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Tumor promotion by exposure to radiofrequency electromagnetic fields below exposure limits for humans



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ABSTRACT

The vast majority of *in vitro* and *in vivo* studies did not find cancerogenic effects of exposure to electromagnetic fields (RF-EMF), *i.e.* emitted by mobile phones and base stations. Previously published results from a pilot study with carcinogen-treated mice, however, suggested tumor-promoting effects of RF-EMF (Tillmann et al., 2010). We have performed a replication study using higher numbers of animals per group and including two additional exposure levels (0 (sham), 0.04, 0.4 and 2 W/kg SAR). We could confirm and extend the originally reported findings. Numbers of tumors of the lungs and livers in exposed animals were significantly higher than in sham-exposed controls. In addition, lymphomas were also found to be significantly elevated by exposure. A clear dose–response effect is absent. We hypothesize that these tumor-promoting effects may be caused by metabolic changes due to exposure. Since many of the tumor-promoting effects in our study were seen at low to moderate exposure levels (0.04 and 0.4 W/kg SAR), thus well below exposure limits for the users of mobile phones, further studies are warranted to investigate the underlying mechanisms. Our findings may help to understand the repeatedly reported increased incidences of brain tumors in heavy users of mobile phones.

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1. Introduction

The increased use of mobile phones during the last two decades was accompanied with fears that their emission of radiofrequency electromagnetic fields (RF-EMF), sometimes also called “radiation”, may have adverse health effects. So far, no biophysical mechanism has been identified which would speak in favor of such effects since the quantum energy in the frequency range used for mobile communication is far too low to break chemical bonds. The only accepted mechanism by which RF-EMF could be harmful is heating

which is prevented at the current exposure limits for the general population (specific absorption rate (SAR) 0.08 W/kg whole body; 2 W/kg local exposure) [1]. Some epidemiological studies, however, have found increased incidences of brain tumors in heavy users of mobile phones [2,3].

In 2010, a study was published [4] showing tumor-promoting effects of life-long exposure to RF-EMF (Universal Mobile Telecommunication System, UMTS) at moderate exposure levels in mice treated with a carcinogen (ethylnitrosourea, ENU) *in utero*. Those results were potentially influenced by an unexpected infection with *Helicobacter hepaticus* (which may have had an influence on the pathological findings in the liver, as suggested by the authors). Nevertheless the data showed clear effects of RF-EMF exposure on the incidences of lung and liver tumors. We have replicated this study with higher numbers of animals per group, but otherwise under similar conditions, in order to clarify whether the previously reported results could be confirmed. In addition, two additional SAR levels of exposure (low and high) were included in order to investigate possible dose–response relationships.

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Furthermore, we ensured that we did not have any infection with *Helicobacter* species in our animals.

2. Materials and methods

2.1. Experimental design

The experiment was performed according to the German Animal Welfare Act and approved by the local authorities (city state of Bremen). Special care was taken to repeat the study by Tillmann et al. [4] as accurately as possible. Male C3H/HeNcrI ($n = 43$) and female C57Bl/6N ($n = 290$) mice were purchased in a staggered design from Charles River Germany, Sulzfeld, Germany, at an age of 8–9 weeks. After acclimatization, at the age of 12 weeks (females), the males and 128 females were mated for one week (ratio 3 females: 1 male) in two rounds, thus a total of 256 potentially pregnant females were obtained. They were distributed to the 128 cages of the exposure devices, two animals per cage. Exposure or sham-exposure of the pregnant females thus started at day 6 p.c. (post conception). All females were weighted at day 13 p.c., and the ones with the highest weight gains remained in the exposure devices while the others were sacrificed (CO_2 overdose). The remaining 34 females, age 12 weeks, were mated with the males, and the female offspring served as the untreated, unexposed cage control ($n = 96$, three animals per cage). At day 14 p.c., the females in the exposure devices were injected (i.p.) with ethylnitrosourea

(ENU; Sigma–Aldrich, Taufkirchen, Germany) at a dose of 40 mg/kg in saline. Six days after birth, after sexing three female F1 animals were left with their mothers, while the surplus females and the males were removed and sacrificed. Litters with too few female pups were filled up with surplus females from other litters of the same exposure group. In total, four groups of female F1 mice were obtained, 96 animals per group. At day 21, pups were weaned, and the dams were sacrificed.

