
CANADA	RÉGIE DE L'ÉNERGIE / ENERGY BOARD
PROVINCE OF QUEBEC DISTRICT OF MONTREAL DOCKET No. R-3770-2011	AUTHORIZATION OF AN INVESTMENT BY HYDRO-QUEBEC DISTRIBUTION – ADVANCED METERING PROJECT PHASE 1
	HYDRO-QUEBEC As Electricity Distributor Petitioner -and- STRATEGIES ENERGETIQUES (S.E.) / ENERGY STRATEGIES (E.S.) ASSOCIATION QUEBECOISE DE LUTTE CONTRE LA POLLUTION ATMOSPHERIQUE (AQLPA) / QUEBEC ASSOCIATION TO FIGHT AGAINST AIR POLLUTION Interveners

ARTICLES MENTIONED IN SECTION 40 OF DR. CARPENTER'S REPORT

(NEUROLOGIC, IMMUNE, ENDOCRINE, REPRODUCTIVE AND CARDIAC ADVERSE HEALTH EFFECTS FROM LOW-DOSE, CHRONIC EXPOSURE TO RF/MW RADIATION IN HUMANS)

Referred to in **David O. CARPENTER**, *Expert Report*, Revised on May 14, 2012,
C-SE-AQLPA-0072, SE-AQLPA-7, Doc. 1.1, parag. 40, 55.

Filed on May 15, 2012

ARTICLES MENTIONED IN SECTION 40 OF DR. CARPENTER'S REPORT

(NEUROLOGIC, IMMUNE, ENDOCRINE, REPRODUCTIVE AND CARDIAC ADVERSE HEALTH EFFECTS FROM LOW-DOSE, CHRONIC EXPOSURE TO RF/MW RADIATION IN HUMANS)

40. Additional studies show neurologic, immune, endocrine, reproductive and cardiac, adverse health effects from low-dose, chronic exposure to RF/MW radiation in humans:

a. Volkow ND, Tomasi D, Wange GJ, Vaska P, Fowler JS, Teland F, Alexoff D, Logan J and Wong C. Effects of cell phone radiofrequency signal exposure on brain glucose metabolism. JAMA 305 : 808-814 : 2011. In healthy participants and compared with no exposure, 50-minute cell phone exposure was associated with increased brain glucose metabolism in the region closest to the antenna. This shows direct effects of RF radiation on the brain with cell phone use.

b. McCarty DE, Carrubba S, Chesson AL, Frilor C, Gonzalex-Toledo E and Marino AA. Electromagnetic hypersensitivity : Evidence for a novel nuerological syndrome. Internat J Neurosci 121 : 670-676 : 2011. In a female physician who is electrosensitive, blinded application of EMFs triggered temporal pain, headache, muscle twitching and skipped heartbeats within 100 s of field application. This study was already filed in the present case as Exhibit C-SE-AQLPA-0037, SE-AQLPA-5, Doc. 5.

c. Papageorgiou CC, Hountala CD, Maganioti AE, Kyprianou MA, Rabavilas AD, Papadimitriou GN, Capsalis CN. Effects of WI-FI signals on the p300 component of event-related potentials during an auditory hayling task. J Integr Neurosci 2011 Jun;10(2):189-202. This study concludes that WI-FI exposure may exert gender-related alterations on neural activity.

d. Altpeter ES, Roosli M et al. Effect of Short-wave magnetic fields on sleep quality and melatonin cycle in humans: The Schwarzenburg shut-down study. Bioelectromagnetics 27:142-150, 2006. Sleep quality improved and melatonin excretion increased when the transmitter was shut down.

e. Abelin T et al. Sleep disturbances in the vicinity of the short-wave broadcast transmitter Schwarzenburg. Somnologie 9:203-209, 2005. There is strong evidence of a causal relationship between operation of a short-wave radio transmitter and sleep disturbances in the surrounding population.

f. Hutter HP et al. Subjective symptoms, sleeping problems, and cognitive performance in subjects living near mobile phone base stations. Occup Environ Med 2006;63:307-313, 2006. There was a significant relation of some symptoms, especially headaches, to measured power density, as well as effects on wellbeing and performance.

g. Preece AW, Georgious AG, Duunn EJ, Farrow SC. Occup Environ Med 2007 64:402-8. Compared to control village, there were highly significant differences in the reporting of migraine, headache and dizziness military and cell phone antenna systems.

h. Robertson HA et al. Low-frequency pulsed electromagnetic field exposure can alter neuroprocessing in humans J. R. Soc. Interface (2010) 7, 467–473 doi:10.1098/rsif.2009.0205. A functional magnetic resonance imaging study demonstrated how the neuromodulation effect of extremely low-frequency magnetic fields influences the processing of acute thermal pain. The study concludes that magnetoreception may be more common than presently thought. This study was already filed in the present case as Exhibit C-SE-AQLPA-0043, SE-AQLPA-5, Document 10.

i. Buchner K, Eger, H. Changes of clinically important neurotransmitters under the influence of modulated RF fields – a long-term study under real-life conditions. Umwelt-Medizin-Gesellschaft 24(1):44-57, 2011. There is clear evidence of health-relevant effects, including increase in adrenaline/noradrenaline, subsequent decrease in dopamine from a new MWemitting base station. During counterregulation, trace amine PEA decreased and remained decreased. Clinically documented increases in sleep problems, cephalgia, vertigo, concentration problems and allergies followed the onset of new microwave transmissions.

j. Eliyahu I, Luria R, Hareuveny R, Margaliot M, Neiran N and Shani G. Effects of radiofrequency radiation emitted by cellular telephones on the cognitive functions of humans. Bioelectromagnetics 27: 119-126: 2006. A total of 36 human subjects were exposed to PM MW and were tested on four distinct cognitive tasks. Exposure to the left side of the brain slows left-hand response time in three of the four tasks.

k. Barth A, Winker R, Ponocny-Seliger E, Mayrhofer W, Ponocny I, Sauter C and Vana N. Occup Environ Med 65: 342-345: 2008. A meta-analysis for neurobehavioural effects due to electromagnetic field exposure emitted by GSM mobiile phones. The authors looked at 19 studies of cognitive function in cell phone users, and found in the meta-analysis that there is evidence for a decreased reaction time, altered working memory and increased number of errors in exposed persons.

l. Augner C, Hacker GW, Oberfeld G, Florian M, Hitzl W, Hutter J and Pauser G. Effects of exposure to base station signals on salivary cortisol, alphaamylase and immunoglobulin A. Biomed Environ Scie 23: 199-207: 2010. This was a human experimental study with exposure to PM MW radiation wherein immune indicators were monitored after five 50-minute sessions. The researchers found dose-dependent changes in cortisol and alpha-amylase.

m. Avendano C, Mata A, Sanchex Sarimiento CA and Doncel GF. Use of laptop computers connected to internet through WI-FI decreases human sperm motility and increases sperm DNA fragmentation. Fert Steril, 2012, In press. In this study human sperm were exposed to WI-FI from a laptop, and were found to show reduced motility after a 4-hour exposure. The results are consistent with other publications (see Agarwal et al., Fert Steril 89: 124-128: 2008) that reported that those who use cell phone regularly have reduced sperm count.

n. Baste V, Riise T and Moen BE (2008) Int J Epidemiol 23: 369-377: 2008. Radiofrequency electromagnetic fields: male infertility and sex ratio of offspring. This is a study of Norwegian Navy personnel chronically exposed to RF fields on the job. The rates of infertility were related to level of exposure in a dose-dependent fashion.

Published in final edited form as:

JAMA. 2011 February 23; 305(8): 808–813. doi:10.1001/jama.2011.186.

Effects of Cell Phone Radiofrequency Signal Exposure on Brain Glucose Metabolism

Nora D. Volkow, MD, **Dardo Tomasi, PhD**, **Gene-Jack Wang, MD**, **Paul Vaska, PhD**, **Joanna S. Fowler, PhD**, **Frank Telang, MD**, **Dave Alexoff, BSE**, **Jean Logan, PhD**, and **Christopher Wong, MS**

National Institute on Drug Abuse, Bethesda, Maryland (Dr Volkow); National Institute on Alcohol Abuse and Alcoholism, Bethesda (Drs Volkow, Tomasi, and Telang and Mr Wong); and Medical Department, Brookhaven National Laboratory, Upton, New York (Drs Wang, Vaska, Fowler, and Logan and Mr Alexoff).

Abstract

Context—The dramatic increase in use of cellular telephones has generated concern about possible negative effects of radiofrequency signals delivered to the brain. However, whether acute cell phone exposure affects the human brain is unclear.

Objective—To evaluate if acute cell phone exposure affects brain glucose metabolism, a marker of brain activity.

Design, Setting, and Participants—Randomized crossover study conducted between January 1 and December 31, 2009, at a single US laboratory among 47 healthy participants recruited from the community. Cell phones were placed on the left and right ears and positron emission tomography with (^{18}F)fluorodeoxyglucose injection was used to measure brain glucose metabolism twice, once with the right cell phone activated (sound muted) for 50 minutes ("on" condition) and once with both cell phones deactivated ("off" condition). Statistical parametric mapping was used to compare metabolism between on and off conditions using paired *t* tests, and Pearson linear correlations were used to verify the association of metabolism and estimated

---

Corresponding Author: Nora D. Volkow, MD, National Institute on Drug Abuse, 6001 Executive Blvd, Room 5274, Bethesda, MD 20892 (nvolkow@nida.nih.gov).

Author Contributions: Drs Volkow and Tomasi had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Volkow.
Acquisition of data: Wang, Vaska, Telang, Alexoff, Wong.
Analysis and interpretation of data: Volkow, Tomasi, Vaska, Fowler, Telang, Logan.
Drafting of the manuscript: Volkow, Wong.
Critical revision of the manuscript for important intellectual content: Volkow, Tomasi, Wang, Vaska, Fowler, Telang, Alexoff, Logan.
Statistical analysis: Tomasi.
Obtained funding: Volkow, Fowler.
Administrative, technical, or material support: Wang, Fowler, Telang, Alexoff, Wong.
Study supervision: Wang, Fowler.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Additional Contributions: We are grateful to BNL employees Donald Warner, AA, for positron emission tomography operations; David Schlyer, PhD, and Michael Schueller, PhD, for cyclotron operations; Pauline Carter, RN, and Barbara Hubbard, RN, for nursing care; Payton King, BS, for plasma analysis; and Lisa Muench, MS, Youwen Xu, MS, and Colleen Shea, MS, for radiotracer preparation; and to NIH employees Karen Appelskog-Torres, AA, for protocol coordination; Millard Jayne, RN, for subject recruitment and nursing care; and Linda Thomas, MS, for editorial assistance. We also thank the individuals who volunteered for these studies. None of the individuals acknowledged were compensated in addition to their salaries for their contributions.

amplitude of radiofrequency-modulated electromagnetic waves emitted by the cell phone. Clusters with at least 1000 voxels (volume >8 cm^3) and $P < .05$ (corrected for multiple comparisons) were considered significant.

Main Outcome Measure—Brain glucose metabolism computed as absolute metabolism (μmol/100 g per minute) and as normalized metabolism (region/whole brain).

Results—Whole-brain metabolism did not differ between on and off conditions. In contrast, metabolism in the region closest to the antenna (orbitofrontal cortex and temporal pole) was significantly higher for on than off conditions (35.7 vs 33.3 μmol/100 g per minute; mean difference, 2.4 [95% confidence interval, 0.67–4.2]; $P = .004$). The increases were significantly correlated with the estimated electromagnetic field amplitudes both for absolute metabolism ($R = 0.95$, $P < .001$) and normalized metabolism ($R = 0.89$; $P < .001$).

Conclusions—In healthy participants and compared with no exposure, 50-minute cell phone exposure was associated with increased brain glucose metabolism in the region closest to the antenna. This finding is of unknown clinical significance.

The dramatic worldwide increase in use of cellular telephones has prompted concerns regarding potential harmful effects of exposure to radiofrequency-modulated electromagnetic fields (RF-EMFs). Of particular concern has been the potential carcinogenic effects from the RF-EMF emissions of cell phones. However, epidemiologic studies of the association between cell phone use and prevalence of brain tumors have been inconsistent (some, but not all, studies showed increased risk), and the issue remains unresolved.[1]

RF-EMFs emitted by cell phones are absorbed in the brain[2] within a range that could influence neuronal activity.[3] Although the intensity of RF-EMFs is very low, the oscillatory frequencies correspond to some of the oscillation frequencies recorded in neuronal tissue and could interfere with neuronal activity.[4] Thermal effects from RF-EMFs have also been invoked as a mechanism that could affect neuronal activity, although temperature changes produced by current cell phone technology are likely minimal.[5] Studies performed in humans to investigate the effects of RF-EMF exposures from cell phones have yielded variable results.[6] For example, imaging studies that used positron emission tomography (PET) to measure changes in cerebral blood flow (CBF) with RF-EMF exposures from cell phones have reported increases,[7,8] decreases and increases,[9,10] or no changes[11] in CBF. The discrepancies among these imaging studies likely reflect their relatively small sample sizes (9–14 participants), and the potential confounding of CBF measures reflecting vascular rather than neuronal signals.[12–14] This highlights the need for studies to document whether RF-EMFs from cell phone use affects brain function in humans.

The objective of this study was to assess if acute cell phone exposure affected regional activity in the human brain. For this purpose we evaluated the effects in healthy participants (N = 47) of acute cell phone exposures on brain glucose metabolism, measured using PET with injection of (^{18}F)fluorodeoxyglucose (^{18}FDG). Brain glucose metabolic activity is a more proximal marker of neuronal activity than measures of CBF, which reflects vascular as well as neuronal components.[15] Also, because brain glucose metabolic measures obtained with ^{18}FDG reflect the averaged brain activity occurring over a 30-minute period,[16] this method allowed assessment of the cumulative effects of cell phone exposure on resting brain metabolism. Because exposure to RF-EMFs from cell phones is well localized and is highest in brain regions closest to the antenna,[2] we hypothesized that the effects on brain metabolism would be greatest in inferior and anterior brain regions, the regions that would be exposed to the highest RF-EMF amplitude for the cell phone model used in this study.

METHODS

Participants

The study was conducted at Brookhaven National Laboratory from January 1, 2009, through December 31, 2009, and was approved by the local institutional review board (Committee on Research Involving Human Subjects, Stony Brook University). We enrolled 48 healthy participants recruited from advertisements in local newspapers and screened for absence of medical, psychiatric, or neurologic diseases. Special attention was given to ensure that participants did not abuse addictive substances (including alcohol and nicotine), and urine toxicology studies were performed prior to the imaging sessions to ensure lack of psychoactive drug use. For technical reasons, data from one of the participants could not be used (see below). Table 1 provides demographic characteristics and cell phone usage histories of the 47 participants whose data were used in the analysis. Participants each received $250 for their participation in the study ($200 for PET scans [$100 per scan] plus $50 for the physical examination and laboratory work). All participants provided written informed consent after receiving a complete description of the study.

Experimental Conditions

All participants had 2 scans performed on separate days using PET with ^{18}FDG injection under resting conditions. For both scans 2 cell phones, one placed on the left ear and one on the right, were used to avoid confounding effects from the expectation of a signal from the side of the brain at which the cell phone was located. For one of the days both cell phones were deactivated (“off” condition). For the other day the right cell phone was on (activated but muted to avoid confounding from auditory stimulation) and the left cell phone was off (“on” condition). For the on condition the cell phone was receiving a call (from a recorded text), although the sound was muted. The order of conditions was randomly assigned, and participants were blinded to the condition. The mean time between the first and the second study was 5 (SD, 3) days.

Two Samsung model SCH-U310 cell phones, capable of transmitting at either cellular or personal communications service frequency bands with code division multiple access modulation, were used for each study. The maximum specific absorption rate in the head for this cell phone model corresponds to 0.901 W/kg. Cell phones were placed over each ear with microphones directed toward the participant’s mouth and were secured to the head using a muffler that did not interfere with the lower part of the cell phone, where the antenna is located. Activation of the right cell phone was started 20 minutes prior to ^{18}FDG injection and maintained for 30 minutes afterward to correspond with the ^{18}FDG uptake period. During the 50-minute period participants sat on a comfortable chair in a quiet, dimly lit room and with their eyes open, with a nurse present to ensure that they kept their eyes open and did not fall asleep.

The RF-EMF emissions were recorded once before the call (background) and every 5 minutes during the stimulation period to ensure that the call was not terminated. This was accomplished with a handheld spectrum analyzer (model FSH6; Rohde & Schwarz, Munich, Germany) connected to a cellular wide-band log periodic directional antenna (model 304411; Wilson Electronics, St. George, Utah) aimed at the head from a distance of 3 feet. The cellular band was active, with a frequency of 837.8 MHz. This frequency was monitored with a resolution bandwidth of 1 MHz. Activation of the cell phone for the experimental period was also corroborated with the records obtained from the cell phone company. For 1 participant the cell phone signal was interrupted at the time of ^{18}FDG injection; this participant’s data were not included in the analysis.

PET Scanning

In preparation for the study, participants had 2 venous catheters placed, one in the antecubital vein for radiotracer injection and the other in a superficial vein on the dorsal surface of the hand for sampling of arterialized blood. Arterialization was achieved by warming the hand to 44°C. The participants were injected with ^{18}FDG (148–222 MBq [to convert to millicuries, divide by 37]) and asked to refrain from moving or speaking during the 30-minute ^{18}FDG uptake period. At the end of the sessions, the cell phones were removed and the participants were positioned in the PET scanner as previously described.[17] Participants were scanned with a whole-body tomograph (ECAT HR+; Siemens/CTI, Munich, Germany), with a resolution of $4.6 \times 4.6 \times 4.2$ mm^3 as measured by National Electrical Manufacturers Association protocols. Emission scans were started 35 minutes after ^{18}FDG injection and lasted 20 minutes. Transmission scans were performed simultaneously.

Radiofrequency Field

The average position of the antenna in the stereotactic space of the Montreal Neurological Institute ($\mathbf{r}_0$) ($\mathbf{r}_0$ = 21 [SD, 10] mm for x [left to right], 30 [SD, 11] mm for y [anterior to posterior], −160 [SD, 7] mm for z [superior to inferior]) was determined for 21 participants using calibrated orthogonal photography that registered orthogonal views (front and sides) of the cell phone positions on the participant's head. The positions of the eyes were used as landmarks to determine $\mathbf{r}_0$ with the aid of the standard brain template (ch2.nii) provided in MRI-cron (available at http://www.sph.sc.edu/comd/rorden/mricron/). The relative amplitude of the cell phone's electric field, $E(\mathbf{r})$, at every position in the brain, $\mathbf{r}$, was computed in Interactive Data Language version 6.0 (ITT Visual Information Solutions, Boulder, Colorado) using the far-field approximation, $E(\mathbf{r}) \sim \|\mathbf{r}-\mathbf{r}_0\|^{-3}$, of a dipole field (Figure 1).

Image Analysis

The data were analyzed using statistical parametric mapping (SPM) in the SPM2 mapping package (Welcome Department of Cognitive Neurology, London, United Kingdom).[18] The SPM analyses were performed on the absolute as well as the normalized (to whole-brain metabolism) metabolic images. For this purpose, the images were spatially normalized using the SPM2 PET template and a 2-mm^3 × 2-mm^3 × 2-mm^3 voxel size and were subsequently smoothed with an 8-mm isotropic Gaussian kernel. Voxel-wise paired t tests were used to assess regional changes in glucose metabolism.

Because the electric field, $E(\mathbf{r})$, produced by the cell phone decreases rapidly with distance to the antenna, we hypothesized that the effects of cell phones on glucose metabolism would occur in regions close to the antenna and that the regions far from the antenna would show no effects. Therefore, the corrections for multiple comparisons were restricted to brain regions in which $E(\mathbf{r})$ was higher than 50% of the maximum field value, E_0, in the brain ($E_0/2 < E(\mathbf{r}) < E_0$) (Figure 1). Thus, the Bonferroni method with a searching volume (S_v) of 201.3 cm^3 (S_v = 25 161 voxels) was used to correct cluster-level P values for multiple comparisons as a function of the cluster volume (C_v) ($P_{corr} = P \times S_v/C_v$). Clusters with at least 1000 voxels (C_v >8 cm^3) and $P < .05$ (corrected for multiple comparisons) were considered significant.

A simple model assuming a linear relationship between cell phone–related increases in metabolism (Δ^{18}FDG; average across participants) and E was used. The paired values ($\Delta^{18}\text{FDG}_i$, E_i) from all voxels that were statistically significant in the SPM2 t test analyses contrasting on vs off conditions within S_v were sorted by E, clustered in groups of 50 voxels, and averaged. These clusters were treated as independent. The Pearson linear correlation factor, R, was used to assess the linear relationship between Δ^{18}FDG and E in Interactive Data Language version 6.0.

The sample-size calculation was based on our preliminary study of the effect of low-frequency magnetic field gradients in glucose metabolism,[19] which demonstrated metabolic differences between stimulation and sham conditions with effect size (ratio between the mean difference and the pooled standard deviation) between 0.65 and 0.80. The minimal important difference in glucose metabolism used to determine the sample size was 1 μmol/100 g per minute. For such effect sizes, to achieve a power of at least 80% using the independent-samples t test with a significance level of .05, at least 40 participants were needed.

RESULTS

Whole-brain glucose metabolism did not differ between conditions, which for the off condition corresponded to 41.2 μmol/100 g per minute (95% confidence interval [CI], 39.5–42.8) and for the on condition to 41.7 μmol/100 g per minute (95%CI, 40.1–43.3). However, there were significant regional effects. Specifically, the SPM comparisons[14] on the absolute metabolic measures showed significant increases (35.7 vs 33.3 μmol/100 g per minute for the on vs off conditions, respectively; mean difference, 2.4 [95% CI, 0.67–4.2]; $P = .004$) in a region that included the right orbitofrontal cortex (BA11/47) and the lower part of the right superior temporal gyrus (BA 38) (Figure 2 and Table 2). No areas showed decreases. Similar results were obtained for the SPM analysis of the normalized metabolic images (normalized to whole-brain glucose metabolism), which also showed significant increases (1.048 vs 0.997 for the on vs off conditions, respectively; mean difference, 0.051 [95% CI, 0.017–0.091]; $P < .001$) in a region that included right orbitofrontal cortex and right superior temporal gyrus (BA 38) (Figure 2).

The regression analysis between cell phone–related increases in metabolism (Δ^{18}FDG) and E revealed a significant positive correlation both for the absolute metabolic measures ($R = 0.95$, $P < .001$) and the normalized metabolic measures ($R = 0.89$, $P < .001$) (Figure 3). This indicates that the regions expected to have the greater absorption of RF-EMFs from the cell phone exposure were the ones that showed the larger increases in glucose metabolism.

CONCLUSIONS

These results provide evidence that the human brain is sensitive to the effects of RF-EMFs from acute cell phone exposures. The findings of increased metabolism in regions closest to the antenna during acute cell phone exposure suggest that brain absorption of RF-EMFs may enhance the excitability of brain tissue. This interpretation is supported by a report of enhanced cortical excitability to short transcranial magnetic stimulation pulses (1 msec) following 40-minute RF-EMF exposures.[20]

Although increases in frontal CBF during acute cell phone exposure had been previously reported by 2 independent PET laboratories, such increases did not occur in brain regions with the highest RF-EMF exposures.[7–10] Moreover, one of these studies reported CBF decreases in the region with maximal RF-EMF exposure.[10] These discrepancies are likely to reflect, among others, the methods used, particularly because the ^{18}FDG method is optimal for detecting long-lasting effects (30 minutes) in brain activity, whereas CBF measures reflect activity over 60 seconds. In this respect, this study is an example of the value of the ^{18}FDG method for detecting cumulative effects in brain activity that may not be observed when using more transient measures of activity. Discrepancies also could reflect uncoupling between CBF and metabolism.[12–14] Moreover, the relatively large sample size (n = 47) improved our ability to detect small effects that may have been missed in prior studies with smaller sample sizes.[11]

The experimental setup also differed from prior studies that used cell phones for which the antenna was closest to superior and middle temporal cortices.[21] However, this is unlikely to have accounted for the differences in results, because the findings in this study show increases in the region with maximal RF-EMF exposure, whereas findings from other studies have shown decreases in regions with the highest RF-EMF exposures, increases in regions far from the antenna, or both. However, the increases in frontal CBF previously reported with acute cell phone exposure possibly could reflect a downstream effect of connections with the regions that had the highest RF-EMF exposures.

The linear association between cell phone–related increases in metabolism (Δ^{18}FDG) and E suggests that the metabolic increases are secondary to the absorption of RF-EMFs from cell phone exposures. The mechanisms by which RF-EMFs from cell phones could affect brain glucose metabolism are unclear. However, based on findings from in vivo animal and in vitro experiments, it has been hypothesized that this could reflect effects of RF-EMF exposure on neuronal activity mediated by changes in cell membrane permeability, calcium efflux, cell excitability, and/or neurotransmitter release.[4] Athermal effect of cell phones on the brain has also been proposed,[22] but this is unlikely to contribute to functional brain changes.[5] Disruption of the blood-brain barrier has also been invoked as a potential mechanism by which RF-EMFs from cell phone exposure could affect brain activity.[23] A recent clinical study reported alterations in a peripheral biomarker of blood-brain barrier integrity (transthyretin) after cell phone exposure, but the significance of this finding is unclear.[24]

The increases in regional metabolism induced by RF-EMFs (approximately 7%) are similar in magnitude to those reported after suprathreshold transcranial magnetic stimulation of the sensorimotor cortex (7%–8%).[25] However, these increases are much smaller than the increases after visual stimulation reported by most studies (range, 6%–51%).[26] The large difference in the magnitude of regional glucose metabolic increases is likely to reflect multiple factors, including differences in glycolytic rate between brain regions,[27] the duration of the stimulation (transient stimulation increases glucose metabolism more than continuous stimulation[26]), and the characteristics of the stimulation used.[28] Indeed, whereas resting glucose metabolism is predominantly supported by glucose oxidation (>90%), with acute visual stimulation the large increases in glucose metabolism appear to reflect predominantly aerobic glycolysis,[29] which is used for purposes other than energy expenditures, and actual energy utilization is estimated to be 8% at most.[13]

Concern has been raised by the possibility that RF-EMFs emitted by cell phones may induce brain cancer.[30] Epidemiologic studies assessing the relationship between cell phone use and rates of brain cancers are inconclusive; some report an association,[31–33] whereas others do not.[34–36] Results of this study provide evidence that acute cell phone exposure affects brain metabolic activity. However, these results provide no information as to their relevance regarding potential carcinogenic effects (or lack of such effects) from chronic cell phone use.

Limitations of this study include that it is not possible to ascertain whether the findings pertain to potential harmful effects of RF-EMF exposures or only document that the brain is affected by these exposures. Also, this study does not provide an understanding of the mechanism(s) by which RF-EMF exposures increase brain metabolism, and although we interpret these exposures as indicators of neuronal excitation, further studies are necessary to corroborate this. Lastly, this model assumes a linear relationship between the amplitude of the radiofrequency field and its effects in neuronal tissue, but we cannot rule out the possibility that this relationship could be nonlinear.

In summary, this study provides evidence that in humans RF-EMF exposure from cell phone use affects brain function, as shown by the regional increases in metabolic activity. It also documents that the observed effects were greatest in brain regions that had the highest amplitude of RF-EMF emissions (for the specific cell phones used in this study and their position relative to the head when in use), which suggests that the metabolic increases are secondary to the absorption of RF-EMF energy emitted by the cell phone. Further studies are needed to assess if these effects could have potential long-term harmful consequences.

Acknowledgments

Funding/Support: This study was carried out at Brookhaven National Laboratory (BNL) and was supported by the Intramural Research Program of the National Institutes of Health (NIH) and by infrastructure support from the Department of Energy.

Role of Sponsor: The funding agencies had no role in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; or the preparation, review, or approval of the manuscript.

REFERENCES

1. Dubey RB, Hanmandlu M, Gupta SK. Risk of brain tumors from wireless phone use. J Comput Assist Tomogr. 2010; 34(6):799–807. [PubMed: 21084892]
2. Schönborn F, Burkhardt M, Kuster N. Differences in energy absorption between heads of adults and children in the near field of sources. Health Phys. 1998; 74(2):160–168. [PubMed: 9450585]
3. Kleinlogel H, Dierks T, Koenig T, Lehmann H, Minder A, Berz R. Effects of weak mobile phone–electromagnetic fields (GSM, UMTS) on event related potentials and cognitive functions. Bioelectromagnetics. 2008; 29(6):488–497. [PubMed: 18421712]
4. Hyland GJ. Physics and biology of mobile telephony. Lancet. 2000; 356(9244):1833–1836. [PubMed: 11117927]
5. Wainwright P. Thermal effects of radiation from cellular telephones. Phys Med Biol. 2000; 45(8): 2363–2372. [PubMed: 10958200]
6. van Rongen E, Croft R, Juutilainen J, et al. Effects of radiofrequency electromagnetic fields on the human nervous system. J Toxicol Environ Health B Crit Rev. 2009; 12(8):572–597. [PubMed: 20183535]
7. Huber R, Treyer V, Borbély AA, et al. Electromagnetic fields, such as those from mobile phones, alter regional cerebral blood flow and sleep and waking EEG. J Sleep Res. 2002; 11(4):289–295. [PubMed: 12464096]
8. Huber R, Treyer V, Schuderer J, et al. Exposure to pulse-modulated radio frequency electromagnetic fields affects regional cerebral blood flow. Eur J Neurosci. 2005; 21(4):1000–1006. [PubMed: 15787706]
9. Haarala C, Aalto S, Hautzel H, et al. Effects of a 902 MHz mobile phone on cerebral blood flow in humans. Neuroreport. 2003; 14(16):2019–2023. [PubMed: 14600490]
10. Aalto S, Haarala C, Bruck A, et al. Mobile phone affects cerebral blood flow in humans. J Cereb Blood Flow Metab. 2006; 26(7):885–890. [PubMed: 16495939]
11. Mizuno Y, Moriguchi Y, Hikage T, et al. Effects of W-CDMA 1950 MHz EMF emitted by mobile phones on regional cerebral blood flow in humans. Bioelectromagnetics. 2009; 30(7):536–544. [PubMed: 19475648]
12. Sirotin YB, Das A. Anticipatory haemodynamic signals in sensory cortex not predicted by local neuronal activity. Nature. 2009; 457(7228):475–479. [PubMed: 19158795]
13. Fox PT, Raichle ME, Mintun MA, Dence C. Non-oxidative glucose consumption during focal physiologic neural activity. Science. 1988; 241(4864):462–464. [PubMed: 3260686]

14. Devor A, Hillman EM, Tian P, et al. Stimulus-induced changes in blood flow and 2-deoxyglucose uptake dissociate in ipsilateral somatosensory cortex. J Neurosci. 2008; 28(53):14347–14357. [PubMed: 19118167]
15. Iadecola C, Nedergaard M. Glial regulation of the cerebral microvasculature. Nat Neurosci. 2007; 10(11):1369–1376. [PubMed: 17965657]
16. Sokoloff L, Reivich M, Kennedy C, et al. The [14C]deoxyglucose method for the measurement of local cerebral glucose utilization. J Neurochem. 1977; 28(5):897–916. [PubMed: 864466]
17. Wang G-J, Volkow ND, Roque CT, et al. Functional importance of ventricular enlargement and cortical atrophy in healthy subjects and alcoholics as assessed with PET, MR imaging, and neuropsychologic testing. Radiology. 1993; 186(1):59–65. [PubMed: 8416587]
18. Friston KJ, Holmes AP, Worsley KJ, et al. Statistical parametric maps in functional imaging. Hum Brain Mapp. 1995; 2:189–210.
19. Volkow ND, Tomasi D, Wang GJ, et al. Effects of low-field magnetic stimulation on brain glucose metabolism. Neuroimage. 2010; 51(2):623–628. [PubMed: 20156571]
20. Ferreri F, Curcio G, Pasqualetti P, et al. Mobile phone emissions and human brain excitability. Ann Neurol. 2006; 60(2):188–196. [PubMed: 16802289]
21. Cardis E, Deltour I, Mann S, et al. Distribution of RF energy emitted by mobile phones in anatomical structures of the brain. Phys Med Biol. 2008; 53(11):2771–2783. [PubMed: 18451464]
22. Cotgreave IA. Biological stress responses to radio frequency electromagnetic radiation. Arch Biochem Biophys. 2005; 435(1):227–240. [PubMed: 15680925]
23. Nittby H, Grafström G, Eberhardt JL, et al. Radiofrequency and extremely low-frequency electromagnetic field effects on the blood-brain barrier. Electromagn Biol Med. 2008; 27(2):103–126. [PubMed: 18568929]
24. Söderqvist F, Carlberg M, Hansson Mild K, Hardell L. Exposure to an 890-MHz mobile phone-like signal and serum levels of S100B and transthyretin in volunteers. Toxicol Lett. 2009; 189(1):63–66. [PubMed: 19427372]
25. Siebner HR, Peller M, Bartenstein P, et al. Activation of frontal premotor areas during suprathreshold transcranial magnetic stimulation of the left primary sensorimotor cortex: a glucose metabolic PET study. Hum Brain Mapp. 2001; 12(3):157–167. [PubMed: 11170307]
26. Vlassenko AG, Rundle MM, Mintun MA. Human brain glucose metabolism may evolve during activation. Neuroimage. 2006; 33(4):1036–1041. [PubMed: 17035047]
27. Vaishnavi SN, Vlassenko AG, Rundle MM, et al. Regional aerobic glycolysis in the human brain. Proc Natl Acad Sci U S A. 2010; 107(41):17757–17762. [PubMed: 20837536]
28. Sanganahalli BG, Herman P, Hyder F. Frequency-dependent tactile responses in rat brain measured by functional MRI. NMR Biomed. 2008; 21(4):410–416. [PubMed: 18435491]
29. Blomqvist G, Seitz RJ, Sjögren I, et al. Regional cerebral oxidative and total glucose consumption during rest and activation studied with positron emission tomography. Acta Physiol Scand. 1994; 151(1):29–43. [PubMed: 8048334]
30. Yakymenko I, Sidorik E. Risks of carcinogenesis from electromagnetic radiation of mobile telephony devices. Exp Oncol. 2010; 32(2):54–60. [PubMed: 20693976]
31. Lehrer S, Green S, Stock RG. Association between number of cell phone contracts and brain tumor incidence in nineteen U.S. States. J Neurooncol. 2011; 101(3):505–507. [PubMed: 20589524]
32. Hardell L, Carlberg M. Mobile phones, cordless phones and the risk for brain tumours. Int J Oncol. 2009; 35(1):5–17. [PubMed: 19513546]
33. Myung SK, Ju W, McDonnell DD, et al. Mobile phone use and risk of tumors: a meta-analysis. J Clin Oncol. 2009; 27(33):5565–5572. [PubMed: 19826127]
34. Inskip PD, Tarone RE, Hatch EE, et al. Cellular-telephone use and brain tumors. N Engl J Med. 2001; 344(2):79–86. [PubMed: 11150357]
35. INTERPHONE Study Group. Brain tumour risk in relation to mobile telephone use. Int J Epidemiol. 2010; 39(3):675–694. [PubMed: 20483835]
36. Inskip PD, Hoover RN, Devesa SS. Brain cancer incidence trends in relation to cellular telephone use in the United States. Neuro Oncol. 2010; 12(11):1147–1151. [PubMed: 20639214]

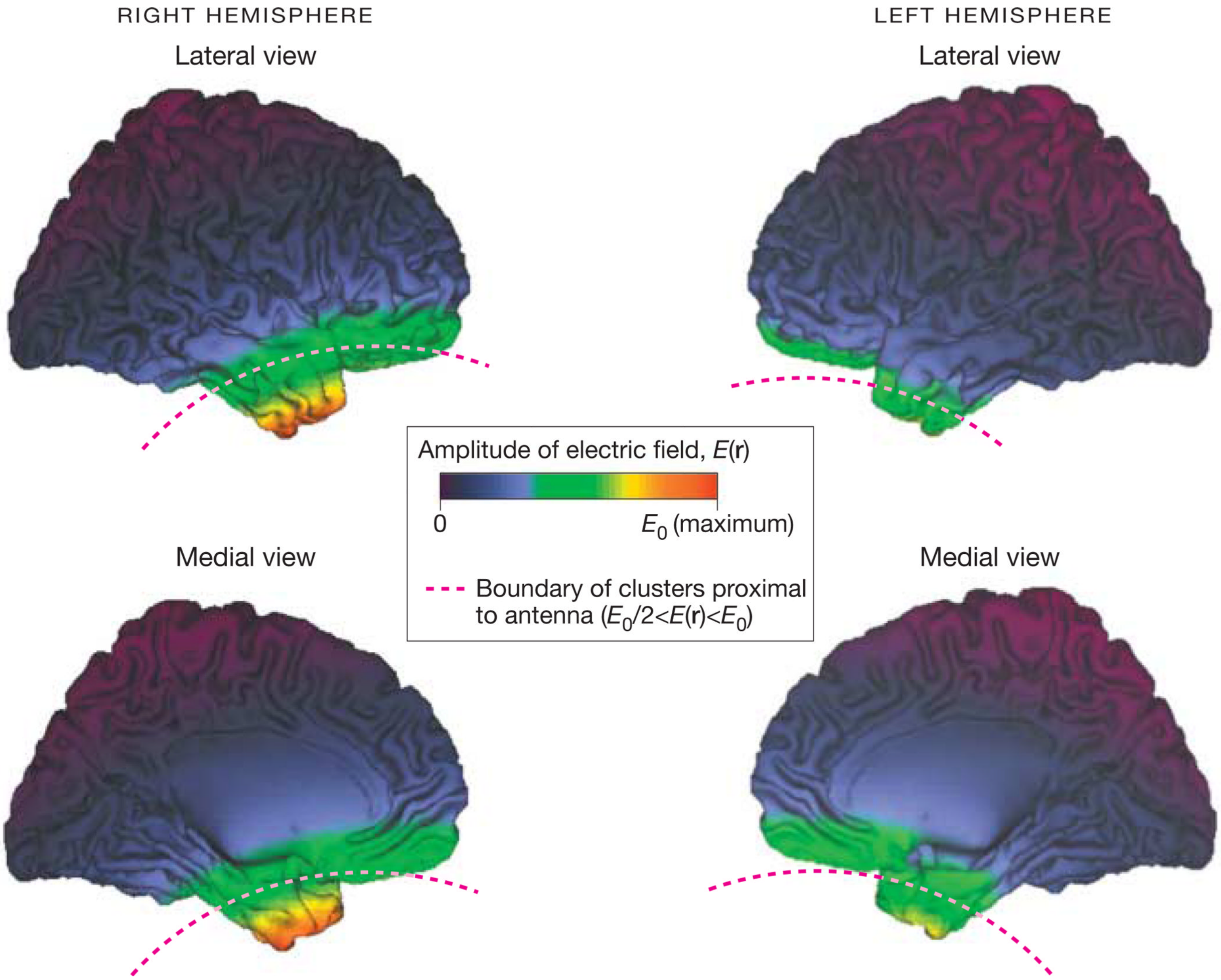


Figure 1. Amplitude of the Electric Field Emitted by the Right Cellular Telephone Antenna Rendered on the Surface of the Human Brain

E_0 indicates maximal field value. Clusters proximal to the antenna are inferior to the red dashed line. Images created using the freeware Computerized Anatomical Reconstruction and Editing Toolkit (CARET) version 5.0 (http://brainvis.wustl.edu/wiki/index.php/Caret:About).

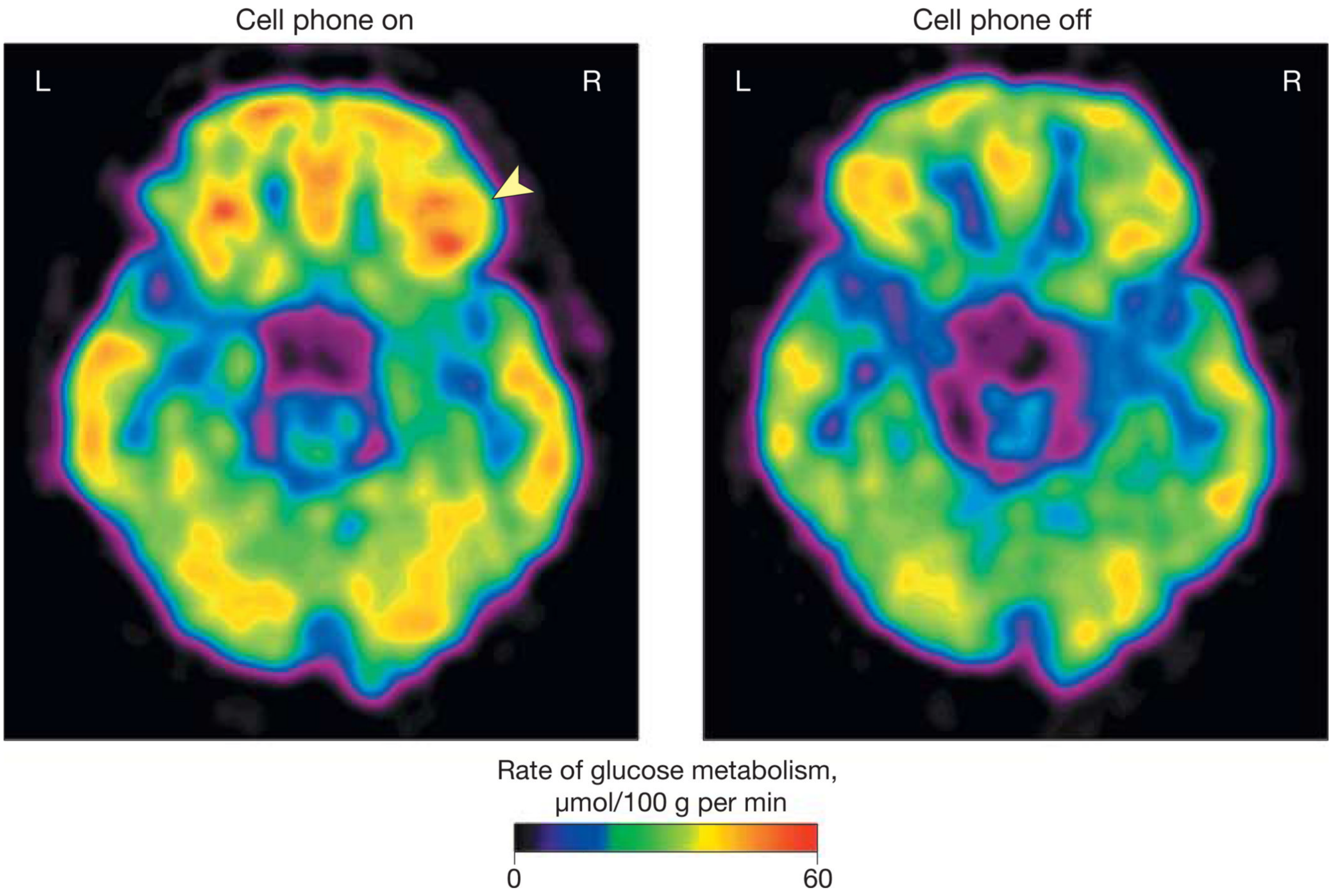


Figure 2. Brain Glucose Metabolic Images Showing Axial Planes at the Level of the Orbitofrontal Cortex

Images are from a single participant representative of the study population. Glucose metabolism in right orbitofrontal cortex (arrowhead) was higher for the “on” than for the “off” condition (see “Methods” for description of conditions).

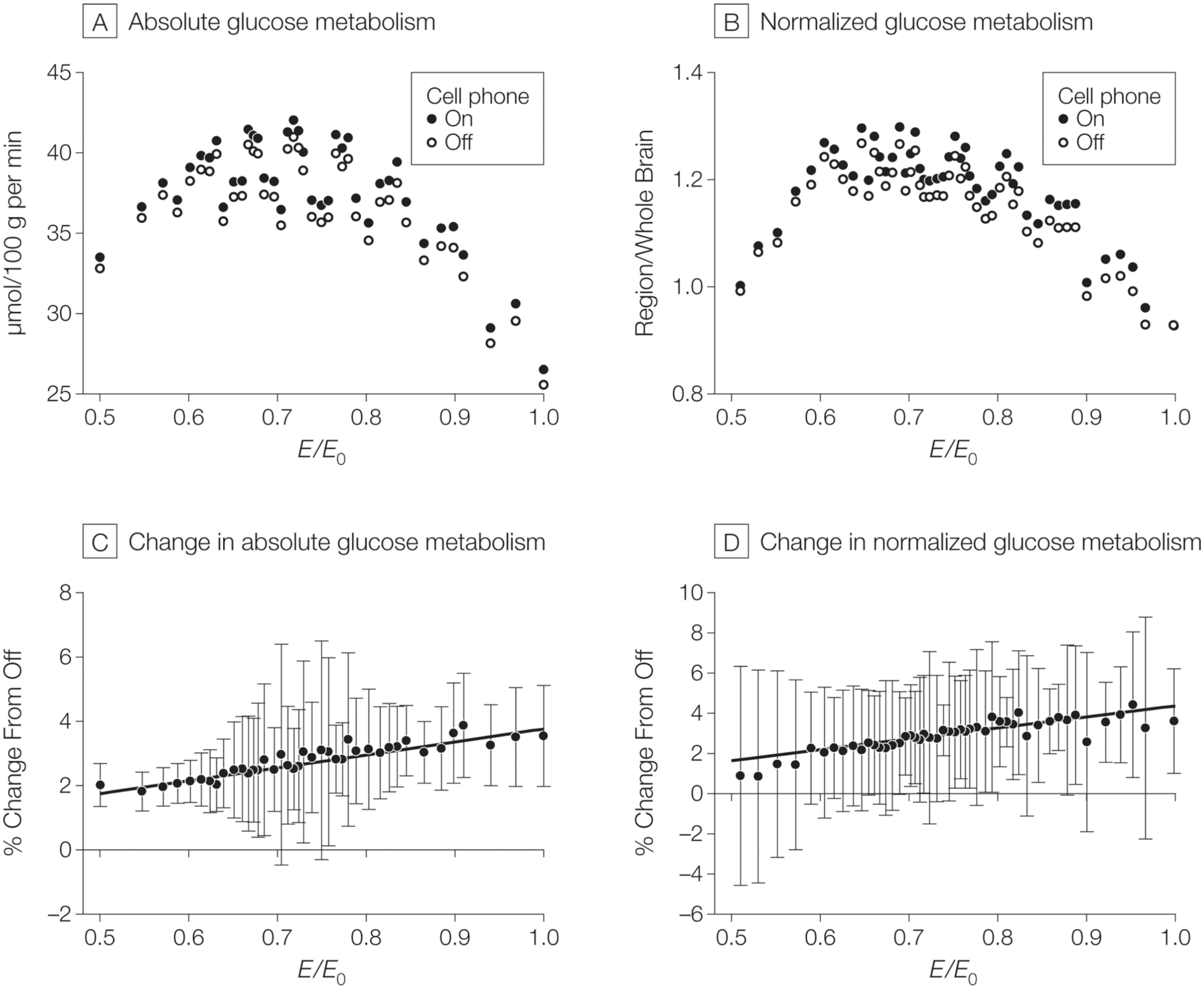


Figure 3. Measures of Absolute and Normalized Glucose Metabolism and Correlation Between Estimated Electromagnetic Field Amplitudes and Increases in Measures (N = 47 Participants)

A and B, Mean measures of absolute glucose metabolism (μmol/100 g per minute) and normalized glucose metabolism (region/whole brain; units cancel) in regions with increased metabolism during "on" vs "off" conditions (see "Methods" for description of conditions) in the brain area within the spherical constraint, $E_0/2 < E(\mathbf{r}) < E_0$ (where E_0 indicates maximal field value and $E(\mathbf{r})$ indicates amplitude of the theoretical electromagnetic field) and the $E(r)$ emitted by the antenna of the right cellular telephone. Absolute = 40 clusters; 2000 voxels were activated within searching volume and grouped into clusters of 50 voxels each; normalized = 48 clusters; 2400 voxels were activated within searching volume and grouped into clusters of 50 voxels each. Range of variability (95% confidence interval [CI]): 9–21 μmol/100 g per minute (panel A) and 0.29–0.57 (panel B). C and D, Regression lines between cell phone–related increases in absolute and normalized glucose metabolism (both expressed as % change from the off condition) in brain regions within the spherical constraint, $E_0/2 < E(\mathbf{r}) < E_0$, and the theoretical electric field, $E(\mathbf{r})$, emitted by the antenna of the right cell phone. Increases significantly correlated with estimated electromagnetic field amplitudes (absolute: $R = 0.95$, $P < .001$; normalized: $R = 0.89$, $P < .001$). Data markers indicate mean metabolic measures; error bars, 95% CIs. Linear regression lines were fitted to the data using Interactive Data Language version 6.0.

Table 1

Characteristics and Cellular Telephone Histories of Participants (N = 47)

Characteristic		No. (%)
Age, mean (SD), y		31 (9)
Sex		
	Men	23 (48.9)
	Women	24 (51.1)
Body mass index, mean (SD)[a]		26 (3)
Handedness		
	Right-handed	43 (91.5)
	Left-handed	4 (8.5)
Education mean (SD), y		14 (2)
Cell phone use, mean (SD) [range], min/mo		1500 (1850) [15–9000]
Ear favored for use		
	Right	38 (80.9)
	Left	9 (19.1)

[a] Calculated as weight in kilograms divided by height in meters squared.

Table 2

Statistical Parametric Mapping For Brain Regions Showing Higher Glucose Metabolism With Cellular Telephone On Than Off

Brain Region	Volume[a]	Brodmann Area	Region Coordinates, mm[b] x	y	z	Z Score, On vs Off	P_{corr}[c]	On vs Off, Mean Difference (95% CI)
Absolute glucose metabolism								
Right inferior frontal	2649	47	18	23	−18	2.7	.05	2.4 (0.67–4.2)[d]
Right superior temporal		38	24	12	−37	2.6		
Right middle frontal		11	23	38	−15	2.6		
Normalized glucose metabolism								
Right superior temporal	2910	38	27	2	−35	3.1	.05	7.8 (2.7–12.9)[d]
Right inferior frontal		47	16	27	−16	3.1		
Right middle frontal		11	23	38	−15	3.1		

Abbreviation: CI, confidence interval.

[a] No. of voxels. One voxel = 0.008 mm^3.

[b] Coordinates on the Montreal Neurological Institute stereotactic space corresponding to distance (in mm) for *x* (left to right), *y* (anterior to posterior), and *z* (superior to inferior).

[c] See “Methods” for details of calculation of Bonferroni-corrected *P* value.

[d] Values for absolute metabolism reported in µmol/100 g per minute; those for normalized metabolism reported as percentages.

Journal of Integrative Neuroscience, Vol. 10, No. 2 (2011) 189–202
© Imperial College Press
DOI: 10.1142/S0219635211002695

ICP Imperial College Press
www.icpress.co.uk

EFFECTS OF WI-FI SIGNALS ON THE P300 COMPONENT OF EVENT-RELATED POTENTIALS DURING AN AUDITORY HAYLING TASK

CHARALABOS C. PAPAGEORGIOU[*,‡], CHRISSANTHI D. HOUNTALA[†,§],
ARGIRO E. MAGANIOTI[†], MILTIADES A. KYPRIANOU[‡],
ANDREAS D. RABAVILAS[‡], GEORGE N. PAPADIMITRIOU[*]
and CHRISTOS N. CAPSALIS[†]

[*]*University of Athens, 1st Department of Psychiatry*
Eginition Hospital, 74 Vas.Sophias Ave
Athens, 11528, Greece

[†]*National Technical University of Athens*
Department of Electrical Engineering
Division of Information Transmission Systems and Material Technology
9 Iroon Polytecneioy str., Athens, 15773, Greece

[‡]*University Mental Health Research Institute (Umhri)*
2 Soranou tou Efesiou (PO Box 66 517) Athens, 15601, Greece
[§]*cchountala@teemail.gr*

Received 25 September 2010
Accepted 7 February 2011

The P300 component of event-related potentials (ERPs) is believed to index attention and working memory (WM) operation of the brain. The present study focused on the possible gender-related effects of Wi-Fi (Wireless Fidelity) electromagnetic fields (EMF) on these processes. Fifteen male and fifteen female subjects, matched for age and education level, were investigated while performing a modified version of the Hayling Sentence Completion test adjusted to induce WM. ERPs were recorded at 30 scalp electrodes, both without and with the exposure to a Wi-Fi signal. P300 amplitude values at 18 electrodes were found to be significantly lower in the response inhibition condition than in the response initiation and baseline conditions. Independent of the above effect, within the response inhibition condition there was also a significant gender X radiation interaction effect manifested at 15 leads by decreased P300 amplitudes of males in comparison to female subjects only at the presence of EMF. In conclusion, the present findings suggest that Wi-Fi exposure may exert gender-related alterations on neural activity associated with the amount of attentional resources engaged during a linguistic test adjusted to induce WM.

Keywords: Wi-Fi; P300 ERP component; Hayling; gender; EMF.

1. Introduction

Concern of health effects due to EMF, specifically radiofrequency (RF) exposure is currently arising. Numerous studies have investigated the potential effects of EMF,

---

[§] Corresponding author.

mainly those emitted by GSM mobile phones (Global System for Mobile communications) on cognitive functioning.

In a recent meta-analytic review [1], taking into consideration 19 studies, it was concluded that EMFs may have a small impact on human attention and working memory without clarifying the exact nature of this impact. In particular, it has been reported that human attention measured by the subtraction task was mildly affected in regard to decreased reaction time. Additionally, working memory being measured by the N-back test seems to be affected. The significant effects concerning the N-back test for working memory showed discrepant effect sizes: under condition 0-back, target response time was lower under exposure, while under condition 2-back, target response time increased. The number of errors under condition 2-back for non-targets appears to be higher under exposure. At other levels of the N-back test, no significant effect sizes were detected.

Event-related potentials (ERPs) are one of the most informative and dynamic methods of monitoring the information stream in the living brain. Because of the high time resolution, ERPs allow the investigation of the time course of auditory processing down to the scale of milliseconds. The P300 component of ERPs is thought to reflect attentional operation resources when working memory (WM) updating is engaged [13, 33, 48]. The P300 amplitude is thought to index attentional processing of target stimulus events — phenomena that appear related to memory processing, while the P300 peak latency is proportional to the time required to detect and evaluate a target stimulus [18, 36, 48].

As far as the effects of EMFs on the P300 component are concerned, the existing literature is rather conflicting. During an oddball task no effect has been found on the P300 component under the exposure of pulsed, GSM or Universal Mobile Telecommunications System (UMTS) signals [31, 55]. However in another study which examined the effects of electromagnetic fields emitted by GSM mobile phones on the human P300 component during an auditory task, results suggested that mobile phone exposure may affect neural activity [22].

A series of studies by our team provided evidence that it is necessary to examine the possible impact of EMF on brain activity separately for males and females, in order to unveil the possible confounding effects of gender and its interaction with EMF [24, 41, 46].

As far as Wi-Fi signals are concerned, due to the fact that daily public exposure to such signals increases rapidly, several investigations on its potential adverse health effects and dosimetry studies are ongoing [11, 17], although the exposure level is low compared to other sources [37].

In view of the above considerations, it can be hypothesized that the electrophysiological brain activity, as reflected by P300, in association with cognitive task operations, could be of value in identifying possible pathophysiological alterations evoked by Wi-Fi signals and their connection with gender. Thus, the present study was designed to determine whether the presence of Wi-Fi signals affects the patterns of P300 ERP component elicited during a Hayling Sentence Completion test adjusted to induce working memory (WM) operation [3, 5, 6]. Contemporary neuropsychological views define WM as the capacity to keep information "online" as necessary for an ongoing task [2, 10]. Accordingly, WM is thought to be in the service of complex cognitive activities, such as reasoning, monitoring, problem solving, decision making, planning, and searching/shifting the initiation or inhibition response, thus comprising (among others) a central executive system [19, 38, 40].

2. Materials and Methods

2.1. *Participants*

Thirty healthy individuals (15 men and 15 women, mean age = 23.76 ± 1.67 years, mean education = 16.9 ± 1.06 years) participated in the experiment. The participants were homogeneous with regards to age and educational level and had no history of any hearing problem. Informed consent was obtained from all subjects.

2.2. *Hayling sentence completion test*

The modified version of the Hayling Sentence Completion test used in the present study is made up from three different conditions: response initiation, response inhibition and baseline. In the response initiation condition, participants completed auditory presented sentences with a word clearly suggested by the context. In the response inhibition condition, participants produced a word that made no sense in the context of an auditory-presented sentence from which the last word was missing. Finally in the baseline condition, subjects were asked to repeat the last word of the presented sentence. The sentences were presented through earphones to the participants and the administration order of the three conditions was counterbalanced. The duration of the sentences was from 3–5 s. After the presentation of each sentence, there was a 500-ms EEG recording period, then a warning stimulus (100-ms duration, 65 dB, 500 Hz) was given, followed by an interval of 900 ms; the warning stimulus was then repeated. Individuals were instructed to give their response after the conclusion of the second warning stimulus. Each condition of the task contained 30 sentences. Before the ERP recording, there was a training period for each condition of the Hayling test in order for the participants to comprehend the nature of a correct response.

It should be noted that the task design involved the 1600-ms period after the participants had heard the sentence and before they were required to respond, in order to avoid interference during the recording session. The onset of ERP recording was 500 ms after the end of the auditory presentation of the sentence (Table 1).

2.3. *EMF exposure*

The subjects performed the tasks twice, with and without radiation, with an interval of two weeks between the measurements. The order in which the subject was exposed

Table 1. Sequence of events in each experimental trial.

Sequence of Action	Duration of Action
Auditory sentence presentation	3–5 s
EEG recording	500 ms
Warning stimulus*	100 ms
ERP recording*,†	1 s
Warning stimulus repetition	100 ms
Response onset	Within 5 s
Period between response completion and onset of next sentence presentation	4–9 s

Notes: *Simultaneous onset of warning stimulus and of ERP recording.

†Peak amplitudes were measured relatively to the mean amplitude of the 100 ms pre-stimulus baseline period; latency measurements were computed relatively to warning stimulus onset.

at the EMF (exposure at the first or second visit) was random. The EMF was emitted by a Wi-Fi access point that was operating at 2.45-GHz frequency. The access point was present at both tasks and the subjects were blinded to the presence or absence of the radiation. The Wi-Fi signal was radiated by a dual dipole antenna, with 20-dBm power and orthogonal frequency-division multiplexing (OFDM) modulation. The access point was placed at a distance of 1.5 m from the head. The field strength was 0.49 V/m at the point where the subjects' head was standing. According to Kapareliotis *et al.* [29] there is no evidence that a Wi-Fi signal causes interference at the EEG recording at the distance of 1.5 m from the EEG electrodes.

The experiment was conducted in a Faraday room, which screened any electromagnetic interference that could affect the measurements. The attenuation of the mean field was more than 30 dB.

2.4. *Recordings*

Electroencephalographic (EEG) activity was recorded from 30 scalp Ag/AgCl electrodes (F7, FC5, C3, CP1, P3, Fpz, Afz, Cz, O1, O2, F8, FC6, T4, CP2, P4, CP6, T6, F3, FC1, T3, CP5, T5, FP1, FP2, Fz, Pz, Oz, F4, FC2, C4) based on the International 10–20 system of electroencephalography [26]. Linked ear lobes served as reference. Electrode resistance was kept constantly below 5 kΩ. The bandwidth of the amplifiers was between 0.05–35 Hz in order to avoid interference of the power supply network's signal, which is at 50 Hz. Eye movements were recorded with the use of electro-oculogram (EOG) and recordings with EEG higher than 75 μV were excluded. The evoked biopotential signal was digitalized at a sampling rate of 1 kHz and was averaged by a computerized system.

The signals were recorded for a 1500-ms interval, which means 500 ms before the first warning stimulus (EEG) and 100 ms after that (ERP).

2.5. *Data transformations*

For each question, 1500 data points, each corresponding to time segments of 1 ms duration for each electrode, were saved. This procedure was done separately for each EMF condition. The final data for analysis for each subject and condition consisted of 1500 amplitude values for each electrode, expressed in μVolts corresponding to the 1500 ms of the time period [46], 500 ms before the onset of the first warning stimulus (EEG), and 1000 ms after the onset (ERP).

