



# In vivo- studies

by Frank Gollnick

**Eleanor Adair**, who has worked for a long time with the research laboratory of the Brooks Air Force Base in Texas, reported on experiments done in six test persons exposed dorsally for 45 min at three ambient temperatures (24 to 31° C) to a non-modulated 220 MHz field (SAR = 0.4 W/kg, 0.53 W/kg and 0.66 W/kg). At the same time, internal body temperature, skin temperature, metabolic rate, local sweat rate, skin blood flow, heart rate, respiration rate and total evaporative water loss were measured. Whereas inner and surface body temperature as well as most other parameters increased only slightly to moderately over the course of field exposure (skin blood circulation) at all ambient temperatures, a vigorous increase in sweat rate was observed already within the first minute. This increase could not be fully explained by external skin heating or elevated ambient temperature. As in previous tests with 100 MHz, the skin was much less heated than in tests using higher frequencies (450 MHz). Due to the relatively large penetration depth, Adair assumes that there is direct stimulation of heat-sensitive nerve cells in the region of the brain stem and in parts of the central nervous system triggering the observed thermoregulative re-

sponse of the body. A very small change in temperature of 0.03° C deep within the body can be sufficient to be perceived and conducted down by approx. 100 primary axons (according to a hypothesis of K. Adair). According to the model calculation, a SAR of  $\geq 1$  W/kg was determined for the respective inner region for the tests with 220 MHz. So it is not temperature sensors within the skin that trigger the observed strong effect, Adair concluded.

**Alexander Lerchl** (International University of Bremen) presented first results of a study he is performing within the German Mobile Radio Research Program promoted by the German Government. In his laboratory experiments in mice, Lerchl aimed at investigating the leukemia risk – a risk that is slightly increased, at least according to several previously performed population studies, at relatively high chronic exposure to 50 Hz or 60 Hz fields (in contrast to lower exposure values).

Lerchl examined a total of 480 female mice (3 groups of 160 animals each) of a particular strain (AKR/J) that has an a priori elevated tendency to develop leukemia due to genetic predisposition (60 to 100%

of the animals within the first year of life). Aged between 4 to 5 weeks and freely moving inside their cages, the animals were daily exposed for 24 h, over 42 weeks, to a sinusoidal 50 Hz magnetic field of 1  $\mu$ T or 100  $\mu$ T, resp. sham-exposed in the third group, and subsequently (or before, at the onset of disease symptoms) pathologically examined (tissue). Other parameters, such as weight gain, blood parameters and swollen lymph nodes, were regularly recorded over the course of exposure. The evaluation of parameters such as lymphoma incidence, survival rate, survival time, gross necropsy, as well as absolute and relative weight gain, showed no statistically significant differences between exposed groups and control group without magnetic field, i.e. no effects of field exposure. Further on in the study, which will extend over several years, blood samples and pathological tissue data of these groups will be evaluated; after that, the study will investigate exposure of AKR/J mice to 1000  $\mu$ T magnetic fields, as well as to 900 MHz GSM and UMTS fields.

**Lutz Haberland** (University of Rostock) presented the results of a literature study commissioned by the FGF. Abstracts of a total of 809 studies either published in scientific journals (peer-reviewed) or presented at meetings (and later on peer-reviewed) covering the range of 2 to 3 GHz were evaluated in detail. The research results taken from three different literature databases span the years 1975 to 2003 and cover a broad spectrum of biological objects and investigation purposes. Only experimental research was considered.


Regarding examined frequencies, the focus was on 2.45 GHz (in 611 of the 809 studies; this frequency e.g. is used by microwave ovens and medical applications). In 330 studies, objects were exposed clearly to fields clearly above permitted limits for humans. The purpose of the literature study was to identify research gaps and to provide recommendations for

further research in the respective fields.

The results showed that there were effects of field exposure close to or below valid limits, but none was clearly reproducible. In contrast, there were clear effects above limits. Regarding the selected biological objects and research purposes, this branch of research seemed to be rather unstraining, without clear foci and lacking background. Often, single findings were not reproduced, or results of similar investigations even were contradictory. Thus, none of the chosen research categories could be classified as having been "fully investigated" with regard to exposure close to limits. Only three of the over 30 identified research fields in the range between 2 to 3 GHz (namely the influence of unmodulated fields on spermatogenesis and heart rate, as well as acute field influence on the blood-brain barrier) were classified as "sufficiently investigated", all three without clearly determined biological effects below limits. A clearly defined recommendation for further research in the respective frequency range could not be given.

**Hideki Harada** of the University School of Medicine in Kurume, Japan, reported on 64 female Wistar rats treated with transcranial magnetic stimulation (short, very strong magnetic field pulses stimulating brain areas) and on ensuing changes in the animals' stimulus and pain sensitivity. For magnetic stimulation, frequencies of 0.1 Hz and 2 Hz, with a field strength of 0.7 Tesla were applied over 30 min. Hypersensitivity of the left back paw artificially induced by inflammation processes was cured over time (up to two days after) by the magnetic field treatment, at least regarding heat stimuli, but not mechanical stimuli. The right back paw served as a control.

