

Spotlight on EMF Research
Spotlight on "The effects of radiofrequency exposure on cognition: A systematic review and meta-analysis of human observational studies" by Benke et al. in Environment International (2024)

Category [radiofrequency, review]

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Competence Centre for Electromagnetic Fields (KEMF)

1 Putting the paper into context by the BfS

The World Health Organization (WHO) is currently updating the Environmental Health Criteria (EHC) monograph on potential health effects of exposure to radiofrequency electromagnetic fields (RF-EMF; frequencies 100 kHz to 300 GHz). In order to prioritize health outcomes that should be systematically reviewed, WHO conducted a survey among 300 international experts in the field. The experts rated cognition among the ten most critical outcomes related to RF-EMF [2]. More information on the systematic reviews commissioned by the WHO in general can be found in another *Spotlight on EMF Research* article (Apr/2024 no.2 [3]).

Although mechanistic effects at low levels of RF-EMF are still unknown, there are a number of studies on a potential effect of RF-EMF exposure on cognitive performance. Numerous studies were motivated by the comparatively high exposure of the brain during mobile phone calls [4]. Possible acute effects on cognition have been studied using experimental studies. In a current systematic review, commissioned by the WHO, these effects have been evaluated. Overall, there was a high to low certainty of evidence that short-term RF-EMF exposure does not reduce cognitive performance [5] (see also *Spotlight on EMF Research Jan/2025* no.1 [6]).

To study potential chronic effects of long-term exposure on cognition, observational studies are needed. Past reviews of observational studies, however, did not fully adhere to systematic review standards [4]. The systematic review and meta-analysis, as part of the WHO-commissioned series, in the present Spotlight [1] aims to overcome these limitations, for example by publishing a protocol before conducting the systematic review and meta-analysis.

2 Results and conclusions from the perspective of Benke et al.

In their systematic review, Benke et al. [1] assessed the available evidence on potential long-term effects of RF-EMF on different indicators of cognition, including domains of learning and memory, executive function, complex attention, language, perceptual motor ability, and social cognition. This primary objective of their systematic review is displayed in the following **PECO** scheme:

- P (population): general population and workers in human observational studies
- E (exposure): long-term (months/years) RF-EMF exposure
- C (comparator): no/low level of RF-EMF exposure
- O (outcome): cognitive function

The methods of the systematic review and meta-analysis have been published in a protocol open-access and a priori [4]. The results are reported in line with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [7]. The protocol includes comprehensive sections on eligibility criteria, the search and selection process, assessment of the Risk of Bias (RoB), methods of the meta-analysis, and certainty of evidence assessment [4].

In brief, in accordance with the PECO scheme, eligible studies were cohort and case-control studies from the general population and occupational settings, covering participants of any age or sex (**Population**). Studies needed to assess RF-EMF exposure and measures of cognitive function, with a follow-up of at least six months. Types of RF-EMF exposure eligible for inclusion contain personal exposure (near-field, e.g., wireless phones), environmental exposure (far-field, e.g., fixed-site transmitters such as broadcast transmitters), and occupational exposure (near-field and far-field, e.g., radar) (**Exposure**). Studies needed to compare at least two different levels of exposure, including a non-exposed or less exposed group as an exposure contrast (**Control**). Eligible studies needed to report at least one measure of cognitive function, including global cognitive function or domain-specific cognitive function such as complex attention, executive function, learning and memory (**Outcome**).

The systematic review is based on a comprehensive search in multiple databases (PubMed, Embase, PsycInfo, EMF-Portal) without any restrictions of date or language of the studies. Furthermore, websites of radiation protection bodies were screened. The selection process, resulting in the eligible studies, was carried out individually by two scientists of the review team. Data from eligible studies were also extracted by multiple scientists, using a standardised form.

To assess the quality of the included studies, a RoB assessment was conducted, again independently by multiple scientists of the team. The Tool for Human and Animal Studies by the National Toxicology Program (NTP) Office of Health Assessment and Translation (OHAT) [8] was used to assess potential bias in the domains of selection, confounding, attrition or exclusion, exposure, outcomes, selection of results, and potential other threats to validity such as financial conflicts of interest. Within each of those domains, the RoB was judged as "definitely low", "probably low", "probably high", or "definitely high". Based on the rating of all domains, each study was classified into Tier 1, Tier 2, or Tier 3. Tier 1 studies are studies with definitely or probably low RoB while the risk increases for each tier.

