Summaries and assessments of selected studies

In the period from May to July 2015, 94 new publications have been identified, and 12 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

Neuritin can reverse deficits in murine recognition memory caused by exposure to extremely low frequency magnetic fields (Zhao et al*. 2015)*

There is evidence from several animal studies that electromagnetic fields lead to behavioural and cognitive disturbances. In a new study in mice, Zhao *et al*. (2015) found that low frequency magnetic field exposure at 1 mT, 50 Hz for 12 hours per day resulted in an impairment of the associative recognition memory. However, this effect was only seen at exposure for 7 and 10 days, while recognition memory was not impaired anymore after exposure for 14 and 21 days. It is important to note that deficits in recognition memory can be due to changes in spontaneous locomotor activity, which is leading to impairment of animal movement rather than the associative recognition memory. This could be excluded in this study. The experiment indicates that the effect is temporary. In addition to the time dependency, a correlation of the recognition memory and dendritic spine density was found on days 7 and 10. From similar animal studies, no mechanism could be deduced so far regarding how magnetic field exposure induces changes in recognition memory. An increase of the neurotrophin neuritin, which was achieved by injecting an adenovirus-associated vector, prevented the transitory effect on the recognition memory induced by the magnetic field. Neuritin is a neurotrophic factor important in the neural development involved in neurite outgrowth, arborisation, synaptic plasticity and maturation. Overexpression of neuritin reversed the effects seen after the magnetic field exposure alone, namely the reduction in dendritic spine density and deficits in recognition memory on exposure days 7 and 10. Earlier studies had shown that neuritin has an anti-depressive effect, and that the neuritin level is reduced under chronic stress. The authors suggest that this effect might be caused by oxidative stress (ROS) leading to a decrease in dendritic spine density and a subsequent decrease in recognition memory. The authors point out the importance of their findings for the elucidation of underlying biological mechanisms.

Extremely low frequency magnetic fields and neuronal activity (Yang et al. *2015)*

The goal of the *in vitro* study by Yang *et al.* (2015) was to investigate the effects of magnetic field exposure on the activity of gamma-aminobutyric acid A ($GABA_A$) receptors, by applying *in vitro* electrophysiological experiments with granule neurons isolated from the cerebellum of rats. From them, they derived basic principles of a putative mechanistic interaction between magnetic field exposure and neuronal effects such as cognitive and behavioural changes or the impact on neuronal development. Neuronal cells were exposed to a 50 Hz ELF-MF at 0.2 or 1 mT flux density for 30 to 120 minutes before assessing the current amplitudes (ion flux) upon administration of the neurotransmitter GABA. GABA causes an increased influx of chloride ions, which in turn decreases the action potential of the neuron. Depending on time and dose, the authors have observed an increased current amplitude of 10 to 20 percent in exposed cells but no impact on the $GABA_A$ receptor excitability. Using specific activators and inhibitors, they also investigated cellular signaling cascades that possibly regulate the ELF-MF-dependent effect. Thereby, the protein kinase C, a

principal signaling molecule, was found to be activated upon exposure. Specific activation or inhibition of the enzyme protein kinase C mimicked or abrogated the increased current amplitudes upon ELF-MF exposure, respectively. Furthermore, the authors showed that the activation of protein kinase C by the magnetic field is mediated by the EP1 receptor. The interesting observations made in this study may provide the basis for further mechanistic experiments in respect to putative effects of magnetic fields on the central nervous system. Weaknesses of the study are the poorly described exposure conditions and not having performed the experiments blinded for the experimenter.

Does exposure to intermediate-frequency magnetic fields alter brain biomarkers and memory functions in adult mice? (Win-Shwe et al. *2015)*

In this study, the effect of intermediate-frequency magnetic fields (21 kHz, 3.8 mT) on neurological and immunological biomarkers in the hippocampi of the brain of mice during pregnancy and adolescence was analysed regarding (a) inflammation, (b) transcription factors associated to signaling pathways for the excitatory N-Methyl D-Aspartate (NMDA) receptor and memory functions, and (c) oxidative stress on RNA level. Furthermore, a potential activation of microglia involved in defending various pathogens was analysed histologically. Pregnant dams were exposed for the first time during foetal organogenesis (day 7-17 of pregnancy) for 1 hour per day, and some of the adolescent male mice were exposed for the second time 27-48 days after birth. Related sham and cage controls were done in parallel. In order to determine and differentiate potential effects during pregnancy and adolescence, biomarkers were analysed 3 and 7 weeks after birth in the one-time-exposed group, and 7 weeks after birth in the two-times-exposed group, immediately after the end of the second exposure. In order to determine recovery, an additional group of mice was exposed two times but examined one day after the end of the second exposure. In 7 week old male mice exposed twice, markers related to the NMDA receptor, inflammation markers, and markers for oxidative stress were significantly increased compared to mice of the same age exposed only once. However, this effect was not observed in the one-time-exposed group where the biomarkers were analysed already 3 weeks after birth. No difference was found in microglia activation between all groups. It can be concluded that exposure to intermediate-frequency magnetic fields during organogenesis is not sufficient for modifying the neurological and immunological biomarkers. However, the data indicate changes in neuroinflammation, oxidative stress and memory function when the animals were also exposed after birth. The effects observed in this experiment are reversible and disappear after ending the magnetic field exposure.

