic studies that have reported a relation between magnetic field exposure and human diseases.

The first report suggesting such a relationship dates back to mid-1960 (1). Its authors declared that exposed Russian workers suffered from fatigue, headaches, sleep disruption, and related disorders. Other studies have reported a possible association between extremely low frequency (ELF) field exposure and increased risk of such health problems as cancer (2, 3), depression (4, 5), and pregnancy outcome (6). Whether or not ELF field exposure is causally related to increased health risks, these and other studies have focused a great deal of scientific interest and some public concern, on the possibility that ELF electromagnetic fields have biological effects in humans. They have led many scientists to examine the mechanisms by which ELF fields might affect human health.

One study showed changes in the activity of the adrenals and the thyroid after chronic and even a single exposure to pulsed low frequency electromagnetic fields; 2 months after a single exposure to 20 mT, the concentration of thyroid hormones remained below normal (7). Other studies report disturbed melatonin circadian patterns in conjunction with abnormally high levels of cortisol secretion, among some patients with endogenous depression (8, 9). Wetterberg et al. hypothesized from these findings that regulation of melatonin secretion might involve a feedback effect from the adrenal to the pineal gland (8). A relation between the pineal gland and the adrenal gland has been documented in vitro (10); as has a relation between the pineal and other glands of the endocrine axis, e.g., thyroid, pituitary, and gonads (11, 12, 13). Indeed, a single dose of melatonin administered to pinealectomized rats at different times of day markedly affects their nocturnal thyroid activity (14). Similarly, melatonin administered late in the afternoon for 10 days inhibits thyroid growth in mice and rats (15). These and other similar results (16, 17, 18) suggest that the pineal gland may be related to thyroid activities.

Considering this hypothesis in light of findings that exposure to electromagnetic fields appears to attenuate the nocturnal melatonin increase in experimental animals (19, 20, 21, 22), we wondered whether and in what ways electromagnetic field exposure might affect the endocrine and neuroendocrine systems. We therefore examined the effects of electromagnetic fields on the adrenocortical system and the hypothalamo-pituitary-thyroid (HPT) axis.

Materials and Methods

Human subjects

Thirty-two healthy young men, aged 20 to 30 years (mean ± SD, 24.44 ± 3.39 and 24.88 ± 3.12 years for exposed and sham-exposed groups respectively) were selected after routine clinical and laboratory examination. They met the following criteria: they had regular sleep habits, no chronic disease or disability, no recent acute illness, did not work nights, had not traveled to another time zone within the preceding 2 months, and were nonsmokers. They were instructed to eat balanced meals and to abstain from consuming alcohol and coffee and from using electric shavers and hair dryers during each experimental session and for 24 hours before each session. They were synchronized with a diurnal activity from 0800 to 2300 and nocturnal rest. The experiment lasted two months (mid-February to mid-April). The subjects were not informed of their exposure status.

Exposure facility

The experimental unit consisted of three independent rooms and a shared bathroom. The exposed subjects slept in the first room (2 beds), and the sham-exposed, in the second (2 beds). The wooden beds (90 x 200 cm) were arranged in parallel in each room and oriented in the north-south axis of the earth's magnetic field. Before the exposure materials and beds were set up, we evaluated the noise of the background magnetic field, using "Linda Wheel and EMDEX II dosimetry systems." In each of the two rooms in which subjects were to sleep, the level of the background magnetic field was less than 40 nanotesla. In the area immediately surrounding the experimental site, the amplitude of the geomagnetic field was approximately 46 μT. Since a minimum distance of 6 m between exposed and sham-exposed beds is required to avoid any effect of the generated field on the sham-exposed group, we spaced them 7 m apart. The devices for generation, calibration, and continuous monitoring of the magnetic field were located in the third room.

Magnetic field generation

The linearly polarized magnetic field (10μT) was generated by a system based on Helmholtz coils. Three rectangular coils (120 x 140 cm) spaced 80 cm apart were used for each bed. They were wrapped in wood, and their horizontal axes were parallel to that of the bed. The coils were positioned at the level of the head, pelvis, and ankles. The device was able to produce both continuous and intermittent exposure conditions. In the intermittent exposure, the device was turned "on" for one hour and "off" for the next hour. Whenever the device was turned "on", the magnetic field was on a 15 second "on-off" cycle. Moreover, the signal generator was monitored by computer. Since "on-off" switching operations induce high frequency transient electric fields that can have a biological effect, all these operations were carefully monitored and synchronized with passages at zero of the current wave to avoid any transient electric field. The magnetic field was generated by a Tollner generator and amplified by a Kepco amplifier, all under a computer control system developed by Electricité de France engineers. A "Positron" dosimetry system was attached to the subject's body at the height of the pelvis, to control the exposure quality and to verify that the device was working. The 10 μT intensity was chosen as representative of the average exposure in occupational settings.

