

Summaries and assessments of selected studies

In the period from August to end of October 2019, 84 new publications have been identified, and eight 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.

1) *Experimental animal and cell studies*

Are there indications for DNA damage associated to radiofrequency radiation from mobile phones? (Smith-Roe et al. 2019)

The publication by Smith-Roe *et al.* (2019) describes the genotoxicity analyses of rat and mice tissue samples, which were conducted as part of the life-long bioassay of the U.S. National Toxicology Program (NTP) on behalf of the U.S. Food and Drug Administration (FDA) regarding carcinogenesis of RF-EMF (see [BERENIS Newsletter – Special Issue November 2018](#)). DNA damage was investigated in cells of three brain regions (frontal cortex, hippocampus, and cerebellum), the liver and in leukocytes by the comet assay. Furthermore, chromosomal damage was assessed in red blood cells (immature and mature erythrocytes) by the so-called micronuclei, which detects faulty repair events and/or problems in the DNA replication. According to the protocol of the NTP study, the animals were exposed to GSM (2G) or CDMA (3G) modulated signals (carrier frequencies, rats: 900 MHz; mice: 1900 MHz) at 10-minute intervals (10 min on, 10 min off) for 18 hours per day and 7 days per week, starting from gestation day 5. This corresponded to a daily cumulative exposure of 9 hours and 10 minutes. After 19 and 14 weeks of exposure for rats and for mice, respectively, tissue samples were collected and refrigerated. For each exposure condition (rats: whole body SAR¹ 1.5, 3 or 6 W/kg; mice: whole body SAR 2.5, 5 or 10 W/kg), and for both sexes and species, 5 animals were included in the comet assay analysis. Thus, DNA damage data of a total of 800 tissue samples were included. The authors considered a clear indication of increased DNA damage, when a dose-effect relationship was found as well as a statistically significant difference to control animals (p-value ≤ 0.025). These criteria were met at the highest dose (6 W/kg) in the hippocampus of male rats, in the frontal cortex of male mice after exposure to both signal modulations (10 W/kg), and in the leukocytes of female mice. In addition, some evidence was found in other exposure groups and classified as "equivocal". In contrast, no evidence for chromosomal damage was found in any of the exposure groups in the micronucleus assays.

It is a well-established concept that induced genome instability results in mutations and thus causes carcinogenesis. Hence, such a study design generally aims to establish a potential causality between tissue-specific DNA damage and increased incidence of tumours. In this regard, the sex-specific differences found in the cancer and the genotoxicological study of the NTP are remarkable. While little evidence for higher tumour incidence was found in female animals, indications were more frequent in males, especially in rats. The DNA damage observed in brain regions could therefore be related to the increased occurrence of malignant gliomas. However, these *ex vivo* analyses do not allow for direct conclusions about the causality. DNA damage could be both the cause and the consequence of neoplastic changes as well as non-neoplastic tissue damage. Notably, the proportion of severely

¹ SAR = specific absorption rate

damaged cell nuclei is relatively high, which could indicate extensive tissue damage, but also be due to the methodology used.

Radiofrequency electromagnetic fields and neurons of the hypothalamus in mice (Kim et al. 2019)

In the study of Kim *et al.* (2019), the effects of RF-EMF (835 MHz, unmodulated, 4 W/kg) on neurons of the hypothalamus in C57BL/6 mice were investigated. The animals were exposed for 5 hours per day over a period of 12 weeks. There is no information available in the manuscript regarding sham exposure of the control group. For the signal transmission between neuronal cells, neurotransmitters are formed and stored in vesicles in the pre-synapse. These vesicles are then released into the synaptic cleft, where the neurotransmitters then bind to receptors at the postsynapse and trigger an effect. In order to assess the effect of exposure on the activity of the synaptic transmission, electron microscopy, protein and gene expression were used. The following parameters were analyzed: a) number and size of synaptic vesicles; b) density of synaptic vesicles (number per unit area) docking and fusing at the active zones of the presynaptic membrane; c) expression levels of synapsin I/II and synaptotagmin 1, two regulators of synaptic vesicle activity in neurons and a voltage-gated calcium channel. Following RF-EMF exposure, the number and size of synaptic vesicles and the expression of both regulators of synaptic vesicle and calcium channel activity were significantly decreased in neurons of the hypothalamus. These findings indicate that after RF-EMF exposure of the cells, fewer neurotransmitters are released at the pre-synapse. The authors also measured body temperature and body weight of the animals and found no differences between exposure groups. In addition, an orientation test was conducted in which the animals had to find hidden food. The results of these experiments showed a reduced ability of the animals to find these pieces of food, which is in line with the neuronal findings.

