ÉTUDE SUR LES EFFETS SANITAIRES DE L'EXPOSITION AUX CHAMPS ELECTROMAGNETIQUES

Note explicative

Ce document est un extrait d'un rapport du « Comité scientifique des risques sanitaires émergents et nouveaux (SCENIHR) » sur les effets sanitaires de l'exposition aux champs électromagnétiques, mis en place par la Communauté Européenne. Il fait état des recherches les plus récentes conduites sur les effets des **champs magnétiques statiques** (en 2007 et 2008) et donne l'opinion des membres du Comité. Les références des articles scientifiques cités ne sont pas incluses, elles sont accessibles dans le document complet téléchargeable sur le site : http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_0022.pdf

Robert Guillaumont, Président de la Commission « Courant continu et santé »

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Scientific Committee on Emerging and Newly Identified Health Risks

SCENIHR

Health Effects of Exposure to EMF

Scientific Committees
- on consumer products
- on emerging and newly identified health risks
- on health and environmental risks

The SCENIHR adopted this opinion at the 28th plenary on 19 January 2009

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They are: the Scientific Committee on Consumer Products (SCCP), the Scientific Committee on Health and Environmental Risks (SCHER) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) and are made up of external experts.

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[1] Declared Interests in his annual Declaration of Interest:
http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/doi_scenihr_mattsson_en.pdf

[2] Declared Interest (see minutes of the 23rd SCENIHR plenary meeting of 2 April 2008):
http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_mi_023.pdf .

[3] Declared Interest (see minutes of the 27th SCENIHR plenary meeting of 26 November 2008):
http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_mi_027.pdf

[4] Declared Interest (see minutes of the 28th SCENIHR plenary meeting of 19 January 2009):
http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_mi_028.pdf

ABSTRACT

The purpose of this opinion is to update the SCENIHR opinion of 21 March 2007 in the light of newly available information, and to provide a methodological framework and corresponding guidelines to evaluate available scientific evidence in order to ensure the best possible quality for risk assessment.

1. Update

Radio frequency fields (RF fields)

It is concluded from three independent lines of evidence (epidemiological, animal and in vitro studies) that exposure to RF fields is unlikely to lead to an increase in cancer in humans. However, as the widespread duration of exposure of humans to RF fields from mobile phones is shorter than the induction time of some cancers, further studies are required to identify whether considerably longer-term (well beyond ten years) human exposure to such phones might pose some cancer risk.

Regarding non-carcinogenic outcomes, several studies were performed on subjects reporting subjective symptoms. In the previous opinion, it was concluded that scientific studies had failed to provide support for a relationship between RF exposure and self-reported symptoms. Although an association between RF exposure and single symptoms was indicated in some new studies, taken together, there is a lack of consistency in the findings. Therefore, the conclusion that scientific studies have failed to provide support for an effect of RF fields on self-reported symptoms still holds. Scientific studies have indicated that a nocebo effect (an adverse non-specific effect that is caused by expectation or belief that something is harmful) may play a role in symptom formation. As in the previous opinion, there is no evidence supporting that individuals, including those attributing symptoms to RF exposure, are able to detect RF fields. There is some evidence that RF fields can influence EEG patterns and sleep in humans. However, the health relevance is uncertain and mechanistic explanation is lacking. Further investigation of these effects is needed. Other studies on functions/aspects of the nervous system, such as cognitive functions, sensory functions, structural stability, and cellular responses show no or no consistent effects.

Recent studies have not shown effects from RF fields on human or animal reproduction and development. No new data have appeared that indicate any other effects on human health.

From the risk assessment perspective it is important to recognise that information on possible effects caused by RF fields in children is limited. Furthermore, there is a lack of information on diseases other than those discussed in this report.

Intermediate frequency fields (IF fields)

Occupational exposure to IF fields in certain areas is considerably higher than exposure to the general public. However, very little research on IF and health risks in occupational settings or for the general public have been presented since the previous opinion, and no epidemiological studies have appeared. Consequently, the data are still too limited for an appropriate risk assessment.

In view of the increasing occupational exposure to IF among workers in e.g. security, shops, and certain industries it is important that research in this area is given priority.

Extremely low frequency fields (ELF fields)

The few new epidemiological and animal studies that have addressed ELF exposure and cancer do not change the previous assessment that ELF magnetic fields are a possible carcinogen and might contribute to an increase in childhood leukaemia. At present, in vitro studies did not provide a mechanistic explanation of this epidemiological finding.

No new studies support a causal relationship between ELF fields and self-reported symptoms.

