UMTS base station like exposure, well being and cognitive performance

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Abstract

Radio-frequency electromagnetic fields (RF EMF) of mobile communication systems are widespread in the living environment, yet their effects on humans are uncertain despite a growing body of literature. The present study investigated the influence of a Universal Mobile Telecommunication System (UMTS) base station-like signal on well being and cognitive performance in subjects with and without self-reported sensitivity to RF EMF. 117 healthy subjects (33 self-reported sensitive, 84 non-sensitive subjects) were exposed for 45 min to an electric field strength of 0, 1 or 10 V/m at weekly intervals in a randomized, double-blind crossover design. Well being, perceived field strength and cognitive performance were assessed with questionnaires and cognitive tasks and statistical analyses were conducted using linear mixed models. Organ and brain tissue specific dosimetry including uncertainty and variation analysis was performed. In both groups, well being and perceived field strength were not associated with actual exposure levels and no consistent condition-induced changes in cognitive performance could be detected except for two marginal effects. At 10 V/m, a slight effect on speed in one of six tasks in the sensitive subjects and an effect on accuracy in another task in non-sensitive subjects was observed. Both effects disappeared after multiple endpoint adjustment. Peak spatial absorption in brain tissue was considerably smaller than during usage of a mobile phone.

In contrast to a recent Dutch study, no evidence was found for a short-term effect of UMTS-like exposure on well being. The reported effect on brain functioning was marginal and may have occurred by chance. Peak spatial absorption in brain tissue was considerably smaller than during usage of a mobile phone. No conclusions can be drawn regarding short term-effects of cell phone exposure or the effects of long-term base station-like exposure on human health.

Introduction

In 2003, a Dutch study on the effects of controlled exposure to mobile communication system radio-frequency fields at base station intensities on human well being and cognitive functions was published (Zwamborn et al., 2003), hereafter called TNO study (TNO Physics and Electronics Laboratory). Effects of two systems were explored, the second generation Global System for Mobile Communication (GSM) that is widely used in Europe and other parts of the world, and the Universal Mobile Telecommunications System (UMTS), the third generation of mobile networks and the successor of GSM. Two groups of subjects were investigated, consisting of individuals with and without self-reported health complaints attributed to daily life exposures to radiofrequency (RF) electromagnetic fields (EMF). Whereas exposure to GSM-like EMF had no effect at the time-averaged incident electric field (E-field) strength of 0.7 V/m, UMTS-like exposure at an E-field strength of 1 V/m reduced well being in both groups. No consistent effects on cognitive performance were found. The 3 dB difference of the averaged incident fields was unlikely to have contributed to the different outcome of GSM and UMTS exposure on well being. The results were hypothesized to be due to the different modulation schemes.

The TNO-study was the first study to investigate UMTS-like exposure and to indicate a reduction in well being. With respect to the stronger but much more localized exposure by mobile phone handsets there is an abundant, yet controversial body of research regarding potential non-thermal effects on humans or human tissues. Data on well being are inconclusive (for a review see Seitz et al. 2005), yet various studies identified subtle effects regarding changes in brain activity or influences on cognitive function such as reaction times, working memory and attention (e.g. Curcio et al. 2005; Freude et al. 2000; Huber et al. 2002: Huber et al. 2005; Hyland 2000; Koivisto

et al. 2000b; Krause et al. 2000). Some of the reported changes (e.g., acceleration of response times in certain cognitive tasks, altered oscillatory activity in the EEG as a function of time and task) were however inconsistent and could not be replicated (Haarala et al. 2003; Krause et al. 2004; Preece et al. 2005).

An ongoing debate in RF EMF research and the general public is concerned with self-reported electromagnetic hypersensitivity (EHS) relating to persons attributing subjective complaints of impaired well being (e.g., headache, nausea, sleep disturbances) to EMF exposure comprising radio frequency, as well as extremely low-frequency fields of domestic power supplies (e.g. National Institute of Environmental Health Sciences – NIEHS Working Group Report 1998; Röösli et al. 2004). Prevalence of EHS was reported to range from 1.5% in Sweden (Hillert et al. 2002) up to 5% in Switzerland (Röösli et al. 2005) according to population based surveys, but so far, no causal link was found between exposure to mobile phones and EHS symptoms (for a review see Rubin et al. 2005) and objective criteria for EHS specification could not be established.

The persisting uncertainty associated with potential adverse health effects of the new UMTS technology, together with its rapidly ongoing implementation has lead to widespread public concern in many countries. The present experiment was designed as a follow-up study to clarify the reliability of the TNO study that was largely debated in the scientific community. Meanwhile, additional follow up studies were initiated in Denmark, the United Kingdom and Japan (Andersen J, Challis L, Watanabe S, personal communications). We used Validated measuring instruments and an improved setup yielding better uniformity of exposure, as well as an additional E-field strength (10 V/m) to establish a dose-response relationship. Based on the results reported by Zwamborn et al. (2003), we hypothesized that exposure to UMTS-

like radiation would attenuate subjective well being in both sensitive and non-sensitive subjects, possibly in a dose-dependent manner, but would not affect cognitive performance.

Methods

Study Participants

The effects of UMTS-like electromagnetic fields were investigated in a group of subjects with self-reported sensitivity to RF EMF (N=37) and in a reference group of subjects without complaints to RF EMF (N=91). Due to non-compliance of three subjects and eight dropouts, the final study group included N=33 sensitive (14 males, 19 females) and N=84 non-sensitive subjects (41 males, 43 females).

Both groups were recruited from the general public by advertisement in a local newspaper and by flyers. Sensitive subjects were also recruited from databases of two previous studies with participants that had indicated their willingness to participate in future research projects. Due to a lack of an operational tool for measuring sensitivity to EMF (WHO 2005), criteria for the recruitment of sensitive subjects were based on self-reported sensitivity to RF EMF, i.e. purported sensing of RF EMF or any afflictions that subjects related to RF EMF such as emitted by mobile or cordless phones and antennas.

More than 500 subjects were contacted by telephone and pre-selected by a standardized interview. Exclusion criteria for both groups were defined a priori, comprising pacemakers, hearing aids or artificial cochlea, regular consumption of narcotics or psychoactive drugs in the previous six months, smoking, polymorbidity with respect to chronic diseases, pregnancy, a medical history of head injuries and or neurologic/ psychiatric diseases, sleep disturbances, an average consumption of

alcohol larger than 10 drinks per week, and of caffeinated beverages amounting to more than 450 mg caffeine per day (e.g., approximately 3 cups of coffee). Shift workers and persons undertaking long-haul flights (>3 hour time zone difference) within the last month prior to or during the experiment were also excluded.

Recruitment started in January 2005 and continued throughout the whole experimental phase to replace subjects that cancelled their appointments prior to the experiment (20% of the recruited population). All subjects were asked to fill in a detailed questionnaire ("entry questionnaire") on their first appointment to verify the information made during the telephone interviews and to survey the exclusion and inclusion as well as the matching criteria (age (in decades), gender and residential area).

The entire reference group of non-sensitive subjects was frequency matched to the sensitive subject group, and a subgroup was post-hoc 1:1 matched with respect to the same criteria, but also including body mass index (BMI).

Recruited subjects were aged between 20 and 60 years (mean age of 37.7 ± 10.9 years (±SD)). Distribution with respect to residential area was even, with 54% of the study population living in an urban as opposed to a rural environment. The majority of subjects lived in a permanent relationship (59%) and was well educated with a high school or higher degree (63%). Similarly, most subjects (88%) were employed at least part-time or still in education, whereas only a few were unemployed. All subjects were right-handed (verified with the Edinburgh Handedness Inventory, Oldfield, 1971) and of normal body weight (BMI >19 and <30 kg/m^2). Overall BMI was 21.97 ± 2.70 for females and 24.06 ± 2.77 for males with no differences found between sensitive and non-sensitive subjects. For a description of the study population, please also refer to Table 1.

