

The following paragraphs refer to recent original scientific studies and papers on effects of high-frequency fields of mobile radio. Publications were selected by the author, Prof. Roland Glaser, reflecting his personal judgement of their relevance.

# News from Science

Can on several occasions found neuronal HF field effects be detected neurochemically, too? To answer this question, rats were surgically implanted with dialysis devices in the brain. Thus it was possible to take samples hourly from the more or less sleeping animals for determination of the concentration of the neurotransmitter acetylcholine (ACh). Though not at 3.26 W/kg, but after one-hour exposure to 6.52 W/kg (2.45 GHz, CW), a significant decrease of ACh concentration could be measured ( $72 \pm 9\%$ ) over several hours. Exposure with 800 MHz (0.325 W/kg, amplitude modulated with 32 Hz) only led to a significant effect when exposure time was not only 1, but 14 hours. The effect after 6.25-W/kg exposure, too, is discussed and seen as being non-thermal, since its maximum is reached only 5 hours after exposure. But considering that this could be a response to some primary effect, the conclusion does not seem compelling (Testylier, G., Tonduli, L., Malabiau, R., and Debouzy, J.C.: Effects of exposure to low level radiofrequency fields on acetylcholine release in hippocampus of freely moving rats. *Bioelectromagnetics* 23, 249-255. 2002).

There is no causal relation between hypersensitivity symptoms and exposure to mobile phones – that is the central message of a newly published Finnish study. The study was aimed at answering two questions: 1. Are there persons showing subjective symptoms caused by mobile phone fields? 2. Can humans possibly perceive such fields, perhaps without suffering from disagreeable feelings? The study is based upon tests performed in 20 participants (13 women, 7 men aged 37 to 67) claiming to respond with subjective symptoms to fields of a mobile phone used by themselves, or in the vicinity of an active device, as early as after at least 30 minutes. In a wooden hut located far from other field sources and without electrification, a test setup was installed allowing testing persons to sit in a comfortable chair during a double-blind experiment using phones that were located 1 to 5 cm to the right and to the left of their ears. Both analogous (900 MHz) and digital GSM phones (900 and 1800 MHz) were used (peak power 2 W, average power 0.25 W). Apart from measuring blood pressure as well as heart and respiratory frequencies, participants were asked to report percep-

tions and symptoms occurring during the 30-min sessions. Though female participants listed 20 symptom categories, men only 13, no correlation between these states and the existence or non-existence of fields could be found. So, experiments provided no positive answer, neither to the first nor to the second question. (Hietanen, M., Hamalainen, A.M., and Husman, T.: Hypersensitivity symptoms associated with exposure to cellular telephones: No causal link. *Bioelectromagnetics* 23, 264-270. 2002).

The Nuclear Factor Kappa B (NF- $\kappa$ B) could be a new indicator of field-induced signal chains within the cell. Normally, this transcription factor is bound in the cell cytoplasm to an inhibitor (I- $\kappa$ B). Triggered by different stress factors, this binding dissociates, NF- $\kappa$ B is released and heads to the nucleus where it leads to sequence-specific gene activations. Some years ago, Mohan et al. already have shown that also gamma radiation is able to trigger this activation (*Radiat. Res.* 140, 97-104. 1994). Goswami et al. (*Radiat. Res.* 151, 300-309. 1999), however, could not find this reaction during HF exposure of

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fibroblasts (847.74 MHz, 0.6 W/kg). The above mentioned group now for the first time demonstrates a three-fold increase in NF- $\kappa$ B activity as a consequence of exposure to microwave pulses. To this end, cultures of human monocytes were exposed to intense pulses of 8.2-GHz fields (50 W/m<sup>2</sup>, pulse duration 2.2  $\mu$ s, 1000 pulses/s, average SAR value  $-10.8 \pm 7.1$  W/kg). In the view of the authors, this result does not point to a thermal effect, since temperature rises lead to a decrease, not an increase of NF- $\kappa$ B activity. On the other side, they point to the high energy density in the pulse not excluding thermal gradient effects. Concerning the above mentioned study on gamma radiation, also oxygen radicals could play a part (Natarajan, M., Vijayalaxmi, Szilagyi, M., Roldan, F.N., and Meltz, M.L.: NF- $\kappa$ B DNA-binding activity after high peak power pulsed microwave (8.2 GHz) exposure of normal human monocytes. *Bioelectromagnetics* 23, 271-277. 2002).

