The Swiss expert group on electromagnetic fields and non-ionising radiation (BERENIS)

In Switzerland, the Federal Office for the Environment (FOEN) is the responsible government body for monitoring and assessing research on health effects of non-ionising radiation (NIR) from stationary sources in the environment. This includes informing and updating the public about the current state of research, which is the basis for the ambient regulatory limits values stated in the Swiss "ordinance relating to protection from non-ionising radiation". In the case of reliable new scientific knowledge and experiences, the FOEN would advise the Federal Council of Switzerland to adapt these ambient regulatory limits.

Assessing the results and conclusions of scientific studies enables early detection of potential health risks of NIR. The FOEN places particular emphasis to not overlook any evidence of harmfulness for public health demanding for corrective regulatory interventions. Furthermore, critical assessment of available scientific data is required to make firm statements about the validity of the presented evidence for biological effects, their relevance for public health, and if so, to estimate the number of potentially affected people.

NIR includes a broad spectrum of frequencies with varying intensities and radiation characteristics, which is becoming more complex and multifaceted as the development and application of technologies emitting them is very dynamic and rapidly increasing. In the context of the work of BERENIS, NIR at frequencies below 10 GHz is addressed. Potential biological effects and the underlying mechanisms of NIR are manifold, and research activities range from the molecular to the population level. As a consequence, specific expertise in various disciplines is needed to assess the related scientific studies rooted in many different biological, medical and technical scientific realms.

The FOEN has therefore nominated a consultative group of Swiss experts from various disciplines with scientific competence regarding electromagnetic fields and NIR, which has commenced its work in July 2014. The group is called "BERENIS", based on the acronym of the respective German term. The BERENIS experts regularly screen the scientific literature, and assess the publications which they consider relevant for the protection of humans from potentially adverse effects. The results of this evaluation are published in quarterly newsletters.

Selection criteria for assessed publications

Critical assessment of scientific studies is labour intensive and time consuming. BERENIS therefore does not attempt to discuss all newly published studies in detail. However, the most important and most relevant studies with regard to health risk assessment shall be identified and considered. Priority is thus given to studies that fulfil as many of the following criteria as possible:

1) General

- high scientific standards
- environmentally relevant exposures, such as NIR by infrastructure facilities
- new or different scientific perspectives
- studies that are publicly or scientifically debated in a controversial manner

2) Epidemiological studies

- findings that may be relevant for human health and well-being
- exposure in the range or below the ambient regulatory limits

- results from Switzerland
- results that are applicable to the Swiss context

3) Experimental studies

- findings that may be relevant for human health and well-being
- well-defined and controlled study conditions, including exposure setup
- results that challenge previous findings or provide new insights

Members of BERENIS

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- Prof. Dr. Peter Achermann, Institute of Pharmacology and Toxicology, University of Zurich
- Dr. Jürg Fröhlich, Fields at Work GmbH, Zurich
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Summaries and assessments of selected studies

In the period from August to October 2014, 91 new publications have been identified, and 18 of these were discussed in depth by BERENIS. Based on the above mentioned criteria, seven of these publications (three experimental studies, three epidemiological studies, one review article) were selected as the most relevant ones. Their summaries and assessments are provided below.

Experimental studies

Baek *et al.* (2014) investigated *in vitro* the influence of extremely low frequency magnetic fields on cells of the connective tissue (fibroblasts) of mice. They continuously exposed them with a magnetic field of 50 Hz and 1 mT for 15-45 days, and observed a substantial stimulation of the reprogramming

efficiency. This process causes the fully differentiated cells to return to a stem cell-like state. Interestingly enough, the authors also showed that the neutralisation of the earth's magnetic field has a contrary effect on this epigenetic process relevant for stem cell research. This data indicates that biological processes are influenced by the geomagnetic field and that additional magnetic fields might be able to interfere with this natural interaction. In the case described here, the exposition to a magnetic field accelerated the epigenetic changes which are required for attaining the stem cell state. The study also stands out due to the fact that elaborated investigations led to the identification of a possible underlying mechanism. The enzyme histone lysine methyltransferase MLL2, which is also linked to the development of leukaemia and brain tumours, was found to play a central role in this process. These interesting observations linking magnetic fields with the regulation of epigenetic processes could be relevant for the development of gametes or early embryos. To assess the relevance for human health, however, further studies are required regarding the impact on similar processes in humans (e.g. development of gonads) or on epigenetic regulation of cells. It would also be desirable to independently replicate the findings with optimised control and exposure conditions and to obtain more information about a potential dose-response relationship and time dependencies.

In the *in vitro* study by Chen *et al.* (2014), the authors were using an innovative approach to investigate the impact of a radiofrequency electromagnetic field of 1800 MHz, widely used in mobile communications, on embryonic neural stem cells. They exposed the neuronal stem cells with an intermittent (5 min field on, 10 min field off) GSM talk signal at specific absorption rates (SAR) of 1, 2 and 4 W/kg for 1-3 days, and observed no effects on programmed cell death (apoptosis), cell proliferation, cell cycle progression and the differentiation potential. However, the authors reported an inhibition of neurites outgrowth at high (4 W/kg, 3 days) but not at lower (1 and 2 W/kg) SAR levels. As the applied SAR values are within the ICNIRP[1] ambient regulatory limits for local exposure, these results might be relevant for brain development and cognitive abilities, especially with regard to exposure of children. A weakness of the study is the missing or at least not described experimental blinding, and the absence of statements about potential other influential factors. With regard to the stated measurement accuracy, temperature effects cannot be completely excluded.