In her lecture, **Maren Fedrowitz** from the working group of Wolfgang Löscher at the University of Veterinary Medicine, Hannover, presented clear differences between effects of two weeks 50 Hz magnetic



field exposure (100  $\mu$ T) in different substrains of DMBA rat models. The substance DMBA (7,12-dimethyl benzanthracene) is used to artificially induce mamma carcinomas in various rat strains for the investigation of breast cancer development.

After initial confusion, it has become obvious over the past years that clear magnetic field effects on the division rate (proliferation) of mamma carcinoma cells in rats - made evident by Löscher's group but for some time non-reproducible by independent scientists, are dependent on applied substrains. In the meantime, a number of strains and substrains have been tested at exposure to magnetic fields, obtaining different, mostly negative results. So the aim of the present study was to find other strains responding to exposure by a change in proliferation.

The cause of the differences between magnetic field sensitivities is of particular interest here. Only one substrain of female Sprague-Dawley rats (SD1) of the many tested rat strains and substrains so far was shown to manifest a reliably reproducible effect in the form of enhanced cell proliferation. This exception among mouse strains coincidentally was the one the group around Löscher had been working with for years in order to give evidence of magnetic field effects.

In addition, also the proliferation in skin and hair follicle cells of the rats was measured now. A significant magnetic field effect in the form of a decreased proliferation rate was demonstrated in the alternatively tested Wistar rat strain. The recently examined Fischer rat strain responded likewise, but only in the case of skin cells. Since rat strains and substrains are genetically different, it became clear that there is now the possibility to look for the genetic causes of magnetic field effects.

Discussion following to the lecture showed that the topic was met by vivid interest. Its focus was the question whether perhaps differences in DMBA absorption across the strains could be the cause of the

determined results instead of the magnetic field. One suggestion was the tests should be reproduced and repeated with other proliferation markers. Moreover it was suggested to compare rat strains of known sensitivity towards DMBA using the same method.

In cooperation with scientists of the University of Bristol and the National Radiological Protection Board (NRPB), **John Tattersall** from the Biomedical Science Department in Salisbury, United Kingdom, tested mouse brain functions and brain physiology at exposure to 900 MHz GSM and unmodulated 900 MHz signals. This was part of the large-scale MTHR Program (Mobile Telecommunication and Health Program). Behavioral tests in a water maze (Morris water maze) were performed; besides, messenger RNA (mRNA) extracts were examined for gene expression, and electrophysiological standard parameters were measured in slice preparations of the hippocampus. Inside plastic tubes (Perspex rockets), the adult mice having been habituated to them over a period of ten days, had their heads exposed for an hour to a GSM-modulated or unmodulated (CW) 900 MHz signal of a ring antenna and were subsequently examined. Moreover, there were control groups in tubes without field exposure, and cage control groups.

The field strength during exposure was adjusted to produce SARs in the head of 3, 6, 18 or 36 W/kg, according to FDTD computer model calculations and temperature measurements in dead tissue. Behavioral tests demonstrated no effects from field exposure compared to controls. However, the cage control group in general showed less activity than the other groups during the tests. The large number of measured electrophysiological parameters neither indicated significant differences, except for the ability to trigger long-term potentiation (LTP) at the synapses (changes observed under CW conditions).

Regarding gene expression, changes after field exposure were determined in less than 0.01% of the ge-



nome. This slight deviation was explained by the restraint inside the plastic tubes. The lively discussion addressed a number of issues:

- How many mice were used in a test group? (Answer: In behavioral tests: 70 in treated groups, 22 in the sham-exposed group, 12 in the cage control group)
- Was statistical power determined prior to the experiments? (Answer: It was not determined)
- Did the restraint inside tubes produce stress? (Answer: No data given)
- Were the animals able to move during exposure? (Answer: No data given)
- Is it possible that the treat given to the animals (food) after leaving the tubes affected the gene expression compared to cage control groups? (Answer: Could be, interesting thought)
- Was exposure non-thermal? (Answer: Highest exposure was designated as thermal control)
- What was the exact GSM test signal? (Answer: No data given)
- Are tests with other frequencies in the vicinity of 900 MHz planned? (Answer: No, but similar follow-up tests at 400 MHz TETRA and 2200 MHz UMTS frequencies, as well as with multiple field exposures).

Another lecture held by Tina Reinhardt from the working group of Volker Hansen (University of Wuppertal) was wrongly allocated to the session on in vivo studies. It described the dosimetric analysis of exposure of rats to a UMTS test signal in a still ongoing two generations study.