Workshop

"Open Questions in the Research on Biological & Health Effects of Low-Intensity RF-EMF"

Abstracts

Organized by

FGF E.V.

STATE MINISTRY OF ENVIRONMENT, BADEN-WÜRTTEMBERG

CONTENTS

page

SCOPE **5**

RF-ABSORPTION AND TEMPERATURE DISTRIBUTION IN HEADS OF CHILDREN **7**
Andreas Christ

STUDIES INVESTIGATING EFFECTS OF RADIO FREQUENCY ELECTROMAGNETIC FIELDS ON CHILDREN **8**
Martin Röösli

COGNITIVE FUNCTION AND MOBILE PHONE USE IN SCHOOLCHILDREN **10**
Geza Benke

SLEEP AND RF-EMF - ARE ELDERLY SUBJECTS AT AN INCREASED RISK FOR SLEEP DISTURBANCES? **11**
Heidi Danker-Hopfe, *Cornelia Sauter and Hans Dorn*

MEASURES FOR THE EXPOSURE OF NEWBORN ANIMALS TO WIFI SIGNALS **12**
Carmela Marino

IN VIVO STUDIES WITH RF-EXPOSURE AT THE FRAUNHOFER INSTITUTE IN HANNOVER **13**
Clemens Dasenbrock, Jochen Buschmann

IN VIVO STUDIES WITH RF-EXPOSURE IN BREMEN **14**
Alexander Lerchl

DIVERGENT EFFECTS OF PERMANENT EXPOSURE TO A GSM-LIKE SIGNAL ON HEALTH AND SURVIVAL OF FEMALE SPRAGUE DAWLEY RATS WITHIN THE SAME ROOMS: POSSIBLE CENTRAL ROLE OF MONTH AS WELL AS YEAR OF BIRTH **15**
Christian Bartsch

USE OF EXPERIMENTAL MODEL SYSTEMS TO IDENTIFY POSSIBLE HEALTH EFFECTS OF EXPOSURE TO RF FIELDS **16**
David McCormick

PREDICTIVITY OF CARCINOGENICITY STUDIES IN ANIMALS FOR HUMAN CANCER RISKS **17**
Wolfgang Dekant

MONITORING THE EFFECTS OF MOBILE PHONE RADIATION BY THE CELLULAR STRESS RESPONSE AND BY OVERALL GENE EXPRESSION ANALYSIS – RECENT APPROACHES AND CHALLENGES (REVIEW) **18**
Matthias Gaestel

MECHANISM OF SHORT-TERM ERK ACTIVATION BY ELECTROMAGNETIC FIELDS AT MOBILE PHONE FREQUENCIES **19**
Rony Seger

THERMAL AND NON-THERMAL EFFECTS OF SHORTWAVE RADIATION IN SINGLE-CELL APPLICATIONS **20**
Magnus S. Jaeger

ON THE RELATION OF THE SUB-CELLULAR RF-FIELD-DISTRIBUTION AND ABSORPTION AND THE DIELECTRIC PROPERTIES OF BIOLOGICAL MEMBRANES **21**
Jan Gimsa

MICROWAVE ABSORPTION OF EMULSIONS CONTAINING AQUEOUS MICRO- AND NANODROPLETS **22**
Markus Antonietti

DOSIMETRY WITH CHILDREN AND PREGNANT WOMEN – STATE OF RESEARCH **23**
Joe Wiart

SCOPE

International Scientific Workshop

„Open Questions in the Research on Biological and Health Effects of Low-Intensity RF-EMF“

Organized by the Forschungsgemeinschaft Funk e.V. (FGF, Research Association for Radio Applications), and the Umweltministerium (Ministry of Environment) Baden/Württemberg

Stuttgart, Tagungshotel der Telekom, 17.-19. November 2008

A lot of research has been done in the last years on the possible and real effects of radiofrequency electromagnetic fields (RF-EMF) on biological matter – in most cases due to considerations of potential health impacts of cell phones and other mobile communication emitters. Many national and international projects have been finished in the meantime. The results are rather an “all-clear”, however, some controversial results remain and also some open questions.
This workshop aims to pick up several of these open questions, to discuss their relevance and the progress in research, and to try to give a guideline how to go on in this field of research. For this reason only two to four presentations per topic will be given, most time is reserved for discussion.

First day:

1. Are children (and other “specific groups”) at higher risk?
Since our last workshop on this topic in 2006 some new results came up: What has been achieved, and what is still to be done?

2. Can animal studies of one or more generations be considered as "long-term" studies regarding the situation with humans? Is thermal regulation a mechanism that has to be taken into account at exposures below the guidelines?

Second day:

3. Are there indications of RF-effects in *in vitro* experiments?

4. Microdosimetry: Are microthermal effects possible and effective in heterogeneous subcellular media, e.g. in double layers?

Third day:

5. Final Discussion: “What is necessary to solve the open questions, and what in fact needs to be solved?”

Some references:

- Boheim et al. EM Field Sensor in Cell Membranes (Influence of EMF on artificial membranes). http://www.fgf.de/english/research_projects/in-vitro_studies.html, Presentation in Rostock 2006: http://www.cost281.org/download.php?fid=986
- Copty AB, Neve-Oz Y, Barak I, Golosovsky M, Davidov D. Evidence for a specific microwave radiation effect on the green fluorescent protein. Biophys J. 2006 Aug 15;91(4):1413-23
- Dimbylow P, Bolch W. Whole-body-averaged SAR from 50 MHz to 4 GHz in the University of Florida child voxel phantoms. Phys Med Biol. 2007 Nov 21;52(22):6639-49
- Divan HA, Kheifets L, Obel C, Olsen J. Prenatal and postnatal exposure to cell phone use and behavioral problems in children. Epidemiology. 2008 Jul;19(4):523-9
- Ebert S, Eom SJ, Schuderer J, Apostel U, Tillmann T, Dasenbrock C, Kuster N. Response, thermal regulatory threshold and thermal breakdown threshold of restrained RF-exposed mice at 905 MHz. Phys Med Biol. 2005 Nov 7;50(21):5203-15. Epub 2005 Oct 19
- 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 Aug 1;405(3):559-68
- Fuhr et al. Semiconductor Microstructures for the Investigation of Radio Frequency Field Effects on Adherent Cells in Physiological Media. http://www.fgf.de/english/research_projects/in-vitro_studies.html
- George, D. F.; Bilek, M. M., and McKenzie, D. R. Non-thermal effects in the microwave induced unfolding of proteins observed by chaperone binding. Bioelectromagnetics. 2008; 29(4)324-330
- Glasser, H. and G. Fuhr. Cultivation of cells under strong ac-electric field—differentiation between heating and trans-membrane potential effects. Bioelectrochemistry and Bioenergetics. Volume 47, Issue 2, December 1998, Pages 301-310
- Holtze C, Sivaramakrishnan R, Antonietti M, Tsuwi J, Kremer F, Kramer KD. The microwave absorption of emulsions containing aqueous micro- and nanodroplets: a means to optimize microwave heating. J Colloid Interface Sci. 2006 Oct 15;302(2):651-7
- Krause CM, Björnberg CH, Pesonen M, Hulten A, Liesivuori T, Koivisto M, Revonsuo A, Laine M, Hämäläinen H. Mobile phone effects on children's event-related oscillatory EEG during an auditory memory task. Int J Radiat Biol. 2006 Jun;82(6):443-50
- Kumlin T, Iivonen H, Miettinen P, Juvonen A, van Groen T, Puranen L, Pitkäaho R, Juutilainen J, Tanila H. Mobile phone radiation and the developing brain: behavioral and morphological effects in juvenile rats. Radiat Res. 2007 Oct;168(4):471-9
- Nagaoka T, Togashi T, Saito K, Takahashi M, Ito K, Watanabe S. An anatomically realistic whole-body pregnant-woman model and specific absorption rates for pregnant-woman exposure to electromagnetic plane waves from 10 MHz to 2 GHz. Phys Med Biol. 2007 Nov 21;52(22):6731-45
- Simeonova M, Gimsa J. The influence of the molecular structure of lipid membranes on the electric field distribution and energy absorption. Bioelectromagnetics. 2006 Dec;27(8):652-66
- Sommer AM, Bitz AK, Streckert J, Hansen VW, Lerchl A. Lymphoma development in mice chronically exposed to UMTS-modulated radiofrequency electromagnetic fields. Radiat Res. 2007 Jul;168(1):72-80
- Wiart J, Hadjem A, Wong MF, Bloch I. Analysis of RF exposure in the head tissues of children and adults. Phys Med Biol. 2008 Jul 7;53(13):3681-95.

RF-ABSORPTION AND TEMPERATURE DISTRIBUTION IN HEADS OF CHILDREN

Dr. Andreas Christ
IT'IS Laboratories, Zeughausstraße 43, 8004 Zürich, Schweiz

STUDIES INVESTIGATING EFFECTS OF RADIO FREQUENCY ELECTROMAGNETIC FIELDS ON CHILDREN

Martin Röösli
Institute of Social and Preventive Medicine, University of Bern

Effects of radiofrequency electromagnetic fields (RF-EMF) on children have been investigated by means of laboratory and epidemiological studies. In this abstract I focus on studies that investigated radiation effects and do not discuss studies about non-radiation health effects related to mobile phones such as use of mobile phones after lights out and implications on the sleep behaviour.

Laboratory studies

In a literature search I identified two studies using a crossover randomized design to investigate effects of a GSM900 mobile phone on cognitive performance of children 10-12 years of age (Preece et al. 2005), or 10-14 years of age (Haarala et al. 2005), respectively. After correction for multiple comparisons, no effects on reaction time and accuracy were observed in both studies. However, the brain oscillatory response during cognitive processing was affected in 15 children 10-14 years of age when exposed to GSM900 mobile phone in another study (Krause et al., 2006). These effects were similar to a comparable study in adults from the same research group. Kramarenko et al. (2003) found somewhat stronger EEG effects for children than for adults, although their study was limited in design and analysis.

Cognitive functions and symptoms due to a 1 V/m exposure from an UMTS mobile phone base station were investigated in 40 adolescents (15-16 years) by means of randomized crossover design in Denmark. Cognitive performance was not affected by the exposure. A tendency of an increased "headache rating" when exposed was observed for the adolescents ($p=0.09$) that reached statistical significance if pooled with the data of the adults from the same study ($p=0.027$).

Nam et al. (2006) investigated the effects of a 30 minutes CDMA cellular phone exposure on systolic and diastolic blood pressures, heart rate, respiration rate, and skin resistance in 21 adults and 21 teenagers. During exposure they found decreased skin resistance for the teenagers ($P < 0.0001$). All other parameters for both groups were unaffected.

Epidemiological studies

In the past, several small ecologic studies that investigated childhood leukaemia in the vicinity of broadcast transmitters emitting RF-EMF reported elevated risks (reviewed in Röösli et al. 2003). However, more recent large case-control studies found either no effect (Merzenich et al. 2008) or reported inconsistent results (Ha, 2007, Schüz et al. 2008).

RF exposure of physiotherapists from the use of diathermy was associated with adverse pregnancy outcomes in several studies (reviewed in Feychting, 2005). However, no specific type of malformation or other adverse outcome has been consistently reported in these studies.

In a case-control study of 538 children diagnosed with neuroblastoma between 1992 and 1994 in the United States or Canada maternal exposure to a broad grouping of sources that produce radiofrequency radiation was associated with a non significant increased risk (odds ratio: 2.8; 95% confidence interval: 0.9-8.7) (De Roos et al., 2001).

Recently, an association has been reported between behavioural problems of children at age 7 and use of mobile phones of their mothers during pregnancy and, to a lesser degree postnatally, in a large cohort of 13,159 Danish children (Divan et al., 2008). This association may be due to unmeasured confounding.