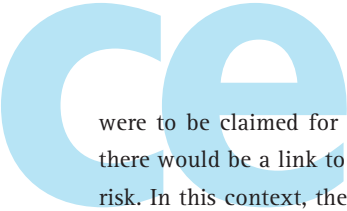
Following to their studies on heat shock protein expression possibly caused by low-frequency magnetic fields (Miyakoshi et al.: *Life Sciences* 66, 1187-1196. 2000), this group devoted its new study to the HF range. In a special temperature-regulated waveguide, standing waves of 2.45 GHz (unmodulated) were produced leading to radially different field intensities in petri dishes 14 cm in diameter. Expression of HSP-70 was measured in cultures of human glioma cells (M054). An exposure of 5 W/kg did not produce any results. There was evidence for a significant increase in heat shock protein concentration in the cells only for SAR values of above 20 W/kg (exposure over 2 hours). The longer the exposure period and the

higher the intensity, the more intense was the expression. From the fact that an increase of thermostat temperature to 39° C had a smaller effect than the same heating caused by the HF field, the authors conclude that the effect is non-thermal – a conclusion we cannot support because of the different heating mechanisms (Tian, F., Nakahara, T., Wake, K., Taki, M., and Miyakoshi, J.: Exposure to 2.45 GHz electromagnetic fields induces hsp70 at a high SAR of more than 20 W/kg but not at 5 W/kg in human glioma M054 cells. *Intern. J. Radiat. Biol.* 78, 433-440. 2002).

The papers of the Japanese group around Imalda already were reported on in the last edition of this newsletter (10<sup>th</sup> year, no. 1, p ??). In the meantime, the authors have published results from their experiments investigating possible effects of HF fields of Japanese PDC-1500 phones on brain tumor development. To this end, they used transgenic mice which were successfully applied in other studies as a sensitive mutagenesis assay via their marker gene. Over 4 weeks, 5 days per week, the animals were exposed to a 2.5-GHz TDM signal for 90 min at a time. The mice were kept in a holder providing a distance of 4 mm between the antenna and their head. To avoid excess heating, the rest of the body, to a large extent, was shielded from radiation. An average SAR value in the head of 2 W/kg was reached, whereas whole-body exposure only led to 0.27 W/kg. DNA sequence analyses were performed, as well as immunohistological tests in the brain; body and brain weight were recorded. The tests showed no significant alterations in the mutation rate of the indicator gene. There was a slight increase in the number of deletions which –

contrary to controls – could be observed already at an exposure of 0.67 W/kg. However, this effect was not significant. The authors are convinced that, in view of this sensitive early-diagnosis system, a 4-weeks exposure is sufficient to conclude that there is no risk of brain tumor development under the used exposure conditions (Takahashi, S., Inaguma, S., Cho, Y.M., Imaida, K., Wang, J.Q., Fujiwara, O., and Shirai, T.: Lack of mutation induction with exposure to 1.5 GHz electromagnetic near fields used for cellular phones in brains of big blue mice. *Cancer Research* 62, 1956-1960. 2002).

Can mobile phone HF fields induce cancer? This much-discussed topic is dealt with by an Australian group. According to the authors, effects on carcinogenesis from high-frequency fields is not clearly proven, but can neither be fully excluded. This assertion is based upon the known uncertain epidemiologic study of Stang et al. (*Epidemiology* 12, 7-12. 2001) on the correlation between mobile phone use and a rare melanoma. As evidence for non-thermal effects in cells, the authors cite their own experiments (French et al.: *Bioelectrochem. Bioenerget.* 43, 13-18. 1997). A year later, though, data from these experiments had to be adjusted concerning dosimetry (French et al.: *Bioelectrochem. Bioenerget.* 46, 311. 1998). They admitted that the experiment was performed at 9 to 50 W/kg instead of with a low SAR (is this still non-thermal, then?). Anyhow, the noteworthy study of De Pomerei et al. (*Nature* 405, 417. 2000) had found effects on heat shock protein (Hsp) formation already at 1 mW/kg, even though experiments were performed in a specific threadworm species. If this effect



were to be claimed for human cells, too, there would be a link to a possible cancer risk. In this context, the authors cite several studies not directly associated with the EMF issue drawing the conclusion that chronic overproduction of Hsp in the end could lead to cell apoptosis inhibition and cancer development. Despite its weak basis, this conclusion is noteworthy (French, P.W., Penny, R., Laurence, J.A., and McKenzie, D.R.: Mobile phones, heat shock proteins and cancer. *Differentiation* 67, 93-97. 2001).

