Summaries and assessments of selected studies

In the period from April to August 2016, 129 new publications have been identified, and nine of these were discussed in depth by BERENIS. Based on the selection criteria, four of these publications were selected as the most relevant ones. Their summaries and assessments are provided below.

1) Experimental animal and cell studies

Extremely low frequency magnetic fields and cancer development in rats (Soffritti et al. 2016)

The effects of ELF-MF on the development of cancer were investigated in this *in vivo* study. Male and female Sprague Dawley rats were exposed for 19 hours per day (1000 µT, 50 Hz) over a period of 104 weeks. The exposure started before the rats were born, thus, in the uterus of the dams. As co-carcinogenic effects of ELF-MF exposure have been previously observed in some *in vivo* studies, effects of concurrent exposure with ELF-MF and a known carcinogen were investigated. Formaldehyde (50 ppm) was added to the drinking water. Formaldehyde causes the development of C-cell carcinomas and lymphoreticular tumours. C-cell carcinomas are malignant thyroid tumours that occur in 1.1% (0.1-2.1%) of untreated animals of this particular rat strain. A previous study (Boorman et al. 1999)[1] described an increased development of C-cell carcinomas in combination with ELF-MF. The exposure combinations in the new study were: a) formaldehyde combined with ELF-MF, b) ELF-MF alone, and c) formaldehyde alone. The size of the experimental groups varied between 200-500 animals. The results of the study did not show significant differences between the groups in regard to food intake, body weight and survival rate. As already observed in the study of Wyde *et al.* (2016)[2] regarding mobile phone radiation (see BERENIS-Newsletter 7), an increased incidence of cancer was only observed in male animals. The combined exposure with ELF-MF and formaldehyde resulted in a significant increase in lymphomas and C-cell carcinomas in male rats. This study confirms the co-carcinogenic effect of ELF-MF. Notably, the same research group has recently published results that showed an enhancement of the carcinogenic effect of gamma radiation[3] by ELF-MF (see BERENIS-Newsletter 6). As usually applied in toxicological studies related to the identification of risks, the doses of the magnetic field tested in this study are higher than commonly occurring in the environment.

Extremely low frequency magnetic fields and impact on apoptosis (Feng et al. 2016)

Feng *et al.* (2016) investigated *in vitro* the influence of ELF-MF exposure (50 Hz; 200, 400, 1000 or 2000 µT) on the regulation of apoptosis. Apoptosis plays an important role in a variety of physiological processes, for example the elimination of degenerated cells from the organism, which could potentially

[1] Boorman GA, McCormick DL, Findlay JC, Hailey JR, Gauger JR, Johnson TR, Kovatch RM, Sills RC, Haseman JK (1999): **Chronic toxicity/oncogenicity evaluation of 60 Hz (power frequency) magnetic fields in F344/N rats.** Toxicol Pathol. 1999 May-Jun;27(3):267-78. https://www.ncbi.nlm.nih.gov/pubmed/10356702

[2] Wyde M, Cesta M, Blystone C, Elmore S, Foster P, Hooth M, Kissling G, Malarkey D, Sills R, Stout M, Walker N, Witt K, Wolfe M, Bucher J (2016): **Report of Partial findings from the National Toxicology Program Carcinogenesis Studies of Cell Phone Radiofrequency Radiation in Hsd: Sprague Dawley® SD rats (Whole Body Exposures).** http://biorxiv.org/content/early/2016/06/23/055699