In order to optimize the signal-to-noise ratio for each subject, each channel ERP amplitudes were averaged using the voltage over the 100-ms pre-stimulus epoch as the baseline. An algorithm was used for identifying the amplitude and latency of the positive peak between 220 and 500 ms after the onset of the first warning stimulus. The sLORETA software was used to calculate and compare the relevant scalp maps [43, 47].

2.6. *Statistical analysis*

The values of the P300 amplitudes at the 30 leads were subjected to multivariate analysis of variance (MANOVA) with the three Hayling conditions (A, B and C), the two radiation conditions (OFF and Wi-Fi exposure) and the gender (male and female) as the between subjects factors. The effects of the interactions between the factors were also taken into consideration. In cases where statistically significant effects were discovered, multiple post-hoc pairwise comparisons were applied with Bonferroni corrections. Statistical significance was set at the 0.05 level.

3. Results

Figure 1 shows the ERP waveforms at the FPz lead averaged over all measurements and over the three different Hayling conditions. The perpendicular dotted lines show the time window (220–500 ms) within which the P300 component was sought. The subjects' ERP patterns at the specific electrode are characteristic of the patterns at virtually all the electrodes. The pattern of the ERPs at condition B is quite distinct from the ones at conditions A and C. There is, for all the conditions, a clearly defined P300 component. Post-hoc comparisons showed that the P300 amplitude values at condition B are lower than at both conditions A and C, while conditions A and C are practically equal. Specifically, differences between conditions A and B achieve statistical significance at 18/30 leads, which (as Fig. 2 shows) form a cohesive network.

Exclusively within Hayling condition B, a significant Gender X Radiation interaction effect is manifested. The nature of this interaction is clarified in Fig. 3 which shows the mean P300 amplitudes at the CP6 lead for male and female subjects at the presence and absence of the Wi-Fi signal. In the absence of the Wi-Fi signal, male subjects had greater P300 amplitudes than female subjects, but the difference was not statistically significant. Switching the Wi-Fi signal on significantly reduces

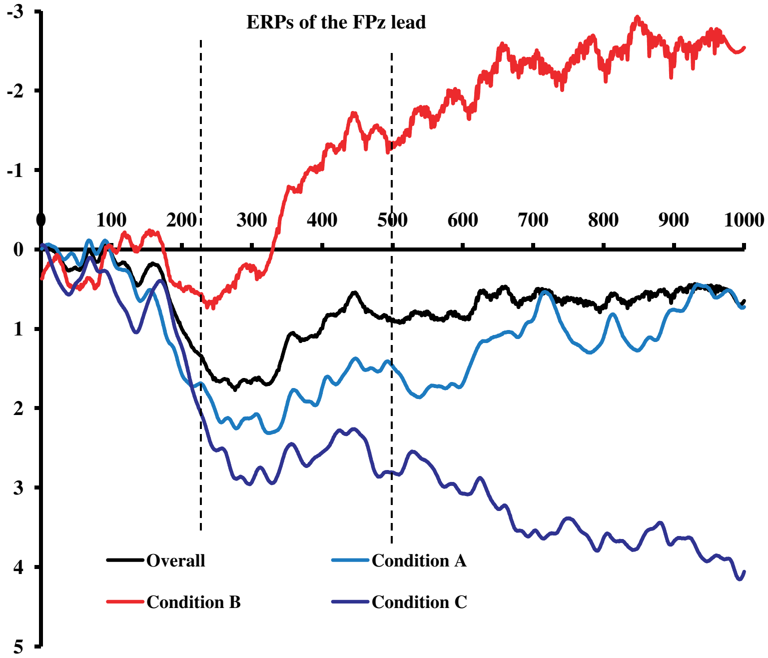


Fig. 1. Average ERP waveforms at the FPz lead for the overall measurements and for the three different Hayling conditions. The perpendicular dotted lines show the time window within which the P300 component was sought.

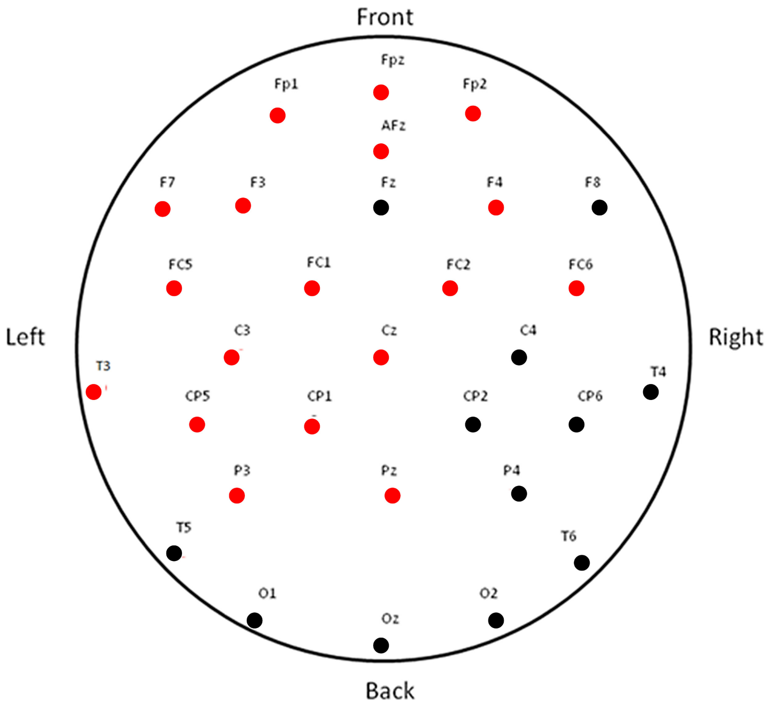


Fig. 2. Comparisons of the P300 component between conditions A and B. Leads at which differences are statistically significant are shown in red.

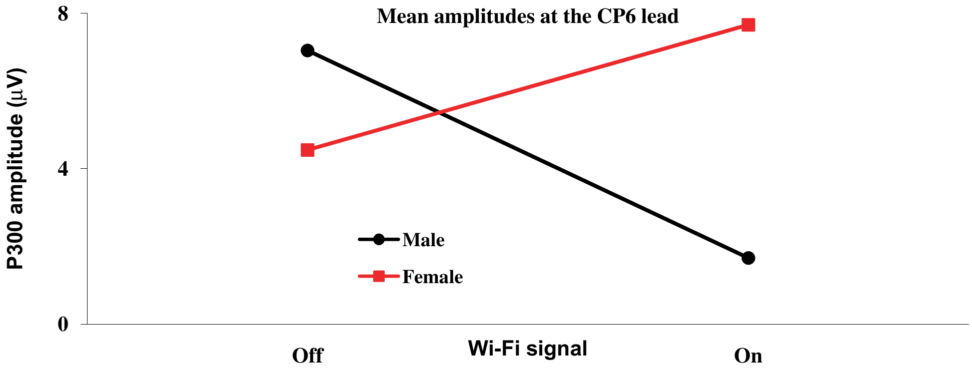


Fig. 3. Mean P300 amplitudes at the CP6 lead for male and female subjects at the presence and absence of the Wi-Fi signal at Hayling condition B.

the P300 amplitudes of the males, while that of the females is enhanced. As a consequence, at the "on" condition, the P300 amplitude of the males is significantly lower than that of the females. The behavior depicted in Fig. 3 is the same for the other leads. As a result of this pattern, while at the "off" condition, there were no significant differences of the P300 amplitudes between males and females (except for electrode AFz), at the "on" condition (as post-hoc pairwise comparisons with Bonferroni corrections proved) significant differences were observed at 15/30 electrodes (Table 2). These leads, as well as the corresponding activation maps, where statistically significant differences between the two genders occur, are shown in Fig. 4.

4. Discussion

There is a significant interaction effect of the gender X radiation that is exclusively manifested in Hayling B condition; this is due to the relative reduction of the amplitudes for the male subjects at the "on" in comparison to the "off" radiation condition and the relative increase in the respective values for the female subjects. As a result, the P300 amplitudes of males are significantly lower than of females at 15 electrodes at the "on" condition.

The comparison between experimental conditions of a modified version of the Hayling Sentence Completion test adjusted to induce WM showed a reduced activation of the P300 component during the inhibition condition (B), than at both the initiation (A) and baseline (C) conditions, while conditions A and C are practically equal. The Hayling condition effect was significant at 18 of the 30 leads over widespread areas of the scalp.

The results of the present study may be interpreted in the light of the psychophysiological and brain-imaging studies related to the P300 ERP waveform and the Hayling test. It has been suggested that P300 originates from task conditions involving working memory operation [13, 33]. In addition, P300 amplitude is thought to be sensitive to the amount of attentional resources engaged during the execution

Table 2. Mean ± standard deviations of the P300 component for male and female subjects at the "off" and "on" radiation condition in Hayling condition B. p-values in bold denote statistically significant differences.

	OFF			ON		
Leads	Male	Female	p-values	Male	Female	p-values
F7	0.74 ± 5.14	2.58 ± 4.57	0.31	1.77 ± 4.50	2.34 ± 4.73	0.74
FC5	2.56 ± 3.19	2.34 ± 4.55	0.88	1.12 ± 2.82	2.79 ± 4.25	0.23
C3	5.62 ± 5.45	2.77 ± 5.34	0.16	1.79 ± 6.53	5.64 ± 4.72	0.08
CP1	2.73 ± 3.34	2.37 ± 4.96	0.81	0.51 ± 2.45	3.43 ± 4.16	**0.03**
P3	2.89 ± 3.78	2.11 ± 4.82	0.63	0.28 ± 2.41	2.84 ± 3.46	**0.03**
Fpz	2.25 ± 3.63	2.08 ± 4.57	0.91	−0.25 ± 2.60	3.12 ± 4.17	**0.02**
Afz	0.62 ± 4.38	4.69 ± 5.71	**0.04**	1.83 ± 5.37	2.94 ± 6.29	0.62
Cz	1.38 ± 3.76	3.63 ± 5.17	0.18	0.74 ± 4.43	2.40 ± 5.42	0.38
O1	2.88 ± 3.55	2.18 ± 4.61	0.65	0.52 ± 2.61	3.19 ± 3.51	**0.03**
O2	2.55 ± 3.73	1.36 ± 3.75	0.39	−1.18 ± 2.83	2.65 ± 3.75	**0.00**
F8	2.54 ± 3.78	0.90 ± 4.67	0.30	−0.21 ± 3.18	1.89 ± 3.24	0.09
FC6	1.21 ± 3.56	2.94 ± 4.59	0.26	0.26 ± 4.48	3.38 ± 5.11	0.09
T4	1.55 ± 3.60	2.86 ± 4.49	0.38	−0.09 ± 6.02	3.73 ± 4.03	**0.05**
CP2	2.70 ± 3.67	2.19 ± 4.59	0.74	0.40 ± 2.92	2.91 ± 5.06	0.12
P4	2.94 ± 3.89	1.94 ± 4.72	0.53	0.76 ± 2.65	2.97 ± 3.93	0.09
CP6	7.04 ± 5.96	4.48 ± 4.90	0.21	1.70 ± 5.59	7.70 ± 6.38	**0.01**
T6	2.14 ± 3.74	2.38 ± 4.54	0.88	−0.36 ± 3.13	3.47 ± 4.66	**0.02**
F3	1.62 ± 3.60	1.82 ± 4.48	0.89	−0.78 ± 3.55	1.70 ± 3.05	**0.05**
FC1	2.29 ± 3.62	2.88 ± 4.07	0.68	0.50 ± 3.00	3.17 ± 3.96	**0.05**
T3	2.18 ± 3.87	2.01 ± 4.54	0.92	−0.35 ± 2.85	2.93 ± 4.59	**0.03**
CP5	2.53 ± 3.59	1.84 ± 4.50	0.65	0.22 ± 2.34	2.67 ± 4.21	0.07
T5	1.78 ± 3.47	1.38 ± 4.32	0.78	−0.50 ± 2.01	2.03 ± 3.51	**0.03**
FP1	0.71 ± 4.31	3.92 ± 6.09	0.11	2.47 ± 5.62	3.72 ± 7.92	0.63
FP2	1.24 ± 5.21	5.06 ± 5.85	0.07	3.26 ± 5.98	2.27 ± 7.31	0.69
Fz	6.09 ± 7.28	4.27 ± 5.96	0.46	3.29 ± 4.84	3.50 ± 2.86	0.89
Pz	2.50 ± 3.88	1.89 ± 4.50	0.70	0.60 ± 2.11	2.18 ± 4.10	0.21
Oz	2.83 ± 3.63	1.05 ± 4.08	0.22	−0.34 ± 2.76	2.16 ± 3.40	**0.04**
F4	1.50 ± 3.73	3.37 ± 5.28	0.27	0.11 ± 3.87	2.61 ± 4.87	0.14
FC2	2.48 ± 2.99	3.22 ± 4.33	0.59	−0.09 ± 3.01	3.44 ± 4.37	**0.02**
C4	2.67 ± 3.81	2.74 ± 4.02	0.96	0.19 ± 4.04	4.42 ± 4.67	**0.01**

of a task [25, 35]. It is postulated that difficult processing tasks that induce high cognitive demand limit attentional resources to resist inhibitory control and produce smaller P300 components [48].

Studies attempting to identify the cerebral generators of the P300 provide evidence that P300 is seen simultaneously, with uniform latency, over widespread areas of the scalp [54] and suggest also, either that it is produced by multiple, relatively independent generators, or that it is a reflection of a central integrated system with widespread connections and impact throughout the brain [14, 44]. However, it is believed that frontal generators are more involved in automated orienting, while temporoparietal generators are more responsive to stimuli, requiring more effort [58].

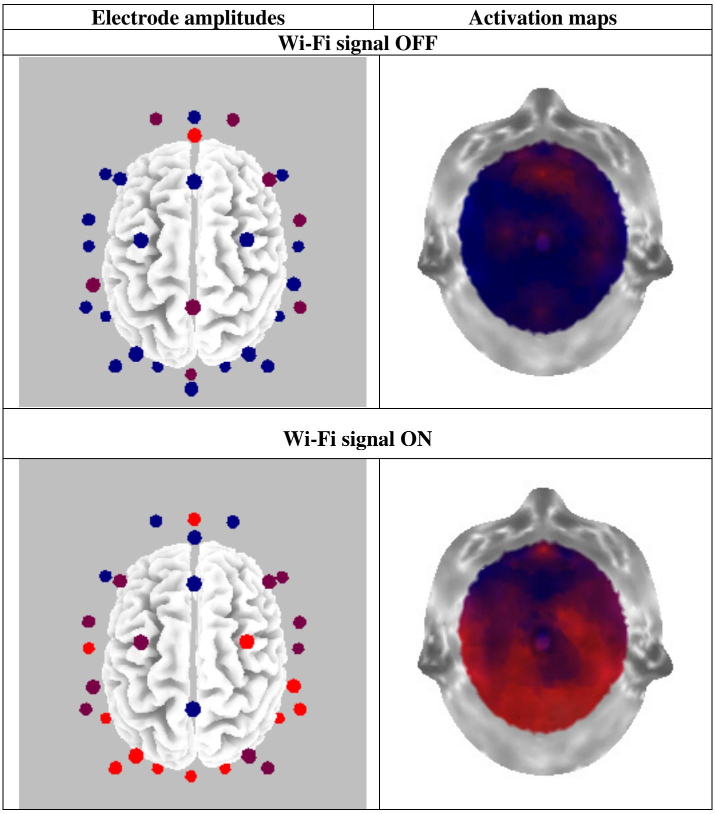


Fig. 4. Comparisons of the electrode amplitudes (left) and activation maps (right) of the P300 component between male and female subjects at the presence (top) and absence (bottom) of the Wi-Fi signal at Hayling B condition. Red color denotes statistically significant differences between the two genders.

In reference to the Hayling test, Collette *et al.* [9] applied PET methodology and found a greater frontal activation during the inhibition than the initiation condition. They attributed the greater activation in the inhibition condition to the complexity of the procedure that involves additional cognitive processes than the processes in the initiation condition that includes planning, semantic search, manipulation of information, selection and evaluation of the response.

Conversely, Nathaniel-James *et al.* [42] using also PET during the application of another version of the Hayling test, found increased activity in prefrontal areas during the initiation as compared to the inhibition condition. A potential explanation provided by the authors is that the initiation condition might rely less on high levels of linguistic processing and more on low levels of word production, generating a functional pattern that could lead to higher frontal activation.

The inconsistency between the findings of the two studies was thought to result from differences in the modified forms of the Hayling test applied in the studies [9]. The Hayling test measures executive functioning and in this regard, although it has been suggested that the prefrontal cortex possesses a pivotal role in executive control [32, 57], research evidence emphasizes the importance of additional brain areas, such as broad cortical and subcortical networks, including thalamic pathways [27]. This broader view might result from the fact that the tests applied for assessment of executive functioning are complex and induce a wide range of skills, thus complicating efforts to identify a unitary interpretation framework.

In the EMF "off" condition, female subjects had significantly lower P300 amplitudes than male subjects. The obtained results may be interpreted in terms of the "neural efficiency hypothesis", which postulates a more efficient use of brain resources in people who are more skilled (trained) than those less skilled [20]. This is in accordance with the notion that a linguistic-related executive functioning has a stronger effect on women than on men [7, 28, 30], and indicate that attentional resources processing when WM updating is engaged during a go and no-go linguistic task undergoes stronger facilitation in women than in men. It is worth noting that previous studies demonstrated also that P300 amplitudes were greater in males than females, supporting the notion that the P300 is sensitive to gender. For example, Oliver-Rodriguez *et al.* [45] studying facial attractiveness and its emotional component, found that P300 amplitudes were greater in male participants.

The relationship between gender and the P300 has been controversial, as some studies found no gender differences [8, 23, 39, 56, 59]. These contradictory findings are difficult to explain. One hypothesis could be based on the account that the difference between the two genders concerning the P300 patterns is attributable to the size and geometry of the head rather than to actual biological and physiological differences [21]. Other possible explanations are seasonal variation [12] and emotion [39, 59]. Furthermore, it has been suggested that hemispheric asymmetry and/or brain lateralization might contribute to these differences [34, 49, 56].

The effect of RF exposure (reduction of amplitudes of the P300 for males and the reverse patterns for females) are in accordance with several studies of our team, regarding gender-related differences in the EEG under 900 MHz and 1800 MHz EMF exposure, similar to that of mobile phones, although the present cognitive task differed from the previous one [24, 41, 46]. Also, Smythe and Costall [53] have reported sex-dependent effects of EMF exposure on the human memory during a memory task.

Emerging evidence provides plausible mechanisms for the explanation of these differences. In particular, central nervous system effects of EMFs have been considered to be secondary to damage to the blood–brain barrier (BBB) permeability [50–52]. It is reasonable to consider the existence of gender-related blood barrier differences, a fact which would explain the fundamental differences between males and females in the intrinsic cognitive processes and in the way they are affected by different types of electromagnetic radiation. Other studies indicate that EMF exposure affects melatonin release. Specifically, a reduced excretion of the urinary metabolite of melatonin among persons using a mobile phone for more than 25 mins per day has been demonstrated [4]. In a study of pubertal individuals, it has been found that nocturnal and diurnal 6-sulfatoxymelatonin excretion is higher in girls [16].

5. Conclusions

To the best of our knowledge, this is the first attempt to investigate the immediate effects of Wi-Fi signals upon brain operation, specifically on the P300 ERP component. Our investigation revealed that P300 amplitude values are decreased for males and increased for females during exposure while performing a Hayling Sentence Completion task. These gender-related differences provide further support to previous studies of our team conducted under different exposure conditions and different auditory tests. As far as the different Hayling tasks are concerned, results show significantly decreased amplitude values for the response inhibition condition in a large area of the brain.

References

[1] Barth A, Winker R, Ponocny-Seliger E, Mayrhofer W, Ponocny I, Sauter C, Vana N, A meta-analysis for neurobehavioural effects due to electromagnetic field exposure emitted by GSM mobile phones, *Occup Environ Med* **65**:342–346, 2008.

[2] Baddeley A, Recent developments in working memory, *Curr Opin Neurobiol* **8**:234–238, 1998.

[3] Beratis I, Rabavilas A, Nanou E, Hountala C, Maganioti A, Capsalis C, Papadimitriou G, Papageorgiou C, Effect of initiation-inhibition and handedness on the patterns of the P50 event-related potential component: A low resolution electromagnetic tomography study, *Behav Brain Funct* **5**:51, 2009.

[4] Burch JB, Reif JS, Noonan CW, Ichinose I, Bachand AM, Koleber TL, Yost MG, Melatonin metabolite excretion among cellular telephone users, *Int J Radiat Biol* **78**:1029–1036, 2002.

[5] Burgess PW, Shallice T, Response suppression, initiation and strategy use following frontal lobe lesions, *Neuropsychologia* **34**:263–273, 1996.

[6] Burgess PW, Shallice T, *Hayling Sentence Completion Test*, Thames Valley Test Co. Ltd, Suffolk-England, 1997.

[7] Canli T, Desmond JE, Zhao Z, Gabrieli JD, Sex differences in the neural basis of emotional memories, *Proc Natl Acad Sci USA* **99**:10789–10794, 2002.

[8] Chu NS, Pattern-reversal visual evoked potentials: Latency changes with gender and age, *Clin Electroencephalogr* **18**:159–162, 1987.

[9] Collette F, Van der Linden M, Delfiore G, Degueldre C, Luxen A, Salmon E, The functional anatomy of inhibition processes investigated with the Hayling task, *Neuroimage* **14**:258–267, 2001.

[10] Collette F, Van der Linden M, Brain imaging of the central executive component of working memory, *Neurosci Biobehav Rev* **26**:105–125, 2002.

[11] de Gannes PF, Taxile M, Duleu S, Hurtier A, Haro E, Geffard M, Ruffié G, Billaudel B, Lévêque P, Dufour P, Lagroye I, Veyret B, A confirmation study of Russian and

Ukrainian data on effects of 2450 MHz microwave exposure on immunological processes and teratology in rats, *Rad Res* **172**:617–624, 2009.

[12] Deldin PJ, Duncan CC, Miller GA, Season, gender, and P300, *Biol Psychol* **39**:15–28, 1994.

[13] Donchin E, Coles MGH, Is the P300 component a manifestation of context updating? *Behav Brain Sci* **11**:357–374, 1988.

[14] Duncan C, Barry R, Connolly J, Fischer C, Michie P, Näätänen R, Polich J, Reinvang I, Van Petten C, Event-related potentials in clinical research: Guidelines for eliciting, recording, and quantifying mismatch negativity, P300, and N400, *Clin Neurophysiol* **120**:1883–1908, 2009.

[15] Eberhardt JL, Persson BRR, Brun AE, Salford LG, Malmgren LOG, Blood–brain barrier permeability and nerve cell damage in rat brain 14 and 28 days after exposure to microwaves from GSM mobile phones, *Electromagn Biol Med* **27**:215–229, 2008.

[16] Fideleff HL, Boquete H, Fideleff G, Albornoz L, Lloret SP, Suarez M, Esquifino AI, Honfi M, Cardinali DP, Gender-related differences in urinary 6-sulfatoxymelatonin levels in obese pubertal individuals, *J Pineal Res* **40**:214–218, 2006.

[17] Foster KR, Radiofrequency Exposure from wireless LANS utilizing Wi-Fi technology, *Health Phys* **92**:280–289, 2007.

[18] Friston K, A theory of cortical responses, *Philos Trans R Soc Lond B Biol Sci* **360**:815–836, 2005.

[19] Glassman RB, A "theory of relativity" for cognitive elasticity of time and modality dimensions supporting constant working memory capacity: Involvement of harmonics among ultradian clocks? *Prog Neuropsychopharmacol Biol Psychiatry* **24**:163–182, 2000.

[20] Grabner RH, Stern E, Neubauer AC, When intelligence loses its impact: Neural efficiency during reasoning in a familiar area, *Int J Psychophysiol* **49**:89–98, 2003.

[21] Guthkelch AN, Bursick D, Sclabassi RJ, The relationship of the latency of the visual P100 wave to gender and head size, *Electroencephalogr Clin Neurophysiol* **68**:219–222, 1987.

[22] Hamblin DL, Wood AW, Croft RJ, Stough C, Examining the effects of electromagnetic fields emitted by GSM mobile phones on human event-related potentials and performance during an auditory task, *Clin Neurophysiol* **115**:171–178, 2004.

[23] Hoffman LD, Polich J, P300, handedness, and corpus callosal size: Gender, modality, and task, *Int J Psychophysiol* **31**:163–174, 1999.

[24] Hountala C, Maganioti A, Papageorgiou C, Nanou E, Kyprianou M, Tsiafakis V, Rabavilas A, Capsalis C, The spectral power coherence of the EEG under different EMF conditions, *Neurosci Lett* **441**:188–192, 2008.

[25] Isreal JB, Chesney GL, Wickens CD, Donchin E, P300 and tracking difficulty: Evidence for multiple resources in dual-task performance, *Psychophysiology* **17**:259–273, 1980.

[26] Jasper H, The ten-twenty electrode system of the international federation, *Electroencephalogr Clin Neurophysiol* **10**:371–375, 1958.

[27] Jurado MD, Rosselli M, The elusive nature of executive functions: A review of our current understanding, *Neuropsychol Rev* **17**:213–233, 2007.

[28] Kansaku K, Kitazawa S, Imaging studies on sex differences in the lateralization of language, *Neurosci Res* **41**:333–337, 2001.

[29] Kapareliotis E, Nanou E, Tsiafakis V, Sotiriou A, Pragiatis L, Capsalis C, Electromagnetic compatibility between Wi-Fi access point and EEG signals, *Proc. 4th International Workshop Biological Effects of Electromagnetic Fields*, Crete-Greece, pp. 545–551, 2006.

[30] Kemp AH, Silberstein RB, Armstrong SM, Nathan PJ, Gender differences in the cortical electrophysiological processing of visual emotional stimuli, *Neuroimage* **21**:632–646, 2004.

[31] Kleinlogel H, Dierks T, Koenig T, Lehmann H, Minder A, Berz R, Effects of weak mobile phone — Electromagnetic fields (GSM, UMTS) on event related potentials and cognitive functions, *Bioelectromagnetics* **29**:488–497, 2008.

[32] Koechlin E, Corrado G, Pietrini P, Grafman J, Dissociating. The role of the medial and lateral anterior prefrontal cortex in human planning, *Proc Natl Acad Sci USA* **97**:7651–7656, 2000.

[33] Kok A, On the utility of P3 amplitude as a measure of processing capacity, *Psychophysiology* **38**:557–577, 2001.

[34] Kolb B, Wilshaw IQ, *Fundamentals of Human Neurophysiology*, 5th edn., Freeman, New York, 1996.

[35] Kramer AF, Wickens CD, Donchin E, Processing of stimulus properties: Evidence for dual-task integrality, *J Exp Psychol Hum Percept Perform* **11**:393–408, 1985.

[36] Magliero A, Bashore TR, Coles MGH, Donchin E, On the dependence of P300 latency on stimulus evaluation processes, *Psychophysiology* **21**:171–186, 1984.

[37] Martínez-Búrdalo M, Martín A, Sanchis A, Villar R, FDTD assessment of human exposure to electromagnetic fields from Wi-Fi and bluetooth devices in some operating situations, *Bioelectromagnetics* **30**:142–151, 2009.

[38] Miyake A, Shah P, *Models of Working Memory*, Cambridge University Press, New York, 1999.

[39] Morita Y, Morita K, Yamamoto M, Waseda Y, Maeda H, Effects of facial affect recognition on the auditory P300 in healthy subjects, *Neurosci Res* **41**:89–95, 2001.

[40] Mueller NG, Knight RT, The functional neuroanatomy of working memory: Contributions of human brain lesion studies, *Neuroscience* **139**:51–58, 2006.

[41] Nanou E, Hountala C, Maganioti A, Papageorgiou C, Tsiafakis V, Rabavilas A, Capsalis C, Influence of a 1,800 MHz electromagnetic field on the EEG energy, *Environmentalist* **29**:205–209, 2009.

[42] Nathaniel-James DA, Fletcher P, Frith CD, The functional anatomy of verbal initiation and suppression using the Hayling test, *Neuropsychologia* **35**:559–566, 1997.

[43] Nichols TE, Holmes AP, Nonparametric permutation tests for functional neuroimaging: A primer with examples, *Hum Brain Mapp* **15**:1–25, 2001.

[44] Nieuwenhuis S, Aston-Jones G, Cohen J, Decision making, the P3, and the locus coeruleus-norepinephrine system, *Psychol Bull* **131**:510–532, 2005.

[45] Oliver-Rodriguez JC, Guan Z, Johnston VS, Gender differences in late positive components evoked by human faces, *Psychophysiology* **36**:176–185, 1999.

[46] Papageorgiou C, Nanou E, Tsiafakis V, Capsalis C, Rabavilas A, Gender related differences on the EEG during a simulated mobile phone signal, *Neuroreport* **15**:2557–2560, 2004.

[47] Pascual-Marqui RD, Standardized low resolution brain electromagnetic tomography (sLORETA): Technical details, *Methods Find Exp Clin Pharmacol* **24**:5–12, 2002.

[48] Polich J, Updating P300: An integrative theory of P3a and P3b, *Clin Neurophysiol* **118**:2128–2148, 2007.

[49] Roalf D, Lowery N, Turetsky BI, Behavioral and physiological findings of gender differences in global–local visual processing, *Brain Cogn* **60**:32–42, 2006.

[50] Salford LG, Brun A, Sturesson K, Eberhardt JL, Persson BR, Permeability of the blood brain barrier induced by 915-MHz electromagnetic radiation continuous wave and modulated at 8, 16, 50 and 200 Hz, *Microsc Res Tech* **27**:535–542, 1994.

[51] Salford LG, Brun AE, Eberhardt JL, Malmgren L, Persson BR, Nerve cell damage in mammalian brain after exposure to microwaves from GSM mobile phones, *Environ Health Persp* **111**:881–883, 2003.

[52] Schirmacher A, Electromagnetic fields (1.8 GHz) increase the permeability of sucrose of the blood–brain barrier *in vitro*, *Bioelectromagnetics* **21**:338–345, 2000.

[53] Smythe JW, Costall B, Mobile phone use facilitates memory in male, but not female, subjects, *Neuroreport* **14**:243–246, 2003.

[54] Soltani M, Knight RT, Neural origins of the P300, *Crit Rev Neurobiol* **14**:199–224, 2000.

[55] Stefanics G, Thuroczy G, Kellenyi L, Hernadi I, Effects of twenty-minute 3G mobile phone irradiation on event related potential components and early gamma synchronization in auditory oddball paradigm, *Neuroscience* **157**:453–462, 2008.

[56] Steffensen SC, Ohran AJ, Shipp DN, Hales K, Stobbs SH, Fleming DE, Gender-selective effects of the P300 and N400 components of the visual evoked potential, *Vision Res* **48**:917–925, 2008.

[57] Stuss DT, Alexander M, Executive functions and the frontal lobes: A conceptual view, *Psychol Res* **63**:289–298, 2000.

[58] Winterer G, Mulert C, Mientus S, Gallinat J, Schlattmann P, Dorn H, Herrmann WM, P300 and LORETA: Comparison of normal subjects and schizophrenic patients, *Brain Topogr* **13**:299–313, 2001.

[59] Yamamoto M, Morita K, Tomita Y, Tsuji K, Kawamura K, Maeda H, Effect of facial affect stimuli on auditory and visual P300 in healthy subjects, *The Kurume Med J* **47**:285–290, 2000.

Bioelectromagnetics 27:142–150 (2006)

Effect of Short-Wave (6–22 MHz) Magnetic Fields on Sleep Quality and Melatonin Cycle in Humans: The Schwarzenburg Shut-Down Study

Ekkehardt-Siegfried Altpeter, Martin Röösli,* Markus Battaglia, Dominik Pfluger, Christoph E. Minder, and Theodor Abelin

Department of Social and Preventive Medicine, University of Berne, Berne, Switzerland

This paper describes the results of a unique ''natural experiment'' of the operation and cessation of a broadcast transmitter with its short-wave electromagnetic fields (6–22 MHz) on sleep quality and melatonin cycle in a general human population sample. In 1998, 54 volunteers (21 men, 33 women) were followed for 1 week each before and after shut-down of the short-wave radio transmitter at Schwarzenburg (Switzerland). Salivary melatonin was sampled five times a day and total daily excretion and acrophase were estimated using complex cosinor analysis. Sleep quality was recorded daily using a visual analogue scale. Before shut down, self-rated sleep quality was reduced by 3.9 units (95% CI: 1.7–6.0) per mA/m increase in magnetic field exposure. The corresponding decrease in melatonin excretion was 10% (95% CI: −32 to 20%). After shutdown, sleep quality improved by 1.7 units (95% CI: 0.1–3.4) per mA/m decrease in magnetic field exposure. Melatonin excretion increased by 15% (95% CI: −3 to 36%) compared to baseline values suggesting a rebound effect. Stratified analyses showed an exposure effect on melatonin excretion in poor sleepers (26% increase; 95% CI: 8–47%) but not in good sleepers. Change in sleep quality and melatonin excretion was related to the extent of magnetic field reduction after the transmitter's shut down in poor but not good sleepers. However, blinding of exposure was not possible in this observational study and this may have affected the outcome measurements in a direct or indirect (psychological) way. Bioelectromagnetics 27:142–150, 2006. © 2005 Wiley-Liss, Inc.

Key words: radiofrequency; electromagnetic fields; insomnia; complex-cosinor-analysis; epidemiology; broadcast antenna

INTRODUCTION

Despite a growing number of experimental and epidemiological studies on the interaction between non-ionising electromagnetic fields (EMF) and biological systems, the effects of radio-frequency (RF) EMF on health remain controversial. Recent reviews have reported a wide variety of phenomena [Roberts and Michaelson, 1985; Juutilainen and Seze de, 1998; Repacholi, 1998; Röösli et al., 2003]. Sleep disorders, a frequent clinical symptom, have been hypothesized to be related to electromagnetic field exposure. So far sleep studies have focused on effects from mobile phone radiation but not from other sources in the high frequency range, such as broadcast transmitters, diathermy devices, radar etc. Randomized controlled cross-over trials examining electroencephalogram (EEG) changes during sleep have found altered amplitude, mostly in the alpha range, when study subjects were exposed to mobile phone handset antennae [Mann and Röschke, 1996, 2004; Borbely et al., 1999; Huber et al., 2000, 2002; Lebedeva et al., 2001]. Two of these studies found evidence of an association with changes in the distribution of the sleep stage during exposure [Mann and Röschke, 1996; Lebedeva et al., 2001]. Only two laboratory studies did not find an effect on EEG under exposure [Wagner et al., 1998, 2000]. There was little evidence that self-rated sleep quality was impaired but these studies were not designed to study such an effect.

Grant sponsor: The Swiss National Science Foundation; Grant number: SNF 32-52733.97; Grant sponsor: SWISSCOM Corporation.

*Correspondence to: Martin Röösli, PhD, Department of Social and Preventive Medicine, University of Berne Finkenhubelweg 11 CH-3012 Berne, Switzerland. E-mail: roeoesli@ispm.unibe.ch

Received for review 29 April 2005; Final revision received 12 August 2005

DOI 10.1002/bem.20183

Previously the effects of amplitude-modulated short-wave broadcast transmitters on sleep quality were investigated in two cross-sectional studies of people living around the Schwarzenburg broadcast transmitter in Switzerland from 1992/1993 [Altpeter et al., 1995] and 1996 [Madarasz and Sprenger, 2002]. An increased prevalence of self-reported sleep disturbances with decreasing distance from the emitting antennas and increasing exposure to magnetic field was found, after controlling for several confounders. This was also the case for various unspecific symptoms of ill health, e.g., nervousness, restlessness, limb pain. However, in a multivariate path analysis (graphical modeling), it has been shown that these latter associations might have been due to difficulties with staying asleep and not directly associated with measured electromagnetic field strength. Similar findings have been reported in a study from the surroundings of a short-wave radio transmitter in Austria [Haider et al., 1992].

Although a biological explanation for an association between exposure to RF-EMF and impaired sleep quality has not been identified, it has been hypothesized that nightly melatonin excretion is suppressed by electromagnetic field exposure [Stevens, 1987]. Melatonin is related to the day–night cycle with higher blood levels during night. Melatonin supplements have been shown to be effective in treating sleep problems due to jet lag, in the blind and to some extent in old people [Arendt et al., 1981; Dahlitz et al., 1991; MacFarlane et al., 1991; Reiter, 1991; Lewy et al., 1992; Jan et al., 1994; Garfinkel et al., 1995; Brzezinski, 1997; Burch et al., 1999]. Two recent observational studies have found evidence of an association between decreased excretion of melatonin during night and increasing use of mobile phones [Burch et al., 2002; Jarupat et al., 2003]. However, four cross-over trials have found no association between exposure to mobile phone handset and melatonin excretion [Mann et al., 1998; de Seze et al., 1999; Radon et al., 2001; Bortkiewicz et al., 2002].

In March 1998, the Swiss government decided to close down permanently the shortwave radio transmitter at Schwarzenburg. We used this opportunity to examine possible chronic and acute effects of radio frequency exposure on sleep quality and salivary melatonin levels in humans, with the hypothesis that an effect would be more pronounced among poor sleepers.

MATERIALS AND METHODS

Study Design

The shortwave transmitter of Schwarzenburg was scheduled to shut down on 29 March 1998 at 2:00 a.m. Our study took place for 1 week before (from 23 March 1998 at noon) and 1 week after the shutdown (until 3 April 1998 at noon). We contacted all participants of two previous studies [Altpeter et al., 1995; Abelin et al., in press] by post and invited them to participate in this study. Study participants recorded sleeping times and self-rated sleep quality in a sleep diary every morning. Salivary melatonin levels were sampled five times a day.

Fifty four participants of the previous studies agreed to participate and gave written consent. The study was approved by the Research Ethics Committee of the Medical Faculty, University of Bern. The participants were between 24 and 70 years (mean

TABLE 1. Descriptive Statistics of the Study Population

	1998	1996
	n (%)	n (%)
Total number of participants	54 (100)	446 (100)
Sex		
Male	21 (39)	199 (45)
Female	33 (61)	247 (55)
Occupation	n (%)	n (%)
General farming	15 (28)	149 (33)
Household work	19 (35)	121 (27)
Other	20 (37)	176 (39)
	Mean (SD)	Mean (SD)
Age	52.8 (12.3)	49.3 (16.8)
Magnetic field strength [mA/m]	1.5 (1.5)	n.a.
Distance to transmitter [km]	1.88 (1.32)	2.27 (1.63)
Years of education (without kindergarten)	12.9 (2.6)	11.8 (2.5)
Socioeconomic status (magnitude prestige scale[a])	39.2 (34.9)	39.0 (29.5)

Schwarzenburg shut-down study [1998] and Schwarzenburg survey [1996].

[a] From Wegener [1992].

52.8 years, Table 1). The characteristics of this study population were similar to those from the previous study with respect to age, sex, and socioeconomic status but it tended to live closer to the transmitter.

Exposure Assessment

The transmitter was situated about 20 km south of the Swiss capital Berne and was built in 1939 to transmit information worldwide. It operated at frequencies of 6.1 to 21.8 MHz, with a maximum power of two times 150 kW. The signal was amplitude modulated. The direction of the transmission beam changed about every 2 h according to the local time in the target areas (America, Asia, Africa, Australia). The beam was elevated by 11° above the horizontal to reach its target by repeated reflection between the stratosphere and the ground.

We used an isotropic sensor system (EH 30KW, EMC-Baden Ltd., Dättwil, made available by Swisscom, operator of the Schwarzenburg transmitter) that had been developed during the previous studies [Altpeter et al., 1995] and took continuous measurements in a hayloft of a cattle stable which was located 925 m north of the shortwave transmitter's star shaped antenna, for the whole study period. The probe had been previously validated and reported [Altpeter et al., 1995; Madarasz and Sprenger, 2002].

We calculated 24 h average H field exposure [mA/m] for each subject's home using Maxwell equations, taking into account the relative position of the residencies to the centre of the antenna (azimuth and distance), the previous exposure measurements (1992, 1993, 1996), and the present broadcasting scheme. The calculations were performed by Swisscom (U. Herrmann and B. Eicher). Before shut down of the transmitter H-field exposure of the study population was in the range of 0.2 to 6.7 mA/m (mean 1.5 mA/m, median 0.92 mA/m). We divided the study population in to groups according to median exposure value. Average exposure level in the low exposure group was 0.4 mA/m (median = 0.40 mA/m), in the high exposure group 2.6 mA/m (median = 2.1 mA/m). After shut-down, there were no emission sources left in this frequency range.

Outcome Measurements

Saliva was sampled using plain, citrate-free spongy polystyrol sticks (Salivetten®; Sarstedt) of 10 mm diameter and 35 mm length. These were kept in the mouth for about a minute and removed when filled with saliva. Salivary sampling times were as follows: before breakfast (median 6:40 AM, interquartile range 65 min), noon (median 12:00 AM, interquartile range 35 min), tea time (median 4:10 PM, interquartile range 60 min), dinner time (median 7:00 PM, interquartile range 75 min), and before bed (median 10:10 PM, interquartile range 70 min). In principle, two samples were taken at the same time point. The saliva samples were stored at below 8 °C in the participant's home refrigerator. Every morning between 8:00 AM and noon samples from the previous 24 h were collected and transferred on dry ice to IBL Laboratories in Hamburg (Germany) where they were stored at −20 °C before saliva melatonin levels were determined by radio-immuno-assay (RIA) tests. Sampling times were specified as before breakfast, noon, tea time, dinner time, and before bed, without giving exact times, in order to improve compliance. The subjects reported the actual sampling times on a form. Participants were requested to complete a standardized sleep log (VIS-M, Collegium Internationale Psychiatriae Scalarum, 4th edn.) every morning. They recorded morning tiredness and sleep quality, time of falling asleep, and duration of sleep. We calculated sleep efficiency as the duration of sleep divided by duration of staying in bed. The primary sleep quality outcome was morning tiredness, which was measured on a 100 arbitrary unit visual analogue scale with low values referring to freshness and high values to tiredness. Every morning the volunteers were supplied with new Salivetten® and new sleep logs. Questionnaires were collected daily so that participants did not compare their daily ratings.

Statistical Analysis

For the data analysis, we divided the study time into two 4-day periods, starting on Monday at noon and ending on Friday at noon. Period 1 (baseline exposure period) lasted from 23 March, 12.00 to 27 May. Period 2 (after shut down) from 30 March, 12.00 to 3 April.

Morning tiredness, melatonin excretion (log transformed), and acrophase (peak time of melatonin excretion) are the main outcome measures of the study. Total melatonin excretion and the acrophase for each period were estimated using a complex-cosinor-model (termed CCA by Lerchl and Partsch, 1994). This corresponds to a cosine-shaped diurnal melatonin excretion pattern. In Figure 1 are shown exemplarily salivary melatonin samples from one individual and the corresponding fitted curve before and after shut down of the transmitter. The total salivary melatonin excretion was then obtained for each individual from the area under the modeled curve (AUC) for both periods. The acrophases were obtained by finding the point in time of the daily maximum of the fitted melatonin cycle. All models were fitted by median regression of the logarithm of the salivary melatonin concentration, implemented in Splus 4.5 for Windows NT by the

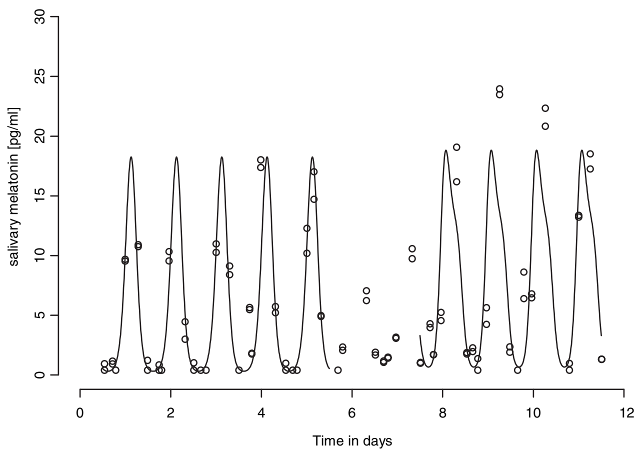


Fig. 1. Salivary melatonin samples from one individual and curve, fitted using a complex-cosinor-models, on workdays before and after shut down of the transmitter. The tick of the day number corresponds to the start of the day: 0:00.

function ‘l1fit’ [Birkes and Dodge, 1993]. Values beyond the laboratory detection limits, i.e., below 0.4 pg/ml and above 250 pg/ml, were excluded. The statistical methods have been described previously [Altpeter and Abelin, 2002].

Chronic effects of short wave radiation were investigated by comparing outcome measurements during the baseline period in association with the magnetic field exposure. Melatonin excretion levels were log transformed. Age and sex were taken into account as possible confounding factors. In order to obtain robust coefficients, a linear median regression model was fitted (L1-norm).

Acute RF effects were studied in a within subject analysis where every subject served as his/her own control. For this analysis, we fitted the outcome measurements in period 2 using a random effects model taking into account the respective baseline value. All models were adjusted for age and sex. We also investigated interaction between sleep quality at baseline and acute exposure in stratified analyses to determine whether EMF exposure affects sleep quality more in poor sleepers than in good sleepers. Sleep quality at baseline was obtained by a principal component analysis (PCA) on diary data from the first period (baseline). Thus, a compound variable was derived as an overall measure of sleep quality at baseline. We constructed two equally sized groups using the median value of the compound variable to classify the study participants as either poor or good sleepers. Mean age of poor and good sleepers was 54 and 50 years, respectively. The sex ratio was similar in both groups (63 and 59%, respectively).

In order to get hints with respect to the biological mechanism, we modelled possible association between rating of sleep quality (freshness vs. tiredness) and the melatonin cycle. We performed two different analyses. First we compared sleep quality at baseline with the melatonin cycle at baseline. Second, we compared change in sleep quality from the period after shut down to the baseline period with the respective change in melatonin excretion at peak time.

The chronic and acute disease models were calculated using Stata 8.1 (Stata Corporation, Austin, TX). $P < 0.05$ was considered statistically significant.

RESULTS

Raw Outcome Measurements

The median melatonin concentrations were 7.02 pg/ ml (interquartile range 13.60) before breakfast, 1.76 pg/ml (interquartile range 2.12 pg/ml) at noon, 1.56 pg/ml (interquartile range 2.54 pg/ml) at tea time, 2.00 pg/ml (interquartile range 3.40 pg/ml) at dinner time, and 10.91 pg/ml (interquartile range 21.53 pg/ml) before bed. One baseline value of a high exposed individual was excluded because there were too few salivary samples. One outlying peak time value (11:30 AM) in a 69-year-old individual was considered as implausible and thus omitted from the analyses.

Table 2 shows the raw outcome measurement during baseline period and after shut-down stratified by exposure status. Morning tiredness was the same before and after shut down in the low exposure group, but the high exposure group reported considerably less tiredness after shut-down. Melatonin excretion (AUC) remained relatively constant in the group with low exposure and increased in the group with high exposure after shut-down of the transmitter. Note that the data distribution of the AUC is skewed and thus logarithm transformed for further data analysis. The peak time for excretion of melatonin in both groups was delayed after shut-down, corresponding to the switch from winter to summer time, when the clock is put forward by one hour. Mean age and sex ratio in the low and high exposure group were similar (51 and 53 years; 63 and 59%, respectively).

Chronic Effects

Table 3 shows the chronic effects of magnetic field exposure. During the baseline period, morning tiredness increased with increasing electromagnetic field values, after controlling for age and sex. Melatonin excretion decreased by a factor of 0.90 for every 1 mA/m increase in magnetic field exposure (95% CI: 0.68–1.20). The peak time of melatonin excretion was put backward by 4.4 min for every 1 mA/m increase in magnetic field exposure (95% CI: −25.4 to 16.6).

TABLE 2. Average Daily Values of Melatonin Excretion (AUC), Peak Time, and Tiredness Before and After Shut Down of Transmitter Stratified by Exposure Status

		EMF low[a]				EMF high			
	Period	n	1st quartile	Median	3rd quartile	n	1st quartile	Median	3rd quartile
EMF [mA/m]	Baseline	27	0.25	0.40	0.57	27	1.47	2.10	3.55
	2	27	0.00	0.00	0.00	27	0.00	0.00	0.00
Morning freshness-tiredness	Baseline	27	41.3	45.0	50.3	27	44.3	54.5	62.3
	2	27	39.5	45.8	51.0	27	31.3	42.5	48.0
Melatonin excretion [pg/ml]	Baseline	27	5.3	12.5	37.9	26	4.9	9.5	17.8
	2	27	9.0	13.7	31.6	27	9.0	14.8	100.6
Peak time [min]	Baseline	26	0:34	1:44	2:20	27	0:37	1:43	3:11
	2	27	1:30	2:19	2:46	27	1:40	2:26	3:04

[a] (cut-off = median).

Acute Effects

Table 4 shows the results of the random effects model comparing within subject changes in outcome measurements. After shut-down study, participants rated their condition in the morning on average 1.74 (95% CI: 0.11 to 3.36) units fresher for each mA/m reduction in magnetic field exposure. There was a tendency for melatonin excretion to increase after shut-down of the transmitter by a factor of 1.15 (95% CI: 0.97 to1.36) per mA/m decrease in magnetic field exposure. The observed change in peak time for melatonin excretion after shut-down of the transmitter was independent of the extent of change in the magnetic field exposure.

In analyses stratified by sleep quality we found evidence of an effect from electromagnetic fields on morning tiredness scores and melatonin excretion in poor sleepers but not in good sleepers (defined as sleep quality below the median for the group) (Table 5). Again, peak time was not related to magnetic field exposure in either good or poor sleepers.

Association Between Sleep Quality and Melatonin

With respect to the biological mechanism, we did not find evidence of an association between rating of sleep quality (freshness vs. tiredness) and the melatonin cycle (Table 6); but due to small numbers, no breakdown by level of EMF exposure was possible.

DISCUSSION

This paper describes the results of a unique ‘‘natural experiment’’ on sleep related effects of the operation and cessation of a short-wave broadcast transmitter. We confirmed that during operation of the transmitter self-rated morning freshness as an indicator of sleep quality decreased with increasing exposure to short-wave magnetic fields. We found that sleep quality improved after the transmitter shut-down, and we found evidence suggestive of a rebound in nightly melatonin excretion in poor sleepers. We did not find any acute or

TABLE 3. Chronic Effects of EMF on Morning Tiredness, Melatonin Excretion (AUC) and Peak Time (Regression Models of Outcomes During Baseline Period)

	Model	Coefficient[a]	Lower 95%-CI	Upper 95%-CI
Morning freshness/tiredness	Crude	2.78	−0.02	5.58
	Adjusted[b]	3.85	1.72	5.99
Melatonin excretion [ratio][c]	Crude	0.86	0.68	1.09
	Adjusted[b]	0.90	0.68	1.20
Peak time [min]	Crude	−14.4	−36.1	7.2
	Adjusted[b]	−4.4	−25.4	16.6

[a] Coefficient refer to a change in outcome parameter per unit increase in EMF exposure [mA/m].

[b] Model includes EMF, age, and sex.

[c] Due to the logarithm transformation the coefficient refers to a change in the ratio (the presented model coefficient is back transformed: in case of statistical significance, the 95% confidence interval does not include 1).

TABLE 4. Acute Effects of EMF on Morning Tiredness, Melatonin Excretion (AUC), and Peak Time

	Model	Coefficient[a]	Lower 95%-CI	Upper 95%-CI
Morning freshness/tiredness	Crude[b]	−1.98	−3.62	−0.34
	Adjusted[c]	−1.74	−3.36	−0.11
Melatonin excretion [ratio][d]	Crude[b]	1.14	0.97	1.35
	Adjusted[c]	1.15	0.97	1.36
Peak time [min]	Crude[b]	2.7	−8.1	13.5
	Adjusted[c]	2.7	−8.2	13.7

[a] Coefficients refer to a change in outcome parameter per unit decrease in EMF exposure [mA/m].
[b] Model includes EMF and outcome measurement at baseline.
[c] Model includes EMF levels and outcome measurement at baseline, age, and sex.
[d] Due to the logarithm transformation the coefficient refers to a change in the ratio (the presented model coefficient is back transformed: in case of statistical significance, the 95% confidence interval does not include 1).

chronic effects of magnetic field exposure on the acrophase of the melatonin cycle.

The strengths of this study are that we were able to exploit the closure of the transmitter to conduct a natural experiment. We compared the same time interval before and after shut-down of the transmitter to minimize data variability. The observed time period allowed us to investigate acute effects of shut-down of the transmitter with a latency of 2 to 6 days. We also collected biological specimens. Although we were particularly interested in melatonin excretion at night, we did not collect nocturnal samples because this might have interfered with sleep quality. Nightly excretion was modelled using the complex-cosinor-analysis model [Lerchl and Partsch, 1994], which fits a characteristic 24-h melatonin excretion curve based on the five samples taken each day. The model takes into account irregularly spaced time series and imperfect compliance, and by using the natural logarithm of salivary melatonin levels and estimating all regression models by L1-norm we could attenuate the influence of outlying observations and measurement error. The estimate of the dose-response relation between melatonin excretion and magnetic field exposure was consistent and independent of the type of model estimated, including a least square approach and a model based on absolute differences.

Some limitations in the study design were due to the natural characteristic of the experiment. First, exposure from short-wave transmitters can cause side effects such as radio sounds in electrical appliances. Thus, we could not blind participants to exposure. Observer bias in the ratings of sleep quality can therefore not be excluded. Melatonin excretion, however, cannot be altered on purpose. Nevertheless, a psychologically triggered interference through other hormonal substances, e.g., adrenaline, cannot be ruled out completely.

Second, it was unfortunate that the change from winter to summer time coincided with the transmitter shut-down. This event was clearly demonstrated by the time difference in the acrophase between the two study periods. On the one hand this observed time shift was not related to magnetic field exposure, which validates our data modeling process. On the other hand, the time change may have influenced sleep quality. This would be expected to increase morning tiredness in period 2 because subjects had to get up 1 h earlier. The observed

TABLE 5. Acute Effects of EMF on Morning Tiredness, Melatonin Excretion (AUC), and Peak Time Stratified by Baseline Sleep Quality

	Sleep quality	Coefficient [a]	Lower 95%-CI	Upper 95%-CI
Morning freshness/tiredness	Poor	−3.54	−5.37	−1.72
	Good	1.30	−1.33	3.93
Melatonin excretion [ratio][b]	Poor	1.260	1.081	1.468
	Good	1.008	0.733	1.386
Peak time [min]	Poor	5.6	−8.2	19.3
	Good	0.8	−16.4	18.0

[a] Coefficients refer to a change in the outcome parameter per unit decrease in EMF exposure [mA/m]. Coefficients are adjusted for age and sex.
[b] Due to the logarithm transformation the coefficient refers to a change in the ratio (the presented model coefficient is back transformed: in case of statistical significance, the 95% confidence interval does not include 1).

TABLE 6. Association Between Freshness/Tiredness Level And Melatonin Excretion (AUC) as Well as Peak Time

	Model	Coefficient[a]	Lower 95%-CI	Upper 95%-CI
Melatonin excretion [ln(pg/ml)]	Baseline	−0.88	−3.96	2.19
Peak time [min]	Baseline	−19.00	−85.38	47.39
Melatonin excretion [ln(pg/ml)]	Difference	1.705	−3.695	7.105
Peak time [min]	Difference	4.0	−118.3	126.3

The baseline model relates baseline tiredness rating to melatonin excretion/peak time. The difference model relates change in freshness/tiredness level to change in melatonin excretion/peak time.

[a] Coefficients are adjusted for age and sex.

lower tiredness after shut-down is therefore more likely to be an underestimation. If a time shift of 1 h had affected melatonin excretion, this effect would not have been dependent on the magnetic field exposure of the study participants. Neither would a time shift explain a dose-response relationship. The same is true for the possible influence of light on the melatonin cycle. Light exposure was increasing during the study period in spring. However, this is unlikely to create a bias in a dose-response manner. The same holds for possible changes in light exposure due to changing weather conditions.

Due to the high natural variability of the melatonin cycle, large sample sizes are needed to obtain strong evidence that magnetic field exposure affects melatonin excretion. We found weak evidence of chronically suppressed melatonin excretion before shut-down of the transmitter. Evidence of an acute increase in melatonin excretion after withdrawal of magnetic field exposure was observed in poor sleepers in accord with our hypothesis. In this context it should be noted that the study had more power to detect acute effects than chronic effects because baseline values of each subject were taken into account.

Our findings are consistent with the hypothesis of a melatonin suppressing effect from magnetic field exposure and a rebound effect after the exposure has ended [Stevens, 1987]. The effect of short wave exposure (3–30 MHz) on melatonin has not previously been investigated except in the area of the Schwarzenburg transmitter [Altpeter et al., 1995; Stärk et al., 1997]. A finding there was an indication of a melatonin rebound effect in cows 3 days after temporary interruption of transmitter activity [Altpeter et al., 1995; Stärk et al., 1997].

A melatonin suppressing or a rebound effect has not been detected so far in randomized crossover trials of mobile phone exposure (radiation in the high frequency range, 900–1800 MHz) [Mann et al., 1998; de Seze et al., 1999; Radon et al., 2001; Bortkiewicz et al., 2002]. Three of those studies investigated melatonin in the night following or during the exposure only [Mann et al., 1998; Radon et al., 2001; Bortkiewicz et al., 2002]. The fourth analyzed melatonin excretion the night after a 4 week exposure had ended and 15 days later [de Seze et al., 1999]. Thus, none of those studies would have captured a 2 to 6 day latency, but a melatonin suppression effect due to a longer exposure period should have been detected, if present. Two recently published observational studies have found a reduction in nocturnal melatonin excretion with increasing use of mobile phones [Burch et al., 2002; Jarupat et al., 2003]. A further observational study found decreased 6-sulfatoxymelatonin urinary excretion in workers exposed to video screen emitting magnetic fields in the kilohertz frequency range [Santini et al., 2003]. However, extrapolating findings from different frequency ranges is still an uncertain endeavor as a common underlying biological mechanism is not known.

Of note, we found evidence that EMF exposure was associated with sleep quality and melatonin excretion, but in poor sleepers only. This suggests that there might be a group of people who are sensitive to electromagnetic field exposure. This phenomenon has been described as electromagnetic hypersensitivity (EHS) [Bergqvist and Vogel, 1997; Radon and Maschke, 1998; Hillert et al., 2002; Levallois, 2002; Mueller et al., 2002; Leitgeb and Schrottner, 2003; Röösli et al., 2004]. It is conceivable, however, that poor sleepers were more emotionally involved in the study and we cannot rule out the possibility of psychologically mediated effects on melatonin excretion.

Irrespective of the frequency, other studies support the hypothesis that melatonin suppression from EMF exposure or rebound effects after exposure termination require extended time to become manifest [Wilson et al., 1990; Pfluger and Minder, 1996; Burch et al., 1999; Graham et al., 2000]. A delayed effect might explain some negative results of short-term exposure trials [Graham et al., 1996a; Graham et al., 1996b]. Overall, the hypothesis of an association between melatonin cycle and EMF exposure requires therefore further investigation [Warman et al., 2003].

In our study there was no shift in the acrophase of the melatonin cycle, although investigating this in detail was hampered by the change from winter to summer time. Our research was not suited to provide evidence of a plausible biological pathway for the effects of melatonin on EMF-associated sleep problems. Given that our results may be due to lack of blinding the question remains whether the present study could be repeated under well controlled laboratory conditions. This, however, is unlikely due to feasibility constraints. Who will accept staying in a sleep lab for more than a week? And where can enough sleep laboratories be found to investigate a sample size of more than 50 persons for several weeks?

CONCLUSIONS

Our findings support a relationship between operation of the radio transmitter under investigation and sleep disturbances in the exposed population, and they are compatible with a causal dose-effect model between radio frequency EMF exposure and sleep quality as well as melatonin excretion. Due to the observational nature of the study, a direct biological cannot, however, have been causality proven, and the possibility of a psychological (Nocebo) rather than a biological effect cannot be excluded. From a public health perspective our findings call for caution in exposing populations to EMF from short-wave radio transmitters. But they do not allow for any firm conclusions about the effects of mobile phone radiation, as short-wave frequency is different from mobile phone radiation. Further studies investigating this particular exposure are needed.

