Extremely low-frequency magnetic fields and health effects: literature review

Abstract

Since an epidemiologic report, in 1979, showed an association between childhood leukemia and exposure to magnetic fields, concerns over the subject have grown, and several other studies have been published. The main goal of this literature review is to present the methods of exposure assessment and the main difficulties in measuring exposure, and also to report the results of epidemiological studies published along the past ten years. The lack of biophysical mechanisms explaining the interaction between magnetic fields and health, and the difficulties regarding exposure assessment have been the main obstacles of research in this area. Leukemia and brain tumors are the most evaluated outcomes. Childhood leukemia has been the most consistently outcome associated with magnetic field exposure. Recent studies have also shown an association between magnetic fields and amyotrophic lateral sclerosis.

Keywords: Magnetic fields. Literature review. Leukemia. Neurodegenerative diseases.

Izabel Marcilio*

Mateus Habermann

Nelson Gouveia

Departamento de Medicina Preventiva da Faculdade de Medicina, USP

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Correspondência: Izabel Marcilio. Faculdade de Medicina da Universidade de São Paulo. Av. Dr. Arnaldo, 455 - São Paulo, SP - CEP 01246-903. E-mail: imarcilio@yahoo.com

Resumo

A partir da publicação, em 1979, dos resultados de um estudo que apontava para o aumento do risco de leucemia em crianças associado à exposição a campos magnéticos, o interesse pelo tema vem aumentando, e diversos estudos foram publicados. O objetivo desta revisão é apresentar os diferentes métodos utilizados na avaliação da exposição aos campos magnéticos de frequência extremamente baixa, bem como as dificuldades enfrentadas na quantificação dessa exposição, além de relatar os resultados de estudos epidemiológicos publicados nos últimos 10 anos. A falta de um modelo fisiopatológico que explique uma possível influência dos campos magnéticos na saúde e a dificuldade para quantificar a exposição têm sido os maiores obstáculos da pesquisa na área. Leucemia e tumores do sistema nervoso central têm sido os efeitos mais estudados. Leucemia em crianças é o desfecho mais consistentemente associado à exposição a campos magnéticos. Estudos mais recentes apontam a associação entre esclerose lateral amiotrófica e campos magnéticos.

Palavras-chave: Campos magnéticos. Revisão de literatura. Leucemia. Doenças neurodegenerativas.

INTRODUCTION

The association of health effects and exposure to magnetic fields has been a major concern and there has been considerable scientific research on the theme. The first paper addressing the issue was published in the 1960's and focused on occupational exposure[1]. In 1979, Wertheimer and Leeper[2] definitely brought the issue to the spotlight by showing a positive association between the risk of childhood leukemia and exposure to electromagnetic fields. Since then, a vast production of papers assessing possible health effects due to exposure to magnetic (MF) and electromagnetic fields (EMF) can be observed.

Magnetic and electric fields are both associated to electric current flow and the term EMF is commonly referred to both. However, the assessment of health effects refers most often to MF, since ordinary civil construction materials cannot block their passage, differently from the electric fields[3]. MFs are radiations generated by different sources, natural or human-made. Around the last one hundred years, man started to be artificially exposed to MF from electric power transmission, and these fields are a key part of industrialized societies[3,4].

Electric fields are generated from differences in voltage, and the higher the voltage, the stronger will be the resultant field. Their intensity decreases with the distance from the source. Magnetic fields happen when there is electric current flow, and their power is directly proportional to the strength of the current[5]. Some of the natural sources of MF include solar radiation and ultraviolet light. Examples of MF generated by man include radiowaves and electric power.

MFs vary in frequency, measured in Hertz (Hz), and size of waves. The lower end of the frequency spectrum (0 Hz) is represented by direct current or static fields. The upper end, with frequency above 10^{16} Hz, comprises ionizing radiations –X-rays, Gama rays, and ultraviolet light[6].

Low frequency fields occupy the range from 3 to 3,000 Hz, with long wavelength.

Electric power generation and transmission networks results in extremely low frequency fields, ranging from 50 to 60 Hz.

MF intensity is measured in Amperes by meter (A/m). For the purposes of research and communication of risk, however, the intensity of magnetic induction is more frequently used and it is described in Gauss (G) or, more commonly, in Tesla (T) or micro-Tesla (μT).