Experimental procedure

This experiment studied four subjects per day, and each subject participated in two 24-hour sessions. They arrived at the laboratory at 0930. Catheters were placed in an antecubital vein for the 24-hour period, and the first blood sample was obtained at 1100. They slept in darkness between 2300 and 0800 and spent their waking time in the laboratory (diurnal activity from 0800 to 2300 and nocturnal rest). Blood samples (tubes without anticoagulant) were taken from 1100 to 0800 of the following day (3-hour intervals from 1100 to 2000 and hourly from 2200 to 0800). From midnight to 0800, the samples were obtained under dim light (less than 50 Lux) without waking the subjects, who slept with eye-masks from 2300 to 0800. Exposure to the magnetic field lasted from 2300 (2300 sampling not included) until 0800. Total urine was collected every 3 hours from 0800 to 2300 and once over the night (at 0800) (for 17-OH-CS). We studied two groups: the first, sham-exposed, i.e., control (N=16), and the other, exposed (N=16). During the first session, a continuous 50-Hz magnetic field of 10 μT was applied. In the second session, a month after the first, the subjects previously exposed to a continuous magnetic field were exposed to an intermittent 50-Hz magnetic field of 10 μT. This protocol was approved by the local ethics committee.

Hormonal assays

Blood was drawn into tubes without anticoagulant, allowed to clot, and then centrifuged to obtain serum that was stored at -20°C until assay. Urinary fractions were also stored at -20°C. All parameters studied here were determined using a commercially prepared enzyme-linked immunosorbent assay (ELISA) (Boehringer Mannheim, France) in a fully automated analyzer (ES 700). The inter- and intra-assay variations are reported in Table 1.

TABLE 1
Hormone Measurements: Inter- and Intra-Assay Variations.

	Inter-assay variation of Mean concentrations	Intra-assay variation of Mean concentrations
Cortisol	13.9 % for 415 nmol/L	6.92 % for 307 nmol/L
17-OH-CS	3.2 % for 0.78 mg	2.4 % for 0.63 mg
LH	3.7 % for 4.4 IU/L	2.3 % for 3.8 IU/L
FSH	6 % for 6.5 IU/L	1.6 % for 5.5 IU/L
TSH	8.5 % for 1.5 IU/L	6 % for 1.2 IU/L
FT4	4.14 % for 17 pmol/L	4.78 % for 12.68 pmol/L
FT3	7.82 % for 6.8 pmol/L	7.19 % for 7 pmol/L
T3	5.05 % for 1.56 nmol/L	5.04 % for 1.3
T4	8.9 % for 70 nmol/L	6.1 % for 65 nmol/L
TBG	5.9 % for 177 nmol/L	4.8 % for 165 nmol/L
TBK	3.48 % for 1.05 TBi	2.78 % for 1.08 TBi

Statistical analysis

All data are expressed in mean ± SEM of raw values. The statistical analysis, which used analysis of variance (ANOVA) for repeated measures, examined the following three factors for each variable studied: the hour factor, the field effect factor, and the hour x field interaction. The F and p values are shown in the annexed tables (2 and 3). The repeated measures factor corresponds to the temporal variation of the variables studied. Our hypothesis was that exposure to a magnetic field might affect the circadian profile of these variables.

Results

In this study, we examined, in 16 exposed and 16 sham-exposed subjects, the circadian profiles of triiodothyronine (T3), thyroxine (T4), free triiodothyronine (FT3), free thyroxine (FT4), TSH, FSH, LH, cortisol, 17-hydroxycorticosteroids in urine (17-OH-CS), thyroxine binding globulin (TBG), and TBK, which represents thyroxine binding capacity and is expressed as the thyroxine-binding index (TBI). Figures (1-4) show the serum levels of all hormones and urinary 17-OH-CS after exposure and sham-exposure to magnetic fields.

Serum cortisol concentration presented a circadian variation with low values during the night (lowest around midnight) and high values during the day (peak at 0800) (Figure 1). Urinary 17-OH-CS showed a profile that peaked at night, in the urine sampled between 2300 and 0800, and was lowest in the sample taken between 2000 and 2300 (Figure 1). The circadian profiles of T4, FT4, and FT3 (Figures 2 and 3) were identical: their highest levels were found around 1100, with some high measurement also at 1400 and decline of values around 1600.