New epidemiological studies indicate a possible increase in Alzheimer's disease arising from exposure to ELF. Further epidemiological and laboratory investigations of this observation are needed.

Recent animal studies provided an indication for effects on the nervous system at flux densities from 0.10-1.0 mT. However, there are still inconsistencies in the data, and no definite conclusions can be drawn concerning human health effects.

Very few recent in vitro studies have investigated effects from ELF fields on diseases other than cancer and those available have very little relevance. There is a need for hypothesis-based in vitro studies to examine specific diseases.

It is notable that in vivo and in vitro studies show effects at exposure levels (from 0.10 mT and above) to ELF fields that are considerably higher than the levels encountered in the epidemiological studies (µT-levels) which showed an association between exposure and diseases such as childhood leukaemia and Alzheimer's disease. This warrants further investigation.

Static fields

Although a fair number of studies have been published since the last opinion, the conclusion drawn there stands: there is still a lack of adequate data for a proper risk assessment of static magnetic fields. More research is necessary, especially to clarify the many mixed and sometimes contradictory results.

Short term effects have been observed primarily on sensory functions for acute exposure. However, there is no consistent evidence for sustained adverse health effects from short term exposure up to several teslas.

Environmental effects

The current database is inadequate for the purposes of the assessment of possible risks due to environmental exposure to RF, IF and ELF.

Research recommendations

The scientific rationale has identified a number of areas characterised by insufficient and contradictory information regarding possible health associated effects from the various frequency bands of the EMF spectrum. It is recommended that certain knowledge gaps are filled.

2. Methodological Framework

The SCENIHR is asked to provide a methodological framework and corresponding guidelines to evaluate available scientific evidence in order to ensure the best possible quality for risk assessment. The subject is covered in detail in chapter 3.8 of the opinion.

The present opinion provides a methodological framework and guidelines as:

- a general outline of criteria used for making EMF health risk assessment
- a description of the work procedure leading to the overall evaluation
- a specialised section where characteristics and quality criteria regarding dosimetry and exposure assessment, epidemiology, human laboratory studies, in vivo studies, and in vitro studies are presented.

Keywords:

EMF, electromagnetic fields, radiofrequency fields, intermediate frequency fields, extremely low frequency fields, static fields, health effects, human health, environmental effects, SCENIHR, Scientific Committee on Emerging and Newly Identified Health Risks

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3.6. Static fields

Previous health risk assessments of static magnetic fields (SMF) principally focused on static fields only. However, the recent increasing use and further development of MRI equipment has also led to studies of exposures to MRI sequences which include combinations of static fields, RF fields, and variable gradient fields. The following section thus considers studies that focus on static fields only, as well as studies where MRI-relevant field combinations have been used.

3.6.1. Sources and distribution of exposure in population

The number of artificial sources of static magnetic fields is small but there is a rapid development of technologies using static magnetic fields. The number of people with implants that can be affected by static magnetic fields is also growing. Static magnetic fields up to some mT are found in certain occupational settings, e.g. in the aluminium and chloralkali industries, in welding processes, and in certain railway and underground systems. A very prominent application is MRI, where different types of tissues in the human body can be identified and located by using static magnetic fields, magnetic gradients and RF fields. Close to the device a few hundred mT can be reached. Common SMF inside MRI scanners are 1.5 and 3 T. Recently developed devices which are currently only used for research purposes and for specialised teams in specific medical applications can generate fields up to 10 T and more.

3.6.2. Health effects

What was already known on this subject?

The previous opinion of 2007 stated that a large number of biological studies have been carried out in search of biological effects of static magnetic fields. The studies include in vitro and in vivo laboratory studies as well as studies on human volunteers (see also WHO 2006 for a comprehensive review). Known effects of magnetic fields are orientation of forces applied on biological molecules with magnetic properties such as haemoglobin, rhodopsin (visual pigment), free radicals, and nitric oxide. These effects are detectable at field levels of about 1 T, without known health consequences.

The WHO report concluded that there are only a few epidemiological studies available and the majority of these have focused on cancer risks. There are some reports on reproductive outcomes, and sporadic studies of other outcomes. Overall, few occupational studies have focused specifically on effects of static magnetic fields and exposure assessment has been poor. In summary, the available evidence from epidemiological studies was deemed not sufficient to draw any conclusions about potential health effects of static magnetic field exposure.

The 2007 opinion concluded that adequate data for proper risk assessment of static magnetic fields are almost totally lacking and that the advent of new technology, and in particular MRI equipment, makes it a priority for research.

What has been achieved since then?

