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(11)

Eighteenth Annual Meeting

Conference Centre, Victoria, B.C., Canada

June 9-14, 1996

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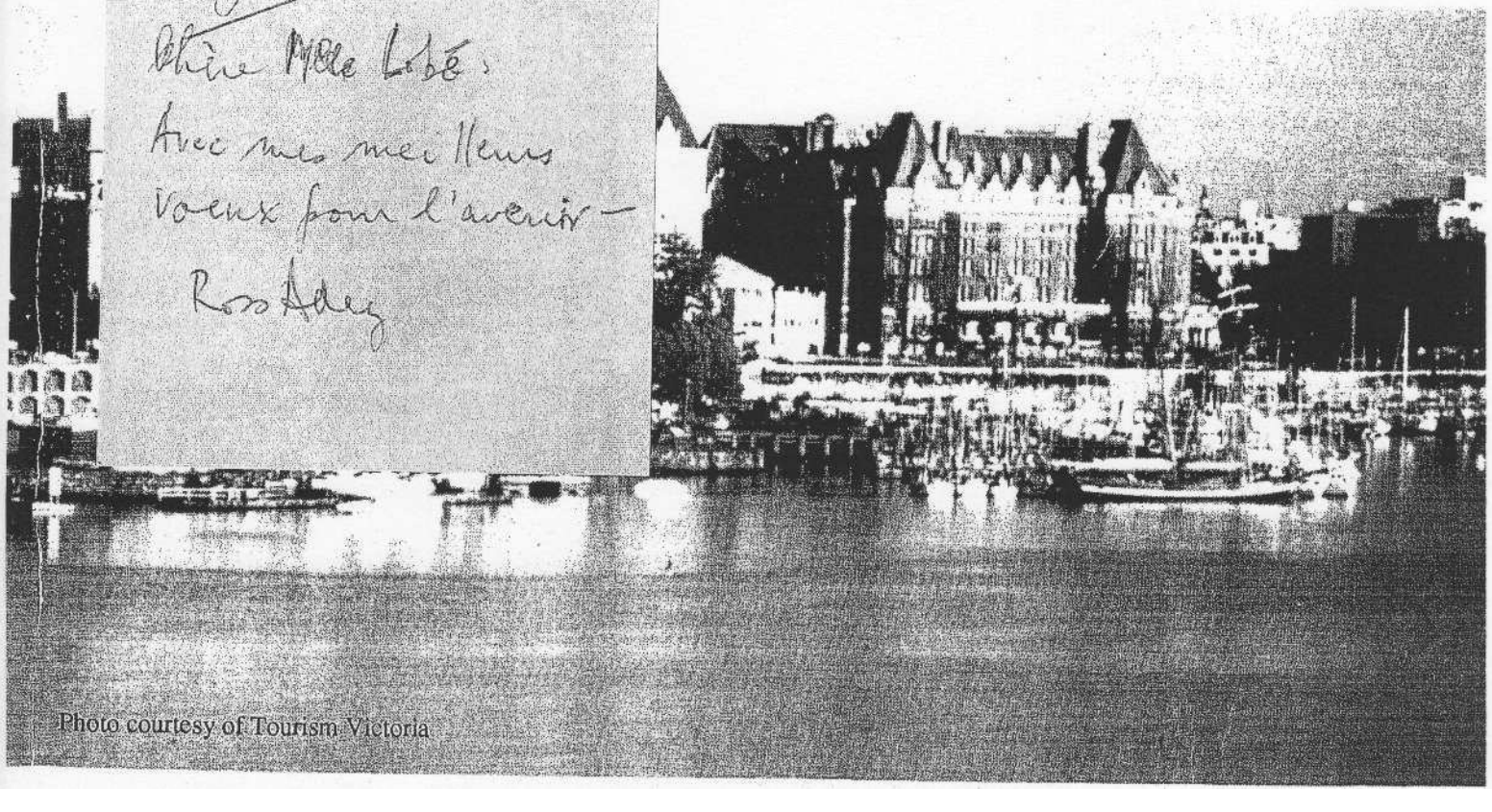

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Bioelectromagnetics 19:271–278 (1998)

GSM Radiocellular Telephones Do Not Disturb the Secretion of Antepituitary Hormones in Humans

René de Seze,[1]* Pascale Fabbro-Peray,[2] and Luis Miro[1]

[1]*Laboratoire de Biophysique Médicale, Faculté de Médecine, Université Montpellier I, CHU de Nimes, Av Kennedy, 30 907, Nimes Cedex 2, France*