2) Epidemiological study

Is there a correlation between extremely low and high frequency electromagnetic fields and physical symptoms? (Baliatsas et al. *2015)*

Baliatsas *et al.* (2015) investigated correlations between ELF-MF as well as RF-EMF and physical symptoms in an epidemiological study comprising 5’933 adults in the Netherlands. The number and duration of non-specific symptoms were assessed using a questionnaire sent out to study participants. In addition, medical records of general practitioners were considered. Various EMF exposure surrogates were derived for each study participant. Exposure to mobile phone base stations as well as radio and television transmitters was assessed by using a propagation model. Distance to the nearest high-voltage overhead power line was calculated with Geographic Information Systems (GIS). Exposure from cordless phone base stations and other people’s mobile phones was estimated by a model which had been calibrated with personal measurements made in another study population. Use and exposure from fields of electrical appliances (e.g. electric alarm

clock near the bed, electric charger, electric blanket, induction hob) was assessed by a questionnaire. The questionnaire also included questions regarding the perceived personal exposure to EMF emission sources at home, at work, and outdoors, on a scale from 0 ("not at all") to 10 ("very much"). The study participants were chosen randomly, with a higher proportion of persons being selected in areas with high modelled RF-EMF from transmitters, in order to include as many potentially highly exposed persons as possible. The participation rate was 46%. Several relevant confounders were considered in the data analysis, such as age, gender, education, smoking habits and alcohol abuse. No association was found between any of the modelled RF-EMF exposures and the number and duration of physical symptoms. However, several associations were observed between occurrence of symptoms and exposure to electrical appliances. The most consistent associations were more and longer symptoms for people using electric chargers in close distance (≤50 cm) during sleep, and for persons using an electric blanket. Sleep quality was, however, not affected in both cases. Persons living in a distance of less than 200 m from a high-voltage overhead power line did not have more symptoms than the rest of the study population. The perceived exposure to all RF-EMF and ELF-MF sources was associated with more self-reported and general practitioner registered symptoms, with longer duration of physical symptoms, and with reduced sleep quality. This study is one of the largest in its field, with a strong emphasis on the exposure assessment. It is unlikely that the exposure modelling for mobile phone base stations as well as radio and television transmitters has led to systematic errors, while this cannot be excluded with regard to self-reported data. For example, there is a possibility that persons with more symptoms reported more frequent use of electric appliances. The weakness of the exposure models is their lack of precision (explained variance below 30%), and the small differences in exposure levels. The latter aspect is of particular importance, because exposure caused by own mobile and cordless phone use is not considered in the study. Another weakness of the study is the fact that it is a cross-sectional study without a temporal component. This implies that no information exists regarding whether the symptoms or the exposure occurred first. It is conceivable, for example, that persons having symptoms use electric blankets more frequently, and not vice versa. Yet, this study confirms the results of previous studies concluding that persons who perceive themselves as being exposed to electromagnetic fields also report more symptoms on average.

3) Review

ANSES report on animals and ELF-MF

The report of ANSES (*Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail*) on „Consequences of extremely low frequency electromagnetic fields for the health of animals and animal breeding performance" has been published in August 2015 and is available at: https://www.anses.fr/fr/system/files/SANT2013sa0037Ra.pdf (in French).

ARIMMORA final report

The EU-funded ARIMMORA project (Advanced Research on Interaction Mechanisms of electroMagnetic exposures with Organisms for Risk Assessment) aimed at scrutinising the underlying biophysical mechanisms and to clarify a possible causal relationship between ELF-MF exposure and cancer, especially childhood leukaemia. The final report is now available at: http://arimmora-fp7.eu/index.php?page=deliverables-and-publications.

4) More information

Potential effects of base station antennas on bovine health (commentary on Hässig et al. *2014)*

The research team of Prof. Michael Hässig has published several articles on potential effects of base station antennas on bovine health. The Swiss Research Foundation for Electricity and Mobile Communication (FSM) has published a commentary (Dürrenberger & Fröhlich 2014, in German) on the publication *„Influence of Non Ionizing Radiation of Base Stations on the Activity of Redox Proteins in Bovines"* (Hässig et al. 2014). The BERENIS experts agree to the content of this commentary. http://www.emf.ethz.ch/fileadmin/redaktion/public/downloads/3_angebot/wissensvermittlung/komment_infobl_broch/Haessig_2014.pdf

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

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

Hässig M, Wullschleger M, Naegeli H, Kupper J, Spiess B, Kuster N, Capstick M, Murbach M (2014): **Influence of non ionizing radiation of base stations on the activity of redox proteins in bovines**. BMC Vet Res. 2014 Jun 19;10:136. http://www.ncbi.nlm.nih.gov/pubmed/24946856

Win-Shwe TT, Ohtani S, Ushiyama A, Kunugita N (2015): **Early exposure to intermediate-frequency magnetic fields alters brain biomarkers without histopathological changes in adult mice.** Int J Environ Res Public Health. 2015 Apr 22;12(4):4406-21. http://www.ncbi.nlm.nih.gov/pubmed/25913185

Yang G, Ren Z, Mei YA (2015): **Exposure to 50 Hz magnetic field modulates GABAA currents in cerebellar granule neurons through an EP receptor-mediated PKC pathway.** J Cell Mol Med. 2015 Jul 14. http://www.ncbi.nlm.nih.gov/pubmed/26176998

Zhao QR, Lu JM, Yao JJ, Zhang ZY, Ling C, Mei YA (2015): **Neuritin reverses deficits in murine novel object associative recognition memory caused by exposure to extremely low-frequency (50 Hz) electromagnetic fields.** Sci Rep. 2015 Jul 3;5:11768. http://www.ncbi.nlm.nih.gov/pubmed/26138388

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)