All subjects were reimbursed for their participation and gave their written informed consent. The ethical committee of the Canton Zurich for research on human subjects approved the study protocol.

		sensitive group (n=33)	Matched non-sensitive (n=33)	All non-sensitive (n=84)
Sex				
	female [%]	57.6	58.1	51.2
	male [%]	42.4	41.9	48.8
Age				
	mean [y] (SD)	37.8 (11.2)	37.8 (11.0)	37.6 (10.9)
	20-30 years [%]	30.3	29.0	29.8
	31-40 years [%]	33.3	32.3	32.1
	41-50 years [%]	21.2	22.6	21.4
	51-60 years [%]	15.2	16.1	16.7
BMI				
	mean [kg/m²] (SD)	21.7 (1.9)	22.8 (3.1)	23.4 (3.1)
	18-20 [%]	24.2	29.0	14.3
	20-25 [%]	72.7	45.2	51.2
	25-30 [%]	3.0	25.8	34.5
Educational status				
	no/little professional education [%]	3.0	0.0	2.4
	apprenticeship [%]	42.4	74.2	61.9
	higher education/ University [%]	54.5	25.8	35.7
Employment status				
	no employment [%]	9.1	0.0	2.4
	jobless [%]	0.0	9.7	10.7
	in education [%]	12.1	16.1	15.5
	part time [%]	36.4	38.7	33.3
	full time [%]	42.4	35.5	38.1
Region				
	urban [%]	51.5	51.6	54.8
	rural [%]	48.5	48.4	45.2

Table 1: Characteristics of the study participants.

Study Design

The study was performed at the Institute of Pharmacology and Toxicology, University of Zurich between February 1 and May 20, 2005. It consisted of three experimental sessions separated by one-week intervals with a tolerance of ±1 day, preceded by a training session 7±1 days prior to the first experimental session. Experimental sessions were always scheduled at the same time of day for each subject (± 2h), Tuesdays to Fridays between 11:30-21:00h and Saturdays between 09:30-19:00h. Subjects were evenly distributed across the experimental period (32% in February, 24% in March, 31% in April and 13% in the first half of May) and across week-days (Tuesday: 22.2%, Wednesday: 24%, Thursday: 21.4% and 16.2% each on Friday and Saturday). The circadian distribution was also equilibrated with each 30% of the subjects performing the experiment in the morning (10-14h) and evening hours (18-22h), and 40% of the subjects having their sessions in the afternoon (14-18h).

Subjects were asked to abstain from any medication 24 h prior to each session and were also requested not to use a mobile or cordless phone for 12 h preceding the sessions.

Exposure was computer controlled providing double blind conditions that were applied in a randomized crossover design. Before and after exposure, subjects filled in the questionnaires in an office room and were then escorted to the exposure chambers. Exposure took place in the basement of the laboratory in two identical and specially adapted, but separate rooms with constant temperature and light conditions (see Figure 1).

Figure 1: Experimental room with exposure chamber.

Two subjects were investigated in parallel and were assigned to either a non-sensitive pair, consisting of two non-sensitive subjects, or a mixed pair, including one sensitive and one non-sensitive subject. Pairs were randomly assigned to one of six possible sequences of the three exposure conditions in a counterbalanced way (sham, 1 V/m, 10 V/m), but subjects in each pair were shifted by 20 min to minimize the contact between them (Table 2).

N (sens/ non-sens)	**Session 1**	**Session 2**	**Session 3**	**Session 4**
5 / 13	Training	Sham	1 V/m	10 V/m
6 / 14	Training	Sham	10 V/m	1 V/m
6 / 14	Training	1 V/m	Sham	10 V/m
5 / 14	Training	1 V/m	10 V/m	Sham
6 / 15	Training	10 V/m	1 V/m	Sham
5 / 14	Training	10 V/m	Sham	1 V/m

Table 2: Treatments and exposure conditions.

With one exception, subjects were always assigned to the same room and generally stayed alone during exposure. The experimenter ensured the safety of the subjects by supervising them and the experiment from outside the room via computer and a web cam, which was also used to record body movements that may affect the SAR distribution (recordings of one frame/s). Four subjects needed to be accompanied by the experimenter, yet the interaction was minimized as far as possible.

When the subject was ready, the experimenter left the room and started the exposure, which lasted 45 min. During exposure, subjects performed two series of cognitive tasks (session 1 and 2), starting at the beginning and after 22 min of exposure, respectively. Between sessions, subjects had to remain in front of the computer and were allowed to read magazines. After finishing the second session, they were presented with landscape movies on the computer screen. Completion of one experimental session took about 55-70 min. Training sessions continued for as long as it took the subjects to fill in the entry questionnaire, get familiar with the procedures and practice the cognitive tasks until they were completely understood.

Exposure and Dosimetry

Each experimental room included an exposure area installed as a one side open chamber shielded with RF radiation absorbers (Figure 2). The antenna (Huber&Suhner type SPA 2000/80/8/0/V) was placed in 1.5 m height and 2 m distance from the subjects, targeting the left side of the body from behind, with a field incidence angle of 25° with respect to the ear-ear vertical plane (see Figures 2 and 7). To produce the same polarization as in the TNO study, the antenna and thus the E-field were tilted 45° from vertical. The antenna possessed a –3 dB beam width of

approximately 75° in horizontal and vertical directions, resulting in a uniform E-field distribution similar to the far field of a base station (Figure 6). Field uniformity was verified before and after the experimental phase by scanning the exposure area with a field probe. The UMTS signal format was identical to the one used by Zwamborn et al. (2003), consisting of four control and synchronization channels (Primary Synchronization Channel (P-SCH) at -8.3 dB below total RF power, Secondary Synchronization Channel (S-SCH), at -8.3 dB, Primary Common Control Physical Channel (P-CCPCH), at -5.3 dB, Common Pilot Channel (CPICH), at -3.3 dB) with a center frequency of 2140 MHz and chip rate of 3.84 Mchips/s. The signal, generated by a commercial generator (Agilent E4433B Options 200, 201, UN8, UN9), corresponded to a UMTS base station frequency division duplex mode downlink configuration with no active voice calls.

Each chamber was equipped with a wooden table and chair, a flat panel monitor with keyboard, a plastic response box for the cognitive tasks and the UMTS antenna with a field probe (Figure 2). The web cam that recorded the subjects from top left (1 frame/s) and the computer hardware were kept outside the exposure chamber. The sum of all magnetic fields (frequency range 30 Hz to 400 kHz) was below 0.2 μT. Background RF radiation levels (80 MHz to 4 GHz) were measured before and after the experiment and they remained below 1 mV/m over the whole exposure area.

