Summaries and assessments of selected studies

In the period from mid of January to beginning of May 2023, 134 new publications have been identified, and seven 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

Biological investigations of breast cancer and breast tissue cells after exposure to extremely low frequency magnetic fields (Lazzarini et al. *2023)*

Assessing various experimental endpoints, the influence of exposure to an ELF-MF (50 Hz, 1 mT for 4 h) was investigated in the *in vitro* study by Lazzarini and colleagues (2023). Therein, they compared triple-negative breast cancer cells (cell line MDA-MB-231) that belong to the most aggressive types of breast cancer with non-cancerous cells (immortalized MCF-10A breast epithelial cells). A key experiment in this study involved a hypothesis-free comparison of abundance of cellular proteins ("proteomics"), an approach rarely used to date in connection with EMF effects. The authors found altered protein levels for approximately 240 and 330 proteins in MCF-10A breast epithelial and breast cancer cells, respectively. The categorization of the altered proteins according to function and cellular mechanisms indicated exposure effects on mitochondria, mRNA processing and protein synthesis, but also different responses of the two cell models. For example, altered proteins involved in the regulation of the cellular interaction with their environment and the extracellular matrix (focal adhesion) were more frequently found in the cancer cells after ELF-MF exposure, while they tended to be reduced in the breast epithelial cells. These cell line-specific differences were supported by further experiments. After exposure, breast epithelial cells showed hardly any differences in cell adhesion, migration and invasion potential as well as morphological changes of the cytoskeleton and cell protrusions (filopodia), whereas reduced adhesion, increased migration and invasion behavior and changes in the cytoskeleton were observed in breast cancer cells. These observations indicated an increased potential of cancer cells for metastasis upon exposure. Based on the altered protein levels, the authors also identified and experimentally validated some transcription factors whose expression was influenced by the exposure. Upon exposure, again, more of these transcription factors were found in the breast cancer cells, whereas they were decreased in the breast epithelial cells. The authors also reported that the exposure led to a faster growth of the cancer cells, while the epithelial cell cultures overall grew more slowly and contained more dead (necrotic) cells. However, no different responses of the two cell lines were found in regard to mitochondria, in which the exposure resulted in ultrastructural changes and slightly increased ROS formation.

The comprehensive and technically sound study by Lazzarini *et al.* (2023) clearly demonstrates once again that the effects of ELF-MF exposure depend on the cell line, and that the findings may be contradictory. This not only hinders the understanding of the mechanism of action, but also makes it difficult to assess putative health effects based on studies in cell models.

Essential elements of the radical pair magnetosensitivity in Drosophila flies (Bradlaugh et al. *2023)*

In the study by Bradlaugh *et al.* (2023), new findings on magnetosensitivity in Drosophila flies were presented. Cryptochrome (CRY), a photoreceptor protein, has been identified as a magnetic field receptor and was shown to play a role in circadian rhythm as a blue light receptor. The mechanism of

action of magnetosensitivity was shown to be a radical pair mechanism in which the chemical reactivity of short-lived intermediates of CRY in a photochemical reaction is influenced by an external magnetic field. The proposed mechanism relies on the blue light-activated electron transfer between flavin adenosine dinucleotide (FAD) and conserved tryptophan chains within the CRY, whereby the spin state of the radical pairs formed by the electron transfer is sensitive to magnetic fields (see e.g. Newsletter 13, 16, 17). Previous studies in Drosophila flies showed that in CRY variants with truncated C-terminus, the light but not the magnetic field dependency was maintained. In the present study, an amino acid variant of the C-terminus of CRY was produced, and behavioral and electrophysiological studies were performed. Compared to sham-exposed flies, the variant led to a shortening of the circadian period when the flies were exposed to a magnetic field of 300 µT (3 Hz). It could thus be shown that the C-terminus and not the light-dependent binding domain of FAD to CRY is sufficient for magnetoreception.