[2]*Departement d'Information Médicale, CHU, 30 029, Nimes Cedex 4, France*

It is known that the endocrine system of experimental animals is susceptible to perturbation by radiofrequency (RF) radiation. Because of the recent interest in health and safety issues of cellular telephones, an experiment was designed to evaluate the effect of a 900 MHz RF radiation emitted by a Global System for Mobile radiotelephone (217 Hz impulses, one-eighth duty cycle, 2 W peak power) on human endocrine functions. Twenty healthy male volunteers aged from 19 to 40 were inducted in the present experiment. Each subject was exposed to RF radiation through the use of a cellular phone 2 h/day, 5 days/wk, for 1 month. Subjects were their own control. End points were serum adrenocorticotropin, thyrotropin, growth hormone, prolactin, luteinizing hormone, and follicle stimulating hormone concentrations. These end points were determined in nine weekly blood samples obtained starting 3 weeks before the commencement of the exposure and ending 2 weeks after exposures. All but one blood sample was drawn 48 h after each weekly session. The seventh drawing was performed the morning after the last weekly exposure. Within each individual, the preexposure hormone concentration was used as a control. Results indicated that all hormone concentrations remained within normal physiologic ranges. A difference was not noted among the nine weekly samples in five of six hormones studied. There was a significant change only in thyrotropin concentration, showing a 21% decrease on the seventh sampling. Because this change recovered fully during the postexposure period, it is concluded that 1 month of intermittent exposures to RF radiation from a cellular telephone does not induce a long-lasting or cumulative effect on the hormone secretion rate of the anterior pituitary gland in humans. Bioelectromagnetics 19:271–278, 1998.

Key words: human study; radiation; non ionising; pituitary hormone secretion; mobile telephone

INTRODUCTION

A rapid worldwide expansion of radiotelephones directs attention to possible effects of the emitted field on the health of users. Exposure standards defined by national and international institutions indicate limit values of specific absorption rate (SAR) of 1.6 to 2 W/kg for local exposure in general public [IEEE, 1992; ICNIRP, 1996]. The interaction of radiotelephones and the brain has been studied by several groups who have modeled the electromagnetic fields in the head. These models give values of SAR approximately 0.1 to 0.3 W/kg [Kuster and Balzano, 1996]. Thus the radiotelephones have an emission level sufficiently far below the defined safety thresholds.

However, these limits were derived from calculated or observed thermal effects, but do not consider possible effects of chronic or repeated nonthermal exposures [IRPA, 1988]. Unexpected nonspecific neurovegetative syndromes have been observed in men exposed to a chronic low-power radar emission: physical and neural asthenia, sleep disorder, humoral changes, headache, myalgia (muscular pain), dysesthesia (disagreeable sensation produced by ordinary stimulus) of extremities [Baranski and Czerski, 1976; Bogucka, 1977; Solon, 1979; Shandala et al., 1981; Kolmodin-Hedman et al., 1988]. Case reports of accidental overexposures to power densities above current safety stan-

Contract grant sponsor: CNET (Research Centre of France Telecom).

*Correspondence to: René de Seze, Laboratoire de Biophysique Médicale, Faculté de Médecine, Université Montpellier I, CHU de Nimes, Av. Kennedy, 30 907, Nimes Cedex 2, France.
E-mail: biomed@zeus.sc.univ-montp1.fr

Received for review 5 August 1997; final revision received 16 January 1998

hours: 0800 h to 1000 h, 1030 h to 1230 h, and 1300 h to 1500 h.

Blood Sampling

This study aimed to look for a cumulative and/or persistent effect on endocrine secretion of a repeated exposure to RF radiation emitted by radiotelephones for 1 month. Thus, most blood drawings were performed on Monday, i.e., more than 48 h after the previous exposure session during the exposure period. Three weekly blood samples were obtained before the beginning of the exposure, four weekly blood samples during the exposure period, and two weekly blood samples after the exposure. In total, nine weekly blood samples were obtained from each subject. To look for an eventual change at times shorter than 48 h, the last blood drawing of the exposure period (the seventh blood sample) was performed on the day after the exposure, i.e., on Saturday. To limit seasonal temperature variations, this study was carried out from mid-September to mid-November when the temperature is relatively moderate and stable. Each week, 15 ml of blood were drawn from overnight fasting volunteers at 0800 h. To reduce the effect of the puncture stress on ACTH and prolactin concentrations, a catheter was inserted into an antecubital vein, and the blood sample was drawn after a 15-min rest. Blood was allowed to clot and was centrifuged to extract serum, which was kept frozen at −20 °C until the time of assay. For each hormone, all samples corresponding to each subject were analyzed together in assay kits of the same manufacturer's lot.