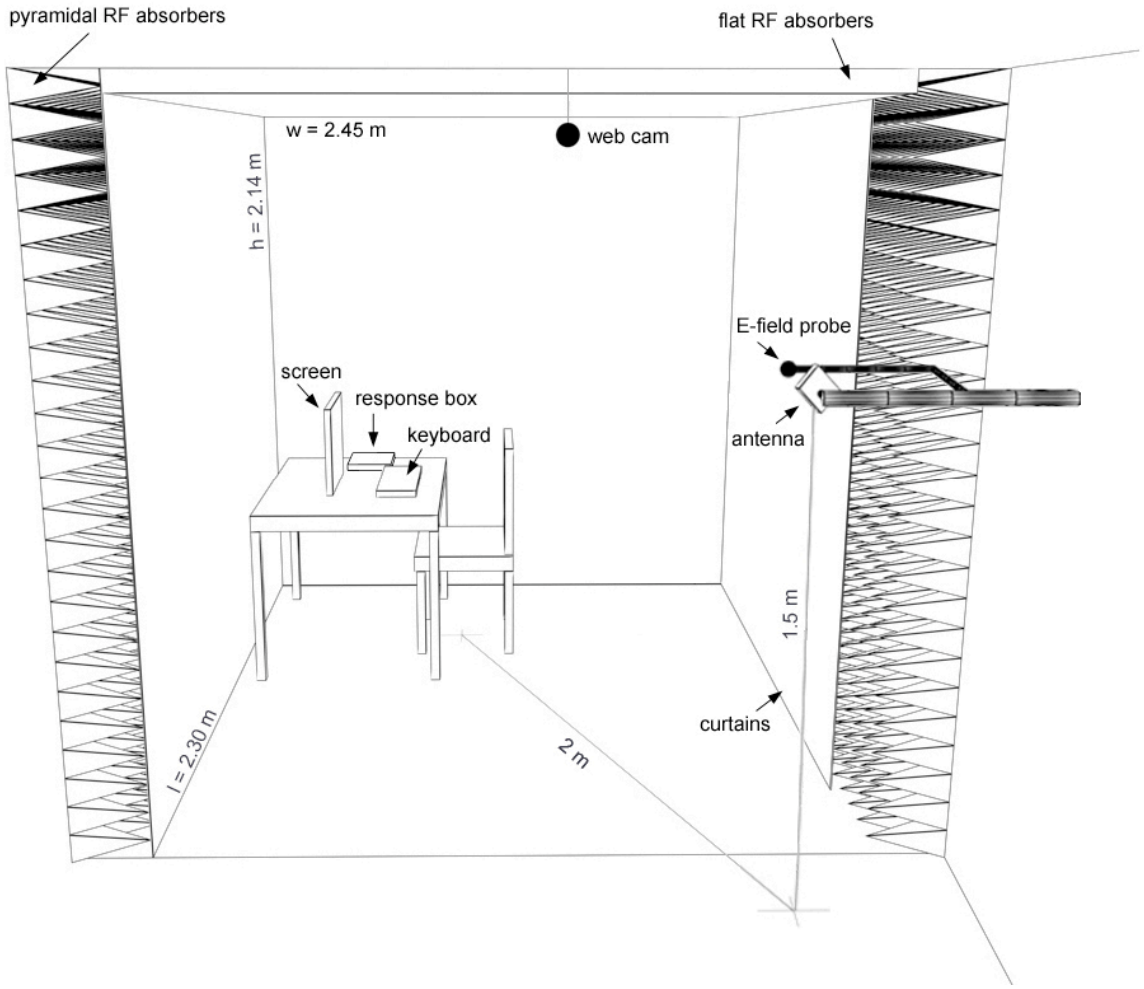

Figure 2: Sketch of the exposure chamber. Walls covered by pyramidal RF absorbers and non-reflecting curtains. Ceiling covered by flat absorbers. Antenna, electric field probe, furniture, screen, keyboard, response box, and web cam, inner dimensions (w: width; h: height; l: length), and position of the antenna are indicated.

Exposure was continuously monitored and regulated (3-axis E-field probe). The software included comprehensive safety and malfunctioning tracking features. Correctness of the applied exposure condition and the actual transmitted electromagnetic field was regularly verified by an external technician not actively involved in the experimental procedure. All recoded data were stored in an encrypted format and saved at two physical locations for evaluations by the technical partner.

Numerical dosimetry was conducted according to Kuster and Schönborn (2000) using the finite-difference time-domain (FDTD) simulation platform Semcad X (SPEAG, Switzerland) and three whole-body anatomical phantoms (two male, one female). Reflections from furniture were treated as uncertainty, reducing the computational space to 2.6 x 1 x 1.8 m^3 (l x w x h). The floor was modeled as concrete ($\varepsilon = 7.5$, $\sigma = 0.12$ S/m), whereas the walls and ceiling were modeled as perfectly absorbing boundaries. The numerical discretization of the chamber was 5 x 5 x 5 mm^3, of the human model 2 x 2 x 2 mm^3, and of parts of the antenna 1 x 0.5 x 1 mm^3, resulting in approximately 335 million voxels.

In dosimetry, an important part of the analysis is the assessment of the uncertainty and exposure variations, understanding uncertainty as the description of the confidence interval of the assessed mean SAR values for all subjects within the study, and variations as the deviations from the mean value for individual subjects in specific orientations to the field, e.g., due to position, posture, weight/size and others. The sources contributing to the absolute uncertainty of the average dosimetry were: 1) antenna modeling: 0.1 dB (experimentally verified); 2) deviation of incident field exposure with respect to the target field including transfer calibration, sensor linearity, feedback control and reflections from furniture: 0.7 dB; and 3) average anatomy, dielectric parameters and discretizations. The variation as function of weight, gender and position was assessed separately by 1) scaling the three phantoms in the range of our subjects (47-110 kg; head tissues were based on non-scaled phantoms), and 2) by rotating the phantoms ±25° around their axis. Due to good uniformity of the field, the effect of movement could be neglected.

Questionnaires

The *Short questionnaire on current disposition* (QCD) (Müller and Basler 1993) measures subjective well being within short test-retest intervals using six bipolar items (tense – calm; apprehensive – unperturbed; worried – unconcerned; anxious – relaxed; skeptical – trusting; uneasy – comfortable). Each item has to be assessed using a six-step scale with a higher score representing a higher perceived burden. The QCD has been validated in various studies during the last decade and a high correlation between QCD, physiological parameters and self-rated general well being was documented. Retest coefficients range between 0.72 and 0.91 and internal consistency (Cronbach's Alpha) ranges between 0.78 and 0.92. The QCD was applied immediately before and after (QCD_{post}) each experimental condition (test-retest interval of approximately 50 min) and completion required 1-2 min (Figure 3). The difference (QCD_{diff}) between post and pre experimental scores was calculated in order to reduce potential influences of daytime on performance. A difference score >0 corresponded to a degradation in current well being during the experiment.

The modified *Quality-of-life questionnaire* (Zwamborn et al. 2003), hence referred to as TNO-Q, was forward and backward translated (Dutch-German, German-Dutch) and used as a reference questionnaire for comparison with the TNO study. The validated, original questionnaire was developed specifically for hypertensive patients, estimating “quality of life” during trials of an antihypertensive drug treatment (Bulpitt and Fletcher 1990) and was modified by Zwamborn et al. (2003) by using a selection of 23 items separated in five subscales (anxiety, somatic symptoms, inadequacy, depression and hostility). For each item, score values included 0 (="not at all"), 1 (="a little bit"), 2 (="quite a bit"), and 3 (="extremely"). Total score as well as the score of all five subscales was calculated with a higher score

indicating more symptoms. The TNO-Q was applied after each experimental condition and completion required 2-5 min (Figure 3).

A self-designed questionnaire was applied after each experimental session to include other factors (QOF) potentially related to well being (sleep duration, quality of sleep in the previous night, suffering from a cold, amount of alcohol and caffeine consumed and medication taken on the day of the experimental session, (pre-) menstrual complaints and stressful events) (Figure 3). Moreover, subjects had to rate the perceived field strength of the same day's exposure condition on a visual analogue scale (100 mm), ranging from "not at all" to "very strong". They were asked to rate each condition independently, so that, in principle, the same assessment could be made for all three conditions.

A paper version of the *Bern questionnaire on well being* (BQW) (Grob 1995) was applied one week prior to the training session and one week after completion of the experiment (Figure 3). The BQW measures well being over a few weeks and consists of 39 items separated into two second-order scales (contentment, negative orientation) and six first-order scales (positive life attitude, self-esteem, depressive mood, vitality, problems, and physical complaints). Each item is assessed using a six-step scale with a higher score representing a higher or smaller perceived burden depending on the scale. The BQW was used to assess whether participation in the study per se had an influence on well being, irrespective of exposure, and whether the effect would differ between sensitive and non-sensitive subjects. As reference values of the BQW exist, well being of our study collective according to age groups (in decades) was also compared to the well being in a sample (N=500) of the general Swiss population (Grob 1995).

A shorter, computerized version including only eight items (BQW-short, Grob 1995) was filled in by the subjects after each experimental session. Test completion required 5-10 min (BQW) and 1-3 min (BQW-short). The paper version was sent and returned by postal mail. Completion of all questionnaires lasted about 5-15 min in total and was verified by a program showing a warning message in case one or more questions were not answered.

