

Appendix 1

2.2. Goals, expected results

A replication of the TNO study with focus on the UMTS field condition will be carried out. Two field strengths of 1 V/m and 10 V/m will be applied. The 1 V/m exposure condition corresponds to the original TNO study and the 10 V/m represent the maximum actual exposure from base stations. Two groups of subjects with and without subjective complaints about sensitivity to electromagnetic fields (hypersensitivity) will be investigated. The main focus will be on non-sensitive subjects. The aim of the study is to provide valuable insights to the influence of UMTS radiation on subjective well being and cognitive performance.

This replication study will be a contribution to the ongoing debate about concerns of possible adverse health effects of the new UMTS technology. The study shall be supervised by an independent expert panel.

2.3. Rationale for the proposed project and state of research

In September 2003 a Dutch study (Zwamborn et al. 2003) about effects of mobile communication system radio-frequency fields on well being and cognitive functions of human subjects was published, hereafter called TNO study. They reported a statistically significant relationship between UMTS-like exposure to electromagnetic fields (EMF) at a field strength of 1 V/m and well being (assessed by questionnaire) in subjects with complaints about EMF and in a symptom free reference group. Both groups showed reduced well being. No consistent effects on cognitive performance were reported.

This study elicited a large debate by the public and by scientists. Furthermore, data analysis in the TNO study was heavily criticized. In Switzerland, there is large public concern about possible adverse health effects of the new UMTS technology. Taken together, there is considerable interest in a rapid replication of the study.

2.4. Detailed research plan (experimental approach, methods, milestones, timetable, personnel, duties of each participant including doctoral students)

The replication study will focus on the UMTS field conditions that resulted in consistent results. Exposure setup and UMTS signals will be identical to the TNO study. In addition to the field strength of 1 V/m, a field strength of 10 V/m will be applied to establish a dose-response relationship.

2.4.1 Design of the study

Subjects will have to report to the institute for an interview and to practice the cognitive tests prior to the experiment.

The three conditions (sham, UMTS 1 V/m, UMTS 10 V/m) will be applied in a randomized, double-blind, counter-balanced cross-over design. Exposure will last 45 min. During exposure subjects will perform cognitive tests. Immediately after the end of exposure they will have to fill in the TNO well-being questionnaire. Before and after exposure, they will have to fill in an additional questionnaire that will be internally validated prior to the experiments. In order to avoid possible carryover effects of the EMF, as demonstrated by Huber et al. (2000, 2002), the three field conditions will be applied on different days. To achieve a higher throughput subjects will be scheduled for morning and afternoon sessions. For a particular subject however, testing will always be at the same time of day to rule out possible circadian effects.

Women showed the largest variance in the TNO study (Zwamborn et al. 2003). Thus, weekly intervals might not be optimal since the menstrual cycle may affect mood, they could however be preferred by subjects for reasons of convenience. Whether the experimental sessions will be scheduled on three consecutive days or at weekly intervals will therefore be decided after consultation of the expert panel.

2.4.2 Exposure setup

Members of the ITIS Foundation will construct the exposure setup and will also perform organ as well as functional brain tissue specific dosimetry including uncertainty analysis.

The exposure system will allow for exposing two subjects at a time. Two Huber + Suhner 1320.41.0012 antennas (same as used in the TNO study) will be installed in the anechoic chamber of the IT'IS laboratories

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second, an additional questionnaire that takes the afore-mentioned criteria into account and that will be applied before and after the sessions.

The data analysis of the well-being questionnaire in the TNO study was subject of criticism. The main criticism was that the data analysis was based on the assumption of normally distributed data, which was however not fulfilled. Most appropriate for such data are non-parametric analysis methods and/or transformation of skewed data (log transformation). As the data are clustered (repeated measurements from the same individual), the use of hierarchical models (random effect models) is most preferable. This allows investigating different exposure situations in the same model by taking into account confounding factors (e.g. sequence effect).