TABLE 2

Repeated measures ANOVA. Comparison between continuously exposed and sham exposed group. For each variable studied, the statistical analysis examined three factors: the hour factor, the field effect factor and the hour-field interaction.

ANOVA repeated measures

Variables/factor	**F**	**p**
Cortisol		
Field	0.04	0.85
Hour	48.53	0.0001
Field x Hour interaction	1.07	0.38
17-OH-CS		
Field	0.002	0.99
Hour	12.96	0.0001
Field x Hour interaction	0.32	0.89
FT4		
Field	0.27	0.61
Hour	18.97	0.0001
Field x Hour interaction	0.65	0.82
FT3		
Field	0.011	0.91
Hour	8.95	0.001
Field x Hour interaction	1.13	0.33
T4		
Field	0.58	0.45
Hour	5.85	0.0001
Field x Hour interaction	0.38	0.98
T3		
Field	0.42	0.52
Hour	8.22	0.0001
Field x Hour interaction	1.36	0.17
LH		
Field	0.70	0.41
Hour	4.051	0.0001
Field x Hour interaction	1.48	0.12
FSH		
Field	0.97	0.43
Hour	3.97	0.0001
Field x Hour interaction	0.49	0.94
TSH		
Field	0.002	0.96
Hour	14.35	0.0001
Field x Hour interaction	1.33	0.18
TBG		
Field	0.15	0.69
Hour	37.95	0.0001
Field x Hour interaction	0.653	0.82
TBK		
Field	0.19	0.66
Hour	5.44	0.0001
Field x Hour interaction	0.63	0.83

TABLE 3
Repeated measures ANOVA. Comparison between intermittently exposed and sham exposed group. For each variable studied, the statistical analysis examined three factors: the hour factor, the field effect factor and the hour-field interaction.

ANOVA repeated measures

Variables/factor	**F**	**p**
Cortisol		
Field	0.04	0.84
Hour	61.90	0.0001
Field x Hour interaction	1.77	0.041
17-OH-CS		
Field	3.36	0.079
Hour	13.49	0.0001
Field x Hour interaction	1.10	0.36
FT4		
Field	0.02	0.88
Hour	33.62	0.0001
Field x Hour interaction	1.11	0.34
FT3		
Field	0.004	0.95
Hour	5.20	0.0001
Field x Hour interaction	0.71	0.76
T4		
Field	0.42	0.52
Hour	8.22	0.0001
Field x Hour interaction	1.36	0.17
T3		
Field	0.17	0.68
Hour	5.19	0.0001
Field x Hour interaction	1.24	0.24
LH		
Field	0.045	0.83
Hour	7.02	0.0001
Field x Hour interaction	1.13	0.33
FSH		
Field	0.72	0.40
Hour	3.17	0.0001
Field x Hour interaction	1.39	0.15
TSH		
Field	0.44	0.52
Hour	10.21	0.0001
Field x Hour interaction	0.79	0.67
TBG		
Field	0.10	0.75
Hour	33.08	0.0001
Field x Hour interaction	0.80	0.66
TBK		
Field	0.17	0.68
Hour	6.48	0.0001
Field x Hour interaction	0.62	0.84