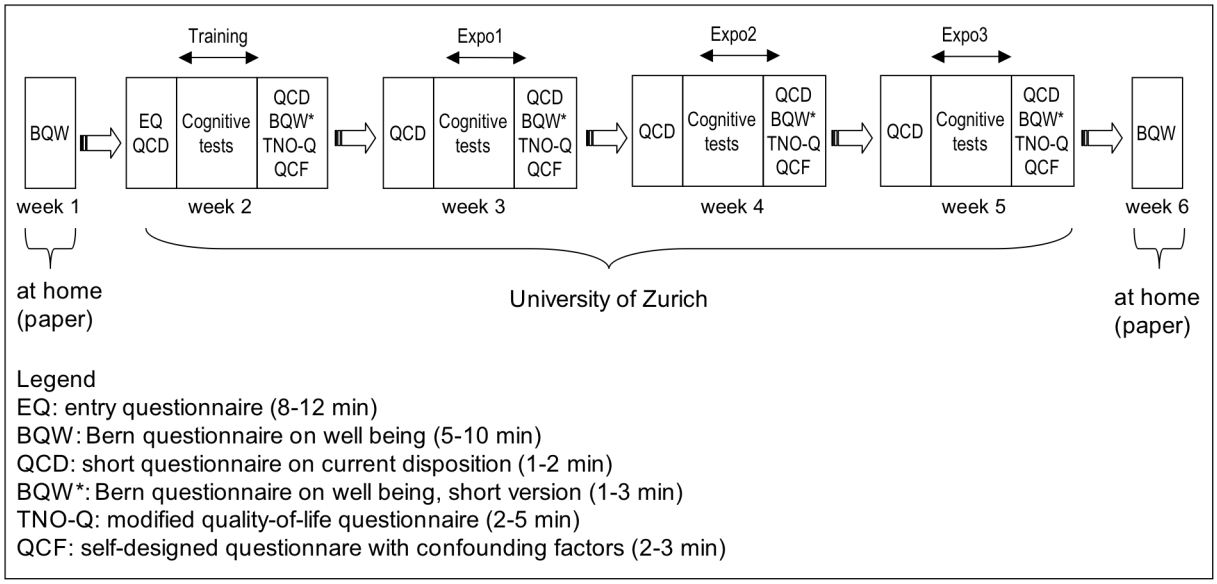

Figure 3: Overview of questionnaires

Cognitive Tasks

Four cognitive tasks previously applied in RF-EMF studies were selected to investigate the effects of UMTS-like radiation on brain functioning: the *Simple Reaction Time Task* (SRT) and *2-Choice Reaction Time Task* (CRT) (Koivisto et al. 2000b; Preece at al. 1999; Preece et al. 1998), the *N-back Task* (N-back) (Koivisto et al. 2000a) and the *Visual Selective Attention Task* (VSAT) adapted from Zwamborn et al. (2003). We implemented the tasks by using software from e-Prime (Psychology Software Tools Inc., USA). In all tasks, black stimuli were presented in a gray box

(SRT: 4.2 x 4.5 cm ; CRT: 5.9 x 4.5 cm ; N-back: 4.8 x 3.4 cm; VSAT: 10.0 x 7.5 cm (length x height)) in the middle of a black screen. The tasks were always applied in a fixed order (SRT, CRT, 1-, 2-, 3-back, VSAT) (Figure 4). Subjects were instructed to respond as quickly and accurately as possible by pressing various buttons corresponding to the respective targets on a response box.

In the SRT, a ”0” appeared on screen until the subjects pressed the corresponding “0” button with the right index finger. The next stimulus appeared with a random delay of 1000-4000 ms (in steps of 500 ms). A total of 42 targets per session was presented. Completion of the task took about 2-3 min.

In the CRT, either "*JA"* (yes) or "*NEIN"* (no) appeared on the screen and subjects had to press the corresponding “J” button with their right index finger and the “N” button with their right middle finger, respectively. The next stimulus appeared with a random delay of 1000-3500 ms (in steps of 500 ms). A total of 24 “yes” and 24 “no” targets per session was presented. Completion of the task took about 2-3 min.

In the N-back task the stimuli were single consonants presented in a random order with varying letter case. Three different memory workload levels were used. In the 1-back task, the target was any letter presented 1 trial back (i.e., G-g). In the 2-back and 3-back task, the target was any letter presented two trials (e.g., G-c-g) or three trials back (e.g., G-c-h-g). Each letter was displayed until the subject responded but maximally for 2000 ms (interstimulus interval 1000 ms). Subjects had to respond to the targets (same letter) with their right index finger, and to non-targets (different letters) with their right middle finger. Each task (1-back, 2-back and 3-back) consisted of 24 targets and 56 non-targets, preceded by a practice block without feedback including three targets and seven non-targets. Completion of the task took about 9-12 min.

In the VSAT a randomized combination of four letters and/or crosses arranged in a grey square was presented on the screen. The targets were the letters “U” and “F” appearing on the diagonal from upper left to lower right. Subjects were instructed to press the “J” button with their right index finger if one or both targets appeared and the “N” button with their right middle finger if no target was presented. Stimuli were displayed until the subject responded but maximally for 2000 ms (interstimulus interval 500 ms). Each session consisted of 16 targets and 64 non-targets, preceded by practice block with feedback including 3 targets and 7 non-targets. Completion of the VSAT took about 2-4 min. Completion of all tasks in one series took 15-20 min.

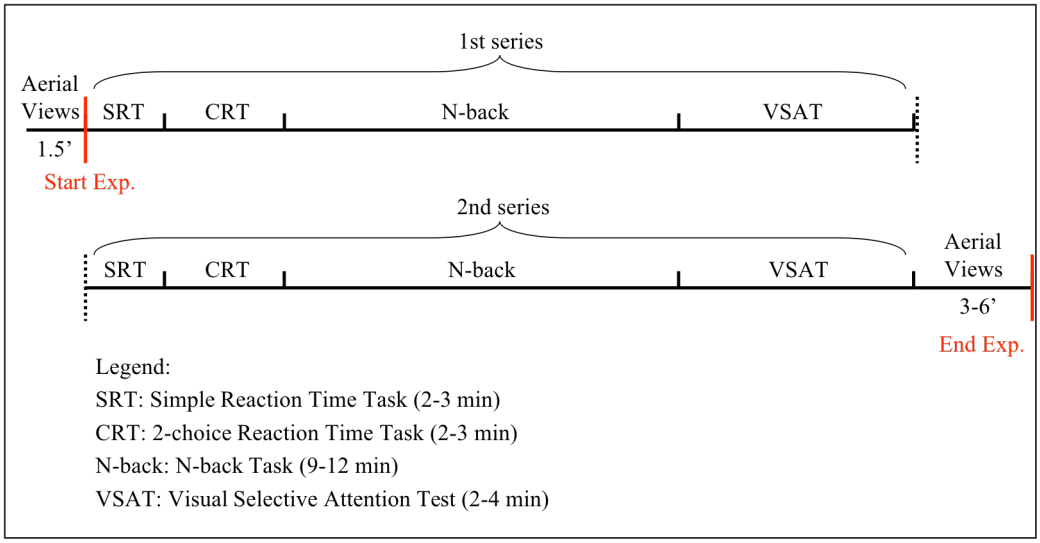

Figure 4: Overview of cognitive tests

Statistical analysis

Linear mixed models were used for statistical analyses (questionnaires: STATA 9.0 (StataCorp, USA); cognitive tasks: SAS 8.2 (SAS Institute Inc., USA)). With respect to reaction times, individual outliers over all sessions were excluded according to a robust rejection-estimation procedure (4* median deviation) (Hampel 1985). Exclusion of outliers accounted for 3.7-6.5% (SRT: 6.5%; CRT: 3.7%; 1-back: 5.4%; 2-back: 5.2%; 3-back: 5.0%; VSAT: 5.7%) and did not alter accuracy scores.

One session each was lost in the SRT and CRT in the sensitive group due to computer problems. In the non-sensitive group, four sessions each were lost for the same reason in the SRT, the N-back and the VSAT, as well as six sessions in the CRT. Other sessions that were excluded comprised two SRT sessions not performed in the right order and two sessions of the 1-back as well as one complete session 1-, 2-, 3-back, where the subject did not follow the instructions.

We transformed reaction times (1/ reaction time), which are referred to as speed [1/s; correct responses only] and checked residuals for normal distribution.

Stratified analyses were performed for the sensitive and non-sensitive group by using a random intercept model presuming an identical intraclass correlation for all subjects (STATA: option "*exchangeable*"; SAS: "*compound symmetry*"). The base model included the factor *Condition* (sham, 1, 10 V/m) and *Week* (1, 2, 3) to account for possible sequence effects. The model for cognitive data also contained the factor *Session* (S1, S2; first or second half of exposure) and corresponding interaction effects.The model was fitted using maximum likelihood and p-values were derived from maximum likelihood ratio tests. The factor *Condition* was modeled as a continuous variable to test for a dose response relationship. We used the values 0, 1, 100, proportional to the energy absorption of the body. Differences between groups were assessed with an overall model that also included the factor *Sensitivity* and a *Sensitivity*Condition* interaction. Robustness of results was evaluated by adjusting the model for potential confounding factors (see Table 3 and 5).

