Summaries and assessments of selected studies

In the period from July to October 2015, 89 new publications have been identified, and 14 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 neurodegenerative diseases (Benassi et al. *2015)*

Using an *in vitro* model for Parkinson's disease, Benassi *et al.* (2015) investigated the association between exposure to ELF-MF and neurodegeneration. The circumstances leading to the loss of dopaminergic neurons in the substantia nigra, and thus to the development of Parkinson's disease, are not yet fully understood. It is assumed that both environmental and genetic factors are involved. One of the theories hypothesizes that the death of neuronal cells is caused by oxidative stress originating from mitochondrial dysfunction. The neurotoxin MPP^+ represents a chemical model for this pathogenesis depending on oxidative stress. It interferes with the mitochondrial electron transport chain and promotes the generation of free radicals. The authors applied it to a brain tumor cell line, which can be differentiated to nerve-like cells. At first, the cells were exposed to an ELF-MF (50 Hz, 1 mT) for up to three days. Compared to the control exposure condition with about 0.3 µT ELF-MF, a slight increase of free radical levels and oxidatively damaged proteins was found, concomitantly with small reductions in the antioxidant defense systems. However, this did not influence cell proliferation and cell death. Then, the magnetic field exposure was combined with MPP^+. Preceding exposure led to a stronger reaction of the cells to the addition of MPP^+ than without magnetic field, including increased dying of cells, particularly at low neurotoxin doses and during the recovery phase. The cumulative increase of free radicals and damaged proteins indicates an association between the increased toxicity and the oxidative stress. These effects were modulated or reduced when the redox regulating system was altered by inhibition of the GSH synthesis or by the addition of antioxidants. The findings of this study may be interpreted in such a way that ELF-MF do not directly cause damage to neurons, but could promote the development of neurodegenerative diseases in the presence of additional environmental factors.

Radiofrequency electromagnetic fields and genetic impact? (Wang et al. *2015)*

Wang *et al.* (2015) explored the controversial issue whether RF-EMF can cause damage to DNA. The authors exposed murine brain tumor cells with a RF-EMF (900 MHz), mimicking the signal during a call with a GSM mobile phone, at different SAR values (0, 0.5, 1, 2 W/kg) for 24 hours. None of the tested SAR values resulted in a significant DNA damage with the alkaline comet assay, which is a standard method for the assessment of acute DNA damage, detecting primarily single- and double-strand breaks as well as lacking bases. Then, the authors applied a less frequently used variation of the comet assay, which also detects oxidative DNA base damage. This assay indicated a significant increase of DNA damage at the highest exposure condition, simultaneously with a rise of free radicals. The DNA repair protein OGG1, which specifically recognizes and removes oxidized guanine bases, plays a central role in the removal of these frequently occurring DNA damages. When the authors reduced the level of this protein in the cells, the exposure-dependent increase of DNA damage became more apparent and detectable in cells exposed at lower SAR values. These observations may indicate that RF-EMF lead to a slight increase of oxidative DNA damage through

the release of free radicals, which can be handled by the intrinsic DNA repair mechanisms under normal physiological conditions. Whether this can eventually lead to cancer-promoting mutations or other detrimental consequences remains open and should be investigated in future studies.

2) Epidemiological study

Amyotrophic Lateral Sclerosis (ALS) in Sweden and occupational exposure to electric shocks and magnetic fields (Fischer et al. *2015)*

The association between ALS and work-related accidental electric shocks, as well as occupational exposure to ELF-MF was investigated in a large population-based nested case-control study in Sweden (Fischer *et al.* 2015). The study included persons who were born in Sweden between 1901 and 1970, and registered in the Swedish Population and Household Census in 1990. Based on the Swedish Patient Register, Migration Register, and Cause of Death Register, it was assessed for all persons whether a disease occurred until 2010. For each of the 4,709 cases included in the study, five control subjects with the same birth year and sex were randomly selected from the population register (n=23,335). The occupations of all selected individuals from both groups were determined based on the register data. For each occupation, the probability of suffering a work-related electric shock and level of ELF-MF exposure was estimated based on corresponding job-exposure matrices. Taking into account socioeconomic status, education, and region of residence, no association between ALS and ELF-MF or electric shocks was observed. However, for individuals less than 65 years old, medium and high electric shock exposure was associated with an increased risk (OR=1.20, 95% CI 1.02-1.40 and OR=1.22, 95% CI 1.03-1.43, respectively). In an analysis of different occupational groups, an increased risk was found for welders <65 years (OR=1.52, 95% CI 1.05-2.21), but not for welders for all ages combined. For electricians, the risk was not increased. The association between ALS and electric shocks in the age group <65 years was consistent, and persisted even when welders were not considered in the analysis. In contrast to two recently published large studies (Huss et al, 2014; Vergara et al. 2015), this study indicates that in the age group <65 years risk factors for ALS are rather occupational electric shocks than ELF-MF exposure. A strength of this large population based study is the prospective collection of exposure and outcome information based on routine records, which makes selection or information bias unlikely. In addition different exposure assessment approaches have been used, which all led to similar results. However, some exposure misclassification is unavoidable. As both, cases and controls, are likely to be affected in a similar manner, such imprecision rather results in an underestimation of the risk, if an association between the exposure and the disease really exists.