The effects of the same type of radiofrequency electromagnetic fields as in Chen *et al*. (2014) were also investigated by Lu *et al*. (2014), but in respect to neurodegenerative diseases. The focus of this *in vitro* study is the pro-inflammatory cell response in two types of brain cells of mice (microglia and astrocytes), exposed with a specific absorption rate of 2 W/kg for 1-24 hours. These brain cells warrant the functionality of neurons, are able to degrade dysfunctional cellular components (phagocytosis), and contribute to immunological processes. The authors showed that exposure activates differentially the pro-inflammatory response of microglia and astrocytes and that the STAT3 signal cascade is involved in the activation of the neuronal immune effector cells (microglia). Similar to a chronic inflammation, the continuous release of cytokines induced by radiofrequency electromagnetic fields could lead to cell death in the long run. The activation of STAT3 signalling represents an interesting finding, as STAT3 is a signal-transmitting protein regulating the responsiveness of astrocytes and the anti-apoptotic pathway during the development of lymphoma, leukaemia and other cancer diseases (i.e. it inhibits programmed cell death of the tumour cells). Furthermore, it has been previously shown that the JAK-STAT3 signalling pathway is involved at the regulation of neurodegenerative diseases. Unfortunately, this study lacks any information about the blinding of the experiments. Moreover, an evaluation of the dose-response relationship would be important in order to assess the relevance to human health. In addition, it would be desirable to

[1] ICNIRP - International Commission on Non-Ionizing Radiation Protection

independently replicate these two studies as both reported cellular effects have previously not been observed.

Epidemiological studies

Numerous epidemiological studies have found a consistent correlation between increased incidence of childhood leukaemia and long-term exposure to extremely low frequency electromagnetic fields (e.g. high voltage power lines). Exposure levels above 0.4 µT were found to be linked to a twofold increase of morbidity risk. However, experimental studies so far could not establish an underlying biological mechanism, and it thus remains unclear if the correlation is causal. Grellier *et al.* (2014) calculated the expected number of cases of childhood leukaemia attributable to extremely low frequency electromagnetic fields, based on the assumption that the epidemiologically observed correlation between extremely low frequency electromagnetic fields and childhood leukaemia was in fact causal. These calculations were made on the basis of data from 27 member states of the European Union (EU) related to exposure to magnetic fields and incidence rates. Under the assumption of a linear effect without a threshold value, 50 to 61 childhood leukaemia cases in the entire EU are attributable to exposure to extremely low frequency electromagnetic fields. This corresponds to roughly 1.5-2% of childhood leukaemia cases occurring in the EU per year. Considering the number of exposed people, an interesting additional finding of this health impact assessment was that numbers estimated by interviewed experts were much higher compared to the measured numbers.

A cohort study conducted in the northwest of England investigated whether the newborns of mothers living in close proximity to high voltage cables, overhead power lines, electricity substations or towers during pregnancy were exposed to an increased health risk (De Vocht *et al.* 2014, De Vocht & Lee 2014). Data from 140'000 singleton live births in the period from 2004 to 2008 were analysed. It was found that the birth weight of children whose mothers were residing 50 meters or less from such extremely low frequency magnetic field sources at the time of birth was significantly decreased by 125 grams on average. Analyses were adjusted for maternal age, ethnicity, parity, and socio-economic status of the postal code area. No effect was found in relation to body size and risk of pre-term birth. Overall, the results might indicate that living in close proximity to high voltage cables during pregnancy could lead to suboptimal growth of the unborn child. However, these findings are based on only 89 births that occurred with mothers living in proximity of 50 meters or less to high voltage cables. This fact considerably weakens the generalisability of this relatively large study. In addition, the exact place of residence was not known, but determined on the basis of the post code, which encompasses several residential blocks. This leads to considerable inaccuracy with regard to exposure assessment. Another weakness of the study is that 120'000 births that occurred during the study period could not be considered in the analysis due to lacking information.

In the *Swiss National Cohort*, Huss *et al.* (2014) addressed the association between amyotrophic lateral sclerosis (ALS) and occupational exposure to extremely low frequency magnetic fields and electric shocks. For this analysis, death certificates and nationwide census data from 1990 and 2000 were combined. Persons with occupational exposure to magnetic fields both in 1990 and 2000 had a 55% higher risk of dying of ALS between 2000 and 2008 (hazard ratio of 1.55; 95% confidence interval: 1.11-2.15). This estimate is based on 15 more cases than expected. No increased risk was observed for persons that were exposed only in 1990 or in 2000. Previous studies have found an increased risk for persons working in an electrical occupation, and have suggested an association with electric shocks (WHO 2007, Vergara *et al.* 2015). However, Huss *et al.* (2014) could not establish an increased risk with regard to electrical occupations and electric shocks. The results thus suggest that longer duration occupational exposures to magnetic fields, rather than electric shocks, may be associated with the risk of dying from ALS. A weakness of this study is the lack of the correct job title

in the census data (e.g. “pensioner”), resulting in only 20% of the population being included in the analysis. Furthermore, case numbers are very low, as both ALS and the specific exposure situation are relatively rare, which prevents from drawing firm conclusions. Positive aspects of the study are the well-made exposure assessment, and the fact that ALS as diagnose on death certificates can be regarded as reliable.

Review article

Based on their review of 41 *in vitro* studies, Mattsson & Simko (2014) conclude that extremely low frequency magnetic fields can influence the oxidative status of cells, including free radical release. With magnetic flux densities of 1 mT or above, this association was found to be consistent, but was sometimes also observed at lower flux densities. The association was found over a relatively broad range of cell types, remarkably being independent of exposure duration. Relevance for health might be given by the circumstance that such oxidative processes can lead to biological damage such as DNA modifications. Methodologically, the authors analysed the studies by grouping relevant biological properties and exposure conditions. A limitation in this field of research is the fact that many of the reviewed studies neither applied blinded protocols, nor included positive controls.

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