ACKNOWLEDGMENTS

The authors' thank the study participants, Mrs. Anke Wunderlich at IBL Hamburg, and Mr. Peter from DHL Switzerland. We are grateful to U. Herrmann for calculating exposure levels. We thank the scientific advisory board for their critical appraisal: C. Bassetti MD, PhD, J. Blum, B. Eicher, Th. Schläpfer MD, PhD, Ch. Schierz PhD. We are grateful to Nicola Low for careful proofreading of this manuscript.

REFERENCES

Abelin T, Altpeter ES, Röösli M. 2005. Sleep disturbances in the vicinity of the short-wave broadcast transmitter Schwarzenburg. Somnologie (in press).

Altpeter ES, Abelin T. 2002. Description of the circadian melatonin cycle in cattle by the complex cosinor analysis and L1-norm. Student 4(2):141–148.

Altpeter ES, Krebs T, Pfluger D, von Känel J, Blattmann R, Emmenegger D, Cloetta B, Rogger U, Gerber H, Manz B, Coray R, Baumann R, Staerk K, Griot C, Abelin T. 1995. Study on health effects of the shortwave transmitter station of Schwarzenburg, Berne, Switzerland. BEW (Bundesamt of Energiewirtschaft); 1995. BEW Publication Series No. 55.

Arendt J, Aldhous M, English J, Marks V, Arendt JH, Marks M, Folkard S. 1981. Some effects of jet-lag and their alleviation by melatonin. Ergonomics 30:1379–1393.

Bergqvist U, Vogel E. (Editors). 1997. Possible health implication of subjective symptoms and electromagnetic fields: A report by a European group of experts for the European Commission DG V. Sona (Sweden): National Instiute for Working Life, Arbete och Hälsa.

Birkes D, Dodge Y. 1993. Least-absolute-deviations regression. Alternative methods of regression. New York: Wiley & Son. pp. 57–84.

Borbely AA, Huber R, Graf T, Fuchs B, Gallmann E, Achermann P. 1999. Pulsed high-frequency electromagnetic field affects human sleep and sleep electroencephalogram. Neurosci Lett 275(3):207–210.

Bortkiewicz A, Pilacik B, Gadzicka E, Szymczak W. 2002. The excretion of 6-hydroxymelatonin sulfate in healthy young men exposed to electromagnetic fields emitted by cellular phone—an experimental study. Neuroendocrinol Lett 23(Suppl 1):88–91.

Brzezinski A. 1997. Melatonin in humans. N Engl J Med 336(3):186–195.

Burch JB, Reif JS, Yost MG, Keefe TJ, Pitrat CA. 1999. Reduced excretion of a melatonin metabolite in workers exposed to 60 Hz magnetic fields. Am J Epidemiol 150(1):27–36.

Burch JB, Reif JS, Noonan CW, Ichinose T, Bachand AM, Koleber TL, Yost MG. 2002. Melatonin metabolite excretion among cellular telephone users. Int J Radiat Biol 78(11):1029–1036.

Dahlitz M, Alvarez B, Vignau J, English J, Arendt J, Parkes JD. 1991. Delayed sleep phase syndrome response to melatonin. Lancet 337:1121–1124.

De Seze R, Ayoub J, Peray P, Miro L, Touitou Y. 1999. Evaluation in humans of the effects of radiocellular telephones on the circadian patterns of melatonin secretion, a chronobiological rhythm marker. J Pineal Res 27(4):237–242.

Garfinkel D, Laudon M, Nof D, Zisapel N. 1995. Improvement of sleep quality in elderly people by controlled-release melatonin. Lancet 346:541–544.

Graham C, Cook MR, Riffle DW, Gerkovich MM, Cohen HD. 1996. Nocturnal melatonin levels in human volunteers exposed to intermittent 60 Hz magnetic fields. Bioelectromagnetics 17: 263–273.

Graham C, Cook MR, Riffle DW. 1996. Human melatonin during continuous magnetic field exposure. Bioelectromagnetics 18: 166–171.

Graham C, Cook MR, Sastre A, Riffle DW, Gerkovich MM. 2000. Multi-night exposure to 60 Hz magnetic fields: Effects on melatonin and its enzymatic metabolite. J Pineal Res 28(1): 1–8.

Haider M, Kundi M, Knasmüller S, Haider TH, Groll-Knapp E, Obermeier G. 1992. Medizinisch-hygienische Untersuchung und Beurteilung der Kurzwellensenderanlage Moosbrunn [Medical-hygiene investigation and evaluatein of the short-wave transmitter Moosbrunn]. Wien: Institut für Umwelthygiene Wien.

Hillert L, Berglind N, Arnetz BB, Bellander T. 2002. Prevalence of self-reported hypersensitivity to electric or magnetic fields in a population-based questionnaire survey. Scand J Work Environ Health 28(1):33–41.

Huber R, Graf T, Cote KA, Wittmann L, Gallmann E, Matter D, Schuderer J, Kuster N, Borbely AA, Achermann P. 2000. Exposure to pulsed high-frequency electromagnetic field during waking affects human sleep EEG. Neuroreport 11(15):3321–3325.

Huber R, Treyer V, Borbely AA, Schuderer J, Gottselig JM, Landolt HP, Werth E, Berthold T, Kuster N, Buck A, Achermann P. 2002. Electromagnetic fields, such as those from mobile phones, alter regional cerebral blood flow and sleep and waking EEG. J Sleep Res 11(4):289–295.

Jan JE, Espezel H, Appleton RE. 1994. The treatment of sleep disorders with melatonin. Dev Med Child Neurol 36:97–107.

Jarupat S, Kawabata A, Tokura H, Borkiewicz A. 2003. Effects of the 1900 MHz electromagnetic field emitted from cellular phone on nocturnal melatonin secretion. J Physiol Anthropol Appl Human Sci 22(1):61–63.

Juutilainen J, Seze de R. 1998. Biolological effects of amplitude-modulated radiofrequency radiation. Scand J Work Environ Health 24:245–254.

Lebedeva NN, Sulimov AV, Sulimova OP, Korotkovskaya TI, Gailus T. 2001. Investigation of brain potentials in sleeping humans exposed to the electromagnetic field of mobile phones. Crit Rev Biomed Eng 29(1):125–133.

Leitgeb N, Schrottner J. 2003. Electrosensibility and electromagnetic hypersensitivity. Bioelectromagnetics 24(6):387–394.

Lerchl A, Partsch C-J. 1994. Reliable analysis of individual human melatonin profiles by complex cosinor analysis. J Pineal Res 16(85):90.

Levallois P. 2002. Hypersensitivity of human subjects to environmental electric and magnetic field exposure: A review of the literature. Environ Health Perspect 110(Suppl 4):613–618.

Lewy AJ, Ahmed S, Latham Jackson JM, Sack RL. 1992. Melatonin shifts human circadian rhythms according to a phase-response curve. Chronobiol Int 9:380–392.

MacFarlane JG, Cleghorn JM, Brown GM, Streiner DL. 1991. The effect of exogenous melatonin on the total sleep time and daytime alertness of chronic insomniacs: A preliminary study. Biol Psychiatry 30:371–376.

Madarasz KN, Sprenger K. 2002. Schlafstörungen und gesundheitliche Beschwerden in der Umgebung des Kurzwellensenders Schwarzenburg. [Sleep disorders and health complaints in the vicinity of the short-wave transmitter Schwarzenburg]. Medical doctor thesis, Medizinische Fakultät der Universität Bern.

Mann K, Röschke J. 1996. Effects of pulsed high-frequency electromagnetic fields on human sleep. Neuropsychobiology 33:41–47.

Mann K, Röschke J. 2004. Sleep under exposure to high-frequency electromagnetic fields. Sleep Med Rev 8(2):95–107.

Mann K, Wagner P, Brunn G, Hassan F, Hiemke C, Röschke J. 1998. Effects of pulsed high-frequency electromanetic fields on the neuroendocrine systeme. Neuroendocrinology 67(2):139–144.

Mueller CH, Krueger H, Schierz C. 2002. Project NEMESIS: Perception of a 50 Hz electric and magnetic field at low intensities (laboratory experiment). Bioelectromagnetics 23(1):26–36.

Pfluger D, Minder CE. 1996. Effects of exposure to 16.7 Hz magnetic fields on urinary 6-hydroxymelatonin sulfate excretion of Swiss railway workers. J Pineal Res 21:91–100.

Röösli M, Rapp R, Braun-Fahrländer C. 2003. Hochfrequente Strahlung und Gesundheit—eine Literaturanalyse [radio and microwave frequency radiation and health—an analysis of the literature]. Gesundheitswesen 65(6):378–392.

Röösli M, Moser M, Baldinini Y, Meier M, Braun-Fahrländer C. 2004. Symptoms of ill health ascribed to electromagnetic field exposure—a questionnaire survey. Int J Hygiene Environ Health 207(2):141–150.

Radon K, Maschke C. 1998. Gibt es Elektrosensibilität im D-Netzbereich? Umweltmed Forsch Prax 3(3):125–129.

Radon K, Parera D, Rose DM, Jung D, Vollrath L. 2001. No effects of pulsed radio frequency electromagnetic fields on melatonin, cortisol, and selected markers of the immune system in man. Bioelectromagnetics 22(4):280–287.

Reiter RJ. 1991. Melatonin: that ubiquitously acting pineal hormone. Physiol Sci 6:223–227.

Repacholi MH. 1998. Low-level exposure to radiofrequency electromagnetic fields: Health effects and research needs. Bioelectromagnetics 19(1):1–19.

Roberts NJ, Michaelson SM. 1985. Epidemiological studies of human exposures to radiofrequency radiation. Int Arch Occup Environ Health 56:169–178.

Santini R, Messagier R, Claustrat B, Fillion-Robin M, Youbicier-Simo BJ. 2003. Video screen exposure and 6-sulfatoxymelatonin urinary excretion in women. Pathologie Biologie 51(3):143–146.

Stevens RG. 1987. Electric power use and breast cancer: A hypothesis. Am J Epidemiol 125(4):556–561.

Stärk KD, Krebs T, Altpeter ES, Manz B, Griot B, Abelin T. 1997. Absence of chronic effect of exposure to short-wave radio broadcast signal on salivary melatonin concentrations in dairy cattle. J Pineal Res 22:171–176.

Wagner P, Röschke J, Mann K, Hiller W, Frank C. 1998. Human sleep under the influence of pulsed radiofrequency electromagnetic fields: A polysomnographic study using standardized conditions. Bioelectromagnetics 19: 199–202.

Wagner P, Röschke J, Mann K, Fell J, Hiller W, Frank C, Grozinger M. 2000. Human sleep EEG under the influence of pulsed radio frequency electromagnetic fields. Results from polysomnographies using submaximal high power flux densities. Neuropsychobiology 42(4):207–212.

Warman GR, Tripp HM, Warman VL, Arendt J. 2003. Circadian neuroendocrine physiology and electromagnetic field studies: Precautions and complexities. Radiat Prot Dosimetry 106(4):369–373.

Wegener B. 1992. Concepts and measurement of prestige. Ann Rev Sociol 18:253–280.

Wilson BW, Wright CW, Morris JE, Buschbom RL, Brown DP, Miller DL, Sommers-Flannigan R, Anderson LE. 1990. Evidence for an effect ELF electromagnetic fields on human pineal gland function. J Pineal Res 9:259–269.

Somnologie **9:** 203–209, 2005

Sleep Disturbances in the Vicinity of the Short-Wave Broadcast Transmitter Schwarzenburg

Schlafstörungen in der Umgebung des Kurzwellensenders Schwarzenburg

Theodor Abelin, Ekkehardt Altpeter and Martin Röösli
Department of Social and Preventive Medicine, University of Berne
[Institut für Sozial- und Präventivmedizin der Universität Bern]

Summary

Objectives The studies reported here investigated the association between health complaints and the vicinity to the short wave transmitter Schwarzenburg, and looked for evidence for a relationship between magnetic field exposure and sleep disturbances.
Subjects and Methods Between 1992 and 1998 two cross-sectional and two panel studies were performed in the area of Schwarzenburg. In each cross-sectional survey about 400 adults living in differently exposed areas were asked about somatic and psycho-vegetative symptoms including sleep disturbances as well as possible confounding factors. Exposure was estimated based on 2621 measurements of magnetic field strength made in 56 locations. In the panel studies, sleep quality and melatonin excretion was studied when the transmission was interrupted or definitively shut down, respectively.
Results In both surveys, prevalence of difficulties of falling asleep and in particular, maintaining sleep, increased with increasing radio frequency electromagnetic field exposure (RF-EMF). Sleep quality improved after interruption of exposure. A chronic change of melatonin excretion following RF-EMF exposure could not be shown, but a parallel study of salivary samples in cows showed a temporary increase after a short latency period following interruption of exposure.
Conclusions The series of studies gives strong evidence of a causal relationship between operation of a short-wave radio transmitter and sleep disturbances in the surrounding population, but there is insufficient evidence to distinguish clearly between a biological and a psychological effect.

Keywords radio frequency – sleep disturbance – insomnia – melatonin – psycho-vegetative symptoms – field study – epidemiology

Zusammenfassung

Fragestellung Die vorliegenden Studien untersuchten den Zusammenhang zwischen gesundheitlichen Klagen und der Nähe zum Kurzwellensender Schwarzenburg, sowie die Beziehung zwischen der Exposition gegenüber elektromagnetischen Feldern und Schlafstörungen.
Untersuchungsbevölkerung und Methoden Zwischen 1992 und 1998 wurden in der Gegend von Schwarzenburg zwei Querschnittstudien und zwei Longitudinalstudien durchgeführt. In jeder Querschnittstudie wurden rund 400 in unterschiedlicher Entfernung vom Sender lebende Erwachsene über somatische und psycho-vegetative Symptome, sowie über mögliche Störfaktoren befragt. Die Schätzung der Exposition erfolgte aufgrund 2621 Messungen der magnetischen Feldstärke an 56 Messstellen. In den longitudinalen Studien wurden die Schlafqualität und die Melatoninexkretion untersucht – je einmal nach vorübergehender Unterbrechung und endgültiger Beendung des Sendebetriebs.

Correspondence: Martin Röösli, PhD, Department of Social & Preventive Medicine, University of Berne, Finkenhubelweg 11, CH-3012 Bern, Switzerland
Tel.: +41 (0)31 631 38 67, Fax: +41 (0)31 631 35 20, E-mail: Roeoesli@ispm.unibe.ch
Received: 18.11.04/Accepted: 11.04.05

Resultate In beiden Erhebungen nahm die Prävalenz von Einschlaf- und namentlich Durchschlafstörungen mit zunehmender Hochfrequenz Strahlungsexposition zu. Die Schlafqualität verbesserte sich nach Unterbruch der Exposition. Eine chronische Veränderung der Melatoninexkretion nach Hochfrequenz Strahlungsexposition konnte nicht gezeigt werden, aber in einer parallel durchgeführten Studie bei Kühen fand sich nach Expositionsunterbrechung eine vorübergehende Zunahme.

Schlussfolgerungen Die Reihe von Studien ergibt deutliche Evidenz für einen Kausalzusammenhang zwischen dem Betrieb eines Kurzwellenradiosenders und Schlafstörungen in der umgebenden Bevölkerung, aber es liegt ungenügende Evidenz vor, um klar zwischen einer biologischen und einer psychologischen Wirkung zu unterscheiden.

Schlussfolgerungen Hochfrequenzstrahlung – Schlafstörung – Insomnie – Melatonin – Psycho-vegetative Beschwerden – Feldstudie – Epidemiologie

Introduction

Although psycho-vegetative symptoms are often reported from populations exposed to radio frequency electromagnetic fields (e.g. [2, 3, 5]), these have not been studied with scientific rigor so far. Nevertheless, in the context of the mobile phone health risk debate, increasing attention is paid to such symptoms. In this paper, results from a series of population studies around a short-wave radio transmitter will be reported.

In 1990, a petition addressed to the Swiss government drew attention to the fact that large numbers of residents living near the transmitter complained about symptoms such as nervousness, headache, sleep disturbance and loss of energy, and that the transmitter was blamed for what was perceived as an accumulation of cases of cancer and other chronic disease. The government agreed to study the situation under the supervision of a panel of scientists convened by the Federal Department of Energy, and our group was charged with designing and conducting appropriate studies. The focus was on psycho-vegetative symptoms, as the study population was too small for studying rare diseases such as cancer. On the basis of the results from the first studies, follow-up studies were designed, leading to a sequence of studies, mostly in the human population surrounding the transmitter, but partly also in cattle:

(1) A first cross-sectional survey in 1992, when little had been published on electromagnetic field (EMF) and psycho-vegetative symptoms. There was no particular focus on sleep disturbances.
(2) An interruption study in 1993, with temporary interruption of exposure and melatonin determination in morning urine in humans, and in two-hourly night salivary samples in cows.
(3) A second cross sectional survey in 1996 with 39 % new participants from an additional exposed zone and use of an extended questionnaire on possible correlates of sleep disturbance.
(4) A shut-down study with monitoring of sleep quality and salivary melatonin excretion before and after the final shut-down of the transmitter in 1998.

Results were published only in a governmental report [1] and a doctoral thesis [4], but with one exception [6] not yet in the scientific literature. The purpose of this publication is to give an overview of these studies. For methodological details reference is made to other sources. Results from the shut-down study will be published elsewhere.

Methodology

The setting is the Swiss national short-wave radio transmitter of Schwarzenburg, about 20 km south of the Swiss Capital city of Berne. Constructed during the pre-World War 2 period, it served to transmit information worldwide since 1939. It operated at frequencies of 3 to 30 MHz, with a maximum power of two times 150 kW. The direction of the transmission beam changed about every two hours according to the local time in the target areas around the world (America, Asia, Africa, Australia). The beam was elevated by 11 degrees against the horizontal axis to reach its target by repeated reflexion between the stratosphere and the ground.

First cross sectional interview survey of 1992

A first study was addressed at all adult persons living up to 1500 meters from the transmitter (exposed) and a simple random sample of persons in comparable areas at 3000 to 5000 meters (assumed unexposed). The exposed area was divided into an inner circle (zone A, up to 900 meters) and an outer circle (zone B). The area assumed to be unexposed was called zone C. 404 persons or 60 % of those invited responded to a structured interview by trained student interviewers. Participation rates were 73.7 %, 55.0 % and 56.3 % in zones A, B and C respectively. The questions concerned frequency of symptoms regardless of a possible relationship with the transmitter, and aspects of working conditions and lifestyle as possible confounders. Prevalence rates of symptoms were compared between the three zones.

A total of 2621 exposure measurements were conducted during day and night time at 56 locations of zones A, B and C.

After an initial analysis showed correlations of several symptoms with distance from the transmitter, a multivariate analysis with graphical modelling was applied to distinguish between direct and indirect correlations with exposure.

Panel studies of 1993 and 1998

In 1993, sleep quality diaries were completed by stratified random sampling with replacement of subjects from the first survey. One hundred and two individuals had to be contacted in order to obtain participation by 65 with approximately equal distribution in terms of exposure zones and presence of sleep complaints. 6-hydroxy-melatonin-sulfate concentration was determined in morning urine during 10 days. After 3 days of baseline measurements the operation of the transmitter was stopped for three days, after which usual exposure was reinstated and measurements were continued for another four days. The results of a parallel study of cows have been published elsewhere [6]. When the transmitter was permanently shut down in March 1998, a convenience sample of 54 volunteers were followed for one week before and one week following shut-down (sleep quality diaries; salivary melatonin excretion) and retested for sleep quality after six months. Fifty-one of these had already participated in the second cross-sectional survey of 1996 (see below). 25 of the 54 participants reported sleep disturbances at the beginning of the shut-down study, of which 17 had reported sleep disturbances in the 1996 survey already.

Second cross-sectional survey of 1996

Local activists criticized the first study for not having included a small exposed mountain farming population in the commune of Rueggisberg to the east of the transmitter ("zone R") and claimed that the omission was in order to weaken the study results. The reason for not including this area in the first survey was however the exceptional situation of zone R. It is an isolated mountain farming area, where medical drug consumption is generally low and other lifestyle characteristics including smoking habits also differ from all other zones. Against the opinion of the supervisory body, we decided to conduct a second cross sectional interview survey using our own resources. This permitted to adapt the interview by deleting questions of no further interest and adding more detailed questions related to sleep disturbances.

399 subjects were fully interviewed, including 244 of the participants from the first survey who could still be located, and 155 subjects from the previously excluded zone R. Participation rate for the full interview among those located was 77 percent. Among 45 persons refusing an interviewer visit, telephone interviews with a few crucial questions were conducted.

As five repeated twenty-four hour exposure measurements in zones A and B showed good correspondence with those of the first survey, previous exposure estimates were used again. Additional measurements were conducted in five locations of the newly added zone R.

The same methods of statistical analysis were applied as in survey 1.

Results

Magnetic field exposure

An emission period lasted generally 2 hours per day due to the changing transmission direction. During the emission period field levels at the participants home from zone A varied from 14 to 41 mA/m (median: 28 mA/m), in zone B from 3 to 37 mA/m (median: 21 mA/m), in zone C from 1–2 mA/m (median 1 mA/m). In zone R a few spot measurements performed in 1996 yielded field levels up to 10 mA/m. The highest values in zone A were close to but did not exceed IRPA exposure limits (73 mA/m). 24 h average were approximately 20 times lower (figure 1). In general,

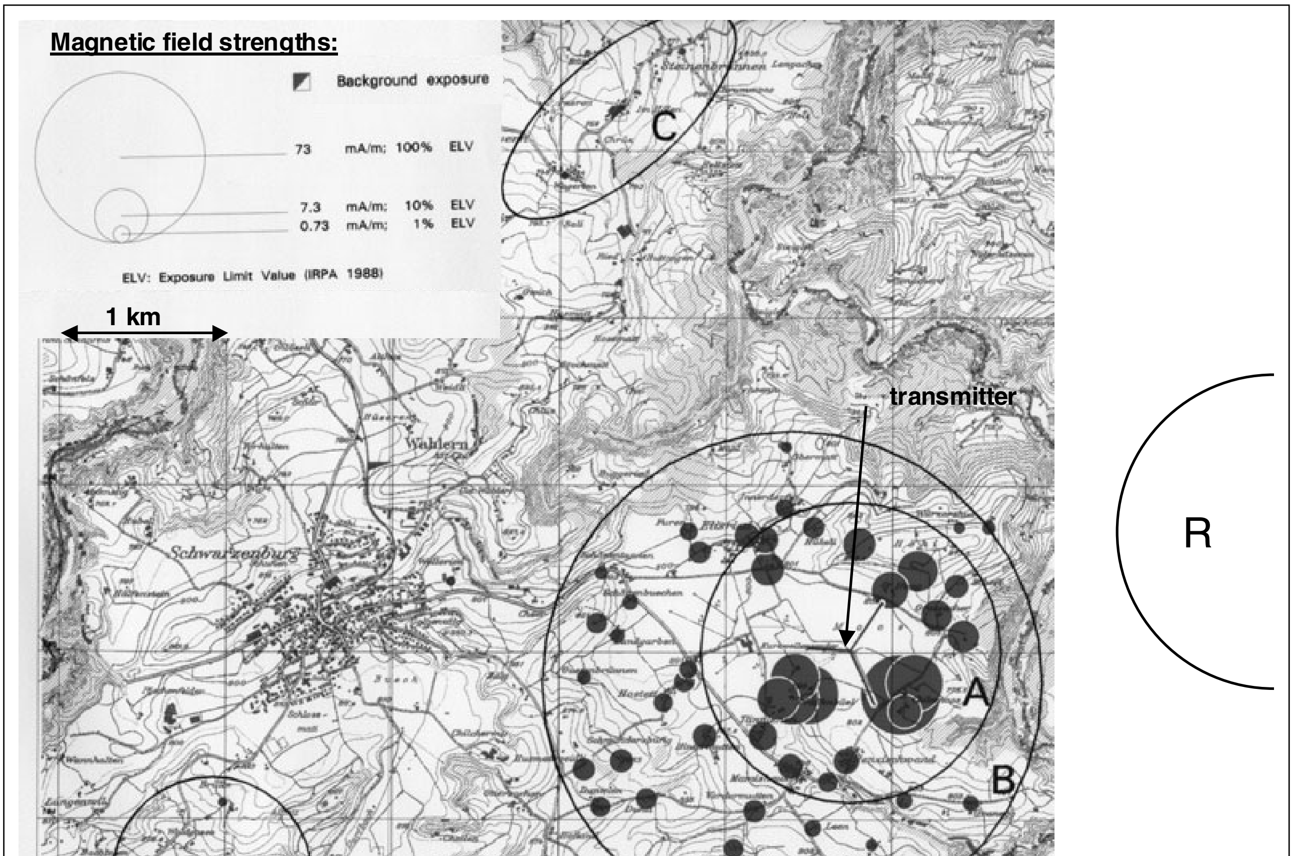


Figure 1. Map of the Schwarzenburg area showing the location of the transmitter, the H-field measurement points and the location of the zones A, B, C and R. The diameters of the circles around the measurement points indicate the 24 hour average magnetic field strengths, as measured between August 1992 and August 1993. (Reproduced with approval from swisstopo (BA046633.))

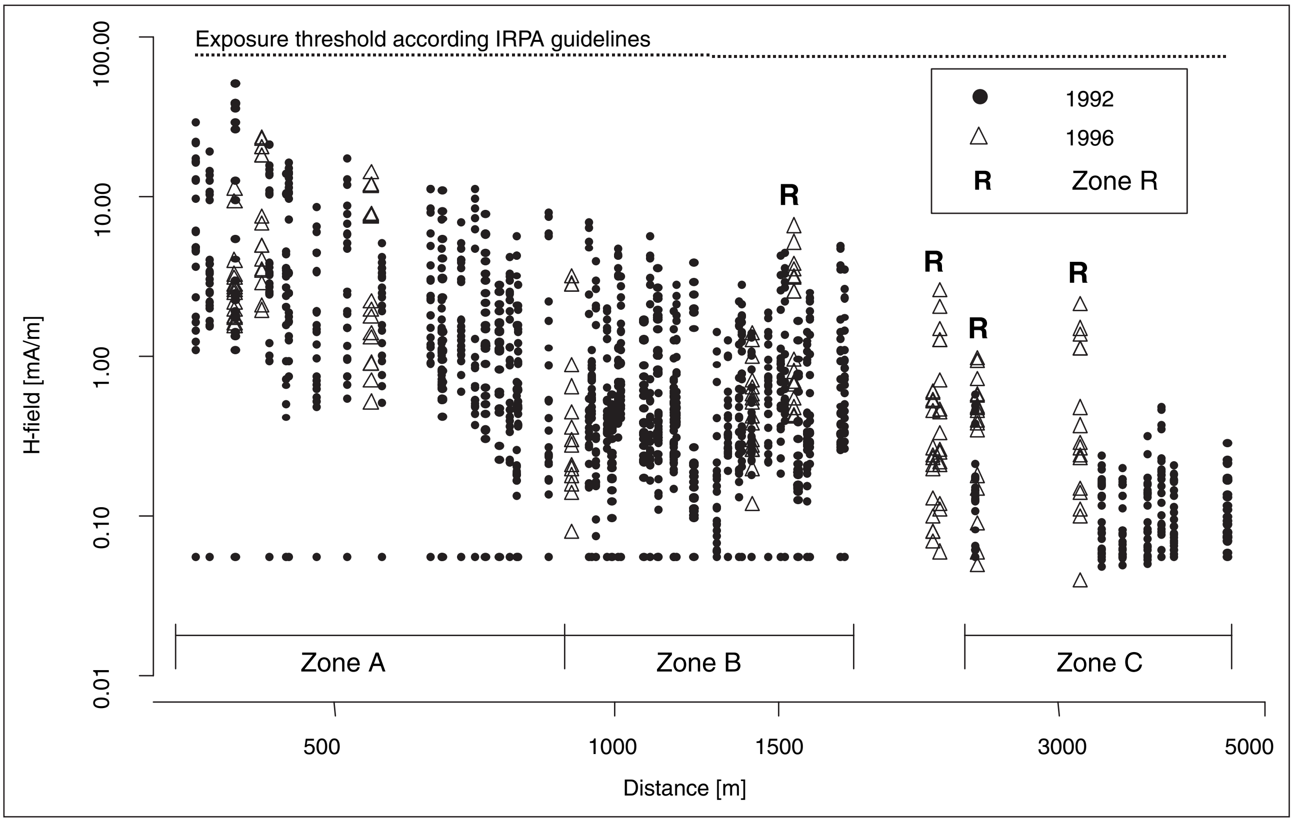


Figure 2. Measured H-field strengths from 56 locations in 1992 and 10 locations in 1996, in relation to distance from transmitter in meters. Each dot represents a mean value over an emission period at a particular location. Measurements of 1996 at or above 1500 meters are from zone R.

exposure increased steadily with decreasing distance from the transmitter (figures 2 and 3). Zone R had higher exposure levels than expected from distance alone, mainly because of its elevated location on a slope facing the transmitter.

The relationship between EMF exposure and psycho-vegetative symptoms

Table 1 shows the prevalence rates of symptoms based on interview responses in relation to distance from the transmitter. Where available, results from surveys 1 and 2 are shown. The p-values are unadjusted. Age is a strong independent risk factor for sleep disturbances, but adjustment for age, gender and education did not affect significance [1, 4]. Based on survey 1, prevalence rates of reported sleep disturbances are highest in zone A and lowest in zone C (control zone), with intermediary values in zone B. Although several other symptoms including nervousness, restlessness, limb pains, etc. show the same gradient, that for sleep disturbance is the most striking. Results from survey 2 confirm those of survey 1 and strengthen them, because in accordance with the observed EMF field strengths, the prevalence of reported sleep disturbance for zone R lies between those of zones B and C. The prevalence rates of reported difficulties of maintaining sleep were considerably higher in the second than in the first survey despite using the same sleep questions, but the gradients are similar in studies 1 and 2.

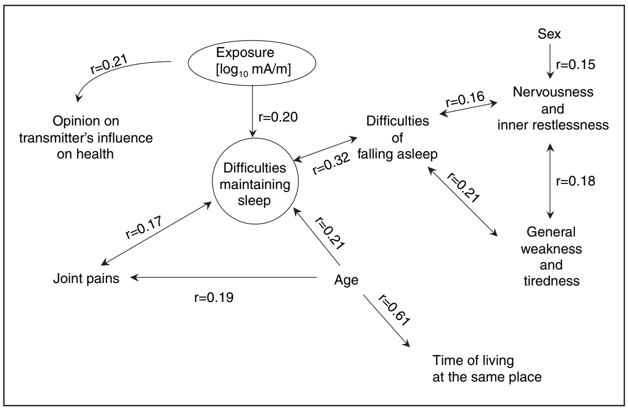


Figure 3. Graph of direct and indirect relationships of measured magnetic field strength with symptoms and personal characteristics of subjects, based on multivariate analysis (graphical model). All variables were correlated with each other, taking into account all other variables. Arrows are only drawn where significant correlations were found. Based on 1992 survey.

Logistic regression yielded an increase in prevalence odds by a factor of 3.2 (95 % confidence limits 1.84 to 5.52) for difficulties falling asleep and by a factor of 3.4 (95 % confidence limits 1.9 to 6.0) respectively for difficulties staying asleep with each increase of field strength by a factor of 10.

Behaviour related to sleep disturbance

In the second survey a number of additional questions on habits possibly related to suffering from sleep disturbance were added. As shown in table 1, the proportion of such habits (e.g. taking sleep drugs, coffee consumption in the evening etc.) was higher in the exposed area. Individuals from farming zone R are probably less comparable to the rest of the study population.

Interrelationship of magnetic field strength, psycho-vegetative symptoms and personal characteristics

Identical multivariate analyses were performed on the results from 1992 and 1996. Figure 2 shows the resulting graphical

Table 1. Prevalence of symptoms and other characteristics of respondents in surveys 1 (1992) and 2 (1996) by zones of different RF-EMF immission.

	Survey	No. respondents	Prevalence Zone A	Prevalence Zone B	Prevalence Zone R	Prevalence Zone C	p-value
No. respondents	1	404	105	119	–	180	–
	2	400	70	83	155	92	–
*Sleep disturbance**			%	%	%	%	
Difficulties in falling asleep	1	404	25.0	18.0	–	7.0	0.000
	2	400	28.7	15.6	14.2	8.7	0.006
Difficulties in maintaining sleep	1	404	32.4	18.5	–	8.9	0.000
	2	400	58.9	43.4	36.8	29.4	0.001
General weakness and tiredness	1	404	22.0	13.0	–	6.0	0.000
	2	399	24.3	17.1	13.6	12.0	0.138
*Other symptoms**			%	%	%	%	
Nervousness, restlessness	1	404	25.0	18.0	–	7.0	0.000
	2	399	30.0	28.6	20.0	13.0	0.024
Limb pain	1	404	14.3	6.7	–	3.3	0.003
	2	400	20.0	15.7	21.3	12.0	0.268
Joint pain	1	404	22.9	10.1	–	10.0	0.004
	2	400	24.3	19.3	23.9	18.5	0.671
Neck and shoulder pain	1	404	17.1	15.1	–	10.0	0.182
Back pain	1	404	7.6	10.1	–	6.7	0.566
Personal characteristics and behaviour			%	%		%	
Believe in transmitter's influence on health at up to 1500 meters distance	1	404	12.4	16.0	–	5.0	0.006
Spare time mainly away from home	1	404	41.9	34.4	5.6	5.0	0.000
Sleep much better/better away from home	2	399	36.2	28.9	24.8	7.8	0.000
Drug use to fall asleep (1/month or more)	2	445**	17.6	14.6	4.3	8.4	0.004
Drug use to maintain sleep	2	442**	8.2	10.1	3.7	6.7	0.135
Coffee before bedtime	2	401	2.9	6.0	3.9	14.1	0.006
Main meal in the evening	2	393	1.4	7.1	9.2	16.1	0.014
Sociodemographic characteristics			%	%	%	%	
Proportion female	1	404	61.9	52.1	–	58.9	–
	2	445**	64.9	53.8	46.6	62.5	–
Age median age	1	404	44	44	–	46	–
	2	446**	53.5	48	44	49.5	–
Education Compulsory only	1	403	39.0	30.3	–	28.5	–
	2	400	41.4	27.7	23.9	23.9	–

*Always or often

**incl. respondents with short telephone interview

model for 1992. The model based on the 1996 data is very similar (and thus not shown), in spite of the fact that almost 40 % of the respondents came from a different exposure group, and although prevalence of reported sleep disturbance was higher in 1996. "Difficulties maintaining sleep" is the only symptom directly related to EMF field strength (1992 data) or distance from the transmitter (1996 data), whereas all other symptoms and personal characteristics show significant correlations with field strength only indirectly through the association with "difficulties staying asleep". For 1992 there is also a correlation between exposure and "believing in health effects of EMF", whereas the correlation between this variable and "difficulties staying asleep" is not significant and therefore not shown in the model.

Sleep disturbance and salivary melatonin after interruption of transmitter activity

In the experimental study of 1993 with 65 human subjects, a decrease of awakenings during the second night after interruption of exposure was correlated to the extent of previous exposure. Urinary 6-hydroxy-melatonin-sulfate levels showed neither a chronic effect between exposure groups nor acute changes after interruption or reinstatement of exposure [1]. In cows, no chronic effect was observed either, but there was a statistically significant temporary increase of salivary melatonin three days after transmitter shut-down [6]. The permanent shut-down of the transmitter in 1998 was followed by improved sleep quality. Morning freshness as an indicator of sleep quality was rated every morning on a visual analogue scale ranging from 0 (=very fresh) to 100 (=very tired). Rating of freshness improved after shut down in the exposed group (24 h average H field >1mA/m) by 11.6 units (95 %-CI: 6.7 to 16.5) whereas in the low exposed group (24 h average H field <1mA/m) only minor improvement was observed: mean = 3.2 units (95 %-CI: −0.8 to 7.2). The improvement persisted in a follow up six months later.

Discussion

In the situation of the short-wave radio transmitter of Schwarzenburg, it was possible to study rather large samples of around 400 persons living at different distances from the transmitter, thus allowing for differentiated analyses of dose-effect relationships. When survey 1 was conducted, there had not been much communication between residents about types of symptoms. To our knowledge the hypothesis that sleep disturbance would become the predominant outcome variable had not been voiced before, and the literature available at that time had not led us to a special interest in sleep disturbance. Therefore suggestion as a mechanism is unlikely to have been responsible for the results of survey 1. This was different in survey 2, because the participants of study 1 had been informed that sleep disturbance was the primary outcome symptom. This, together with an increased age of the subjects may explain the higher prevalence of difficulties of maintaining sleep in study 2, while the consistent correlation between sleep disturbance and EMF exposure cannot be explained by confounding factors. The direct correlation of sleeping disturbance with magnetic field strength in multivariate analysis and the pattern of secondary behaviour (consumption of sleeping pills, avoidance of coffee and large meals in the evening, sleeping better when away from home) further strengthen the hypothesis of a real increase of prevalence of sleep disturbance with increasing exposure to RF-EMF.

Several difficulties have to be considered in the study of "soft" effects of electromagnetic fields, including sleep disturbances. These symptoms are rather prevalent in all populations, requiring comparison of prevalence rates between subgroups with different exposure. Many of these symptoms, in particular sleep disturbances can be caused or aggravated by anxiety, including fear of effects from EMF exposure. Soft outcomes cannot be measured objectively in this large number of subjects, but are based on subjective reporting. Thus, blinding in terms of exposure would be desirable, but persons living close to radio stations are experienced in recognizing transmitter activity through physical effects such as resonance phenomena from household appliances (e.g. radio sound from washing machine).

The cross-sectional approach was chosen by necessity in this situation of long-term exposure. Its value is limited for drawing conclusions on causal association, but this was compensated partially by longitudinal observation of morning freshness as an indicator of sleep quality immediately and six months following the shut-down of the transmitter. As no information about non-responders is available, selection bias cannot be ruled out, in particular in the second survey when the public was more aware of the objective of the study. In the first survey decisive selection bias was ruled out, when rates of disturbed sleep maintenance remained statistically significant even when computed under the assumption that all persons experiencing sleep disturbance had participated in the study.

The main strengths of our studies are the detailed exposure measurements and the large numbers of subjects allowing for differentiated data analysis. Two instances of interruption of exposure (of which one, in 1993, without previous information of the subjects) led to improvement of sleep quality as reported in detailed sleep diaries.

How can the study results be interpreted? The series of studies successively revealed consistent evidence of a close association between operation of the Schwarzenburg transmitter and health relevant sleeping disturbances. Believing in negative health effects of the radio transmitter explained only a small part of the association between magnetic field strength and difficulties maintaining sleep. But also, the search for a causal mechanism mediated by melatonin was unsuccessful, except for an isolated observation in cows [6], which can hardly have been influenced by psychological factors. Therefore, further research in humans with longer observation periods is desirable to replicate this observation.

In practical terms, a governmental scientific advisory group examined our results and recognized a causal relationship between operation of the transmitter and sleep disturbances – but left open whether the mechanism was biological or by suggestion. In either case, the population would be suffering and remedial action was thought to be indicated. But generalization and consideration in adjusting general exposure standard limits would only be justified, if more evidence was available for a biological effect.

What is the significance for mobile phone studies? The measured field levels in the vicinity of the short-wave transmitter correspond roughly to maximal but in practice rarely observed field levels close to mobile phone base station. As frequency and signal characteristics are not identical, results cannot directly be transferred. Nevertheless, some of the open questions are comparable, and when psycho-vegetative symptoms including sleep disturbance are suspected as a health consequence, similar study designs, interview constructions and approaches to data analysis might be indicated. Laboratory studies allow to study exposure effects under well controlled conditions using sophisticated measurement devices. However, sufficiently large observation periods, which are relevant to study latency periods, can hardly be achieved in the laboratory. Epidemiologic field studies may therefore be a valuable complement.

Acknowledgements

The studies reported here were supported by the Swiss Federal Office of Energy, the Swisscom Corporation and the Swiss National Science Foundation (SNF 32-52733.97). The authors would like to thank the study participants, the interviewers, the staff of earlier study phases and the supervisory panel of scientists convened by the Federal Office of Energy.

References

[1] Altpeter ES, Krebs Th, Pfluger DH et al. Study on Health Effects of the Shortwave Transmitter Station of Schwarzenburg, Berne, Switzerland. BEW Publication Series, Study No. 55. The Federal Office of Energy, Berne, Switzerland, 1995.

[2] Hillert L, Berglind N, Arnetz BB, Bellander T: Prevalence of self-reported hypersensitivity to electric or magnetic fields in a population-based questionnaire survey. Scand J Work Environ Health 28: 33–41, 2002.

[3] Levallois P: Hypersensitivity of human subjects to environmental electric and magnetic field exposure: a review of the

literature. Environ Health Perspect 110 (Suppl 4): 613–618, 2002.

[4] Katrin MM, Katharina S: Schlafstörungen und gesundheitliche Beschwerden in der Umgebung des Kurzwellensenders Schwarzenburg. Doctoral Thesis, University of Berne, Berne, 2002.

[5] Röösli M, Moser M, Baldinini Y, Meier M, Braun-Fahrländer C: Symptoms of ill health ascribed to electromagnetic field exposure - a questionnaire survey. Int J Hygiene Environl Health 207: 141–150, 2004.

[6] Stärk KD, Krebs T, Altpeter ES, Manz B, Griot B, Abelin T: Absence of chronic effect of exposure to short wave radio broadcast signals on salivary melatonin concentrations in dairy cattle. J Pineal Res 22 (4): 171–176, 1997.

ORIGINAL ARTICLE

Subjective symptoms, sleeping problems, and cognitive performance in subjects living near mobile phone base stations

H-P Hutter, H Moshammer, P Wallner, M Kundi

Occup Environ Med 2006;**63**:307–313. doi: 10.1136/oem.2005.020784

See end of article for authors' affiliations

Correspondence to:
Dr H-P Hutter, Institute of Environmental Health, Medical University of Vienna, Kinderspitalgasse 15, A-1095 Vienna, Austria; hans-peter.hutter@univie.ac.at

Accepted
11 November 2005

Background: The erection of mobile telephone base stations in inhabited areas has raised concerns about possible health effects caused by emitted microwaves.
Methods: In a cross-sectional study of randomly selected inhabitants living in urban and rural areas for more than one year near to 10 selected base stations, 365 subjects were investigated. Several cognitive tests were performed, and wellbeing and sleep quality were assessed. Field strength of high-frequency electromagnetic fields (HF-EMF) was measured in the bedrooms of 336 households.
Results: Total HF-EMF and exposure related to mobile telecommunication were far below recommended levels (max. 4.1 mW/m^2). Distance from antennae was 24–600 m in the rural area and 20–250 m in the urban area. Average power density was slightly higher in the rural area (0.05 mW/m^2) than in the urban area (0.02 mW/m^2). Despite the influence of confounding variables, including fear of adverse effects from exposure to HF-EMF from the base station, there was a significant relation of some symptoms to measured power density; this was highest for headaches. Perceptual speed increased, while accuracy decreased insignificantly with increasing exposure levels. There was no significant effect on sleep quality.
Conclusion: Despite very low exposure to HF-EMF, effects on wellbeing and performance cannot be ruled out, as shown by recently obtained experimental results; however, mechanisms of action at these low levels are unknown.

Hand-held cellular telephones were introduced in the early 1980s. Due to the relatively high microwave exposure for users while they are on the telephone, the potential health effects of mobile phones have been studied in recent years. However, exposure to the much lower emissions from mobile phone base stations has been neglected. There have been only two observational pilot investigations,[1–2] and one experimental study.[3]

The World Health Organisation (WHO)[4] has recently recommended investigating the effects of exposure to emissions from mobile phone base stations to address public concerns.

It has often been argued that if there are detrimental long term effects from high-frequency electromagnetic fields (HF-EMF) as transmitted by mobile phone base stations, then such effects should have been found near powerful radio and television transmitters. This argument is invalid as: (1) there are very few studies on effects from radio and TV transmitters, ecological and cluster studies on cancer,[5–10] and studies on sleep and other endpoints;[11–12] (2) the results of these studies are compatible with the assumption of a moderately elevated risk; and (3) emissions from base stations differ substantially from those of other sources of HF-EMF.

There are numerous reports from physicians that base stations are associated with a number of health symptoms in neighbours. However, these symptoms might be due to fear about negative effects. Nevertheless there is evidence that long term, low level exposure to HF-EMF may result in a number of symptoms (for example, headaches, fatigue, sleep disorders, memory impairments),[13] attributed as microwave sickness syndrome.[14]

This study investigated the relation between exposure from mobile telecommunication and other sources of HF-EMFs and the associations between exposure and symptoms.

METHODS

Selection of base stations

The study covers urban as well as rural areas in Austria. The city of Vienna was selected as the urban area while villages in Carinthia represented the rural areas. Two network providers were each asked to identify about five base stations within both regions that fulfilled the following requirements:

- The antenna must have been operating for at least two years
- There had been no protests by neighbours against the base station
- There was no other base station nearby (this could only be achieved in rural areas)
- Transmission was preferably only in the 900 MHz band.

Twenty one base stations were specified, from which 10 were selected for the study based on inspection of the local conditions (population density, other sources of exposure).

Selection of study area and participants

Data from the 10 selected antenna locations, including the antenna diagram, were provided by the network companies. In order to ensure a sufficient gradient of exposure, these data were used to define the study area around the selected base station. The investigation was carried out by trained students and a medical technical assistant in Carinthia and

Abbreviations: ANCOVA, analysis of covariance; BCCH, broadcast channel; CI, confidence interval; GSM, global system for mobile telecommunication; HF-EMF, high-frequency electromagnetic fields; MHz, megahertz; POR, prevalence odds ratio; SAR, specific (energy) absorption rate; SD, standard deviation; TDMA, time division multiple access; WHO, World Health Organisation

Table 1 Demographic characteristics of subjects by exposure category

	Exposure category (mW/m^2)			
	<0.1	0.1–0.5	>0.5	p value
Age	45 (SD 16)	40 (SD 14)	44 (SD 15)	0.390
Females	60%	58%	56%	0.829
Years of residence	19 (SD 16)	17 (SD 13)	20 (SD 16)	0.403
Hours at home	10 (SD 5)	10 (SD 4)	10 (SD 5)	0.413
Employed	56%	60%	61%	0.689
Urban residence	55%	42%	49%	0.171
Education > 12 y	42%	38%	40%	0.784
Mobile phone use	75%	77%	78%	0.866

p value from Kruskal–Wallis or χ^2 test.

Vienna. Based on power calculations, the projected number was 36 subjects for each of the 10 locations.

In Vienna, households were randomly selected from telephone register entries. Subjects were contacted by telephone. If after three attempts no contact could be achieved, the next entry in the telephone list was chosen. Subjects were told that the relationship between environmental factors and health would be investigated. They had to be older than 18 years, have been living in their present house for at least one year, and been staying there for a minimum of eight hours a day on average. Refusal was slightly above 40% and mainly due to time constraints. On acceptance of participation an appointment was made for a visit. In Carinthia the procedure was different because no clear relation of address to study area could be ensured (houses are not always numbered consecutively). Therefore a random selection of houses based on the site plan was performed. Investigators contacted subjects directly in their homes. In the case of acceptance, either an appointment for the investigation was made or it was carried out immediately. Rate of refusal was somewhat lower than in the urban area (32%). On contact, gender, age, and duration of residence in their present house (eligibility criteria) were registered. Nonparticipants were insignificantly more frequently males (47% *v* 41%) and significantly younger (40 *v* 44 years), and had a significantly shorter time living in their present house (13 *v* 16 years).

Data collection and measurements

All investigations were done in the homes of the subjects using a laptop computer. Performance tests as well as questionnaires were presented along with instructions on the screen. Handling was so simple that after a short introduction all subjects were able to fulfil the tasks without further assistance by the investigators. The investigation consisted of the following:

- Sociodemographic data, sources of EMF exposure within the household, regular use of mobile telephones.
- Evaluation of environmental quality, subjective scaling of the impact different environmental factors could have on the health of the subjects. Among the items listed were traffic noise, particulate matter, and mobile phone base station. Assumed impact was rated on a five point scale from 0 = not at all, to 4 = very strong impact.
- Subjective scaling of symptoms (Zerssen scale).[15] Symptoms were rated on a four point scale from 0 = not at all, to 3 = strong. Symptoms of special interest were headaches, symptoms of exhaustion, and circulatory symptoms (see table 4). For analysis, ratings were dichotomised (0/1–3).
- Investigation of sleeping problems (Pittsburgh sleeping scale).[16] Problems falling asleep and staying asleep were rated by the participants on a frequency scale ranging from never to more than 3 days a week. The global index is

Table 2 Exposure categories and results of analysis of covariance for tests of cognitive performance

	Exposure category (mW/m^2)			
Test	<0.1	0.1–0.5	>0.5	p value
Memory				
Immediate memory*	6.2 (1.4)	5.6 (1.4)	5.9 (1.5)	0.166
Short term memory (1 min)†	29.1 (4.3)	29.5 (4.1)	29.3 (3.9)	0.354
Short term memory (5 min)†	33.9 (2.9)	33.1 (3.1)	34.0 (1.9)	0.761
Short term memory (15 min)†	33.4 (2.9)	33.6 (2.4)	33.7 (2.0)	0.883
d′ (1 min)‡	0.87 (0.48)	0.88 (0.42)	0.86 (0.41)	0.737
d′ (5 min)‡	1.54 (0.39)	1.48 (0.62)	1.53 (0.32)	0.579
d′ (15 min)‡	1.56 (0.39)	1.54 (0.32)	1.62 (0.27)	0.198
ln β (1 min)§	−0.34 (0.45)	−0.19 (0.32)	−0.29 (0.30)	0.235
ln β (5 min)§	−1.09 (0.58)	−1.11 (0.72)	−1.04 (0.54)	0.605
ln β (15 min)§	−1.36 (0.53)	−1.21 (0.52)	−1.47 (0.53)	0.095
Perceptual speed				
Speed score (sec)	4.3 (0.9)	4.0 (1.1)	3.8 (1.0)	0.061
Items solved (max. 8)	4.6 (2.4)	4.1 (2.3)	4.1 (2.5)	0.147
Choice reaction task				
Reaction time (msec)	582 (217)	511 (139)	585 (244)	0.485

Results expressed as mean (SD).
p values for exposure factor are shown.
*Highest number of correctly reproduced digits.
†Number of correctly identified items (sum of correct detections (from 20) and correct rejections (from 20 distraction items)).
‡d-prime from signal detection analysis.
§Natural logarithm of detection bias beta.

computed as the sum of seven sub-scales (see table 5) with each component scored 0 to 3 (higher score indicates greater problems).

- Cognitive performance.
  - Memory tasks consisted of a short term memory test using 1–10 digit numbers that had to be reproduced immediately after presentation. The score was defined as the highest number of digits correctly reproduced. The assessment of medium term memory was based on 20 simple everyday objects in silhouette drawings presented together for 30 seconds on the screen. After 1, 5, and 15 minutes these items together with 20 distraction items (different for the three tests) were presented in random sequence, one at a time, and the subjects had to decide whether or not the picture was among those presented. Each response was followed by immediate feedback. After each test all objects were again presented for 15 seconds. The score was defined as the number of correct responses. In addition, d-prime and response bias (beta) from signal detection analysis were computed (d-prime is the normalised distance between the signal and noise answer distributions, the higher the d-prime, the less likely is confusion between target and distraction items; beta measures the bias to respond ''yes'' whether it is a target or distraction item).
  - The choice reaction task consisted of a random sequence of squares of three different colours (red, green, and yellow) appearing at random locations on the screen. Subjects had to react as fast as possible by pressing a specified button for each colour. The score was defined as the average correct reaction time across 25 trials.
  - Perceptual speed was tested by presenting two series of 10 letters (''meaningless words'') that differed at exactly one position. Eight of these double series were presented in random sequence. Subjects had to find the differing letter under time constraints (maximum 6 seconds) and place a cursor below it. These position varied between the 3rd and 7th letters. Score was defined as the average time to achieve the correct solution. In addition, the number of items solved within the time window was computed.

After completion of the questionnaires and tests, dates were arranged for exposure measurements. Measurements of high frequency EMFs were done by a specialist from a certified centre in Vienna (TGM). A biconic field probe (PBA 10200, ARC Seibersdorf) was used connected to a spectrum analyser (FSP, Rhode & Schwarz). Measurements were performed in the bedroom (this being typically the only place in the house where people consistently spend many hours a day). As exposure may vary at this location, in addition to the sum of power densities across all mobile phone frequencies, the maximum exposure from the base station was computed based on measurements of broadcast channels. Broadcast channels (BCCH) operate all the time at maximum power with all time slots occupied. Hence multiplication of measurements of BCCH by the ratio of the sum of the power of all channels to that of the BCCH results in maximum possible exposure level, while the sum of BCCH measurements gives the minimum. The former is the result of all channels operating at maximum power with all time slots occupied, while the latter occurs if no traffic channel is active.

Distance from the antenna was calculated based on the coordinates of the measurement location and the base station. It ranged between 24 m and 600 m in rural areas and between 20 m and 250 m in urban areas. The smaller range in the latter was due to the vicinity of other base stations and the shadowing effect of high buildings.

Subjects

In total, 365 subjects were investigated (185 in Vienna and 180 in Carinthia). In some cases EMF measurements were not possible due to the absence of the inhabitants at the arranged date. Therefore, only data from 336 subjects could finally be evaluated.

Subjects were between 18 and 91 years of age (mean 44, SD 16 years). Fifty nine per cent were female. Average duration of residence in the house was 19 (SD 16) years, and subjects stayed for 10 (SD 5) hours a day in the immediate neighbourhood. Overall, six subjects occupied the place only after erection of the base station. All subjects slept normally at home.

Statistical analysis

Statistical evaluation of exposure from the base stations was done by analysis of covariance (ANCOVA) for components of the Pittsburgh Sleeping Scale and performance measurements, and by logistic regression analysis for subjective symptoms based on the following procedure. First the maximal power density estimates from base station frequencies were classified into three groups: $\leqslant 0.1$ mW/m^2 (approximately up to median), 0.1–0.5 mW/m^2 (between median and 3rd quartile), and >0.5 mW/m^2. Originally it was planned to define four exposure categories based on quartiles. However, it turned out that the level of exposure was too low for the two lowest exposure categories to be meaningfully discriminated and consequently these categories were combined. Average exposure levels were 0.04 mW/m^2, 0.23 mW/m^2, and 1.3 mW/m^2, respectively. Exposure level, area (rural *v* urban), and interaction were included as fixed factors, age, sex, regular use of a mobile telephone, and the subjective rating of negative consequences of the base station on health were used as covariables. Normality was assessed by Kolmogorov–Smirnov tests using Lilliefors p values, homogeneity of variance by Levene's tests. For all analyses the model with separate slopes was first tested. If none of the interactions with fix factors were significant at the 10% level, the model with homogenous slopes was computed. In addition, homogeneity of variance–covariance matrices of covariables and dependent variables across groups was tested by Box M tests. Unconditional logistic regression was performed using the same covariables. For all tests a p value below 0.05 was considered significant. No correction for multiple testing was applied.

RESULTS

Table 1 gives an overview of features of participants across exposure categories. Although none of the variables reached statistical significance, the somewhat higher proportion of subjects from the urban area in the lowest exposure category should be noted.

Exposure to high frequency EMFs was generally low and ranged from 0.0002 to 1.4 mW/m^2 for all frequencies between 80 MHz and 2 GHz; the greater portion of that exposure was from mobile telecommunications (geometric mean 73%), which was between 0.00001 and 1.4 mW/m^2. Maximum levels were between 0.00002 and 4.1 mW/m^2. Overall 5% of the estimated maximum exposure levels were above 1 mW/m^2. Average exposure levels were slightly higher in the rural area (0.05*/7.6 mW/m^2) than in the urban area (0.02*/7.1 mW/m^2).

Most subjects expressed no strong concerns about adverse health effects of the base station. In the urban and rural test areas, 65% and 61% respectively stated no concerns at all.

Table 3 Detailed results of analysis of covariance for speed score of perceptual speed as a dependent variable

Source of variation		df	MSQ	F value	p value
Covariates	Combined	4	54.980	19.721	0.000
	Concerns about base station	1	2.618	0.939	0.333
	Age	1	216.469	77.648	0.000
	Sex	1	0.028	0.010	0.920
	Use of mobile phone	1	0.803	0.288	0.592
Main effects	Combined	3	28.562	10.245	0.000
	Area (rural/urban)	1	69.948	25.090	0.000
	GSM exposure	2	7.869	2.823	0.061
Interaction		2	0.036	0.001	0.999

Factors and covariables are shown in the column ''source of variation''.
df, degrees of freedom; MSQ, mean sum of squares.

Table 2 gives an overview of results from ANCOVA on the different tests of cognitive performance for the exposure factor only; table 3 shows the full results for the test of perceptual speed. For perceptual speed a tendency for faster reaction in the higher exposure category was found. Omitting the three insignificant covariates from analysis resulted in a significant ($p = 0.009$) main effect for exposure. Logistic regression with the median chosen as a cut-off point was statistically significant. The estimated risk of a value below the median speed score relative to the lowest exposure category was 0.73 (95% CI 0.33 to 1.58) for the second and 0.42 (95% CI 0.18 to 0.98) for the third exposure categories. Accuracy of perceptual speed indicated by number of correct reactions showed the opposite effect, although not

Table 4 Relative risk estimates of subjective symptoms of primary interest for categories of exposure to microwaves from base stations in the bedroom against lowest exposure category

Symptom	Exposure category (mW/m^2)	% with symptom	Relative risk*	95% CI	p value
Headaches	≤0.1†	61	1.00		0.017
	0.1–0.5	66	1.36	0.62–2.99	
	>0.5	79	3.06	1.22–7.67	
Vertigo	≤0.1 †	17	1.00		0.306
	0.1–0.5	27	1.27	0.50–3.22	
	>0.5	32	1.54	0.68–3.50	
Palpitations	≤0.1†	26	1.00		0.444
	0.1–0.5	32	1.06	0.45–2.47	
	>0.5	38	1.37	0.61–3.11	
Tremor	≤0.1†	12	1.00		0.062
	0.1–0.5	9	0.68	0.19–2.41	
	>0.5	26	2.37	0.96–5.87	
Hot flushes	≤0.1†	32	1.00		0.739
	0.1–0.5	26	0.90	0.39–2.09	
	>0.5	26	0.87	0.37–2.01	
Sweating	≤0.1 †	34	1.00		0.455
	0.1–0.5	38	1.05	0.47–2.32	
	>0.5	40	1.35	0.61–2.97	
Cold hands or feet	≤0.1†	40	1.00		0.019
	0.1–0.5	46	1.03	0.40–2.63	
	>0.5	62	2.57	1.16–5.67	
Loss of appetite	≤0.1†	13	1.00		0.069
	0.1–0.5	17	1.23	0.42–3.57	
	>0.5	24	2.40	0.93–6.18	
Loss of energy	≤0.1†	63	1.00		0.886
	0.1–0.5	63	1.32	0.61–2.84	
	>0.5	58	1.06	0.49–2.27	
Exhaustion	≤0.1†	44	1.00		0.098
	0.1–0.5	41	0.77	0.30–2.02	
	>0.5	51	2.07	0.87–4.89	
Tiredness	≤0.1†	64	1.00		0.258
	0.1–0.5	89	1.97	0.64–6.10	
	>0.5	88	1.92	0.62–5.96	
Difficulties to concentrate	≤0.1†	60	1.00		0.035
	0.1–0.5	64	1.32	0.61–2.86	
	>0.5	76	2.55	1.07–6.08	
Feeling strained	≤0.1†	44	1.00		0.450
	0.1–0.5	51	1.67	0.76–3.65	
	>0.5	40	0.74	0.33–1.63	
Urge for sleep	≤0.1†	47	1.00		0.630
	0.1–0.5	54	1.21	0.56–2.61	
	>0.5	51	1.17	0.53–2.54	

p values for exposure factor are shown.
*Adjusted for age, sex, region, regular use of mobile telephone, and fear of adverse effects of the base station.
†Reference category.

