Summaries and assessments of selected studies

In the period from beginning of November 2023 to mid of January 2024, 58 new publications have been identified, and six of these were discussed in depth by BERENIS. Based on the selection criteria, three of these publications were selected as the most relevant ones. Their summaries and assessments are provided below. In addition, due to the thematic overlap, one publication from the next screening period is also discussed in this newsletter (Crespi *et al.* 2024).

1) Experimental animal and cell studies

Radiofrequency electromagnetic fields and zebrafish embryo development (Torres-Ruiz et al. *2023)*

The study of Torres-Ruiz *et al.* (2024) investigated the effect of RF-EMF (700 and 3500 MHz) on behavioral aspects (anxiety and general activity, learning, habituation to stimuli) and morphological changes (eye size and structures of the vestibular organ) in zebrafish embryos. Because of similarities to humans, zebrafish are a well-suited model organism for investigating potential health effects during early development.

The study is based on the hypothesis that early stages of embryonic development are particularly sensitive to environmental influences. For both frequencies, zebrafish embryos were exposed to RF-EMF with an exposure level of 34-35 V/m for 1 and 4 hours. Thus, the exposure levels were below the limits recommended by ICNIRP (61 V/m for 3500 MHz and 36.4 V/m for 700 MHz) and corresponded to SAR values of 1-1.2 W/kg. Subsequently, the authors analyzed the embryos for movement activities in light and dark conditions, toxicity and effects on development as well as habituation to sounds and visual stimuli.

After 4 hours of exposure to the 700 MHz RF-EMF, the authors found reduced activity of the embryos (approx. 24%) and reduction in anxiety behavior, while no effect on activity but increased anxiety behavior was documented at 3500 MHz. The animals' learning ability was reduced after exposure to either frequency. Only for exposure to 700 MHz RF-EMF (for 1 and 4 hours) a significant reduction in acetylcholinesterase of approx. 20% was observed. This enzyme inactivates the active neurotransmitter acetylcholine in the synaptic cleft. Acetylcholine mediates the signal transmission between nerve cells and plays a key role in controlling many bodily functions, such as breathing, memory, cognitive functions and muscle activity. Reduction of the acetylcholinesterase means that more acetylcholine is permanently present, which can at least partially explain the reduced activity. Results of the study also show that RF-EMF exposure at 700 MHz (1 and 4 hours) and 3500 MHz (1 hour) is associated with reduced habituation to stimuli and thus impairs non-associated learning. Such learning impairments have been reported in people with neurological disorders such as autism, Parkinson's disease, schizophrenia or attention deficit disorder.

RF-EMF exposure had no effect on mortality, hatching or body length (i.e. overall embryonic development) of the young zebrafish. Thus, no evidence was found that short-term exposures had a toxic effect on embryonic development. Minor morphological changes in structures of the vestibular organ and eye size (5%) were found.

Experiments of this study were controlled for temperature, but there was no sham exposure, only a control group kept in the same room. In general, the various observed effects were dependent on the frequency and duration of exposure and the effects were often more pronounced for 700 MHz than for 3500 MHz RF-EMF.

2) Epidemiological studies

Residency near electrical transformers and risk of childhood leukemia (Malavolti et al. *2024 and Crespi* et al. *2024)*

Both Malavolti *et al.* (2024) and Crespi *et al.* (2024) investigated a possible association between childhood leukemia and exposure to extremely low frequency electromagnetic fields (ELF-MF), specifically from electrical transformers, often used in apartment buildings. Neither study found indications of such an association.

The Malavolti study considered 182 cases of childhood leukemia and 726 controls matched by sex, year of birth and province (in northern Italy). The Crespi study considered cases from five countries (Finland, Israel, Hungary, the Netherlands and Switzerland), conducting a pooled case-control study which included 76 cases and 20491 controls.

While the Malavolti study considered all residences within 15 or 25 m of a transformer as highly or intermediately exposed, the Crespi study only considered residences directly sharing a wall or floor with the transformer room as exposed (which have a typical distance of less than 15m to the transformer). Nevertheless, neither the Malavolti study (with two cases within 15m and 5 cases within 25m radius) nor the Crespi study (3 cases with high exposure and 16 with intermediate exposure) identified many children as highly exposed. Both studies rightfully acknowledge that high exposure scenarios are extremely rare, and that detecting an association with a disease as rare as leukemia is unlikely even when data from several countries are pooled.