Hormone Assays

The following hormones were measured: ACTH, TSH, GH, prolactin (PRL), and we benefited from the protocol to also screen in a rather systematic way the luteinizing hormone (LH) and the follicle stimulating hormone (FSH). Hormone concentrations were determined by radioimmunology, immunofluorometry, or chemoluminescence. The biological characteristics of assay kits are described in Table 1.

Statistical Analysis

Interindividual variation is greater than intraindividual variation. To increase statistical power, comparison should be made to individual baseline or by multivariate analysis. In this study, each subject served as his own control. For each subject and for each hormone, a baseline value was obtained from the mean of the first three hormone concentrations obtained weekly during the preexposure period. The effect of exposure on serum hormone concentrations was evaluated by the Friedman test, looking at a time-effect amongst the

TABLE 1. Biological Characteristics of Assay Kits for ACTH, TSH, GH, PRL, and LH*

Characteristic	Hormone					
	ACTH	TSH	GH	PRL	LH	FSH
Assay kit	ACTHK-PR	BeriLux® hTSH	hGH RIA	Stratus® Prolactin control	LH IRMA	FSH kit
Normal values of the laboratory	2 to 20 pmol/l	0.1 to 3 mU/l	below 12 mUI/l	in man: 100 to 40 mU/l	in man: 3.1 to 10 UI/l	in man: 2.0 to 10 UI/l
Within-assay CV (%)	6.2	3.5	5.1	3.1	6.7	2.2
Between-assay CV (%)	8.3	4.0	5.6	1.6	4.4	6.3
Manufacturer	CIS bio International Gif-sur-Yvette, France	Hoechst-Behring, Rueil-Malmaison, France	Pharmacia Diagnostics, Uppsala, Sweden	Baxter, Maurepas, France	Immunotech, Marseille, France	Immunotech, Marseille, France

*ACTH, adrenocorticotropin; TSH, thyrotropin; GH, growth hormone; PRL, prolactin; LH, luteinizing hormone; FSH, follicle stimulating hormone; CV, coefficient of variation.

TABLE 2. Mean Inter- and Intraindividual Coefficients of Variation for ACTH, TSH, GH, PRL, LH, and FSH*

	Hormone					
Value	ACTH	TSH	GH	PRL	LH	FS
Mean interindividual CV (%)	61	43	153	46	48	6
Range (min–max) (%)	42–148	33–48	130–258	42–85	43–55	51-
Intraindividual CV (%)	47	29	71	30	27	1
Range (min–max) (%)	16–104	14–65	0–192	12–95	11–45	6-

*The interindividual CV is the ratio of the standard deviation over the mean between the 18 individuals at each time; the intraindivic CV is the ratio of the standard deviation over the mean of the 9 sampling times for each individual. For abbreviations, see Table 1.

baseline hormone concentration and the six following samples. The null hypothesis was rejected at 0.05. When the overall time effect was significant for one hormone, Bonferroni's multiple comparison test was used for post hoc analysis of values from each exposure or postexposure date versus baseline values. Possible influence of confounding factors, such as exposure group (i.e., month of exposure), smoking habit, time of exposure within the day, were evaluated in comparison to an observed change greater than the mean intraindividual variation. For each defined factor, the Fisher's exact test was used because of the small size of subgroups. The volunteer's age could also be a confounding factor; Spearman's correlation coefficient was used on the last sample of the exposure period to evaluate an age-related change in TSH concentration.

RESULTS

Two subjects were excluded from the experiment: one was excluded because of a genetic hormonal disease, the other because of one missing blood sample. Thus, the data from 18 persons were analyzed statistically.

Scattering of Hormone Concentrations Between Subjects

A large variation in serum hormone levels between individuals was noted. The interindividual variation (or coefficient of variation [CV]) at the different dates ranged from 33 to 48% for TSH up to 131 to 258% for GH.