Personality inventory

An open issue in the context of the electromagnetic hypersensitive syndrome (EHS) is the question whether hypersensitive persons differ from the general population with respect to the personality. This was investigated in the TNO study with the Big-Five evaluation (Neo-FFI). There are also other personality inventories available such as 'Freiburger Persönlichkeitsinventar (FPI)'. Previous experiences have shown that application of psychological questionnaires in EHS individuals may be crucial for discerning the groups (Rössli et al., 2004). EHS individuals tended to fill in the questionnaire in a biased way, i.e. EHS individuals tried to appear as psychologically "normal" as possible. Thus, different scores between the two groups in such personality inventories may not represent real differences, rather they may be due to information bias. We therefore think that the study design is not suitable to evaluate possible differences in the personalities between hypersensitive subjects and the general population and we propose not to include personality inventories.

2.4.5 Cognitive tests

In the TNO study 4 cognitive tasks (Taskomat) were applied:

- reaction time test (speed [ms])
- memory comparison test (speed of memory comparison [ms])
- visual selective attention test (speed of focusing attention [ms])
- dual tasking test (general reaction time [ms]; indicator for filtering irrelevant information)

Completion of the 4 tasks lasted approximately 20 min. Zwamborn et al. (2003) did not provide a reason for selecting this particular cognitive test battery for investigating the effects of EMP.

EMP at intensities corresponding to mobile phones were reported to influence cognitive functions (Koivisto et al., 2000a; Koivisto et al., 2000b; Preece et al., 1999) and attention (Edelstyn and Oldershaw, 2002). In recent studies, however, previously reported changes in cognitive functioning could not be replicated (Haarala et al., 2003b; Krause et al., 2004). The following tests were applied: "N-Back Task" (Koivisto et al., 2000), "Simple Reaction Time Task" and "2-Choice Reaction Time Task" (Koivisto et al., 2000a; Preece et al., 1998). Target variables were reaction time and accuracy.

Preliminary analysis of own data with the above mentioned tasks revealed increased accuracy in the "3-back task" during 30-min exposure to handset-like EMP. Subjects performed the test battery twice, once during the 1st and once during the 2nd 15 min of exposure. The effect was observed in the 2nd session indicating that subjects had to be exposed for 15 min before cognitive performance was affected.

Based on these results, we will use the "N-Back Task", "Simple Reaction Time Task" and "2-Choice Reaction Time Task" together with a visual selective attention test similar to the one used in the TNO-study, which showed significant effects in the UMTS-like exposure conditions in both groups.

Tests in the replication study will also be performed 2 or 3 times in order to assess whether there is a temporal evolution of a possible effect.

2.4.6 Hypothesis

Based on the results of Zwamborn et al. (2003) the following hypothesis will be tested:

- (1) Exposure to UMTS radiation leads to a reduction of well being
- (2) Cognitive performance is not affected by exposure to UMTS radiation of 1 V/m

In addition we hypothesize

2.5. Available resources for realization of the project (equipment, staff, knowledge, experience)

No further funding is available. However, the study consortium will provide basic infrastructure.

2.6. Expected cooperations

A study consortium consisting of the following three institutions

- Institute of Pharmacology and Toxicology, University of Zurich (IPT; represented by PD Dr. Peter Achermann)
- Foundation for Research on Information Technologies in Society (IT²IS; represented by Prof. Niels Kuster)
- Department of Social and Preventive Medicine, University of Bern (ISPM; represented by Dr. Martin Röösli)

will conduct the study. The responsible project leader will be PD Dr. Peter Achermann.

All partners have previously conducted research about the effect of EMF of mobile phones on humans. IPT and IT²IS have successfully collaborated in previous projects.