Table 5 Results of analysis of covariance for components and global score of the Pittsburgh Sleep Quality Index and logistic regression for "poor sleepers" (global score >5)

	Exposure category (mW/m²)			
Component	<0.1	0.1–0.5	>0.5	p value
Subjective sleep quality	0.71 (0.79)	0.60 (0.77)	1.00 (0.89)	0.240
Sleep latency	0.76 (0.93)	0.74 (0.95)	0.94 (0.98)	0.295
Sleep duration	1.06 (0.98)	1.14 (1.03)	1.21 (1.09)	0.504
Habitual sleep efficiency	0.54 (0.92)	0.70 (0.98)	0.74 (1.15)	0.061
Sleep disturbances	0.92 (0.58)	0.91 (0.66)	0.91 (0.62)	0.338
Daytime dysfunction	0.66 (0.75)	0.54 (0.70)	0.82 (0.90)	0.099
Sleep medication	0.10 (0.46)	0.17 (0.71)	0.21 (0.73)	0.216
Global score	4.74 (3.52)	4.78 (3.86)	5.87 (4.21)	0.282
Poor sleepers (%)	35%	31%	41%	0.225

Results expressed as mean (SD).
p values for exposure factor are shown.

to a significant extent. Hence there is some speed–accuracy trade-off.

For subjective symptoms of primary interest, effects of exposure from the base station are shown in table 4. Many symptoms were more frequent at higher exposure levels; headaches, cold hands or feet, and difficulties in concentrating, and to a lesser degree, tremor, loss of appetite, and feelings of exhaustion showed increased prevalence after correction for confounding factors.

Results for sleep quality are shown in table 5. Two subscales (sleep efficiency and daytime dysfunction) showed indications of poorer sleep at higher exposure categories. A highly significant effect of concerns about negative health implications of the base station was found for overall sleep quality (global score), with poorer quality in those concerned. As expected, age also had a significant influence. Without considering the influence of the subjects' concerns about the base station, the effect of exposure would have been statistically significant. Logistic regression analysis with the median score as a cut-off point showed no pronounced effect of exposure ($p = 0.131$).

DISCUSSION

Mobile phone base stations easily comply with current guidelines (for example, ICNIRP (International Commission on Non-Ionizing Radiation Protection) guidelines).[17] Our measurements show that exposure of the public in the vicinity of base stations is indeed low. However, considering all HF-EMF exposures above 80 MHz, mobile telecommunication is responsible for an average of 73% of these exposures. This is consistent with representative measurements in Sweden[18] and the UK.[19]

The present study was conducted to provide answers to intriguing methodological problems of the epidemiological investigation of base stations.

How is it possible to attribute effects to a specific source of HF-EMF? In study areas, exposure from other sources of HF-EMFs was from distant transmitters and therefore more or less constant. Effects from these exposures will therefore not confound the effects of base stations. As study areas were selected to guarantee a gradient of exposures from base stations, the only relevant contribution to the variance of HF-EMF exposure was from base stations (93% of variance).

Another problem is the time variation of exposure, depending on the number of connected calls (due to the TDMA (time division multiple access) mode of the GSM system). Of course the best approach would be a long term measurement of exposure, or to use personal "dosimeters". However, there are no such dosimeters available and long term measurements are not feasible due to economic restrictions as well as problems of compliance. A possible solution is to conduct a short term measurement at a location where subjects are assumed to spend considerable periods of time (we chose the bedroom), analyse the spectrum of exposure, and select the broadcast channels that are operating at constant maximum power. Based on these measurements a range of exposures can be computed. We analysed data based on broad categories so that this categorisation leads to almost equal allocation whether "average", minimum, or maximum exposure estimation is used. A broad categorisation was used because of other sources of variance of exposure (like movements of subjects) that cannot be accounted for.

A further problem is the dynamic development of telecommunication networks. For the present study, we selected base stations emitting with unchanged features for

Table 6 Results of analysis of covariance (ANCOVA) for global score of the Pittsburgh Sleep Quality Index as dependent variable

Source of variation		df	MSQ	F value	p value
Covariates	Combined	4	323.407	11.770	0.000
	Concerns about base station	1	482.088	17.545	0.000
	Age	1	661.076	24.059	0.000
	Sex	1	87.286	3.177	0.076
	Use of mobile phone	1	63.176	2.299	0.130
Main effects	Combined	3	42.571	1.549	0.202
	Area (rural/urban)	1	57.795	2.103	0.148
	GSM Exposure	2	34.959	1.272	0.282
Interaction		2	58.404	2.126	0.121

Factors and covariables are shown in the column "source of variation".
df, degrees of freedom; MSQ, mean sum of squares.

Main messages

- Exposure from mobile phone base stations is orders of magnitude below current guideline levels.
- Self-reported symptoms like headache and difficulties in concentrating show an association with microwave exposure from base stations, not attributable to subjects' fear of health effects from these sources.
- Other symptoms, like sleeping problems, seem to be more due to fear of adverse health effects than actual exposure.

Policy implications

- Despite very low emissions from mobile phone base stations, more research concerning the effects of radiofrequency radiation from base stations is indicated.
- As a precautionary measure, siting of base stations should be such as to minimise exposure of neighbours.

at least two years. Furthermore, it was important that no other base station was nearby (which, however, could only be achieved in rural areas).

Because of the much higher exposure during telephoning compared to exposure from base stations, it is hardly conceivable that such small additional exposure could have an effect. However, these exposures have fundamentally different features. Exposure from the base station will be at low, but more or less constant levels for many hours a day, especially during the night. Comparing these levels is inappropriate if long term effects actually exist. If, for example, a subject is using a GSM mobile with a specific energy absorption rate (SAR) of 0.04 W/kg[20] for 10 minutes, this would be roughly equivalent to a 15 day exposure from a base station at an exposure level of 1 mW/m^2 if the principle of time–dose reciprocity is valid. However, it is not known whether this principle holds for exposure to HF-EMFs.

There is no a priori argument why the much lower levels from base stations should have no effect in the presence of widespread use of mobile telephones. Possible confounding by using a mobile has been considered in this study.

Generally, ratings were higher for most symptoms in subjects expressing concerns about health effects from the base station. Subjects who experience health problems might search for an explanation in their environment and blame the base station; another explanation would be that subjects with concerns are more anxious and also tend to give a more negative view of their body functions, or that some people generally give quite negative answers. Irrespective of these explanations there seem to be effects of exposure that occur independently of the fear of the subjects about the base station affecting their health. This is the case for headaches, cold hands or feet, and difficulties in concentrating, for example. These effects were robust with respect to additional potential confounders (for example, for headaches, inclusion of an indicator of socioeconomic status—years of education and type of occupation—slightly increased the risk estimator for exposure and decreased the p value from 0.017 to 0.016; inclusion of years of living in the present home and overall rating of environmental quality slightly increased the p value to 0.019; inclusion of hours staying at home did not change effect estimates at all). Interestingly these symptoms as well as some others that tended to be increased at higher exposure levels belong to those attributed to the microwave sickness syndrome. However, no clear relationship has been found for sleeping problems that are often mentioned in the public debate. The effect on sleep is dominated by concerns of the subjects of negative health effects of the base station. Many factors are known to influence sleep quality. Only a few could be considered in this study. Since some aspects of sleep quality, like sleep efficiency, showed a tendency for being affected by exposure, future studies should attempt to eliminate additional confounders.

Concerning symptom reporting there are a number of personality factors for which an association has been established. Among these are state anxiety, depression, and negative affectivity. The main question concerning this range of factors is whether they might act as confounders. In discussions of the microwave sickness syndrome, depression has also been mentioned among the possible effects of exposure; confounding is therefore conceivable. Sleep quality, unspecific symptoms, depression, affectivity, and other personality characteristics are connected with each other in a network of relationships such that a clear understanding of the possible long term effects of exposure may only be determined by longitudinal studies.

No influence of the subjects' fear about negative effects of the base station was found for cognitive performance. There was a small but significant reduction of reaction time for perceptional speed at increased exposure levels. It is interesting to note that such facilitating effects have also been reported during short term experimental exposures[20 22] and a study in teenagers using mobile phones.[21] On the other hand, a study[12] in children chronically exposed to emissions from a radio tower reported increased reaction times and reduced performance in cognitive tasks. We found a reduction of reaction time in adults, but an insignificant decrease of accuracy. Recognition in the medium term memory task showed a reasonable and increasing differentiation between target and distraction items and a decreasing response bias over repeated tests, but there was no indication of an influence of exposure from the base station. Furthermore, cognitive performance varies with factors that have not been controlled or considered in this study. Indices of socioeconomic status, however, were tested and did not modify effect size of base station exposure.

The results of this study indicate that effects of very low but long lasting exposures to emissions from mobile telephone base stations on wellbeing and health cannot be ruled out. Whether the observed association with subjective symptoms after prolonged exposure leads to manifest illness remains to be studied.

ACKNOWLEDGEMENTS

This study was supported by the Scientific Medical Funds of the Mayor of the City of Vienna and the Government of the County of Carinthia. The assistance of Dr M LMathiaschitz, Mrs G Pridnig, and Mrs B Piegler is gratefully acknowledged.

. . . .

Authors' affiliations

H-P Hutter, H Moshammer, P Wallner, M Kundi, Institute of Environmental Health, Medical University of Vienna, Austria

Competing interests: none

REFERENCES

1 **Santini R**, Santini R, Le Ruz P, *et al.* Survey study of people living in the vicinity of cellular phone base stations. *Electromagnetic Biology and Medicine* 2003;**22**:41–9.

2 **Navarro EA**, Segura J, Portosolés M, *et al.* The microwave syndrome: a preliminary study in spain. *Electromagnetic Biology and Medicine* 2003;**22**:161–9.

3 **Zwamborn A**, Vossen S, van Leersum S, *et al. Effects of global communication system radio-frequency fields on well being and cognitive functions on human beings with and without subjective health complaints. TNO-report FEL-03-C148*. The Hague: TNO Physics and Electronic Laboratory, 2003.

4 **World Health Organisation**. International EMF Project, Agenda for research. http://www.who.int/peh-emf/research/agenda/en (accessed 13 June 2004).

5 **Hallberg Ö**, Johansson O. Melanoma incidence and frequency modulation (FM) broadcasting. *Arch Environ Health* 2002;**57**:32–40.

6 **Dolk H**, Shaddick G, Walls P, *et al.* Cancer incidence near radio and television transmitters in Great Britain, Part I. Sutton Coldfield Transmitter. *Am J Epidemiol* 1997;**145**:1–9.

7 **Dolk H**, Elliot P, Shaddick G, *et al.* Cancer incidence near radio and television transmitters in Great Britain, Part II. All high-power transmitters. *Am J Epidemiol* 1997;**145**:10–17.

8 **Hocking B**, Gordon IR, Grain ML, *et al.* Cancer incidence and mortality and proximity to TV towers. *Med J Aust* 1996;**165**:601–5.

9 **Maskarinec G**, Cooper J, Swygert L. Investigation of increased incidence in childhood leukemia near radio towers in Hawaii: preliminary observations. *J Environ Pathol Toxicol Oncol* 1994;**13**:33–7.

10 **Selvin S**, Schulman J, Merrill DW. Distance and risk measures for the analysis of spatial data: a study of childhood cancers. *Soc Sci Med* 1992;**34**:769–77.

11 **Altpeter E**, Battaglia M, Bader A, *et al.* Ten years experience with epidemiological research in the vicinity of the short-wave broadcasting area Schwarzenburg: what does the story tell us? *Proceedings of the International Conference on Cell Tower Siting*. Salzburg, Austria, 7–8 June, 2000:127–32.

12 **Kolodynski AA**, Kolodynska VV. Motor and psychological functions of school children living in the area of the Skundra Radio Location Station in Latvia. *Sci Tot Environ* 1996;**180**:87–93.

13 **Silverman C**. Nervous and behavioral effects of microwave radiation in humans. *Am J Epidemiol* 1973;**97**:219–24.

14 **Johnson Liakouris AG**. Radiofrequency (RF) sickness in the Lilienfeld study: an effect of modulated microwaves? *Arch Environ Health* 1998;**53**:236–8.

15 **Zerssen D v, Koeller DM**. Die Befindlichkeitsskala. Testzentrale Göttingen. 1976.

16 **Buysse DJ**, Reynolds III CF, Monk TH, *et al.* The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research. *Psychiat Res* 1989;**28**:193–213.

17 **International Commission on Non-Ionizing Radiation Protection**. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). *Health Phys* 1998;**74**:494–522.

18 **Hamnerius I**, Uddmar Th. Microwave exposure from mobile phones and base stations in Sweden. *Proceedings of the International Conference on Cell Tower Siting*. Salzburg, Austria, 7–8 June, 2000:52–63.

19 **Mann SM**, Cooper TG, Allen SG, *et al. Exposure to radio waves near mobile phone base stations,* NRPB-R321, 2000.

20 **Persson T**, Törnevik C, Larsson LE, *et al.* GSM mobile phone output power distribution by network analysis of all calls in some urban, rural and in-office networks, complemented by test phone measurements. *24th Meeting of the Bioelectromagnetics Society*. Quebec, Canada, June, 2002:181–3.

21 **Edelstyn N**, Oldershaw A. The acute effects of exposure to the electromagnetic field emitted by mobile phones on human attention. *Neuroreport* 2002;**13**:119–21.

22 **Lee T**, Ho S, Tsang L, *et al.* Effect on human attention of exposure to the electromagnetic field emitted by mobile phones. *Neuroreport* 2001;**12**:729–31.

23 **Preece AW**, Iwi G, Davies Smith A, *et al.* Effect of a 915-MHz simulated mobile phone signal on cognitive function in man. *Int J Radiat Biol* 1999;**75**:447–56.

ORIGINAL ARTICLE

Health response of two communities to military antennae in Cyprus

A W Preece, A G Georgiou, E J Dunn, S C Farrow

Occup Environ Med 2007;**64**:402–408. doi: 10.1136/oem.2006.028894

See end of article for authors' affiliations

Correspondence to:
Professor A W Preece,
Biophysics Research Unit,
Department of Medical
Physics, Clinical Sciences
South Bristol, Bristol
Haematology & Oncology
Centre, Horfield Road,
Bristol BS2 8ED, UK;
a.w.preece@bristol.ac.uk

Accepted 19 January 2007

Objectives: This study investigated concerns that have been raised about past and future health effects caused by high power transmissions of high frequency (7–30 MHz) radio waves from military antenna systems at Akrotiri, Cyprus.

Methods: A cross-sectional study of three villages (two exposed, one unexposed) collected longitudinal and short-term radiofrequency measurements. Health data were collected using questionnaires containing information on demographic factors, specific illnesses, general health (SF-36 well-being questionnaire), reproductive history, childhood illnesses, risk perception and mortality. Analysis was with SPSS v11.5 using cross tabulations of non-parametric data and tests for significance. Key health outcomes were subjected to logistic regression analysis.

Results: Field strengths within the two ''exposed'' villages were a maximum of 0.30 (Volts/Vm^{-1} metre) from the 17.6 MHz military transmissions and up to 1.4 Vm^{-1} from unspecified sources, mainly cell phone frequencies. The corresponding readings in the control village were <0.01 Vm^{-1}. Compared with the control village there were highly significant differences in the reporting of migraine (OR 2.7, $p<0.001$), headache (OR 3.7, $p<0.001$), and dizziness (OR 2.7, $p<0.001$). Residents of the exposed villages showed greater negative views of their health in all eight domains of the SF-36. There were also higher levels of perceived risk, particularly to noise and electromagnetic ''pollution''. All three villages reported higher values of risk perception than a UK population. There was no evidence of birth abnormalities or differences in gynaecological or obstetric history. Numbers of cancers were too small to show differences.

Conclusion: It was clear that even this close (1–3 km) to powerful transmissions, the dominant sources of radiofrequency fields were cell phone and national broadcast systems. There was no excess of cancer, birth defects or obstetric problems. There was heightened risk perception and a considerable excess of migraine, headache and dizziness, which appears to share a gradient with radiofrequency exposure. The authors report this association but suggest this is unlikely to be an effect of radiofrequency and more likely to be antenna visibility or aircraft noise.

The Akrotiri salt lake site is part of the UK Sovereign Base Areas Administration (SBAA) in Cyprus and contains a military air base and a large antenna array. The proposal to build a larger phased array (Pluto 2) to supplement the existing Pluto 1 antenna was greeted with demonstrations and media campaigns. The inhabitants expressed fears about cancer and childbirth problems, and cited concerns expressed in other countries that had led to restrictions outside the usually accepted International Commission on Non-Ionizing Radiation Protection (ICNIRP) levels[1] for radiofrequency exposure. Indeed the operational guidelines used at the time were National Radiological Protection Board (NRPB)[2] levels that were some five times higher than ICNIRP since the former did not distinguish public and occupational exposure differences. The public are to some extent confused because different countries have set different levels,[3] for ''precautionary'' reasons related to possible non-thermal effects. Thermal effects and their consequences are well established, and national guidelines, albeit at variance[3] with each other, have been set out to control these. However non-thermal effects have been seen to occur at low levels and probably represent no more than minor physiological responses.[4]

At a public meeting there was a call for a health survey to be linked to measurements of the fields from the military system. To meet these requirements the SBAA agreed to set up a monitoring antenna in Akrotiri village that relayed data to the Ministry of Telecommunications in Nicosia, and to commission this health survey (under the direction of the Ministry of Health, Cyprus) that began in June 2001. The survey consisted of two distinct elements: a health survey and a measurement survey.

METHODS

Subjects

A cross-sectional survey was conducted across three sites: the ''exposed'' sites of Akrotiri village and the smaller community of Asomatos, and the ''unexposed'' Pano Kyvides. This enabled comparisons to be made between the exposed communities and non-exposed village for both the electromagnetic field (EMF) profiles and health information collected. The spatial relationship of the villages and the antenna site is shown in figure 1.

Questionnaires

The prevalence of specific symptoms and diseases among the residents of all three communities was investigated using specifically designed questionnaires, a risk perception survey, and the collection of health and mortality data from available registry and other sources. Different questionnaires were used for age and gender specific issues:

1. The adult questionnaire comprised four sections. The first was concerned with basic demographic information. The second contained a list of 11 specific conditions or illnesses

---

Abbreviations: EMF, electromagnetic field; ICNIRP, International Commission on Non-Ionizing Radiation Protection; NRPB, National Radiological Protection Board; SMR, standardised mortality ratio

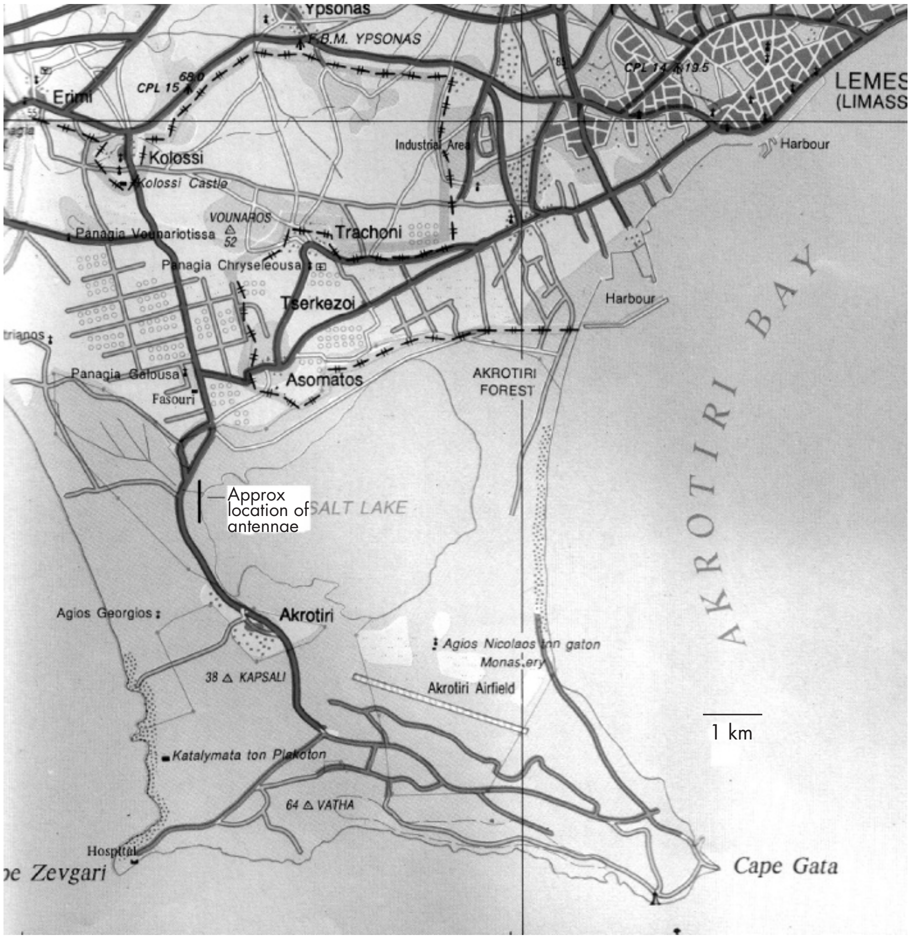


Figure 1 Location of antenna array in relation to Akrotiri and Asomatos. Note that the control village was approximately 15 km to the northeast of the antenna site (obtained from the Department of Land and Surveys, Cyprus).

under a general header "Have you had any of the following conditions?" and included, among others, migraine, headache and dizziness. Previous research[5–8] conducted on the health of populations living near broadcast media sites and electricity installations, provided an indication of the diagnoses and disease patterns of interest. This section went on to explore certain health behaviours such as smoking and mobile phone use, which may have a confounding effect on other responses. The third section used the SF-36 as a standard measure of health status. The SF-36 is a multipurpose, short-form health survey with only 36 questions. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index.[9] Our version was a validated instrument in Greek obtained from the suppliers. Finally, the fourth section was concerned with an individual's relative perceptions of risk. A series of questions, previously developed at Bristol University, UK from a Swedish Occupational Health study and also used in the US,[10–12] was adapted for use with regard to proximity to military antennae. Respondents were invited to consider a series of situations and apply a "risk category" to each on a 5-point scale. The majority of items were identical to questions that had been used in the UK so that cultural comparisons would be possible.

2. The female questionnaire was an additional questionnaire for completion by all female residents of the communities aged 18–50 years. Previous research had suggested that electromagnetic field exposure may be associated with certain reproductive health effects,[13] and so this questionnaire was concerned with reproductive history including pregnancy, miscarriage, fetal loss and infertility.

3. The child questionnaire concerned the health of children under 16 years.

All questionnaires were translated into Greek and back translated into English.

Questionnaire data analysis

Analysis was carried out using a standard statistical package (SPSS v11.5). Most of the analyses were simple cross-tabulations for non-parametric data using the Pearson χ^2 test. Logistic regression analysis was used on four key outcome variables—migraine, headache, dizziness and depression. Models were developed incorporating all independent variables that had been shown to have an association with the particular outcome. This was assessed using the Pearson χ^2 statistic ($p<0.05$). These were entered in a stepwise way based on their level of association.

Mortality data collection

As official sources of mortality data were insufficient for our purpose, an alternative approach was used. Each family was asked to complete a questionnaire concerning family members (resident in the village) who had died within the previous 10 years. Details pertaining to the cause of death and the attending physician were requested. Data were then checked later against hospital records to confirm diagnosis. Because of the interest in brain tumours and leukaemia, special attention was paid to checking the cause of death and the site of specific cancers.

Table 1 Percentage of respondents reporting health problems or illnesses, percentage for each of the eight SF-36 domain scales and results of risk perception on a scale of 1 to 5

	Akrotiri (%)	Asomatos (%)	Pano Kyvides (%)		p Value
Condition					
Migraine	23.1	14.8	9.9		<0.001
Headache	51.3	35.1	22.2		<0.001
Dizziness	35.7	20.9	10.2		<0.001
Depression	10.2	9.7	3.9		0.002
Name of scale					
Physical functioning	75.7	70.7	80.9		<0.001
Role physical	71.4	71.5	81.0		0.001
Bodily pain	72.1	71.2	79.9		0.001
General health	55.2	56.9	59.6		0.025
Vitality	56.7	55.4	62.9		<0.001
Social functioning	72.3	70.8	82.4		<0.001
Role emotional	74.2	73.3	82.4		0.004
Mental health	64.6	63.1	73.6		<0.001
Risk perception statement	Score	Score	Score	Total	
Smoking	4.58	4.03	4.36	4.40	<0.001
Passive smoke	4.63	4.41	4.64	4.60	0.007
High alcohol consumption	4.64	4.55	4.62	4.62	0.515
Moderate alcohol consumption	3.54	3.15	2.36	3.01	<0.001
High fat diet	4.35	4.37	3.87	4.16	<0.001
Low fibre diet	3.80	3.72	3.51	3.67	0.001
Sedentary lifestyle	4.11	4.17	3.81	4.00	<0.001
Exposure to industrial chemicals	4.83	4.62	4.81	4.79	0.001
Living near nuclear power plant	4.85	4.75	4.87	4.84	0.104
Living near electric power station	4.45	4.55	4.24	4.39	0.001
Radioactive fallout from nuclear plant	4.88	4.86	4.85	4.87	0.802
Living near mobile phone transmitter	4.26	3.83	4.01	4.10	<0.001
Living near an overhead powerline	4.66	4.42	4.64	4.62	<0.001
Using a mobile phone	3.82	3.21	2.95	3.39	<0.001
EMF exposure overhead powerline	4.69	4.37	4.70	4.65	<0.001
EMFs from home appliances	2.37	2.68	2.13	2.31	<0.001
Living near a military antenna	4.85	4.62	4.62	4.73	<0.001
Exposure to noise	4.58	4.02	4.05	4.29	<0.001
Exposure to poor air quality	4.70	4.54	4.66	4.66	0.086
Driving twice legal limit of alcohol	4.81	4.82	4.86	4.83	0.383
Involved in RTA when sober	4.31	3.05	4.35	4.16	<0.001
Radiation exposure medical *x* ray	2.44	3.60	2.36	2.59	<0.001

EMF, electromagnetic field; RTA, road traffic accident.

Additionally, an estimate of the number of deaths was made from the cemeteries. Information on age and date of death was collected from the gravestones. These methods (though crude) provided the only possible mechanism for calculating standardised mortality ratios (SMRs) for all three sites.

Radiofrequency field measurements

Radiofrequency measurement was carried out using Delta T environmental multichannel loggers (Delta-T Devices Ltd, Cambridge, UK). Inside each of three loggers two radiofrequency amplifiers were connected to an antenna and signals approximately band-passed at below and above 100 MHz. The units were calibrated at 27 MHz (high frequency) and 900 MHz (ultra high frequency) with 1 Vm^{-1} signals. The outputs of the amplifiers were recorded every 10 min for maximum, average, and minimum signal for the high and ultra high frequency channels during the 10 min interval. One was sited on the upper floor of the Akrotiri community centre and later at the local bank, another at Asomatos Greek Orthodox Church behind the altar, and the third at Pano Kyvides medical centre. Measurements of the military Pluto antenna were undertaken on two occasions using a spectrum analyser, fed by a calibrated vehicle-mounted antenna, coupled to a computer and GPS. The military powered the antenna with 100 kW constant wave at 17.6 MHz and steered the beam either south towards Akrotiri or north to Asomatos whilst the vehicle was moved to key points in the village. Simultaneously a Narda handheld field meter (EMR 20C; Narda Safety Test Solutions, Pfullingen, Germany) was used to record the integrated field strength from all sources from 100 kHz to 3 GHz. Maximum operational power for that antenna was 500 kW. One limitation was that the constant wave transmission was available only after airfield operations, effectively at night, and subject to short notice cancellation.

RESULTS

Response rates

The estimates of the numbers of people living in each village were: 800 in Akrotiri, 350 in Asomatos and 1000 in Pano Kyvides. Questionnaires were distributed to all households, with an overall response rate of 87%. Individual village response rates were Akrotiri 87%, Asomatos 77% and Pano Kyvides 92%

Adult questionnaire: general personal information

There was no overall significant difference between villages when looking at age or gender ratio. The differences in marital status were of borderline significance. There were small differences in educational level that were just significant ($p = 0.048$) but there was no consistent pattern. There were significant differences in the number of years that adults had lived in each of three villages. For those who had lived in their village for >20 years the percentage for Akrotiri was 77.6%; for Pano Kyvides 72.9%; and for Asomatos 57.6%. There was no difference in smoking and mobile phone ownership between the three villages. On the question of frequency of mobile phone use there were significant differences ($p = 0.013$). The percentage results for several times a day were 74.3% for Akrotiri, 68.9% for Asomatos and 81.1% for Pano Kyvides.

Adult questionnaire: health

There were significant differences by village for the seven conditions: migraine, headache, dizziness, depression, asthma, heart problems and other respiratory problems. No significant differences were found for diabetes, epilepsy, diseases of the nervous system, cancer or leukaemia. Asthma was present in 9.4% of adults in Asomatos compared with 3.2% in Akrotiri and 3.1% in Pano Kyvides. 7.2% experienced other breathing/lung problems in Akrotiri, compared with 5.6% in Asomatos and 2.9% in Pano Kyvides. There were significant differences in heart problems between the villages, with Asomatos showing 16.2% of the adult population compared with 10.5% in Akrotiri and 7.1% in Pano Kyvides.

There were highly significant differences by village for migraine, headache, dizziness and depression. Table 1 shows the percentage of adults complaining of those symptoms for each of the three villages. For migraine, headache and dizziness there was a marked gradient with Akrotiri having the highest figures and Pano Kyvides the lowest.

Further analysis was undertaken to describe the association of these conditions with other factors.

Migraine

Given the highly statistically significant association between village and migraine ($p<0.001$) logistic regression was carried out with migraine as the outcome variable. The reference district was Pano Kyvides and odds ratios were calculated for both Akrotiri and Asomatos against the reference village. The unadjusted odds ratio for Akrotiri was 2.73 ($p<0.001$, 95% CI 1.826 to 4.091). Initially the logistic regression model was developed by adding first one and then two independent variables in a stepwise way. Estimates were terminated at iteration number 5 because parameter estimates changed by less than 0.001.

In the final model (table 2) the average perceived risk score, age, smoking and mobile phone use were not significant. The variables that remained significant in the model ($p<0.05$) were two of the higher educational levels (adjusted odds ratio 3.26 95% CI 1.34 to 7.93; and adjusted odds ratio 2.38 CI 1.15 to 4.95), female gender (adjusted odds ratio 5.5 95% CI 3.35 to 9.03) and living in Akrotiri (adjusted odds ratio 3.32 95% CI 2.14 to 5.15). The Hosmer and Lemeshow goodness of fit test suggested a good match (χ^2 5.670, 8 df, significance level 0.684.). The full output from the logistic regression analysis is shown in table 2.

Table 2 Migraine: logistic regression analysis final table*

Education to university	Reference Odds ratio	95% CI lower	95% CI upper
No education	2.37	0.82	6.87
Education to age 12	3.26	1.34	7.93
Education to age 15	2.22	0.87	5.61
Education to age 18	2.38	1.15	4.95
Age group†	0.90	0.71	1.13
Gender (female)	5.50	3.35	9.03
Smoking	0.77	0.45	1.31
Mobile phone	1.02	0.62	1.67
Risk score (median used)	0.91	0.627	1.31
Village			
Village (1)	3.32	2.14	5.14
Village (2)	1.56	0.86	2.85

*All risk factors were considered within a single statistical model.
†Age was not significant as decades, nor as <40 vs 40 and over, which is shown here.

Headache

A logistic regression was carried out with the odds of experiencing headache in villages one and two against village three. It demonstrated significantly greater unadjusted odds of headache in Akrotiri (OR 3.69, $p<0.001$, 95% CI 2.71 to 5.00) and Asomatos (OR 1.89, $p<0.002$, 95% CI 1.26 to 2.85). Both gender and educational level stayed in the model. Gender showed an OR of 2.84 (95% CI 2.00 to 4.04). The adjusted OR for Akrotiri were 4.16 (95% CI 2.96 to 5.84) and for Asomatos 1.78 (95% CI 1.14 to 2.79). The Hosmer and Lemeshow goodness of fit test was χ^2 10.65, 8 df, significance level 0.222.

Dizziness

The adjusted odds ratios were significant for gender (OR 3.32, 95% CI 2.18 to 5.05); Akrotiri (OR 5.64, 95% CI 3.69 to 8.62) and Asomatos OR 2.37, 95% CI 1.37 to 4.12). The Hosmer and Lemeshow goodness of fit test was χ^2 15.77, 8 df, significance level 0.046.

Depression

The adjusted odds ratios were significant for gender (OR 3.00, 95% CI 1.54 to 5.84), Akrotiri OR 3.82, 95% CI 1.89 to 7.74) and Asomatos (OR 3.45, 95% CI 1.50 to 7.97). The Hosmer and Lemeshow goodness of fit test was χ^2 6.64, 8 df, significance level 0.595).

Adult questionnaire: SF-36

This section contained the 36 questions that comprise the validated health questionnaire, the SF-36. There are eight scales and each scale value is a number between 1 and 100. Table 1 gives the values of each scale by village and illustrates the extent of the differences in self-reported health between the villages. The similarity between Akrotiri and Asomatos contrasts with the results from the control village.

Adult questionnaire: risk perception

The final section of the adult questionnaire asked questions about risk perception. There were 22 questions and respondents were invited to select one of five comments: "no possible harm"; "low harm"; "moderate harm"; "high harm"; or "extremely high harm". Table 1 shows the mean score for each of the three villages, together with the total for all villages and the significance value of the differences between villages.

Computed perceived risk score

The average risk score for each subject was computed. Analysis showed that there was a significant difference between the villages (χ^2 80.67, 2 df, $p<0.001$. Residents in Akrotiri had the highest perception of risk across the whole range of risks.

Table 3 Incidence of reported conditions and infections in the three villages

	Akrotiri (%)	Asomatos (%)	Kyvides (%)	p Value
Condition				
Migraine	7.4	1.8	0	0.001
Headaches	12.9	10.7	2.8	0.001
Dizziness	7.1	5.6	1.9	0.045
Infections				
Lung or chest infections	11.8	18.2	5.5	0.006
High temperatures	78.6	61.0	65.7	0.009
Rubella (German measles)	6.7	21.1	12.4	0.013
Mumps	1.3	9.4	4.4	0.029
Tonsillitis	36.8	53.7	34.6	0.034
Measles	7.3	9.1	2.4	0.041

Table 4 Standardised mortality ratios using the different mortality data

	Akrotiri	Asomatos	Pano Kyvides
Questionnaire	0.97	1.01	1.50
Cemetery	1.37	1.53	1.60
National records	1.26	2.01	1.32

Residents in Asomatos were intermediate and those in Pano Kyvides showed the lowest perceived risk.

Female questionnaire

Eighty three per cent of women who completed this questionnaire had been pregnant. Miscarriages were reported by 35%, terminations of pregnancy by 17%, infant deaths by 12%, stillbirths by 4.6%, births of less than 2500 grams by 9.2% and births that arrived more than three weeks early by 9.7%. On average 8.1% of respondents reported problems with conception. Analysis of the female questionnaire indicated that there were no significant differences between villages with regard to pregnancy and childbirth.

Child questionnaire

The male:female ratio was 48.7:51.3 and the differences between villages was not statistically significant. There were no differences in the ages of the children between villages or in the number of abnormalities at birth: Akrotiri (4), Asomatos (6) and Pano Kyvides (8).

There were no significant differences for diabetes, asthma, other breathing and lung problems, epilepsy, depression, heart problems or cancer. There were, however, significant differences in relation to migraines, headaches and dizziness (table 3)

With regard to infections there were no differences between villages for head cold, chicken pox, pneumonia, meningitis, otitis media, skin infections, urinary tract infections and glandular fever. There were significant differences among the infections.

In five of the six infectious diseases where there were significant differences between villages, Asomatos had the highest percentage.

Qualitative data

Adult questionnaire

The majority of comments were provided by the residents of Akrotiri. The presence of the antennae dominated these responses. Comments also included reference to aircraft noise (because of the topography, noise was sudden and certainly startled researchers making readings in Asomatos), but the overwhelming majority of comments made reference to the antennae and the ‘‘effect’’ on health. The consensus of opinion recorded was that the antennae ‘‘damaged’’ health. The responses from both Akrotiri and Asomatos when viewed together suggested that these communities firmly believe that their health was being damaged by the antennae. Residents' perception of the risk involved was, in many ways, as important as the actual risk.

Female questionnaire

Women providing comments did not make any reference to the military antennae. This is very different from the other questionnaires that definitely associated health problems with exposure.

Child questionnaire

All the additional comments provided came from the exposed sites. The military antennae (perhaps unsurprisingly) were the concern of almost all the respondents. There was anxiety that the antennae were damaging the future health of the children living in the villages.

Mortality

Overall mortality and standardised mortality ratios

The Cyprus Ministry of Health has good information on age-specific death rates for all causes on a national basis, based on the 2001 population census. Death information is based on the three-year period from 2001 to 2003. The annualised age-specific death rates were applied to the census population for each village to provide an expected number of deaths: Akrotiri, 4.76; Asomatos, 1.78; and Pano Kyvides 3.92.

The calculation of the standardised mortality ratio (SMR) required information on the actual number of deaths. There were three different ways of calculating ‘‘observed’’ deaths: mortality questionnaires, cemetery information and national records.

There was a discrepancy between the three methods of calculating the SMR suggesting that we do not have any satisfactory method of determining the effect of any extraneous factor specific to location.

Results of the measurement study

The results of spot measurements in Akrotiri and Asomatos are summarised below and covered the limits and key points within the village. Readings were all in Vm^{-1} that can be converted to power density by the formula:

$$\frac{V^2}{377}\ Wm^{-1}$$

Field measurements of the radiofrequency during a 100 kW transmission were as follows: for Akrotiri in 12 different locations, the average broadband outdoor field strength (all sources, military, civil and broadcast) was 0.57 Vm^{-1} (SD 0.24, max 1.04, min 0.19), and for the military transmission at 17.6 MHz was 0.11 Vm^{-1} (SD 0.09, max 0.29, min 0.002).

For Asomatos in 14 locations, the average broadband was 0.46 Vm^{-1} (SD 0.32, max 1.38, min 0.10), and for the military transmission was 0.04 Vm^{-1} (SD 0.02, max 0.64, min 0.012).

Readings from the loggers, being inside buildings, were generally lower and did not exceed 1 Vm^{-1} at any time over the study period, consisting of a maximum of 0.57 Vm^{-1} from the high frequency transmissions and up to 0.9 Vm^{-1} very high frequency from unspecified sources, possibly nearby cell phone use. The average logger readings for all 10-min samples over the period in Akrotiri were 0.050 Vm^{-1} (there were long ‘‘quiet’’ periods) for high frequency and 0.110 Vm^{-1} for ultra high frequency, and 0.040 Vm^{-1} and 0.060 Vm^{-1} respectively in Asomatos. The corresponding readings in the control village were <0.01 Vm^{-1} for both high and ultra high frequency, and this was confirmed with the handheld meter. That village had no cell phone mast nearby and the nearest broadcast antenna was more than 10 km.

DISCUSSION

In common with many other countries, the population of Cyprus show concerns about exposure to EMFs. In most countries this is focused on cell phone masts and broadcast systems, leading to claims of hypersensitivity and other poorly defined health effects such as cancer and birth defects.[14] In 1999 the inhabitants of Akrotiri, in particular, voiced concerns about the presence of large antenna arrays. These concerns escalated to extensive civil unrest, the imprisonment of a politician and an attack on a police station. Assurances from the Sovereign Base Area Administration (SBAA) that all transmissions met international guidelines for safety were not accepted by the local community.

Measurement in individual houses would have been desirable, but considered not feasible: the attenuation due to walls is highly variable necessitating personal data logging or multiple measurements, and this will differ for different frequencies. The military transmission on a particular frequency that could be tracked was only available when normal operations were shut down. This depended on field operations and ionospheric conditions, and for short times. This was incompatible with house-to-house appointments and measurement. Also the effect of raising awareness of radiofrequency exposure was considered undesirable. Although this resulted in a lack of accurate exposure assessment and an overestimate, exposure was in fact exceedingly low. The field measurements consisted of a set of longitudinal samples over two years taken at 10-min intervals, at central locations in all three villages. These were broadband, to include the military frequencies as well as broadcast and civilian communication frequencies. In addition, with the collaboration of the SBAA, limited high power measurements were made of the equipment of main public concern, namely the Pluto high frequency system covering 10–30 MHz. This enabled the contribution of the military system to public exposure to be assessed. The longitudinal measurements addressed the concerns of residents that there were no emissions of any extraordinary nature taking place while there was no surveillance. The questionnaire analysis has shown that the three villages were in fact reasonably well matched demographically and provided an appropriate basis for the comparison of exposed and unexposed populations.

The measurement study during military transmission confirmed an average value of 0.57 Vm^{-1} in Akrotiri and 0.46 in Asomatos. In Pano Kyvides the levels were <0.01 Vm^{-1}. The other sources were various broadcast antennae, in particular the cell phone mast in Akrotiri. It seems unlikely that the electromagnetic level was contributing to the neurological symptoms reported by those living close to the antenna.

A number of important issues emerged from the questionnaire results. Firstly, the responses to the adult health questionnaire provided significant differences between the villages (and not just between exposed and unexposed). In Akrotiri there was increased reporting of migraine, headache, dizziness and depression. A similar trend was noted in Asomatos although at lower levels. There is a consistent literature that cognitive and neurological effects are associated with EMF exposure. However, this is normally found at higher levels and higher frequencies and associated with mobile phone use, as covered in detail in the Stewart Report.[4] There are also reports of similar effects at lower levels, such as associated with mast exposure.[15] [16] In particular the study by Hutter *et al*[15] shows remarkable similarities in the relative risk for headache and dizziness (vertigo) for those ''exposed'' compared with the ''unexposed'' population. The field strengths are also of similar magnitude.

The adult questionnaire was designed to explore general physical and mental health using a standard validated instrument (SF-36) and risk perception. The results showed significant differences between the two exposed villages and the unexposed. It is possible to compare the results from this study with other values from studies in Greece. One of these studies was in hospital staff, a healthy working population, by Tountas *et al* in 2003.[17] The values for that study were as follows (the figures in brackets are the results from Akrotiri): physical functioning, 84.2 (75.7); role physical, 75.7 (71.4); bodily pain, 74.4 (72.1), general health, 69.0 (55.2); vitality, 63.5 (56.7); social functioning, 69.5 (72.3); role emotional, 74.1 (74.2) and mental health, 66.6 (64.6). This perceived low health status may well have been causing distress and anxiety, which may in part explain the reported neurological symptoms. The risk perception sections of the questionnaire shows that Akrotiri respondents had a higher level of perceived risk than the other two villages. For example they showed a high level of concern for external and physical factors including noise and electromagnetic pollution.

Similar studies in the UK have produced a lower mean risk score (2.6) and lower values for all the 22 variables. Although it is not possible to compare the score between one question and another, this does indicate a particular bias in risk perception for Akrotiri (median 4.41) compared even with Asomatos (median 4.27), and Pano Kyvides (median 4.14). This is surprising, as Akrotiri and Asomatos are approximately equidistant from the antennae, although it has to be said that the antennae were more visible from Akrotiri because of the topography. However this result may also in part explain the observed symptoms. In comparison with the results found in the UK, all three villages scored highly, possibly reflecting a national difference. Furthermore, the analysis of the open comments provided in all three questionnaires demonstrated a heightened state of anxiety concerning the presence of the antennae. The consensus of opinion recorded was that the antennae ''damage health'', albeit in an unspecified manner.

Given the importance of the high levels of neurological symptoms reported in Akrotiri the information provided by the adult questionnaire gave the opportunity to analyse the relative importance of location (ie, village) in explaining this outcome. The logistic regression analysis confirmed the importance of village, but also the contribution made by several other key factors including gender and education.

The visibility of the antennae from each village and the amount of aircraft noise appears to be positively related to an

Main messages

- Health effects (within the WHO definition) can occur when there is perceived to be exposure to radiofrequency, and may be related to anxiety.
- Other factors which are associated, such as aircraft movement and noise, could be contributory.
- Actual radiofrequency exposure can be very low in spite of proximity to very high power systems.
- A cell phone base station is likely to be a dominant source because it is within the community.

Policy implications

- Consideration needs to be given to dissemination of information from a trusted source to allay anxiety.
- Visibility of sources of radiofrequency is likely to be as, if not more, important than actual exposure, and consideration of planning issues is required when deciding on location.
- Alternatively, consideration needs to be given to separating communities from perceived sources of threat.

increased reporting of health problems or illnesses (ie, migraine, headache, dizziness) and higher perceived risk scoring, with Akrotiri having the highest figures and Pano Kyvides having the lowest figures. These three symptoms reported are similar to those in many, if not all, of the studies of electrical hypersensitivity.[18–20] Hypersensitivity to EMFs has reportedly been associated with a general increase in sensitivity and anxiety, even though provocation experiments with EMFs have not been able to demonstrate an objective association.[21]

The findings from the female questionnaires do not provide evidence of any differences between exposed and unexposed sites in gynaecological and obstetric history. Miscarriage has been associated with exposure to high levels of EMFs in previous studies; however, this has not been found in this research.

No evidence of birth abnormalities was found in the child questionnaire, although this phenomenon is suggested by the wider literature.[14] There were, however, significant differences in the reporting of migraine, headache and dizziness, with exposed sites reporting increased incidence.

These present results are in accordance with a recently concluded study in the US on PAVE PAWS radar on Cape Cod. The local inhabitants were anxious about the health effects from the ultra high frequency radar system which, although in a higher frequency range than PLUTO and of higher power density, had many similarities in being a phased array and beamed at a low angle. A study carried out by the US National Academy of Sciences concluded that there was no evidence of a health hazard, in particular no increased cancer risk. However a recommendation of continued epidemiological studies has been made.[22]

In summary this study has established that the levels of EMF exposure in all three sites are comparable with many civilian urban situations (a thousand times lower than recommended guidelines), with the majority of exposure coming from broadcast or cell phone systems. We could find no evidence of increased cancer incidence, childhood illness or negative reproductive effects. The only health effects identified in the exposed sites were headaches, migraine, dizziness and depression. These symptoms are surprisingly similar to the results of Hutter *et al*[15] on subjective symptoms in subjects living near mobile phone base stations showing that, despite very low exposure to high frequency EMF, effects on well-being and performance cannot be ruled out and that the symptom of headache had the highest significant relation to measured power levels.

The results of the Akrotiri study do not exclude the possibility that proximity to EMF sources have an effect on well-being and health. However the field levels do not suggest any causal association. Part of the explanation could be heightened risk perception. Proximity to the antennae may also be associated with general pollution, including noise.

ACKNOWLEDGEMENTS

This work was funded through the Cyprus Ministry of Health. In particular we wish to thank the village leaders for their kindness and support, and the staff of the Ministry of Health for their help and guidance.

Authors' affiliations

A W Preece, E J Dunn, Department of Medical Physics, University of Bristol, Bristol, UK
A G Georgiou, Division of Medical Research, Ministry of Health, Nicosia, Cyprus
S C Farrow, Public Health, Middlesex University, London, UK

REFERENCES

1 **ICNIRP**. Guidelines for limiting exposure to time varying electric, magnetic, and electromagnetic fields (up to 300 GHz). *Health Phys* 1998;**744**:494–522.
2 **NRPB**. Board statement on restrictions on human exposure to static and time varying electromagnetic fields and radiation. Documents of the NRPB. Vol 4, No 5, 1993.
3 **Swanson J**. *EMF Exposure standards applicable in Europe and elsewhere.* Brussels: Eurelectric, 2006, Available at http://www.jrc.cec.eu.int/emf-net/doc/Reports/Euroelectric%20Exposure%20Standards%202006.pdf (accessed March 2007).
4 **Independent Expert Group on Mobile Phones**. *The Stewart Report: Mobile Phones and Health*. Chilton, UK: NRPB, 2000.
5 **Dolk H**, Shaddick G, Walls P, *et al.* Cancer incidence near radio and television transmitters in Great Britain. 1: Sutton Coldfield transmitter, *Am J Epidemiol* 1997;**145**:1–9.
6 **Dolk H**, Elliott P, Shaddick G, *et al.* Cancer incidence near radio and television transmitters in Great Britain: all high power transmitters. *Am J Epidemiol* 1997;**145**:10–17.
7 **Hocking B**, Gordon IR, Grain HL, *et al.* Cancer incidence and mortality and proximity to TV towers. *Med J Aust* 1996;**165**:601–5.
8 **Ha M**, Lim HJ, Cho SH, *et al.* Incidence of cancer in the vicinity of Korean AM radio transmitters. *Arch Environ Health* 2003;**58**:756–62.
9 **Reed PJ**. Moore DD. SF-36 as a predictor of health states. *Value Health* 2000;**3**:202–7.
10 **MacGregor DG**, Slovic P, Morgan MG. Perception of risks from electromagnetic fields: a psychometric evaluation of a risk-communication approach. *Risk Anal* 1994;**14**:815–28.
11 **Morgan MG**, Slovic P, Nair I, *et al.* Powerline frequency electric and magnetic fields: a pilot study of risk perception. *Risk Anal* 1985;**5**:139–49.
12 **McMahan SG**, Meyer JF. Reducing exposure to extremely low frequency electromagnetic fields: the effect of high and low threat messages. Review of research. San Antonio, Texas: US Department of Energy, 1996.
13 **Li DK**, Odouli R, Wi S, *et al.* A population-based prospective cohort study of personal exposure to magnetic fields during pregnancy and the risk of miscarriage. *Epidemiology* 2002;**13**:9–20.
14 **California EMF program**. An evaluation of the possible risks from electric and magnetic fields (EMFs)from power lines, internal wiring, electrical occupations and appliances. Oakland CA: California EMF Program, 2002, Available at http://www.dhs.ca.gov/ehib/emf/RiskEvaluation/riskeval.html (accessed March 2007).
15 **Hutter HP**, Moshammer H, Wallner P, *et al.* Subjective symptoms, sleeping problems, and cognitive performance in subjects living near mobile phone base stations. *Occup Environ Med* 2006;**63**:307–13.
16 **Santini R**, Seigne M, Bonhomme-Faivre L. Danger of cellular telephones and their relay stations. *Pathol Biol (Paris)* 2000;**48**:525–8.
17 **Tountas Y**, Demakakos PT, Yfantopoulos Y, *et al.* The health related quality of life of the employees in the Greek hospitals: assessing how healthy are the health workers. *Health Qual Life Outcomes* 2003;**1**:61.
18 **Bergdahl J**. Psychologic aspects of patients with symptoms presumed to be caused by electricity or visual display units. *Acta Odontol Scand* 1995;**53**:304–10.
19 **Hillert L**, Hedman B, Soderman E. Hypersensitivity to electricity: working definition and additional characterization of the syndrome. *J Psychosom Res* 1999;**47**:429–38.
20 **Roosli M**, Moser M, Baldinini Y, *et al.* Symptoms of ill health ascribed to electromagnetic field exposure-a questionnaire survey. *Int J Hyg Environ Health* 2004;**207**:141–50.
21 **Rubin GJ**, Das Munshi J, Wessely S. Electromagnetic hypersensitivity: a systematic review of provocation studies. *Psychosom Med* 2005;**67**:224–32.
22 **National Academy of Sciences**. *An assessment of potential health effects from exposure to PAVE PAWS low level phased array radiofrequency.* Washington DC: The National Academies Press, 2005.

Changes of Clinically Important Neurotransmitters under the Influence of Modulated RF Fields—A Long-term Study under Real-life Conditions

Klaus Buchner and Horst Eger

This follow-up of 60 participants over one and a half years shows a significant effect on the adrenergic system after the installation of a new cell phone base station in the village of Rimbach (Bavaria).
After the activation of the GSM base station, the levels of the stress hormones adrenaline and noradrenaline increased significantly during the first six months; the levels of the precursor dopamine decreased substantially. The initial levels were not restored even after one and a half years. As an indicator of the dysregulated chronic imbalance of the stress system, the phenylethylamine (PEA) levels dropped significantly until the end of the study period.
The effects showed a dose-response relationship and occurred well below current limits for technical RF radiation exposures. Chronic dysregulation of the catecholamine system has great relevance for health and is well known to damage human health in the long run.

Keywords: cell phone base station, long-term study, stress hormones, radiofrequency radiation, GSM transmitter, far-field radiation

-- Introduction

Despite the distribution of numerous wireless transmitters, especially those of cell phone networks, there are only very few real-life field studies about health effects available. In 2003, the Commission on Radiation Protection was still noticing that there are no reliable data available concerning the public's exposure to UMTS radiation near UMTS base stations (1).

Since the 1960s, occupational studies on workers with continuous microwave radiation exposures (radar, manufacturing, communications) in the Soviet Union have shown that RF radiation exposures below current limits represent a considerable risk potential. A comprehensive overview is given in the review of 878 scientific studies by Prof. Hecht, which he conducted on behalf of the German Federal Institute of Telecommunications (contract no. 4231/630402) (2, 3).
As early as the 1980s, US research projects also demonstrated in long-term studies that rats raised under sterile conditions and exposed to "low-level" RF radiation showed signs of stress by increased incidences of endocrine tumors (4, 5).

Concerned by this "scientific uncertainty" about how radiofrequency "cell tower radiation" affects public health, 60 volunteers from Rimbach village in the Bavarian Forest decided to participate in a long-term, controlled study extending about one and a half years, which was carried out by INUS Medical Center GmbH and Lab4more GmbH in

Original study in German: BUCHNER K, EGER H (2011) Umwelt-Medizin-Gesellschaft 24(1): 44-57.

Zusammenfassung

Veränderung klinisch bedeutsamer Neurotransmitter unter dem Einfluss modulierter hochfrequenter Felder - Eine Langzeiterhebung unter lebensnahen Bedingungen

Die vorliegende Langzeitstudie über einen Zeitraum von eineinhalb Jahren zeigt bei den 60 Teilnehmern eine signifikante Aktivierung des adrenergenen Systems nach Installation einer örtlichen Mobilfunksendeanlage in Rimbach (Bayern).

Die Werte der Stresshormone Adrenalin und Noradrenalin steigen in den ersten sechs Monaten nach dem Einschalten des GSM-Senders signifikant; die Werte der Vorläufersubstanz Dopamin sinken nach Beginn der Bestrahlung erheblich ab. Der Ausgangszustand wird auch nach eineinhalb Jahren nicht wieder hergestellt. Als Hinweis auf die nicht regulierbare chronische Schieflage des Stresshaushalts sinken die Werte des Phenylethylamins (PEA) bis zum Ende des Untersuchungszeitraums signifikant ab. Die Effekte unterliegen einem Dosis-Wirkungs-Zusammenhang und zeigen sich weit unterhalb gültiger Grenzwerte für technische Hochfrequenzbelastung. Chronische Dysregulationen des Katecholaminsystems sind von erheblicher gesundheitlicher Relevanz und führen erfahrungsgemäß langfristig zu Gesundheitsschäden.

Schlüsselwörter: Mobilfunk-Basisstationen, Langzeituntersuchung, Stresshormone, Mobilfunkstrahlung, Fernfeld

in cooperation with Dr. Kellermann from Neuroscience Inc.[1].

Common risk factors such as external toxic agents, parameters of the catecholamine system (6) were determined prior to the activation of the GSM transmitter and followed up in three additional tests for a period of more than 18 months. The informed consent of all participants included the condition that the data were to be published anonymously.

-------------------------------- Materials and Methods

Study Setting and Selection of Study Subjects

In spring 2004, a combined GSMD1 and GSMD2 cell transmitter (900 MHz band) was installed on Buchberg mountain in D-93485 Rimbach (Lower Bavaria) with two sets of antenna groups each. The installation height of the antennas for both systems is 7.9 m; the horizontal safety distance along the main beam direction is 6.3 or 4.3 m, respectively. At the same tower, there is also a directional antenna at 7.2 m (7).

Shortly after it had become known that the wireless transmitters were to be installed, all inhabitants of Rimbach had been asked to participate in a mass screening. The municipality has approximately 2,000 inhabitants. In 60 volunteers (27 male, 33 female) aged between 2 and 68, the levels of adrenaline, noradrenaline, dopamine, and PEA (phenylethylamine)—which cannot be consciously regulated—were determined in their urine at the end of January/beginning of February 2004 (shortly before the activation of the antennas and the RF emissions beginning) as well as in July 2004, in January 2005, and in July 2005.

Most of these study participants signed up immediately after an informational gathering in late January 2004, at which the course of action by the cell phone service providers was criticized. Others signed up following a call for participation in the local paper. Since Rimbach is a small municipality, mouth-to-mouth propaganda also played a role. Participation was made attractive to the volunteers because a lab test that usually would be very expensive was offered for a small fee. Since the study required to show the status of the biological parameters over a given time period, only those study subjects participating in all four tests are included.

The data presented below come primarily from volunteers who have a certain interest in the life of their community and their health. Other persons joined the stress hormone investigation because of the recommendation of, or request by, their fellow citizens. This does not meet the requirements for a random sample. The result of this study, however, is hardly affected because Rimbach is a very small municipality. Therefore, the social contacts that lead to participation are very important. Most probably they do not affect the blood parameters. Furthermore, numerous large families participated as a whole whereby the health status of the individual family members did not play any role. For this reason, but especially because of the population structure, the study includes many children but only a few adolescents and young adults: there are hardly any opportunities for occupational training in Rimbach. In contrast, the municipality is attractive to young families with many children.

Sample Collection

The second morning urine was collected at INUS Medical Center on Mondays between 9:00 and 11:00 a.m. We made sure that each participant's appointment was always scheduled for the same time and that the time of breakfast or the state of fasting was the same for each participant at all tests. On the same day, the samples were sent by express to *Labor Dr. Bieger* in Munich where they were processed. In addition, samples were also sent to a laboratory in Seattle for control analyses (8-11).

Medical History

Medical doctors of the INUS Medical Center took a thorough medical history of each participant. At the initial test, the following data were also gathered: exact address, average time spent at home, indoor toxins, stress due to heavy-traffic roads, and the number of amalgam fillings. The latter number also included fillings that had already been removed. A nine-year-old child was noted to be electro-

---

1) INUS Medical Center, Dr. Adam-Voll Str. 1, 93437 Furth im Wald, Tel.: 09973/500 5412, www.inus.de; Lab4more GmbH, Prof. Dr. W. Bieger, Paul-Heyse-Straße 6, 80336 München, Tel.: 089/54321 730, info@lab4more.de; NeuroScience Inc., Dr. Kellermann, 373 280th Street - Osceola, WI 54020 - USA, Tel.: +1/715/294-2144, www.neuroscienceinc.com.

sensitive to the effects of household wiring and connected appliances. All other study participants declared themselves to be not electrosensitive.

When taking their medical history, participants were also questioned about subjective symptoms and chronic diseases at the start of the study and during its course; if overweight, this was also noted. In this study, overweight in adults is defined as a weight greater than the "body height in cm minus 100 plus 5 kg tolerance."

Consistency checks for the parameter "overweight," however, indicate that—especially with regard to children—different criteria have been applied during the taking of the medical history. These data, therefore, can only serve as a reference point. They are listed here anyhow since they can provide suggestions for further studies.

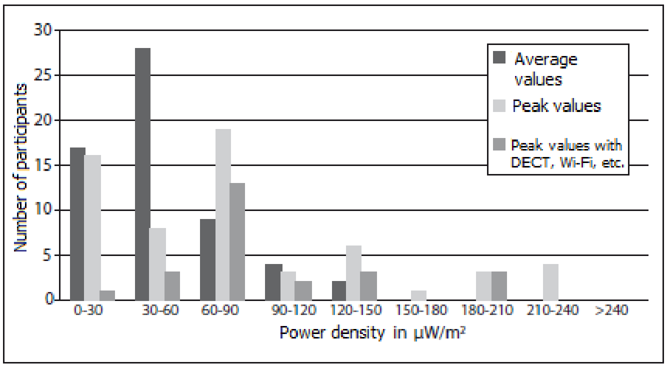


Fig. 1: Classification of participants based on average or peak value of the GSM power density level

All atopic disorders such as:

1. Hay fever, neurodermatitis, allergies, asthma, eczema are referred to as "chronic disorders;" as well as
2. All chronic inflammations such as interleukin- or COX-2-mediated problems;
3. All autoimmune diseases such as rheumatism, multiple sclerosis (MS);
4. All chronic metabolic disorders such as diabetes, liver diseases, intestinal diseases, kidney diseases.