2.2. Exposure to electromagnetic fields

The exposure devices consisted of eight radial waveguides with 16 cages each, arranged in stacks of two and connected to power amplifiers and RF-generators. Details have been published earlier [5]. Extensive numerical calculations of the field distributions and the corresponding SAR values revealed unavoidable substantial variations for animals in different positions and within animals (local maximum SAR values) which could be as much as 3–5 times higher than the whole-body SAR. Two waveguides per exposure group with 16 cages each (32 cages in total, 96 animals) were one out of four groups with the following nominal whole-body SAR levels: sham-exposed (0 W/kg), 0.04 W/kg (low), 0.4 W/kg (moderate) and 2 W/kg (high) for a reference configuration of three mice (body weight 20 g each) per cage, with a standard deviation for this configuration of around 36%. The exposure was comparably homogeneous with standard deviations of the whole body SAR within

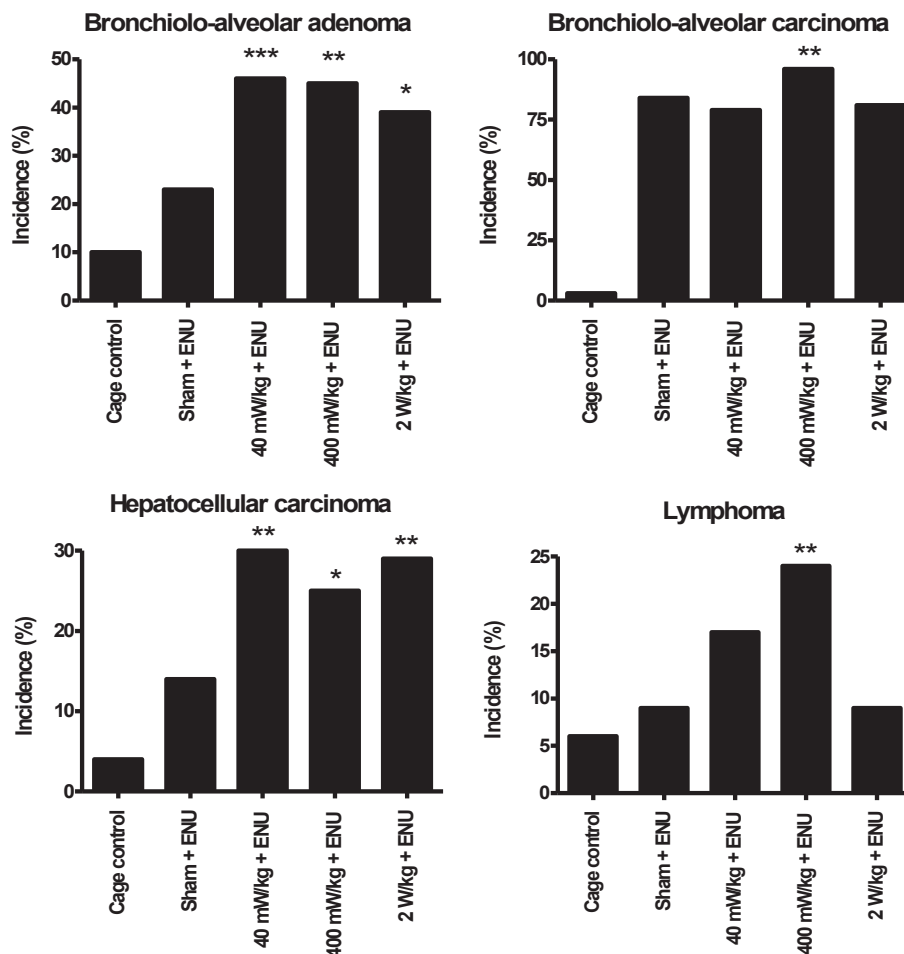


Fig. 1. The effects of life-long exposure to RF-EMF in mice treated with ENU *in utero*. Shown are the tumor incidences as percentages of animals, based on histopathological analyses of 93–96 animals per group. Significant differences are indicated by asterisks (Fisher's one-tailed exact test): *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

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