The percentage of correct answers in the CRT, 1-, 2-, 3-back and VSAT was used as a measure of accuracy. Except for the 3-back, residuals were not normally distributed and differences were assessed using non-parametric Wilcoxon-Signed-Rank tests. Comparisons of 1 V/m vs. sham and 10 V/m vs. sham were performed for

S1, S2, and the difference between the two sessions. The significance level was adjusted for multiple testing according to Bonferroni-Holm (Holm 1979).
In order to generally control for multiple testing, a multiple endpoint adjustment was performed for the cognitive outcomes using the method proposed by Tukey and colleagues (Tukey et al. 1985).

The ability to perceive EMF was analyzed by calculating Spearman rank correlations between perceived field intensity and true exposure status for each subject. We tested the number of positive and negative correlations using Sign test and used the same procedure to evaluate the association between perceived field intensity and well being (QCD, TNO-Q).

To assess whether participation per se had an effect on general well being within our two subject groups, differences in scores of the BQW_{prior} and BQW_{post} were analyzed using paired t-tests and the difference between the two groups assessed with a regression analysis. For the comparison of our study population with the general public with respect to general well being as assessed by the BQW_{prior}, differences in scores were evaluated with two sample t-tests.

Post hoc power analysis

A post hoc power analysis based on the observed data characteristics (N, mean, SD, within subject correlation) was conducted in order to estimate the power of the study. A repeated measurement power analysis (ANCOVA) was performed treating the 0 V/m condition as baseline and the exposure conditions as follow-up measurements. Minimal detectable differences refer to the mean difference between baseline and follow-up measurements assuming a power of 0.8 and a significance level of 0.05.

Results

Questionnaires

Well being as measured by the QCD and the TNO-Q was not affected by exposure (Table 3). With respect to the six items in the QCD and the five subscales of the TNO-Q, we found no significant exposure-response associations in any of the two groups. Irrespective of the actual condition, sensitive subjects generally reported more health problems, particularly in the TNO-Q.

Outcome	**Group**	**Sham**	**1V/m**	**10V/m**	**Cond[1]**	**Cond[2]**
		mean (SD)	mean (SD)	mean (SD)	p-value	p-value
QCD_{diff}	Sensitive	0.30 (0.83)	0.24 (0.99)	0.24 (0.95)	0.88	0.95
	Non-Sensitive	0.05 (0.73)	-0.04 (0.59)	0.02 (0.55)	0.93	0.95
QCD_{post}	Sensitive	2.57 (1.06)	2.65 (1.22)	2.61 (0.97)	0.97	0.96
	Non-Sensitive	2.19 (0.76)	2.05 (0.80)	2.13 (0.78)	0.97	0.89
TNO-Q	Sensitive	10.53 (9.51)	9.61 (8.96)	9.79 (8.38)	0.84	0.65
	Non-Sensitive	5.23 (5.09)	4.45 (4.92)	4.96 (5.08)	0.78	0.92
Field	Sensitive	26.0 (31.9)	31.2 (33.7)	29.4 (29.7)	0.89	0.67
perception	Non-Sensitive	12.9 (22.8)	5.7 (13.1)	12.2 (23.2)	0.24	0.33

[1] Adjusted for order; [2] Adjusted for order, age, gender, BMI, caffeine intake, medication, (pre-) menstrual complaints, sleep quality and suffering from a cold

Table 3: Results of applied questionnaires (mean scores; SD in parenthesis; N=33 sensitive and N=84 non-sensitive subjects). Outcomes of the QCD (*Short questionnaire on current disposition*) comprise the difference between pre and post experimental scores (QCD_{Diff}) as well as post experimental scores (QCD_{post}). A difference score >0 corresponds to a degradation in current well being during the experiment. In the QCD_{post} and the TNO-Q (*Quality-of-life questionnaire*) higher scores refer to a lower well being. We measured subjective field perception by means of a 100 mm visual analogue scale ranging from "*not at all"(0)* to *"very strong" (100 mm)*. We only report p-values of *Condition* (Cond) (for details see Methods).

Neither group showed a relationship between perceived field intensity and true exposure status (Table 4). Sensitive subjects indicated higher field strengths in all conditions ($p<0.001$), even though score values were not associated with exposure levels. 17 out of 31 sensitive subjects had a positive correlation between perceived and real field intensity, 13 a negative correlation (non-sensitive group: 22 and 27 out of 57 subjects, respectively), which can be expected by chance (Table 4). Irrespective of exposure condition, perceived field intensity was positively correlated with impaired well being in 68% of sensitive (QCD_{diff}: $p=0.043$) and 64% of non-sensitive subjects ($p=0.001$). Similar results were found with respect to the QCD_{post} and TNO-Q (data not shown).

		Correlation between perceived and real field			
	N	positive	negative	zero	p-value[1]
All	88	39	40	9	1
Sensitive	31	17	13	1	0.58
Non-Sensitive	57	22	27	8	0.56

[1] Sign Test

Table 4: Correlations between perceived electric field strength and real exposure condition (sham, 1 V/m, 10 V/m). Two sensitive and 27 non-sensitive subjects perceived no field in all three conditions and were omitted from the analysis.

In the BQW, comparison of scores one week prior to and after study participation showed no significant changes for satisfaction and ill health in the sensitive group. In the non-sensitive group, the score for ill health was lower after the experiment ($p=0.004$), but satisfaction remained unchanged (Table 5). Changes in well being over the experimental period as assessed by the BQW_{prior} and BQW_{post} did not differ between the two subject groups, indicating that participation per se did not affect sensitive and non-sensitve subjects differently.

	Sensitive			Non-sensitive		
Scale	**prior** mean (SD)	**post** mean (SD)	**p-value**	**prior** mean (SD)	**post** mean (SD)	**p-value**
Satisfaction	4.88 (0.49)	4.80 (0.57)	0.158	4.69 (0.55)	4.71 (0.63)	0.621
Ill-being	2.15 (0.63)	2.06 (0.71)	0.298	1.95 (0.55)	1.80 (0.48)	0.004
Positive life attitude	4.83 (0.58)	4.78 (0.64)	0.679	4.58 (0.56)	4.66 (0.64)	0.083
Problems	2.19 (0.54)	2.02 (0.69)	0.054	2.28 (0.67)	2.02 (0.60)	<0.001
Somatic complaints	2.10 (1.00)	2.11 (0.97)	0.913	1.61 (0.71)	1.58 (0.57)	0.586
Self-esteem	5.10 (0.58)	4.95 (0.66)	0.101	4.95 (0.63)	4.93 (0.72)	0.658
Depressive mood	1.64 (0.53)	1.79 (0.65)	0.055	1.91 (0.67)	1.95 (0.68)	0.67
Joy in life	4.63 (0.74)	4.28 (0.85)	0.024	4.35 (0.93)	4.22 (1.09)	0.166

Table 5: BQW score values in the sensitive and non-sensitive group one week before (prior) and one week after the experiment (post).

In comparison with the general Swiss population, scale values in non-sensitive subjects were similar but higher for ‘self-esteem’ and ‘joy in life’. Sensitive subjects differed more strongly from the general population. Whereas scale values indicated a higher amount of somatic complaints in sensitive subjects, the other scales pointed towards a higher well being in all other scales comprising a more positive life attitude, higher self esteem, larger joy in life and less problems (Table 6).

	CH population		Non-Sensitive group			Sensitive group		
Scale	Mean	SD	Mean	SD	p-value	Mean	SD	p-value
POS	4.53	0.64	4.58	0.56	0.501	4.83	0.58	0.009
PRO	2.44	0.75	2.28	0.67	0.067	2.19	0.54	0.06
SOM	1.53	0.44	1.61	0.71	0.165	2.10	1.00	<0.001
SEL	4.60	0.71	4.95	0.63	<0.001	5.10	0.58	<0.001
DEP	1.90	0.74	1.91	0.67	0.908	1.64	0.53	0.048
JOY	4.01	0.86	4.35	0.93	0.001	4.63	0.74	<0.001

Table 6: Population means (standardized for age according to our study collective) for the BWQ.

Cognitive Tasks

In the course of the entire study, subjects got faster in all tasks (*Week*: $p<0.02$) except the SRT. In both groups and irrespective of condition, speed decreased significantly from S1 to S2 in both the SRT and CRT, but increased in the 1-, 2-, 3-back and VSAT (*Session*: $p<0.0001$). In the following, only effects including *Condition* or a *Condition*Session* interaction are described.