Ongoing research

In the near future results can be expected from the MobilEe study that investigated exposure to mobile phone radiation in the everyday life of children and adolescents and symptoms (K. Radon, Munich). In the UK a case-control study is ongoing investigating the relationship between mobile phone base station radiation and childhood leukaemia (P. Elliot, London). The international case-control study CEFALO study addresses the association between use of mobile phones and brain tumour in children and adolescents (M. Feychting, Stockholm; L. Klaeboe, Oslo; P. McKinney, Leeds; M. Röösli, Bern; J. Schüz, Copenhagen). Additional studies that I am not aware of may be ongoing as well.

Conclusions

Little research about RF-EMF effects in children has been published so far. The few and heterogeneous available studies do not allow to draw firm conclusions.

References

De Roos A.J., Teschke K., Savitz D.A., Poole C., Grufferman S., Pollock B.H., Olshan A.F.: Parental occupational exposures to electromagnetic fields and radiation and the incidence of neuroblastoma in offspring. Epidemiology 2001: 12 (5), 508-517.

Divan HA, Kheifets L, Obel C, Olsen J. Prenatal and postnatal exposure to cell phone use and behavioral problems in children. Epidemiology. 2008;19(4):523-9.

Feychting M. Non-cancer EMF effects related to children. Bioelectromagnetics. 2005;Suppl 7:S69-74.

Ha M, Im H, Lee M, Kim HJ, Kim BC, Gimm YM, Pack JK. Radio-frequency radiation exposure from AM radio transmitters and childhood leukemia and brain cancer. Am J Epidemiol. 2007;166(3):270-9.

Haarala C, Bergman M, Laine M, Revonsuo A, Koivisto M, Hämäläinen H. Electromagnetic field emitted by 902 MHz mobile phones shows no effects on children's cognitive function. Bioelectromagnetics. 2005;Suppl 7:S144-50.

Kramarenko A.V.;Tan U.: Effects of high-frequency electromagnetic fields on human EEG: a brain mapping study. Int J Neurosci 2003: 113 (7), 1007-19.

Krause CM, Björnberg CH, Pesonen M, Hulten A, Liesivuori T, Koivisto M, Revonsuo A, Laine M, Hämäläinen H. Mobile phone effects on children's event-related oscillatory EEG during an auditory memory task. Int J Radiat Biol. 2006 Jun;82(6):443-50.

Merzenich H, Schmiedel S, Bennack S, Brüggemeyer H, Philipp J, Blettner M, Schüz J. Childhood leukemia in relation to radio frequency electromagnetic fields in the vicinity of TV and radio broadcast transmitters. Am J Epidem, 2008, ahead of print (Doi:10.1093/aje/kwn230)

Nam KC, Kim SW, Kim SC, Kim DW: Effects of RF exposure of teenagers and adults by CDMA cellular phones.. Bioelectromagnetics 2006: 27 (7), 509-514.

Preece AW, Goodfellow S, Wright MG, Butler SR, Dunn EJ, Johnson Y, Manktelow TC, Wesnes K. Effect of 902 MHz mobile phone transmission on cognitive function in children. Bioelectromagnetics. 2005;Suppl 7:S138-43.

Riddervold IS, Pedersen GF, Andersen NT, Pedersen AD, Andersen JB, Zachariae R, Mølhave L, Sigsgaard T, Kjaergaard SK. Cognitive function and symptoms in adults and adolescents in relation to rf radiation from UMTS base stations. Bioelectromagnetics. 2008;29(4):257-67.

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

Schüz J, Philipp J, Merzenich H, Schmiedel S, Brüggemeyer H. Re: "Radio-frequency radiation exposure from AM radio transmitters and childhood leukemia and brain cancer". Am J Epidemiol. 2008;167(7):883-4.

COGNITIVE FUNCTION AND MOBILE PHONE USE IN SCHOOLCHILDREN

Geza Benke
Geza Benke[1,2], Christina Dimitriadis[1,2], Imo Inyang[1,2], Malcolm Sim[1,2], Rory Wolfe[1], Rodney Croft[2,3], Michael Abramson[1,2]

[1]Department of Epidemiology & Preventive Medicine, Monash University
[2]Australian Centre for Radiofrequency Bioeffects Research
[3]Brain Sciences Institute, Swinburne University of Technology

Introduction:
The Mobile Radiofrequency Phone Exposed Users Study (MoRPhEUS) is an epidemiological cohort study investigating possible associations of mobile (cellular) telephone use and cognitive function, hearing and blood pressure in Australian secondary school students.

Methods: A total of 479 students were invited into the study of whom 317 (66%) took part. Almost all (299 or 94%) students had ever used a mobile phone and 243 (77%) had their own phones. Cognitive function was assessed by use of the CogHealth™ test battery and the Stroop colour word test. Mobile phone use was assessed by self report. Regression models were fitted to cognitive outcomes adjusting for age, gender, ethnicity, handedness and clustering by school.

Results: Median age of students was 13 (range 11-14 years). There were 144 (45%) boys and 173 (55%) girls. The analysis of the cognitive data in the cross-sectional part of the study showed that the completion time for the Stroop word naming tasks was longer in those reporting more mobile phone use (p=0.012). The CogHealth test battery showed that the accuracy of working memory was poorer in students reporting more mobile phone use (p=0.006). In addition, the reaction time for a simple learning task was shorter (p=0.03); associative learning response time was shorter (p=0.03) and accuracy poorer with more mobile phone use (p=0.002).

Conclusion: Overall we found that mobile phone use was associated with faster and less accurate responding on higher level cognitive tasks. These findings may either be due to more impulsive behaviour with increasing use or alternatively, they may be learnt through frequent use of a mobile phone. As findings for SMS messages were very similar, they are unlikely to be due to radiofrequency (RF) exposure.

Supported by NHMRC

SLEEP AND RF-EMF - ARE ELDERLY SUBJECTS AT AN INCREASED RISK FOR SLEEP DISTURBANCES?