Since the groups around Bawin (1975) and Blackman (1979) first published their related studies, the issue of low- and high-frequency field effects on the calcium (Ca) signal system in the cell has been repeatedly investigated and discussed. Though these findings never could be reproduced and many follow-up studies pointed to methodological faults, they still serve as an argument for potential field effects. Behind this is, among others, the hypothesis of Adey presented in 1981 of a long reaction chain based upon such alterations. A working group of biophysicists and engineers from the University of Technology, Melbourne (Australia), recently published a study dealing with the question whether GSM signals (915 GHz, 2 W/kg) can cause alterations of Ca concentrations in human leukemia cells (Jurkat cells). The study impresses by its high-quality application setup, its dosimetry, temperature regulation, and evaluation methods. To avoid the meanwhile well-known UV effect methodologically caused by fluorescent spectroscopy using Fura-2, as a Ca indicator, Fluo-3 was applied which is excitable by the UV-distant light of an Argon laser. Each test

consisting of a pre-test phase (600 s), an exposure or sham-exposure phase (600 s), and a final Ca influx phase (after induction of the Ca ionophore A23187), measured approximately 20 individual cells using microscopic imaging. As usual, in the course of experiments there were spontaneous peaks of Ca concentration of different type and frequency. Neither the average value of Ca concentration nor peak frequency, nor steepness or height show significant differences during exposure. Fourier analysis/the averaged power spectrum only showed a slight effect at pulse-modulated exposure of cells activated by phytohemagglutinin. However, the authors see this as a statistical anomalia without biological relevance. (Cranfield, C.G., Wood, A.W., Anderson, V., and Menezes, K.G.: Effects of mobile phone type signals on calcium levels within human leukaemic T-cells (Jurkat cells). *Intern. J. Radiat. Biol.* 77. 1207-17. 2001)

Psychologists of the University Keel (United Kingdom) report an effect of a mobile phone held to the ear on the cognitive performance of participants. Experiments were performed in 38 psychology students (aged 20 to 22) who were asked to hold a phone (900 MHz, 1.19 W/kg, switched on or off) with their left hand to the left ear over 30 minutes. 15 min before, 15 min after onset, and 30 min after the end of the test, an 8-min attention test was conducted. The test persons had to repeat a number series and/or sequences of touching 9 cubes forward and backwards. A distinct increase in attentional capacity was demonstrated when the mobile phone was activated. This effect is explained by alterations of blood circulation in certain brain areas (Edelstyn, N.

and Oldershaw, A.: The acute effects of exposure to the electromagnetic field emitted by mobile phones on human attention. *Neuroreport* 13, 119-121. 2002).

A Finnish working group (11 authors from 5 cooperating institutes) performed a comprehensive and thorough study on the issue of possible cancer-promoting effects from mobile phone radiation. Contrary to publications investigating only one single chemically induced or genetically determined cancer type, this study conducted an exceptionally broad-scoped analysis of different tumors induced by gamma radiation (4 Gy) in a total of 200 female CBA/S mice. Over 78 weeks, animals previously exposed to gamma radiation were exposed on 5 days per week for 1.5 hours in a waveguide (902.5 MHz FM, 1.5 W/kg, or: 902.4 MHz, 217 Hz pulsed, 0.35 W/kg). The animals were fixated in special acrylic tubes inside the waveguide (the longitudinal axis of the animals was parallel to field lines) thus ensuring a controlled and exactly dosed exposure. Parallel to HF exposure, both sham-exposure using the same holders but without field, as well as controls in normal cage holders with and without gamma radiation were carried through. Irrespective of HF exposure, 66-68% of the animals had survived gamma radiation after 78 weeks. Apart from the continuous recording of weight as well as feed and water consumption, in all animals comprehensive hematological and histopathological tests were performed. While gamma radiation definitely led to an increase of lymphoma and primary malignant neoplasms, as well as to different hyperplastic lesions, additional effects from HF exposure could not be detected at all (Heikin-

en, P., Kosma, V.M., Hongisto, T., Huuskonen, H., Hyysalo, P., Komulainen, H., Kumlin, T., Lahtinen, T., Lang, S., Puranen, L., and Juutilainen, J.: Effects of mobile phone radiation on X-ray-induced tumorigenesis in mice. *Radiation Research* 156, 775-785. 2001).