Out of the 16 chronically affected participants 12 had allergies.

It was also asked whether there were DECT, Wi-Fi, or Bluetooth devices in the house or apartment during the study period from late January 2004 until July 2005. Also included were those devices present only for part of the study period, but not those turned off at night.

Exposure Level Measurements

For the most part, Rimbach municipality is located at one side of a narrow V-shaped valley. The cell phone base station is situated almost right across from the village center on the other side. RF radiation levels were measured at the outside of the residences of all study participants, wherever possible with direct line of sight of the transmitter. Because the municipality is located on a slope, great differences were noted inside homes—depending on whether or not a line of sight to the transmitter existed. In three cases, it was possible to measure the exposure levels at the head end of the bed. In these cases, the peak value of the power density was lower by a factor of 3.5 to 14 compared to measurements in front of the house with direct line of sight to the transmitter. The exact location of DECT, Wi-Fi, and Bluetooth base stations (if present) as well as possible occupational exposures, etc. were not determined by most participants.

At first, the measurements were taken with a broadband RF meter HF38B of Gigahertz Solutions, for which the manufacturer guarantees an error margin of max. ±6 dB (+ 7 decimal places; but this error can be mostly eliminated by selecting the appropriate measurement range). However, an inspection revealed that the error margin was less than ±3 dB. In addition, the broadband RF meter HF59B (±3 dB, ±5 decimal places) was used at several points. With this RF meter, relevant frequencies can be analyzed with variable filters, the ELF modulation frequencies via fast Fourier analysis.

By using broadband RF meters, the testing effort and expense are reduced compared to spectrum analyzers. Thus, it was possible to take measurements at a greater number of points, and as a result, it was easier to determine the maxima and minima of the power density levels. Furthermore, the accuracy of high-quality broadband RF meters is similar to that of spectrum analyzers.

In this study, only cell phone signals are considered: not DECT, Wi-Fi, or Bluetooth devices inside homes or emissions from broadcast or TV stations at *Hohenbogen*, a mountain above Rimbach. For the most part, the emissions from the latter transmitters remained stable during the study period, whereas the focus of this study is on changes in exposure levels. For almost all sample measurements, the portion of the exposure due to the transmitter at *Hohenbogen* was at maximum 35 μW/m^2 (peak value). It was higher in the residences of only two study participants: 270 μW/m^2 (average) or 320 μW/m^2 (peak), respectively. At these residences, the GSM exposure was approximately 10 μW/m^2.

For the assessment, the peak values of the signals are used because, in the case of GSM radiation, they are less dependent on the usage level than average values. The peak value of the power density for all study participants from Rimbach was on average 76.9 μW/m^2 (Tab. 1).

In Figure 1 the exposure of the participants is given as power density levels in increments of 30 μW/m^2.

Classification of Participant Group and Exposure Levels

Sixty persons participated in the study; their age distribution is shown in Figure 2 according to year groups. In order to capture the effect of the cell phone base station, other environmental factors must be excluded as much as possible. It is vitally important to ensure that no major differences between high-exposure and low-exposure persons influenced the results.

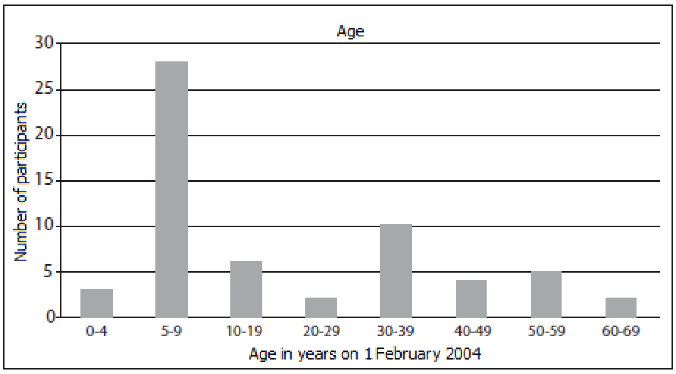


Fig. 2: Age distribution of study participants on 1 February 2004

	All	<=60 μW/m^2	60-100 μW/m^2	>100 μW/m^2
Participants	60	24	20	16
Power density, avg (μW/m^2)	76.9	21.7	68.1	170.7
Healthy adults	20	9	5	6
Sick adults	9	6	2	1
Healthy children	24	9	7	8
Sick children	7	0	6	1
Overweight	14	7	3	4
Amalgam number	12	5	3	4
Evaluation of amalgam/person	120	76.4	32.7	240
Street	8	0	8	0
Indoor toxins	17	7	6	4
DECT, Wi-Fi, Bluetooth	25	4	14	7

Tab. 1: Data on the 60 study participants who are classified into exposure groups 0 - 60 μW/m^2, 60 - 100 W/m^2, and above 100 μW/m^2, based on relevant peak values of GSM exposure in front of their residence.

Additional information:

Power density, avg (μW/m^2) means: average peak value of GSM exposure level in the relevant category;
Healthy adults: adults without chronic diseases. Participants who were born after 1 February 1994 are referred to as children, all others as adults;
Sick adults: adults with chronic diseases;
Healthy children: children without chronic diseases;
Sick children: children with chronic diseases;
Overweight: see text;
Amalgam number: number of participants who had at least one amalgam filling (which may have been removed prior to the study period);
Evaluation of amalgam/person: For each tooth with an amalgam filling of a participant, the size of the filling (values from 1 to 3) is multiplied with the number of years this filling has been placed prior to the date of the initial test of this study (rounded up to the nearest whole number). The value in the table is the sum of these numbers for all amalgam fillings of a person in the respective category divided by the number of participants with amalgam fillings (= "amalgam number");
Street: number of participants who live at a busy street;
Indoor toxins: number of participants who have had contact with toxins, varnishes, preservatives, etc. at home or at work;
DECT, Wi-Fi: number of persons who had DECT, Wi-Fi, Bluetooth or the like at home at the end of January 2004 or later.

As shown in Table 1, the group with exposure levels greater than 100 μW/m^2 included fewer chronically ill persons and fewer residences at heavy-traffic roads, but considerably higher amalgam exposures by dental fillings compared to the average of the participants. These differences, however, cannot explain the observed development of the blood parameters as will be shown further below. It should also be noted that the number of children in the group of <= 60 μW/m^2 is considerably lower than in the other two groups.

Statistics

Because of the large individual differences in blood values, their asymmetrical distribution, and because of the many "outliers," the assessment presented here focuses on the following problem: "Did the level of a given substance predominantly increase (or decrease, respectively) in the test subjects?" For this problem, the so-called signed-rank paired Wilcoxon test (12) is applied. How to determine the confidence intervals of medians is described in an easy-to-understand form in (13).

Due to the rather large differences in individual values, we refrained from carrying out additional statistical analyses, especially those with parametric methods.

-- Results

1 Clinical Findings

Adrenaline, noradrenaline, and dopamine as well as phenylethylamine (PEA) levels were determined at the time when the medical history was taken at INUS Medical Center. Out of the 60 participants, eleven had sleep problems until the end of 2004. During the study period (until July 2005), eight additional cases with these problems were reported. At the end of January 2004, only two participants complained about headaches; eight additional cases were reported thereafter. For allergies, there were eleven cases in the beginning and 16 later; for dizziness five and eight; and for concentration problems ten and fourteen. Due to the limited number of participants, no meaningful statements can be made about changes during the study period regarding the conditions tinnitus, depression, high blood pressure, autoimmune diseases, rheumatism, hyperkinetic syndrome, attention deficit hyperactivity disorder (ADHD), tachycardia, and malignant tumors. (Tab. 2)

Symptoms	Before activation of transmitter	After activation of transmitter
Sleep problems	11	19
Headache	2	10
Allergy	11	16
Dizziness	5	8
Concentration problems	10	14

Tab. 2: Clinical symptoms before and after activation of transmitter

2 Adrenaline

The adrenaline level trends are shown in Figure 3. After the activation of the transmitter from January until July 2004, a clear increase is followed by a decrease. In participants in the exposure category above 100 µW/m², the decrease is delayed.

Since the distribution of the adrenaline levels is very asymmetrical as shown in Figure 4, the median values are better suited for evaluation than the average values. However, there is no significant difference between the trend of the median and the trend of the average values (Tab. 3). But it stands out that, in the lowest exposure group with a power density below 60 µW/m², median values do not decrease between July 2004 and January 2005.

The statement "The adrenaline values of study subjects increased after the activation of the transmitter, i.e. between January and July 2004" is statistically confirmed ($p<0.002$), as well as the statement "The adrenaline level of the study participants decreased from July 2004 to July 2005" ($p<0.005$). In the lowest exposure group, the increase is the smallest. Until the end of the study period, these values do not drop.

A certain dose-response relationship can be observed for the increase in adrenaline levels from January 2004 until July 2004. The increase in medians was 2.3 µg/g creatinine for all subjects. At an RF radiation level up to 60 µW/m², creatinine was 1.0 µg/g, and by contrast, for power density levels between 60-100 µW/m² it was 2.6 µg/g.

For subjects in the exposure group above 100 µW/m², creatinine levels were found to be 2.7 µg/g, i.e. this value did not increase. We refrain from any additional statistical analysis because, as shown further below, the increase in adrenaline levels was mainly observed in children and chronically ill participants whose numbers were not sufficient to be broken down into further subgroups.

		January 2004	July 2004	January 2005	July 2005
All	Average	8.56	10.79	8.84	9.14
	Median	7.44	9.75	8.40	7.45
	CI	5.9 - 8.4	6.6 - 11.7	6.1 - 10.0	6.5 - 9.6
0-60 µW/m²	Average	8.9	10.3	7.7	9.0
	Median	6.4	7.4	7.8	7.4
	CI	3.8 - 10.3	4.6 - 13.2	3.4 - 9.4	5.5 - 11.1
60-100 µW/m²	Average	7.9	10.4	8.4	9.0
	Median	7.4	10.2	8.1	7.2
	CI	5.3 - 10.0	6.6 - 12.8	5.0 - 11.2	6.4 - 9.7
>100 µW/m²	Average	8.9	12.0	11.1	9.6
	Median	8.2	10.9	10.6	8.6
	CI	5.3 - 10.9	5.7 - 19.6	5.8 - 15.2	4.9 - 13.4

Tab. 3: Results for adrenaline levels in µg/g creatinine
CI = 95% confidence interval of median

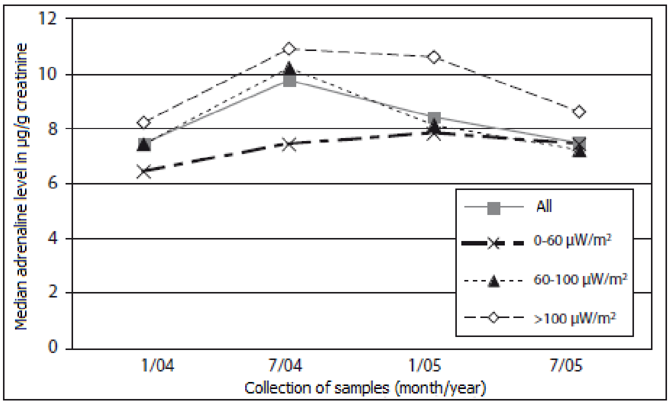


Fig. 3: Median adrenaline levels for all participating citizens of Rimbach whose cell phone base station exposure was above 100 µW/m², between 60 and 100 µW/m², or up to 60 µW/m². The power density levels refer to peak values of the GSM radiation exposure in front of a given residence.

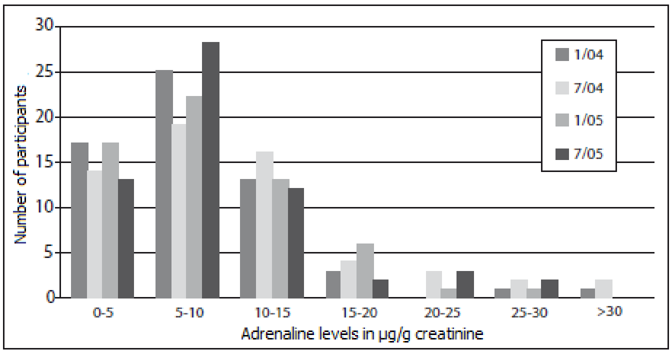


Fig. 4: Distribution of adrenaline levels in µg/g creatinine

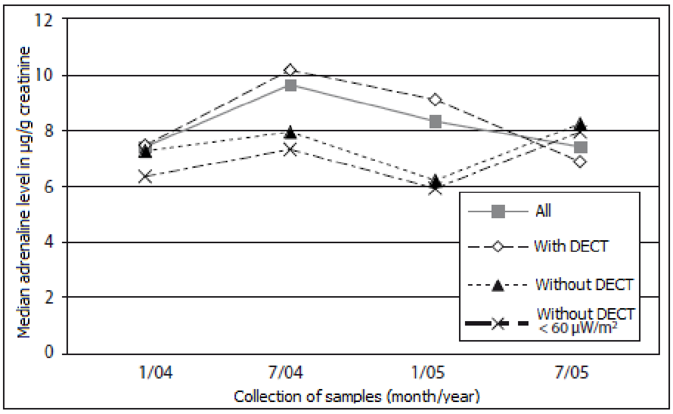


Fig. 5: Median adrenaline levels for all participating citizens of Rimbach who have a DECT phone, Wi-Fi, Bluetooth, or similar device, for those who do not have such wireless devices, and for the lowest exposure group without indoor wireless transmitters and with a GSM power density level up to 60 µW/m².

The impact of indoor wireless devices such as DECT, Wi-Fi, and Bluetooth (the latter are not specifically mentioned in the graphs) are shown in Fig. 5. Within the first year after the activation of the GSM transmitter, i.e. until and including January 2005, the group with indoor wireless devices shows the strongest responses.

It is possible that in the less exposed subjects seasonal fluctuations or other factors such as "overshooting" of the values could have played a role.

It should be noted here that both the average as well as the median adrenaline values increased after the activation of the transmitter and decreased again after one year. This, however, only applies to exposure levels >60 µW/m^2. Chronically ill subjects and children showed especially strong responses; except for some "outliers," no effect was observed in healthy adults.

The adrenaline level of overweight subjects and those with an amalgam burden hardly changed during the study period (Fig. 6). In contrast, chronically ill subjects showed especially strong responses above average. In fact, the increase in the median values between January and July 2004 for all study subjects was predominantly caused by children and chronically ill subjects; adults without any chronic disease show a flat curve. During this period, an increased adrenaline level between 5 and 10.3 was measured in three healthy adults. Because of these "outliers," the average values for healthy adults clearly increased in contrast to the median values.

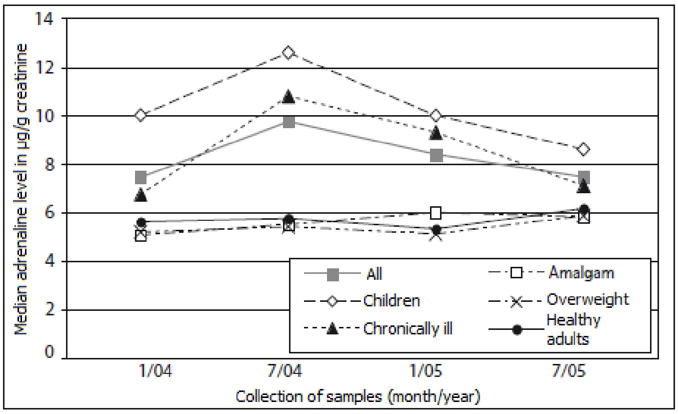


Fig. 6: Median adrenaline levels for participating children, for chronically ill subjects, for those with amalgam burden, and overweight subjects in Rimbach in comparison to the median levels of all study subjects and adults without chronic disease

The lower sensitivity of subjects with an amalgam burden can be explained by the fact that the effect occurs more often in children and that children according to our definition are younger than 10 years. They have hardly any fillings with amalgam.

3 Noradrenaline

The results for noradrenaline are similar to those for adrenaline (Tab. 4, Fig. 7). The statement that individual noradrenaline levels from January to July 2004 increased is statistically well supported with $p<0.001$. The fact that the levels dropped between July 2004 and July 2005 is also well supported with $p<0.0005$. Like in the case of adrenaline, the period under investigation is July 2004 to July 2005 to take the delayed decrease in the high exposure group into consideration. According to Table 4, the median of all noradrenaline levels increased from January to July 2004 for 11.2 µg/g creatinine; for exposures up to 60 µW/m^2, there were 2.2 µg/g creatinine, at 60-100 µW/m^2 12.4 µg/g creatinine, and above 100 µW/m^2 12.3 µg/g creatinine. As in the case of adrenaline, the increase for the last two groups is almost the same. Again, it is not possible to statistically verify a dose-response relationship. In Figure 7, a dose-response relationship

		January 2004	July 2004	January 2005	July 2005
All	Average	55.8	64.9	57.7	55.7
	Median	49.8	61.0	52.2	53.5
	CI	44.3-59.1	53.3-72.2	45.0-60.3	41.9 -60.5
0-60 µW/m^2	Average	54.7	59.3	56.5	53.5
	Median	45.2	47.4	48.7	48.1
	CI	35.1-67.8	36.3-75.6	40.1-60.0	36.3-65.6
60-100 µW/m^2	Average	51.4	63.6	49.1	55.9
	Median	47.5	59.9	45.8	54.8
	CI	38.0-59.1	53.1-74.8	40.5-58.4	34.9-66.5
>100 µW/m^2	Average	62.9	74.9	70.1	58.8
	Median	58.8	71.1	71.6	56.3
	CI	49.9-87.3	54.9-91.6	48.7-89.1	36.9-81.6

Tab. 4: Results for the noradrenaline levels in µg/g creatinine
CI = 95% confidence interval of the median

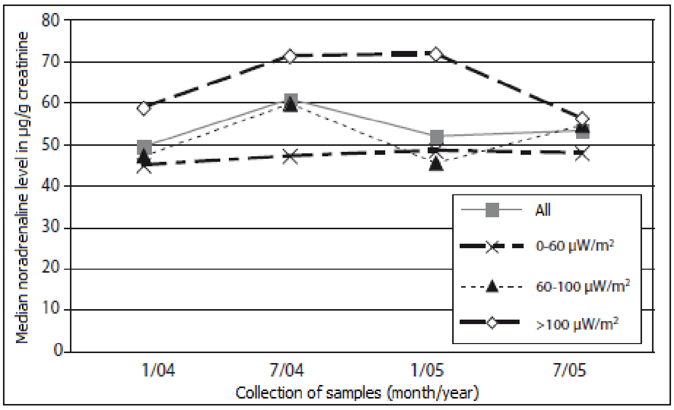


Fig. 7: Median noradrenaline levels in all participating citizens of Rimbach as a function of GSM power density levels (peak values)

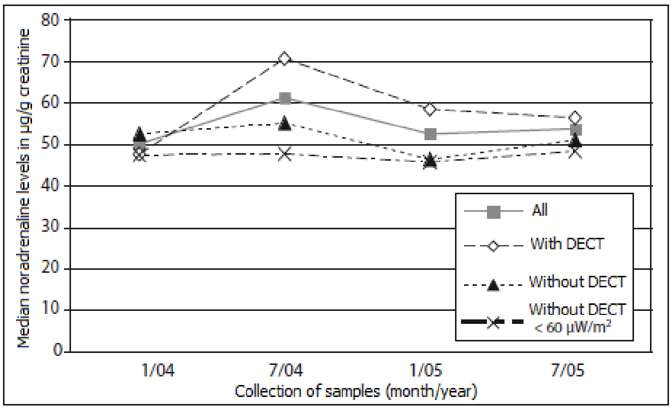


Fig. 8: Median noradrenaline values for subjects who had a DECT phone or other wireless devices at home, for those without indoor wireless devices, as well as for subjects without indoor wireless devices and with a GSM radiation exposure up to 60 µW/m^2 (peak value measured in front of residence)

is seen, whereby the dot-dashed line serves as reference for persons with very low exposures. It stands out that the "recovery period," i.e. the decrease in values in 2005, drags on for longer in subjects in the exposure group with GSM radiation levels above 100 μW/m^2. This also corresponds with the behavior of the adrenaline levels.

In comparison with adrenaline, noradrenaline plays a somewhat greater role in residences where wireless devices existed before the beginning of this study (Fig. 8).

The trend in Figure 9 shows that children and chronically ill subjects in contrast to overweight subjects express strong responses to cell tower radiation. The ratios, however, are not as clearly visible as with adrenaline. Especially in overweight subjects, they indicate a slow response to GSM radiation.

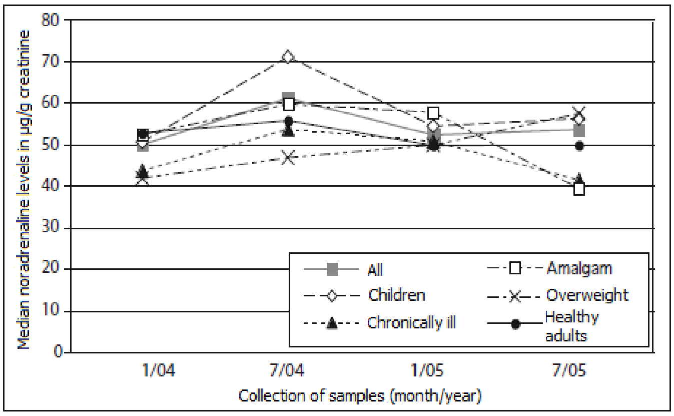


Fig. 9: Median noradrenaline levels of children, chronically ill subjects, those with amalgam burden and overweight subjects in Rimbach in comparison to the median values of all study subjects and healthy adults

Noradrenaline and adrenaline, however, responded very similarly.

4 Dopamine

For dopamine, inverse effects to those for adrenaline and noradrenaline were observed. The median dopamine levels decreased from 199 to 115 μg/g creatinine between January and July 2004 (Tab. 5). The fact that the dopamine levels of the study subjects decreased during this period is highly significant ($p<0.0002$). Thereafter, the median increased again: In January 2005, it was at 131 μg/g creatinine, in July of this year 156. This increase is also significant (for increase between July 2004 and July 2005 $p<0.05$).

This, too, is a dose-response relationship: from January to July 2004, the median for all subjects decreased for 84 μg/g creatinine, in the exposure group up to 60 μW/m^2 for 81, in the exposure group above 100 μW/m^2 even 153 μg/g (see Tab. 5 and Fig. 10). This dose-response relationship is statistically significant based on the signed-rank Wilcoxon test (12) with $p<0.025$. The following statement applies: "The decrease in dopamine levels for exposure levels up to 100 μW/m^2 is smaller than at exposure levels above 125 μW/m^2."

In subsequent laboratory tests, the dopamine levels do not return to the same level as in January 2004. From Figure 11, it is obvious that the correlation with prior exposures to indoor wireless devices is small.

		January 2004	July 2004	January 2005	July 2005
All	Average	233	158	138	164
	Median	199	115	131	156
	CI	168-273	86-160	111-153	145-175
0-60 μW/m^2	Average	217	183	130	148
	Median	189	108	116	147
	CI	142-273	80-254	90-157	129-167
60-100 μW/m^2	Average	242	161	140	178
	Median	223	150	131	175
	CI	137-335	94-168	93-164	126-207
>100 μW/m^2	Average	244	115	147	170
	Median	244	91	151	156
	CI	139-316	48-202	117-169	138-209

Tab. 5: Results for dopamine levels in μg/g creatinine
CI = 95% confidence interval of median

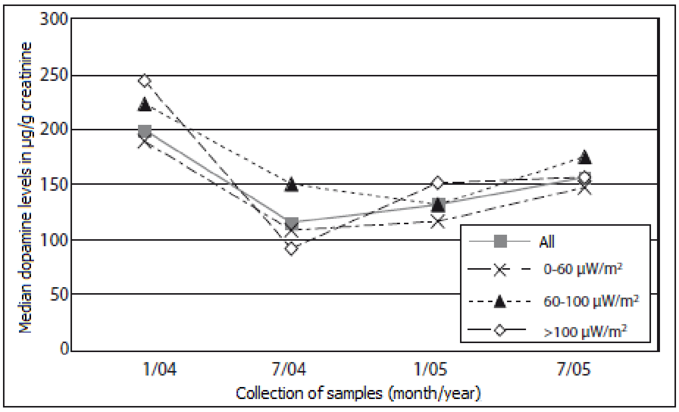


Fig. 10: Median dopamine levels for different GSM power density levels

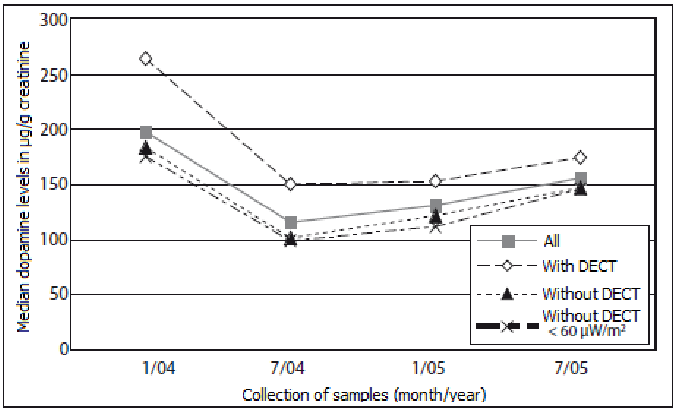


Fig. 11: Median dopamine levels for all participating citizens of Rimbach, for those with and without DECT phone, Wi-Fi, or Bluetooth, and for those without indoor wireless devices who had a GSM exposure level below 60 μW/m^2 (peak value).

It is to be emphasized that the lowest exposure group without such indoor wireless devices and with a GSM power density level < 60 µW/m^2 responds almost as strongly as all other study subjects. This is consistent with the data in Figure 10: the data suggest that the effect of the radiation on the dopamine levels can already be observed at very low power density levels; however, it still can increase at levels above 100 µW/m^2.

Figure 12 shows that the radiation effect is somewhat more pronounced in children compared to the average, i.e. the gradient of the curves between the first two data points is somewhat greater. However, the difference is far too small to be statistically significant.

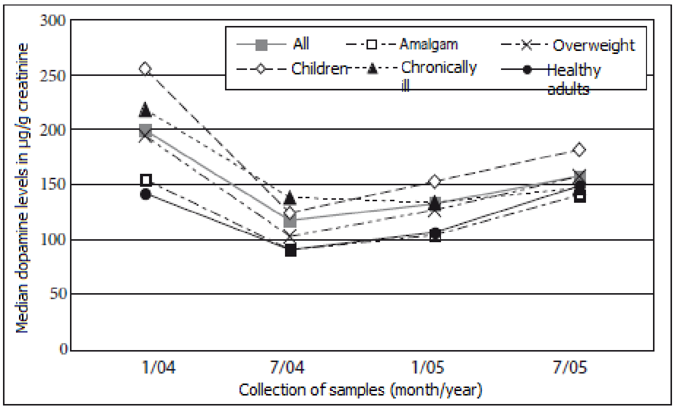


Fig. 12: Median dopamine levels of children, the chronically ill, with amalgam burden, overweight subjects, and healthy adults in Rimbach

In summary, dopamine levels decreased after the activation of the GSM transmitter and were not restored to the initial level over the following one and a half years. A significant dose-response relationship is observed. In children, the decrease is somewhat more pronounced than in adults.

5 Phenylethylamine (PEA)

Phenylethylamine (PEA) levels respond more slowly to the radiation compared to the substances investigated so far (Tab. 6, Fig. 13). Only in the exposure group above 100 µW/m^2 GSM radiation do the PEA levels decrease within the first six months. Thereafter, hardly any differences can be discerned between PEA values of the various power density levels investigated here.

The decrease of PEA levels between July 2004 and July 2005 is highly significant ($p<0.0001$)

Similar to adrenaline and noradrenaline, a previous exposure to indoor wireless devices intensifies the effect of the GSM radiation (see Fig. 14). The subjects of the low-exposure groups without indoor wireless devices do respond in a time-delayed fashion, but after six months they respond just as clearly as the subjects of the highest exposure group. In this regard, the PEA levels behave like those of dopamine in contrast to adrenaline and noradrenaline, which only respond to stronger fields.

		January 2004	July 2004	January 2005	July 2005
All	Average	725	701	525	381
	Median	638	671	432	305
	CI	535 -749	569 - 745	348 - 603	244 - 349
0-60 µW/m^2	Average	655	678	523	329
	Median	604	653	484	243
	CI	477 - 835	445 - 835	279 - 675	184 - 380
60-100 µW/m^2	Average	714	699	535	451
	Median	641	678	426	330
	CI	492 - 746	569 - 790	310 - 804	293 - 438
>100 µW/m^2	Average	843	739	514	371
	Median	780	671	413	305
	CI	451 - 1144	334 - 822	338 - 748	157 - 513

Tab. 6: Results for phenylethylamine (PEA) levels in ng/g creatinine
CI = 95% confidence interval of median

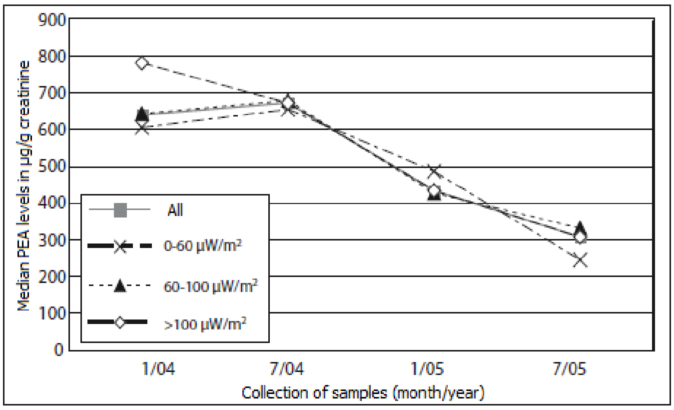


Fig. 13: Median phenylethylamine (PEA) levels for various GSM power density levels

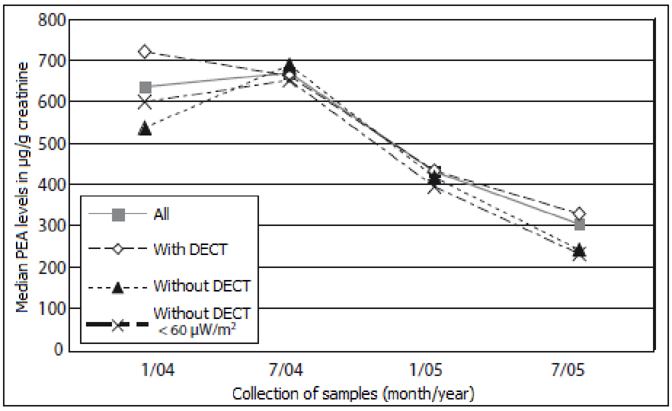


Fig. 14: Median phenylethylamine (PEA) concentrations in µg/g creatinine of subjects with and without indoor wireless devices at home and subjects without indoor wireless devices with a GSM power density level below 60 µW/m^2

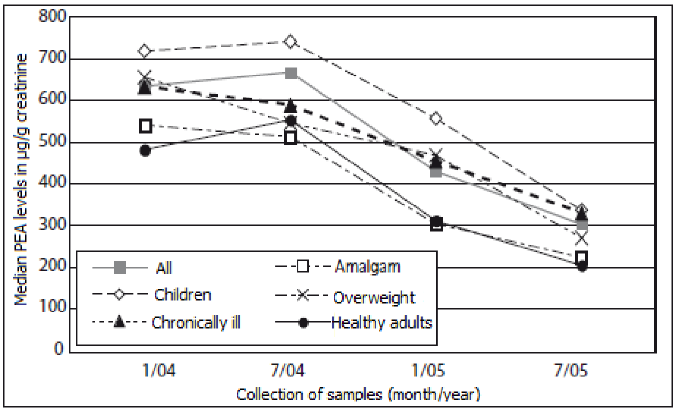


Fig. 15: Median phenylethylamine (PEA) concentrations in µg/g creatinine of children, the chronically ill, with amalgam burden, and overweight subjects, as well as health adults in Rimbach

In children, the effect of GSM radiation on their PEA levels is no greater than in the average of the study subjects; healthy adults also do not respond substantially differently. In contrast to the other substances looked at so far, the group of overweight subjects does respond particularly rapidly to PEA.

------------------------------------ Summary of Results

Adrenaline and noradrenaline levels increase during the first six months after the GSM transmitter had been activated; thereafter, they decrease again. After an exposure period of one and a half years, the initial levels are almost restored. Only at power density levels above 100 µW/m^2 is this decrease delayed for several months. In contrast, dopamine levels decrease substantially after the exposure begins. Even after one and a half years, the initial levels are not restored. Six months after the activation of the transmitter, PEA levels decrease continuously over the entire exposure period. Only in the exposure group above 100 µW/m^2 is this effect observed immediately. All findings were observed well below current exposure limits (14).

Wireless devices used at home such as DECT, Wi-Fi, and Bluetooth amplify the effect of the GSM radiation. In the case of adrenaline and noradrenaline, almost exclusively children and chronically ill subjects (here mostly subjects with allergies) are affected. However, the response of chronically ill subjects to dopamine and the response of children to PEA are very similar to those found in the average of the study subjects. Except for PEA, overweight subjects show only very weak responses to GSM radiation.

--- Discussion

Catecholamine System and Phenylethylamine (PEA)

The survival of mammals depends on their ability to respond to external sources of stress. An established, well-researched axis of the human stress system represents the catecholamine system (6, 15, 16). It can be activated by psychic or physical stressors. Impulses mediated by nerves are responsible for an induction of the catecholamine biosynthesis at the level of tyrosine hydroxylase as well as dopamine beta-hydroxylase, whereby the effect is based on an induction of both enzymes. Many biochemical regulatory mechanisms tightly control catecholamine synthesis (8, 15, 17). Chronic dysregulation always leads to health problems in the long run. The development of high blood pressure under continuous stress serves as a clinical example; so-called "beta blockers" directly block the action of adrenaline and noradrenaline on the target receptors, and it is impossible to imagine medication-based therapy without them (15).

PEA can be synthesized from the essential amino acid phenylalanine either via tyrosine, dopamine, noradrenaline, and adrenaline or via a direct biochemical path (15) (Fig. 16). The sympathetic-mimetic effect of PEA was first described by Barger in 1910 (18).

PEA is also synthesized from phenylalanine and is considered a superordinate neuromodulator for the regulation of catecholamine synthesis (19-22).

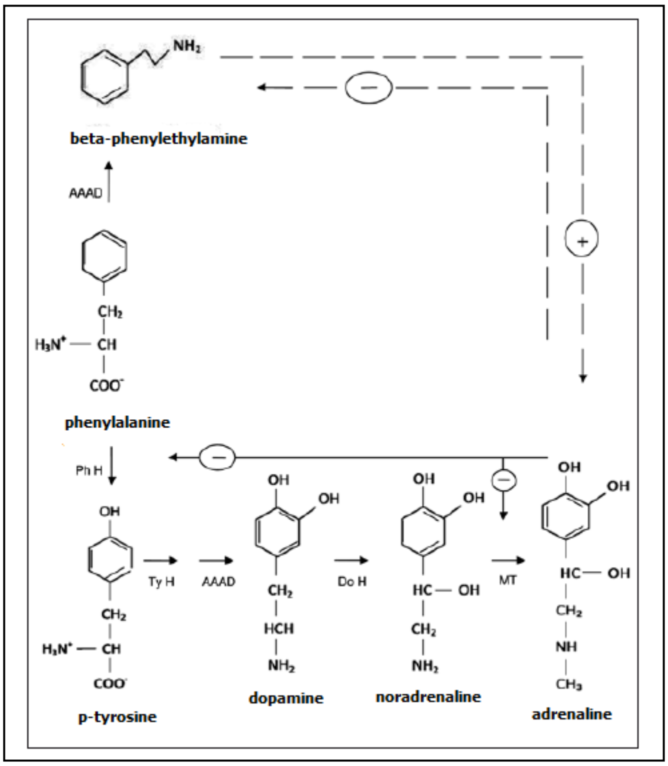


Fig. 16: Chemical structure of derivatives of the essential amino acid phenylalanine and the simplified synthesis pathways of catecholamines or phenylethylamine, respectively, simplified according to Löffler (15).

Abbreviations
AAAD: aromatic l-amino acid decarboxylase,
DoH: dopamine beta-hydroxylase,
PhH: phenylalanine hydroxylase,
MT: n-methyltransferase,
TyH: tyrosine hydroxylase
—(—)— ---- known feedback loop, - - (---) - - postulated feedback loop

In 1976, Zeller described the physiological relationships (23) and points out that PEA is released by the brain via electrical stimulation (24).

The effect mechanism of PEA in the catecholamine system is the center of current pharmaceutical research efforts. In molecular biological terms, intracellular TAAR (trace amine-associated receptor) G-protein-coupled receptors that mediate modulatory effects of PEA are verified (20).

For high nanomolar to low micromolar PEA concentrations, in vivo studies have shown amphetamine-like effects. During an increase of PEA, an increased amount of noradrenaline and dopamine is also released and the reuptake of these substances is impaired (25, 26).

According to Burchett, the following effects of PEA amplifying the catecholamine effect are assumed to be known: Direct agonist action via increased release of transmitters, reuptake inhibition, and stimulation of transmitter synthesis as well as inhibition of monoamine oxidase (MAO) (19). PEA's high lipophilia—a prerequisite for the permeability of membrane barriers such as the blood-brain barrier—is of note here; PEA levels in the brain, serum, and urine correlate quite well (10, 21, 25, 27).

The clinical relevance of changed PEA levels is well documented for mental illnesses. Endogenous depression is associated with lowered PEA levels, whereby the transition from depression to maniac episodes is accompanied by an increase in PEA levels (28-32).

The therapeutic increase in the PEA level has a positive impact on the course of the disease. Phenylalanine improves the effectiveness of antidepressants; PEA by itself is a good antidepressant—effective in 60% of the cases of depression.

In persons with ADD/ADHD (attention deficit hyperactivity disorder), PEA levels are substantially lower; the ADHD treatment with methylphenidate (Ritalin®) normalizes PEA excretion in the urine of responders (33, 34).

Contributing Factors

Laboratory tests of catecholamine have been established for years. Increased values are found in disorders such as pheochromocytoma, neuroblastoma, and arterial hypertension, whereby it is impossible for a subject to consciously regulate these values. Especially urine tests offer a sufficient level of sensitivity and specificity because urine contains 100 to 1000 times higher levels than blood plasma. The intraindividual variation coefficient ranges from 7% to 12% from one day to another; stored under appropriate conditions, the stability of the samples can be guaranteed without problems (8).

In Rimbach, urine samples were always collected at the same time of the day so that a circadian dependence could be ruled out. Other contributing factors such as increased physical activity as well as large meals were also ruled out by collecting the urine in the morning. Seasonal factors of the samples collected twice in winter and summer should have been reflected as undulating levels in the testing results. Only in the adrenaline levels of the lower exposure groups (Fig. 5) can such a corresponding correlation be found. All other data did not indicate any seasonal influences.

In the study presented here, the selection of the participating citizens of Rimbach was not based on random assignment, but on self-selection. We can assume that the subjects, especially the adults, had informed themselves about the issue of cell tower radiation. However, because it is impossible to consciously regulate these levels, this self-selection should not make any difference in this study.

Especially in children below age ten, it is not thought possible to maintain a chronic state of anxiety for one and a half years due to an abstract term such as cell tower radiation.

This study limits itself to the following type of questions: "Did the level of a given substance predominantly increase or decrease during the study period?" Independent of each model, this question can be clearly answered with the Wilcoxon test and the indication of the confidence interval. The corresponding results are statistically very well supported. Any statements beyond this—e.g. the dependence of levels on certain parameters—cannot be made because with 60 study subjects the number of cases is too small to establish the same type of statistical significance.

The great advantage of the "Rimbach data" is that prior to January 2004 the exposure levels were very low because there was no cell phone tower and because only a few citizens had installed DECT, Wi-Fi and similar devices. In addition, due to the testing equipment with a measurement accuracy of less than ± 3 dB combined with repeated control measurements, the classification of the exposure groups can be considered to be verified.

For the stress hormones adrenaline and noradrenaline, the increase occurred only after the installation and activation of the transmitter, and thereafter, levels continued to decrease but did not fully normalize.

For dopamine, significant differences in the dose-response relationship according to exposure group could be shown after the activation of the new cell tower antenna. Also, the consistently decreasing levels of the hypothetically superordinate regulatory PEA do not support the hypothesis that the stress factor for the observed changes in the adrenergic system would exclusively be found in the realm of psychological factors.

Mode of Action of Microwave Radiation

There is a wide range of evidence to interpret the newly emerging microwave exposures as an invisible stressor.

Microwaves are absorbed by living tissue. The frequencies used for cell phone technologies have a half-life penetration depth of several centimeters, whereby cell membranes constitute no obstacle (35).

Microwaves cause enzymes to malfunction directly by, for example, monomerization (36). Thus, it is conceivable that enzymes of the catecholamine system could be affected directly.

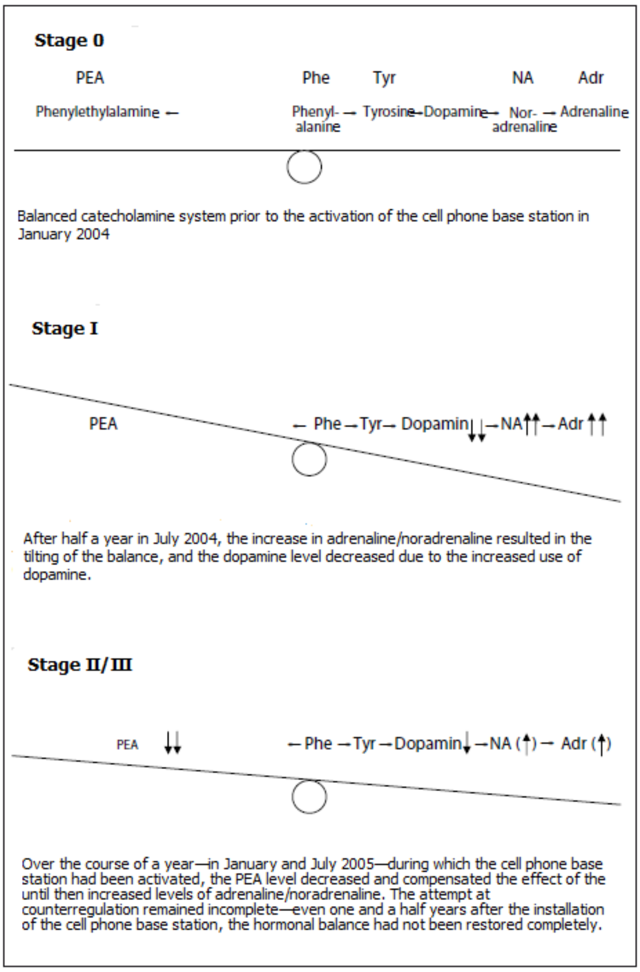
Intracellular processes are changed, and cellular mitosis is disturbed by forces acting on the cellular spindle apparatus (37, 38). The human body is required to provide a higher level of repair services that is comparable to a chronic state of stress. A decrease in adenosine triphosphate (ATP) due to microwave exposure could be demonstrated by Sanders in intracerebral tissue already in 1980 (39).

Within current exposure limits, Friedman could show the stress caused by microwaves in the cell membranes of a cell model (40). The oxygen radicals formed by NADH have an activating effect on subsequent intracellular cascades that amplify the membrane effect by a factor of 10^7, which in turn substantially change intracellular processes (17). Even reproductive impairments due to microwaves are mediated by the formation of free radicals (41).

In industry, more and more microwave devices are being used for chemical peptoid syntheses, which allow for a 100 times faster and more precise production even without any measurable heating (42). The toxic effects of free radicals formed by microwaves are used in such technical applications as water purification (43).

In several studies, the chronic symptoms of residents near cell tower antennas were described (44-48). Interestingly, the expansion of wireless networks corresponds with the increase in prescription expenses for methylphenidate, a drug whose chemical structure is related to PEA and which is indicated in cases of attention deficit disorder (ADD) (49).

Long-term studies over five years suggested an increased cancer incidence due to microwave exposure (50, 51). Since the catecholamine system is directly linked with the nervous system within the psychoneuroimmunological framework beside its organ-specific effects, the observed increase in cancer incidence can now also be understood from a pathophysiological perspective (6, 15, 52, 53).



Balanced catecholamine system prior to the activation of the cell phone base station in January 2004

After half a year in July 2004, the increase in adrenaline/noradrenaline resulted in the tilting of the balance, and the dopamine level decreased due to the increased use of dopamine.

Over the course of a year—in January and July 2005—during which the cell phone base station had been activated, the PEA level decreased and compensated the effect of the until then increased levels of adrenaline/noradrenaline. The attempt at counterregulation remained incomplete—even one and a half years after the installation of the cell phone base station, the hormonal balance had not been restored completely.

Fig. 17: Stage-like course of the stress response in Rimbach

Hypothesis of the Course of the Stress Response in Rimbach

Significant research on the stress-response axis was carried out in the 1950s. Selye established the nowadays generally accepted theory of the general adaptation syndrome of the human body to a stressor (16). He distinguished between three stages in the stress response, which can be found again in the description of the microwave syndrome according to Hecht (2, 3). Thus, after the stages of alarm and resistance, the last stage of exhaustion sets in (Fig. 17). The parameters investigated in the Rimbach study follow this pattern.

STAGE I—Activation Stage

The results of the long-term study presented here show an immediate activation of the adrenergic system. After the activation of the cell phone base station under investigation, the parameters adrenaline and noradrenaline increase significantly within a period of one and a half years. Because of the increased production of the final hormones noradrenaline/adrenaline, the use of dopamine increases, and as a result, the dopamine level decreases. The decrease in the dopamine level is the more pronounced, the higher the GSM radiation exposure level is at the residence of the individual participants.

STAGE II—Adaptation Stage

After this sympathicotonic activation stage, the body tries to compensate the increase in adrenaline and noradrenaline. In order to inhibit the overshooting catecholamine production and to ensure a stable regulation, the phenylethylamine level (PEA level) decreases. Here the decrease in PEA starts in the highest exposure group first.

STAGE III—Premorbid Stage

According to our hypothesis, the effects of adrenaline and noradrenaline are inhibited by feedback mechanisms at the expense of a chronically, over six continuous months, lowered PEA level. However, the attempt at counterregulation remains incomplete—even one and a half years after the installation of the cell phone base station; the hormonal balance had not been restored completely. The PEA level remains at a low level, which is to be interpreted as evidence for the beginning of exhaustion.

-- Conclusion

Thus, the following hypothesis is proposed: Although participants maintained their usual lifestyle, they developed chronic stress with a primary increase in adrenaline/noradrenaline and a subsequent decrease in dopamine in response to the microwave exposure from the newly installed cell phone base station. During the stage of counterregulation, the "trace amine" PEA decreases and remains decreased.
This is of considerable clinical relevance because psychiatric symptoms also exhibit altered PEA levels. In Rimbach, the increase in sleep problems, cephalgia, vertigo, concentration problems, and allergies could be clinically documented after the cell phone base station had been activated. The newly developed symptoms can be explained clinically with the help of disturbances in the humoral stress axis (53).

After having exhausted the biological feedback mechanisms, major health problems are to be expected. The possible long-term consequences of remaining caught in the exhaustion stage have already been described by Hecht and Selye (3, 16).

Thus, the significant results presented here not only provide clear evidence for health-relevant effects in the study subjects of Rimbach after a new GSM base station had been installed there, but they also offer the opportunity to carry out a causal analysis. This has already been successfully done in the "shut-down study" of Schwarzenburg, Switzerland (54). In Rimbach, the documented levels should return to normal once the relevant base station is shut down.

Epidemiological Evidence

There is current epidemiological evidence for the considerable clinical relevance of the dysfunction of the humoral stress axis with its endpoints of PEA decrease and adrenaline increase, as documented by us.

1. Decreased PEA levels can be found in a large portion of ADD/ADHD patients. As therapy methylphenidate is used, a substance that is structurally related to PEA. Between 1990 and 2004, the boom time of cell phones, prescription costs for this medication had increased by a factor of 86 (49, 55).

2. As part of the German Mobile Telecommunication Research Programme, approximately 3000 children and adolescents were studied in Bavaria for their individual cell phone radiation exposure levels in relation to health problems. Among the various data sets, the data set regarding behavioral problems showed a significant increased risk for both adolescents (OR: 3.7, 95%-CI: 1.6-8.4) and also children (OR: 2.9, 95%-CI: 1.4-5.9) in the highest exposure group (56). For the first time, the "Rimbach Study" provides a model of explanation in biochemical terms.

3. Pheochromocytomata are adrenaline- and noradrenaline-secreting tumors of the adrenal gland (57). This type of tumor due to microwave exposure has already been demonstrated in animal experiments in 1985 (5). The increase of this disease in the US population is highly significant. Concurrent with the increase in local microwave exposures due to an increased number of base stations and use of wireless communication technologies, the number of cases have increased from 1,927 to 3,344 between 1997 and 2006 (58, 59).

It is a physician's responsibility—not bound by directives—to work toward the preservation of the natural basis of life regarding human health (60). Now it is the duty of the responsible agencies (public health department, Bavarian State Ministry of the Environment and Public Health as well as other federal ministries) to investigate the current situation.

Note
For the data collection, financial and personnel support was provided by INUS Medical Center and the two laboratories Lab4more GmbH and Neuroscience Inc.
The above-listed institutions were so kind to provide clinical examinations as well as the laboratory tests for the evaluation without external funding.

Acknowledgement
Many thanks to the Rimbach participants as well as the staff of the supportive clinics and laboratories, without whose efforts this study would not have been carried out. For the deciphering of cryptic handwriting, we owe Christina Panchyrz our gratitude.

Contact:

Professor Dr. rer. nat. Dr. habil. Klaus Buchner
Straßbergerstraße 16
80809 München

Dr. med. Horst Eger (Korrespondenz)
Ärztlicher Qualitätszirkel „Elektromagnetische Felder in der
Medizin - Diagnostik, Therapie, Umwelt'; (Code-Nr. 65143 KV Bayern)
Marktplatz 16
95119 Naila
E-mail: horst.eger@arcormail.de

Editor's Note

The above paper is identified as an original scientific paper and it was subject to a special peer-review process in cooperation with the Scientific Advisory Board.

The Editorial Team

Translation
By Katharina Gustavs and authorized by the authors and publisher
Original publication: BUCHNER K, EGER H. (2011): Veränderung klinisch bedeutsamer Neurotransmitter unter dem Einfluss modulierter hochfrequenter Felder - Eine Langzeiterhebung unter lebensnahen Bedingungen (Wissenschaftlicher Originalbeitrag). Umwelt-Medizin-Gesellschaft 24(1): 44-57.

(Submitted: 9 July 2010)
(Revised version accepted: 13 December 2010)

Literature

(1) STRAHLENSCHUTZKOMMISSION (2003): Forschungsbedarf im Sonderforschungsprogramm Mobilfunk, 3./04.07.2003.

(2) HECHT, K. (2001): Auswirkungen von Elektromagnetischen Feldern - Eine Recherche russischer Studienergebnisse 1960-1996, [Erhebung im Auftrag des Bundesinstituts für Telekommunikation (Auftrag Nr. 4231/630402)], umwelt-medizin-gesellschaft 14(3): 222-231.

(3) HECHT, K., SAVOLEY, E. N. (2007): Überlastung der Städte mit Sendeanlagen - eine Gefahr für die Gesundheit der Menschen und eine Störung der Ökoethik International Research Centre of Healthy and Ecological Technology, Berlin.

(4) BECKER, R. O. (1990): Cross Currents, J. P. Tarcher, Los Angeles.

(5) GUY, A. W., CHOU, C. K., KUNZ, L. L.,CROWLEY, J., KRUPP, J. (1985): Effects of long-term low-level radiofrequency radiation exposure on rats, summary, august 1985, Prepared for USAF SCHOOL OF AEROSPACE MEDECINE, Seattle, USAFSAM-TR-85-64, contract number F33615-80-C-0612, 9: 1-20.

(6) SCHMIDT, R. F., THEWS, G. (1983): Physiologie des Menschen, 21. Auflage, Springer Verlag, Berlin: 124

(7) BUNDESNETZAGENTUR (2004): STANDORTBESCHEINIGUNG Nr. 680 894 vom 5. 4 2004

(8) THOMAS, L. (1992): Labor und Diagnose, 4. Auflage, Die Medizinische Verlagsgesellschaft, Marburg.

(9) LABOR DIAGNOSTIKA Nord GmbH & Co. KG (Hrsg) (2008): Instructions For Use 3-Cat ELISA, [http://www.ldn.de/index.php/Catecholamines-ELISA/View-all-products.html, letzter Zugriff: 11.11.2010].

(10) BIEGER, W. P. (2004): Neuroscience - Grundlagen, Diagnostik und Therapie von Neurotransmitter-vermittelten Erkrankungen, [http://dr-bieger.de/neurostress-aktuallisierte-kurzuebersicht/#0, letzter Zugriff: 08.06.2010].

(11) HUISMANN, H., WYNVEEN, P., SETTER, P. W. (2009): Studies on the immune response and preparation of antibodies against a large panel of conjugated neurotransmitters and biogenic amines: specific polyclonal antibody response and tolerance, Journal of Neurochemistry, 10.1111/j.1471-4159.2009.06492.x.

(12) BÜNING, H., TRENKLER, G. (1978): Nichtparametrische statistische Methoden, W. de Gruyter, Berlin, New York.

(13) BOSCH, K. (2005): Elementare Einführung in die angewandte Statistik, vieweg studium, Wiesbaden.

(14) INTERNATIONAL COMMISSION ON NON-IONIZING RADIATION PROTECTION - ICNIRP (1998): Guidelines for Limiting Exposure to Time-Varying Electric, Magnetic, and Electromagnetic Fields (up to 300 GHz). Health Physics 74 (4): 494-522; 1998. [http://www.icnirp.org/PubMost.htm, letzter Zugriff 11.11.2010].

(15) LÖFFLER, G., PETRIDES, P. (1997): Biochemie und Pathochemie, 6. Auflage, Springer Verlag, Berlin: 800-821.

(16) SELYE, H. (1953): Einführung in die Lehre von Adaptations-Syndrom, Thieme Verlag, Stuttgart.

(17) LINDER, H. (2005): Biologie, 22. Auflage, Schroedelverlag, Braunschweig: 155

(18) BARGER, A., DALE, H. (1910): Chemical structure and sympathomimetic action of amines, J. Physiol. (Lond.) 41: 19-59.

(19) BURCHETT, S. A., HICKS, T. P. (2006): The mysterious trace amines: Protean neuromodulators of synaptic transmission in mammalian brain, Progress in Neurobiology 79: 223-246.

(20) LINDEMANN, L., HOENER, M. (2005): A renaissance in trace amines inspired by a novel GPCR family, TRENDS in Pharmacological Sciences 26(5): 274-281.

(21) BERRY, M. D. (2004): Mammalian central nervous system trace amines Pharmacologic amphetamines, physiologic neuromodulators, J. Neurochem. 90: 257-271.

(22) XIE, Z., MILLER, G. M. (2008): ß-Phenylethylamine Alters Monoamine Transporter Function via Trace Amine-Associated Receptor 1: Implication for Modulatory Roles of Trace Amines in Brain, The journal of pharmacology and experimental therapeutics 325: 617-628.

(23) ZELLER, E. A., MOSNAIM, A. D, BORISON, R. L, HUPRIKAR S. V. (1976): Phenylethylamine: Studies on the Mechanism of Its Physiological Action, Advances in Biochemical Psychopharmacology 15: 75-86.

(24) ORREGO, H. (1976): pers. Mitteilung, in: ZELLER, E. A., MOSNAIM, A. D, BORISON, R. L, HUPRIKAR S. V. (1976): Phenylethylamine: Studies on the Mechanism of Its Physiological Action, Advances in Biochemical Psychopharmacology 15: 83.

(25) BOULTON, A. (1976): Identification, Distribution, Metabolism, and Function of Meta and Para-Tyramine, Phenylethylamine and Tryptamine in Brain, Advances in Biochemical Psychopharmacology 15: 57-67.

(26) BERRY, M. D. ET AL. (1994): The effects of administration of monoamine oxidase-B inhibitors on rat striatal neurone responses to dopamine, Br. J. Pharmacol. 113: 1159-1166.

(27) RAO, T. S., BAKER, G. B., COUTTS, R. T. (1987): N-(3-Chloropropyl) Phenylethylamine as a possible Prodrug of ß-Phenylethylamine: Studies in the rat brain, Progress in neuro-psychopharmacology & biological psychiatry 11: 301 -308.

(28) SABELLI, H. C., MOSNAIM, A. D. (1974): Phenylethylamine hypothesis of affective behavior, Am. J. Psychiatry 131: 695-699.

(29) SABELLI, H. C. (1995): Phenylethylamine modulation of affect, Journal of neuropsychiatry and clinical neurosciences 7: 6-14.

(30) BIRKMAYER, W., RIEDERER, P., LINAUER W., KNOLL, J. (1984): The antidepressive efficacy of l-deprenyl, Journal of Neural Transmission 59: 81-7.

(31) DAVIS, B. A., BOULTON, A. A. (1994): The trace amines and their acidic metabolites in depression - an overview, Prog. Neuropsychopharmacol. Biol. Psychiatry 18: 17-45.

(32) SABELLI, H., FINK, P., FAWCETT. J., TOM, C. (1996): Sustained Antidepressant Effect of PEA Replacement, The journal of neuropsychiatry and clinical neurosciences 8: 168-171.

(33) BAKER, G. B., BORNSTEIN, R. A., ROUGET, A. C., ASHTON, S. E., VAN MUYDEN, J. C., COUTTS, R. T. (1991): Phenylethylaminergic Mechanisms in Attention-Deficit Disorder, Biologic Psychiatry 29: 15-22.

(34) KUSAGA, A., YAMASHITA, Y., KOEDA, T., HIRATANI, M., KANEKO, M., YAMADA, S., MATSUISHI, T. (2002): Increased urine phenylethylamine after methylphenidate treatment in children with ADHD, Annals of neurology, 52(3): 372-4.

(35) SCHLIEPHAKE, E. (1960): Kurzwellentherapie, Stuttgart, Fischer Verlag [mit Zitat aus: Deutsche Medizinische Wochenschrift, Heft 32: 1235 (5. August 1932)].

(36) BARTERI, M. (2005): Structural and kinetic effects of mobile phone microwaves on acetylcholinesterase activity, Biophysical Chemistry 113: 245-253.

(37) SCHMID, E., SCHRADER, T. (2007): Different biological effectiveness of ionizing and non-ionising radiations in mammalian cells, Adv. Radio Sci. 5: 1-4.

(38) SCHRADER, T., SCHMID, E., MÜNTER, K., KLEINE-OSTMANN, T. (2008): Spindle Disturbances in Human-Hamster Hybrid (AL) Cells Induced by Mobile Communication Frequency Range Signals, Bioelectromagnetics 29: 626 - 639.

(39) SANDERS, A. P., SCHAEFER, D. J., JOINES, W. T. (1980): Microwave effects on energy metabolism of rat brain, Bioelectromagnetics 1: 171-182. 42

(40) FRIEDMAN, J., KRAUS, S., HAUPTMAN, Y., SCHIFF, Y., SEGER, R. (2007): Mechanism of a short-term ERK activation by electromagnetic fields at mobile phone frequency, Biochemical Journal 405(Pt 3): 559-568.

(41) DESAI, N. R., KESARI, K. K., AGARWAL, A. (2009): Pathophysiology of cell phone radiation: oxidative stress and carcinogenesis with focus on male reproductive system, Reproductive Biology and Endocrinology 7: 114: 1-9.

(42) OLIVOS, H. J., ALLURI, P. G., REDDY, M. M., SALONY, D., KODADEK, T. (2002): Microwave-Assisted Solid-Phase Synthesis of Peptoids, Organic Letters 4(23): 4057-4059.

(43) HORIKOSHI, S., HIDAKA, H., SERPONE, N. (2003): Hydroxyl radicals in microwave photocatalysis. Enhanced formation of OH radicals probed by ESR techniques in microwave-assisted photocatalysis in aqueous TiO2 dispersions, Chemical Physics Letters 376: 475-48.