Intraindividual Reproducibility

TSH, LH, and FSH concentrations were homogeneous for each subject throughout the experiment. Concentrations of ACTH and GH varied greatly, and PRL at a lesser extent. Only two ACTH values were outside the normal range: one at 79 pmol/l without known physiologic reason and the other at 45 pmol/l characterized by fainting spells. Both were accompanied by elevated PRL. Such secretion increases are known to related to puncture stress. GH values varied from c session to the other in four volunteers; many valu were above the usual 12 mUI/l upper limit of norn values of the laboratory. It seems then that for GH, t 15-min rest was not long enough to rule out the pur ture stress. Except for these values, the repetition measurements in 9 consecutive weeks shows good r producibility, so that the data dispersion decreases the mean intraindividual CV of 18% for FSH (6–34' and 71% for GH (0–192%) (Table 2). As a nonpar metric test was used for statistical analysis, it was r necessary to exclude any value. However, excludi outliers did not modify the statistical results (data r shown).

Study, Hormone by Hormone

There were no pathologic hormone changes du ing or after the exposure period (Table 3). Althou the mean hormone concentrations remained within t limits of the physiologic variations, the Friedman te was significant in two hormones: TSH ($P = .045$) ar FSH ($P = .036$). For TSH, Bonferroni's test was si nificant for the seventh sample ($P = .032$; see Table and Fig. 1). For FSH, Bonferroni's test was not signi cant for any sample. The largest difference was al on the seventh sample, but was less than 10%. Tl isolated and transient decrease of TSH level will l discussed further.

Influence of Confounding Factors

Data about possible confounding factors are give in Table 5. No difference between the various subgrou was statistically significant. Age of the volunteers ar TSH changes on the seventh sample in comparison the baseline are shown in Table 6. The Spearman correlation coefficient between TSH change and age w. −0.036, which was not significantly different from ze ($P = .89$). It could be concluded that the observed TS decrease was not correlated to the age of the subjects

TABLE 3. Mean Concentrations of ACTH, TSH, GH, PRL, LH and FSH Before, During, and After the 1-Month Cellular Telephone Use (n = 18)*

	Period								
	Preexposure week			Exposure week				Postexposure week	
Hormone	1	2	3	4	5	6	7	8	9
ACTH									
Mean (pmol/l)	7.6	9.0	11.6	10.2	7.8	6.4	6.4	7.9	7.4
Coefficient of variation	61	62	148	96	51	60	67	51	42
Delta (%)	−19	−4	24	8	−17	−32	−32	−16	−22
TSH									
Mean (mU/l)	1.69	1.61	1.51	1.40	1.44	1.36	1.27	1.53	1.64
Coefficient of variation	37	34	48	34	33	35	46	41	48
Delta (%)	5	0	−6	−13	−10	−15	−21[a]	−4	3
GH									
Mean (mU/l)	1.97	5.47	2.29	9.94	1.39	1.99	2.64	0.84	1.36
Coefficient of variation	258	228	202	250	180	166	204	131	169
Delta (%)	−39	69	−29	206	−57	−39	−18	−74	−58
PRL									
Mean (mU/l)	232	283	268	257	221	211	213	244	237
Coefficient of variation	43	52	85	52	46	42	47	52	42
Delta (%)	−11	8	3	−2	−15	−19	−18	−7	−9
LH									
Mean (UI/l)	4.7	4.7	5.0	4.9	5.2	5.0	4.5	5.0	4.9
Coefficient of variation	56	48	44	50	43	49	46	50	49
Delta (%)	−2	−2	4	1	8	4	−6	5	3
FSH									
Mean (UI/l)	4.5	4.3	4.7	4.7	4.8	4.6	4.2	4.5	4.4
Coefficient of variation	51	58	65	58	51	58	59	59	60
Delta (%)	0	−5	4	5	7	3	−6	0	−1

*Delta is the relative difference "(concentration − reference)/reference" in percent between the mean hormone concentration of each date and the reference. For each hormone, the reference was obtained from the mean for the 18 volunteers of the first three mean hormone concentrations obtained weekly during the preexposure period. Delta can easily be compared with the coefficient of variation.
[a]P = 0.32.

Individual Responses

Close examination of data from each individual did not show any change in hormone concentrations with respect to RF exposure from using cellular phone. Changes were noted mainly in GH concentrations and to a lesser degree in ACTH and PRL concentrations. However, the serum concentrations of these hormones are influenced by several physical or psychologic stresses. In some cases, increases of these hormones could be related to known causes of stress, such as a home burglary or a child's illness, but in other cases, no such cause could be found. These variations in GH, ACTH, and PRL concentrations did not coincide with RF exposure from using cellular phone.