In both groups, we observed no condition-induced effects on speed in the SRT, 1-, 2-, 3-back and VSAT. Accuracy was neither affected by exposure in any of the cognitive tasks. In the CRT, response times decreased in the sensitive group from S1 to S2 in the sham and 1 V/m condition (~20 ms), but not in the 10 V/m condition (*Condition*Session*: $p=0.007$, Table 7, Figure 5). In contrast, we observed a decrease in speed between sessions irrespective of exposure condition in the non-sensitive group ($p=0.254$, Table 7). A mixed model ANOVA including the factor *Sensitivity* (sensitive, non-sensitive) corroborated the observed differences between groups (*Condition*Sensitivity*: $p=0.005$).

Accuracy was not affected by exposure in a dose response manner in any of the cognitive tasks, except for the 1-back task in the non-sensitive group, where it decreased from 98.2% (sham) to 97.3% (10 V/m; $p=0.046$) in session 1.

Adjusting the models for potential confounding factors (see Table 3 and 7) or performing the analyses with only the 1:1 matched subjects did not alter the results. After multiple endpoint adjustment (alpha=0.05; number of tests=44, overall correlation among cognitive outcomes=0.39), however, all reported p-values exceeded the significance level of $p=0.0051$ (Tukey et al. 1985).

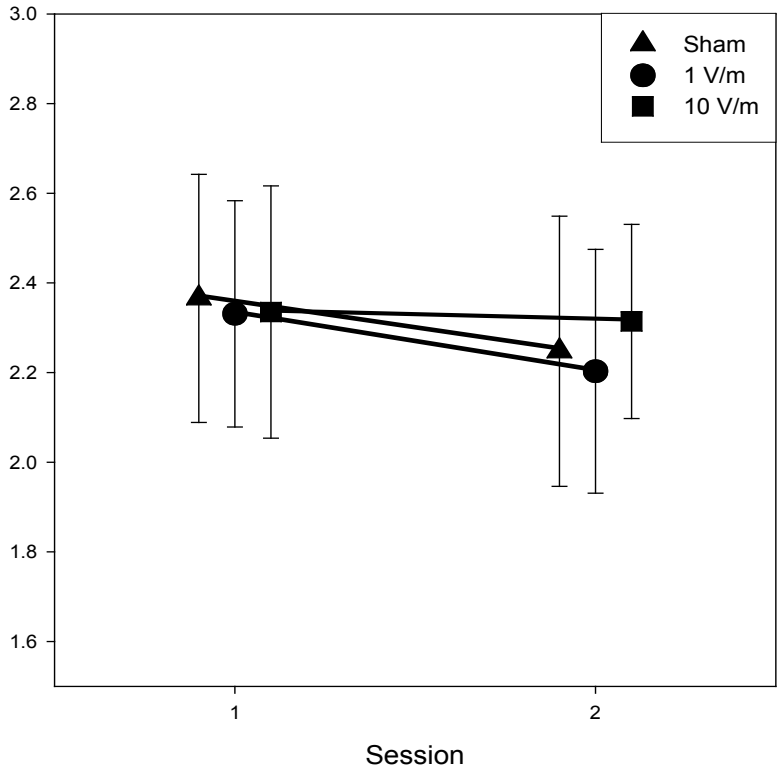

Figure 5: Changes in mean speed (1/ reaction time [1/s]) in the two-choice reaction time task (CRT) from the first to the second session (1st and 2nd half of exposure) in sensitive subjects (N = 32). Three experimental conditions were applied (sham, 1 V/m, 10 V/m).

Table 7: Results of cognitive performance. Mean speed (1/Reaction time [1/s]; SD in parenthesis; N=33 sensitive and N=84 non-sensitive subjects) in the two sessions (1st and 2nd half of exposure) in the SRT (*Simple reaction time task*), CRT (*Two choice reaction time task*), N-back task (*1-, 2-, 3-back*), and VSAT (*Visual selective attention time task*). We only report p-values of *Condition* (Cond) and of the interaction *Condition*Session* (for details see Methods). Statistical analysis is based on data of all subjects. Due to a missing session in some subjects, mean values are based on subjects who completed both sessions in each condition (N= at least 32 sensitive and at N= at least 77 non-sensitive subjects).

Outcome	**Group**	**Session**	**Sham** mean (SD)	**1V/m** mean (SD)	**10V/m** mean (SD)	**Cond**[1] p-value	**Cond*Session**[1] p-value	**Cond**[2] p-value	**Cond*Session**[2] p-value
SRT	Sensitives	1	3.86 (0.52)	3.78 (0.44)	3.84 (0.48)	0.09	0.27	0.07	0.27
		2	3.73 (0.56)	3.65 (0.43)	3.78 (0.47)				
	Non-Sensitives	1	3.85 (0.37)	3.85 (0.38)	3.84 (0.43)	0.59	0.51	0.37	0.50
		2	3.70 (0.44)	3.70 (0.49)	3.68 (0.41)				
CRT	Sensitives	1	2.37 (0.28)	2.33 (0.25)	2.33 (0.28)	**0.03**	**0.01**	**0.02**	**0.01**
		2	2.25 (0.30)	2.20 (0.27)	2.31 (0.22)				
	Non-Sensitives	1	2.27 (0.26)	2.27 (0.27)	2.24 (0.25)	0.13	0.25	0.08	0.24

		2	2.22 (0.27)	2.21 (0.27)	2.21 (0.25)				
1-Back	Sensitives	1	2.15 (0.56)	2.12 (0.55)	2.13 (0.55)				
		2	2.27 (0.57)	2.29 (0.54)	2.29 (0.49)	0.90	0.67	0.93	0.67
	Non-Sensitives	1	2.12 (0.44)	2.12 (0.48)	2.10 (0.42)				
		2	2.25 (0.44)	2.28 (0.48)	2.24 (0.43)	0.57	0.97	0.46	0.98
2-Back	Sensitives	1	1.59 (0.46)	1.53 (0.44)	1.53 (0.35)				
		2	1.70 (0.49)	1.71 (0.53)	1.71 (0.47)	0.61	0.44	0.50	0.43
	Non-Sensitives	1	1.63 (0.39)	1.58 (0.39)	1.60 (0.38)				
		2	1.74 (0.42)	1.74 (0.43)	1.72 (0.39)	0.44	0.52	0.37	0.52
3-Back	Sensitives	1	1.48 (0.40)	1.48 (0.46)	1.48 (0.39)				
		2	1.56 (0.42)	1.60 (0.51)	1.54 (0.37)	0.57	0.52	0.39	0.51
	Non-Sensitives	1	1.56 (0.44)	1.57 (0.51)	1.51 (0.36)				
		2	1.70 (0.55)	1.64 (0.50)	1.70 (0.49)	0.59	0.11	0.64	0.11
VSAT	Sensitives	1	1.74 (0.33)	1.72 (0.31)	1.75 (0.31)	0.28	0.94	0.22	0.94

	2	1.85 (0.29)	1.85 (0.31)	1.87 (0.28)				
Non-Sensitives	1	1.69 (0.34)	1.69 (0.33)	1.68 (0.29)	0.64	0.70	0.50	0.71
	2	1.78 (0.32)	1.83 (0.36)	1.79 (0.31)				

[1] Adjusted for order; [2] Adjusted for order, age, gender, BMI, caffeine intake, medication, (pre-) menstrual complaints, sleep quality and suffering from a cold.

Dosimetry

Penetration depth was low and highest specific absorption rate (SAR) values occurred predominantly at the illuminated side close to skin (Table 8, Figure 6 and 7). Whole-body average absorption was 6.2 ±1.8 and 620 ±180 µW/kg for 1 V/m and 10 V/m, respectively, with an absolute uncertainty of 41% (Table 8). Peak spatial SAR (averaged over 10 g) was 45 ±13 and 4500±1300 µW/kg for brain tissue. At 10 V/m, all values were at least 100x below recommended safety limits (International Commission on Non-Ionizing Radiation Protection 1998). Compared to usage of a mobile phone at the ear or to exposure levels used in other studies, the peak spatial SAR of the brain was more than 100x lower at 10 V/m in our study. SAR values for head tissues and left/ right differences are provided in Table 9.