Heidi Danker-Hopfe, Hans Dorn, Cornelia Sauter
Charite Universitaetsmedizin Berlin, Dept. of Psychiatry and Psychotherapy, Berlin, Germany

The question whether elderly subjects are at an increased risk for sleep disturbances due to potential effects resulting from RF-EMF sources of mobile phone base stations and mobile phone handsets is still open. Almost all studies on the effects of mobile phones on sleep investigated young male subjects and only a few middle-aged subjects of both sexes, and not older than 45 years. Only one study dealt with the effects of electromagnetic fields emitted by digital mobile phone handsets on sleep in subjects aged 18 to 60 years (Loughran et al. 2005). So far, no subjects older than 60 years were studied. Since it is known that sleep architecture and structure changes in the course of a lifetime, with an increase in light sleep and a higher frequency and longer duration of nocturnal awakenings in older subjects, resulting in lower sleep efficiencies, sleep might be more vulnerable to external influences like electromagnetic fields. Furthermore, certain characteristic elements occurring during sleep in the EEG (electroencephalogram) of light sleep, i.e. sleep spindles, which have recurrent been reported to be influenced by electromagnetic fields of mobile phone telephony, change with increasing age. In our own study on healthy young male subjects (aged 18-30 years), exposure to GSM900 resulted in a decrease of the duration of stage 1 and stage 2 sleep and an increase of power in these light sleep stages mainly in the beta-frequency range, whereas under exposure to UMTS, the number of significant results did not exceed the number expected by chance.

In the case of potential effects of mobile phone base stations, our own field study on a total number of 376 subjects, representative of the German population, and aged between 18 to 81 years, older subjects were more concerned on possible health effects resulting from mobile phone base stations and from mobile phones than younger ones. In this study, we found a decreased objective and subjective sleep quality in subjects, who worried about health risks evolving from mobile phone base stations: objective and subjective sleep efficiency and wake after sleep onset, and subjective sleep latency were negatively influenced by concerns about mobile phone base stations.

In the light of age-related sleep changes and its increased vulnerability, and the observed influences of electromagnetic fields - predominately observed on light sleep parameters - it is indispensable to expand studies on the effects of electromagnetic fields of mobile telephony on the increasing population of older people.

MEASURES FOR THE EXPOSURE OF NEWBORN ANIMALS TO WIFI SIGNALS

C. Marino, Paolo Galloni, Francesca Nasta, Rosanna Pinto,
Claudio Pioli and Giorgio A. Lovisolo
Unit of Toxicology and Biomedical Sciences, Casaccia Research Center, ENEA, Rome, Italy

Introduction: New research programs have been devoted to investigate the possible effects of WiFi (frequency band 2412-2484 MHz) signal on biological systems. Studies on the biological effects of electromagnetic fields on newborns have been encouraged by scientific community. Processes occurring during early life, such as maturation of immune system and CNS, body growth, and other ones are, indeed, considered potentially susceptible targets.

Objective: Development of dosimetric methodologies and experimental procedures for whole-body RF exposure of newborn mice.

Experimental procedure and results: Exposure of newborn animals require specific considerations and measures for animal handling and restrain, temperature control, body weight and size (both length and width) growth and, therefore, for dosimetry analysis. Pilot experiments with reduced numbers of animals were performed. Two TEM cells were utilized as exposure systems; their length allowed to expose simultaneously up to 12 restrained mice/cell organized in three groups of four animals each at the fixed field conditions. A SAR vs. body weight curve was defined and used to keep constant the chosen SAR level (0 to 4 W/kg) for the whole exposure period (up to 5 weeks of age). Numerical and experimental dosimetry showed the high variability of induced dose with the averaged weight of mice: During the exposure period, mice were restrained in different kind of jigs according to the animal size: newborn mice (up to 5 g weight) were placed in polystyrene supports to prevent wounding during the first days of exposure; for bigger mice perspex jigs were used, with the inner diameter varying according to body size. During the first weeks of age newborn mice belonging to different families or even to the same family (brothers) may reach different body weights. Number of pups per mother and therefore accessibility to breast feeding is one of the main factors affecting body weight and size in this period. In order to reduce weight variability (and consequently inter-individual variability in SAR level), the number of pups per mother was kept uniform. Newborn mice are hairless and usually lie very close each other and to dams to keep their body temperature. On the other hand, restrainment and EM power absorption at the highest exposure level may overheat the animals. A system devoted to temperature conditioning was added to the exposure system. The conditioning system is constituted by two metallic guides, lining one side of each cell, in which water from a thermostatic bath, at controlled temperature, can be run. Results showed that in the first 8-10 days the environment inside TEM cells should be warmed in order to keep constant the body temperature (36°C ± 1), regardless of SAR level of exposure. After ten days of age, exposed animals required the TEM cells be refrigerated. In conclusion, our pilot experiments showed that to perform experiments with newborn animals under controlled EM field conditions, specific procedures should be adopted.

IN VIVO STUDIES WITH RF-EXPOSURE AT THE FRAUNHOFER INSTITUTE IN HANNOVER

Clemens Dasenbrock, Jochen Buschmann
Fraunhofer Institut Hannover

The presentation will summarize the results of the recent studies performed at Fraunhofer ITEM addressing subchronic effects incl. immunotoxicity, as well as fertility, pregnancy, developmental neurotoxicity, genotoxicity and co-carcinogenicity, particularly for PERFORM-A.

Regarding PERFORM-A, the first two projects included mice (PERFORM-A1) and rats (-A2), both exposed either to GSM or to DCS signals. These subprojects were performed as "classical" combined chronic toxicity and carcinogenicity studies, equivalent to studies routinely performed to evaluate the health risks of chemicals, pharmaceuticals or environmental agents. Two additional PERFORM-A studies were conducted using animals predisposed to tumor [e.g., mammary tumor (-A3) or lymphoma (-A4)] development.
All animal studies, including histopathology, were performed blind to all scientists involved except for the IT'IS staff controlling/monitoring the daily RF-exposure. Reversely the IT'IS staff did not know the group identifier. For each of the single studies three different exposure levels were applied to the animals. The studies were performed GLP-compliant and are presented in separate publications, provided as handouts.
Uniform whole-body exposure was achieved by restraining the animals in tubes at fixed positions in the exposure setup. Mice or rats were exposed to three whole-body SAR levels (SAR: Specific Absorption Rate) or sham exposed during the entire exposure period. The exposure units ("wheels") consisted of two parallel stainless steel plates at a defined distance. A conical antenna was placed in the center between the plates. Encased between the plates cylindrical (plexiglass) tubes were arranged radially around the antenna. Animals were placed in these tubes with adjustable backstops.