The results of studies on health effects and static magnetic fields carried out since the last opinion will be presented in the following chapters on human, in-vivo and in-vitro studies.

3.6.2.1. Human studies

Several studies have been performed where volunteers were exposed to either the static field of an MRI only, or to a diagnostic procedure which also includes exposure to low and high frequency fields.

Nervous system effects

Toyomaki and Yamamoto (2007) observed an increase in the activity in the theta band of brain activity during exposure to a 1.5 T SMF of an MRI scanner, especially when a task was performed. Atkinson et al. (2007) observed no effects on vital signs and cognitive ability of a sodium imaging procedure in a 9.4 T MRI scanner. Patel et al. (2008) exposed MRI workers to the SMF of a 9.4 T MRI. All subjects noted sensory symptoms during exposure, but no effects on vestibular function could be detected at 30 min and 3 months after exposure.

De Vocht et al. (2007) studied cognitive effects of standardised head movements in a 0.8 or 1.6 T SMF. Negative effects were observed on a visual tracking task. A trend for decreased performance in two cognitive-motor tests was also found, but no effects on working memory were observed.

Kuipers et al. (2007) observed no effect of a 1 h exposure to a SMF of 0.06 T on pain perception, sympathetic function, and hemodynamics at rest or during noxious stimuli.

Other studies

Sirmatel et al. (2007a, b) observed contradictory effects on oxidative stress from a 30 min SMF exposure in a 1.5 T MRI scanner. In the first paper Sirmatel et al. (2007b) reported an increased total nitrite concentration in blood samples, an indicator for nitric oxide concentration and indicating increased oxidative stress. In the second paper Sirmatel et al. (2007a) reported an increased total antioxidant capacity and a decreased total oxidant status, and also calculated a decreased oxidative stress index.

No new epidemiological studies have been published since the 2007 opinion.

3.6.2.2. In vivo studies

Nervous system effects

The group of László has published a series of studies on the effects of SMF exposure on pain perception in mice. László et al. (2007) observed pain reduction with exposures between 0.4 and 1.47 mT for up to 30 min in preliminary experiments in search for an optimal exposure arrangement. Once found, it was used to study the effect of 0-45 min to approximately 1.6 mT (Sandor et al. 2007). Depending on the method used to inflict pain (by injection of chemicals such as acetic acid); pain reduction was already measurable after 5 min. It was concluded that capsaicin-sensitive nerves are involved in the SMF-induced antinociceptive action. In a subsequent paper, Gyires et al. (2008) concluded that the antinociceptive effect of SMF is likely to be mediated by opioid receptors. László and Gyires (2009) repeated these experiments by exposing the animals to the SMF in the bore of a 3 T MRI unit and observed a stronger antinociceptive action than with the weaker SMF.

Behaviour of rats was studied by Houpt et al. (2007a, b). In their first paper the animals were trained to climb though the bore of a sham NMR unit (large vertical magnet). When this was switched for a real magnet with a field strength of 14.1 T, half of the animals avoided climbing into the magnetic field. Upon further testing the animals had already stopped climbing at a field strength of about 2 T. Surgical removal of the peripheral vestibular apparatus abolished this avoidance behaviour. In a parallel study, Houpt et al. (2007b) found increased locomotor circling and aqcuired taste aversion when the animals were exposed to a uniform 14.1 T SMF, but not when exposed to a gradient field (maximally 54 T/m). Ammari et al. (2008b) exposed mice to a 128 mT SMF for 1 h/d, 5 d. No effect on anxiety was observed, but the mice developed an altered emotional behavior and cognitive impairment.

Effects on individual neurons have been studied in several species. Todorovic et al. (2007) exposed neurons of the beetle *Morimus funereus* to 2 mT for 5 min and observed both excitation and inhibition. Nikolic et al. (2008) studied the activity of neurons of the snail *Helix pomatia.* In the Br neuron (an easily accessible nerve cell with a prominent axon and thus well suited for electrophysiological studies), exposure to 2.7 mT resulted in changes in amplitude and duration of the action potential, while 10 mT changed the resting potential, amplitude spike, firing frequency, and duration of the action potential. No effects were observed in the N(1) neuron. In the crayfish nerve cord, exposure to 8.08 mT for 30 min increased the efficacy of synaptic transmission in the tail-flip escape circuit (Yeh et al. 2008).