3) Human qualitative study

Is electromagnetic hypersensitivity caused by nocebo responses? (Dieudonné, 2015)

The aim of the qualitative study of Dieudonné (2015) was to investigate how electromagnetic hypersensitivity (EHS) originates, and the role of nocebo effects in this process. There are no objective diagnostic criteria for EHS, and by definition EHS is based on the affected person's individual assessment. A nocebo effect is defined as the pathogenic effect of an exposure caused by the expectations of the affected persons, therefore the opposite of a placebo effect. For this study 40 individuals were interviewed (11 men and 29 women) who suffer from EHS and have adjusted their lifestyles accordingly (e.g. by removing electrical devices from the apartment).

The study participants were recruited through adverts distributed in EHS self-help groups and other networks of EMF-sensitive people in France. Interviews were conducted in venues of choice of the participants, using a standardized qualitative study approach. Based on the interviews a model for the EMF attribution process was developed. The typical linear model is composed of seven stages: (1) onset of symptoms, (2) no (medical) explanation and solution, (3) discovery of EHS, (4) gathering of information about EHS, (5) implicit appearance of conviction, (6) experimentation (conducting small self-experiments), (7) conscious acceptance of conviction. The author emphasizes that a typical feature of all interviews was that symptom onset occurred before environmental factors were suspected, and that most of the participants did not show a specific interest in EMF at the time when the symptoms started. Thus, a nocebo effect seems to be unlikely as an explanation for the start of the symptoms but may happen at the sixth stage of the process leading to a reinforcement of the attribution to EMF. Taking the study design into account, the affected persons probably suffer from severe forms of EHS. The author makes several suggestions: (1) for a better understanding of EHS, the affected persons should be conceived as patients suffering from medically unexplained symptoms, which they attribute to EMF exposure. (2) This attribution allows them, firstly, to make sense of symptoms, and then to act upon them, which may be a mean of empowering themselves against their symptoms or disease. (3) The attribution of the symptoms to EMF is the only feature that is common among all EHS patients, and it is thus not surprising that EHS cannot be objectified in clinical or experimental categories.

Contact

Dr. Stefan Dongus
BERENIS Secretariat
Swiss Tropical and Public Health Institute
Department of Epidemiology and Public Health
Environmental Exposures and Health Unit
Socinstr. 57, P.O. Box, CH-4002 Basel, Switzerland
Tel: +41 61 284 8111
Email: stefan.dongus@unibas.ch

References

Benassi B, Filomeni G, Montagna C, Merla C, Lopresto V, Pinto R, Marino C, Consales C (2015): **Extremely Low Frequency Magnetic Field (ELF-MF) Exposure Sensitizes SH-SY5Y Cells to the Pro-Parkinson's Disease Toxin MPP.** Mol Neurobiol. 2015 Jul 30.
www.ncbi.nlm.nih.gov/pubmed/26223801

Dieudonné M (2015): **Does electromagnetic hypersensitivity originate from nocebo responses? Indications from a qualitative study.** Bioelectromagnetics. 2015 Sep 15.
www.ncbi.nlm.nih.gov/pubmed/26369906

Fischer H, Kheifets L, Huss A, Peters TL, Vermeulen R, Ye W, Fang F, Wiebert P, Vergara XP, Feychting M (2015): **Occupational Exposure to Electric Shocks and Magnetic Fields and Amyotrophic Lateral Sclerosis in Sweden.** Epidemiology. 2015 Nov;26(6):824-30.
www.ncbi.nlm.nih.gov/pubmed/26414853

Huss A, Spoerri A, Egger M, Kromhout H, Vermeulen R; Swiss National Cohort (2015): **Occupational exposure to magnetic fields and electric shocks and risk of ALS: the Swiss National Cohort.** Amyotroph Lateral Scler Frontotemporal Degener. 2015 Mar;16(1-2):80-5. Epub 2014 Sep 17.
http://www.ncbi.nlm.nih.gov/pubmed/25229273

Vergara X, Mezei G, Kheifets L (2015): **Case-control study of occupational exposure to electric shocks and magnetic fields and mortality from amyotrophic lateral sclerosis in the US, 1991-1999.** J Expo Sci Environ Epidemiol. 2015 Jan;25(1):65-71. Epub 2014 Jun 11.
http://www.ncbi.nlm.nih.gov/pubmed/24917188

Wang X, Liu C, Ma Q, Feng W, Yang L, Lu Y, Zhou Z, Yu Z, Li W, Zhang L (2015): **8-oxoG DNA Glycosylase-1 Inhibition Sensitizes Neuro-2a Cells to Oxidative DNA Base Damage Induced by 900 MHz Radiofrequency Electromagnetic Radiation.** Cell Physiol Biochem. 2015;37(3):1075-88. Epub 2015 Sep 25. www.ncbi.nlm.nih.gov/pubmed/26401913

Additional information related to the Swiss expert group on electromagnetic fields and non-ionising radiation (BERENIS) and a list of abbreviations can be found at
http://www.bafu.admin.ch/elektrosmog/01095/15189/index.html?lang=en

Link to list of abbreviations (pdf)