The exposure of male and female B6C3F1 mice to 902 MHz GSM and 1747 MHz DCS wireless communication signals at a whole body absorption rate of up to 4.0 W/kg, 2 h/d, 5 d/week, over a period of up to 24 months produced no evidence of any adverse health effect of the exposure or of any influence on the incidence or severity of the background non-neoplastic and neoplastic lesions observed mice (PERFORM-A1) and rats (PERFORM-A2). It is not known whether the presence of 4 prostate adenomas in the 1747 MHz DCS Wireless Communication Signals high dose group in the rat experiment can be directly attributed to treatment (PERFORM-A2).
The long term repeated exposure (4 h/d, 5 d/week over 6 months) to 902 MHz GSM signals (SAR levels of 0.4, 1.3 or 4.0 W/kg) produced a borderline evidence affecting the DMBA-induced mammary tumour response in Sprague Dawley rats with an equivocal biological relevance (PERFORM-A3).
Finally, the exposure of *Pim 1* transgenic mice to a pulsed 900 MHz electromagnetic field at an absorption rate of 0.5, 1.4 or 4.0 W/kg, daily for one hour, over a period of not less than 18 months produced no evidence of any effect of the exposure on the incidence or severity of any neoplastic or non-neoplastic findings (PERFORM-A4).

As an overall conclusion, three out of four studies produced no evidence of any effect of the exposure on the incidence or severity of any neoplastic or non-neoplastic lesions (with one equivocal finding in one study). The only effect observed is a borderline one in the study investigating effects on the DMBA-induced mammary tumour response.

IN VIVO STUDIES WITH RF-EXPOSURE IN BREMEN

Alexander Lerchl
School of Engineering and Science, Jacobs-University Bremen, Campus Ring 6, 28759 Bremen, a.lerchl@jacobs-university.de

Animal experiments are valuable additional sources of information dealing with the possible biological effects of radiofrequency electromagnetic fields (RF-EMF). Unlike cell cultures, animals can respond with a variety of physiological responses, and also multi-factorial processes, especially the induction and promotion of cancer, are possible to be studied only in animals. Likewise, fertility and developmental studies are not possible in cells. In Bremen, a number of studies were performed to address the possible effects of RF-EMF on mice. All studies were done blinded.

AKR mice, which have a high incidence of spontaneous lymphomas, were chronically (life-long) exposed to GSM-modulated 900 MHz RF-EMF at 0.4 W/kg SAR (Sommer A. M. et al. 2004). Their health status as well as repeated blood samples was investigated, while the most important endpoints were onset of disease and survival time. The group sizes (160 sham-exposed and 160 exposed mice) ensured statistical analyses with high power. The survival rates and the other parameters investigated were not affected by exposure, while a slight, but significant difference in body weight development was observed. The same experiment was repeated later (Sommer A. M. et al. 2007), this time exposing AKR mice to UMTS-type RF-EMF, again at 0.4 W/kg SAR. As in the earlier investigation, no harmful effects were observed; surprisingly, a tendency to longer survival was observed in exposed animals at the end of exposure. Unlike in the GSM-900 experiment, no effects on body weight development were seen.

In a multi-generation study which was recently accepted for publication (Sommer A. et al. 2008), we have exposed normal male and female mice life-long to UMTS-type RF-EMF. The mean whole-body SAR values, calculated for adult animals at the time of mating, were 0 (sham), 0.08, 0.4, and 1.3 W/kg. Power densities were kept constant for each group (0, 1.35, 6.8, and 22 W/m²), resulting in varying SAR levels due to the different numbers of adults and pups in the course of the experiment. The results show no harmful effects of exposure on fertility and development of the animals. The number and the development of pups were not affected by exposure. Some data, albeit without a clear dose-response relationship, indicate effects of exposure on food consumption which is in accordance with some previously published data.

In summary, the results of our studies do not indicate harmful effects of long-term exposure of mice to GSM- or UMTS-type RF-EMFs, even when animals are exposed over several generations. These results are reassuring but should be interpreted with caution when drawing conclusions for humans' health, mainly for two reasons: first, the life span of mice is much shorter than that of humans. "Life-long" therefore covers quite different periods of time. Second, the SAR values have different physiological meanings since the metabolic rates of mice and rats are considerably different, too. Nonetheless are the negative findings of our studies in accordance with the vast majority of epidemiological and other animal studies where no harmful effects of RF-EMF exposure could be identified. Our multi-generation study extends this notion considerably.

Acknowledgements: The studies were supported by the Bundesamt für Strahlenschutz (BfS) within the German Mobile Phone Research Program (Deutsches Mobilfunk-Forschungsprogramm).

References

Sommer AM, Streckert J, Bitz AK, Hansen VW, Lerchl A (2004) No effects of GSM-modulated 900 MHz electromagnetic fields on survival rate and spontaneous development of lymphoma in female AKR/J mice. BMC Cancer 4: 77

Sommer AM, Bitz AK, Streckert J, Hansen VW, Lerchl A (2007) Lymphoma development in mice chronically exposed to UMTS-modulated radiofrequency electromagnetic fields. Radiat Res 168: 72-80

Sommer A, Grote K, Reinhardt T, Streckert J, Hansen V, Lerchl A (2008) Effects of Radiofrequency Electromagnetic Fields (UMTS) on Reproduction and Development of Mice: A Multi-Generation Study. Radiat Res in press

DIVERGENT EFFECTS OF PERMANENT EXPOSURE TO A GSM-LIKE SIGNAL ON HEALTH AND SURVIVAL OF FEMALE SPRAGUE DAWLEY RATS WITHIN THE SAME ROOMS: POSSIBLE CENTRAL ROLE OF MONTH AS WELL AS YEAR OF BIRTH

Christian Bartsch
C. Bartsch[1], H. Bartsch[1], H. Küpper[1], U. Scheurlen[2], F. Deerberg[6†], E. Seebald[1], I. Herget[5], K. Dietz[3], H. Lehmann[7], D. Mecke[4], H. Probst[4], T. Stehle[4]

