

Summaries and assessments of selected studies

In the period from mid of October 2022 to mid of January 2023, 122 new publications have been identified, and six 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

Impact of ELF-MF exposure on stress responses and hormesis effect in rats (Klimek et al. 2022)

The experimental animal study by Klimek and colleagues (2022) investigated whether there is evidence for stress and associated stress responses in rats after repeated exposure to ELF-MF (50 Hz, 1 mT and 7 mT). With intervals of three weeks, the authors exposed three-month-old male Wistar rats three times. After each exposure period and the subsequent stress test, stress hormones and their receptors were measured, as well as the animals' exploration and anxiety behaviour. This study focused in particular on the stress response of the hypothalamic-pituitary-adrenal axis. The production of corticosteroids by the adrenal gland is influenced by a signal from the pituitary gland. High plasma corticosteroid levels lead to signaling to the adrenal gland to produce fewer corticosteroids, as there is a feedback mechanism between the hypothalamic pituitary gland and adrenal cortex. The investigations showed that the ELF-MF changed, depending on the field strength/flux density, the sensitivity to trigger stress responses. While the results indicated for 1 mT ELF-MF a neuroprotective and thus therapeutic effect and anxiolysis (reduced anxiety) at, the opposite was observed after exposure with 7 mT. This corresponds to the principle of hormesis (adaptive response, Greek: "stimulation, impetus"), a phenomenon already described by Paracelsus , where low doses of harmful or toxic substances can have a positive biological effect on the organism.

Analogous to hormesis, the results show that mild stress protects against further stressors when applied repeatedly, while more intense stress has the opposite effect. After a previous study in Drosophila fruit flies, this effect of ELF-MF of different flux densities has been shown in mammals for the first time.

Impact of WiFi-related radiofrequency electromagnetic fields on the chromatin of fruit flies (Cappucci et al. 2022)

This study investigated the effect of an RF-EMF (2.436 GHz) on the activation state and structure of chromatin (nuclear DNA and associated structural proteins) in larval and adult fruit flies (*Drosophila melanogaster*). Using an appropriate exposure device (TEM cell coupled to a commercial WiFi router), fruit flies were exposed to a continuous WiFi signal (average E-field of 1.35 V/m) throughout their development to the adult stage, and compared with animals in a control TEM cell with approximately 13-fold weaker background E-fields. The authors calculated a SAR value of 60.8 mW/kg for the exposed group. An increased expression (gene activity) of mobile genome sequences (transposons) was observed in the heads and ovaries, but not in the testes, of 10-day-old exposed adult animals. Such an activation of transposon was already described for other cellular stressors such as heat shock. As the authors have demonstrated in a control experiment with heat shock treatment of the flies, however, the increase in transposon expression after RF-EMF exposure is caused by a different mechanism. WiFi exposure led to the decondensation of the constitutive heterochromatin (inactive and condensed



chromatin), indicated by a decrease in biomarkers for inactive chromatin (HP1 and histone modifications) and a change in heterochromatin-dependent gene inactivation in a genetic test model. Moreover, exposed larvae showed signs of genome instability and chromatin decondensation in dividing brain cells and a moderate increase in ROS formation in different brain regions. Compared to sham-exposed control animals, WiFi exposure resulted in reduced locomotor behaviour of larvae and adult flies, as well as in reduced light avoidance by larvae. Lastly, the influence of RF-EMF on tumour metastasis formation was investigated in a genetic model. An increase in metastases upon exposure was found, which the authors explained with the mutagenic potential of transposon activation.

The observations of this study are noteworthy as there are so far hardly any comparable studies regarding the effect of EMF on heterochromatin. The repetitive genomic regions composed of transposon and viral sequences make up a considerable proportion of the genetic material depending on the organism (approx. 40-45% in humans). They are kept inactivated in the cells to prevent mutations by active elements. For a long time, these regions were regarded as "junk DNA", since they do not contain any coding genes essential for the cells. Nowadays, however, it is assumed that they also have structural and gene-regulating functions. For instance, activation of retroviral elements in heterochromatin was recently linked to the ageing of cells and organisms. In this regard, the findings of Cappucci *et al.* (2022) about the decondensation of heterochromatin, activation of transposons and increased metastasis as well as the behavioural changes by exposure to RF-EMF might be a relevant starting point for further investigations.