(44) SANTINI, R., SANTINI, P., DANZE, J. M., LE RUZ, P., SEIGNE, M. (2002): Symptoms experienced by people living in vicinity of mobile phone base stations: Incidences of distance and sex, Pathol. Biol. 50: 369-373.

(45) NAVARRO, E. A., SEGURA, J., PORTOLES, M., GÖMEZ-PERRETTA DE MATEO, C. (2003): The Microwave Syndrome: A Preliminary Study in Spain, Electromagnetic biology and medicine 22(2 & 3): 161 -169.

EGER, H., JAHN, M. (2010): Spezifische Symptome und Mobilfunkstrahlung in Selbitz (Bayern) - Evidenz für eine Dosiswirkungsbeziehung, umwelt-medizin-gesellschaft 23(2):130-139.

(46) AUGNER, C., HACKER, G.W., OBERFELD, G., FLORIAN, M., HITZL, W., HUTTER, J., PAUSER, G. (2010): Effects of Exposure to GSM Mobile Phone Base Station Signals on Salivary Cortisol, Alpha-Amylase, and Immunoglobulin A., Biomed Environ Sci 23 (3): 199-207.

(47) ABDEL-RASSOUL, G., EL-FATEH, O.A., SALEM, M.A., MICHAEL, A., FARAHAT F., EL-BATANOUNY, M., SALEM, E. (2007): Neurobehavioral effects among inhabitants around mobile phone base stations. NeuroToxicology 28(2): 434-40.

(48) FEGERT, J., GLAESKE, G., JANHSEN, K., LUDOLPH, A., RONGE, C. (2002): Untersuchung zur Arzneimittel-Versorgung von Kindern mit hyperkinetischen Störungen anhand von Leistungsdaten der GKV. Projektbericht für das Bundesministerium für Gesundheit und Soziale Sicherung, [http://www.home.uni-osnabrueck.de/kjanhsen/ unter Bücher, Buchartikel, Projektberichte, letzter Zugriff 11.11.2010].

(49) EGER, H., NEPPE, F. (2009): Krebsinzidenz von Anwohnern im Umkreis einer Mobilfunksendeanlage in Westfalen, Interview-basierte Piloterhebung und Risikoschätzung, umwelt-medizin-gesellschaft 22(1): 55-60.

(50) EGER, H., HAGEN, K. U., LUCAS, B., VOGEL, P., VOIT, H. (2004): Einfluss der räumlichen Nähe von Mobilfunksendeanlagen auf die Krebsinzidenz, umwelt-medizin-gesellschaft 17(4): 326-332.

(51) FELTEN, D. L., MAIDA, M. E. (2002): Psychoneuroimmunology, in: FINK, G. (Hrsg.): Encyclopedia of the Human Brain, Vol. 4, Academic Press, San Diego: 103-127.

(52) STRAUB, R. H. (Hrsg.) (2007): Lehrbuch der klinischen Pathophysiologie komplexer chronischer Erkrankungen, Band 1 und 2, Vandenhoeck und Ruprecht, Göttingen: (2) 89-98.

(53) ABELIN, T., ALTPETER, E., RÖÖSLI, M. (2005): Sleep Disturbances in the Vicinity of the Short-Wave Broadcast Transmitter Schwarzenburg - Schlafstörungen in der Umgebung des Kurzwellensenders Schwarzenburg, Somnologie 9: 203-209.

(54) PAFFRATH, D., SCHWABE, U. (Hrsg.) (2004): Arzneiverordnungs-Report 2004, Aktuelle Daten, Kosten, Trends und Kommentare. Springer-Verlag, Berlin. [http://wido.de/arzneiverordnungs-rep.html unter download, letzter Zugriff 11.11.2010].

(55) THOMAS, S., HEINRICH, S.,VON KRIES R., RADON K. (2010): Exposure to radio-frequency electromagnetic fields and behavioural problems in Bavarian children and adolescents. Eur J Epidemiol 25(2): 135-141.

(56) SIEGENTHALER, W. K., HORNBOSTEL, H. D. (1984): Lehrbuch der Inneren Medizin, Georg Thieme Verlag, Stuttgart, New York.

(57) MILHAM, S. (2010): Dirty electricity - electrification and the diseases of civilization, universe, Bloomington.

(58) OSSIANDER, E. (2010): persönliche Mitteilung [Numbers of hospitalizations per year for ICD-9 code 227.0 (benign tumor of the adrenal gland, 1987-2007, Epidemiology Office, Washington State Department of Health Pheochromocytoma, ICD 227.0, 1997-2006, US Department of Health and Human Services, H.CUPnet.

Bioelectromagnetics 27:119–126 (2006)

Effects of Radiofrequency Radiation Emitted By Cellular Telephones on the Cognitive Functions of Humans

Ilan Eliyahu,[1]* Roy Luria,[2] Ronen Hareuveny,[1] Menachem Margaliot,[1] Nachshon Meiran,[2] and Gad Shani[3]

[1]*Radiation Safety Division Soreq NRC, Yavne, Israel*
[2]*Department of Behavioral Sciences, Ben-Gurion University, Beer-Sheva, Israel*
[3]*Department of Biomedical Engineering, Ben-Gurion University, Beer-Sheva, Israel*

The present study examined the effects of exposure to Electromagnetic Radiation emitted by a standard GSM phone at 890 MHz on human cognitive functions. This study attempted to establish a connection between the exposure of a specific area of the brain and the cognitive functions associated with that area. A total of 36 healthy right-handed male subjects performed four distinct cognitive tasks: spatial item recognition, verbal item recognition, and two spatial compatibility tasks. Tasks were chosen according to the brain side they are assumed to activate. All subjects performed the tasks under three exposure conditions: right side, left side, and sham exposure. The phones were controlled by a base station simulator and operated at their full power. We have recorded the reaction times (RTs) and accuracy of the responses. The experiments consisted of two sections, of 1 h each, with a 5 min break in between. The tasks and the exposure regimes were counterbalanced. The results indicated that the exposure of the left side of the brain slows down the left-hand response time, in the second—later—part of the experiment. This effect was apparent in three of the four tasks, and was highly significant in only one of the tests. The exposure intensity and its duration exceeded the common exposure of cellular phone users. Bioelectromagnetics 27:119–126, 2006. © 2005 Wiley-Liss, Inc.

Key words: cognitive function ability; left hemisphere; right hemisphere; GSM

INTRODUCTION

The dramatic increase in cellular phones usage raises the question of the existence of possible biological effects of radio-frequency electromagnetic radiation (RFR) [Stewart, 2000]. Although the effects of the utilized frequencies (~0.9 and ~1.8 GHz) have been studied before, two new developments in cellular technology warrant our attention:

1. Never before have so many people (especially children) been exposed to RFR, at non-negligible intensities with such proximity to the head (although within permitted levels according to IRPA/ICNIRP, 1998, FCC, 1996, CENLEC, 2001 exposure standards).
2. Most modern cellular systems operate in a pulsating mode in which the data is accumulated and transmitted in short pulses. Such modulated RFR at low average power has been reported to have effects on the central nervous system [Bawin et al., 1975; Blackman et al., 1979, 1980].

Several recent studies on the effects of exposure to RFR from cellular phones report that exposure to 900 MHz has an identifiable effect on electroencephalogram (EEG). Klaus and Joachim [1996] found changes in the EEG pattern of sleeping subjects during the exposure to GSM RFR. The radiation source in the said report had an 8 W output and the power density at the head was estimated to be 0.05 mW/cm^2. The subjects were exposed for 8 h from one side only. Further studies [Wagner et al., 1998] tried, but failed, to replicate the results of this study.

A study by Krause et al. [2000] tested the effects of GSM cellular phone on the EEG during an auditory

---

*Correspondence to: Ilan Eliyahu, Radiation Safety Division Soreq NRC, Yavne 81800, Israel. E-mail: ilan@soreq.gov.il

Received for review 29 November 2004; Final revision received 30 June 2005

DOI 10.1002/bem.20187

memory test. A standard GSM phone (at 902 MHz) was attached to the right posterior temporal region of the head under two exposure conditions: on or off. Their findings indicated that EMF decreased the theta band activity only during their memory retrieval task, and increased the alpha band activity. However, a replication study by Krause et al. [2004] did not confirm these findings.

An epidemiological study by Oftedal et al. [2000] in Sweden and Norway looked for symptoms such as headaches, feelings of discomfort or warmth behind/around the ear in GSM users and NMT users. Their results indicated that mobile phone users experienced a variety of symptoms either during or shortly after a phone call. A study by Koivisto et al. [2001] compared subjective symptoms or sensations, such as head aches, dizziness, fatigue, itching, tingling of the skin, redness and sensations of warmth on the skin in two groups of 48 subjects, who were exposed to RFR for 30–60 min. Their results did not reveal significant differences between the exposure and non-exposure conditions.

The effects of RFR on cognitive functions were examined in several studies. Preece et al. [1999] conducted tests on a variety of short-term and long-term memory tasks, and reaction time (RT) tests. The subjects were exposed to RFR at 915 MHz (1 and 0.25 W powers). They reported a reduction in RT, with the shortest response time when the subjects were exposed to 915 MHz at 1 W.

Similar tests were conducted by Koivisto et al. [2000a]: 12 different RT tests were conducted under the exposure to 902 MHz at 0.25 W. In three of the tests, a reduction in the RT was observed. Another study by Koivisto et al. [2000b] examined the effects on the working memory, and revealed a reduction in RT under exposure to 902 MHz at 0.25 W.

In two replications and an extension study done by Haarala et al. 2003, 2004, 64 subjects in two different laboratories in Finland and Sweden performed double-blind cognitive and short-term memory tasks. The phone was attached to the left side of the head. No statistically significant differences were found between laboratories, and they did not replicate the Koivisto et al. [2000a,b] results.

The Present Study

The goal of the present study was to examine whether RFR can affect cognitive functions. The subjects were asked to perform four different tasks while being exposed to different RFR condition. The tasks chosen were those that are known to have high hemisphere specificity, i.e., they activate mostly one side of the brain (see Smith and Joindes, 1999 for a review article). The four tasks were a verbal item recognition task (left side), a spatial item recognition task (right side), and two spatial compatibility tasks (the left compatible stimuli activate the right side, while the right compatible stimuli activate the left side).

Subjects were exposed to RFR alternatively to the left side, to the right side and sham exposed. To the best of our knowledge this is the first study that compares effects of exposure to the two head sides within the same task. This allows us to test the hypothesis of the present work, that performance of specific tasks is affected by one side exposures only.

MATERIALS AND METHODS

Thirty-six healthy right-handed male subjects were chosen. The mean age was 24 years, ranging from 19 to 27. The experiment was approved by the Ben-Gurion University Medical School Ethical Committee (Beer–Sheva, Israel). The subjects gave an informed written consent. The subjects completed a questionnaire concerning intakes of tea, coffee, alcohol and the amount of sleep they had prior to the experiment. The participants reported adequate sleep in the night prior to the experiment, and they did not drink excessively or use CNS-affecting drugs.

Cognitive Tasks

The subjects were requested to perform four different tasks. The examined parameters were the response time (RTs) and the percentage of erroneous responses made by the subjects. In all tasks, subjects were instructed to react to the stimuli presented on a computer screen by pressing given buttons (‘‘/’’—using the index finger of their right hand or ‘‘z’’—using the index finger of their left hand) on the computer keyboard as quickly and accurately as possible.

As differentiation between hemispheres was one of the objects of the present study, the tasks chosen were those for which hemisphere differentiation is well established.

The tasks were coded as follows:

Spatial item recognition task—“FACE”. In this task, three targets ‘‘faces’’ were presented sequentially, for 650 ms each, in three random locations on the screen, chosen out of eight possible locations. After a 3.5 s interval, another face appeared in a random location. The subject had to decide whether the last face matched the location of any of the three target faces. They were instructed to press the ‘‘/’’ when there was a match, or ‘‘z’’ when there was no match. This task is known to activate a region in the right premotor cortex [Smith et al., 1998; Smith and Jonides, 1999]. Figure 1 illustrates this experiment.

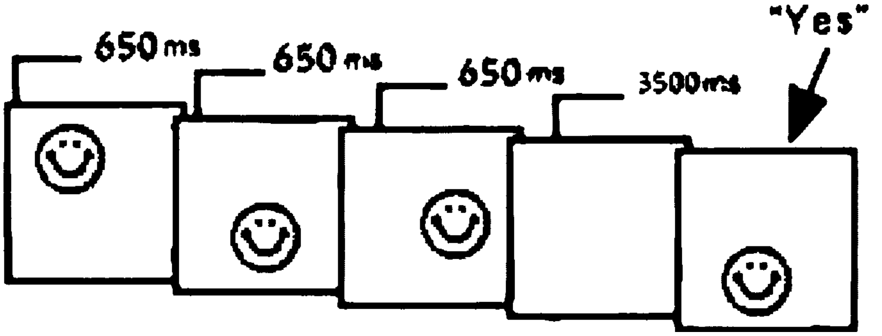


Fig. 1. "FACE"—spatial item recognition task—the subjects task is to decide whether the probe face is in the same location as any of the target faces.

Verbal item recognition task—"LETTER". In this task, a small set of target uppercase letters was presented simultaneously for 0.5 s, followed by a single lowercase probe letter after a delay interval of 3 s. The subject had to decide whether the probe matched any of the target letters by pressing "/" when there was a match or "z" when there was no match. This task is known to activate the left posterior parietal cortex, three frontal sites, and the left supplementary motor and premotor areas [Smith et al., 1998; Smith and Jonides, 1999]. Figure 2 illustrates this experiment.

Spatial compatibility—"SPAT". In this task, a letter was presented either on the left or on the right side of a fixation letter. The subject had to activate the left or the right hand according to the side of the letter. This task is assumed to activate the right posterior parietal cortex, when the letter is in the right side of the fixation letter, and the left posterior parietal cortex when the letter is on the left side of the fixation point [Peri and Zeki, 2000]. Figure 3 illustrates this experiment.

Spatial compatibility—"SIMON". In this task, the subject had to respond to stimuli that appeared either on the left or the right side of a fixation letter. When the symbols Π or θ appeared, the subject had to respond with his left or right hand, respectively. Previous studies indicate that [Simon and Rudell, 1967; Simon, 1990] when the side of the stimulus' presentation matches the responding hand (the compatible condition), responses were faster than when there is no match between the side of the stimulus and the responding hand (the incompatible condition). This is called the Simon effect [Simon and Rudell, 1967; Simon, 1990]. Figure 4 illustrates this experiment.

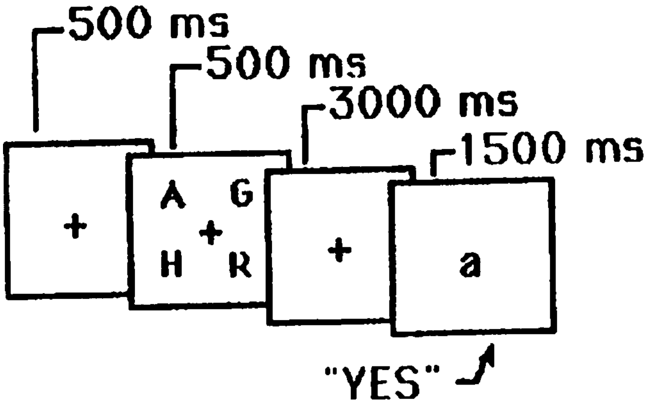


Fig. 2. "LETTER"—verbal item recognition task—the subjects task is to decide whether the probe matches any of the target letters.

The test was divided into two sessions: a first 1 h series of tasks, a 5 min break, and then another hour of tasks. Before the first hour the subjects performed a 5 min training session of the four tasks employed in the experiment in order to minimize training effects.

All subjects performed all four tasks under either, left, right, or sham exposure conditions. This resulted in 12 sub-sessions per subject. Each subject performed a total of 1614 trials in all four experiments.

RF Exposure

Each subject had two standard Nokia™ 5110 GSM cellular phones attached to his head by a specially designed non-conductive frame. The phones were placed on both sides of the head, as shown in Figure 5.

We controlled the cellular phones power by using an HP GSM test system model E6392B. The phones were operated with test SIM cards (Wavetek). This

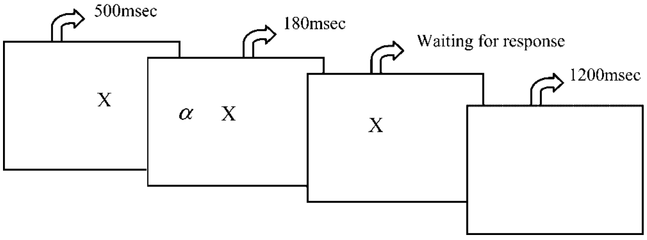


Fig. 3. "SPAT"—spatial compatibility—the subject has to activate the left or the right hand according to the side of the letter.

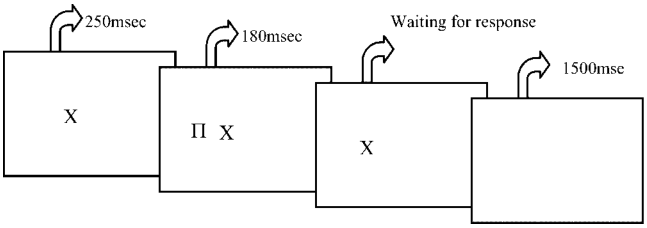


Fig. 4. "SIMON"—spatial compatibility—when the symbols Π and θ appeared, the subject had to press his left or right hand, respectively.

system maintained the phones at either no transmission or full power transmission (890.2 MHz, 33 dBm = 2 W peak power, using the typical GSM pulse duration of 577 µs and duty cycle of 1/8, yielding 0.25 W average power). The communication between the phones and the test system was wireless, at an extremely small output power (0.01 mW peak output power, as compared to the 2 W peak output of the phones); thus, we consider it negligible. During the experiment, the phones were battery operated. The phones were mounted on the subject's heads before the first task and dismounted after the final task.

At the end of the experiments, the subjects were requested to assess whether and when the phones operated. They were unable to distinguish between exposure/sham-exposure situations, and between the sides of the exposures.

All tasks utilized the standard laboratory PC-based software (Micro Experimental Laboratory 2.0$^{\mathrm{TM}}$) and experiments were presented on 14 inch screens. The subjects used standard 104-key computer keyboards.

In case of an erroneous response, the computer emitted a 400 ms beep at 500 Hz. The exposure regime and the order of the tasks were counterbalanced across subjects according to a balanced Latin square design. Each subject served as his own control, namely, his performance without exposure was compared to his own performance under exposure (a repeated measures design). The RF exposure regime was single-blinded, i.e., the experiment manager was aware of the exposure mode, while the subjects were not, since the phones were silent all the time. An opaque partition was placed between the experiment manager and the subjects during the experiment.

Fig. 5. A subject during the experiment, with the phone frame attached. [The color figure for this article is available online at www.interscience.wiley.com.]

RESULTS

In each task, trials with response times longer than 3 s and shorter than 100 ms were screened out. Only trials in which the response was correct were included in the response time analyses. In the present work, Greenhouse–Geisser correction was applied to the df's, and corrected P-values were reported for all factors (when df > 2). No speed-accuracy trade-off was observed in any of the tasks.

A repeated measures analysis of variance (ANOVA) including Exposure condition (right hemisphere, left hemisphere, and sham exposure), Session (part one or part two), and Responding Hand (right or left) as within dependent variables on the average RT in each condition was performed.

Results for the FACE Task

The triple interaction between exposure, session and side was significant ($F(2, 62) = 3.40$, $P = .037$) see Figure 6a and b. For most exposure conditions, we observed a reduction in the response/RT from the first to the second session (with either sham exposure, or exposure to the right side of the brain). This result is probably due to training (see Fig. 6a). However, in the left hemisphere exposure condition, a reversed pattern was observed when subjects responded with their left hand: the RT in the second part of the experiment was significantly prolonged relative to the first part, from 907 to 931 ms ($F(1, 32) = 6.30$, $P = .01$) and this pattern was significantly different from the sham exposure and right side exposure averaged together ($F(1, 32) = 5.17$, $P = .02$) see Figure 6b.

There was also a significant main effect of Responding Hand, ($F(1,32) = 13.3$, $P < .001$) indicating that RT was 48 ms (from 864 to 912 ms) faster for the right hand responses (recall that all subjects were right handed).

Results for the LETTER Task

The main effect for the factor session ($F(1, 29) = 4.79$, $P = .036$) and Hand ($F(1, 29) = 26.74$, $P < .0001$) was significant, as was the interaction between these

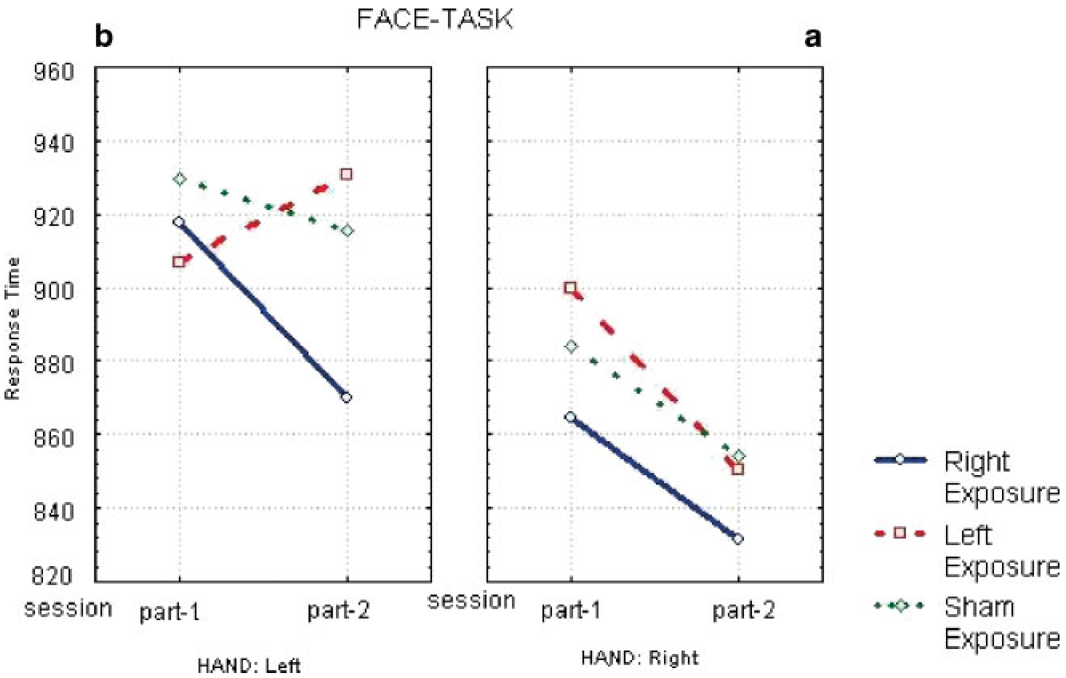


Fig. 6. Response times in milliseconds—left hand response (**b**) and right hand response (**a**)—"FACE" task. Triple interaction between exposure, session, and side was significant. For three of the exposure conditions, a reduction in the response time from the first to second session was observed. Only in the setup in which the exposure was to the left side and the left hand responded was the response time prolonged.

factors ($F(1, 29) = 9.54$, $P < .005$). Subject improvement from the first to the second part of the experiment was limited to the right hand (60 ms improvement for the right hand as opposed to 0 ms for the left hand—see Fig. 7). The results also indicate a trend similar to the FACE experiment—RTs in the left hand were increased under the left side exposure condition (by 13 ms—from 1014 to 1027 ms) as opposed to a slight decease in RT in the right side and sham exposure (2 and 9 ms respectively). This trend was not significant. It is possible that the effect of RFR is less evident on the average RT analysis, but it may still affect other parts of the RT distribution [Ratcliff, 1979]. In order to verify this point, we reanalyzed the data, this time using the 25th (fast RT) percentile as the independent variable. The left-side exposure condition slowed left hand responses by 14 ms as opposed to acceleration for the right side and sham exposure conditions (15 and 29 ms, respectively). For left hand responses, the left exposure condition was significantly slower than sham exposure in the second part of the experiment ($F(1, 29) = 4.28$, $P = .04$). This difference was not significant in the first part of the experiment, $F < 1$.

Results for the SPAT Task

The only significant observable effect was the main effect for the factor of responding hand ($F(1, 29) = 7.75$, $P < .01$). Right hand responses were 9 ms faster than left hand responses (340 and 349 ms, respectively). Importantly, the same trend for the left side exposure condition appeared also in this experiment (see Fig. 8): left hand responses were slowed down by 5 ms from the first to the second part of the experiment (from 349 to 354 ms), but under the right side and the sham exposure conditions, the left hand responses was accelerated (2 and 9 ms, respectively). The difference between the left side exposure condition and the sham exposure condition was significant in the second part of the experiment ($F(1, 30) = 6.43$, $P = .01$), but this difference was not significant in the first part of the experiment, $F < 1$.

Results for the SIMON Task

The ANOVA was the same as in the previous analysis, but it included the variable compatibility (compatible vs. incompatible responses) as an additional independent variable. The main significant effect was the difference between the examination sessions ($F(1,29) = 10.86, P < .005$), namely: the first part of the experiment was on the average, 24 ms faster than the second part.

Another effect observed was the so-called Simon effect [Simon and Rudell, 1967; Simon, 1990]—the compatibility between the visual stimulus side and the

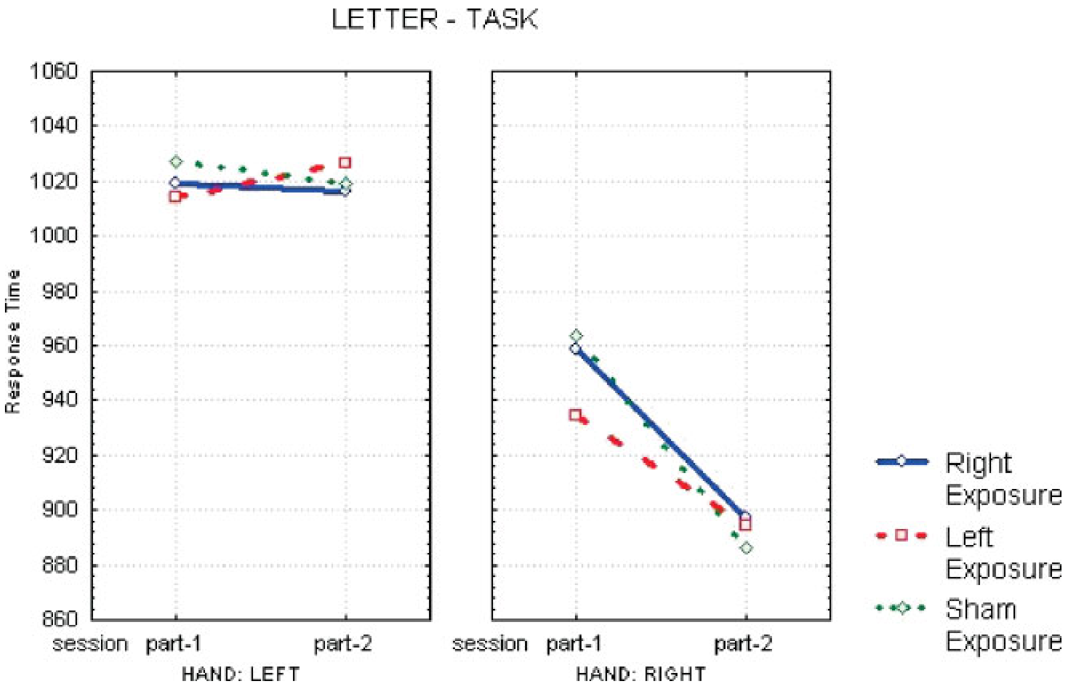


Fig. 7. Response times in milliseconds—first and second sessions—LETTER task.

responding hand ($F(1, 29) = 7.06$, $P = .01$), namely: compatible responses were 16 ms faster than incompatible responses (from 499 to 515 ms). There was no indication of any effects of RFR either in the average RT analysis or in the fast RT analysis.

DISCUSSION

The scientific literature dealing with the effects of low intensity radio waves emitted by cellular handsets shows a growing interest in the existence of cognitive

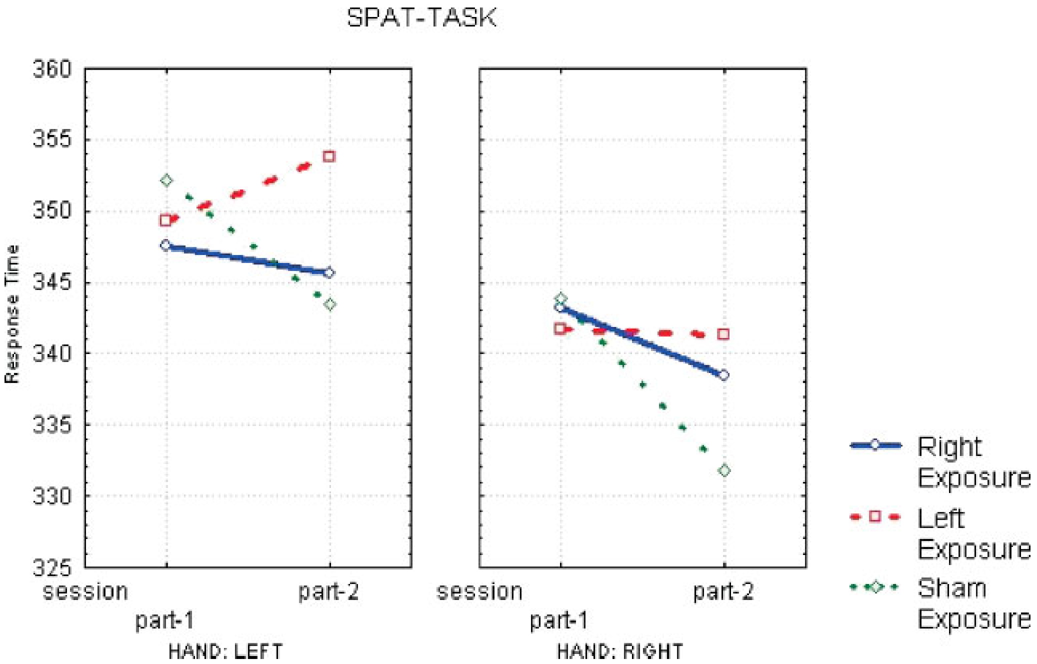


Fig. 8. Response times in milliseconds—first and second sessions—SPAT task.

effects. This is due to the assumption that cognitive functions might express very weak basic effects, if they exist, in an observable manner, because of CNS amplification.

Of these effects, the linkage between RFR exposure and RT to external stimuli has been previously examined. In particular, Preece et al. [1999] and Koivisto et al. [2000a,b] reported a shortening of the RT. Some work on verification of these reports failed to confirm their findings [Haarala et al., 2003, 2004].

In these studies only one side of the head was exposed: the left side [Preece et al., 1999; Koivisto et al., 2000a,b; Haarala et al., 2003, 2004] and the right side [Krause et al., 2000]. The responding hand was the right hand in some works [Koivisto et al., 2000a,b; Haarala et al., 2003, 2004], while in the other publications this was not clearly specified.

In the present work, we thus added specific examinations of possible differences between right/left side exposures and right/left responding hand.

We considered these details to be of relevance, due to the differentiation between the right/left brain hemispheres functions.

The present work is, to the best of our knowledge, the first attempt to examine directly these two responding conditions. To achieve these purposes, we used two phones, placed simultaneously on both sides of the head, and in fact, our results indicated that the effect of RFR was evident only in the left head side exposure and left hand responding combined condition.

The statistically significant finding was a slowing effect in left hand responses under left side RFR exposure condition only (found in the spatial item recognition task—"FACE"). This effect became evident only in the second part of the experiment (namely: after an hour of test, of which 40 min were under full power exposure). The same trend was also observed in the spatial compatibility task—"SPAT", but was significant only in the specific comparison analysis.

While the effects of RFR were not evident in all experiments, it is possible that the dependent variable of average RT is not sensitive enough to detect those effects [Ratcliff, 1979]. In this respect we have shown that at least in one task (Verbal item recognition—"LETTER") the effects were not apparent in the usual average RT but were detectable in other parts of the RT distribution. Specifically, we found changes on the 25th percentile (the fast part of the RT distribution).

It is noteworthy that although all the detected effects were expressed in left hand slowing, and appeared under left side exposure, we cannot state that a hemisphere dependence was detected, as the functions affected are related to activities of both hemispheres.

The origin of the differences between our results and the former studies is unclear, and could result form several reasons such as: the exposure methodology—right and left hemispheres, the responding hand—left or right, the exposure time, and the differences in the cognitive tasks. These differences seem to be significant and should be examined in future studies.

It can be concluded that more work is required to verify our results and to reconcile the differences between our study, and the former studies in which an opposite effect, or no effect were found. In addition, the involvement of confounding factors must be examined further.

REFERENCES

Bawin SM, Kaczmarek LK, Adey WR. 1975. Effects of modulated VHF fields on the central nervous system. Ann NY Acad Sci 247:74–80.

Blackman CF, Elder JA, Weil CM, Benane SG, Eichinger DC, House DE. 1979. Induction of calcium-ion efflux from brain tissue by radiofrequency radiation, effects of modulation frequency and field strength. Radio Sci 14:93.

Blackman CF, Elder JA, Lampe JA, Benane SG, Faulk JM, House DE. 1980. Induction of calcium-ion efflux from brain tissue by radiofrequency radiation effects of sample number and modulation frequency on the power density window. Bioelectromagnetics 1:35.

CENELEC. 2001. European Committee for Electrotechnical Standardization. Product standard to demonstrate the compliance of mobile phones with the basic restrictions related to human exposure to electromagnetic fields (300 MHz–3 GHz).

FCC/Federal Communications Commission. 1997. Evaluating compliance with FCC Guidelines for human exposure to radiofrequency electromagnetic fields. OET Bulletin 65 Edition 97-01. August 1997.

Haarala C, Bjornberg L, Ek M, Laine M, Revonsuo A, Koivsto M, Hamalainen H. 2003. Effect of a 902 MHz electromagnetic field emitted by mobile phones on human cognitive function: A replication study. Bioelectromagnetics 24:283–288.

Haarala C, Ek M, Bjornberg L, Laine M, Revonsuo A, Koivsto M, Hamalainen H. 2004. 902 MHz mobile phone does not affect short term memory in humans. Bioelectromagnetics 25:452–456.

IRPA/ICNIRP. 1998. Guidelines for limiting exposure to time-varying electric magnetic and electromagnetic fields (up to 300 GHz). Health Phys 74(4):494.

Koivsto M, Revonsuo A, Krause MC, Haarala C, Sillanmak L, Laine M, Hamalainen H. 2000a. Effects of 902 MHz electromagnetic field emitted by cellular telephones on response times in humans. Cognitive Neurosci Neuropsychol II(2): 413–415.

Koivsto M, Krause MC, Revonsuo A, Laine M, Hamalainen H. 2000b. The effects of electromagnetic field emitted by GSM phones on working memory. Cognitive Neurosci II(8):1641–1643.

Koivsto M, Haarala C, Krause MC, Revonsuo A, Laine M, Hamalainen H. 2001. GSM phone signal does not produce subjective symptoms. Bioelectromagnetics 22:212–215.

Krause CM, Sillanmaki L, Koivisto M, Haggqvist A, Saarela Carina, Revonsuo A, Laine M, Hamalainen H. 2000. Effects of electromagnetic field emitted by cellular phones on the EEG during a memory task. Cognitive Neurosci II(4):761–764.

Krause CM, Haarala C, Sillanmaki L, Koivisto M, Alanko K, Revonsuo A, Laine M, Hamalainen H. 2004. Effects of electromagnetic field emitted by cellular phones on the EEG during an auditory memory task: A double blind replication study. Bioelectromagnetics 25:33–40.

Mann K, Roschke J. 1996. Effects of pulsed high frequency electromagnetic fields on human sleep. Neuropsychobiology 33:41–47.

Oftedal G, Wilen J, Sandstrom M, Mild KH. 2000. Symptoms experienced in connection with mobile phone use. Occup Med 50(4):237–245.

Peri R, Zeki S. 2000. The neurology of saccades and covert shifts in spatial attention. An event-related fMRI study. Brain 123: 2273–2288.

Preece AW, Iwi G, Davies-Smith A, Wesnes K, Butler S, Lim E, Varey A. 1999. Effect of a 915 MHz simulated mobile phone signal on cognitive function in man. Int J Radiat Biol 75(4):447–456.

Ratcliff R. 1979. Group reaction time distributions and an analysis of distribution statistics. Psychol Bull 86:446–461.

Simon JR. 1990. The effects of an irrelevant directional human information processing. In: Proctor RW, Revve TG, Editors. Stimulus response compatibility: an integrated perspective. Amsterdam: Elsevier, pp 31–88.

Simon JR, Rudell AP. 1967. The effect of an irrelevant cue on information processing. J Appl Psychol 51:300–304.

Smith E, Jonides J. 1999. Storage and executive process in the frontal lobes. Science 283:1657–1661.

Smith E, Jonides J, Christy M, Robert AK. 1998. Components of verbal working memory: Evidence from neuroimaging. Proc Natl Acad Sci USA 95:876–882.

Stewart W. 2000. Mobile phones and health. Independent expert group on mobile phones.

Wagner P, Roschke J, Mann K, Hiller W, Frank C. 1998. Human sleep under the influence of pulsed radiofrequency electromagnetic field. Bioelectromagnetics 19:199–202.

A meta-analysis for neurobehavioural effects due to electromagnetic field exposure emitted by GSM mobile phones

A Barth,[1] R Winker,[2] E Ponocny-Seliger,[3] W Mayrhofer,[4] I Ponocny,[3] C Sauter,[5] N Vana[6]

[1] Institute of Management Science, Division Ergonomics and Organization, Vienna University of Technology, Vienna, Austria; [2] Division of Occupational Medicine, Medical University of Vienna, Vienna, Austria; [3] Empirical Research & Statistical Consulting, Vienna, Austria; [4] Fraunhofer Project Group for Production- and Logistics Management in Vienna (Fraunhofer PPL), Vienna, Austria; [5] Department of Neurology, Medical University of Vienna, Vienna, Austria; [6] Atomic Institute of the Austrian Universities, Vienna, Austria

Correspondence to: Dr A Barth, Institute of Management Science, Division Ergonomics and Organization, Vienna University of Technology, Theresianumgasse 27, A-1040 Vienna, Austria; barth@imw.tuwien.ac.at

AB and RW contributed equally to this study.

Accepted 27 September 2007
Published Online First
10 October 2007

ABSTRACT

Background and objective: Numerous studies have investigated the potential effects of electromagnetic fields (EMFs) emitted by GSM mobile phones (~900 MHz to ~1800 MHz) on cognitive functioning, but results have been equivocal. In order to try and clarify this issue, the current study carried out a meta-analysis on 19 experimental studies.

Design: Meta-analysis.

Methods: Nineteen studies were taken into consideration. Ten of them were included in the meta-analysis as they fulfilled several minimum requirements; for example, single-blind or double-blind experimental study design and documentation of means and standard deviation of the dependent variables. The meta-analysis compared exposed with non-exposed subjects assuming that there is a common population effect so that one single effect size could be calculated. When homogeneity for single effect sizes was not given, an own population effect for each study and a distribution of population effects was assumed.

Results: Attention measured by the subtraction task seems to be affected in regard to decreased reaction time. Working memory measured by the N-back test seems to be affected too: under condition 0-back target response time is lower under exposure, while under condition 2-back target response time increases. The number of errors under condition 2-back non-targets appears to be higher under exposure.

Conclusion: Results of the meta-analysis suggest that EMFs may have a small impact on human attention and working memory.

In view of the widespread and increasing use of GSM mobile phones, potential health risks have been a key focus of concern. Over the past years, several studies have investigated the effects of electromagnetic fields (EMFs) emitted by mobile phones on cognitive functioning. It is still unclear, however, whether there are effects and, if so, which functions of the central nervous system may be influenced. Although a number of studies have been conducted to examine this issue, results are inconsistent. Some research suggests that acute exposure to mobile phones affects cognitive performance. Lee *et al* recorded a mild facilitating effect on attention.[1] Preece *et al* found a small decrease in reaction time in choice reaction task.[2] Tests conducted by Smythe and Costall reflected facilitated memory performance, but only in male subjects.[3] Koivisto *et al* found that response times in simple reaction task and vigilance tests increased.[4] Cognitive time to complete an arithmetic task, however, decreased. In a second study, Koivisto *et al* revealed that response times in some working memory tasks decreased.[5] Edelstyn and Oldershaw demonstrated a facilitatory effect on attention.[6] Eliyahu *et al* investigated spatial recognition, verbal recognition and spatial compatibility tasks and reported a slowdown of response time.[7] Curcio *et al* also showed an improvement of the performance in simple and choice reaction tasks.[8] In contrast, Keetley *et al* showed an impairment in simple and choice reaction tasks, while performance on trail making was improved.[9]

Other studies, however have shown no effects. Haarala *et al*[10 11] tried to replicate the findings of Koivisto *et al*[4 5] but were unable to find any significant difference on cognitive function. Besset *et al* found no effects in the following neuropsychological categories: information processing, attention capacity, memory function and executive function.[12] Russo *et al* demonstrated no change in performance in attention tasks.[13] Hladky *et al* found no impact in memory load and attention.[14] Recent findings from Haarala *et al* indicate that electromagnetic exposure (differentiated in continuous wave and pulse modulated EMFs) have no effect on human cognitive functions.[15]

The current paper uses a meta-analysis to examine whether cognitive functions are affected by acute exposure to EMFs emitted by GSM mobile phones.

METHODS

PubMed was used for a literature search on original articles published before 28 February 2007 using the phrases "mobile phone" or "cellular phone" and "cognitive". The search revealed 40 articles. In addition, relevant articles were identified by personal reference lists. We decided to investigate all abstracts from these articles. Then, the full text articles of all relevant human studies examining the question of neuropsychological effects of mobile phones were assessed for inclusion in the meta-analyses.

Nineteen studies published between 1999 and January 2007 were taken into consideration: Russo *et al*;[13] Besset *et al*;[12] Haarala *et al*;[10] Haarala *et al*;[11] Lee *et al*;[1] Edelstyn and Oldershaw;[6] Koivisto *et al*;[4] Koivisto *et al*;[5] Elihayu *et al*;[7] Smythe and Costall;[3] Preece *et al*;[2] Maier *et al*;[18] Krause *et al*;[19] Hladky *et al*,[14] and Lee *et al*;[16] Keetley *et al*;[9] Curcio *et al*;[8] Wilen *et al*;[17] and Haarala *et al*.[15]

These studies investigated the effect of GSM mobile phones on cognitive functions using test

Table 1 Characterisation of the 10 studies according to sociodemographic variables and study design

Study	n (gender)	Mean age (range)	Handedness	Design		Source/duration of exposure	Head side of exposure
Russo *et al*[13]	84 (NA)	23.5 (17–41)	NA	Double-blind	One group (on/off)	GSM; 888 MHz 35–40 min	42 left, 42 right irrespective of handedness
Besset *et al*[12]	55 (28 F, 27 M)	24.3 (18–40)	8 left 47 right	Double-blind	Two groups: 28 (on); 27 (off) matched by IQ	GSM; 900 MHz; 28 sessions; 120 min/session	Preferred hand
Haarala *et al*[10 11]	64 (32 F, 32 M)	26.8 (20–42)	Right	Double-blind	One group (on/off)	GSM; 902 MHz 65 min	Left
Haarala *et al*[10 11]	64 (32 f, 32 M)	26.8 (20–42)	Right	Double-blind	One group (on/off)	GSM; 902 MHz 65 min	Left
Lee *et al*[1]	78 (53 F, 35 M)	19.8 (NA)	Right	Single-blind	Two groups: 39 (on); 39 (off) matched by age, education	GSM; 1900 MHz 25 min	Right
Edelstyn *et al*[6]	38 (NA)	21 (20–22)	Right	Single-blind	Two groups: 19 (on); 19 (off)	GSM; 900 MHz 30 min	Left
Koivisto *et al*[4]	48 (24 F, 24 M)	26.0 (18–49)	Right	Single-blind	One group (on/off)	GSM; 902 MHz 60 min	Left
Koivisto *et al*[5]	48 (24 F, 24 M)	23.2 (18–34)	Right	Single-blind	One group (on/off)	GSM; 902 MHz 30 min	Left
Curcio *et al*[8]	20 (10 F, 10 M)	26.4 (22–31)	Right	Double-blind	One group (on/off)	GSM; 902 MHz 45 min.	Left
Keetley *et al*[9]	120 (58 M, 62 F)	33.0 (18–70)	NA	Double-blind	One group (on/off)	GSM; not specified 60 min	Left

procedures for recording change in performance: information processing; reaction time; attention; memory and executive functions. The minimum criteria for inclusion in our meta-analysis encompassed the following:

1. Either: treatment group (mobile phone switched on) and control group (mobile phone switched off) with baseline measures; or repeated measurement of subjects with mobile phone switched on and switched off.
2. Means and standard deviation of the dependent variables are documented for both groups or both time points or test statistics (t or F values).
3. Single-blind or double-blind experimental study design was applied.
4. Exposure by a GSM mobile phone specified at a range of ~900 MHz to ~1800 MHz under two conditions: on versus off.
5. Enrolled subjects were considered healthy.
6. The study must include at least one neuropsychological test that is used in another study, which fulfils requirements 1–4.

Nine studies did not fulfil at least one of these minimum requirements: Hladky *et al*,[14] Preece *et al*,[2] Smythe and Costall,[3] Eliayhu *et al*,[7] Lee *et al*, [16] Wilen *et al*,[17] Haarala *et al*,[15] Maier *et al*,[18] and Krause *et al.*[19]

Ten studies fulfilled all the requirements mentioned above. Table 1 gives an overview of the design, sample size and sociodemographic variables, showing that three studies used a double-blind method; five single-blind; five used a repeated design while three others used independent variables, which were matched via education/intelligence or subjects were randomly allocated to either an experimental or control group. In total 555 subjects were tested; 470 subjects were exposed to GSM cellular phones and 421 were tested under sham condition. As the studies of Haarala *et al*[10] and Haarala *et al*[11] described different cognitive tests administered to the same samples, they will be treated as one study in the following.

The minimum requirement for the inclusion of a single test procedure in the analysis was that test results were provided from at least two different studies. The remaining 10 studies provided data in order to analyse the results of 10 tests comprising a total of 29 psychological parameters. The following provides a brief outline of the tests included in the meta-analysis:

- Simple Reaction Task (SRT): measured subjects' reaction time to a stimulus (compare Haarala *et al*[10]).
- Choice Reaction Task (CRT): measured reaction time to complex stimuli. Subjects were shown a number and had to press the corresponding button (compare Haarala *et al*[10]).
- Vigilance (VIG): single capital letters were presented and subjects were to press a button when one of the target letters appeared (compare Russo *et al*[13]).
- Subtraction (SUB): subjects had to solve subtraction exercises, in which a one-digit number was to be subtracted from the number nine. Correct answers and reaction times were recorded (compare Russo *et al*,[13] Haarala *et al*[10]).
- Sentence Verification (VER): measured attention. Statements, including numbers, were presented to subjects in the form of $x<y$, $x>y$, $x=y$. Subjects had to respond by pressing "yes" or "no". Correct answers and reaction time were recorded (compare Haarala *et al*[10]).
- N-back test: measured short-term or working memory. Stimuli (capital letters) were presented, and subjects had to respond to target letters by pressing "yes" and to non-target letters by pressing "no". There are four memory load conditions: 0-back, 1-back, 2-back and 3-back. Under these conditions the target letter was any letter presented 0, 1, 2, 3 trials back. Correct answers and reaction times were recorded (compare Haarala *et al*[11]).
- Trail Making Test: measured visual-conceptual and visual motor tracking skills. Subjects are asked to draw a continuous line connecting 25 circled digits/letters (compare Keetley *et al*[9]).
- Digit span forward and digit span backward: measured attentional capacity. Seven pairs of random number sequences were read aloud. Subjects were asked to repeat the same sequence in either the same or reverse order (compare Edelstyn and Oldershaw[6]).
- Spatial span forward and spatial span backward: measured attentional capacity. Increasingly larger amounts of information were presented. Subjects had to estimate spatial span using white cubes fastened in a random order to a board. In each trial the blocks were tapped in a prearranged sequence. Subjects were asked to repeat this sequence in either the same or reverse order (compare Edelstyn and Oldershaw[6]).

The meta-analysis was done as a group comparison between exposed and non-exposed subjects. The results of all studies

Table 2 Homogeneity measure, mean effect size and 95% CI for the comparable cognitive parameters

Cognitive parameter/studies	Homogeneity (χ^2)	Effect size† ($\bar{\Delta}$)	95% CI
Simple Reaction Task/[4, 8–13]	4.84	−0.05	−0.25 to 0.15
Choice Reaction Task‡/[1, 4, 8–13]	4.27	−0.03	−0.20 to 0.14
Vigilance§/[4, 10, 11, 13]	6.71*	0.01	−0.22 to 0.23
Subtraction			
Correct/[4, 8, 10, 11]	0.51	−0.05	−0.18 to 0.07
Time/[4, 8, 10, 11, 13]	0.40	−0.09	−0.16 to −0.02
Sentence Verification/[4, 10, 11]			
Correct	0.49	0.01	−0.12 to 0.14
Time	0.46	0.01	−0.12 to 0.13
N-back test/[5, 10, 11]			
Targets			
0-back			
Time	0.01	−0.04	−0.06 to −0.02
Errors	0	0	NA
1-back			
Time	0.22	0.02	−0.06 to 0.11
Errors	1.70	0.01	−0.23 to 0.26
2-back			
Time	2.54	0.10	0.098 to 0.99
Errors	0.45	0.01	−0.12 to 0.13
3-back			
Time	0.59	−0.04	−0.18 to 0.11
Errors	0.60	0.07	−0.08–0.21
Non-targets			
0-back			
Time	0.28	0.003	−0.09 to 0.10
Errors	3.13	−0.14	−0.46 to 0.18
1-back			
Time	0.25	0.002	−0.09 to 0.10
Errors	0.19	−0.04	−0.12 to 0.05
2-back			
Time	0.11	0.04	−0.02 to 0.10
Errors	0.009	0.05	0.03 to 0.07
3-back			
Time	0.02	0.0004	−0.03 to 0.03
Errors	0.02	0.01	−0.01 to 0.04
Trail Making Test			
TMT A/[1, 9]	0.41	−0.04	−0.13 to 0.05
TMT B/[1, 9]	0.54	0.05	−0.05 to 0.15
Digit span forward§/[6, 9, 12]	10.95**	0.08	−0.27 to 0.43
Digit span backward/[9, 12]	0.42	−0.09	−0.21 to 0.03
Spatial span forward/[6, 9, 12]	3.38	0.29	−0.05 to 0.63
Spatial span backward/[6, 12]	3.24	0.15	−0.21 to 0.51

$*p \leq 0.05$; $**p \leq 0.01$.

†A positive effect size indicates higher values under exposure; a negative effect size indicates lower values under exposure.

‡The studies of Besset *et al*[12] and Koivisto *et al*[4] used two forms measuring choice reaction time. In both cases the average delta is used as the reference effect size.

§The assumption of a common effect size is violated, computations follow a random effects model.

were first transformed into their respective effect sizes, indicating whether there exists an effect of mobile phones, and then these effect sizes were transformed into the meta-analytic delta-measure (Δ). The analysis begin with the assumption that there is a common population effect in the different studies and that one single effect size could be determined for the different studies. When the assumed homogeneity for single effect sizes was not given (the variance of population effects was unequal zero, tested via χ^2 test), a random effects model was applied; otherwise computations were according to the fixed effects model. A correction of the estimators of the effect sizes based on the reliabilities was not possible because of missing documentation from the cognitive tests in the studies. As a result of missing documentation on the correlations, the effect sizes of repeated measures were calculated according to the formulae of independent samples, taking into account a reduction of the power.

RESULTS

Table 2 summarises the results of the meta-analyses. For all eligible parameters (except for vigilance (time) and digit span backward) the effect sizes of the studies can be seen as homogeneous and the mean effect size ($\bar{\Delta}$) describes the population effect. For vigilance and digit span backward the single effect sizes of the included studies are not homogenous and $\bar{\Delta}$ describes the mean effect size of the studies. The confidence interval depicts the range of the population effect based on the variance of the population effects.

Significant effect sizes were found in two tests: reaction time in the subtraction task was facilitated by exposure—that is, subjects reacted faster. In the N-back test under condition 0-back target reaction time was also facilitated. However, under condition 2-back target, reaction time was impaired from exposure. The errors in condition 2-back non-target are higher—that is, subjects make more errors under exposure. No significant effect sizes were found in all the other tests. All effect sizes are shown in figure 1.

DISCUSSION

The meta-analysis confirms the assumption that cognitive performance measured by the subtraction task is mildly facilitated from EMF exposure. This effect appears only in reaction time, not accuracy. The significant effects concerning the N-back test for working memory show discrepant effect sizes: under condition 0-back target response time is lower under exposure, while under condition 2-back target response time increased. The number of errors under condition 2-back for non-targets appears to be higher under exposure. At the other levels of the N-back test no significant effect sizes were detected.

No effects were found in the following tasks: Simple and Choice Reaction Task (SRT, CRT), Vigilance (VIG), Sentence Verification (VER), all parameters of the N-back test except the three ones mentioned above; digit span forwards and spatial span forwards/backwards.

What conclusions can be drawn from this analysis? The results of the meta-analysis show that the original spectrum of cognitive abilities, which might be influenced by EMF emitted by mobile phones, can be reduced to two areas, which are measured by two tests: short-term memory (N-back test) and cognitive time needed in a mental arithmetic task (subtraction task). Furthermore, the effects seem to be so small that implications for human performance in everyday life can be practically ruled out.

However, several problems arise in the interpretation of our results. Firstly, the results of the N-back test seem to be paradoxical. On a low level of difficulty, there is a facilitatory effect, but on a higher one there is an inhibitory effect. From a scientific point of view, this conflicts with conventional patterns of dose-response relation. Another anomaly is that there are no discernable effects on the levels between 0-back target and 2-back target as well as on the higher level 3-back target. One explanation for this paradoxical result could be that Koivisto *et al*,[5] whose study is included in the analysis, only used a single-blind study design. In such a design, non-optimal

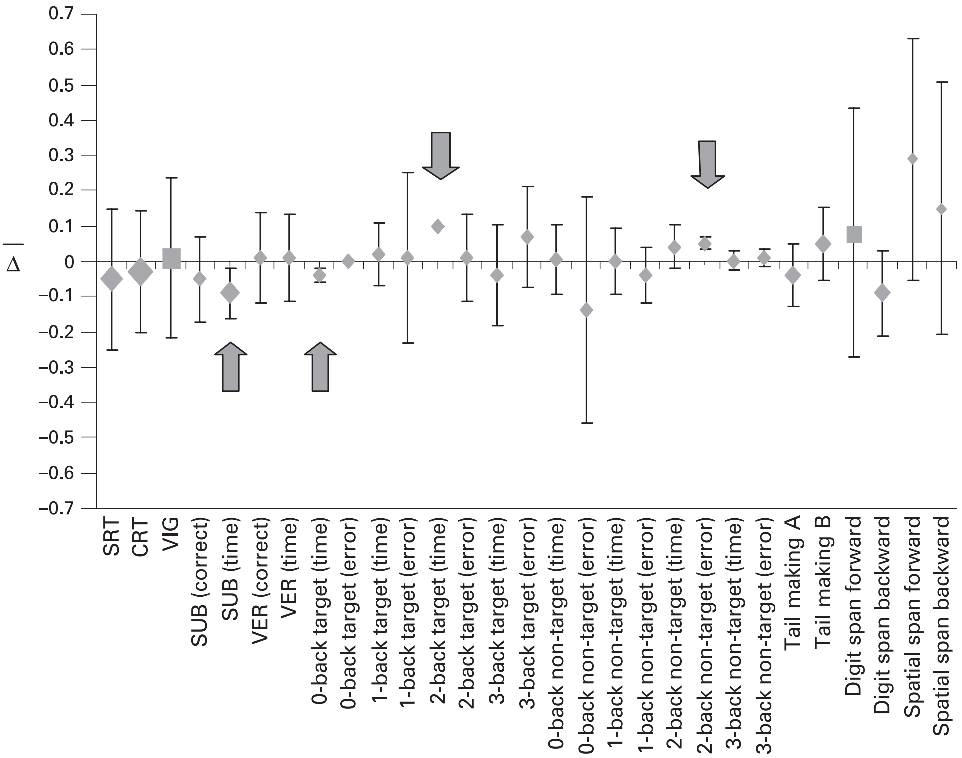


Figure 1 Meta-analytic effect sizes ($\overline{\Delta}$) and their confidence intervals (diamonds represent fixed effects models, rectangles random effects models and the size of the squares indicates the number of subjects included). SRT, Simple Reaction Task; CRT, Choice Reaction Task; VIG, Vigilance; SUB, Subtraction; VER, Sentence Verification.

administration of the exposure source as well as the test procedure may influence the results.

Secondly, the problem of single-blind study designs also occurs in the subtraction task. The single-blind study of Koivisto *et al*[4] shows the highest and per se the only significant effect size. Russo *et al*,[13] Haarala *et al*[10 11] and Curcio *et al*[8] showed no significant effect size in the subtraction task.

Thirdly, the biological mechanism influencing the test outcomes is unknown. There are only vague speculations that potential negative effects may be due to a rise in brain tissue temperature, but empirical evidence is lacking.[2] The absence of a biological mechanism complicates interpretation of the results.

What are the limitations of this study? In general, the administered meta-analysis is a very useful technique to objectively aggregate single results of a number of separate studies. It not only gives a conclusive overview about a certain field of research, but also overcomes the problem of reduced power due to small sample sizes by an enhanced pooled sample size, and therefore leads to more accurate estimations of the effect size. However, to conduct a conclusive meta-analysis the requirements already mentioned in the statistical section must be fulfilled. Moreover, the main problem was the fact that many instruments were applied in only one study and therefore could not be included in the meta-analysis—for example, spatial item recognition task (FACE) used by Eliyahu *et al*,[7] word-recall task used by Smythe and Costall[3] or tests from the Cognitive Drug Research (CDR) used by Preece *et al*.[2] From a scientific point of view, it is not efficacious to apply new and non-standardised test procedures. Moreover, some studies omitted certain statistics—for example, Hladky *et al*[14] and Smythe and Costall[3] did not include means and standard deviations in their results. As meta-analyses will be used more frequently in the future, a statistical standard should be set, such as documenting effect sizes or correlations in the case of repeated measurements.

CONCLUSION

Summarising the current analysis, the following can be concluded: there may be two cognitive areas that are mildly affected by exposure to EMF by GSM mobile phones. Firstly, human attention measured by the subtraction task may be mildly affected in regard to decreased reaction time. Secondly, working memory measured by the N-back test seems to be affected. However, as the latter result cannot be explained by conventional patterns of scientific dose-response relation, it should be judged with caution. As both effects are quite small, the implication in everyday life can virtually be ruled out.

Further research should focus on attention and working memory using the same tests included in this meta-analysis. Basis requirements such as a double-blind study design should also be considered. A final conclusion—if possible—can only be reached on a biological level once it is clarified how electromagnetic fields influence cognitive functions.

Competing interests: None declared.

Main message

Electromagnetic fields emitted by GSM mobile phones may have a small impact on two cognitive functions. Firstly, human attention may be affected mildly in regard of decreased reaction time. Secondly, working memory seems to be affected too.

Policy implication

Health policy should emphasise the necessity of further research on the neurobehavioural effects of electromagnetic fields.