Tissue	**Averaged SAR (SD)** (µW/kg)	**Uncertainty** (95 % CI) (%)
Whole body	6.2 (1.8)	41
Whole body 10g (Peak Spatial)	150 (49)	39
Whole body 1g (Peak Spatial)	320 (130)	41
Brain	11 (2.4)	48
Brain 10g (Peak Spatial)	45 (13)	45
Brain 1g (Peak Spatial)	73 (16)	44
Skin 10g (Peak Spatial)	230 (48)	50
Skin 1g (Peak Spatial)	380 (76)	39
Muscle 10g Peak Spatial)	120 (31)	48
Muscle 1g (Peak Spatial)	190 (62)	39

Table 8: Averaged SAR values (SD of variations in parenthesis) and the absolute uncertainty (CI, confidence interval) over all subjects for an electric field strength of 1 V/m for whole body and brain, as well as peak spatial averaged SAR for whole body, brain, skin, and muscle (1 g and 10 g). To obtain SAR values at a field strength of 10 V/m, SAR values in the table have to be multiplied by 100.

Organ/Tissue	Organ or tissue / whole body	Ratio left / right
Grey matter (left hemisphere)	3.5	2.9
White matter (left hemisphere)	2.0	2.6
Cerebellum	0.52	-
Hippocampus (left hemisphere)	0.84	1.6
Hypothalamus (left hemisphere).	0.52	1.9
Thalamus (left hemisphere)	0.64	0.81
Parotid gland	4.6	-
Ear pinna (left)	17	18
Eye ball (left)	5.6	8.8

Table 9: Ratio between organ or tissue averaged SAR values and whole-body (6.2 μW/kg at 1 V/m) for brain parts, ear, and eye, as well as the ratio between the averaged SAR of the left and right part of the head.

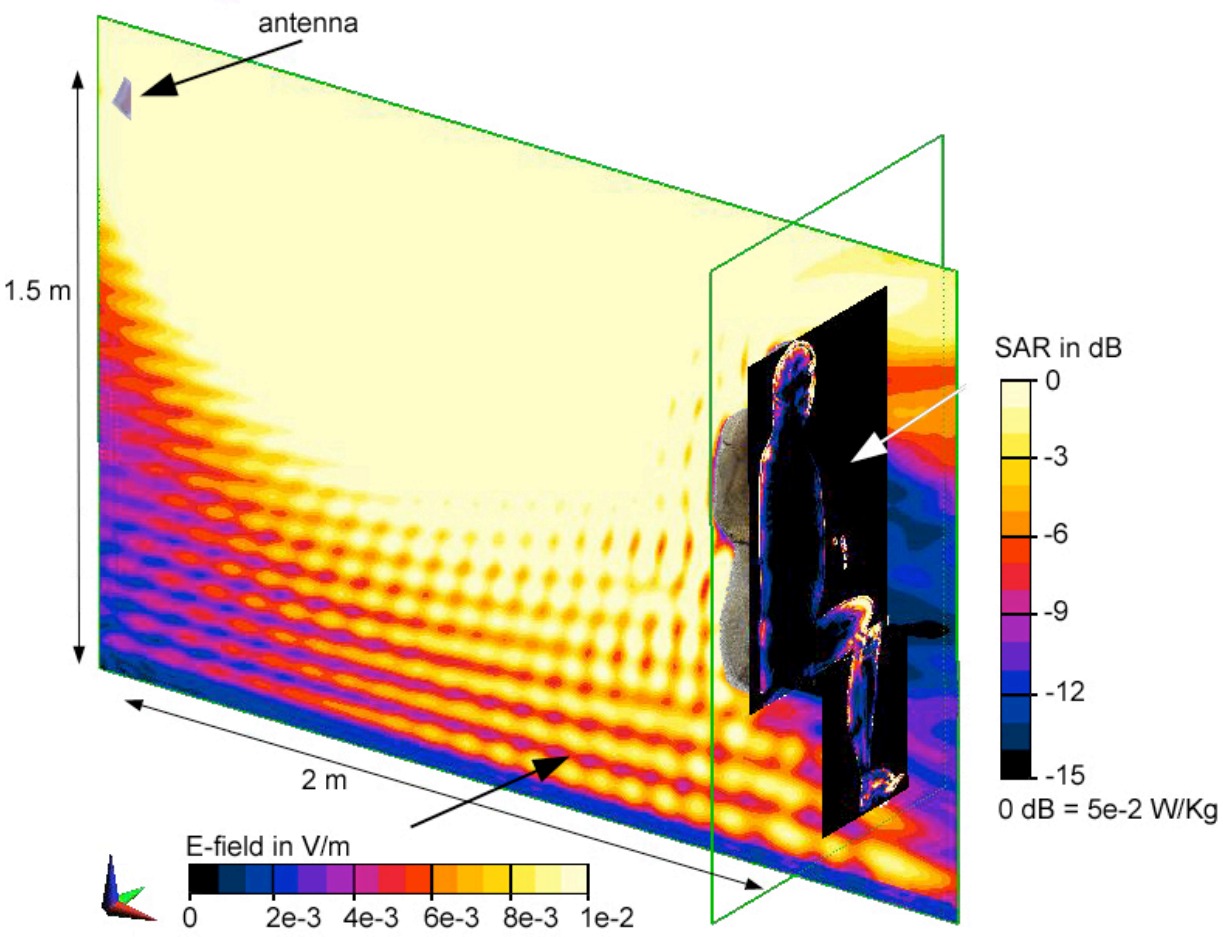

Figure 6: Plane view showing the E-field pattern between the antenna and the subject as well as the SAR distribution in a male human model on a plane at 2 m distance from the antenna.