[3] Soffritti M, Tibaldi E, Padovani M, Hoel DG, Giuliani L, Bua L, Lauriola M, Falcioni L, Manservigi M, Manservisi F, Panzacchi S, Belpoggi F (2016): **Life-span exposure to sinusoidal-50 Hz magnetic field and acute low-dose γ radiation induce carcinogenic effects in Sprague-Dawley rats.** Int J Radiat Biol. 2016 Feb 19:1-13. http://www.ncbi.nlm.nih.gov/pubmed/26894944

cause tumour development. The authors have exposed a human amniotic cell line for 30, 60 and 120 minutes to the ELF-MF. The exposure did neither cause any direct impact on cell viability nor apoptosis. However, when the cultures were subsequently treated with the antibiotic staurosporine, a relative reduction of early apoptotic cell stages was observed after exposure for 60 minutes, but not after 30 and 120 minutes. With the applied concentration, staurosporine triggered a 50% increase of apoptotic cells. This exposure time-dependent decrease of apoptosis was only observed with magnetic flux densities of 400 µT and 1000 µT, but not with weaker and stronger magnetic fields (200 µT and 2000 µT). Moreover, a possible explanation for this effect was elaborated. After 30 and 120 minutes of exposure, an increase in free radicals / reactive oxygen species (ROS) in the mitochondria was seen, which could not be detected after 60 minutes. This suggests a specific mechanism for the removal of the ROS within this time slot. Indeed, the authors showed that the blocking of a pore in the mitochondrial membrane not only caused an increase of ROS after 60 minutes of exposure, but also protected from staurosporine-induced apoptosis. Opening of this pore, thus, causes an outflow of ROS and other molecules from the mitochondria influencing the cell response to the additional stressor staurosporine. By means of specific inhibitors, it was possible to show that the release of ROS into the cytoplasm leads to the activation of the Akt signaling pathway. This signaling pathway is known for supporting cell viability and counteracting apoptosis. Nevertheless, it remains open whether this interesting mechanism caused by ELF-MF exposure can be universally applied to various cell types, and whether these effects have a relevant impact on physiological processes of the organism.

2) Epidemiological studies

Non-specific symptoms in the vicinity of mobile phone base stations (Baliatsas et al. 2016)

A retrospective cohort study conducted in the Netherlands with 1069 adults explored whether exposure to radiation from mobile phone base stations was correlated to prevalence of non-specific symptoms (Baliatsas *et al.* 2016). Based on interviews with 5933 adults in 2010/2011[4] (see BERENIS-Newsletter 4) all individuals with symptoms data available from electronic health records of general practices that did not move residence since 2004 were included in the present survey. A total of 27 non-specific symptoms that are often mentioned in relation to EMF were selected. Residential exposure to RF-EMF emitted from mobile phone base stations was modeled for 2010/2011. For 2004, the exposure was extrapolated based on the ratio of the number of antennas at both points in time within a 500m distance of houses. The number of antennas increased by 30% between 2004 and 2010/2011. Average exposure in the study population was 0.12 V/m in the year 2010/2011 and 0.11 V/m in the year 2004. Cross-sectional analysis of the whole study sample did not reveal associations of any of the symptoms with exposure to RF-EMF from mobile phone base stations. A total of 55 out of the 1069 individuals stated that they are sensible to mobile phone radiation. This group reported more symptoms in 2010/2011 compared to 2004, and for several symptoms, a correlation with modeled exposure at the place residence was seen. A weakness of this analysis is that it was retrospective, i.e. that the statement regarding sensibility to RF-EMF from mobile phone base stations was made in 2010/2011. It thus remains unclear whether newly emerged symptoms are attributed to RF-EMF from mobile phone base stations, simply because such base stations are present at the residential location, or whether indeed a causal link exists. The statistical analyses only accounted for age, sex, and ownership of a house. Other confounders could therefore bias the result. The exposure model is simple and does not account for relevant factors such as the tilt of the base station. The

[4] Baliatsas C, Bolte J, Yzermans J, Kelfkens G, Hooiveld M, Lebret E, van Kamp I (2015): **Actual and perceived exposure to electromagnetic fields and non-specific physical symptoms: An epidemiological study based on self-reported data and electronic medical records.** Int J Hyg Environ Health 2015; 218 (3): 331 – 344. http://www.ncbi.nlm.nih.gov/pubmed/25704188

differences in exposure between the two points in time are relatively small. Furthermore, a longitudinal analysis would have been desirable.