2) Review article

Systematic review of methodological limitations in electromagnetic hypersensitivity studies (Schmiedchen et al. 2019)

From a scientific point of view, many uncertainties exist regarding electromagnetic hypersensitivity (EHS). While there are numerous individuals who claim to suffer from health problems due to EMF exposure, many experimental studies conducted on this topic have not been able to establish a causal relationship with EMF. The systematic review conducted by Schmiedchen *et al.* (2019) focused on published blinded experimental studies in volunteers in the frequency range from 0 to 300 GHz with study participants claiming to suffer from EHS. The analysis aimed at evaluating these studies with regard to their methodological limitations, since the respective study approaches can lead to biased results due to implicit assumptions. The authors performed a "risk of bias" assessment by evaluating the individual studies with regard to possible systematic bias. Such bias can occur, for example, if some of the study participants had physical illnesses that could explain their EHS symptoms, or due to the sequence and duration of the exposure conditions applied, since these can result in different stress levels. A total of 28 studies were included in the analysis, 7 of which found statistically significant associations between EMF exposure and health effects in EHS persons. Both increased and decreased occurrence of symptoms was observed under exposure conditions. However, 21 studies found no evidence that the symptoms reported by the study participants were related to EMF exposure. For 82% of the studies examined, the authors criticized the heterogeneity of the study participants, as the exposure scenarios applied were probably not suitable for some of the participants. This could have led to false negative results (i.e. a study does not find a link between exposure and symptoms, even though it does exist) if effects only occur under very specific exposure conditions. The results of studies

with relatively few methodological limitations show less likely exposure-related effects. In almost one third of the studies examined, the nocebo effect² plays a role with regard to symptoms in people with EHS. According to the authors, this review suggests absence of a causal relationship between EMF exposure and health effects. However, it still cannot be ruled out that there might be weak health effects, or some individuals who actually do react to EMF. For future studies, the authors thus recommend to identify subgroups and to conduct studies at the individual level.

3) Information on additional publications

ANSES reports on EMF and health

In mid-2019, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) has published two reports on EMF and health:

- Opinion on the “Health effects associated with exposure to low-frequency electromagnetic fields”³
- Opinion on the possible health effects associated with high SAR values from mobile telephones carried close to the body⁴

ANFR reports on 5G

Also in mid-2019, the French National Frequency Agency (ANFR) has published two reports on 5G (available in French):

- General information on 5G exposure⁵
- First results from measurements in 5G pilot projects (3400-3800 MHz)⁶

² A nocebo effect is defined as the pathogenic effect of an exposure caused by the expectations of the affected persons, therefore the opposite of a placebo effect ([BERENIS Newsletter No. 5, March 2016](#))

³ <https://www.anses.fr/en/system/files/AP2013SA0038EN.pdf>

⁴ <https://www.anses.fr/en/system/files/AP2017SA0229EN.pdf>

⁵ <https://www.anfr.fr/fileadmin/mediatheque/documents/expacement/CND/Rapport-ANFR-presentation-generale-5G.pdf>

⁶ <https://www.anfr.fr/fileadmin/mediatheque/documents/expacement/CND/Rapport-ANFR-resultats-mesures-pilotes-5G.pdf>

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Kim JH, Huh YH, Kim HR (2019): **Trafficking of synaptic vesicles is changed at the hypothalamus by exposure to an 835 MHz radiofrequency electromagnetic field.** Gen Physiol Biophys. 2019 Sep;38(5):379-388. Epub 2019 Aug 14. <https://www.ncbi.nlm.nih.gov/pubmed/31411574>

Schmiedchen K, Driessen S, Oftedal G (2019): **Methodological limitations in experimental studies on symptom development in individuals with idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF) - a systematic review.** Environ Health. 2019 Oct 22;18(1):88. <https://www.ncbi.nlm.nih.gov/pubmed/31640707>

Smith-Roe SL, Wyde ME, Stout MD, Winters JW, Hobbs CA, Shepard KG, Green AS, Kissling GE, Shockley KR, Tice RR, Bucher JR, Witt KL (2019): **Evaluation of the genotoxicity of cell phone radiofrequency radiation in male and female rats and mice following subchronic exposure.** Environ Mol Mutagen. 2019 Oct 21. <https://www.ncbi.nlm.nih.gov/pubmed/31633839>

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Additional information:

[BERENIS - Swiss expert group on electromagnetic fields and non-ionising radiation](#)

[List of abbreviations \(pdf\)](#)