In the meta-analysis, mean difference (MD), the standardised mean difference (SMD), or odds ratios (ORs) were reported as a measure of the effect size, depending on whether a continuous or ordinal scale was present in the single original studies. Regarding the interpretation of MDs or SMDs, Cohens's guiding rules for interpretation were used. For interpretation of the ORs, an OR > 1.25 or < 0.80 was considered an important effect. Fixed effects meta-analyses were conducted because of the limited number of sufficiently similar studies to combine. Studies with only children or adolescents were analysed separately from those with only adults.

For the overall rating of the certainty of evidence, the OHAT decision rules were applied and the summary of evidence tables were set up according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines. [8]. According to the GRADE approach, every outcome of cognitive function was evaluated in five categories (RoB, inconsistency, indirectness, imprecision, and publication bias), resulting in high, moderate, low, or very low certainty in the evidence.

Initially, 3,945 articles were screened, of which 3,625 papers were excluded during the title/abstract screening. Of the 320 remaining articles, five studies were finally included in the systematic review, based on the inclusion and exclusion criteria, after performing the full-text screening. All five studies were prospective co-hort studies conducted between 2006 and 2017. The length of follow-up was approximately one year in four studies and nearly four years in the fifth study. The population in all except one study consists of children or adolescents from Switzerland, Australia and Singapore. In one study, adults aged 55 years or older were included. The sample size of each study varied between 317 and 2808 participants. The exposure types investigated in the included studies were mainly personal exposures to mobile or cordless phones (near-field). One study also investigated environmental exposure to RF-EMF (far-field). Most studies reported complex attention, learning and memory, and executive function as outcomes.

In the RoB assessment, three studies were rated as probably high and two studies with probably low RoB. A major reason for a high RoB rating was the exposure domain, showing, e.g., indirect assessment of exposure via self-reported use of wireless phones. Two studies calculated brain dose of RF-EMF based on self-reported information, which was validated through operator data. These two studies were rated as probably low RoB.

Results of the systematic review and meta-analyses were stratified for children and elderly. Meta-analyses were carried out for complex attention, executive function, and learning and memory in children. The authors conducted fixed effects meta-analyses, because of the limited number of available studies (n=2) [9, 10]. There was a third study on complex attention and learning and memory in children [11]. This study used a different test for the outcomes and therefore was not included in the meta-analyses. However, the results were in line with the results from the meta-analyses based on two studies. Random effects meta-analyses were presented in the appendix. Results of the meta-analyses were based on data of 615 children and a one-year follow-up (table 1).

There were no studies available on global cognitive functioning in children, both for near-field (personal exposure) and far-field (environmental) exposure to RF-EMF. For far-field exposure (environmental exposure) and complex attention in children, one study was identified. For near-field exposure (personal exposure) and

Outcome	No. of studies	Exposure metric ^a	Effect measure, effect size (95 % CI) ^b	Statistically significant effects	Certainty of the evidence
Results of meta-analysis on effects of personal RF-EMF exposure on cognition in children (Near-field personal exposure to the head via mobile phones)					
Complex attention	3*	Mobile phone calls per week: increase, decrease or same number	MD 0,02 [†] (-0,04 — 0,08)	No	Low
Executive function	2	Mobile phone calls per week: increase, decrease or same number	MD 0,02 [†] (-0,01 — 0,04)	No	Very low
Learning and memory	3*	Mobile phone calls per week: increase, decrease or same number	MD -0,03 [†] (-0,07 — 0,02)	No	Low
Results of single studies on effects of environmental RF-EMF exposure on cognition in children (Far-field exposure from fixed-site transmitters)					
Complex attention	1	Per interquartile change in personal exposure	SMD -0,09 [†] (-0,76 — 0,57)	No	Very low
Results of single studies on effects of personal RF-EMF exposure on cognition in elderly people (Near-field personal exposure to the head via mobile phones)					
Global cognitive function	1	Mobile phone use: frequent vs. never/rarely	OR 0,81 (0,42 — 1,58)	No	Very low
Complex attention	1	Mobile phone use: frequent vs. never/rarely	OR 0,67 (0,27 — 1,68)	No	Very low
Executive function	1	Mobile phone use: frequent vs. never/rarely	OR 1,07 (0,37 — 3,05)	No	Very low
Learning and memory	1	Mobile phone use: frequent vs. never/rarely	OR 0,75 (0,29 — 1,99)	No	Very low

^a Mobile phone use: frequent = daily, \geq 7 calls per week, never/rarely = <1 call per week.

Table 1: Summary of the results.

the outcomes global cognitive functioning, complex attention, executive function, and learning and memory, only one study in elderly persons was identified [12] (table 1). There were no studies on far-field (environmental) exposure and cognition in elderly, and no study on occupational exposure.