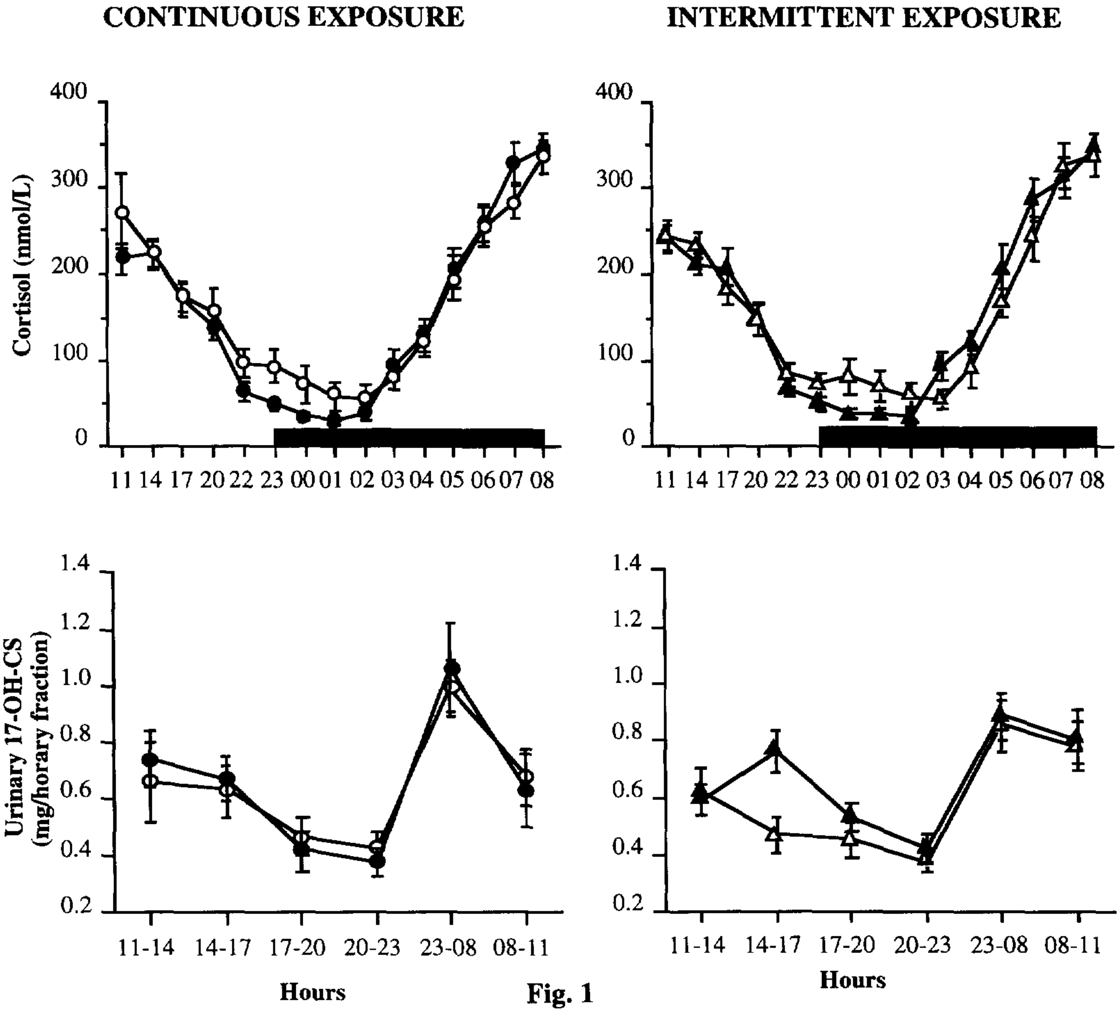

Fig. 1

Circadian profiles of serum Cortisol (top) and urinary 17-OH-CS (bottom) under continuous and intermittent exposure to a 50-Hz magnetic field (10 μT). The dark bar shows the duration of exposure, i.e., time in bed. Each time point is the mean ± SEM of data. Control group: (○, △) ; exposed group: (●, ▲)

The circadian profile of T3 was lowest in the afternoon around 1600 and peaked during the late night and early morning hours (Figure 2).

TBG and TBK levels peaked during the day and reached their low levels during the dark phase (Figure 3). The circadian profile of TSH showed peak values at 2300, that is, bedtime. Its lowest values were found in the afternoon, around 1400 (Figure 4).

In comparing data for the different variables, it is important to note that the amplitudes of each are similar for each 24-hour profile between the control and exposed groups; they are also similar within groups for the experiments spaced a month apart.

The results show no significant differences between the groups. Indeed, comparisons of the control and the exposed groups, using repeated measures ANOVA ($p > 0.05$), disclosed no effect from either the continuous or the intermittent magnetic field.