Radiofrequency electromagnetic fields from mobile phone base stations, TV and radio broadcast transmitters and symptoms in Swiss adolescents (Schoeni et al. 2016)

In BERENIS-Newsletter 6 (June 2016), results of the prospective Swiss cohort study HERMES were discussed which indicated that changes in the memory performance within one year are related to the cumulative EMF dose of the brain. The latter is mainly determined by the own mobile phone use. In a new publication of this cohort study based on the same 439 adolescents aged 12 to 17 years from Switzerland (Schoeni *et al.* 2016), it was investigated whether RF-EMF from mobile phone base stations, TV and radio broadcast transmitters caused an increase of non-specific symptoms such as headache, tiredness or lack of concentration within one year. For this purpose, exposure at home and school of the participants was modeled and time-weighted average exposure was calculated by assuming that the adolescents spend an average of 4.8 hours per day at school. Three exposure groups were formed: low exposure (below median; <0.048 V/m), medium exposure (between median and 75th percentile; 0.048-0.073 V/m) and high exposure (>0.073 V/m). Symptoms were recorded with standardised questionnaires. All analyses were adjusted for age, sex, nationality, school level, physical activity, alcohol and education of parents. The longitudinal analyses were also adjusted for change in body height between baseline and follow-up. The cross-sectional analysis did not reveal a correlation between the modeled RF-EMF exposure and any of the recorded symptoms. The longitudinal analyses found an increased incidence of tiredness in the highest exposure group (Odds Ratio: 2.94; 95%CI: 1.43 to 6.05). No correlations were found for the other symptoms. A change analysis revealed a two-fold decrease in exhaustibility (Odds Ratio: 0.50; 95%CI: 0.27-0.93) for persons with an exposure increase within a year compared to those with unchanged or decreased exposure. The authors interpret the few significant and opposite results as chance findings. This is the first longitudinal study with adolescents regarding environmental exposure to RF-EMF from fixed site transmitters. A strength of the study is the systematic assessment of RF-EMF exposure by means of a validated propagation model. However, the identified differences in exposure are very small. According to dosimetric evaluations, the average contribution of all far field sources (including WLAN and cordless phones) was only 1.6% of the absorbed total brain dose, and 6.0% of the absorbed total whole-body dose[5]. In this respect, it is not surprising that no correlations with symptoms were found. A weakness of the study is the relatively small sample size.

3) Review

ANSES report on radiofrequency electromagnetic fields and health of children

The report of ANSES (*Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail*) on „Exposure to radiofrequency electromagnetic fields and health of children" has been published in July 2016 and is available at:
https://www.anses.fr/fr/system/files/AP2012SA0091Ra.pdf (in French).

[5] Roser K, Schoeni A, Bürgi A, Röösli M (2015): **Development of an RF-EMF Exposure Surrogate for Epidemiologic Research.** Int J Environ Res Public Health. 2015 May 22;12(5):5634-56. http://www.ncbi.nlm.nih.gov/pubmed/26006132

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Feng B, Ye C, Qiu L, Chen L, Fu Y, Sun W (2016): **Mitochondrial ROS Release and Subsequent Akt Activation Potentially Mediated the Anti-Apoptotic Effect of a 50-Hz Magnetic Field on FL Cells.** Cell Physiol Biochem. 2016;38(6):2489-99. Epub 2016 Jun 17. http://www.ncbi.nlm.nih.gov/pubmed/27310130

Schoeni A, Roser K, Bürgi A, Röösli M (2016): **Symptoms in Swiss adolescents in relation to exposure from fixed site transmitters: a prospective cohort study.** Environ Health. 2016 Jul 16;15(1):77. http://www.ncbi.nlm.nih.gov/pubmed/27422272

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List of abbreviations (pdf)