REFERENCES

1. **Lee TMC,** Lam PK, Yee LTS, *et al*. The effect of the duration of exposure to the electromagnetic field emitted by mobile phone on human attention. *Neuroreport* 2003;**14**:1361–4.
2. **Preece AW,** Iwi G, Davies-Smith A, *et al*. Effect of a 915-MHz simulated mobile phone signal on cognitive function in man. *Int J Radiat Biol* 1999;**75**:447–56.
3. **Smythe JW,** Costall B. Mobile phone use facilitates memory in male but not female, subjects. *Neuroreport* 2003;**14**:243–6.
4. **Koivisto M,** Revonsuo A, Krause C, *et al*. Effects of 902 MHz electromagnetic field emitted by cellular telephones on response times in humans. *Neuroreport* 2000;**11**:413–15.
5. **Koivisto M,** Krause CM, Revonsuo A, *et al*. The effects of electromagnetic field emitted by GSM phones on working memory. *Neuroreport* 2000;**11**:1641–3.
6. **Edelstyn N,** Oldershaw A. The acute effects of exposure to the electromagnetic field emitted by mobile phone on human attention. *Neuroreport* 2002;**13**:119–21.
7. **Eliyahu I,** Luria R, Hareuveny R, *et al*. Effects of radiofrequency radiation emitted by cellular telephones on the cognitive functions of humans. *Bioelectromagnetics* 2006;**27**:119–26.
8. **Curcio G,** Ferrara M, Gennaro L, *et al*. Time-course of electromagnetic field effects on human performance and tympanic temperature. *Neuroreport* 2004;**15**:161–4.
9. **Keetley V,** Wood A, Spong J, *et al*. Neuropsychological sequelae of digital mobile phone exposure in humans. *Neuropsychologia* 2006;**44**:1843–8.
10. **Haarala C,** Björnberg L, Ek M, *et al*. Effect of a 902 MHz electromagnetic field emitted by mobile phones on human cognitive function: a replication study. *Bioelectromagnetics* 2003;**24**:283–8.
11. **Haarala C,** Ek M, Björnberg L, *et al*. 902 MHz mobile phone does not affect short term memory in humans. *Bioelectromagnetics* 2004;**25**:452–6.
12. **Besset A,** Espa F, Dauvilliers Y, *et al*. No effect on cognitive function from daily mobile phone use. *Bioelectromagnetics* 2005;**26**:102–8.
13. **Russo R,** Fox E, Cinel C, *et al*. Does acute exposure to mobile phones affect human attention? *Bioelectromagnetics* 2006;**27**:215–20.
14. **Hladky A,** Musil J, Roth Z, *et al*. Acute effects of using a mobile phone on CNS functions. *Cent Eur J Public Health* 1999;**7**:165–7.
15. **Haarala C,** Takio F, Rintee T, *et al*. Pulsed and continuous wave mobile phone exposure over left versus right hemisphere: effects on human cognitive function. *Bioelectromagnetics* 2007;**28**:289–95.
16. **Lee TMC,** Ho SMY, Tsang LYH, *et al*. Effect on human attention of exposure to the electromagnetic field emitted by mobile phones. *Neuroreport* 2003;**12**:729–31.
17. **Wilen J,** Johansson A, Kalezic N, *et al*. Psychophysiological tests and provocation of subjects with mobile phone related symptoms. *Biolelectromagnetics* 2006;**27**:204–14.
18. **Maier R,** Greter SE, Maier N. Effects of pulsed electromagnetic fields on cognitive processes: a pilot study on pulsed field interference with cognitive regeneration. *Acta Neurol Scand* 2004;**110**:46,52.
19. **Krause C,** Haarala C, Sillanmäki L, *et al*. Effects of electromagnetic field emitted by cellular phones on the EEG during an auditory memory task: a double blind replication study. *Bioelectromagnetics* 2004;**25**:33–40.

Echo

Mesothelin in effusions marks out malignancy

An ELISA assay for mesothelin should make it easier and faster to identify malignant mesothelioma from patients' pleural effusions, especially in centres with limited expertise in cytopathological diagnosis.

Researchers have found that the test, which has already been used to detect soluble mesothelin–a marker for the cancer—in serum, can be successfully applied to effusions.

In a six year prospective study they used the assay on pleural and peritoneal effusions collected from consecutive patients at outpatient respiratory clinics in two centres in Perth, Western Australia.

The assay had a diagnostic specificity of 98% at a cut off value of 20 mM soluble mesothelin and cross validated sensitivity of 67% in pleural effusions from patients with confirmed malignant mesothelioma. Mesothelin concentrations in pleural effusions and matched serum samples correlated significantly and were raised 3 weeks to 10 months before diagnosis in 70% (7/10) of patients, in half (4/8) of whom amounts were higher than in serum. They were not raised in effusions from patients with non-mesothelioma respiratory cancers or benign conditions. Peritoneal effusions seemed to be similarly valuable in patients with suspected mesothelioma and ovarian cancer.

Assays were performed on pleural effusions from 192 patients: 52 had a subsequent diagnosis of malignant mesothelioma, 56 non–mesothelioma, and 84 benign conditions. Peritoneal effusions from 42 patients were tested, 7 with mesothelioma, 14 non-mesothelioma, and 21 benign conditions.

Diagnosing this aggressive cancer—usually by cytology of exudates—can be difficult, but measuring soluble mesothelin to supplement serum analysis in tricky cases would speed up diagnosis.

- Creaney J, Yeoman D, Naumoff LK, *et al*. Soluble mesothelin in effusions: a useful tool for the diagnosis of malignant mesothelioma. *Thorax* 2007;**62**:569–76.

BIOMEDICAL AND ENVIRONMENTAL SCIENCES **23**, 199-207 (2010) www.besjournal.com

Effects of Exposure to GSM Mobile Phone Base Station Signals on Salivary Cortisol, Alpha-Amylase, and Immunoglobulin A[1]

CHRISTOPH AUGNER[*,2], GERHARD W. HACKER[*], GERD OBERFELD[#], MATTHIAS FLORIAN[*],
WOLFGANG HITZL[+], JÖRG HUTTER[±], AND GERNOT PAUSER[°]

[*]IGGMB-Research Institute for Frontier Questions of Medicine and Biotechnology, Salzburg Federal Hospital-University Clinics of the Paracelsus Medical Private University, Salzburg Federal Clinics (SALK), Salzburg, Austria; [#]Public Health Department Salzburg, Salzburg, Austria; [+]Research office, Paracelsus Medical Private University, Comma Salzburg, Austria; [±]University Clinic of Surgery, Salzburg Federal Hospital University Clinics of the Paracelsus Medical Private University, Salzburg Federal Clinics (SALK), Salzburg, Austria; [°]University Clinic for Anesthesiology, Perioperative Medicine and General Intensive Care, Salzburg Federal Hospital-University Clinics of the Paracelsus Medical Private University, Salzburg Federal Clinics (SALK), Salzburg, Austria

Objective The present study aimed to test whether exposure to radiofrequency electromagnetic fields (RF-EMF) emitted by mobile phone base stations may have effects on salivary alpha-amylase, immunoglobulin A (IgA), and cortisol levels. **Methods** Fifty seven participants were randomly allocated to one of three different experimental scenarios (22 participants to scenario 1, 26 to scenario 2, and 9 to scenario 3). Each participant went through five 50-minute exposure sessions. The main RF-EMF source was a GSM-900-MHz antenna located at the outer wall of the building. In scenarios 1 and 2, the first, third, and fifth sessions were “low” (median power flux density 5.2 µW/m²) exposure. The second session was “high” (2126.8 µW/m²), and the fourth session was “medium” (153.6 µW/m²) in scenario 1, and vice versa in scenario 2. Scenario 3 had four “low” exposure conditions, followed by a “high” exposure condition. Biomedical parameters were collected by saliva samples three times a session. Exposure levels were created by shielding curtains. **Results** In scenario 3 from session 4 to session 5 (from “low” to “high” exposure), an increase of cortisol was detected, while in scenarios 1 and 2, a higher concentration of alpha-amylase related to the baseline was identified as compared to that in scenario 3. IgA concentration was not significantly related to the exposure. **Conclusions** RF-EMF in considerably lower field densities than ICNIRP-guidelines may influence certain psychobiological stress markers.

Key words: GSM base stations; Mobile phone; Salivary IgA; Alpha amylase; Cortisol; Radiofrequency electromagnetic fields (RF-EMF)

INTRODUCTION

The use of mobile phones has increased dramatically over the last decade. Simultaneously, public concern about possible adverse effects of exposure to radiofrequency electromagnetic fields (RF-EMF) emitted by mobile phones and mobile phone base stations on health has emerged. Although there is a large number of studies dealing with effects associated with using mobile phones, the number of publications on possible influences of base stations is still comparatively small (a Medline search performed on July 23, 2008 revealed 46 related articles only, with only 8 reporting original research in humans).

A few cross sectional studies have shown correlations between base-station originated EMF-exposure and subjective symptoms[1-5]. Experimental studies of short term exposure to EMFs emitted by base stations are rare, and their results are not unambiguous[6-8], except the one reported by Eltiti and his colleagues[7] which included physiological measurements as well.

Most of the reports focusing on endocrine responses or the immune system published so far were limited to *in vitro* studies or animal assays[9-12]. The experiments which were conducted under laboratory conditions applied mobile phone signals differing considerably from base station signals. The advantage of a better control of relevant conditions

---

[1] This study was funded by the Land Salzburg Federal Government, Science Department, and Mr. Daniell Porsche, Chairman of the Paracelsus-School at St. Jakob am Thurn, Salzburg, Austria.

[2] Correspondence should be addressed to Dr. Christoph Augner, E-mail: c.augner@salk.at

Biographical noto of the first author: Dr. Christoph Augner, PhD in Psychobiology, Deputy Head of IGGMB-Research Institute for Frontier Questions of Medicine and Biotechnology, Salzhurg Federal Hospital-University clinics of the Paracelsus Medical Private University, Salzburg Federal Clinics (SALK), Salzburg, Austria.

0895-3988/2010
CN 11-2816/Q

has to be balanced against the artificiality of the exposure scenario. Our present study is an attempt to improve ecological validity and at the same time to preserve internal validity by performing experiments in a field laboratory (a room in a kindergarten suitably adapted for the purpose of the study), with a real world exposure source (a continuously operating base station) where actual exposure of participants was manipulated by different amounts of shielding. In order to identify potential effects on the bodily defence system, we immunochemically or enzymatically measured the concentrations of cortisol, alpha-amylase, and immunoglobulin A (IgA) in the saliva of 57 healthy persons. Cortisol is a well-established indicator of stress, used in routine clinical practice and research and also in experiments on EMF[13]. Another marker of stress that has recently gained acceptance is the salivary enzyme alpha-amylase, also representing a surrogate pointer of the psychobiology of stress[14]. The major immunoglobulin class present in saliva is IgA and has been discussed to function as an immediate defence protein against possible infections via food and air[15]. In addition, IgA is of major interest in connection to stress [16].

MATERIALS AND METHODS

Study Design and Ethical Considerations

Our study followed the design of a double blinded experiment. In our recent publication dealing with effects on well-being, the study design used had been described in detail[17]: 57 participants were exposed to different levels of RF-EMF and randomized into three experimental scenarios. The age range was from 18 to 67 years; 61.4% of the volunteers were female, and 38.6% male. Detailed oral and written information about the test design and possible risks was given. After the test persons had signed informed consent letters, medical histories were questioned. All procedures, and especially all actions in the context of data security, were consistent with the ethical guidelines stated by the expanded Helsinki Declaration and by the American Psychological Association[18-19].

Exposure System and Procedure

Experiments were performed in a kindergarten room located in Salzburg city. Outside the experimental room, a GSM micro-cell omni antenna (900 MHz) was mounted on the outer wall, and a number of further GSM 900 and 1 800 MHz base stations were situated in the area surrounding the building. During all the experimental sessions, band-specific exposure levels, variations of GSM 900 uplink and downlink, GSM 1 800 uplink and downlink, UMTS uplink and downlink, DECT and ISM 2.4 GHz were permanently recorded using a microwave dosimeter (ESM-140, Maschek, Kaufering, Germany). In addition, frequency selective measurements were performed using a professional FSH-3 spectrum analyzer (Rhode und Schwarz; Munich, Germany) that continuously recorded spectra and their electrical field strengths within the frequency band 30 to 3.000 MHz. Technical oversight of the study was done by an accredited expert for EMF measurements (Dr.-Ing. Martin Virnich, ANBUS Analytik GmbH, Fuerth, Germany).

Different exposure levels were produced by variation of shielding (“Swiss Shield Naturell”; ESAG GmbH., Vienna, Austria) and non-shielding placebo curtains that were optically indistinguishable. To produce a defined area of entry of the base station signal, the walls had been covered with shielding paint (“HSF53”, YShield, Pocking, Germany) except for an area in close proximity to the base station antenna mounted at the outer edge of that wall. Every experiment consisted of 5 sessions of 50 min each and was carried out between 9:00 a.m. and 1:30 p.m., to minimize chronobiological variation across the subjects. During a pre-experimental period of one hour in between 8:00 and 9:00 a.m., persons were kept in maximum shielding, while health status information was obtained and psychological questionnaires were filled in. Each test person was then subjected to one of the three exposure scenarios following computerized randomization tables. Before the first session and during every of the 5 min breaks in between the sessions, participants were asked to leave the test room, to drink a glass of tap water, and to use a bath room if necessary.

During the experiments, the test persons sat on a upholstered wooden chair in a distance of about 6 meters from the micro cell antenna mounted on the outside of the building but invisible to them. Changing shielding curtains to obtain experimental variation of exposure levels was done by a technician during breaks, imperceptible to both the test person and the experimenter. The shielding curtains were always concealed by normal white curtains; therefore, neither the participants nor the experimenter had a clue as to the exposure condition. During the first five min of every session, measurements of field strength and field distributions were carried out by scanning head and thorax areas in an approximate five centimeters distance to the sitting test person using a dosimeter (ESM-140, Maschek, Kaufering, Germany; dynamic body measurements). Afterwards, the dosimeter remained fixed about 30 centimeters from the head of the test person and recorded field strengths during the whole experiment (permanent static body measurements).

Twenty-two persons were subjected to experimental scenario 1 and 26 to scenario 2. Among them exposure level was low in the first and third of the five test sessions. Medium or high exposure levels were established in sessions 2 and 4, respectively. Scenario 3 included only nine persons and served as a control group with four subsequent sessions of low exposure level. In order to possibly gain additional information, these four low exposure sessions were followed by a fifth session with high exposure level. The small sample size in scenario 3 was due to earlier termination of measurements because the kindergarten was no longer available as a field laboratory.

Biochemistry

Saliva sample preparation In every session saliva samples were taken after 10, 25, and 45 min for biochemical analyses, using Salivette saliva collection devices (Sarstedt, Nürnbrecht, Germany). For each sampling, Salivettes were left for 5 min in the mouth. Immediately after sample collection, Salivettes were centrifuged for 5 min at 1000 x *g*, and the saliva specimen spun into 100 µL of 100 mmol/L HEPES pH7.0, 1 mg/mL bovine aprotinin to protect against proteolytic degradation. Thereafter, all saliva samples were stored in an ice water bath until the end of the daily exposure scheme. Individual saliva samples were then aliquoted and frozen at –20 ℃ until analysis. Aliquoted samples were used only once and residual material discarded after the test and autoclaved.

Biochemical analyses All chemicals and biochemicals used for saliva assays were purchased from Sigma-Aldrich (Taufkirchen, Germany) unless noted otherwise. 96-well microplates were from *Greiner BioOne* (Nuertingen, Germany). For absorbance measurement, a *Sunrise* microplate reader (Tecan, Grödig bei Salzburg, Austria) was used. Washing of ELISA-plates was done with a *Wellwash 4* microplate washer (Thermo Electron, Waltham, MA, USA). Data calculation was performed using *Deltasoft* software (Biometallics, Princeton, NJ, USA).

Determination of the total protein content of saliva samples was done following the method of Bradford[20] using bovine serum albumin as standard.

Salivary cortisol levels were examined by a competitive enzyme-linked immunoadsorbent assay (ELISA) on microplates coated with goat-anti-rabbit-IgG with rabbit anti-cortisol-antiserum (Fitzgerald, Concord, MA, USA) and a cortisol-3-O-adipic acid dihydrazide-horseradish peroxidase (HRP) conjugate as specific competitor, synthesized essentially as described by Basu *et al.*[21]. HRP activity was measured with 0.1 mg/mL tetramethyl benzidine and 0.01% H_2O_2 in 0.1 mol/L sodium acetate pH 6.0 at room temperature and detected at 450 nm (reference 595 nm). Saliva samples were prediluted in PBS immediately prior to the assay. All samples were assayed in triplicates, and cortisol concentrations calculated with respect to appropriate standard concentrations of cortisol (hydrocortisone) run on each plate using a 4 parameter fit equation. Detection range was 0.05 to 20 ng cortisol/mL as defined by 10 versus 90% $B/B_{0.}$

Salivary α-Amylase (1,4 a-D-glucanohydrolase, EC 3.2.1.1) was assayed essentially according to the method of Gillard *et al.*[22] using 1 mmol/L p-nitrophenyl α-maltoside as substrate with some minor modifications and adaptation to a microplate format. Briefly, 10 µL of saliva samples were diluted with 100 µL of 11 mmol/L p-nitrophenyl α-maltoside in 11 mmol/L HEPES pH 7.0 prewarmed to 37 ℃. Absorbance was immediately measured at 405 nm (reference 595 nm). Plates were then further incubated for 4 h at 37 ℃, or in case of very low activities, also overnight. Absorbance was measured again at the end of the incubation period and subtracted by the respective zero-time-point values, and the increase of specific absorbance was calculated per hour. Assays were performed in triplicates, and enzyme activities calculated as mU/mL with respect to the molar extinction coefficient of p-nitrophenole, with 1 mU defined as a substrate conversion of 1 nmol/min in an assay volume of 1 mL.

Salivary IgA (sIgA) concentrations were measured using a sandwich ELISA with a matched pair of mouse monoclonal anti-human-IgA antibodies (G18-1 for capture, and alkaline phosphatase-labeled G20-359 for detection, both from Pharmingen (Becton-Dickinson, Vienna, Austria). Just before the assay, saliva samples were prediluted in phosphate buffered saline (PBS). Alkaline phosphatase activity was measured with 10 mmol/L 4-nitrophenyl-phosphate in 0.1 mol/L diethanolamine-HCl, 2 mmol/L $MgCl_2$, pH 9.5 at room temperature, and detected at 405 nm (reference 595 nm). All samples were assayed in triplicates, and sIgA concentrations were calculated with respect to appropriate standard concentrations of human IgA run on each plate. Linear detection range was 25 to 500 ng IgA/mL.

Data Handling

Values obtained for the different parameters of each individual test person were corrected for dilution by the aprotinin-buffer additive and normalized to the mean values of the first exposure phase (i.e. maximum shielding) to compensate for the variation in individual levels of the parameters tested. For cortisol, each sample was corrected for the diurnal drift in morning cortisol levels based on the individual awakening times of the test persons using a 3rd degree polynomial equation deduced from the data published by Westermann and his co-workers[23].

Statistics

For statistical data analyses, the software packages *SPSS* 14.0 (SPSS, Chicago, IL, USA), *Statistica 6.0* (Statsoft, Tulsa, OK, USA) and Sigma Plot 10.0 were used. All values for each of the sessions were related to the baseline concentrations (session 1) of the particular parameter.

All saliva parameters were analyzed by ANOVA for repeated measurements in one factor (sessions) and fixed between-subjects factor (scenario). Scenario/ sessions interaction would indicate exposure effects. In addition, linear contrasts were used to compare the different exposure levels. In a second step, the mean concentrations of sessions 2-4 of cortisol, IgA and alpha-amylase were calculated. Means were then related to the baseline. In order to obtain homogeneity of variances the values were log transformed.

Age, gender, and degree of self rated electromagnetic hypersensitivity were included as covariates in these analyses.

Dosimetry

Narrow band measurements via spectrum analyzers showed that the RF-EMF spectrum was dominated by two GSM-900 MHz downlink signals, one broadcast control channel (BCCH) plus one traffic channel (TCH), originating from a 50-cm-micro-cell omni-directional antenna mounted on *the outer wall of the building. During the experiments, the GSM* 900 *antenna operated with constant BCCH and variable TCH output, leading to a fluctuation in field strength by a factor of two (3 dB).* At exposure situation "high", other RF-EMF sources like public radio, TV channels, GSM 1800, DECT, UMTS, WiFi etc., had power densities of at least a factor of 400 below the GSM-900 downlink signals mentioned before.

Results of the permanent (static) measurements showed stable exposure conditions during each of the sessions. Overall power flux densities given as a median were 5.2 $\mu W/m^2$ (5th percentile (*P5*)=1.4, 95th percentile (*P95*)=15.5) for low, 153.6 $\mu W/m^2$ (*P5*=21.3, *P95*=468.0) for medium, and 2126.8 $\mu W/m^2$ (*P5*=827.3, *P95*=4908.4) for high. Table 1 shows power flux densities by scenario and session. The dynamic body measurements via the ESM-140 showed comparable power densities for the three key body regions (forehead, mouth, chest) examined.

TABLE 1

Power Flux Densities During the Different Scenarios

R	**Scenario 1**			**Scenario 2**			**Scenario 3**		
Session	P5	P50	P95	P5	P50	P95	P5	P50	P95
1	1.6	5.2	15.7	1.5	5.7	14.7	1.9	6.5	26.0
2	694.5	1858.0	3829.8	30.5	168.4	446.5	1.5	5.1	16.5
3	1.1	3.9	13.8	1.4	5.4	16.0	1.6	5.0	16.0
4	16.0	128.8	490.8	912.6	2130.5	5389.7	1.6	5.2	14.3
5	1.2	4.7	14.3	1.6	5.6	14.1	1289.8	2939.0	4967.7

Note. 5th, 50th (median), and 95th percentiles of the distribution of microwave power densities for each session and scenario, measured by microwave dosimeter ESM-140 placed 30 cm from the head of the person. Results for "High exposure" sessions are presented in dark grey background, and "medium exposure" sessions in light grey background.

RESULTS

Sample Characteristics

Among the 57 participants, 35 were female, and 22 were male, aged 18-67 years (mean 40.72, *SD* 12.75). Table 2 shows some important characteristics of the sample. There were no statistically significant differences between the groups allocated to the three scenarios in none of these variables and in baseline levels of saliva parameters as well.

Exposure and Variation of Concentrations of Saliva Parameters

Variance analysis revealed a significant effect for session (*P*<0.001) in cortisol, but not for alpha-amylase and IgA. No significant effects for scenario and for scenario/session-interaction were detected for any parameter. *A posteriori* tests showed a significant increase of the cortisol concentration in scenario 3 from session 4 (low exposure; M=1.40, SD=0.46) to session 5 (high exposure; M=2.01, SD=0.76) (*P*=0.002).

Linear contrasts of sessions 2-4 in scenario 1 (HM=high-low-medium exposure) and scenario 2 (MH=medium-low-high exposure) *vs.* scenario 3 (LL=low-exposure throughout) reached the level of significance in alpha-amylase (*P*=0.037) (Table 3). Participants in scenarios 1 and 2 had a significantly higher alpha-amylase concentration, related to the baseline, than those in scenario 3. Cortisol and IgA showed no significant contrasts between the scenarios.

TABLE 2

Test Person Characteristics and Mean Concentrations of Biochemical Parameters Measured From Saliva

	Scenario 1	Scenario 2	Scenario 3	P
Age	38 (13)	44 (13)	39 (12)	0.298
Female	55%	69%	56%	0.538
City >20.000 Inhabitants	59%	58%	78%	0.544
Health Concerns with Base Stations	28.95 (20.37)	27.08 (22.06)	24.89 (23.40)	0.814
sCortisol (ng/mL)	2.97 (1.36)	3.66 (2.18)	2.92 (1.07)	0.341
sAlpha-Amylase (mU/mL)	1.75 (1.09)	2.47 (1.47)	2.14 (1.02)	0.142
sIgA (µg/mL)	263 (236)	180 (111)	142 (131)	0.154

Note. Characteristics of subjects allocated to the scenarios, age, gender, city of inhabitance, and health concerns regarding base stations (higher value indicates higher concern). Alpha amylase, IgA, and cortisol in saliva from baseline measurements. *P*-values from Kruskal-Wallis-Test or Chi-Square-Test. Results are expressed as means+SD (standard deviations).

TABLE 3

Mean Relative Changes of Saliva Parameter Concentrations (Linear Contrast Analysis)

	HM	MH	LL	P*	P**	P***
Cortisol	1.213 (0.257)	1.186 (0.380)	1.356 (0.345)	0.333	0.228	0.244
Alpha-Amylase	1.049 (0.351)	1.004 (0.228)	0.843 (0.130)	0.055	0.052	0.037
IgA	0.973 (0.277)	0.972 (0.245)	1.167 (0.359)	0.100	0.127	0.087

Note. Mean relative changes (in brackets: standard deviations) in relation to baseline concentrations of saliva parameters during sessions 2 to 4 per scenario. (HM = high-low-medium exposure, scenario 1; MH = medium-low-high exposure, scenario 2; LL=low-low-low exposure, scenario 3. *P* values indicate results from univariate linear contrasts, log-transformed data: *= HM *vs*. LL, **= MH *vs*. LL, ***= HM, and MH *vs*. LL. Diurnal change correction was applied for cortisol.

Single Case Analysis

In an explorative analysis of individual participants, we found some cases worth to be mentioned. The cortisol curve of a male scenario 2-participant shows a delayed, but extremely strong reaction in the last session. Here, an increase to about 400% of the normalized base level was observed. Amylase concentration changes in a female subjected to scenario 2 suggested visible dose-related exposure effects in sessions 2 (medium) and 4 (high). The opposite reaction was observed in IgA of another female participant of scenario 2. For a participant of scenario 3, we found an increase of the IgA concentration during the experiment that stopped abruptly during the high exposure in session 5, in effect even leading to a decrease.

DISCUSSION

Compared to traditional laboratory experiments, field laboratory experiments in the area of EMF research show some distinct advantages. First, in our daily life situations, we are not exposed to constant flux densities like those present in an anechoic chamber usually applied in most experimental setups. In real life, as in field laboratory experiments, the organism has to permanently adapt to varying exposure levels with uneven distributions of the field, for instance, because of reflections. Second, for the test person, the situation present in a field laboratory is much less artificial. This is a central issue, since psychological and physiological coping of the experimental situation could overlay EMF effects. On the other hand, in laboratory experiments, a number of confounding variables can be controlled.

Biochemically measuring the concentrations of certain stress and immune system parameters is regarded reliable. Assays used in our study for analyzing cortisol and IgA are widely accepted methods applied in routine clinical work as well as in experimental investigations. The method used to detect alpha-amylase is an enzymatic assay available for more than thirty years[22]. Another well-established method, the Bradford-assay, was applied to assess the summative protein concentration as a control parameter[20]. Research reports have shown that the reliability of measurements in saliva is comparable to that obtained in serum, and today saliva measurement methodologies are increasingly used[14, 16, 24-28].

In the present study, analyses of variance with repeated measurement factor (time) revealed a significant effect for time in cortisol, but no effects in the other parameters tested. We also found a significant cortisol level change in scenario 3 from session 4 (low exposure) to session 5 (high exposure) (P=0.002). Such kind of change could not be detected in the other scenarios in that intensity. Furthermore, this was accompanied by an insignificant decrease (P<0.10) of IgA level detected in parallel. These results seem to be consistent with other studies that identified cortisol as a modulator of immune function, down regulating immune parameters such as IgA[23-24,29].

In line with available evidence, the normal daily cortisol concentration pattern should not increase at midday unless there is a stressor. Therefore, it is justified to assume that the higher exposure was responsible for this change in scenario 3. Nevertheless we did not find any exposure effects on cortisol in scenarios 1 and 2-although these scenarios included a higher number of participants. This situation might be explained with a finding that was assumed to be present, but had not yet been described elsewhere to the best of our knowledge; when analyzing individual time course curves of cortisol (and, to a lighter degree, possibly also of the other parameters tested in this study), it appeared evident to us that in some persons, effects on concentration seemed to be present during the same phase of exposure, and in other individuals, up to approximately one hour or probably even longer delayed effects can be observed. In other words, there might be some types of responders who reacted immediately, while others reacted in a delayed fashion, or even did not react at all at higher exposure doses applied for 50 min only. This observation might also explain why in scenarios 1 and 2, statistical significance was not reached for cortisol, because such effects “subtract” each other when analyzing time curses.

The missing significance in scenarios 1 and 2 might also be attributed to the different exposure patterns in the scenarios used. In scenarios 1 and 2, test persons were shielded much shorter before a high exposure condition. It was likely that participants had already been exposed to EMFs on their way to the field laboratory. When they arrived at the test place, they came into a situation that shielded them much higher than in usual daily life situations. In scenario 3, participants remained in that situation for more than 4 hours (including the pre-testing period). It was likely therefore that their stronger cortisol reaction during high exposure came from a more relaxed, regenerated body, already somewhat adapted to optimum shielding during the prolonged period of low exposure.

It is obvious that some of these results raise great doubt that changes of the stress and immune parameters measured would always occur exactly within the session in which people are subjected to higher exposure levels. As onset of possible changes and symptoms are discussed controversially[30-31], we tried to focus on further analysis of a longer period of time. For this, we summed up sessions 2 to 4 and compared scenarios 1 and 2 with scenario 3. In scenarios 1 and 2 during that time, all three different exposure levels were allocated, while in scenario 3 there was low exposure throughout the phases. Using that kind of analysis, statistically significant differences in alpha-amylase levels were observed: higher exposed participants in scenarios 1 and 2 showed higher concentrations of alpha-amylase in relation to the baseline than scenario 3 participants. For cortisol and IgA, no significant change was found using that kind of analysis.

On one hand, alpha-amylase was used as a substitute parameter to indirectly measure the adrenalin *vs.* noradrenalin balance[32]. On the other hand, recent research on salivary alpha-amylase gave strong evidence that alpha-amylase itself was a reliable parameter for stress, although its exact connections to cortisol remained largely unclear[25]. Higher alpha-amylase concentrations seem to show higher levels of stress. Therefore, one could interpret that the differences presented here are caused by higher exposure levels in scenario 1 and 2. On the other hand, amylase does not increase in session 5 at high exposure, but cortisol does. Any possible delayed effect on amylase concentration of session 5 in scenario 3 might be present but could not be measured in our study, as saliva sampling ended within session 5.

In addition to our statistical analyses, we explored reactions of individual participants. We found noticeable curves in some individuals, as described in the results section. In sum these findings suggest that some people seem to react strongly on exposure. Further, there seemed to be inter-individual differences regarding ignition of reaction: some of the participants showed immediate changes, others delayed changes. There was no intra-individual association between different parameters.

In general, the results presented give additional indications strengthening existing reports that contradict the hypothesis that flux densities lower than the security standards of ICNIRP (International Commission on Non-Ionizing Radiation Protection) would not induce stress or might have negative effects on the human immune system. These findings were also supported by the large reviews contained in the Bioinitiave Report 2007, especially those of section 7 dealing with stress response[33], and section 8 on effects on the human immune system[34]. Nevertheless, studies with the same or comparable parameters in the EMF area are scarce. Mann and his colleagues[35] investigated cortisol concentrations during RF-EMF exposure at night. Cortisol showed a slight increase immediately after the onset of exposure, persisting for approximately 1 hour. The authors concluded that a kind of adaptation took place - as also discussed by us above. Radon *et al.*[13] measured salivary IgA, melatonin and cortisol in eight male persons. Although they used rather high power flux densities (1 W/m^2), they found no significant differences between exposure and sham. Unfortunately, sample size was very small and raw data instead of relative changes had been analyzed by that research group, although variance in saliva parameters is usually large. Djeridane *et al.*[36] measured serum cortisol in 20 men for four weeks of regular mobile phone RF-EMF exposure. During the test period, cortisol concentration decreased by 12 % and increased again to pre-level in the post-experimental period. Obviously, this seems to be opposite to our findings and to the findings of Mann and his colleagues. Nevertheless, this actually makes sense: it is very likely that healthy subjects exposed only a short time to EMF react “healthily” to this stressor, with an increased cortisol level. After longer periods of exposure-several days, weeks, months-the body cannot keep on this short time-reaction to the stressor. Research on Multiple Chemical Sensitivity (MCS) had shown that MCS-patients partly could not adequately react to stress and show very low levels of cortisol[37]. This could be understood as a long term result of exposure to environmental hazards, in our case RF-EMFs.

Our results presented here must be seen in the context with other scientific work published recently. Friedman et al. showed that RF-EMF emitted by mobile phones could change a whole cascade of biochemical reactions[38]. The spectrum of possible effects reaches from the induction of transcription and other cellular processes to proliferation. Schwarz et al.[39] showed that EMF-signals from UMTS (Universal Mobile Telecommunication System) at 1950 MHz could cause genetic alterations in some human cells *in vitro*. They observed a significant increase of comet tail factor and centromere-negative micronuclei in human cultured fibroblasts from a specific absorption rate (SAR) of 0.05 W/kg on (SAR-safety limit: 2 W/kg). Others observed similar adverse effects following GSM exposure, and several studies identified chromosomal instabilities and even genotoxic effects which also included double-strand breaks[40-45]. It is common medical study knowledge that a combination of possible genotoxic effects, a possible increase of proliferation, and a possible weakening of the bodily defence system finally might lead to severe health consequences. As reviewed by Nittby et al.[46], RF-EMFs can also show effects on the blood-brain barrier.

CONCLUSION

In conclusion, our work supports the assumption that RF-EMF in considerably lower field densities than ICNIRP-guidelines[47] can potentially influence certain psychobiological stress markers. Additional scientific work needs to be carried out, aiming to better identify the various possibilities of stress response, chronobiological mechanisms and interactions of common immune parameters. Furthermore, studies on long term effects of RF-EMF would be especially important.

ACKNOWLEDGEMENTS

We would like to thank the team of the *KOKO-Kinderbetreuungs-Einrichtung* (Salzburg City) for allowing us to rent the room which we used as field laboratory. We would like to thank Dr. Günter Schwamberger (Salzburg University) for performing the biochemical tests as requested, and Dr. Ing. Martin Virnich (Anbus GmbH, Fürth, Germany) for his perfect accredited technical contributions to the study. The following institutions and companies helped us with their know-how and apparatus / materials: Salzburg Federal Hospital; Paracelsus Medical University, Salzburg; Salzburg Government, Health Department; Maschek (Kaufering, Germany); ESAG (Vienna, Austria); Y-Shield (Pocking, Germany); Gigahertz-Solutions (Langenzenn, Germany). For her expert help in bringing this manuscript into English language, we would like to thank Mrs. Hannah Leigh Wapshott (Annapolis, MD, USA).

Declaration of Interests: No competing interests.

REFERENCES

1. Abdel-Rassoul G, El-Fateh O A, Salem M A, *et al.* (2007). Neurobehavioral effects among inhabitants around mobile phone base stations. *Neurotoxicology* **28**(2), 434-440.
2. Blettner M, Schlehofer B, Breckenkamp J, *et al.* (2009). Mobile phone base stations and adverse health effects: phase 1 of a population-based, cross-sectional study in Germany. *Occupational and Environmental Medicine* **66**(2), 118-123.
3. Hutter H P, Moshammer H, Wallner P, *et al.* (2006). Subjective symptoms, sleeping problems, and cognitive performance in

subjects living near mobile phone base stations. *Occupational and Environmental Medicin* **63**(5), 307-313.

4. Santini R, Santini P, Danze J M, *et al.* (2002). Study of the health of people living in the vicinity of mobile phones base stations: I/ Influence of distance and sex. *Pathologie Biologie* **50**(6), 369-373.
5. Santini R, Santini P, Danze J M, *et al.* (2003). Symptoms experienced by people in vicinity of base stations: II/ Incidences of age, duration of exposure, location of subjects in relation to the antennas and other electromagnetic factors. *Pathologie Biologie* **51**(7), 412-415.
6. Regel S J, Negovetic S, Röösli M, *et al.* (2006). UMTS base station-like exposure, well-being, and cognitive performance. *Environmental Health Perspectives* **114**(8), 1270-1275.
7. Eltiti S, Wallace D, Ridgewell A, *et al.* (2007). Does short-term exposure to mobile phone base station signals increase symptoms in individuals who report sensitivity to electromagnetic fields? A double-blind randomized provocation study. *Environmental Health Perspectives* **115**(11), 1603-1608.
8. Furubayashi T, Ushiyama A, Terao Y, *et al.* (2009). Effects of short-term W-CDMA mobile phone base station exposure on women with or without mobile phone related symptoms. *Bioelectromagnetics* **30**(2), 100-113.
9. De Seze R, Fabbro-Peray P, Miro L (1998). GSM radiocellular telephones do not disturb the secretion of antepituitary hormones in humans. *Bioelectromagnetics* **19**(5), 271-278.
10. Nakamura H, Seto T, Nagase H, *et al.* (1997). Effects of exposure to microwaves on cellular immunity and placental steroids in pregnant rats. *Occupational and Environmental Medicine* **54**(9), 676-680.
11. Nasta F, Prisco M G, Pinto R, *et al.* (2006). Effects of GSM modulated radiofrequency electromagnetic fields on B-cell peripheral differentiation and antibody production. *Radiation Research* **165**(6), 664-670.
12. Tuschl H, Novak W, Molla-Djafari H (2006). In vitro effects of GSM modulated radiofrequency fields on human immune cells. *Bioelectromagnetics* **27**(3), 188-196.
13. Radon K, Parera D, Rose D M, *et al*. (2001). No Effects of Pulsed Radio Frequency Electromagnetic Fields on Melatonin, Cortisol, and Selected Markers of the Immune System in Man. *Bioelectromagnetics* **22**(4), 280-287.
14. Nater U M, Rohleder N (2009). Salivary alpha-amylase as a non-invasive biomarker for the sympathetic nervous system: current state of research. *Psychoneuroendocrinology* **34**(4), 392-401.
15. Akimoto T, Kumai Y, Akama T, *et al.* (2003). Effects of 12 months of exercise training on salivary secretory IgA levels in elderly subjects. *British Journal of Sports Medicine* **37**(1), 76-79.
16. Philips A C, Douglas C (2006). Stressful life events are associated with low secretion rates of immunglobulin A in saliva in the middle aged and elderly. *Brain, Behavior and Immunity* **20**, 191-197.
17. Augner C, Florian M, Pauser G, *et al.* (2009). GSM base stations: short-term effects on well-being. *Bioelectromagnetics* **30**(1), 73-80.
18. World Medical Association declaration of Helsinki (1997). Recommendations guiding physicians in biomedical research involving human subjects. *JAMA* **277**, 925-926.
19. American Psychological Association (2002). Ethical principles of psychologists and code of conduct. Retrieved June **22**, 2009, from www.apa.org/ethics.
20. Bradford M M (1976). A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Analytical Biochemistry,* **72**, 248-254.
21. Basu A, Shrivastav T G, Kariya K P (2003). Preparation of enzyme conjugate through adipic acid dihydrazide as linker and its use in immunoassays. *Clinical Chemistry* **49**, 1410-1412.
22. Gillard B K, Marksman H C, Feig S A (1977). Direct spectrophotometric determination of alpha amylase activity in saliva, with p-nitrophenyl alpha-maltoside as substrate. *Clinical Chemistry* **23**, 2279-2282.
23. Westermann J, Demir A, Herbst V (2004). Determination of cortisol in saliva and serum by a luminescence-enhanced enzyme immunoassay. *Clinical Laboratory* **50**, 11-24.
24. Hucklebridge F, Clow A, Evans P (1998). The relationship between salivary secretory immunoglobulin A and cortisol: neuroendocrine response to awakening and the diurnal cycle. *International Journal of Psychophysiology* **31**(1), 69-76.
25. Nater U M, La Marca R, Florin L, *et al.* (2006). Stress-induced changes in human salivary alpha-amylase activity-association with adrenergic activity. *Psychoneuroendocrinology* **31**(1), 49-58.
26. Ohira H (2004). Social support and salivary secretory immunoglobulin A response in women to stress making a public speech. *Perceptual and motor skills* **98**, 1241-1250.
27. Rantonen P J, Meurman J H (2000). Correlations between total protein, lysozyme, immunoglobulins, amylase and albumin in stimulated whole saliva during daytime. *Acta odontologica Scandinavia* **58**, 160-165.
28. Sjogren E, Leanderson P, Kristenson M (2006). Diurnal saliva cortisol levels and relations to psychosocial factors in a population sample of middle-aged Swedish men and women. *International Journal of Behavioral Medicine* **13**(3), 193-200.
29. Kirschbaum C, Steyer R, Eid M, *et al.* (1990). Cortisol and behavior: 2. Application of a latent state trait model to salivary cortisol. *Psychoneuroendocrinology* **15**(4), 297-307.
30. Eltiti S, Wallace D, Ridgewell A, *et al.* (2008). Mobile Phone Base Stations: Eltiti et al. Respond. *Environmental Health Perspectives* **116**(2), A64-A65.
31. Zinelis, S A (2008). Short-Term Exposure to Mobile Phone Base Station Signals. *Environmental Health Perspectives* **116**(2), A62.
32. Chatterton R T Jr., Vogelsong K M, Lu Y C, *et al.* (1996). Salivary alpha-amylase as a measure of endogenous adrenergic activity. *Clinical Physiology* **16**(4), 433-448.
33. Blank M. (2007). Bioinitiave Report 2007: Section 7: Evidence for Stress Response (Stress Proteins). Health Risks of the Electromagnetic Fields: Research on the Stress Response. Retrieved April **17**, 2008, from:http://www.bioinitiative.org/report/docs/section_7.pdf
34. Johansson O (2007). Bioinitiave Report 2007: Section 8: Evidence for effects on the immune system. Retrieved April **17**, 2008, from:http://www.bioinitiative.org/report/docs/section_8.pdf
35. Mann K, Wagner P, Brunn G, *et al.* (1998). Effects of pulsed high-frequency electromagnetic fields on the neuroendocrine system. *Neuroendocrinology* **67**(2), 139-144.
36. Djeridane Y, Touitou Y, de Seze R (2008). Influence of electromagnetic fields emitted by GSM-900 cellular telephones on the circadian patterns of gonadal, adrenal and pituitary hormones in men. *Radiatiation Research* **169**(3), 337-343.
37. Mayer W, Bieger W (2003). [Diagnostics of Chronic Multisystem Illnesses] Article in German: Diagnostik von chronischen Multisystemerkrankungen / Chronic Multisystem Illnesses. *Journal fuer Orthomolekulare Medizin* **11**(4), 391-404.
38. Friedman J, Kraus S, Hauptman Y, *et al.* (2007). Mechanism of short-term ERK activation by electromagnetic fields at mobile phone frequencies. *Biochemical Journal* **405**(3), 559-568.
39. Schwarz C, Kratochvil E, Pilger A, *et al.* (2008). Radiofrequency electromagnetic fields (UMTS, 1,950 MHz) induce genotoxic effects in vitro in human fibroblasts but not in lymphocytes. *International Archives of Occupational and Environmental Health* **81**(6), 755-67.
40. Hardell L, Sage C (2008). Biological effects from electromagnetic field exposure and public exposure standards. *Biomedicine & Pharmacotherapy* **62**(2), 104-149.
41. Lai H, Singh N P (1996). Single- and double-strand DNA breaks in rat brain cells after acute exposure to radiofrequency

electromagnetic radiation. *International Journal of Radiation and Biology* **69**(4), 513-521.

42. Lai H, Singh N P (2004). Magnetic-field-induced DNA strand breaks in brain cells of the rat. *Environmental Health Perspectives* **112**(6), 687-694.
43. Lixia S, Yao K, Kaijun W, *et al.* (2006). Effects of 1.8 GHz radiofrequency field on DNA damage and expression of heat shock protein 70 in human lens epithelial cells. *Mutation Research* **602**(1-2), 135-142.
44. Mashevich M, Folkman D, Kesar A, *et al*. (2003). Exposure of human peripheral blood lymphocytes to electromagnetic fields associated with cellular phones leads to chromosomal instability. *Bioelectromagnetic* **24**(2), 82-90.
45. Nylund R, Leszczynski D (2006). Mobile phone radiation causes changes in gene and protein expression in human endothelial cell lines and the response seems to be genome- and proteome-dependent. *Proteomics* **6**, 4769-4780.
46. Nittby H, Grafström G, Eberhardt J L, *et al.* (2008). Radiofrequency and extremely low-frequency electromagnetic field effects on the blood-brain barrier. *Electromagnetic Biology and Medicine* **27**(2), 103-126.
47. International Commission on Non-Ionizing Radiation Protection (ICNIRP) (1998). Guidelines for Limiting Exposure to Time-Varying Electric, Magnetic, and Electromagnetic Fields (up to 300 GHz). *Health Physics* **74**(4), 494-522.

(*Received December* 4, 2009 *Accepted May* 3, 2010)

Use of laptop computers connected to internet through Wi-Fi decreases human sperm motility and increases sperm DNA fragmentation

Conrado Avendaño, M.S.,[a] Ariela Mata, M.S.,[a] César A. Sanchez Sarmiento, M.D., Ph.D.,[a] and Gustavo F. Doncel, M.D., Ph.D.[b]

[a] Nascentis Medicina Reproductiva, Córdoba, Argentina; and [b] CONRAD, Department of Obstetrics and Gynecology, Eastern Virginia Medical School, Norfolk, Virginia

Objective: To evaluate the effects of laptop computers connected to local area networks wirelessly (Wi-Fi) on human spermatozoa.
Design: Prospective in vitro study.
Setting: Center for reproductive medicine.
Patient(s): Semen samples from 29 healthy donors.
Intervention(s): Motile sperm were selected by swim up. Each sperm suspension was divided into two aliquots. One sperm aliquot (experimental) from each patient was exposed to an internet-connected laptop by Wi-Fi for 4 hours, whereas the second aliquot (unexposed) was used as control, incubated under identical conditions without being exposed to the laptop.
Main Outcome Measure(s): Evaluation of sperm motility, viability, and DNA fragmentation.
Result(s): Donor sperm samples, mostly normozoospermic, exposed ex vivo during 4 hours to a wireless internet-connected laptop showed a significant decrease in progressive sperm motility and an increase in sperm DNA fragmentation. Levels of dead sperm showed no significant differences between the two groups.
Conclusion(s): To our knowledge, this is the first study to evaluate the direct impact of laptop use on human spermatozoa. Ex vivo exposure of human spermatozoa to a wireless internet-connected laptop decreased motility and induced DNA fragmentation by a nonthermal effect. We speculate that keeping a laptop connected wirelessly to the internet on the lap near the testes may result in decreased male fertility. Further in vitro and in vivo studies are needed to prove this contention. (Fertil Steril® 2012;97:39–45. ©2012 by American Society for Reproductive Medicine.)
Key Words: Laptop computer, Wi-Fi, sperm quality, fertility, sperm DNA fragmentation

In recent years, the use of portable computers (laptops, connected to local area networks wirelessly, also known as Wi-Fi) has increased dramatically. Laptops have become indispensable devices in our daily life, offering flexibility and mobility to users. People using Wi-Fi may be exposed to radio signals absorbing some of the transmitted energy in their bodies. Portable computers are commonly used on the lap (1–3), therefore exposing the genital area to radio frequency electromagnetic waves (RF-EMW) as well as high temperatures (3, 4).

Infertility is a common worldwide condition that affects more than 70 million couples of reproductive age (5). It has been suggested that male fertility has declined during the past several decades (6). Such decline has been attributed to the direct or indirect exposure to certain environmental factors such as RF-EMW (7).

Extremely low frequency magnetic fields can initiate a number of biochemical and physiological alterations in biological systems of different species (8–12). Many of these effects have been associated with free-radical production (13, 14). Free radicals are causative factors of oxidative damage of cellular structures and molecules such as lipids, proteins, and nucleic acids. Free radicals react with polyunsaturated fatty acids in cell membranes promoting a process called lipid peroxidation. In human spermatozoa the presence of unesterified polyunsaturated fatty acids is causally associated with the induction of reactive oxygen species (ROS) generation and lipid peroxidation (15). Damage may occur at the membrane level, leading to immotility and cell death, or at the DNA level. DNA integrity is essential to normal conception. Sperm DNA fragmentation has been associated with impaired fertilization, poor embryonic development, high

Received June 14, 2011; revised September 9, 2011; accepted October 11, 2011; published online November 23, 2011.
C.A. has nothing to disclose. A.M. has nothing to disclose. C.A.S.S. has nothing to disclose. G.F.D. has nothing to disclose.
Reprint requests: Conrado Avendaño, M.S., Nascentis Medicina Reproductiva, Montevideo 359, Córdoba, Córdoba X5000AXA, Argentina (E-mail: cavendano@nascentis.com or andrologiachubut@yahoo.com.ar).

Fertility and Sterility® Vol. 97, No. 1, January 2012 0015-0282/$36.00

doi:10.1016/j.fertnstert.2011.10.012

rates of miscarriage, and increased incidence of morbidity in the offspring, including childhood cancer (16, 17). It has been proposed that genetic and environmental factors would be involved in the etiology of sperm DNA damage (18).

The RF-EMW from mobile phones may cause DNA damage (19), in addition to decreased motility and viability (20, 21). Increased levels of intracellular ROS (22) would be the cause of these deleterious effects.

Portable computers using Wi-Fi emit RF-EMW and are typically positioned close the male reproductive organs. Their potential negative effects on male germ cells have not been elucidated. To assess this potential association we used an in vitro model incubating human sperm in the presence of an active portable computer connected to the internet by Wi-Fi. Sperm viability, motility, and DNA fragmentation were the main study end points.

MATERIALS AND METHODS

Subjects

Use of these samples for research purposes was approved by the Institutional Ethics Committee of Nascentis Medicina Reproductiva, Córdoba, Argentina, and all participants gave written informed consent. Twenty-nine semen samples were collected by masturbation from healthy donors after 2–5 days of sexual abstinence. After liquefaction, sperm concentration and motility were determined by light microscopy, using a Makler chamber (Mid Atlantic Diagnostics Inc.). Sperm morphology was examined at ×1,000 oil immersion microscopy by strict criteria after staining with the Papanicolau method as previously described (23). Preparation and assessment were performed by a single experienced operator. Semen samples with more than 0.5 million/mL of peroxidase-positive leukocytes were discarded and not used in the study.

Motile spermatozoa were selected by swim up performed in modified human tubal fluid (HTF; Irvine Scientific) supplemented with 10% synthetic serum substitute (SSS; Irvine). Briefly, each sperm sample was diluted 1:1 with modified HTF and then centrifuged at 300 × g for 10 minutes. The supernatant was discarded and the pellet was gently layered with 1 mL of modified HTF/SSS and incubated at 37°C, at a 45° angle, for 1 hour. After the incubation period, the top 0.5 mL of the supernatant, which is enriched in the motile sperm, was withdrawn carefully and sperm concentration and motility were determined. The sperm concentration was adjusted to 10–20 million/mL with modified HTF/SSS.

Each sperm suspension sample was aliquoted in two fractions (A and B) and a drop of 400 μL was placed in 35 × 10 mm Petri dishes (Falcon 3001). This was covered with 3 mL of embryo oil (Irvine) to avoid evaporation. Fractions B were incubated under a laptop computer. Fractions A (control group) were incubated under similar conditions without the computer.

Incubation of Spermatozoa Under Laptop

For each sperm sample, one of the dishes (fraction B) was incubated at room temperature under a laptop computer (Toshiba Satellite M305D-S4829) connected to the internet wirelessly (Wi-Fi, frequency 2.4 GHz defined by IEEE 802.11b). To induce the greatest possible effect, the laptop worked actively (uploading and downloading information) throughout the period of exposure (24). To maximize the likelihood of observing deleterious effects the distance between the computer and each specimen was kept constant at 3 cm. This distance was the estimated distance between the computers resting on the lap and the testis/epididymis (Fig. 1B and C). The duration of exposure was 4 hours (Fig. 1A). The temperature under the laptop was kept at 25°C during the incubation time by an air conditioning system. The temperature on each medium drop was thoroughly controlled by an IVF Thermometer (Research Instruments) and recorded every 5 minutes. Unexposed aliquots (fraction A) were used as control and kept under identical temperature and conditions in another room away from any computers or electronic devices. After the incubation period, sperm vitality, motility, and DNA fragmentation were determined on each aliquot.

Vitality and Motility

Sperm vitality was evaluated by eosin stain according to specifications of the World Health Organization (25). Sperm motility was assessed microscopically using a Makler chamber (Mid Atlantic Diagnostics Inc.), and sperm movement was classified as progressive motility, nonprogressive motility, and immotility.

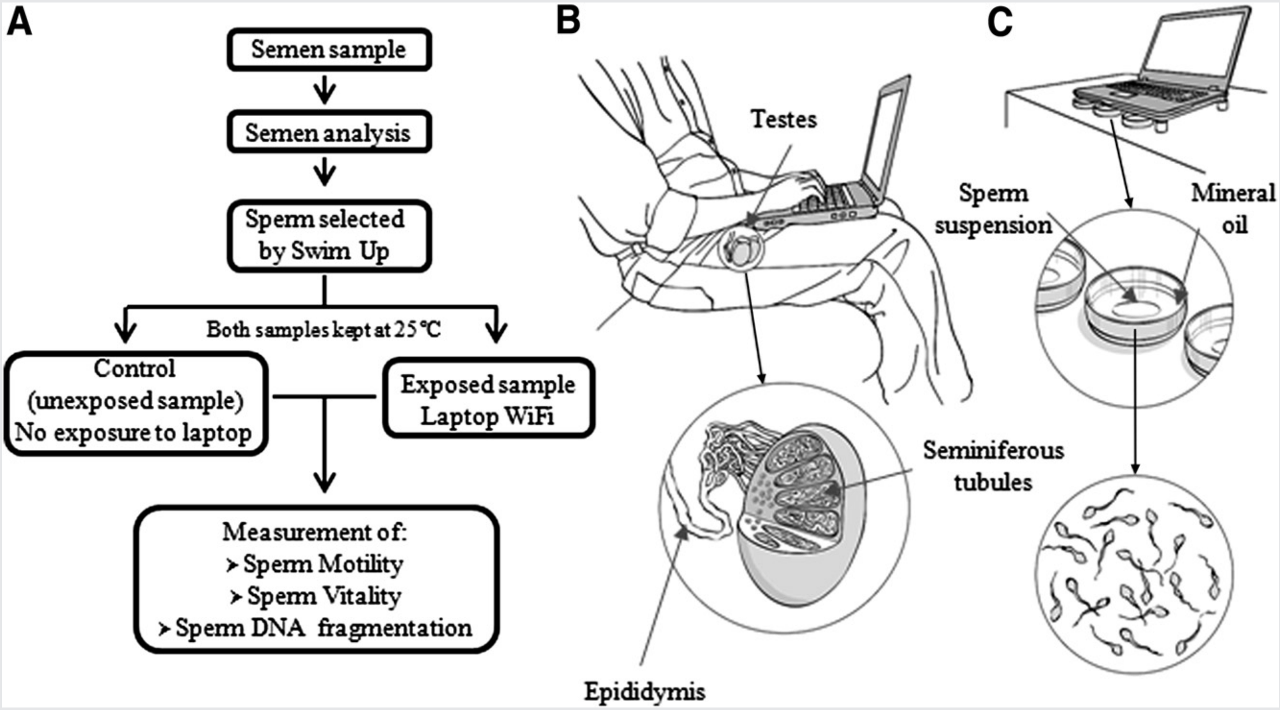
TUNEL Assay

Sperm DNA fragmentation was evaluated with TUNEL assay using the in situ cell death detection kit, fluorescein (Roche Diagnostics GmbH). The assay uses fluorescein-dUTP to label single and double DNA strand breaks according to manufacturer's instructions and was performed as previously described (26). Briefly, spermatozoa were fixed with paraformaldehyde (final concentration 2%, permeabilized with 0.1% Triton X-100) and incubated in the dark at 37°C for 1 hour in TUNEL reaction mixture containing 0.5 IU/μL of calf thymus terminal deoxynucleotidyl transferase and fluorescein-dUTP. Negative (omitting the enzyme terminal transferase) and positive (using deoxyribonuclease I, 1 U/mL for 20 minutes at room temperature) controls were included in each experiment. Mounting medium for fluorescence (Vectashield, Vector Laboratories) was added before the evaluation to prevent fluorescence quenching. A total of 500 cells were randomly analyzed per sample in a Zeiss Axioplan (Carl Zeiss MicroImaging) microscope with a ×1,000 oil immersion objective. Each sperm cell was classified as having intact DNA (no fluorescence) or fragmented DNA (green nuclear fluorescence). As expected, none of the cells showed fluorescent staining in the negative control, whereas 100% of the cells showed fragmentation in the positive control (treated with DNase). The results were expressed as percentage of sperm with fragmented DNA.

Power Density

A RF Field Strength Meter (Alphalab) was used to measure radiation under the experimental conditions. The RF Field Strength Meter detects the electric field of radio and

FIGURE 1



Study design and set-up for the exposure of human sperm to laptop. (A) Experimental design. (B) Schematic situation of the use of the laptop on the lap near the testes. (C) Diagram of the in vitro study. The Petri dishes were placed at 3 cm from a laptop computer. Each Petri dish contained a drop of 400 μL of sperm suspension in human tubal fluid/synthetic serum substitute (HTF/SSS) covered with mineral oil to prevent evaporation.

Avendaño. Laptop usage and sperm quality. Fertil Steril 2012.

microwaves from 0.5 MHz–3 GHz, and expresses the field strength as power density (0.001–2,000 $\mu W/cm^2$). The RF Field Strength Meter is directional and detects only the component of the electric field that has the same polarization as the long axis of the meter. To find the highest reading, the meter was located at the same distance as the Petri dishes and positioned vertically and horizontally, according to the manufacturer's specifications. The horizontal way showed higher reading and was recorded. Power density was monitored at the same distance of the Petri dishes, during basal condition (no exposure to laptop), laptop without Wi-Fi connection and laptop working in Wi-Fi mode throughout the experiment.

Statistical Analysis

Data were expressed as mean ± SD. The Mann-Whitney test was used to identify differences between two groups. $P < .05$ was considered statistically significant.

RESULTS

Donors' mean age was 34.1 ± 5.6 years (range 26–45 years). Semen parameters (volume, concentration, motility, vitality, and morphology) are presented in Supplemental Table 1 (available online). Many samples showed normozoospermia, whereas four samples showed low semen volume (LS6, LS13, LS27, and LS29) and three (LS15, LS16, and LS25) presented isolated teratozoospermia, according to World Health Organization reference values (25, 27).

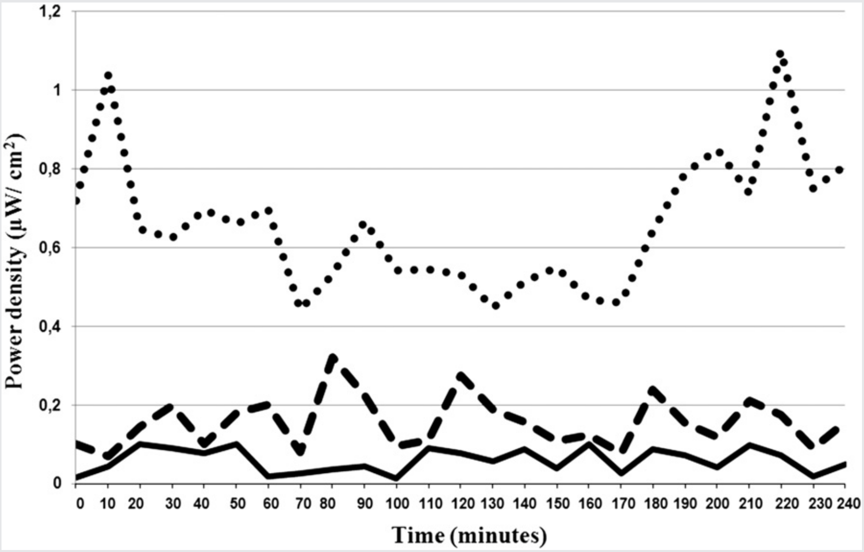
Room and under-the-laptop temperatures were monitored during the incubation time and kept at 25°C for both sperm fractions (A and B) by an air conditioning system (Supplemental Fig. 1, available online). The RF-EMW were recorded every 10 minutes in both groups throughout the experiment. The RF-EMW from a laptop working without Wi-Fi connection were checked in a pilot experiment (Fig. 2). The radiation from the computer operating with Wi-Fi was three or more times higher than without Wi-Fi and 7–15 times higher than basal conditions (not exposed to laptop).