Biological Mechanisms

The known interaction between extremely low-frequency MF and the human body is the induction of weak electric currents. These fields are not capable of breaking chemical bonds and are known as "non-ionizing radiations"[3,7].

Despite the many studies on the theme, there is no agreement to the moment about adverse health effects generated by extremely low frequency MF, since they seem to have insufficient energy to break DNA bonds and trigger a carcinogenic process [8,9], except for acute exposures equal or above 100 μT[10]. Therefore, the current hypothesis is that extremely low-frequency MF acts as a cocarcinogenic factor[11,12].

Experimental evidences suggest that MF may influence some cell functions, such as cell proliferation and intercellular communication[11-13]. Exposure to high levels of MF can lead to tumor promotion or to other types of cell damage through the production of endogenous free radicals or by interfering in calcium channels[11,13-15].

Another hypothesis to explain the association of leukemia and breast cancer with MF is the influence of the latter in the melatonin system[15-17]. Melatonin is mainly produced by the pineal gland. Its secretion is directly related to the circadian cycle, influenced by the perception of absence of light by sensitive cells in the eye. Some studies showed that MFs reduce different parameters of the production of melatonin by the pineal glands of mammals. From the literature review, however, we may conclude that, despite the results attained in some experiments with animals, there is no sufficient evidence of alteration in the melatonin physiology in humans related to extremely low-frequency MF exposure [18-20].

The nervous system works by electric stimulation and is considered particularly vulnerable to the effects of MF and the electric currents they induce[15]. Although extremely low-frequency MF provoke smaller currents than those physiologically present and capable of stimulating the peripheral nervous tissue, evidence suggests that the former may modulate the functional electric activity in the central nervous system (CNS)[13,15].

Experimental studies assessing MF health effects show some limitations. A large part of them use exposures way above the levels that, in general, are present in home environments[16,21]. Such is the case of the studies of Iorio et al.[22], who found an increase in the mobility of spermatozoids exposed to fields starting from the minimum intensity of 2.5 mT, and Tokalov and Gutzeit[23], who found differences in the expression of stress proteins upon cell stimulation by MF from 10 to 140 μT.

Non-identification of a target organ (or target mechanism) for MF poses a challenge for experimental studies about their health effects[23]. Lack of independent replication is also frequent in such studies, which makes it difficult to establish a causal association between MF exposure and health effects[16].

Thus, to the present, experimental studies have not been capable of establishing a biophysical mechanism that can explain a biological response induced by MF. It is worth noting, however, that since epidemiological studies show that MF exposure may be harmful to health, there must be a mechanism of interaction, even if in the moment this mechanism cannot be demonstrated, or even seems implausible[15].

OBJECTIVE

The goal of this review is to present the different methods used in the assessment of exposure to extremely low-frequency MF, as well as the difficulties faced in quantifying this exposure, in addition to reporting the results of epidemiological studies published in the past 10 years.

METHOD

A literature search was conducted in PubMed and Scielo database using the terms: electromagnetic, electric or magnetic fields (EMF) + health effects and *campo eletromagnético*, *campo magnético*, and *efeitos na saúde*. The terms health effects and *efeitos na saúde* were also replaced by*:* cancer*,* leukemia and neurodegenerative disorders and *câncer, leucemia* and *doenças neurodegenerativas.*

All papers found were included in the analysis of exposure assessment. Description of results on health effects studies, however, was limited to the last 10 years (1998 to June 2008).

RESULTS

Exposure assessment

One of the main problems faced in investigating MF health effects is the assessment and quantification of exposure[9,12,15]. This difficulty permeates the prevalence and ubiquity of exposure. There is, also, complexity on characterizing and adding up the effects of different MF sources[15].

The lack of a dose-response model or a pathological mechanism, in addition to difficulty in defining the induction period of harmful effects are obstacles to establish relevant parameters to be quantified for risk assessment[9,15].

Despite the difficulty to characterize MF exposure, apparently there is not a trend of bias on accessing exposure. It is presumed that the same probability of error lies in the classification of subjects into exposed and non-exposed categories[10]. This fact would imply the so-called "non-differential classification error" and any difficulties found would not result in a false risk to health. To the contrary, they would tend to underestimate an existing real risk[24].