DISCUSSION

This study evaluated the effect of RF exposure from radiotelephone use on serum hormone levels during 9 consecutive weeks. The overall analysis of the results showed that exposure of men to the electromagnetic fields emitted by radiotelephones 2 hours per day, 5 days per week, for 4 weeks, did not produce any persistent or cumulative modification in the secretion of the anterior pituitary hormones. The unusual peaks, mainly for GH, could be linked to stress reactions or the pulsatile nature of GH secretion and could not be attributed to the exposure, because some of these peaks were already present before the beginning of the RF exposure session. The Friedman test showed a time effect only for FSH and TSH. This significant difference was confirmed by Bonferroni's test for TSH in the seventh sample.

This isolated and transient decrease of TSH concentration corresponded to the end of the exposure and was carried out on the day after the last exposure session of the week. However, the existence of a causal relationship between TSH decrease and RF exposure

TABLE 4. Concentration and Reference Values of TSH (mU/l)*

	Preexposure week			Exposure week				Postexposure week		
Volunteer	1	2	3	4	5	6	7	8	9	Ref
V1	1.2	1.3	1.2	0.6	0.7	1.0	0.5	0.8	1.3	1.2
V2	1.0	0.8	0.2	0.8	0.3	0.7	0.5	0.6	0.5	0.7
V3	1.7	1.7	1.6	1.7	1.6	1.7	1.2	2.1	1.6	1.7
V4	2.0	1.2	0.3	1.4	1.6	0.7	0.7	0.5	0.2	1.2
V5	2.3	2.0	3.3	2.2	2.0	1.9	1.5	2.0	1.9	2.5
V6	1.2	1.4	1.8	1.4	1.1	1.3	0.9	1.7	1.8	1.5
V7	1.4	0.9	1.1	1.1	1.0	1.3	1.0	1.1	1.1	1.1
V8	1.3	1.4	1.6	1.7	1.8	1.3	1.2	1.6	1.3	1.4
V9	1.0	1.6	1.9	1.2	1.2	0.6	0.9	1.4	1.0	1.5
V10	2.1	1.3	1.8	1.3	1.1	1.6	0.8	2.0	1.7	1.7
V11	2.0	2.9	1.0	1.0	1.5	1.5	2.5	3.0	1.3	2.0
V12	1.0	0.8	1.7	1.2	1.2	0.8	1.3	0.9	1.1	1.2
V13	2.3	2.2	1.9	1.2	2.0	0.9	1.4	2.1	2.2	2.1
V14	1.6	2.0	2.6	2.5	2.0	1.8	2.3	1.1	2.2	2.1
V15	2.7	2.2	1.2	2.0	1.8	1.8	1.8	1.6	3.5	2.0
V16	2.2	1.9	1.2	1.5	1.8	2.2	2.0	1.6	2.8	1.8
V17	2.7	1.7	1.6	1.3	1.6	1.7	1.6	1.5	2.2	2.0
V18	0.7	1.7	1.2	1.1	1.6	1.6	0.8	2.0	1.9	1.2
Mean	1.69	1.61	1.51	1.40	1.44	1.36	1.27	1.53	1.64	
Sem	0.14	0.12	0.16	0.11	0.11	0.11	0.13	0.14	0.18	

*The TSH concentrations are tabulated for each week 1 to 9 and for each volunteer V1 to V18. The reference values (Ref) are the means of the three preexposure period values. For abbreviations, see Table 1.

could not be ascertained without a replicate or a double-blind experiment. From this work, we can calculate that to perform a powerful double-blind study, 24 persons would be needed in each group, based on an α risk of 0.05, a significant difference of 21% in the TSH concentration between exposed and control groups and the mean of intraindividual CV of 29%. If a 21% difference would not be significant in these conditions, the power of the study would, however, be 80%.

Although there are many papers on dosimetry and standards in the literature, few papers have been published on the effects in humans of GSM-type microwaves: Mann and Röschke [1996] showed a slight change in the sleep structure of volunteers exposed for 1 night to low-power radiofrequency electromagnetic fields emitted by a radiotelephone (0.05 mW/cm^2). Navakatikian and Tomashevskaya [1994] observed an inhibition of testosterone and insulin secretions in rats by low intensity microwaves. The intensity of this effect depended on the duration of exposure (0.5–12 h), the schedule of exposure (single or repeated for 15–60 days, 7–12 h/day), and the modulation (pulsed or continuous wave), with a threshold level at 10 μW/cm^2, far below the power density produced by radiotelephone exposure at the surface of the head. This inhibition was more pronounced with longer exposure duration (7–12 h compared with 0.5 h) and depended on the number of daily sessions: −50% after 15 days with a continuous wave exposure (no more effect after 60 days) or −20% to −50% after 60 days with a pulsed exposure

