Bundesamt
für Strahlenschutz

Spotlight on EMF Research

Spotlight on “Effects of Radiofrequency Electromagnetic Fields (RF-EMF) exposure on pregnancy and birth outcomes: A systematic review of experimental studies on non-human mammals” by Cordelli et al. in Environment International (2024)

Category [radiofrequency, review]

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Competence Centre Electromagnetic Fields (KEMF)

1 Putting the paper into context by the BfS

In autumn 2019 the World Health Organization initiated an international project aiming at systematically reviewing the evidence regarding the association between exposure towards radiofrequency electromagnetic fields (RF-EMF) and adverse health effects. Within the project, several endpoints were prioritised by an expert group, which include reproductive health outcomes [2]. A possible impairment of human reproductive health through exposure to RF-EMF has been discussed for years. Experimental studies published on this subject are inconsistent with regard to study quality and results – and thus also contradictory. The present systematic review evaluated the comprehensive data on pregnancy and birth outcomes available from studies on experimental non-human mammals, a second systematic review on male fertility will follow [3]. Another systematic review summarizing and evaluating observational studies in humans is also expected.

2 Results and conclusions from the authors‘ perspective

The authors analysed all relevant data from peer-reviewed scientific papers that investigated the effects of RF-EMF on fecundity and health of the offspring at birth and at later life stages. All criteria for literature search, eligible papers, review design and analysis procedures were described in a published protocol beforehand [4]. The authors followed the guidelines for systematic reviews, which included an assessment of the study quality according to the Risk of Bias criteria [5]. A question regarding the consideration of temperature increases was added because this aspect is especially relevant in the case of RF-EMF exposure during pregnancy. Based on the Risk of Bias assessment, studies were assigned to “low concern”, “some concern” or “high concern”. For the calculation of the effect estimates, study results were pooled in a

random effects meta-analysis comparing average exposure to no-exposure and in a dose-response meta-analysis using all exposure doses. Depending on the data, different effect estimates were calculated: Mean Difference (MD) or Standardized Mean Difference (SMD) for continuous data, and Odds Ratio (OR) for binary data. For each endpoint, pooled effect size estimates for studies with "low or some concern" Risk of Bias rating and studies with "high concern" Risk of Bias rating were calculated separately. For the final assessment of the body of evidence (i.e. the GRADE assessment), a modified version of the GRADE approach, specified for experimental studies, was used [6, 7]. Only studies with "low concern" or "some concern" Risk of Bias rating were considered for the GRADE assessment.

From 3194 studies found in the literature search, a total of 215 studies remained after title and abstract screening. These studies were screened for eligibility by two independent reviewers, which left 88 papers that were included in the systematic review. Most studies investigated effects in rats.

In terms of the Risk of Bias assessment, most included studies were evaluated as "some concern", followed by "high concern" and only a very low number of studies as "low concern". The main reasons for "some concern" were limited confidence in the outcome assessment and a lack of blinding during the experimental procedures. The main reasons for "high concern" were insufficient exposure characterisation, insufficient assessment of exposure induced temperature elevations and small size of experimental groups. The authors noted that the highest confidence in exposure characterisation seemed to correlate with studies with the largest sample size.

Overall, 14 endpoints in three categories were investigated:

Reduction of fecundity:

- For *Pre-implantation loss*, no meta-analysis was performed due to overall low study quality.
- For *litter size*, the meta-analysis of 24 studies showed no statistically significant difference between sham exposed and RF-EMF exposed groups with MD= 0.05 (95% CI [-0.21, 0.30]) at an average SAR of 4.92 W/kg. The certainty of the evidence was high.
- For *resorbed or dead foetuses*, the meta-analysis of 21 studies showed a statistically significant increase of the incidence in RF-EMF exposed animals with OR= 1.84 (95% CI [1.27 to 2.66]) at an average SAR of 20.26 W/kg. The certainty of the evidence was low.

Adverse effects on the offspring health at birth:

- For *foetal weight*, the meta-analysis of 48 studies showed a small, statistically significant decrease of foetal weight in RF-EMF exposed groups with SMD= 0.31 ([95% CI 0.15 to 0.48]) at an average exposure level of 9.83 W/kg. The certainty of the evidence was moderate.
- For *foetal length*, the meta-analysis of 13 studies showed a small, statistically significant decrease of foetal length in RF-EMF exposed groups with SMD= 0.45 (95% CI [0.07 to 0.83]) at an average SAR of 4.55 W/kg. The certainty of the evidence was low.
- For *fraction of malformed foetuses*, the meta-analysis of 13 studies showed a moderate statistically significant increase of malformed foetuses with SMD= -0.45 (95% CI [-0.68 to -0.23]) at an average SAR of 6.75 W/kg. The certainty of the evidence was low.
- For *numbers of litters with malformed foetuses*, the meta-analysis of 28 studies showed a large, statistically significant increase of litter with malformed foetuses with OR = 3.22 (95% CI [1.9 to 5.46]) at an average SAR of 16.63 W/kg. The certainty of the evidence was very low.
- For *sex ratio*, no RF-EMF effect was found in the meta-analysis of 13 studies with OR= 1.08 (95% CI [0.92, 1.28]) at an average exposure level of 4.29 W/kg. The certainty of the evidence was low.