[1]Center for Research in Medical and Natural Sciences, [2]Department of Laboratory Animals, [3]Department of Biometrics, [4]Interfaculty Institute of Biochemistry, University of Tübingen, Tübingen; [5]Graupnerweg 9, Darmstadt; [6]Central Institute for Laboratory Animals, Hannover, Germany; and [7]Swisscom Innovations, Swisscom AG, Bern, Switzerland

During 1997-2008 four long-term experiments were performed testing the effect of permanent exposure to a low-energy GSM-like signal (900 MHz pulsed with 217 Hz, 100 µW/cm² mean power flux density, 44 mW/kg mean SAR for whole body of 300g) on health and survival of unrestrained female Sprague-Dawley rats obtained from the same breeder and kept within the same rooms. Radiofrequency(RF)-exposure started at 52-70 days of age and was continued for 24 months (exp. I), 17 months (exp. II) and up to 34 months (exps. III/IV).

In exps. I and II animals were allowed to live until they were 770 resp. 580 days old observing 12 exposed and sham-exposed animals each. No adverse health effects of permanent RF-exposure were detected, neither by macroscopic nor detailed microscopic pathological examinations of more than 20 tissues in each animal (exp. I); on the contrary, the overall number of pituitary tumors was *reduced* by 47%.

In the course of two survival experiments (III and IV) 30 RF- and 30 sham-exposed animals each were followed up until their natural end or when they became moribund necessitating euthanasia. In exp. III (2002-2005) RF-exposure significantly shortened survival times (median: 705 vs. 832 days in controls; P=0.0078) and more life-terminating polypathologies (20% vs. 3% in controls; P=0.1028) were found. In exp. IV (2005-2008) survival times were not affected despite significantly more life-terminating polypathologies (31% vs. 3% in controls; P=0.021), primarily due to pituitary tumors (+42%). From these two experiments it appears that the animals' capacity to cope with life-terminating diseases was enhanced in exp. IV so that survival times under RF-exposure remained substantially unaffected by polypathologies. A decisive difference between exps. III and IV probably was that animals were born in October (III) and May (IV) indicating that the month of birth modulated the animals' capacity to resist polypathology under permanent RF-exposure. These two survival studies (2002-2008), inspite of differences in response patterns, consistently showed that exposure to a GSM-like signal exerted negative health effects, particularly favouring pituitary tumors. This, however, is in total contrast to exps. I (1997-1999) and II (1999/2000) where the overall incidence of pituitary tumors under chronic RF-exposure was *reduced* (- 47%).

These findings indicate that biological response patterns to the same type of RF-signal, applied under identical laboratory conditions, not only vary within certain limits (depending on e.g. month of birth) but can be diametrically opposite if the same experiment is repeated over several years. To render a possible explanation for these puzzling observations we hereby extend our previous hypothesis regarding a regulatory role of natural geomagnetic variations (detectable in our animal rooms) to generate seasonal variations in laboratory animals under constant photoperiods and now take into consideration that the earth's magnetic field is profoundly modulated by the 11-years' cycle of solar activity. On this basis, it appears that RF-exposure when applied during the ascending limb of a solar cycle (e.g. in exps. I and II: 1997-2000) possesses no or even favourable health effects whereas exposure during the descending limb (e.g. in exps. III and IV: 2002-2008) influences adversely.

USE OF EXPERIMENTAL MODEL SYSTEMS TO IDENTIFY POSSIBLE HEALTH EFFECTS OF EXPOSURE TO RF FIELDS

David L. McCormick, Ph.D., D.A.B.T.
Senior Vice-President and Director, IIT Research Institute, Chicago, Illinois 60616 U.S.A
Professor of Biology, Illinois Institute of Technology, Chicago, Illinois 60616 U.S.A.

In situations where epidemiologic data are conflicting or inadequate, studies performed using experimental models may provide information that is critical to the identification of exogenous agents that impact human health. Radiofrequency (RF) radiation emitted by cellular telephones and other wireless communications devices provides an excellent example of this situation: although millions of people are exposed to cell phone RF fields every day, the relatively short period of time in which wireless communications devices have been in wide public use currently precludes a comprehensive epidemiologic evaluation of their possible impact on the risk of cancer and other chronic diseases.

The rational application of experimental data to identify human health hazards requires both the generation of an experimental data set that is relevant to the disease processes being studied, and an objective analysis of the strengths and limitations of the model system in which those data were generated. Important considerations in this evaluation include:

- relevance of the biology of disease in the experimental model to the human disease
- relevance of the exposure metrics used in the experimental study to human exposures
- sensitivity of the experimental model to disease induction
- magnitude and statistical significance of effects observed in the model system
- level of confidence that the experimental model will accurately predict human responses.

In this presentation, our current understanding of the possible effects of exposure to RF fields on the risk of cancer and other chronic diseases will be discussed in the context of the scientific approaches used to generate such data. A brief review of current research and potential gaps in our knowledge will also be included.

PREDICTIVITY OF CARCINOGENICITY STUDIES IN ANIMALS FOR HUMAN CANCER RISKS

Wolfgang Dekant
Institut für Toxikologie, Universität Würzburg, Versbacherstr. 91, 97080 Würzburg, Germany

Testing for induction of malignant tumors is an important aspect in the hazard identification for chemical agents and contributes to health risk assessment of occupational, therapeutic, and environmental exposures. Chemicals are tested for induction of malignant tumors (carcinogenicity) in animals and more then 500 chemicals have been assessed regarding carcinogenicity in animals. In humans, epidemiology has identified 50 individual chemicals as carcinogenic to humans. Such chemicals are classified as group 1 carcinogens by the International Agency for Research on Cancer (IARC). All group 1 carcinogens identified by IARC also have been shown to cause induction of malignant tumors in appropriate animal studies showing that, regarding carcinogenicity, animal studies are highly predictive of human cancer. When using the presently performed protocols, animal carcinogenicity studies may be even considered as overestimating health risks, since the experimental design using specific exposure conditions (high doses, lifetime application) is conservative (probably overestimating risk for an optimal protection of public health). The high doses used may induce tumors by cytotoxicity and saturation of repair mechanisms.