Sperm parameters were evaluated after 4 hours of incubation of motile sperm selected by swim up and exposed to an active laptop computer under controlled temperature conditions. There were no differences in the percentage of viable sperm between the test and control groups (Fig. 3A). On the contrary, laptop exposure induced a significant decrease in sperm progressive motility with a concomitant increase in nonmotile sperm compared with the unexposed controls ($P < .05$). The percentage of nonprogressive sperm did not show statistically significant differences (Fig. 3B). Important, a significant increase in sperm DNA fragmentation was found in the fraction incubated under the computer compared with the control group (3.3 ± 6.0 vs. 8.3 ± 6.6; $P < .05$; Fig. 4A and B).

DISCUSSION

To our knowledge, this is the first study to examine the effect of portable computers on human spermatozoa in vitro. In the

FIGURE 2



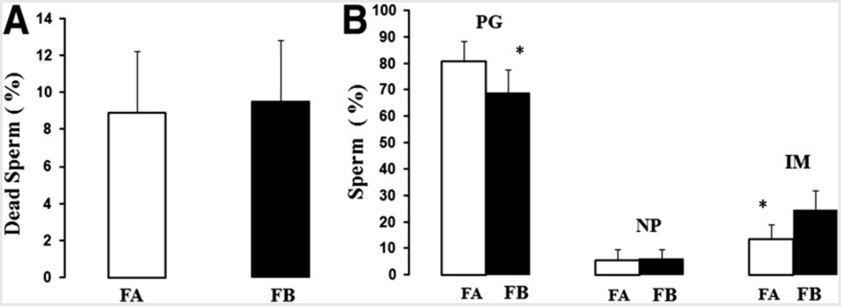
Variation of electromagnetic radiation (in microwatts per centimeter squared) during incubation time under the following experimental conditions: ●●● laptop conneted to Wi- Fi; ▬ ▬ ▬ laptop without connection to Wi-Fi; —— no laptop (basal conditions). The radio frequency electromagnetic waves were 7–15 times higher under the laptop than in basal conditions. They were significantly decreased when the Wi-Fi was turned off compared with the laptop working with Wi-Fi.

Avendaño. Laptop usage and sperm quality. Fertil Steril 2012.

present study we demonstrate that laptop computers connected wirelessly to the internet decrease sperm quality by a nonthermal effect. We evaluated vitality, motility, and DNA fragmentation in sperm selected by swim up after incubation under a laptop connected to the internet by Wi-Fi. The results demonstrate a significant decrease in sperm progressive motility and a significantly higher proportion of sperm with DNA fragmentation when samples were incubated for 4 hours under the laptop. These differences were seen in comparison with aliquots of the same semen samples incubated under similar conditions but outside the proximity of any computer or electronic device.

Several lifestyle and environmental factors may adversely impact human health and, in particular, reproductive performance (18). Approximately 15% of the sexually active population is affected by clinical infertility and in 50% of the cases a male factor is involved, either as a primary problem or in combination with a problem in the female partner (28). In this regard it has been proposed that the increased use of certain new technologies may decrease fertility

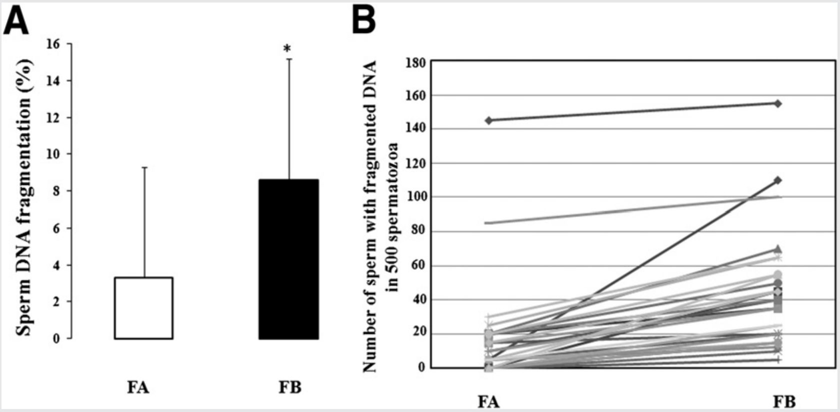
FIGURE 3



Laptop exposure and human sperm quality. Spermatozoa (10–20 × 10^6 cells/mL) were suspended in modified human tubal fluid/synthetic serum substitute (HTF/SSS) medium and incubated under a laptop computer connected to internet to Wi-Fi (FB). Another sperm aliquot was placed outside the reach of other computers or electronic devices (FA). Both groups were incubated for 4 hours at 25°C. (A) Percentage of dead sperm were not significantly different between the laptop exposed and unexposed groups and the unexposed cells (9.5% ± 3.3% vs. 8.9% ± 3.3%, $P>.05$). (B) Progressive sperm motility (PG) was significantly reduced in the group incubated under the laptop compared with that of control group (68.7% ± 8.8% to 80.9% ± 7.5%, $*P<.01$). No difference was found in the percentage of nonprogressive (NP) spermatozoa between groups. Immotile sperm (IM) were significantly increased after laptop exposure (24.5% ± 7.6% vs. 13.6% ± 5.6%, $*P<.01$).

Avendaño. Laptop usage and sperm quality. Fertil Steril 2012.

FIGURE 4



Laptop exposure and human sperm DNA fragmentation. Sperm suspensions were incubated under a laptop computer connected to the internet by Wi-Fi (FB) during 4 hours at 25°C. Aliquots of the same samples were placed outside of the reach of other computers or electronic devices, in a separate room (FA). (A) Sperm DNA fragmentation was increased after 4 hours of laptop exposure. In the test group, 8.6% ± 6.6% of the cells were fragmented, whereas only 3.3% ± 6.0% of the controls showed DNA fragmentation (*$P<.01$). (B) Plot of individual responses of sperm DNA fragmentation to laptop exposure. The number of sperm with fragmented DNA was evaluated in two aliquots of the same sample (500 cells/aliquot).

Avendaño. Laptop usage and sperm quality. Fertil Steril 2012.

potential by increasing long-term exposure to nonionizing radiation (18).

Laptop computer usage has increased significantly in recent years, especially in people of reproductive age. Frequently laptops are connected to the internet through Wi-Fi and commonly placed on the lap near the testes. Portable computers actively generate high temperatures that can increase the scrotal temperature and may produce deleterious effects on spermatogenesis (3, 29). In addition, laptop computers working by Wi-Fi are connected through RF-EMW (4, 24), which may damage spermatozoa in the male reproductive organs through microwave radiation.

To set up this study we first evaluated the radiation emitted from a laptop. The radiation varied during the test and depended on the flow of information between the computer and the network to which it was connected (Fig. 2).

Overall, however, the RF-EMW were 7–15 times higher under the laptop than under basal conditions (no laptop). Compared with the laptop working with Wi-Fi, RF-EMW were significantly decreased when the Wi-Fi was turned off.

It is well known that increased temperature may decrease sperm quality (30) and the use of portable computers on the lap increases scrotal temperature (3). Therefore to prevent confounding thermal effects, room and incubation temperatures were kept constant in both the unexposed and the under-the-laptop groups (Fig. 1) during the incubation time.

The first relevant finding of this study was a significant decrease in sperm progressive motility after exposure to the laptop. A plausible explanation for the impaired sperm motility could be magnetic and electromagnetic fields inducing oxidation of phospholipids, which are a major component in the sperm mitochondrial sheath (31). Several studies have shown that higher ROS values have detrimental effects on the motility of normal human spermatozoa (15, 32). Furthermore, it has been reported that infertile men with high seminal ROS levels have a lower percentage of motile sperm (27). This can be explained by a disturbance of the mitochondrial membrane potential, which causes high levels of ROS to be released into the cytoplasm, depleting the energy supply and affecting both sperm motility and kinetics (33, 34). Interestingly, in our study, sperm vitality was not different between the two experimental groups (Fig. 3).

Concerning spermatozoa, RF-EMW generated by mobile phones cause a decrease in their progressive movement, in both human and rat cells (21, 22, 35). In vitro human spermatozoa exposed to mobile phone radiation showed reduced sperm head area and decreased sperm binding to the zona pellucida (ZP) without an increase in acrosomal reaction compared with controls (36). High levels of sperm ROS (22, 37), as well as an increased percentage of sperm DNA fragmentation (37), have been reported after mobile phone exposure. However, other studies did not find any changes in DNA integrity or the induction of proapoptotic markers (22, 38). The lack of DNA damage observed in these studies might be explained by the shorter time of exposure to cell phone radiation or by the antioxidant effect of seminal plasma. The RF-EMW generated by mobile phones are similar to those generated by laptop computer and other mobile devices connected wirelessly to the internet (4).

In this regard we found that ex vivo exposure of human spermatozoa for 4 hours in the absence of seminal plasma induces DNA damage by a nonthermal effect (Fig. 4). This effect is similar to that observed by De Iuliis and co-workers (37) with sperm exposed to mobile phones in vitro. These investigators observed highly significant relationships between RF-EMW emitted by mobile phones, covering a range of specific absorption rates, the oxidative DNA damage marker, 8-hydroxy-2′-deoxyguanosine, and sperm DNA fragmentation. These changes were unrelated to thermal effects.

Research has shown negative consequences of electromagnetic fields on biological mechanisms. Genotoxic damage by 1.8 GHz in human fibroblast has been proposed as a direct consequence of intermittent exposure to RF-EMW (39). After exposure to 2.45 GHz, alteration of gene expression was found in cultured human cells mediated by a nonthermal mechanism (40). Electromagnetic radiation from mobile phones induces activation of the extracellular signal-regulated kinases (ERK)-cascade thereby altering transcription and other key cellular processes (8). Chronic exposure to low intensity microwaves (2.45 and 16.5 GHz) causes statistically significant increase in DNA strand breaks in rat brain cells (41). A recent work showed that the exposure of oviducts to extremely low frequency electromagnetic field negatively affects early embryo development, causing a slowdown in the embryo cleavage rate (42).

In an in vivo study, it was demonstrated that acute exposure to radiofrequency fields of cellular phones may modulate the oxidative stress of free radicals by enhancing lipid peroxidation, and a decrease in the activity of the antioxidants, superoxide dismutase, and glutathione peroxidase, in erythrocytes from human volunteers (43). In addition, genotoxic effect on epididymal spermatozoa has been reported when mice were irradiated for 7 days at 12 hours per day (19).

As opposed to somatic cells, the spermatozoon is a highly specialized cell with a condensed DNA (packaged by protamines) and very small cytoplasmic area (44). During spermatogenesis, human spermatozoa may take up to 1 week to move from the seminiferous tubules in the testes to the cauda epididymis (45) and throughout this time they would be highly vulnerable to RF-EMW exposure (19, 37), especially from a source close to the testes and epididymis such as a Wi-Fi laptop computer.

Our data suggest that the use of a laptop computer wirelessly connected to the internet and positioned near the male reproductive organs may decrease human sperm quality. At present we do not know whether this effect is induced by all laptop computers connected by Wi-Fi to the internet or what use conditions heighten this effect. The mechanisms involved in mediating the decrease in sperm motility and DNA integrity also need further study. We speculate that RF-EMW from laptop computers wirelessly connected to the internet may be the cause of sperm damage. However, we cannot discard the possibility that damage to sperm is caused by the low radiation produced by the computer without internet connection. With the caveat that these data were obtained with sperm samples incubated in vitro, our findings suggest that prolonged use of portable computers sitting on the lap of a male user may decrease sperm fertility potential. The potential implications of these findings warrant this report and further basic and clinical investigation.

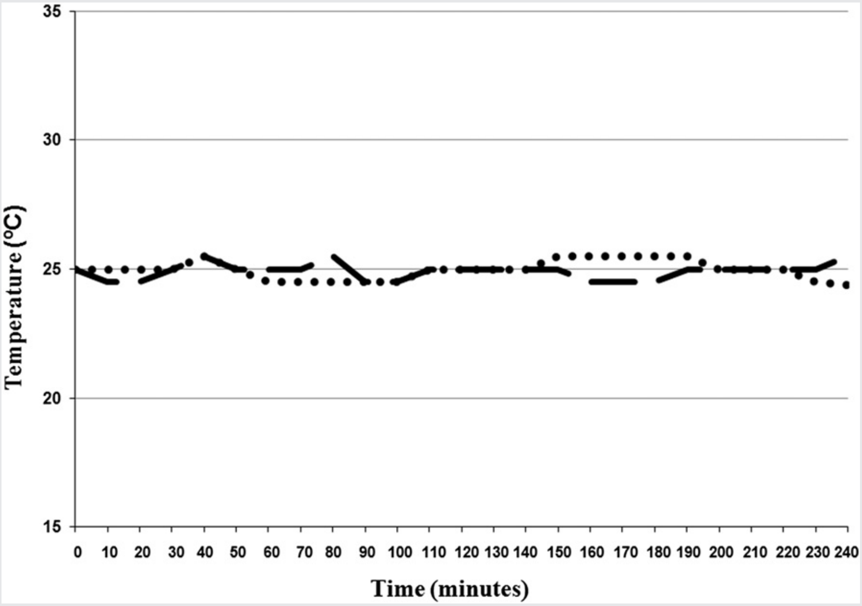
Acknowledgments: The authors thank Professor Nestor Hugo Mata for invaluable contribution in RF-EMW measurements, Valeria Martinez for her assistance and technical support, and the staff of Nascentis Medicina Reproductiva for their helpful input. Conrado Avendaño is grateful to the Instituto de Fisiología, Facultad de Ciencias Médicas and Centro de Investigaciones en Química Biológica de Córdoba, Facultad de Ciencias Químicas from Universidad Nacional de Córdoba, Argentina, for allowing the use of their fluorescence microscope. Special thanks to Cecilia Sampedro for her help in the fluorescence microscope.

REFERENCES

1. Paulius K, Napoles P, Maguina P. Thigh burn associated with laptop computer use. J Burn Care Res 2008;29:842–4.
2. Ostenson CG. Lap burn due to laptop computer. Lancet 2002;360:1704.
3. Sheynkin Y, Jung M, Yoo P, Schulsinger D, Komaroff E. Increase in scrotal temperature in laptop computer users. Hum Reprod 2005;20:452–5.
4. World Health Organization. WHO research agenda for radio frequency fields. Available at: http://whqlibdoc.who.int/publications/2010/9789241599948_eng.pdf. Accessed May 11, 2011.
5. Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Hum Reprod 2007;22:1506–12.
6. ESHRE Capri Workshop Group. Europe, the continent with the lowest fertility. Hum Reprod Update 2010;16:590–602.
7. Agarwal A, Desai NR, Ruffoli R, Carpi A. Lifestyle and testicular dysfunction: a brief update. Biomed Pharmacother 2008;62:550–3.
8. Friedman J, Kraus S, Hauptman Y, Schiff Y, Seger R. Mechanism of short-term ERK activation by electromagnetic fields at mobile phone frequencies. Biochem J 2007;405:559–68.
9. Lupke M, Frahm J, Lantow M, Maercker C, Remondini D, Bersani F, et al. Gene expression analysis of ELF-MF exposed human monocytes indicating the involvement of the alternative activation pathway. Biochim Biophys Acta 2006;1763:402–12.
10. Yamaguchi DT, Huang J, Ma D, Wang PK. Inhibition of gap junction intercellular communication by extremely low-frequency electromagnetic fields in osteoblast-like models is dependent on cell differentiation. J Cell Physiol 2002;190:180–8.
11. Volkow ND, Tomasi D, Wang GJ, Vaska P, Fowler JS, Telang F, et al. Effects of cell phone radiofrequency signal exposure on brain glucose metabolism. JAMA 2011;305:808–13.
12. Cuccurazzu B, Leone L, Podda MV, Piacentini R, Riccardi E, Ripoli C, et al. Exposure to extremely low-frequency (50 Hz) electromagnetic fields enhances adult hippocampal neurogenesis in C57BL/6 mice. Exp Neurol 2010;226:173–82.
13. Blank M. Do electromagnetic fields interact with electrons in the Na, K-ATPase? Bioelectromagnetics 2005;26:677–83.
14. Palumbo R, Capasso D, Brescia F, Mita P, Sarti M, Bersani F, et al. Effects on apoptosis and reactive oxygen species formation by Jurkat cells exposed to 50 Hz electromagnetic fields. Bioelectromagnetics 2006;27:159–62.
15. Aitken RJ, Wingate JK, De Iuliis GN, Koppers AJ, McLaughlin EA. Cis-unsaturated fatty acids stimulate reactive oxygen species generation and lipid peroxidation in human spermatozoa. J Clin Endocrinol Metab 2006;91:4154–63.
16. Avendano C, Franchi A, Duran H, Oehninger S. DNA fragmentation of normal spermatozoa negatively impacts embryo quality and intracytoplasmic sperm injection outcome. Fertil Steril 2010;94:549–57.
17. Aitken RJ, De Iuliis GN. Origins and consequences of DNA damage in male germ cells. Reprod Biomed Online 2007;14:727–33.
18. Pacey AA. Environmental and lifestyle factors associated with sperm DNA damage. Hum Fertil (Camb) 2010;13:189–93.
19. Aitken RJ, Bennetts LE, Sawyer D, Wiklendt AM, King BV. Impact of radio frequency electromagnetic radiation on DNA integrity in the male germline. Int J Androl 2005;28:171–9.
20. Erogul O, Oztas E, Yildirim I, Kir T, Aydur E, Komesli G, et al. Effects of electromagnetic radiation from a cellular phone on human sperm motility: an in vitro study. Arch Med Res 2006;37:840–3.
21. Yan JG, Agresti M, Bruce T, Yan YH, Granlund A, Matloub HS. Effects of cellular phone emissions on sperm motility in rats. Fertil Steril 2007;88:957–64.
22. Agarwal A, Desai NR, Makker K, Varghese A, Mouradi R, Sabanegh E, et al. Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: an in vitro pilot study. Fertil Steril 2009;92:1318–25.

23. Menkveld R, Kruger TF. Sperm morphology—predictive value? Fertil Steril 1992;57:942–3.
24. Foster KR. Radiofrequency exposure from wireless LANs utilizing Wi-Fi technology. Health Phys 2007;92:280–9.
25. World Health Organization. WHO laboratory manual for the examination of and procesing of human semen. 5th ed. Cambridge, UK: Cambridge University Press; 2010.
26. Avendano C, Franchi A, Taylor S, Morshedi M, Bocca S, Oehninger S. Fragmentation of DNA in morphologically normal human spermatozoa. Fertil Steril 2009;91:1077–84.
27. Cooper TG, Noonan E, von Eckardstein S, Auger J, Baker HW, Behre HM, et al. World Health Organization reference values for human semen characteristics. Hum Reprod Update 2010;16:231–45.
28. Thonneau P, Marchand S, Tallec A, Ferial ML, Ducot B, Lansac J, et al. Incidence and main causes of infertility in a resident population (1,850,000) of three French regions (1988–1989). Hum Reprod 1991;6:811–6.
29. Sheynkin Y, Welliver R, Winer A, Hajimirzaee F, Ahn H, Lee K. Protection from scrotal hyperthermia in laptop computer users. Fertil Steril 2011;95:647–51.
30. Thonneau P, Bujan L, Multigner L, Mieusset R. Occupational heat exposure and male fertility: a review. Hum Reprod 1998;13:2122–5.
31. Tremellen K. Oxidative stress and male infertility—a clinical perspective. Hum Reprod Update 2008;14:243–58.
32. Plante M, de Lamirande E, Gagnon C. Reactive oxygen species released by activated neutrophils, but not by deficient spermatozoa, are sufficient to affect normal sperm motility. Fertil Steril 1994;62:387–93.
33. Mahfouz R, Sharma R, Thiyagarajan A, Kale V, Gupta S, Sabanegh E, et al. Semen characteristics and sperm DNA fragmentation in infertile men with low and high levels of seminal reactive oxygen species. Fertil Steril 2010;94:2141–6.
34. Pasqualotto FF, Sharma RK, Nelson DR, Thomas AJ, Agarwal A. Relationship between oxidative stress, semen characteristics, and clinical diagnosis in men undergoing infertility investigation. Fertil Steril 2000;73:459–64.
35. Falzone N, Huyser C, Fourie F, Toivo T, Leszczynski D, Franken D. In vitro effect of pulsed 900 MHz GSM radiation on mitochondrial membrane potential and motility of human spermatozoa. Bioelectromagnetics 2008;29:268–76.
36. Falzone N, Huyser C, Becker P, Leszczynski D, Franken DR. The effect of pulsed 900-MHz GSM mobile phone radiation on the acrosome reaction, head morphometry and zona binding of human spermatozoa. Int J Androl 2010;34:20–6.
37. De Iuliis GN, Newey RJ, King BV, Aitken RJ. Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro. PLoS One 2009;4:e6446.
38. Falzone N, Huyser C, Franken DR, Leszczynski D. Mobile phone radiation does not induce pro-apoptosis effects in human spermatozoa. Radiat Res 2010;174:169–76.
39. Diem E, Schwarz C, Adlkofer F, Jahn O, Rudiger H. Non-thermal DNA breakage by mobile-phone radiation (1800 MHz) in human fibroblasts and in transformed GFSH-R17 rat granulosa cells in vitro. Mutat Res 2005;583:178–83.
40. Lee S, Johnson D, Dunbar K, Dong H, Ge X, Kim YC, et al. 2.45 GHz radiofrequency fields alter gene expression in cultured human cells. FEBS Lett 2005;579:4829–36.
41. Paulraj R, Behari J. Single strand DNA breaks in rat brain cells exposed to microwave radiation. Mutat Res 2006;596:76–80.
42. Bernabo N, Tettamanti E, Russo V, Martelli A, Turriani M, Mattoli M, et al. Extremely low frequency electromagnetic field exposure affects fertilization outcome in swine animal model. Theriogenology 2010;73:1293–305.
43. Moustafa YM, Moustafa RM, Belacy A, Abou-El-Ela SH, Ali FM. Effects of acute exposure to the radiofrequency fields of cellular phones on plasma lipid peroxide and antioxidase activities in human erythrocytes. J Pharm Biomed Anal 2001;26:605–8.
44. Eddy EM. The spermatozoon. In: Knobil E, Neil J, editors. The physiology of reproduction. New York: Raven Press; 1994:3–54.
45. Turner TT. On the epididymis and its role in the development of the fertile ejaculate. J Androl 1995;16:292–8.

SUPPLEMENTAL FIGURE 1



Incubation temperature in test (under the laptop; - - -) and control (unexposed; ● ● ● ●) groups. Room temperature was kept constant during incubation (4 hours) both in the control and the experimental groups.

Avendaño. Laptop usage and sperm quality. Fertil Steril 2012.

SUPPLEMENTAL TABLE 1

Basic semen parameters of study samples.

Semen parameter	Mean
Volume (mL)	2.8 ± 1.6[a]
Concentration (× 10^6 / mL)	111.0 ± 49.8
Vitality (%)	85.3 ± 4.6
Progressive motility (%)	60.2 ± 9.3
Morphology (%)	8.2 ± 4.7

[a] Mean ± SD.

Avendaño. Laptop usage and sperm quality. Fertil Steril 2012.

Eur J Epidemiol (2008) 23:369–377
DOI 10.1007/s10654-008-9236-4

ENVIRONMENTAL EPIDEMIOLOGY

Radiofrequency electromagnetic fields; male infertility and sex ratio of offspring

Valborg Baste · Trond Riise · Bente E. Moen

Received: 5 June 2007 / Accepted: 13 March 2008 / Published online: 16 April 2008

Abstract Concern is growing about exposure to electromagnetic fields and male reproductive health. The authors performed a cross-sectional study among military men employed in the Royal Norwegian Navy, including information about work close to equipment emitting radiofrequency electromagnetic fields, one-year infertility, children and sex of the offspring. Among 10,497 respondents, 22% had worked close to high-frequency aerials to a "high" or "very high" degree. Infertility increased significantly along with increasing self-reported exposure to radiofrequency electromagnetic fields. In a logistic regression, odds ratio (OR) for infertility among those who had worked closer than 10 m from high-frequency aerials to a "very high" degree relative to those who reported no work near high-frequency aerials was 1.86 (95% confidence interval (CI): 1.46–2.37), adjusted for age, smoking habits, alcohol consumption and exposure to organic solvents, welding and lead. Similar adjusted OR for those exposed to a "high", "some" and "low" degree were 1.93 (95% CI: 1.55–2.40), 1.52 (95% CI: 1.25–1.84), and 1.39 (95% CI: 1.15–1.68), respectively. In all age groups there were significant linear trends with higher prevalence of involuntary childlessness with higher self-reported exposure to radiofrequency fields. However, the degree of exposure to radiofrequency radiation and the number of children were not associated. For self-reported exposure both to high-frequency aerials and communication equipment there were significant linear trends with lower ratio of boys to girls at birth when the father reported a higher degree of radiofrequency electromagnetic exposure.

Keywords Electromagnetic fields · Infertility · Occupational exposure · Offspring sex ratio · Male infertility · Radiofrequency electromagnetic fields

Abbreviations

CI	Confidence interval
OR	Odds ratio

In recent decades, concern and discussion has been growing about decreasing fecundity and fertility in many countries [1, 2]. The reasons for this possible decreasing fertility are complex, as both social and behavioral changes in societies contribute in addition to biological mechanisms. However, several studies indicate that semen quality may have decreased in the past half century [3–5] and that reduced semen quality is associated with reduced fertility [6]. Various types of environmental and occupational exposure have been suggested as possible causes for the reduced semen quality [1, 7], but few factors have been consistently identified. One of the exposures have been non-ionizing electromagnetic fields and in special radiofrequency electromagnetic fields [8].

Non-ionizing electromagnetic fields are usually divided into groups according to frequency bands ranging from 50 Hz to several gigahertz, including extremely low-frequency electromagnetic fields emitted by electric equipment and radiofrequency fields emitted by radio communication and navigation equipment, mobile phones and radar.

V. Baste (✉)
Department of Public Health and Primary Health Care, Section for Occupational Medicine, UNIFOB AS, University of Bergen, Kalfarveien 31, 5018 Bergen, Norway
e-mail: valborg.baste@isf.uib.no

T. Riise · B. E. Moen
Department of Public Health and Primary Health Care, Section for Occupational Medicine, University of Bergen, Kalfarveien 31, 5018 Bergen, Norway

Many Royal Norwegian Navy employees are exposed to non-ionizing radiation. Employees use technical equipment creating electromagnetic fields both onshore and especially on board the ships. Navy personnel are exposed to fields in the whole range of frequencies but differ from other parts of the population because they are frequently exposed to radiofrequency electromagnetic fields during work. All ships have radar, transmitters and antennas causing exposure to radiofrequency fields. On several ships the distance between the personnel on deck and the antennas and the radars is short, and the personnel use this equipment whenever the ships are sailing. One study [9] has indicated adverse reproductive health outcome in a subgroup of employees in the Royal Norwegian Navy and suggested that this was related to electromagnetic radiation from the electronic equipment on board.

Little is known about exposure to non-ionizing electromagnetic fields and male reproductive health. Some studies on semen quality have reported that exposure to radiofrequency radiation has adverse reproductive effects [10–13], whereas others have not found such an effect [14, 15]. Recent studies have shown that using mobile phones negatively affects semen motility [16–18] and sperm concentration [17]. The sex ratio of offspring is important as an indicator of reproductive hazard [19], and there have been reported decreased sex ratio among fathers after exposure to radiofrequency electromagnetic fields [20–23] but only one was significant [22].

We investigated the association between men's self-reported occupational exposure to radiofrequency electromagnetic fields in the Navy and infertility and sex ratio of the offspring.

Methods

Design and data collection

The study population comprised all current and former male military employees in the Royal Norwegian Navy, defined by the military employment list. The data were collected during two time periods depending on whether they were currently or formerly employed. All military employees currently employed in September 2002 ($n = 2{,}497$) received a postal questionnaire during autumn 2002. The response rate was 62% ($n = 1{,}550$). Former military employees were defined as those employed in the Royal Norwegian Navy for more than 16 months from 1950 to September 2002. Sixteen month was chosen to exclude conscripts. A total of 15,259 received a questionnaire at the end of 2004 and 9,666 of them responded (63%). Among the respondents, 719 men were excluded because they answered that they had been employed less then 1 year or had only worked as a civilian in the Navy, leaving 8,947 formerly employed military men.

The employees were identified by both name and personal identification number, and their current address was found by using the National Population Registry. In both surveys we sent two reminders to nonrespondents. We finally included 10,497 currently and formerly employed military men in the analysis.

Questionnaires

The questionnaire sent to the current employees was 20 pages long including various topics related to work and health. The questionnaire sent to the former employees contained only a subset of these questions. This study only used questions that were identical in the two surveys.

The questionnaire included three questions on exposure to radiofrequency electromagnetic fields: work closer than 10 m from high-frequency aerials, work closer than 3 m from communication equipment and work closer than 5 m from radar. Further questions asked about exposure to organic solvents or paint, welding or torch-cutting or working with the hull and lead. These types of exposure were considered because of the possible effects on reproductive health [24–28]. Each of these six work exposure items was asked separately for exposure in the Navy and for exposure at other workplaces or at leisure. They were formulated as "Have you ever worked with…" with response categories "not at all", "low", "some", "high", "very high" or "do not know". We combined the exposure in the Navy and exposure at other workplaces or at leisure separately for each exposure, such that the new combined exposure variables were given the highest exposure of these two. If the answer was missing or the response was "do not know" for exposure both in the Navy and outside the Navy, the combined variable was set to "missing".

Infertility was determined by a single question: "Have you and your partner ever tried to become pregnant without success for more than 1 year?" The response categories were "yes", "no" and "do not know". The analysis only included those who answered "yes" or "no" ($n = 9{,}925$, 95%).

We also asked whether the participants had biological children, and how many. For each of the children the participants should give the year of birth and gender of the child. In the analyses of sex ratio only children born the year after first employment in the Navy was included.

Some participants had probably not started their reproductive career. Two new variables were therefore defined as a combination of infertility and whether they had children. (1) Fertility problems: reported infertility and had children. (2) Involuntary childlessness: reported infertility and had no children. For both variables, we used the respondents who had not reported infertility and had children as the reference group. For these two variables, we excluded those who did not answer the question on infertility or answered "do not know" and those who reported no problems with infertility and did not have children. Analyses including this people into the reference group did not change the results.

We also asked the participants about current smoking habits, which was categorized into ever-smokers (current smokers, former smokers and sometime smokers) or never-smokers. We dichotomized information on current alcohol consumption into >13 and ≤13 alcohol units of 4 cl. per week [29]. We obtained information on the dates employment in the Navy started and stopped from the military employment list. Age was divided into 10-years age groups, which reflect birth cohorts.

Statistics

We performed tests for linear trend between radiofrequency electromagnetic fields and infertility by Mantel–Haenszel chi-square analysis. We used logistic regression to estimate the effect of radiofrequency electromagnetic fields on infertility and whether they had biological children in two separate analyses. The estimated odds ratios (OR) with 95% confidence interval (CI) were adjusted for smoking habits, alcohol consumption and exposure to organic solvents, welding and lead. To investigate which of the three exposure variables of radiofrequency electromagnetic fields most strongly affected infertility, we included each of the radiofrequency variables and exposure to organic solvents, welding and lead, and age as continuous variables in addition to smoking habits and alcohol consumption in a backwards stepwise logistic regression.

In analyzing associations between working near high-frequency aerials and fertility problems and involuntary childlessness, we adjusted the OR for smoking habits and alcohol consumption. Adjustment for exposure to organic solvents, welding and lead did not change the estimates in the analysis of infertility, and since the number of cases with infertility problems or involuntary childlessness was relatively low we did not adjust for this exposure in analyzing these two variables.

The dose response association between exposure for radiofrequency electromagnetic fields and offspring sex ratio was analyzed by Mantel–Haenszel chi-square and the OR were estimated from an unadjusted logistic regression.

We calculated Pearson bivariate correlation coefficients to quantify the associations between the exposure variables.

To test the differences in the number of children between personnel with different exposure levels, we performed linear regression adjusted for alcohol consumption and smoking habits.

Because reproductive history depends on age, we stratified the analysis by age groups according to the respondents' age when answering the questionnaire: <29, 30–39, 40–49 and ≥50 years. Statistical significance was set at $P < 0.05$.

Results

The mean age among the 10,497 respondents was 49 years. They had joined the Navy at a mean age of 20 years and had worked in the Navy on average 11 years (Table 1). Sixty percent were ever-smokers, and 6% drank more than 13 standard alcoholic drinks per week. Among those younger then 30 years, 17% reported that they had experienced infertility, 18% of those 30–39 years old, 19% of those 40–49 years old and 12% of those 50 years or older (Table 1). The percentages refer to the study population after excluding those who did not answer the question on infertility or answered "do not know" and those who reported no problems with infertility and did not have children.

A total of 22% reported that they had been working closer than 10 m from high-frequency aerials to a "high" degree or "very high" degree; 19% worked closer than 3 m from communication equipment and 21% worked closer than 5 m from radar (Fig. 1). Exposure to lead was slightly lower, and exposure to organic solvents or paint and welding, torch-cutting or working with the hull was considerably lower. In each of the three radiofrequency exposure groups, about one fourth of the respondents reported that they had never worked close to the specific exposure.

When analyzing the relation between the exposure and infertility in the whole study population, all three radiofrequency exposure variables gave significant linear trends, with higher reported levels of exposure related to more reported infertility. The OR for infertility among those who had worked to a "low" degree closer than 10 m from high-frequency aerials relative to those who reported no work near high-frequency aerials was 1.39 (95% CI: 1.15–1.68), adjusted for age, smoking habits, alcohol consumption and exposure to organic solvents, welding and lead. The OR for "some", "high" and "very high" exposure to high-frequency aerials were 1.52 (1.25–1.84), 1.93 (1.55–2.40) and 1.86 (1.46–2.37), respectively (data not shown).

When dividing the analysis into four age groups, all three radiofrequency exposure variables showed a significant linear trend in all age groups, except for those younger than 30 years and exposed to communication equipment (Table 2). Those who reported exposure to a "high" or "very high" degree showed significantly more infertility for all three radiofrequency exposure variables in all age

Table 1 Descriptive data from all participants in two cross-sectional studies of infertility among current (2002) and former (1950–2002) employed in the Royal Norwegian Navy

				First time in Navy	Duration in Navy	Smoking		More than 13 standard alcoholic drinks per week		Infertility	
Age group	*n*	%	Mean age (years)	Mean age	Mean year	Yes	%	Yes	%	Yes	%
−29	960	9.1	25.6	19.6	5.3	377	39.4	163	17.1	30	17.3
30–39	2,276	21.7	34.9	20.0	7.7	989	43.5	96	4.3	305	17.8
40–49	2,319	22.1	44.3	19.8	12.4	1,277	55.1	113	4.9	380	18.6
50+	4,940	47.1	62.9	20.3	13.7	3,668	74.3	313	6.6	516	11.7
Total	10,495	100.0	49.3	20.0	11.4	6,313	60.1	685	6.5	1,231	14.7
Missing	2			176.0	143.0	19		242		2,151[a]	

[a] Those who did not answer the question on infertility or answered "do not know" and those who reported no problems with infertility and did not have children

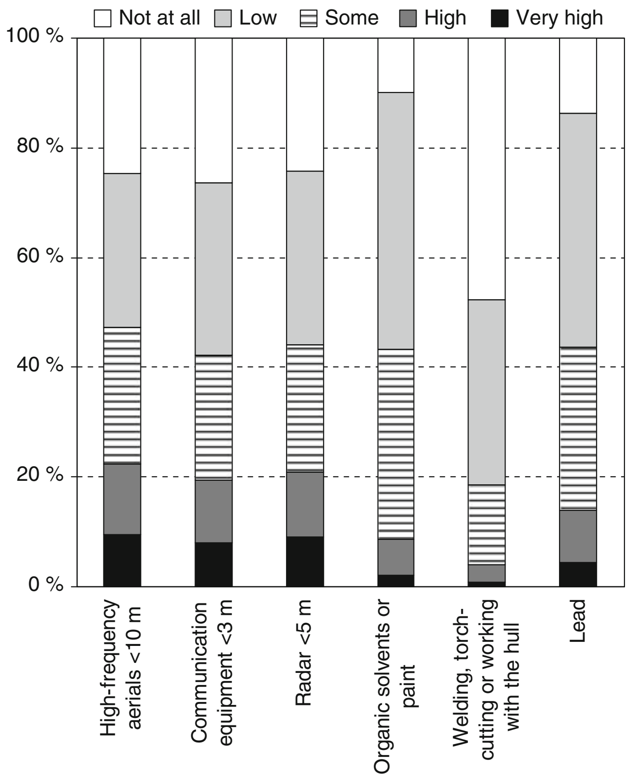


Fig. 1 Distribution of male military Navy workers working close to radiofrequency equipment, organic solvents, welding and lead in the Navy, at other workplaces or at leisure

groups, except for those younger than 30 years and exposed to communication equipment. The greatest and most significant effect was for high-frequency aerials in the two oldest age groups. Among those 40–49 years old, those reporting a "high" degree of working closer than 10 m from high-frequency aerials had an OR of 1.82 of infertility relative to "not at all", and the OR was 1.90 for "very high" relative to "not at all". The associations were similar among those 50 years or older.

The correlation coefficients between the three electromagnetic field exposure variables varied between 0.70 and 0.78. The other correlation coefficients between the six exposure variables ranged from 0.06 to 0.22, except for organic solvents and welding (0.48).

We performed stepwise backward logistic regression analysis including all three radiofrequency exposure variables as continuous variables in addition to exposure to organic solvents, welding, lead, age, smoking and alcohol consumption. The last step of this model included as significant variables working with high-frequency aerials, working with communication equipment and smoking habits. This model showed that high-frequency aerials had the strongest and most significant effect on infertility, and each step of increase in degree of self-reported exposure for high-frequency aerials increased the risk of infertility by 10% (OR = 1.10, 95% CI: 1.01–1.19).

Self-reported exposure to high-frequency aerials was also significantly related to the two constructed variables fertility problems and involuntary childlessness (Table 3). There was a significant linear trend with more fertility problems with higher exposure to high-frequency aerials in the two oldest age groups, and there was a significant linear trend between exposure to high-frequency aerials and involuntary childlessness for all age groups. Generally, the OR was higher for involuntary childlessness than for fertility problems. OR for involuntary childlessness among those who had worked closer than 10 m from high-frequency aerials to a "very high" degree relative to "not at all" were 3.14 among those 40–49 years old and 3.16 among those ≥50 years old.

Analysis of how working near communication equipment and working near radar influenced fertility problems and involuntary childlessness gave similar associations as for working near high-frequency aerials (results not given).

In our population 80% had biological children, varying from 17% among those younger than 30 years when answering the questionnaire to 92% among those 50 years

Table 2 Risk of infertility by exposure to self-reported radiofrequency electromagnetic fields in four age groups

		Work closer than 10 m from high-frequency aerials					Work closer than 3 m from communication equipment					Work closer than 5 m from radar				
		Total	Infertility				Total	Infertility				Total	Infertility			
Age (years)[a]	Degree of exposure level		%	OR[b]	95% CI[c]	*P*[d]		%	OR[b]	95% CI[c]	*P*[d]		%	OR[b]	95% CI[c]	*P*[d]
−29	Not at all	197	2.0	1.00			256	1.6	1.00			258	1.9	1.00		
	Low	256	2.3	1.10	0.30–4.07		292	2.7	1.86	0.54–6.40		318	1.9	0.87	0.25–2.99	
	Some	202	1.5	0.71	0.15–3.34	**0.013**	171	5.3	**3.56**	**1.05–12.08**	0.077	155	4.5	2.13	0.64–7.06	**0.001**
	High	114	7.0	**3.84**	**1.09–13.52**		86	4.7	3.50	0.83–14.78		88	2.3	1.11	0.20–6.00	
	Very high	144	5.6	2.70	0.76–9.53		105	3.8	2.49	0.60–10.42		93	9.7	**5.09**	**1.59–16.30**	
30–39	Not at all	368	10.9	1.00			439	9.3	1.00			411	10.0	1.00		
	Low	621	12.9	1.24	0.83–1.87		736	13.6	**1.53**	**1.04–2.26**		758	14.1	1.46	0.99–2.15	
	Some	576	14.2	1.36	0.90–2.04	**0.011**	491	16.7	**1.88**	**1.25–2.82**	**0.007**	494	13.2	1.32	0.87–2.02	**0.005**
	High	332	15.7	1.51	0.97–2.37		286	15.4	**1.76**	**1.11–2.80**		287	16.7	**1.79**	**1.14–2.82**	
	Very high	270	17.0	**1.72**	**1.08–2.74**		218	15.6	**1.80**	**1.10–2.96**		233	17.6	**1.91**	**1.19–3.07**	
40–49	Not at all	464	11.6	1.00			488	13.7	1.00			463	13.0	1.00		
	Low	684	17.4	**1.46**	**1.03–2.07**		755	15.8	1.04	0.75–1.45		755	17.2	1.22	0.87–1.71	
	Some	553	17.9	1.43	0.99–2.07	**<0.001**	534	19.3	1.28	0.91–1.81	**<0.001**	528	17.8	1.24	0.87–1.79	**0.002**
	High	286	20.6	**1.82**	**1.21–2.75**		244	19.7	1.37	0.91–2.08		247	20.6	**1.59**	**1.05–2.41**	
	Very high	184	22.8	**1.90**	**1.20–3.01**		155	25.2	**1.86**	**1.18–2.94**		195	21.5	1.50	0.95–2.35	
50+	Not at all	1312	8.5	1.00			1330	9.8	1.00			1203	9.5	1.00		
	Low	1123	10.5	1.28	0.96–1.69		1242	9.8	1.02	0.78–1.34		1249	10.2	1.11	0.84–1.46	
	Some	1042	12.6	**1.59**	**1.20–2.11**	**<0.001**	992	12.5	1.31	0.99–1.73	**<0.001**	1059	13.4	**1.58**	**1.20–2.09**	**0.001**
	High	505	15.4	**2.02**	**1.45–2.81**		463	15.1	**1.71**	**1.23–2.37**		518	12.7	1.39	0.98–1.97	
	Very high	305	15.4	**1.84**	**1.23–2.74**		293	16.0	**1.71**	**1.16–2.53**		349	13.8	**1.50**	**1.01–2.23**	

[a] Age when answering questionnaire

[b] Adjusted for smoking habits, alcohol consumption, organic solvents or paint, welding, torch-cutting or working with hull and lead. OR, Odds ratios

[c] CI, Confidence interval

[d] Test for linear trend (Mantel–Haenszel chi-square)

Statistically significant results are in bold

or older. The exposure was not linearly associated with whether they had biological children (chi-square). Nor were exposure and number of children significantly associated (linear regression). This analysis was stratified by age groups and adjusted for alcohol use and smoking habits.

A total of 18,625 children were born after the fathers have had occupation in the Navy. For both self-reported exposure to work closer then 10 m from high-frequency aerials and 3 m from communication equipment there were a significant linear trend with lower sex ratio (boys to girls births) with higher degree of exposure (Table 4). A similar, but weaker and not significant trend was seen for father's exposure to radar.

Discussion

Self-reported exposure to radiofrequency electromagnetic fields among Navy personnel was significantly and linearly associated with 1 year infertility. This applied to work close to high-frequency aerials, communication equipment and radar both for the whole population and for all age groups (except personnel younger than 30 years working close to communication equipment). The correlation with infertility was even stronger among those who were involuntarily childless. In addition there was a decrease in the offspring sex ratio, boys to girls, when the fathers reported that they had worked with a higher degree of exposure to radiofrequency fields.

Our findings on infertility are in accordance with previously findings where semen quality was reduced after occupational exposure to electromagnetic fields. In a study of 365 infertile couples, Irgens et al. found that among men occupationally exposed to electromagnetic fields (worked as welders, cooks or electricians) had reduced semen quality [10]. Another study among 31 men with long-term occupational exposure to microwaves (10,000–

Table 3 Fertility problems and involuntary childlessness by degree of self-reported exposure to high-frequency aerials in four age groups

	Work closer than 10 m from high-frequency aerials		Fertility problems[a]				Involuntary childlessness[b]			
Age (years)		Total	*n*	OR[c]	95% CI[d]	*P*[e]	*n*	OR[c]	95% CI[d]	*P*[e]
≤29	Not at all	47	1	1.00			3	1.00		
	Low	43	6	6.24	0.71–55.03		0	–	–	
	Some	29	1	1.41	0.08–23.93	.065	2	1.15	0.18–7.42	**0.010**
	High	24	1	2.54	0.15–43.60		7	**7.21**	**1.62–32.09**	
	Very high	26	5	**10.92**	**1.17–101.71**		3	2.23	0.40–12.40	
30–39	Not at all	278	28	1.00			12	1.00		
	Low	488	60	1.28	0.79–2.06		20	1.01	0.49–2.11	
	Some	450	54	1.23	0.76–2.00	0.194	28	1.48	0.74–2.99	**0.011**
	High	257	33	1.35	0.79–2.31		19	1.90	0.90–4.01	
	Very high	216	29	1.45	0.83–2.53		17	2.08	0.96–4.48	
40–49	Not at all	426	47	1.00			7	1.00		
	Low	628	91	1.36	0.93–1.98		28	**2.84**	**1.23–6.59**	
	Some	517	71	1.26	0.84–1.87	**0.003**	28	**3.40**	**1.46–7.91**	**0.007**
	High	266	46	**1.73**	**1.11–2.70**		13	**3.22**	**1.26–8.21**	
	Very high	169	33	**1.99**	**1.22–3.26**		9	**3.14**	**1.11–8.86**	
≥50	Not at all	1259	81	1.00			31	1.00		
	Low	1090	82	1.20	0.87–1.66		36	1.42	0.87–2.32	
	Some	1009	90	**1.40**	**1.02–1.93**	**<0.001**	41	**1.78**	**1.10–2.87**	**<0.001**
	High	487	58	**2.06**	**1.44–2.96**		20	**1.90**	**1.07–3.39**	
	Very high	290	25	1.45	0.90–2.34		22	**3.16**	**1.76–5.68**	

[a] Had children and reported infertility for 1 year

[b] No children and reported infertility for 1 year

[c] OR relative to those who have had children and reported no infertility. Adjusted for smoking habits and alcohol consumption. OR, Odds ratio

[d] CI, Confidence interval

[e] Test for linear trend (Mantel–Haenszel chi-square)

Statistically significant results are in bold. The analysis excludes those who did not answer the question on infertility or answered “do not know” and those who reported no problems with infertility and did not have children

3,600 MHz) also reported significantly reduced sperm quality compared with 30 controls [11].

Recently, male reproductive health and the use of mobile phones have been studied. In an in vitro study [16], semen samples from each of the 27 men participating were divided in two parts. One part was exposed to an activated 900 MHz cellular phone and the other part was unexposed. The exposed group had significantly decreased sperm motility. A study in Australia found significantly lower sperm motility and sperm concentration among 52 men who carried mobile phone close to the testes compared with those who did not [17]. Another study of 371 men also associated reduced sperm motility with prolonged use of mobile phones, information of use of hands free was not available in this study [18].

In addition, a study among soldiers who had experienced microwave exposure as radar equipment operators (intelligence radar) showed significantly lower sperm counts and a lower percentage of motile sperm than the comparison group [12]. Another military study reported reduced semen quality ($P = 0.07$) among 19 men operating military missile tracing radar compared with other non-military workers [13]. In contrast, soldiers exposed to communication radar in the military had no significantly reduced semen quality [14]. Schrader et al. [14] suggested that the differences in the results were caused by low exposure in their study [14]. However, some of these studies [11, 12, 14] were based on volunteers and may therefore be biased. Grajewski et al. [15] measured several parameters of semen quality and hormone levels among 12 men exposed to non-ionizing radiation and 34 men without such exposure. The groups differed slightly in semen quality and hormone levels, but a low participation rate and multiple testing make the results unreliable.

The effect of radiofrequency electromagnetic exposure on sex ratio of offspring has been debated lately [23, 30]. Several studies have reported a decrease in sex ration of offspring, with less boys borne, but these studies are small [20–23] and only one of these studies has shown significant findings [22]. Opposite to these findings Mjoen et al. [31]

Table 4 Sex ratio of offspring by father's exposure to self-reported radiofrequency electromagnetic fields

Exposure	Degree of exposure level	Children[a]		Boys			
		N	%	%	OR	95% CI	*P*[b]
Work closer then 10 m from high-frequency aerials	Not at all	4595	25.9	52.1	1.00		
	Low	4898	27.6	51.8	0.99	0.91–1.07	
	Some	4528	25.5	52.6	1.02	0.94–1.11	**0.008**
	High	2282	12.8	50.0	0.91	0.83–1.01	
	Very high	1457	8.2	47.6	**0.84**	**0.74–0.94**	
	Total	17760	100.0				
Work closer then 3 m from communication equipment	Not at all	4738	26.5	51.9	1.00		
	Low	5610	31.4	52.2	1.01	0.94–1.09	
	Some	4222	23.7	51.8	0.99	0.92–1.08	**0.031**
	High	1991	11.2	50.2	0.93	0.84–1.04	
	Very high	1286	7.2	48.1	**0.87**	**0.77–0.98**	
	Total	17847	100.0				
Work closer then 5 m from radar	Not at all	4321	24.0	52.2	1.00		
	Low	5612	31.1	51.7	0.98	0.90–1.06	
	Some	4377	24.3	52.0	0.99	0.91–1.08	0.062
	High	2158	12.0	48.8	**0.87**	**0.79–0.97**	
	Very high	1559	8.6	50.9	0.93	0.83–1.05	
	Total	18027	100.0				

[a] Children borne after first occupation in the Navy

[b] Test for linear trend (Mantel–Haenszel chi-square)

Statistically significant results are in bold

reported recently a borderline significant increase in proportion of males borne by fathers possible exposed to radiofrequency electromagnetic fields. This study was a large register study, but the exposure classification was very crude and may have led to misclassification.

Radiofrequency electromagnetic radiation may have both thermal and non-thermal effects. There is no agreement on which might be most important for possible adverse effects on reproductive health. The effects caused by temperature rise are basically understood; this may reduce sperm quality [32]. However, the existence of non-thermal effects is more hotly debated. Foster [33] discussed that radiofrequency electromagnetic radiation could have effects on the cell membrane excitation and breakdown and also direct electrical forces on cells or cell constituents in addition to thermal effects on biological systems. Fejes et al. [18] have formulated two hypotheses on how radiofrequency radiation may affect male fertility. One suggests that the testis is affected by a change in melatonin level. The other hypothesis is that radiofrequency radiation may cause DNA damage in the genital tract.

Sex ratio at birth is related to a number of different mechanisms, among them changes in hormone profile [34]. A lowered ratio of testosterone/gonadotrophin in male has been suggested to be causally associated with lower sex ratio in offspring [30]. The lowered hormone ratio is also reported among men exposed to radiofrequency radiation [15].

We focused on non-ionizing radiation, but the workers may have been exposed to other factors as well. A study in Germany [35] described ionizing radiation related to three types of radar in Germany's army. However, the Norwegian Navy has not used any of these types of radar [36], and we have no knowledge about exposure to ionizing radiation in our population.

Our study participants reported exposure both at work and outside work, which is a strength. However, the exposure was rather roughly described and includes no objective measures so the relevance of the findings for similar exposure in civilian setting is difficult. The three different sources of exposure to radiofrequency radiation were highly correlated and seem to coexist to a high degree. This makes them difficult to separate. Further, exposure to non-ionizing electromagnetic fields at lower frequencies may have been present. No information on the duration of the exposure was obtained nor whether the specific exposure had taken place before planning a pregnancy or whether they were exposed at the time they tried to achieve pregnancy. However, we can assume that the participants had been exposed to radiofrequency radiation before they started family planning, as most of the exposure was reported from their work in the Navy and the vast majority began in the Navy (mean age 20 years) before they started their reproductive career.

Duty on board a ship often means long journeys away from home. Sailing time was not measured and might have been a confounding factor since such long journeys could be related to reduced possibility of conceiving, and since we assume that the exposure was highest on board ships. Nevertheless, since exposure to all three electromagnetic field variables was likely associated with time on board ships, adjusting for one of the electromagnetic field variables might therefore be considered as a proxy adjustment for being on board a ship. The effect of high-frequency aerials was not reduced when adjusted for exposure to communication equipment. This indicates that our findings are unlikely to be an effect of long periods away from home.

The response rate was 63%, but the prevalence of infertility of 15% among the responders was in accordance with other studies of infertility [37, 38] and does not indicate that those with infertility problems were overrepresented in our study.

In a cross-sectional survey, there are several potential sources for bias. The information about exposure and outcome was self-reported and obtained from the same questionnaire. Common method bias was therefore possible: a person reporting high exposure might tend to over report the outcome. In addition, there may have been recall bias: a person with a negative outcome might remember exposure better. However, since the exposure was classified from not at all to a very high degree and the results showed significant linear trends for all age groups, ascribing all the results to bias is less likely. Further, the fact that the effect of exposure to high-frequency aerials did not change when adjusted for other types of radiofrequency exposure indicates that common method bias cannot explain all the results. Finally the effect on the sex ratio cannot be ascribed common method bias or recall bias and it has been clamed that offspring's sex ratio for this reason has an advantage as a monitor of reproductive hazard [19].

Although infertility increased among men exposed to radiofrequency electromagnetic fields, the degree of exposure was not related to the proportion of respondents reporting having children. Further, the mean number of children was the same in the exposure subgroups. However, the number of children is not solely a biological issue. Today it is also a social decision, due to family planning, and the number of children is therefore not an optimal measure of fertility as a health parameter. Also, an effect of occupational factors might be temporary. One study has reported that, among men with long-term occupational microwave exposure, two thirds had improved spermatogenesis after 3 months without the exposure [11].

In conclusion, increasing self-reported work near equipment emitting radiofrequency electromagnetic fields among Navy personnel was significantly linearly associated with more reported infertility. Among those who had no children, the association was even stronger. The offspring's sex ratio showed a significant linear trends with lower ratio of boys to girls at birth when the father reported a higher degree of exposure to high-frequency aerials and communication equipment.

Acknowledgments We thank The Royal Norwegian Navy for funding the research program Health, Safety and Work Environment in the Royal Norwegian Navy and the employees in the Royal Norwegian Navy for participating in the study. We are also grateful to Stein Emil Vollset, University of Bergen for important comments in the process of the study and on the article.

References

1. Skakkebaek NE, Jorgensen N, Main KM, et al. Is human fecundity declining? Int J Androl. 2006;29:2–11.
2. Sallmen M, Weinberg CR, Baird DD, Lindbohm ML, Wilcox AJ. Has human fertility declined over time? Why we may never know. Epidemiology. 2005;16:494–9.
3. Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Evidence for decreasing quality of semen during past 50 years. BMJ. 1992;305:609–13.
4. Auger J, Kunstmann JM, Czyglik F, Jouannet P. Decline in semen quality among fertile men in Paris during the past 20 years. N Engl J Med. 1995;332:281–5.
5. Andersen AG, Jensen TK, Carlsen E, et al. High frequency of sub-optimal semen quality in an unselected population of young men. Hum Reprod. 2000;15:366–72.
6. Bonde JP, Ernst E, Jensen TK, et al. Relation between semen quality and fertility: a population-based study of 430 first-pregnancy planners. Lancet. 1998;352:1172–7.
7. Bonde JP. Environmental fertility research at the turn of the century. Scand J Work Environ Health. 1999;25:529–36.
8. Ahlbom A, Green A, Kheifets L, Savitz D, Swerdlow A, ICNIRP. Epidemiology of health effects of radiofrequency exposure. Environ Health Perspect. 2004;112(17):1741-54.
9. Mageroy N, Mollerlokken OJ, Riise T, Koefoed V, Moen BE. A higher risk of congenital anomalies in the offspring of personnel who served aboard a Norwegian missile torpedo boat. Occup Environ Med. 2006;63:92–7.
10. Irgens A, Kruger K, Ulstein M. The effect of male occupational exposure in infertile couples in Norway. J Occup Environ Med. 1999;41:1116–20.
11. Lancranjan I, Maicanescu M, Rafaila E, Klepsch I, Popescu HI. Gonadic function in workmen with long-term exposure to microwaves. Health Phys. 1975;29:381–3.
12. Weyandt TB, Schrader SM, Turner TW, Simon SD. Semen analysis of military personnel associated with military duty assignments. Reprod Toxicol. 1996;10:521–8.
13. Hjollund NHI, Bonde JPE, Skotte J. Semen analysis of personnel operating military radar equipment. Reprod Toxicol. 1997;11:897.
14. Schrader SM, Langford RE, Turner TW, et al. Reproductive function in relation to duty assignments among military personnel. Reprod Toxicol. 1998;12:465–8.

15. Grajewski B, Clinton C, Schrader SM, et al. Semen quality and hormone levels among radiofrequency heater operators. J Occup Environ Med. 2000;42:993–1005.
16. Erogul O, Oztas E, Yildirim I, et al. Effects of electromagnetic radiation from a cellular phone on human sperm motility: an in vitro study. Arch Med Res. 2006;37:840–3.
17. Kilgallon SJ, Simmons LW. Image content influences men's semen quality. Biol Lett. 2005;1:253–5.
18. Fejes I, Zavaczki Z, Szollosi J, et al. Is there a relationship between cell phone use and semen quality? Arch Androl. 2005;51:385–93.
19. James WH. Male reproductive hazards and occupation. Lancet. 1996;347:773.
20. Knave B. Long-term exposure to electric-fields—cross-sectional epidemiologic investigation of occupationally exposed workers in high-voltage substations. Scand J Work Environ Health. 1979;5:115–25.
21. Nordstrom S. Reproductive hazards among workers at high-voltage substations. Bioelectromagnetics. 1983;4:91–101.
22. Mubarak Aas. Does high voltage electricity have an effect on the sex distribution of offspring? Hum Reprod. 1996;11:230–1.
23. Saadat M. Offspring sex ratio in men exposed to electromagnetic fields. J Epidemiol Community Health. 2005;59:339.
24. Kumar S. Occupational exposure associated with reproductive dysfunction. J Occup Health. 2004;46:1–19.
25. Luderer U, Bushley A, Stover BD, et al. Effects of occupational solvent exposure on reproductive hormone concentrations and fecundability in men. Am J Ind Med. 2004;46:614–26.
26. Winker R, Rudiger HW. Reproductive toxicology in occupational settings: an update. Int Arch Occup Environ Health. 2006;79:1–10.
27. Shiau CY, Wang JD, Chen PC. Decreased fecundity among male lead workers. Occup Environ Med. 2004;61:915–23.
28. Joffe M, Bisanti L, Apostoli P, et al. Time to pregnancy and occupational lead exposure. Occup Environ Med. 2003;60:752–8.
29. Aasland OG, Amundsen A, Bovim G, Fauske S, Morland J. [Identification of patients at risk of alcohol-related damage]. Tidsskr Nor Laegeforen. 1990;110:1523–7.
30. James WH. Offspring sex ratios of people exposed to electromagnetic fields. J Epidemiol Community Health. 2005;59:810.
31. Mjoen G, Saetre DO, Lie RT, Tynes T, Blaasaas KG, Hannevik M, Irgens LM. Paternal occupational exposure to radiofrequency electromagnetic fields and risk of adverse pregnancy outcome. Eur J Epidemiol. 2006;21:529–35.
32. Hietanen M. Establishing the health risks of exposure to radiofrequency fields requires multidisciplinary research. Scand J Work Environ Health. 2006;32:169–70.
33. Foster KR. Thermal and nonthermal mechanisms of interaction of radio-frequency energy with biological systems. IEEE Trans Plasma Sci. 2000;28:15–23.
34. James WH. Evidence that mammalian sex ratios at birth are partially controlled by parental hormone levels at the time of conception. J Theor Biol. 1996;180:271–86.
35. Rapport fra ekspertkommissionen vedrørende spørsgsmålet om den fare, der utgår fra stråling fra tidligere radaranlæg i "Bundeswehr" og "Nationale Volksarmee" (Radarkommission). Berlin, den 2.juli 2003.
36. Frogner T. Historisk granskning av radar i det norske forsvar. Forsvarets laboratorietjeneste, EMC/Kraftforsyning laboratorium 2006-03-31.
37. Bonde JP, Hjollund NH, Kolstad HA, Abell A, Larsen SB. Environmental semen studies—is infertility increased by a decline in sperm count? Scand J Work Environ Health. 1999;25(Suppl 1):12–6.
38. Schmidt L, Munster K. Infertility, involuntary infecundity, and the seeking of medical advice in industrialized countries 1970–1992—a review of concepts, measurements and results. Hum Reprod. 1995;10:1407–18.