Circulatory system

Several groups studied the influence of SMF exposure on blood flow. Gmitrov (2007) exposed rabbits to 350 mT for 40 min and observed increased arterial baroreflex sensitivity as well as increased blood flow. Brix et al. (2008) studied blood flow in hamster muscle. At exposures higher than 500 mT for up to 3 h, red blood cell flow velocity was reduced by more than 40%. No effect was found on the capillary and arteriolar diameter and on the amount of functional vessels. In hamster A-Mel-3 tumours, an SMF of 150 mT and higher induced a ~40% reduction of red blood cell velocity already after 1 min, with no further increase thereafter (Strieth et al. 2008). With 587 mT these authors found also a decreased number of functional vessels and a time-dependent increase in platelet-endothelial cell adherence.

Morris et al. (2008) observed effects of SMF exposure on edema formation in rats after specific treatments. Exposure was to 10, 70 or 400 mT for 15 or 30 min, or 2 h. A reduction in histamine-induced edema formation was seen after 10 or 70 mT for 15 or 30 min, while Ca^{2+}-induced edema formation was reduced only after exposure to 70 mT for 2 h. The same authors also continuously exposed rat skin flaps to a 25–85 mT/cm SMF gradient for 7 days. They observed a reduction in arteriolar diameter and in venular diameter and length, indicating regulation of vessel growth.

Growth and metabolism

Abbasi et al. (2007) exposed mice to 50 mT for at least 10 h per day for 10 and 15 days and found no effect on weight gain and blood glucose levels. Hashish et al. (2007) exposed mice to gradient SMF of permanent magnets (-2.9 µT to +2.9 µT) for 30 d. They observed a gradual loss of body weight, coupled with decreased glucose and total protein levels and alkaline phosphatase activity in serum. Increased hepatic enzyme activity and lipid peroxidation levels were found. The numbers of monocytes, platelets, peripheral and splenic lymphocytes decreased, but the number of granulocytes increased.

Peric-Mataruga et al. (2008) exposed pupae of the mealworm *Tenebrio molitor* to 320 mT for 8 days and observed an increase in cell number, cell and nuclei size, number of nucleoli in the nuclei, and size of corpora allata in protocerebral neurosecretory neurons.

3.6.2.3. In vitro Studies

Gene expression and genotoxicity

In some studies using cultured cell lines, exposure to several hundreds of millitesla resulted in altered gene expression or DNA damage (Amara et al. 2007, Tenuzzo et al. 2008a, Tenuzzo et al. 2008b, Denaro et al. 2008), while in others, exposure to much stronger SMF such as those used in clinical MRI (up to several tesla) did not cause any effects (Schwenzer et al. 2007a, Schwenzer et al. 2007b). Sakurai et al. (2008a, 2009) observed in both insulin-secreting cells and osteoblasts an increased expression of specific mRNAs after exposure to 6 T / 41.7 T/m for 1 h, but not after 3 T / 26.9 T/m or 10 T / 0 T/m.

In the nematode *Caenorhabditis elegans* several genes were transiently induced after 3 or 5 T, but not after 2 T (Kimura et al. 2008). No DNA damage was observed.

Micronucleus (MN) induction is indicative of DNA damage. Simi et al. (2008) exposed lymphocytes taken from healthy volunteers to up to four consecutive sequences in a 1.5 T MRI scanner and investigated MN formation directly and 24 h after exposure. The baseline level of the MN frequency (the percentage of cells with MN) varied between 7 and 19%. A dose-response effect was observed with an increase in MN frequency at all four levels. After 24 h recovery at room temperature the MN frequency was decreased, returning to control levels at the two lowest levels. MN induction and recovery was also evaluated in lymphocytes taken from the volunteers after they had been submitted to a cardiac scan. The MN frequency was approximately doubled directly after the scan but returned to control level at 48 h.

Oxidative stress, apoptosis and membrane effects

Several studies using different types of cancer cells have shown contradictory effects on oxidative stress. No effect was found in HL-60 cells exposured to 100 mT for 13 min by Rozanski et al. (2008), while a 2 h exposure to 6 mT increased oxidative stress in U937 monocytic tumour cells (De Nicola et al. 2006).

Reduction of apoptosis (programmed cell death) may result in an increased risk for carcinogenesis. Nuccitelli et al. (2006) observed in U937 monocytic tumour cells a correlation between reduction of apoptosis and modulation of membrane potential induced by exposure to 6 mT SMF. Combined with the results from De Nicola et al. (2006), who observed that modification of the redox balance prevented the antiapoptotic effect of SMF, this indicates a link between reduction of apoptosis and alteration of the intracellular redox balance induced by SMF.