Responsibilities of the partners:

IPT: Project management and project responsibility, subject recruitment, cognitive tests, running the experiment, data analyses

IT²IS: Building setup, providing shielded room for experiment, dosimetry, exposure scheme and randomization

ISPM: Identification of EMF sensitive subjects by questionnaire; German version of TNO questionnaire; analysis of questionnaires

EMF sensitive subjects will be recruited from the database of the Federal Office of Public Health (BAG). Personnel of BAG will establish a first contact with this group of subjects. Thus, a close collaboration between BAG and the study consortium will be needed in the recruitment phase.

The TNO study group and the expert panel will be contacted and their advice will be included in finalizing the design of the replication study.

2.7. List of own relevant publications (preferably the latest papers)

IPT:

Achermann P, Huber R, Schuderer J, Kuster N, Borbély AA. Effects of exposure to electromagnetic fields of type GSM on sleep EEG and regional cerebral blood flow. Proceedings of the 15th International Zurich Symposium on Electromagnetic Compatibility 2003; 289-292.

Borbély AA, Huber R, Graf T, Fuchs B, Gallmann E, Achermann P. Pulsed high-frequency electromagnetic field affects human sleep and sleep electroencephalogram. Neuroscience Letters 1999; 275(3):207-10.

Huber R, Graf T, Cote KA, Wittmann L, Gallmann E, Matter D, Schuderer J, Kuster N, Borbély AA, Achermann P. Exposure to pulsed high-frequency electromagnetic field during waking affects human sleep EEG. Neuroreport 2000; 11(15):3321-5.

Huber R, Schuderer J, Graf T, Jutz K, Borbély AA, Kuster N, Achermann P. Radio frequency electromagnetic field exposure in humans: Estimation of SAR distribution in the brain, effects on sleep and heart rate. Bioelectromagnetics 2003; (4):262-76.

Huber R, Treyer V, Borbély AA, Schuderer J, Gottselig JM, Landolt HP, Werth E, Berthold T, Kuster N, Buck A, Achermann P. Electromagnetic fields, such as those from mobile phones, alter regional cerebral blood flow and sleep and waking EEG. Journal of Sleep Research 2002; 11(4):289-95.

Koivisto M, Krause CM, Revonsuo A, Laine M, Hamalainen H. The effects of electromagnetic field emitted by GSM phones on working memory. *Neuroreport* 2000; 11:1641-3.

Koivisto M, Revonsuo A, Krause CM, Haarala C, Sillanmaki L, Laine M, Hamalainen H. Effects of 902 MHz electromagnetic field emitted by cellular telephones on response times in humans. *Neuroreport* 2000; 11:413-415.

Krause CM, Haarala C, Sillanmaki L, Koivisto M, Alanko K, Revonsuo A, Laine M, Hamalainen H. Effects of electromagnetic field emitted by cellular phones on the EEG during an auditory memory task: a double blind replication study. *Bioelectromagnetics* 2004; 25(1):33-40

Preece AW, Iwi G, Davies-Smith A, Wesnes K, Butler S, Lim E, Varey A. Effect of a 915-MHz simulated mobile phone signal on cognitive function in man. *Int J Radiat Biol.* 1999;7 5(4):447-56.

Preece AW, Wesnes KA, Iwi GR. The effect of a 50 Hz magnetic field on cognitive function in humans. *Int J Radiat Biol.* 1998; 74(4):463-70.

Zwamborn APM, Vossen SHJA, van Leersum BJAM, Ouwens MA, Makel WN. Effects of Global Communication system radio-frequency fields on Well Being and Cognitive Functions of human subjects with and without subjective complaints. Netherlands Organisation for Applied Scientific Research (TNO). FEL-03-C148 (2003).

2.9. Significance of project to "Swiss Research Foundation on Mobile Communication"

This project is in the line of research that is supported by the "Swiss Research Foundation on Mobile Communication". In fact, the "Swiss Research Foundation on Mobile Communication" was essential in the fund-raising process for this study. Without their effort this project would not have been possible.

2.10. Related projects of the Research Unit

All partners of the study consortium have previously conducted research about the effect of EMF of mobile phones on humans.