Delayed effects on the offspring health:

- For *brain pathology*, the meta-analysis of 12 studies showed no effect of RF-EMF exposure with SMD= 0.10 (95% CI [-0.09, 0.29]. The certainty of the evidence was moderate.
- For *behavioural ontogeny*, no meta-analysis was performed due to low study quality
- For *learning and memory functions*, no significant impact of RF-EMF exposure was found in the meta-analysis of two studies, with SMD= -0.54 (95% CI [-1.24, 0.17]). The certainty of the evidence was very low.
- For *motor activity*, the meta-analysis of four studies showed a decrease of the endurance capacity in the progeny of RF-EMF exposed dams with SMD= 0.79 (95% CI [0.21, 1.38]). The certainty of the evidence was very low.
- For *motor and sensory functions*, the meta-analysis of two studies indicated a moderate increase of the magnitude of the startle response in the RF-EMF exposed animals with SMD= -0.66 (95% CI [-1.18, -0.14]). The certainty of the evidence was very low.
- For *female infertility* (F2 litters), no RF-EMF effect was found in the meta-analysis of four studies with SMD= 0.08 (95% CI [-0.39, 0.55]). The certainty of the evidence was low.

In terms of limitations, the authors claim that the database for this systematic review was sufficiently large, with 88 included studies. However, there was a high heterogeneity of study characteristics, parameters, metrics and endpoints, which reduced the comparability and the number of studies for each meta-analysis. Furthermore, most studies were rated with “some concern” Risk of Bias level due to frequent deficits in exposure characterisation, blinding, sample size and outcome assessment, which increased uncertainty. Most studies did not follow a standardised experimental design and reporting of results as recommended by international guidelines (The Organisation for Economic Co-operation and Development (OECD)), likely because most studies did not have a focus on risk assessment, but a rather explorative approach.

According to the authors, the systematic literature review does not provide sufficient evidence for an impairment of female fertility, pregnancy and offspring in animal studies due to RF-EMF exposure and only sees a possible small effect on foetal weight, but taking into account the very high exposure levels used in the studies.

The authors conclude that the SR could only partly answer the initial PECO question, and it does not provide conclusions certain enough to inform decisions at the regulatory level, but it can be considered as a starting point to direct future research on this topic.

3 Comments by the BfS

This systematic review is important from a radiation protection point of view and remains of interest to the scientific community as well as to the general public.

The study was performed according to the high quality standards for systematic reviews [5]. The eligibility criteria were not overly stringent in terms of publication dates, animal populations and exposure conditions and included a wide variety of exposure durations and specific absorption rate (SAR) values, as well as RF-EMF induced temperature increases. Data were carefully synthesized, statistical heterogeneity was examined by subgroup analyses, and dose-response analyses were performed when possible.

Particular attention was given to the extraction of dosimetric information. When data on the exposure levels in the included studies were not reported, a SAR estimate was calculated based on other dosimetric information and biophysical assumptions. However, traceability is hampered by the lack of detailed information on the exact calculation methods.

The authors’ decision not to include studies with “high concern” in the overall assessment of the body of evidence (GRADE) is reasonable, because including low quality studies would have further decreased the certainty of the evidence.

For most results found in the meta-analyses, the certainty of the evidence was low or even very low, mostly due to high risk of bias and inconsistency between the studies. Only the results for litter size, foetal weight and brain pathology were moderate or high. However, for these and all other endpoints, it is obvious that the average exposure levels (wbSAR) used in studies exceeded the limit value for humans of 0.08 W/kg by far [8]. The authors stated themselves that the exposure levels used in the included studies were very high on average, and that many effects measured were most likely due to temperature increases that occur at the high field strengths used. Heating effects are known to be detrimental for the development of foetuses, affecting e.g. foetal weight [9]. Based on the included data, it cannot be determined at which exposure level RF-EMF starts to affect birth outcomes in experimental animal studies and whether effects occur at lower RF-EMF levels, closer to relevant human exposure levels.

Overall, this systematic review provides a comprehensive and transparent analysis of the current evidence for an association between RF-EMF exposure and pregnancy and birth outcomes in animal experimental studies. From a radiation protection point of view, this systematic review does not provide evidence for impairment of female fertility, pregnancy and offspring health due to RF-EMF exposure in humans, particularly for typical exposure scenarios relevant for human exposures (e.g. from telecommunications transmitters or wireless devices). Based on the overall low certainty of the evidence, further research that meets high quality standards and assesses relevant exposure levels is needed. The need for higher quality studies is in line with conclusions from SCHEER [10], the German Radiation Protection Commission [11] and the conclusion of the authors of this systematic review.

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