These observations are supported by the study of Tenuzzo et al. (2008b). They exposed human lymphocytes to 6 mT for up to 24 h and observed a reduction of apoptosis and modification of the influx of free calcium. The effect of SMF exposure on the response of cytosolic free calcium to ATP stimulation was also studied in HL-60 cells by Belton et al. (2008). In this study, exposure to 1, 10 or 100 mT for 13 min had no effect.

Shen et al. (2007) studied the effects of exposure to 125 mT SMF on the voltage-gated potassium channel (VGPC) currents in trigeminal root ganglion neurons. Their observations are consistent with modification of physiological characteristics of ion channels in the membrane, resulting from membrane deformation.

Cell growth, differentiation and viability

The formation of microtubules in human endothelial cells was influenced only by a gradient field, and not by a 120 mT SMF (Okano et al. 2007, Okano et al. 2008).

Exposure to a SMF of 5 mT for 24 h had no effect on growth of a Schwann cell line (Gamboa et al. 2007). No changes in cell proliferation were observed by Coletti et al. (2007) in L6 myogenic cells grown under continuous exposure to 80 mT SMF, but in MG63 osteoblast-like cells a 24-h exposure to 0.4 T reduced the proliferation effects of growth factors (Chiu et al. 2007). In rat GH3 cells (which are of pituitary origin) continuous exposure to 0.5 T increased cell size after 3 weeks and reduced cell growth by 51% after 4 weeks (Rosen et al. 2008). A 2 h exposure to 3 T did not have any effect on the clonogenic ability and proliferation of Hel 299 human embryonic lung fibroblasts (Schwenzer et al. 2007c).

Exposure to a SMF of 5 mT for 24 h had no effect on differentiation of a Schwann cell line (Gamboa et al. 2007), but increased differentiation was observed in U937 cells continuously exposed to 6 mT (Tenuzzo et al. 2008a), in L6 myogenic cells grown under continuous exposure to 80 mT SMF (Coletti et al. 2007), and in MG63 osteoblasts after exposure to 0.25 or 0.4 T for up to 8 h (Lin SL et al. 2008). In human neuronal SH-SY5Y and PC12 cells, exposure to 12 mT influenced the direction of outgrowth of neurites (Kim S et al. 2008).

A higher cell viability was observed in fibroblasts after exposure for 12 h to 0.4 T SMF (Lin CT et al. 2008), in U937 cells continuously exposed to 6 mT (Tenuzzo et al. 2008b), and in human chondrocytes after exposure for 72 h to 0.6 T (Stolfa et al. 2007).

3.6.3. Conclusions about static fields

The human volunteer studies indicate that instantanuous effects on neuronal functioning of movement in particular, through a SMF or SMF gradient as used in clinical practice might be possible. These studies need confirmation.

Recent animal studies confirm earlier findings that SMF of several mT can have direct effects on neurons in some in vivo systems. In vitro studies also show that exposure to SMF in the millitesla range may change membrane properties. These changes may lead to changes in neuronal functioning. The effects seem to be reversible.

The studies on pain reduction in animals by exposure to millitesla SMF are interesting. The question is whether rodents are an adequate model for humans in this respect, since no pain reduction in humans was observed after SMF exposure one order of magnitude higher.

Earlier studies indicated effects on rodent behaviour at SMF of 4 T and higher. The current findings at lower levels also need confirmation.

The recent results from animal experiments on blood flow and vessel growth, as well as on growth and development are contradictory and do not clarify the mixed results of previous studies.

The recent experimental data support results from earlier studies that SMF can affect the expression of specific genes in human and other mammalian cells and that these effects may depend on exposure duration and field gradients. Genotoxic effects have been reported, although it seems that these effects can be repaired and are not permanent.

The many earlier studies on cell growth showed contrasting results. The occurrence of effects appeared highly cell-type dependent. The more recent experimental results do not clarify this picture. The recent studies on apoptosis also provide contrasting results as in earlier studies.

Although a fair number of studies have been published since the last opinion, the conclusion drawn there still stands: there is still a lack of adequate data for a proper risk assessment of static magnetic fields. More research is necessary, especially to clarify the many mixed and sometimes contradictory results.

Short term effects have been observed primarily on sensory functions for acute exposure. However, there is no consistent evidence for sustained adverse health effects from short term exposure up to several teslas.

3.7. Environmental Effects

Studies on individual species living in close proximity to EMF sources are important in identifying whether ecosystems can be affected substantially by EMF. In addition such studies may be a potential source of information on the potential of EMF to cause adverse effects in man.

What was already known on this subject?

In the past the main themes of research have been:

- effects on reproduction
- influence on species that use magnetic fields for navigation purposes