Different groups, beginning with Peters et al. (1979) to several publications of the group around Cleary (1990-1996), found effects of high-frequency fields on cell proliferation drawing conclusions on possible mechanisms of cancer development and growth. In the meantime, methods have been refined. Instead of looking for radio-thymidine uptake, researchers use fluorescence methods allowing for more detailed quantifying insights into the cell cycle. Such a study was performed in two different cell lines: embryonic fibroblasts (C3H 10T1/2) and human glioblastoma cells (U87MG) under scrupulously controlled experimental conditions (dosimetry, temperature and gassing control, etc). Both FMCW fields (835.62 MHz) as well as CDMA fields (847.74 MHz) were applied; the average SAR was determined as being 0.6 W/kg. For an exposure setup, a radial transmission line was used – a system being able to parallelly and simultaneously expose several samples (Moros et al.: *Bioelectromagnetics* 20, 65-80. 1999). It was located in a thermostated room. Evidence was found by immunofluorescence using a flow cytometer. Short-term experiments

(13 hours) observed passage through the different stages of cell proliferation; long-term tests (100 hours) were meant to show possible cumulative effects. However, none of the tests could confirm field effects on the cell cycle. The sensitivity of the method was demonstrated by distinct alterations already occurring at very slight temperature shifts. Thoroughly, the authors discuss the above mentioned preceding studies pointing to methodological faults mainly caused by the tritium-thymidine method and the lack of local temperature regulation (Higashikubo, R., Ragouzis, M., Moros, E.G., Straube, W.L., and Roti, J.L.R.: Radiofrequency electromagnetic fields do not alter the cell cycle progression of C3H 10T1/2 and U87MG cells. *Radiat. Res.* 156, 786-795. 2001).

To date, studies on potential behavioral effects on animals from high-frequency fields have been conducted under conditions of whole-body exposure. For the first time now there is a behavioral study in rats (48 Sprague-Dawley rats) which were daily exposed for 45 min prior to the tests with their head, whereas the rest of the body, to large extent, was shielded (900 MHz, GSM pulsed, 1 W/kg and/or 3.5 W/kg average head SAR). They were compared to sham-exposed animals kept for the same time period in the corresponding holder. On 14 subsequent days, the animals' learning capacity was measured: a – chocolate cookies put at the ends of an 8-arm maze were to be found as fast

as possible without returning to the arms already emptied; b – 13 small boxes mounted to a 120-cm disc and closed by white lids were to be opened and emptied. There were visual orientation marks in the room helping the animals along. The learning curves, that is, the decrease of error frequency, showed no differences between exposed and non-exposed animals. An ANOVA evaluation neither showed field effects. Moreover, the authors discuss the experiments leading to positive results performed by Lai, Wang, and others (*Bioelectromagnetics* 15, 95-104. 1995; *Bioelectromagnetics* 12, 52-56. 2000). According to them, these experiments are unrealistic, since they deal with whole-body exposure. Obviously, the findings rather were based upon physiological whole-body than on specific brain reactions, as is shown, too, by the paper on the cholinergic effect published by the same authors (*Pharmacol. Biochem. Behav.* 33, 131-138. 1989). The authors believe head-only exposure to be essential for methodological progress, an important step to a realistic human-mobile phone model, but do not deny still existing inadequacies (only 14-days observation, symmetrical effect on the whole rat brain). Further, they demand that the developing brain should receive more attention (Dubreuil, D., Jay, T., and Edeline, J.M.: Does head-only exposure to GSM-900 electromagnetic fields affect the performance of rats in spatial learning tasks? *Behavioural Brain Research* 129, 203-210. 2002).