In summary, for none of the investigated combinations of outcomes, exposure types, and populations an effect of the exposure could be identified based on the available scientific literature, but the certainty of the underlying evidence is low to very low.

Benke et al. interpret their results as indicating a consistent lack of evidence for an effect of RF-EMF on cognition. However, they clearly point out several limitations: Firstly, the evidence consists of a very small study base, with only four studies on children and one study on elderly persons. Secondly, there is a high risk of detection bias in the two studies included in the meta-analyses as a result of the crude assessment of RF-EMF exposure via self-reported mobile phone use through questionnaires. In addition, in these two studies, the exposure contrast at hand is crude. Only any change in exposure at all and not the amount of change was considered. Therefore, small amounts of change in exposure would be similarly weighted as a large amount of change in exposure. Thirdly, there is long-standing evidence from neuroscience that specific regions of the brain are involved in specific domains of cognition, but the included studies do not provide de-

 $[^]b$ CI = Confidence Interval, MD = Mean Difference, SMD = Standardised Mean Difference, OR = Odds Ratio

^{*} Meta-analysis is based on two studies.

[†] A positive MD indicates better outcome, such as more complex attention, while a negative MD indicates a worse outcome, such as less complex attention.

tailed spatially resolved exposure data for specific regions of the brain that are relevant for different cognitive domains.

Finally, Benke et al. highlight important research gaps based on their findings. They outline that there is currently no observational study on far-field (environmental) exposure and cognition in adults or elderly and no study on occupational exposure. Furthermore, the authors call for a uniform method in terms of exposure and outcome assessment in future studies to enable a better synthesis and comparison of findings.

3 Comments by the BfS

From a radiation protection perspective, the question of whether there is an association between exposure to RF-EMF and cognitive effects, is very relevant. The study by Benke et al. provides a comprehensive overview of the current scientific evidence from human observational studies on potential effects of RF-EMF exposure on cognitive functions, such as learning and memory. The systematic review is based on a detailed a priori published and registered study protocol that covers all mandatory areas, such as a clearly defined PECO scheme, information on the systematic literature search, data extraction, and RoB assessment.

Benke et al. convincingly demonstrate that the available evidence base is very limited. Despite an extensive search process, only five relevant studies could be identified, of which four are on cognition in children and one is on elderly people. Since the studies themselves were quite different, only results of two studies could be combined in a meta-analysis. In a previous narrative review on cognition in children, a significantly larger number of studies were identified, which however also included cross-sectional studies [13]. Benke et al. provide a compelling argument, that in cross-sectional studies outcome and exposure data are assessed at the same time, which does not allow reliable conclusions to be drawn about causal effects of exposure on the outcome. Despite the differences in methodology and numbers of included studies, both reviews point to no effect of the exposure.

A shortcoming, that is present in four of the five included studies, is a potential training effect of computer usage for cognitive testing. The training effect can result in an improvement in test results simply because the individual has taken the test before and is now familiar with it. Becoming familiar with the test format, the types of questions, and the testing process, can potentially lead to better results on a repeated test compared to the initial one. This improvement is not due to genuine cognitive enhancement but rather a training effect [14]. When assessing changes over time, this might lead to a bias toward the null effect. This means, the results are more likely to underestimate or fail to detect an effect, even if one existed [15]. Benke et al. discuss this issue critically and highlight the need for thorough pre-testing of cognitive tests to address the potential training effect.

Overall, there was a consistent lack of evidence for an association between RF-EMF exposure and cognitive function. This included different cognitive functions, such as learning and memory, executive function, and complex attention in human observational studies with a follow-up of > six months. However, the certainty of evidence for all included studies, ranged from very low to low. The results of these observational studies are in line with the results of experimental studies, namely another recent independent systematic review and meta-analyses commissioned by the WHO and carried out by Pophof et al. [5]. Overall, Pophof et al. identified mostly moderate to high certainty of evidence that in human experimental studies, short-term RF-EMF exposure at SAR levels within recommended ICNIRP limits does not negatively affect cognitive function [5]. Furthermore, no established biophysical mechanisms that might explain potential adverse effects of RF-EMF exposure at levels below recommended exposure restrictions have been identified [16].

To increase the certainty of the evidence regarding long-term exposure, more high-quality observational studies would be needed, especially among different age groups. However, given the challenges in exposure assessment, it is unrealistic that such studies are feasible unless new and reliable methodologies for exposure assessment become available.

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