Residential exposure

Assessment of residential exposure to MFs has been most often conducted based on surrogates models. The first study published used an exposure classification developed by authors themselves, the wire code system[2]. Subsequent studies used, in addition to the wire code, several combinations of exposure assessment surrogates, such as:

1. Wire code system: most commonly used in the US, the wire code system classifies exposure based on visual inspection of transmission lines and equipment close to households, taking into consideration characteristics like probable load in transmission lines (TL), thickness of wires, location of transformers and household proximity to lines. The first classification categorized households as high current configurations (HCC) or low current configurations (LCC)[2]. Later, categorization was refined and 5 ranges of exposure were created[25,26].
   The wire code system has the advantage of being relatively stable along the years. Another advantage is that it can be carried out independently from subject's participation, which decreases the chances of bias due to refusal or even memory bias[15]. On the other hand, it does not take into account other sources of exposure, such as the electric equipment present in households.
2. Calculation of distance between households and energy transmission equipment: Coleman et al.[27] considered distance from household to TL, dividing subjects into groups: 0-24 m, 25-49 m, 50-99 m and ≥100 m (reference group). After this, several other studies used the distance between households and TL to assess MF exposure[28-33]. The use of distance to assess exposure has become more common with the advent of geo-referenced information systems [29,34].
3. Historical calculation MF history

through information provided by electric power companies[30-35]: The field in each household is calculated based on information about the distance between household and TL, type, load, and current flow in TL, height of towers, distance between towers, distance and ordering of phases, and date of TL construction.

As in the wire code classification, assessment based on calculation of the distance between households and TL and based on historical calculation of MF has the advantage of being relatively stable along time and of being independent of participation of subjects. Despite their advantages, both assessment methods have the same limitations as the classification in wire codes.

4. Focal measurements of MF: focal MF measurement close to household entrance doors and in the rooms of parents and children was used by Savitz et al.[36] together with application of questionnaires and classification of households based on wire codes. Other authors used MF measured in households, schools and day care centers as an indicator, isolatedly or associated to other indicators[37-40].
5. Personal measurements by dosimeters held by subjects during specific periods[41,42].

   If, on one hand, focal and personal measurements represent apparently more precise ways of quantifying exposure by measuring the influence of different sources of MF; on the other hand, they can be influenced by changes of behavior and consumption along time and depend on subject participation in the study. In addition, exposure assessment based on personal measurement in case-control studies may be influenced by factors related to behavioral changes determined by sickness or health status[15].

Occupational exposure

Difficulties similar to those present in residential exposure studies are described in literature for the assessment of occupational exposure, such as rare outcomes and unawareness of the relevant period of exposure. Added to those, there are some peculiarities in the work environment. MF intensity in certain jobs, for instance, can reach much higher levels than in residential exposure. In addition, occupational exposure is characterized by major variation in field intensity, both in space and time. An example of such variation was described in the ICNIRP[9] review, assuming the situation of a worker that while repairing the line may be exposed to fields that exceed 100 μT and while moving from one site to another may be exposed to null fields.

Occupational exposure has been estimated based on surrogates, such as job categories or more complex matrixes of exposure. Other possibility includes detailed assessment of a sample of workers through personal dosimeters, extrapolating results to a larger target group[9].

Exposure classification based on job categories was primarily used by Milham, in 1982[9], and is the first assessment model of occupational exposure to MF[9,15]. It has the advantage of being based on information relatively easy to obtain, in that it is possible to use secondary data, in addition to being a simple manner to communicate the study's results. On the other hand, it has an important disadvantage: classification merely based on job category may show disconnection to real exposure. It is the case of line engineers who work most of their time in the office, away from electric facilities[15].

Aiming at enhancing the quantification of occupational exposure, several researchers invested in the development of exposure matrixes. Such matrixes comprised algorithms of lesser or higher complexity that may take into account job title, workplace, description of activities developed, utilization of electric equipment, and even MF measured by personal dosimeters in a sample of workers[9,43-50].

Studies that use dosimeters to build the occupational matrix have the advantage of being more easily replicated. They also can be compared to other studies, including those studies that assessed residential exposure[9].