MONITORING THE EFFECTS OF MOBILE PHONE RADIATION BY THE CELLULAR STRESS RESPONSE AND BY OVERALL GENE EXPRESSION ANALYSIS – RECENT APPROACHES AND CHALLENGES (REVIEW)

Matthias Gaestel
Matthias Gaestel, Institute of Biochemistry, Hannover Medical School, Carl-Neuberg-Str.1, 30625 Hannover, Germany, e-mail: gaestel.matthias@mh-hannover.de

Summary

The aim of this review is to understand the recent developments in analysing the influence of radio-frequency electromagnetic fields (RF-EMFs) on biological systems by monitoring cellular stress response as well as overall gene expression. The stress response of mammalian cells is activated by a wide variety of extracellular conditions and characterised by rapid activation of specific protein kinase cascades and increased biosynthesis of heat shock proteins. Since thermal effects of RF-EMF initiate the heat shock response, a description of non-thermal effects by this response is inherently problematic and has failed due to technical problems and non-adequate experimental settings in many cases. However, the heat shock response can be used for both, monitoring and excluding thermal effects of RF-EMF on biological samples. Hence, the RF-EMF-dependent activation of signalling enzymes, such as ERKs, in the absence of a general stress response could be an example for a specific non-thermal response RF-EMF in cell culture. To bring the field beyond the recent confusion arising from possible thermal "non-thermal" effects, I propose to neglect possible non-thermal stress responses leading to activation of stress-dependent protein kinases and increased expression of heat shock proteins. Instead, future studies searching for non-thermal biological effects of RF-EMF should monitor the short term and long term stress response by looking at stress-activated protein kinases, such as JNKs or p38 MAPK, and Hsp expression, respectively. Only if these responses are negative after "non-thermal" or completely isothermal-controlled RF-EMF exposure, thermal effects can definitively be excluded and further non-thermal effects can be searched for and characterised. For such a search, "Omic" techniques will be well suited and enable a more general and rather unbiased investigation. However, due to their high-throughput-characteristics, "omic" approaches generate false positive results and require statistical evaluation based on a sufficient number of independent experiments with identical parameters. Apart from that, statistically significant positive results from "Omics" approaches must be confirmed by independent quantitative methods. Finally, confirmed results from cell culture have to be evaluated *in vivo*. Following these intentionally strict criteria, non-thermic biological effects of RF-EMF should be proven by statistically significant quantitative changes in gene expression under conditions where the cellular stress response is not elucidated to avoid confusion with possible thermal effects.

MECHANISM OF SHORT-TERM ERK ACTIVATION BY ELECTROMAGNETIC FIELDS AT MOBILE PHONE FREQUENCIES

Rony Seger
Department of Biological Regulation,
The Weizmann Institute of Science, Israel

The exposure to non-thermal microwave electromagnetic fields generated by mobile phones affects the expression of many proteins. This effect on transcription and protein stability can be mediated by the MAPK (mitogen-activated protein kinase) cascades, which serve as central signalling pathways and govern essentially all stimulated cellular processes. Indeed, long-term exposure of cells to mobile phone irradiation results in the activation of p38 as well as the ERK (extracellular-signal-regulated kinase) MAPKs. In the present study, we have studied the immediate effect of irradiation on the MAPK cascades, and found that ERKs, but not stress-related MAPKs, are rapidly activated in response to various frequencies and intensities. Using signalling inhibitors, we delineated the mechanism that is involved in this activation. We found that the first step is mediated in the plasma membrane by NADH oxidase, which rapidly generates ROS (reactive oxygen species). These ROS then directly stimulate MMPs (matrix metalloproteinases) and allow them to cleave and release Hb-EGF [heparin-binding EGF (epidermal growth factor)]. This secreted factor activates the EGF receptor, which in turn further activates the ERK cascade. Thus this study demonstrates for the first time a detailed molecular mechanism by which electromagnetic irradiation from mobile phones induces the activation of the ERK cascade and thereby induces transcription
and other cellular processes.

THERMAL AND NON-THERMAL EFFECTS OF SHORTWAVE RADIATION IN SINGLE-CELL APPLICATIONS

Magnus S. Jaeger[1], Torsten Mueller[2], Thomas Schnelle[3], Katja Uhlig[1], Michael Kirschbaum[1], Guenter R. Fuhr[1]

[1]Fraunhofer Institute for Biomedical Engineering (IBMT), Am Muehlenberg 13, 14476 Potsdam, Germany
[2]JPK Instruments AG, Aufgang C, Haus 2, Bouchéstrasse 12, 12435 Berlin, Germany
[3]Zimmermann and Partner, European Patent Attorneys, Oranienburger Strasse 90, 10178 Berlin, Germany

Abstract

Today, shortwave radio-frequency radiation is regularly employed in biotechnological applications of dielectrophoresis, i. e. for exerting low-stress forces on living cells in microfluidic channels. In such chip-based configurations, the cells experience two forms of stress. Firstly, applying an electric field to an electrically conductive medium, e. g. as used in animal cell culture, causes Ohmic warming. This depends on the electric conductivity and especially on the electric field strength but - in first approximation - not on the frequency. We present and compare different approaches to quantifying this warming in microstructures. Secondly, a non-thermal stress results from membrane polarisation effects. These latter can be separated from the first group by their frequency dependency. To this end, we investigated cell growth rates in electric fields of 1 MHz to 10 MHz and at 0.6 kV / m.

In addition, we show experiments on using intracellular calcium as an early indicator of immune cell activation in on-chip assays. In this context, we found that the same parameter also provides valuable and clear information on electric field-induced stress.

While dielectrophoresis is usually performed in the frequency range from 10 kHz up to 500 MHz, we currently prepare analogous tests at 10 GHz to 1 THz.