2) Epidemiological studies

Analysis of the metabolic profile of individuals with fibromyalgia and electromagnetic sensitivity (Piras et al. 2022)

The metabolic profile ("metabolomics") of 31 participants (30 female, 1 male) with a fibromyalgia diagnosis and self-declared electromagnetic sensitivity (EHS) was compared with 23 healthy controls (21 female, 2 male). Metabolites in blood plasma were determined by gas chromatography-mass spectrometry (GC-MS). Nineteen metabolites involved in different metabolic pathways differed between the two groups. These metabolic pathways involve energy metabolism, metabolic muscle processes, oxidative stress defense and chronic pain. Comparisons of the two groups using H-NMR spectroscopy have been presented earlier (Piras *et al.* 2020)¹

Fibromyalgia is defined as generalised soft tissue rheumatism of unknown cause. The diagnosis is based on validated criteria. The main symptom is chronic soft tissue pain, often accompanied by fatigue, sleep disturbances, cognitive symptoms, depression and anxiety. Routine laboratory tests and diagnostic imaging are normal. Fibromyalgia often occurs together with other functional diseases, for example irritable bowel syndrome or migraine. EHS patients also suffer from various medically unexplainable symptoms. In this respect, there are parallels between fibromyalgia and EHS. It is interesting but neither surprising nor new that the complex multi-organ symptomatology is accompanied by metabolic changes. According to the authors, the results suggest a possible metabolic alteration in EHS patients. This conclusion is an over-interpretation, given the simultaneous presence of fibromyalgia and EHS, and the lack of a comparison group with fibromyalgia but without EHS. The alterations described could also have been caused by other factors (e.g. food intake, concomitant diseases).

¹ Piras C, Conte S, Pibiri M, Rao G, Muntoni S, Leoni VP, Finco G, Atzori L (2020): **Metabolomics and psychological features in fibromyalgia and electromagnetic sensitivity**. Sci Rep. 2020 Nov 24;10(1):20418. doi: 10.1038/s41598-020-76876-8. <u>https://pubmed.ncbi.nlm.nih.gov/33235303/</u>



Extremely low frequency magnetic field exposure from power lines in Slovenia and cancer risk in children and adolescents (Zagar et al. 2023)

Previous epidemiological studies have shown that long-term ELF-MF exposure stronger than 0.3 µT, as it occasionally occurs in houses located close to high-voltage power lines, may be a risk factor for the incidence of leukaemia in children. One aim of the study by Zagar et al. (2023) was a detailed nationwide modelling of ELF-MF exposure from power lines in Slovenia. The second aim was to investigate whether living in the proximity of power lines has an effect on cancer incidence, particularly on leukaemia and brain tumours in children and adolescents. National cancer registry data over a 12year period were used (2005-2016, cancer in the age group 0-14 years, leukaemia in the age group 0-19 years, brain tumours in the age group 0-29 years). All cases were classified into five exposure categories with regard to ELF-MF exposure at the place of residence (lowest category: <0.1 μT, highest category: $\geq 0.4 \mu$ T, three intermediate categories in the range of 0.1 - 0.4 μ T). The exposure category below 0.1 µT comprised 99.5% of the study population and 516 cancer cases. Only 0.5% of children and adolescents in Slovenia lived in places where the average ELF-MF exposure was $0.1 \,\mu T$ or more. Merely 0.09% of all children lived for at least one year in an area exposed to more than 0.4 µT. One leukaemia case occurred in the 0.1-0.2 μ T category, and one brain tumour case in the 0.2-0.3 μ T category. No cancer cases were observed above 0.3 μ T. The authors compared the number of observed cases with the expected number of cases in their analysis. No significant differences in cancer risk were found among children and adolescents with higher exposure compared to their peers.

The exposure modelling using high-resolution electricity flow data from electricity suppliers is a strength of the study. However, it does not take into account domestic sources (wiring, electrical appliances). No confounders were considered in the analysis. However, for these outcomes no relevant confounders are known in this age group. The study provides a good illustration of the difficulties in researching this topic. Cancer cases in children and adolescents are rare, and only a very small part of the population is exposed to high ELF-MF levels at the place of residence. The statistical power of a single study of this kind is therefore very limited. At the same time, the study shows that even with an hypothetical doubling of the cancer risk due to ELF-MF, the number of expected additional cancer cases would be small, because only a small part of the population is exposed to intensities above the suspected threshold level.

3) Further information

Computational modelling of exposure from 5G network topologies in Switzerland

Castellanos *et al.* (2022)² have published a study that evaluates different 5G network topologies in Switzerland in terms of EMF exposure, connection quality and sustainability based on computational modelling.

EU report on health risks of RF-EMF

Following a request from the European Commission, the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) has prepared a report on health risks of RF-EMF. After the

² Castellanos G, De Gheselle S, Martens L, Kuster N, Joseph W, Deruyck M, Kuehn S (2022): **Multi-objective optimisation of human exposure for various 5G network topologies in Switzerland.** Comput Netw 2022; 216: 109255. <u>https://doi.org/10.1016/j.comnet.2022.109255</u>



preliminary version had been made available for public consultation from August to September 2022, the final report was published in June 2023.³

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

List of abbreviations (pdf)

³ SCHEER (2023): **Opinion on the need of a revision of the annexes in Council Recommendation 1999/519/EC and Directive 2013/35/EU, in view of the latest scientific evidence available with regard to radiofrequency (100kHz - 300GHz)**. Scientific Committee on Health, Environmental and Emerging Risks, adopted by written procedure on 18 April 2023. <u>https://health.ec.europa.eu/consultations/scheer-public-consultation-preliminary-opinion-scientific-evidence-radiofrequency_en</u>)