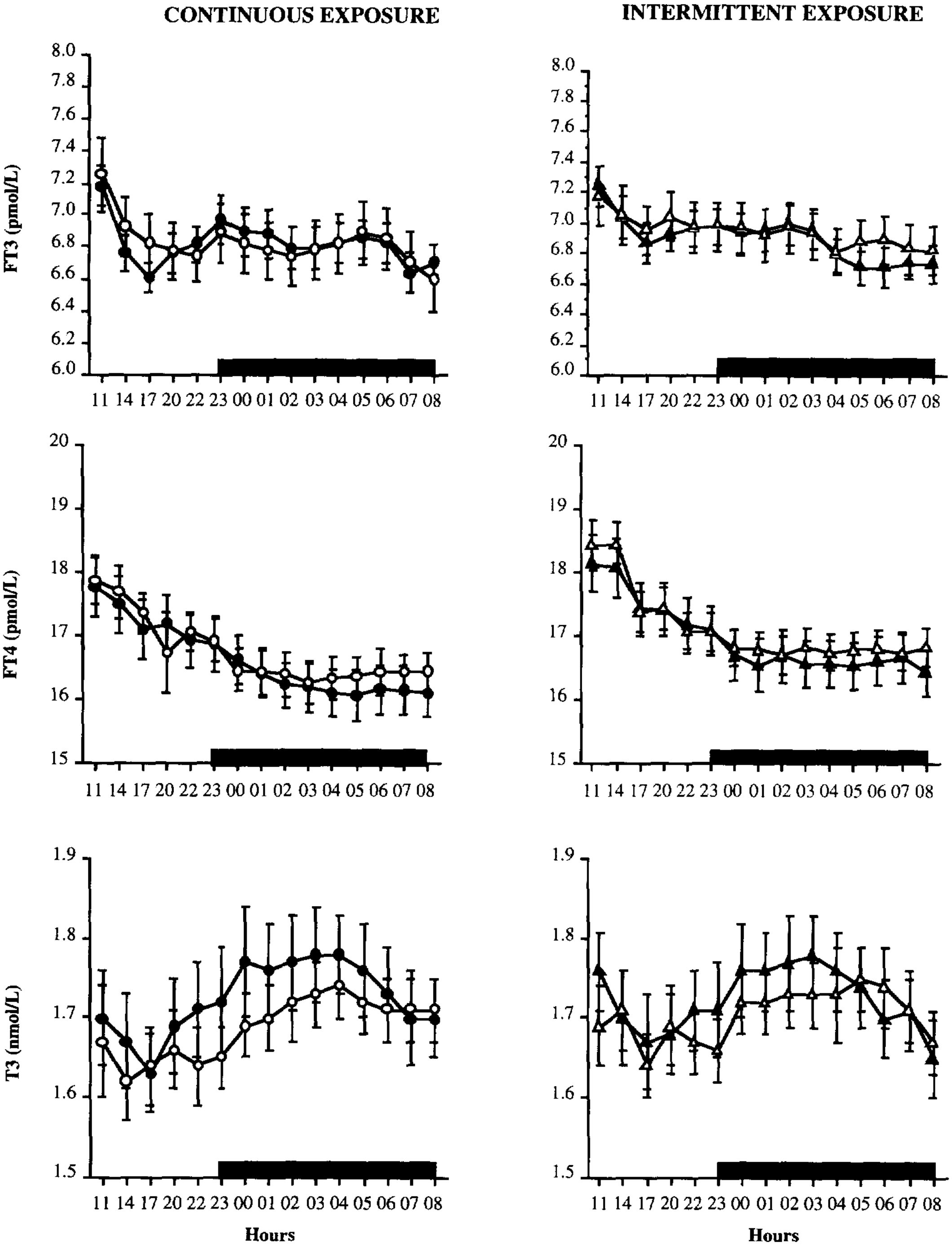

Fig. 2

Circadian profiles of FT3, FT4, and T3 under continuous and intermittent exposure to a 50-Hz magnetic field (10 μT). The dark bar shows the duration of exposure, i.e., time in bed. Each time point is the mean ± SEM of data. Control group: (○, △) ; exposed group: (●, ▲).