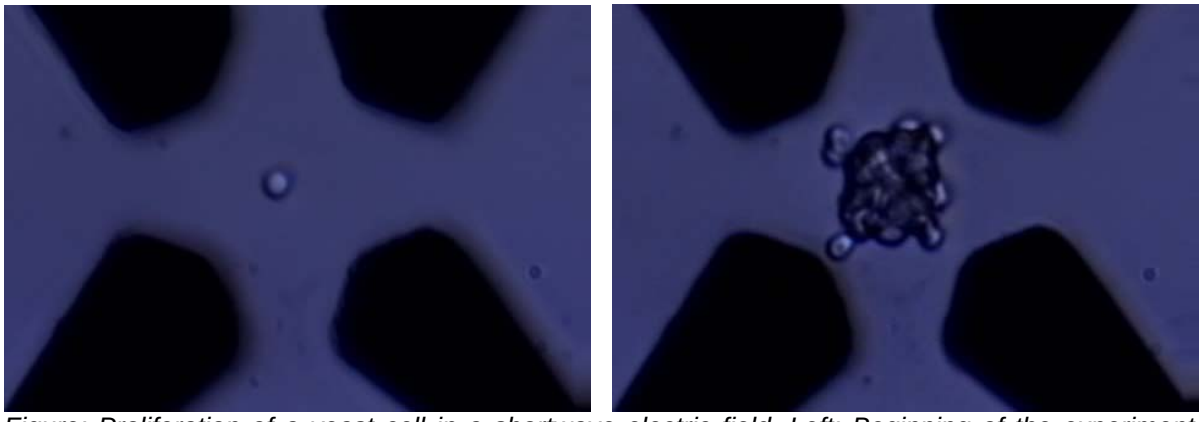

Figure: Proliferation of a yeast cell in a shortwave electric field. Left: Beginning of the experiment, right: after one day, the cell has divided repeatedly - about every two hours - and formed an aggregate. Under appropriate electric field conditions, the cell cycle time remains unaffected (distance of diagonally opposite electrodes: 40 µm).

ON THE RELATION OF THE SUB-CELLULAR RF-FIELD-DISTRIBUTION AND ABSORPTION AND THE DIELECTRIC PROPERTIES OF BIOLOGICAL MEMBRANES

Jan Gimsa
Chair of Biophysics, Department of Biology, University of Rostock, Gertrudenstr.11A, D-18057 Rostock, Germany, Tel.: +49-381-498 6020, Fax: +49-381-498 6022
e-mail: jan.gimsa@uni-rostock.de,
http://www.biologie.uni-rostock.de/biophysik/

Cells are compartmentalized and consist of complexly arranged various media with very different frequency-dependent properties. The electric field distribution at the cellular and sub-cellular levels is based on electric double layer, interfacial, bulk and molecular properties [1].
Compartmentalization is the reason for the dominating structural (interfacial and bulk) dispersions. Nevertheless, electric double layer or molecular properties can strongly modulate structural dispersions. In the GHz-range, structural and molecular contributions dominate the frequency-dependencies of the field distribution and the local absorption at the subcellular level.

Field distribution and energy absorption have been considered for two model systems, the human red blood cell (HRBC) [2, 3] and lipid vesicles [4].

The frequency-dependent properties of the most abundant molecules were obtained from literature studies and own experiments, respectively. The cytoplasmic properties for HRBCs are mainly determined by the properties of hemoglobin (Hb) and cytoplasmic water. For modeling, the lipid phase properties of the membranes can be taken into account by a sandwich model. The model comprises strata of different frequency-dependent behaviors, i.e. bound water, hydrophilic lipid headgroup, and hydrophobic lipid chain-regions as well as orthogonal segments formed by transmembrane proteins.

We found that the anisotropic properties of the lipid headgroup region might have a strong influence on the subcellular field distribution.
Further, membrane absorption is commonly calculated for averaged membrane properties. We found an increase in the absorption when it was calculated as the average of the absorption in the different strata.

The new way of calculation together with the anisotropy effects may lead to an increase of the absorption in the lipid phase by one order of magnitude.

References

[1] J. Gimsa, L. Haberland. 2005. Electric and magnetic fields in cells and tissues. in: F. Bassani, J. Liedl, P. Wyder (eds.) Encyclopedia of Condensed Matter Physics. Elsevier Ltd. Vol. Biophysics. pp. 6-14.
[2] D. Wachner, M. Simeonova, J. Gimsa. 2002. Cellular Absorption of Electric Field Energy: Equations for a Single Shell Model of the General Ellipsoidal Shape", Bioelectrochemistry 56:211-213.
[3] M. Simeonova, D. Wachner, J. Gimsa. 2002. Cellular Absorption of Electric Field Energy: Influence of Molecular Properties of the Cytoplasm", Bioelectrochemistry 56:215-218.
[4] M. Simeonova, J. Gimsa. 2005. Dielectric anisotropy, volume potential anomalies and the persistent Maxwellian equivalent body. J. Phys.: Cond. Matter 17:7817-7831.
[5] M. Simeonova, J. Gimsa. 2006. The influence of the molecular structure of lipid membranes on the electric field distribution and energy absorption. Bioelectromagnetics 27:652-666.

MICROWAVE ABSORPTION OF EMULSIONS CONTAINING AQUEOUS MICRO- AND NANODROPLETS

*Christian Holtze, Markus Antonietti **
Max Planck Institute of Colloids and Interfaces, Department of Colloid Chemistry, Research Campus Golm, D-14424 Potsdam, Germany; e-mail: markus.antonietti@mpikg.mpg.de

Microwave absorption at frequencies between 10 MHz - 4 GHz is measured for aqueous brine droplets dispersed in a dielectric medium (ε' = 2.0). By varying the size of the droplets, ion type and ion concentration, an anomalous absorption mechanism is identified which is attributed to surface polarization of ions in the water phase. It is found that this microwave absorption goes through a maximum in size and ion concentration which in addition depends on the type of ions and their concentration. The mechanisms allows to optimize microwave heating in convenience food and dewatering of crude oil emulsions, but also may represent an unwanted absorption and damping scenario for mobile telecommunication and radar devices.

DOSIMETRY WITH CHILDREN AND PREGNANT WOMEN – STATE OF RESEARCH

Joe Wiart
Orance Labs France Telecom R&D - DMR/IIM; Mobile Services + Radio Systems,
38, Rue du General Leclerc, F-Issy les Moulineaux Cedex 92131