An intracellular increase in FAD alone is sufficient to increase blue light and magnetic field sensitivity. FAD alone can act as a magnetoreceptor if this protein is present in high concentrations. Thus, the primary role of CRY appears to be rather a transducer of magnetosensation than a magnetoreceptor. The results suggest that the radical pair mechanism can cause responses to blue light and magnetic field independently of CRY. This carefully conducted study is a good basis for better understanding the underlying mechanism of magnetoreception of the earth's magnetic field by animals. It remains to be seen to what extent this mechanism also plays a role for other electromagnetic fields and in humans.

Effects of prenatal stress and extremely low frequency magnetic fields on anxiety behavior in female rats (Hosseini et al. *2023)*

In the study by Hosseini *et al.* (2023), effects of ELF-MF with and without additional prenatal stress were investigated. Alongside with a control group, female rats were divided into three groups with different stressors (e.g. noise, light, water deprivation, no bedding in the cage), ELF-MF (100 µT, 50 Hz, 4 hours/day) and combined stress/ELF-MF exposure. The prospective dams were then subjected to the environmental exposure conditions 21 days before and after conception. 40 days after birth, behavioral tests were performed in the female offspring. On day 41, hippocampal and other brain tissues were examined histologically by light microscopy. Additional immunohistochemical methods were used to detect functional changes.

Compared to sham controls, the anxiety behavior of the animals increased in all groups, with the increase being most pronounced when stress was combined with ELF-MF. In the brain areas associated with anxiety behavior, the prefrontal cortex and the hippocampus, various biomarkers (BDNF, caspase, GAP-43) were measured, which are associated with apoptosis but also neuronal plasticity, neurite formation and growth, survival of neurons and neurotransmitter regulation. The marker caspase, which is important for apoptosis but also synaptic plasticity, was increased in both brain regions, whereas BDNF and GAP-43 were decreased in the hippocampus and in the prefrontal cortex.

The strength of the study is that morphological and behavioral changes were examined in parallel. The study shows that prenatal exposure to ELF-MF can have the same effects on offspring as prenatal stress, manifesting in increased anxiety behavior, and that both effects potentiate each other. Linked to anxiety behavior, the morphological changes in the brain regions indicate neurodegenerative changes and reduced synaptic plasticity.

2) Epidemiological studies

Acute RF-EMF exposure and cognitive performance, health-related quality of life and sleep (Eeftens et al. *2023)*

Eeftens et al. (2023) conducted a panel study in 121 adults from France and Switzerland to investigate possible correlations between several markers of EMF exposure and cognition, health-related quality of life and sleep. Every evening over the course of ten days, the study participants completed six game-like cognitive tests, assessing verbal and visuo-spatial performance. Furthermore, they rated their fatigue, mood and stress on a scale from 1 to 10, and estimated the duration of their cordless and mobile phone calls as well as their mobile screen time for the four-hour period before each test. In the morning, the participants reported screen time on their smartphone for the last hour before going to bed. Other relevant confounders such as time spent outdoors, coffee and alcohol consumption were also surveyed. Duration and quality of sleep were recorded using a wearable monitoring movement. The median time for mobile phone calls preceding the cognitive tests was 3 minutes, 0 minutes for cordless phones, and 40 minutes for smartphone screen time. The sporadically observed significant associations between exposure markers and cognition test results were attributed rather to chance than to exposure. There was no correlation between self-reported mobile phone use and screen time and sleep duration or sleep quality. A significant correlation was found between the self-reported stress level and duration of mobile phone screen time.

The results indicate that rather screen time than RF-EMF exposure is critical for health-related quality of life. However, this observational study cannot resolve whether screen time increased the stress level of the participants or conversely, distressed participants tend to spend more time in front of a mobile phone screen. The strengths of the study are the prospective design, consideration of various confounders and the real-life setting. Repeated observations per participants compensate at least partly for the relatively small sample size.

References

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

List of abbreviations (pdf)