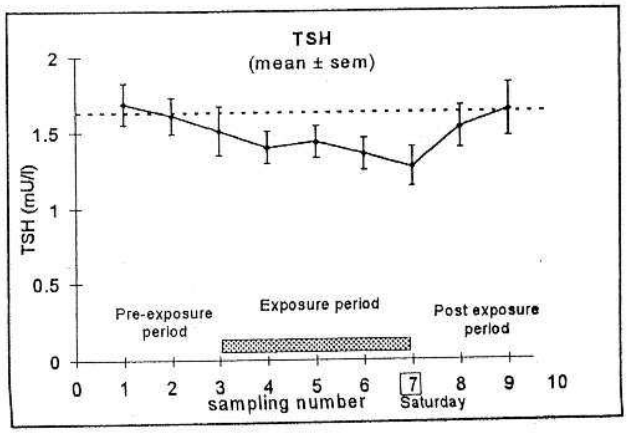

Fig. 1. Time course of the values of the TSH changes (mean ± SEM; n = 18). The dotted line represents the reference value, i.e., the mean of the three preexposure values. All drawings were performed at 0800 h. The seventh drawing was performed on Saturday (first day after exposure) as others were on Monday (third day after exposure). *P = 0.032

TABLE 5. Possible Confounding Factors for TSH Decrease on the Seventh Sample*

Parameter	TSH Decrease > intra-CV: No	TSH Decrease > intra-CV: Yes
Group 1 (September)	4	4
Group 2 (October)	6	4
Smoker	5	5
Nonsmoker	5	3
Exposure time		
0800 h–1000 h	3	4
1030 h–1230 h	4	1
1300 h–1500 h	3	3

*The factors considered are the group (seasonal variation over 2 successive months), smoking habit, and time of exposure (looking for a circadian variation of an effect). For abbreviations, see Table 1.

TABLE 6. TSH Decrease on the Seventh Sample in Comparison to Volunteer's Age

Group 1 (September)			Group 2 (October)		
Volunteer	Age (yr)	TSH decrease (%)	Volunteer	Age (yr)	TSH decrease (%)
V1	29	−59.5	V9	39	−40
V2	23	−24.6	V10	21	−53.8
V3	27	−28	V11	24	27.1
V4	31	−40	V12	35	11.4
V5	23	−40.8	V13	35	−34.4
V6	30	−38.6	V14	33	11.3
V7	29	−11.8	V15	19	−11.5
V8	40	−16.3	V16	22	13.2
			V17	25	−20
			V18	20	−33.3

(carrier frequency, 3000 MHz; pulse duration, 2 μs; repetition frequency, 400 Hz; i.e., duty cycle: 1/1250). Considering these phasic changes, the inhibition that we observed in our experiment could be larger when measured closer to exposure (on Saturday instead of on Monday) and at an earlier time, for example on the fifth sampling after the second week of exposure. This is to be investigated in a further study.

Electromagnetic fields have mainly been shown to inhibit nocturnal melatonin secretion in animals [Lambrozo et al., 1996]. This effect has been observed with static and extremely low frequency (<300 Hz) magnetic fields. It would also be interesting to study the effect on this hormone of RF electromagnetic fields such as those emitted by cellular radiotelephones.

CONCLUSION

This study was designed to search for a possible effect in humans exposed to electromagnetic fields emitted by hand-held radiotelephones at 900 MHz, used at their maximal power. The end point was the anterior pituitary function. The results are reassuring: (i) no pathologic modification of the hormone concentrations was noted during or after exposure; (ii) a 21% decrease of TSH concentration was noted on the seventh sample, which remained within the physiologic range. Although the TSH change occurred during the radiotelephone exposure period, the causality cannot be attested with this protocol. A replicate study would be required to test the reproducibility of this effect and the significance of the TSH concentration decrease in relation to health and safety issues of radiotelephone use.

ACKNOWLEDGMENTS

This work has been funded by CNET (Research Centre of France Telecom) Issy les Moulineaux, France, which provided the exposure system. Volunteers have been managed by C. Bec. Dr. Baudin (CHU Nimes) is acknowledged for his help in conceiving the protocol, performing biochemical analysis, and interpreting some of the results.

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