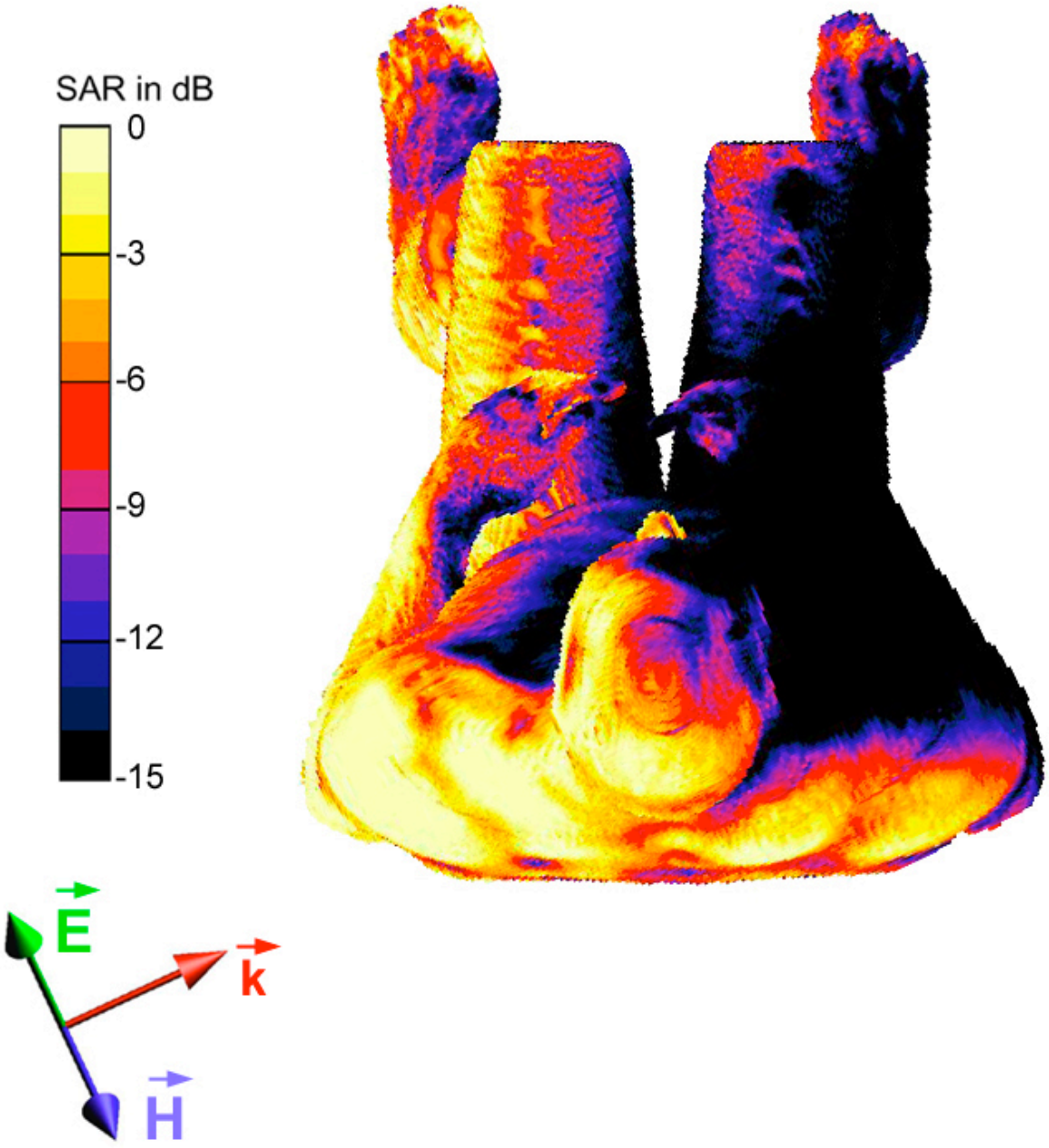

Figure 7: SAR distribution on the surface of a male human model in a sitting position (top view). 0 dB corresponds to 0.05 W/kg for an electric field strength of 1V/m. The orientation of the electric field ($\vec{E}$), the magnetic field ($\vec{H}$), and the propagation direction ($\vec{k}$) of the EMF are indicated.

Post hoc Power Analysis

The post-hoc power analysis yielded a power of 80% to detect a difference of 0.32 for sensitive and 0.14 for non-sensitive subjects in the QCD_{Diff}. The difference score for the QCD in the two subject groups was 0.324 (sensitive) and 0.135 (non-sensitive). The respective post score values for the QCD resulted in 0.315 (sensitive) and 0.13 (non-sensitive), for the TNO_Q in 2.37 (sensitive) and 0.87 (non-sensitive), respectively. For the SRT, the minimal detectable difference in speed yielded 0.11 in sensitive and 0.07 in non-sensitive subjects. For the CRT the respective values were 0.07 (sensitive) and 0.037 (non-sensitive), for the VSAT 0.09 (sensitive) and 0.057 (non-sensitive), respectively. For 1-, 2- and 3-back, the minimal detectable difference ranged between 0.12-0.13 for sensitive subjects and between 0.075-0.085 for non-sensitive subjects.

Discussion

In contrast to our hypothesis, well being as assessed by the QCD and TNO-Q questionnaires was not affected by UMTS radiation, neither at the 1 V/m nor at the 10 V/m condition. Even though the sensitive group generally reported more health problems, there was no difference overall between the two groups with respect to the applied field conditions.

Similarly, cognitive performance was not affected, except for two separate and marginal effects in the 10 V/m condition. In the CRT, a slight decrease in speed across sessions in sensitive subjects could not be observed and in the 1-back task, accuracy was reduced in non-sensitive subjects compared to the sham condition.

Cognitive tasks with moderate to high workload have frequently been used as a tool to assess RF EMF effects on brain physiology by measuring simple motoric responses requiring

selective attention as well as higher cognitive functions such as working memory (e.g. Krause et al. 2000b). Except for the VSAT, which was taken from the TNO battery of cognitive tasks for follow-up reasons, the SRT, CRT and N-back were chosen on the basis of recently published work attempting to assess EMF-induced changes with respect to brain physiology (Koivisto et al. 2000a; Koivisto et al. 2000b; Preece et al. 1999). However, the described effects showed no consistent picture and could not be replicated (Haarala et al. 2003; Preece et al. 2005).

In general, exposure in these studies was poorly defined and the inconsistencies in cognitive outcome may be due to differences in the design, blinding, study population and sample size, thus preventing a comparison of the results. Alternatively, cognitive tasks used so far may not be sensitive enough to reliably measure potential RF EMF effects on brain functioning, leading to a masking of existing effects or resulting in significant effects of tests that stochastically respond to RF EMF. Moreover, statistical analysis of several tests increases the risk of false positive findings.

In the present study, speed was affected in the sensitive group in one of six cognitive tasks and accuracy in the non-sensitive group in one of five tasks. Although an actual *Condition*Session* interaction in the CRT in sensitive subjects and, similarly, a *Condition* effect in the 1-back task in non-sensitive subjects cannot be excluded, the findings seem to be coincidental because they did not reach significance after multiple endpoint adjustment. Both the sensitive and the non-sensitive group were unable to identify the applied fields better than expected by chance. Because only three conditions per subject were investigated, the likelihood of correct field rating by chance was relatively high. The observed distribution of 39 individuals with a positive correlation between the applied and estimated exposure condition and 40 individuals with a negative correlation was likely to be expected by chance.

Nevertheless, we cannot exclude that among these subjects a minority was actually able to perceive the applied exposure. The identification of such individuals has failed in several provocation studies so far (reviewed in Rubin et al. 2005) and would require a multiple testing approach in order to reduce the likelihood of a correct rating by chance. Perceived field strength correlated with an impairment of current well being in both groups irrespective of exposure condition. Also, sensitive subjects rated perceived field strengths higher than non-sensitive subjects, yet ratings in both groups were not better than expected by chance and not associated with exposure levels. This indicates that sensitive subjects overestimate their ability to better perceive RF EMF than the general public (Leitgeb and Schröttner 2003).

Our results differ with respect to both well being and cognitive performance from the results reported by Zwamborn et al. (2003). The TNO-Q is an adapted and not validated version of the original questionnaire (Bulpitt and Fletcher 1990) and was not designed for short retest intervals. Our findings were corroborated by the results of the QCD, a standardized questionnaire that more reliably measures changes in well being over short test-retest intervals (Müller and Basler 1993). Contrary to the TNO study, we found no significant effect on speed in the VSAT. It was however the only task applied in both studies; all other cognitive tasks were distinct. Zwamborn et al. (2003) found other effects with respect to cognitive tasks and exposure conditions (GSM and UMTS) and we also report an effect on speed in one out of six tasks and an effect on accuracy in one out of five tasks used. No clear picture therefore emerges across the two studies showing reproducible effects of exposure condition or cognitive task.

A number of other factors may have contributed more generally to the discrepancies between the TNO study and our study. Sample sizes differ substantially (sensitive subjects: 24 versus 33; non-sensitive subjects: 24 versus 84). Our reference group was frequency matched

to the sensitive group and a subgroup was 1:1 matched with respect to gender, age, residential area and BMI. In the TNO study, all conditions in a particular subject were carried out on a single day, whereas we investigated the subjects at the same time of day in weekly intervals to rule out possible circadian and carry-over effects. We further controlled circadian influences by a uniform distribution of experimental sessions across the time of day. Carry-over effects may lead to an accumulation of RF EMF radiation over time, thus falsifying potential effects of discrete conditions. Furthermore, inclusion of an additional E-field strength of 10 V/m is likely to have contributed to a more reliable assessment of RF EMF effects.

Technical improvements necessitated the modification of the exposure setup used in the TNO study to achieve a more uniform and reproducible base station-like exposure. Whereas the signal (carrier frequency and modulation) and the angle of incidence were identical, the spatial incident field distribution was less uniform in the TNO study, where a narrow exposure beam of only 5° width was used resulting in a larger variation due to differences in height and position of the subjects. In addition, the whole-body exposure conditions applied in this study correspond better to a base-station exposure scenario. However, exposure of head tissues was equivalent in both studies, even though we had a smaller inter-subject variability. Further insights regarding the discrepancies between the present and the Dutch study might be gained from other follow up studies underway in Denmark, the U.K. and Japan, which are also investigating the effect of UMTS base station-like radiation on well being and cognitive function (personal communications).

In summary, no causal relationship between RF EMF and a decrease in well being or adverse health effects was found under the given exposure conditions, but an effect of UMTS-like EMF on brain functioning cannot be excluded. The described effects were weak and not consistent in the two groups. Regarding the implications for public health due to widespread

exposure in the living environment, no conclusions about long-term effects of UMTS base station-like EMF can be drawn from the present study, as only a short-term exposure was applied.

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