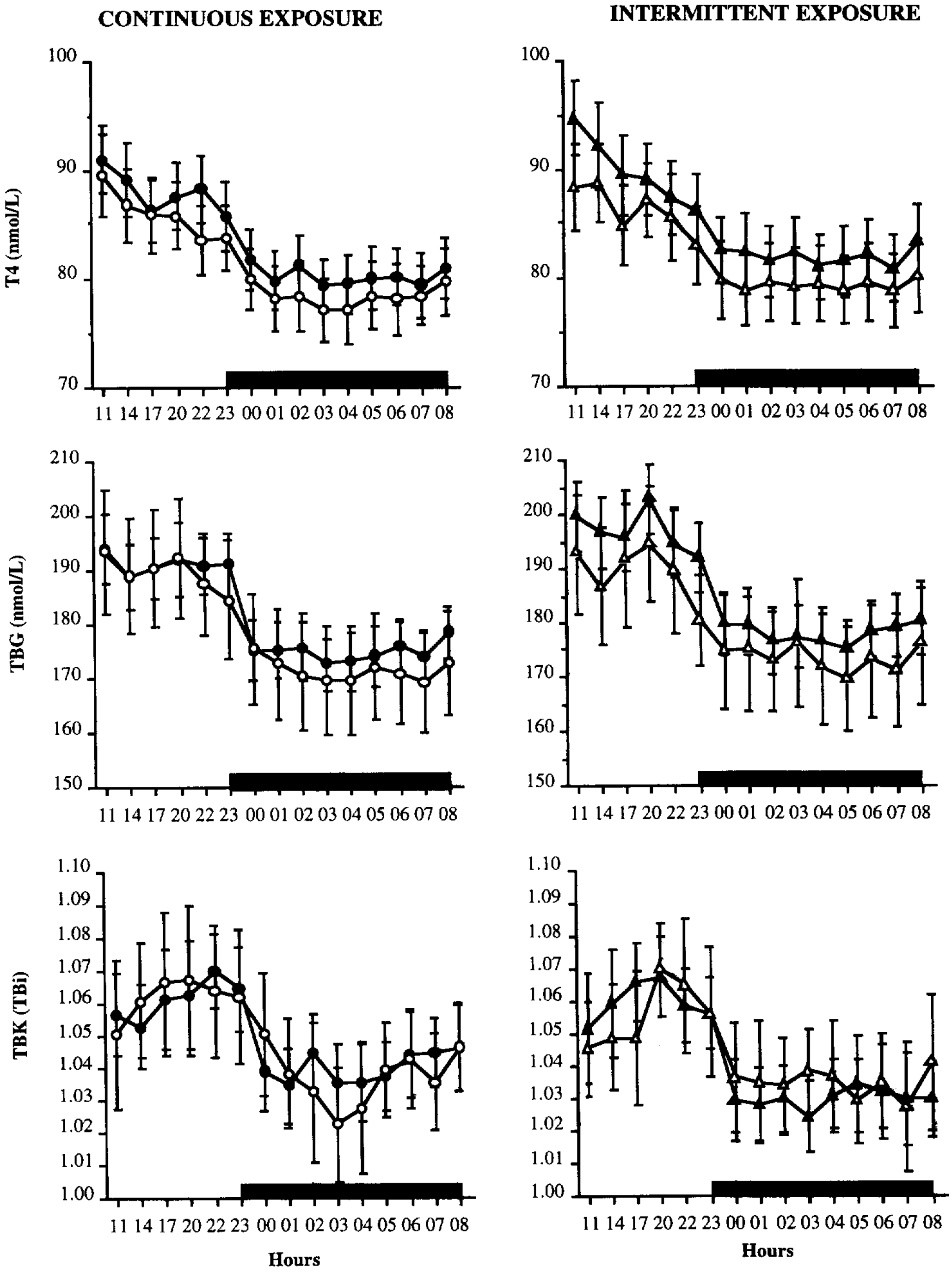

Fig. 3

Circadian profiles of T4, TBG, and TBK under continuous and intermittent exposure to a 50-Hz magnetic field (10 μT). The dark bar shows the duration of exposure, i.e., time in bed. Each time point is the mean ± SEM of data. Control group: (○, △) ; exposed group: (●, ▲).