Both the Crespi study (1.39; 95% Confidence Interval (CI): 0.77-2.52) and the Malavolti study (1.0; 95% CI 0.2-4.9) found exclusively odds ratios[1] indicating no association, surrounded by wide confidence intervals for the risk of developing leukemia when highly exposed to ELF-MF from transformers (within 15m for the Malavolti study, “high” exposure for the Crespi study). Considering transformers within 25m (Malavolti) or intermediate exposures (Crespi) did not change results. Neither did a specific analysis of two highly and eight intermediately exposed cases against 2396 and 15050 controls in a nested cohort approach using only the Finnish data (Crespi). This analysis, which also took into account residential history, yielded equally uncertain odds ratios for both high (1.7; 95% CI: 0.2-13.6) and intermediate exposure (0.6; 95% CI 0.1-2.6). The “stronger association” found by the Malavolti study in children aged five years and older (1.3; 95% CI: 0.1-12.8) is an overinterpretation by the authors, and they ignore the finding of a “protective” and equally uncertain association in children under five years (0.7; 95% CI 0.1-6.6).

Regarding exposure assessment, a critical point to note is that both studies assume that distance to the transformer station is a proxy for the strength of the magnetic field, which in reality can be non-uniform. Both studies acknowledge the possibility of some exposure misclassification, and point out that it is extremely hard to obtain information about the exact location and installation time of transformers. Nevertheless, the most likely explanation for the imprecise outcomes is the combination of an extremely rare exposure with an extremely rare disease.

[1] An odds ratio describes the increased «odds» of contracting a disease, in this case leukemia if the child is living close to a transformer. An odds ratio of 1 indicates that the odds of getting leukemia is the same in those who are highly exposed as in those who have low exposure. The 95% confidence interval describes the uncertainty surrounding the odds ratio; in this study, the precision is extremely low. The confidence interval thus leaves open the possibility of both a protective and an adverse effect.

3) Studies with humans

Do radiofrequency electromagnetic fields influence the sleep of preterm neonates? (Besset et al. *2023)*

The aim of the study was to assess the influence of RF-EMF on the sleep patterns of preterm newborns. Preterm newborns are constantly exposed to low-intensity RF-EMF in the neonatal intensive care unit. The RF-EMF exposure levels were measured continuously during the first 21 days after birth in 29 preterm neonates (18 girls, 11 boys). The measuring device was attached to the incubator wall. Additionally, after this period, sleep was recorded over a period of 12 hours and the sleep parameters were determined. The RF-EMF exposure over 3 weeks (chronic) was 0.03 ± 0.01 V/m at the median level (mean exposure; predominant during 50% of the time) and 0.24 ± 0.11 V/m at the 99th percentile (high exposure; predominant during 1% of the time). The respective values of the last 24 hours were considered as acute exposure (0.03 ± 0.02 and 0.12 ± 0.09 V/m). To determine the effect of exposure, correlations between exposure values and sleep parameters were analyzed. For chronic exposure, a mainly positive correlation with sleep fragmentation was found for mean and high exposure values. During acute exposure, mean exposure values showed a negative correlation with the sleep period, while high exposure values correlated positively with sleep fragmentation. The correlations explain about 15-25% of the variation. However, the significance disappears after correction for multiple testing, which leads to the interpretation that RF-EMF exposure in the neonatal intensive care unit does not disturb sleep in preterm infants.

The study presents an interesting approach to investigate potential effects of RF-EMF on preterm neonates. For preterm newborns, there is no alternative to the intensive care unit, and thus there is no control condition without RF-EMF exposure. Sleep is of interest because increasing sleep continuity is a sign of brain maturation. In this study, rather a fragmentation was observed. However, it is questionable whether sleep in the first three weeks of life is able to provide any information about brain maturation. In addition, there are many other important factors that were not accounted for in the study, such as contact with caregivers, parents or noise.

References

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

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List of abbreviations (pdf)