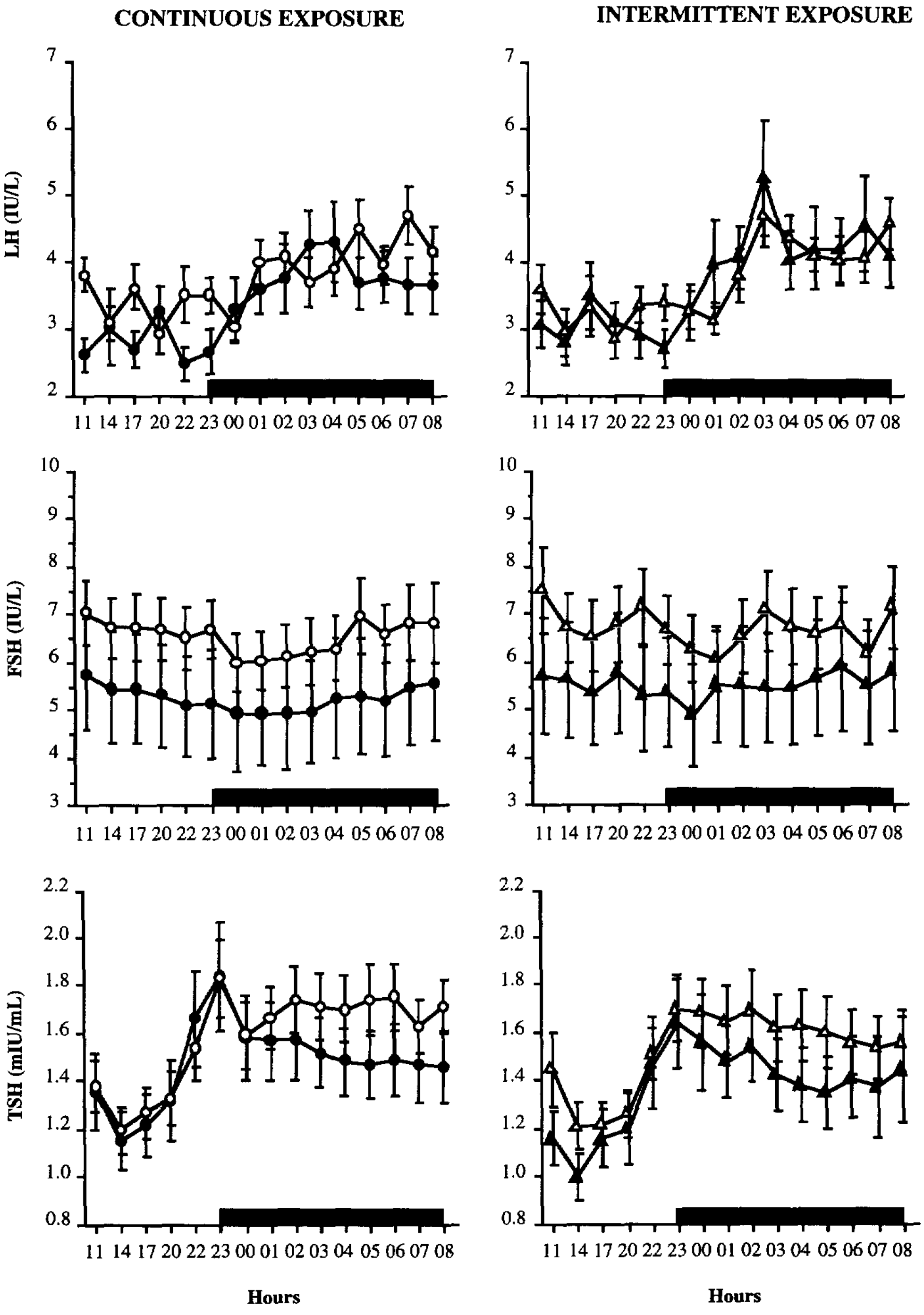

Fig. 4

Circadian profiles of LH, FSH, and TSH under continuous and intermittent exposure to a 50-Hz magnetic field (10 μT). The dark bar shows the duration of exposure, i.e., time in bed. Each time point is the mean ± SEM of data. Control group:(○, △) ; exposed group: (●, ▲).

Discussion

The HPT and HPA axes are part of a complex web of neuroendocrine functions. The hypothalamus regulates the secretion of pituitary hormones. Most of these stimulate peripheral glands, which in turn secrete hormones that act on target cells.

The hypothalamus-pituitary system has been studied in great detail (23, 24). Of the hormones produced by the pituitary gland, those that stimulate most strongly are TSH, FSH, LH and ACTH. The thyroid gland, on the other hand, is regulated by the pituitary hormone TSH in its own hormonal production, thereby illustrating the complexity of the HPT and HPA systems.

These axes have an intricate time structure: rhythmic variations of multiple frequencies are found at all levels of the system from hypothalamic neurons to the cells of the peripheral target tissues. The frequencies observed range from neuronal discharges to ultradian rhythms and pulsatile secretions to circadian and circannual rhythms.

The stability of this endocrine system, which is one of the body's primary physiological regulators, maintains homeostasis in mammals. In fact, perturbation by environmental factors can be manifested by functional changes in this regulatory system.

In our study we were interested in magnetic fields: epidemiologic studies have hypothesized that these fields are an environmental factor that may have a toxic influence on human biological systems. To our knowledge, this study is the first to examine the effect of a magnetic field on the circadian rhythms of the HPT and HPA functions in humans.

Our results indicate that the circadian rhythm of the HPT and HPA functions was not affected by acute exposure (9 hours) to either a continuous or an intermittent 50-Hz magnetic field. Looking at the circadian rhythm of serum cortisol, we observe a remarkable resemblance between the profiles of the exposed and sham-exposed groups in both experiments (continuous and intermittent). Cortisol values were highest around 0800, at the hour the subjects awoke, and then dropped, reaching a minimum around midnight. Comparing cortisol data for the different groups of subjects shows that, for each 24-hour profile, the amplitudes for the control and the exposed groups are remarkably similar; they are also similar within each individual experimental group, tested twice, a month apart. These results confirm the previously reported existence of a reproducible circadian rhythm in cortisol (25, 26, 27). In fact, cortisol is a strong marker for circadian rhythms. Urinary 17-OH-CS measured in these young healthy men showed a profile that peaked at night, in the urine sample taken between 2300 and 0800 and was lowest in the sample taken between 2000 and 2300. Here again, statistical analysis showed no effect on 17-OH-CS excretion from either a continuous or an intermittent magnetic field. Our overall results do not indicate that the magnetic field had any effect on either serum cortisol or urinary 17-OH-CS.

Thyroid function results showed the highest levels of serum T4, FT4, and FT3 during the day, around 1100, and the lowest levels at night. In contrast, the circadian profile of T3 was lowest in the afternoon around 1600 and peaked during the late night and early morning hours, as previously reported (28, 29, 30). Comparing the circadian profiles of exposed and sham-exposed subjects, we did not uncover any effect from either the continuous or the intermittent 50-Hz magnetic field. Likewise, the circadian profiles of TBG and TBK in exposed subjects did not differ from those of the sham-exposed: both peaked during the day and reached their lowest level during the dark phase. These data also accord with those reported by others (28, 29).

TSH is normally secreted by the pituitary gland in a series of discrete pulses (31). But our longer sampling intervals (3-hour intervals during the day, hourly at night) did not allow us to characterize individual TSH pulses. The circadian profile of TSH showed peak values at 2300, that is, bedtime, and the lowest values were found in the afternoon, around 1400. The statistical analysis showed no differences between exposed and sham-exposed subjects. These results suggest that exposure to either a continuous or an intermittent magnetic field has no effects on TSH secretion in humans. LH secretion, which has a circadian profile with low values during the day and high values at night, was also unaffected by the 50-Hz magnetic field.

Nor was FSH secretion affected by exposure to either the intermittent or the continuous magnetic fields. On the other hand, ANOVA of repeated measures indicated a time variation in FSH secretion (Table 2 and 3). The single cosinor method (32), however, did not validate this time variation as a circadian rhythm. It may instead be explained by the differences in FSH concentrations between some sampling times that could not be considered as a circadian rhythm.

Our results are consistent with those of animal experiments that have not found any clear effect from electric fields on the hypothalamic-pituitary-thyroid and adrenal axes (33, 34, 35). Free et al. (33) have reported that 60-Hz electric fields have no effect on testosterone or corticosterone in rats exposed to 68kV/m for 30 days. Surprisingly, however, after 120 days of electric exposure, testosterone and corticosterone levels were significantly depressed. The duration of exposure may influence the secretion of these hormones: indeed, we have previously demonstrated the role which duration and intensity of exposure play in the effects of magnetic fields on rats (19). A short-term exposure (12 hours) of rats to a 50-Hz magnetic field resulted in a significant reduction of rat serum melatonin and pineal NAT activity only at an intensity of 100 µT; there was no significant reduction at lower levels. In contrast, chronic exposure (one month) resulted in a significant decrease of serum melatonin concentration and pineal NAT activity, at both 10 µT and 100 µT. However, we did not find any effects of 50-Hz magnetic field (10 µT) on serum melatonin and urinary 6-sulfatoxymelatonin concentration in controlled study on young healthy volunteers exposed for one night (36).

Our results, which indicate that magnetic fields had no effect on the circadian rhythm of the endocrine functions studied here, must be interpreted with prudence. Higher intensity, longer duration, and a different timing might all affect the findings. While further studies are needed to examine the role of these factors in humans, the experimental variation of exposure and intensity in humans raises delicate problems. Another question concerns the possibility of a phase response curve for the effects of magnetic fields on the hypothalamic-pituitary-thyroid and adrenal axes, i.e., the response of subjects might be different when exposure takes place at other circadian times than during the night time.

Our results revealed, for the first time, that a nocturnal (from 2300 to 0800) and controlled acute exposure to a 50-Hz magnetic field (10 µT) had no effect on the hypothalamic-pituitary-thyroid and adrenal function in men. The present data are in good agreement with the lack of effects of one night exposure of magnetic field we have reported on pineal function (36) and on hematologic and immunologic functions (37).

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