MF HEALTH EFFECTS

Bibliographic search for epidemiological studies investigating MF health effects published between 1998 and June 2008 resulted in 82 papers. Most of them assessed the occurrence of leukemia (25 papers) and cancers of several types, particularly brain tumors (17 papers). There are also studies on cardiovascular diseases[43-45], miscarriage and congenital malformation[33,42,46,47], neurodegenerative diseases[48-51] and psychological disorders[49,52].

Among the studies found, 47 were case-control and 19 were cohort. The other papers found were 8 reviews, 3 meta-analyses, 2 grouped analyses, one case-cohort study, one ecological study and one cluster study.

The papers published were mainly produced in the US (25 papers) and Europe (30 papers). In the European production, it is worth highlighting the importance of the Scandinavian countries, with 20 publications. Only 4 studies were conducted in Latin America—3 in Brazil and one in Mexico.

Childhood leukemia

Wertheimer and Leeper[2] conducted a pioneering study evaluating MF residential exposure and occurrence of childhood leukemia. This population-based case-control study assessed exposure based on wire codes. The odds ratio (OR) found was 2.3 (1.8 - 5.0) among children that lived in HCC households.

As of this, several other studies were published in different countries and using different ways of accessing MF exposure. Most suggested increased risk associated to higher exposure, although, in general, 95% Confidence Intervals had null risk included[41,53,54,55,56,57].

In 2000, two grouped analysis were published. Ahlbom et al.[58] analyzed nine studies that investigated the relationship between children leukemia and residential exposure. They included all population-based studies that accessed exposure through MF estimation or field direct measurement at the child's household. For children exposed to MF levels between 0.2 and 0.4 μT, a risk close to null was calculated (OR: 1.1; 95% CI: 0,8 - 1,5). For children exposed to MF ≥ 0,4 μT, an OR of 2.0 was found (95% CI: 1.3 - 3.1).

Another grouped analysis, with less restrictive inclusion criteria, was published by Greenland et al.[59]. Analysis of data from the 15 studies included resulted into an OR of 1.7 (95% CI: 1.2 - 2.3) for children exposed to MF > 0.3 μT, in comparison to those exposed to ≤ 0.1 μT.

Some studies were also published exploring the risk of leukemia in children based on parents' occupational exposure. A cohort developed in Sweden found an RR of 2.0 (95% CI: 1.1 - 3.5) among children whose parents were exposed to MF ≥ 0.3 μT, in relation to those whose parents had exposure ≤ 0.12 μT[60].

In 2002, based on these studies, the International Agency of Research in Cancer (IARC), classified extremely low-frequency MF as possibly carcinogenic for humans (Group 2B)[18].

After IARC's publication[18], other two studies published results that did not change significantly what had been previously established:

Draper et al.[29] conducted a case-control study in Great Britain assessing the risk of childhood leukemia based on distance between their households and the closest TL. They detected raised risk among children who lived up to 200 m from TL (OR: 1.7; 95% CI: 1.1 – 2.5).

Kabuto et al.[40] recent study found a statistically significant association between exposure to MF ≥ 0.4 μT and incidence of leukemia, with OR of 2.6 (95% CI: 0.8 - 8.6) when compared to the reference group (MF < 0.1 μT). MF intensity was measured by a dosimeter placed on the child's bedroom.

Two case-control studies conducted in Canada and England both found a raised risk for leukemia among children whose parents had higher occupational exposure to MF (OR: 2.5; 95% CI: 1.2 – 5.0 and OR*:* 1.4; 95% CI: 1.1 – 1.8; respectively)[61,62].

Mejia-Arangure et al.[39] study assessed the risk of leukemia exclusively among children with Down Syndrome. The authors reported an OR of 3.7 (95% CI: 1.1 – 13.1) for children with higher residential exposure.

Table 1 brings a summary of the epidemiological studies published after IARC[18] risk assessment analyzing the occurrence of childhood leukemia based on MF exposure.

Adult leukemia

Most studies addressing the risk of adult leukemia associated to MF assessed occupational exposure.

Two population-based case-control studies assessing residential exposure were conducted after IARC publication, in 2002[18]. Tynes and Haldorsen[63] and Lowenthal et al.[64] studies found augmented risk among people with higher MF exposure. The former analyzed exposure by calculating magnetic induction in each household and found the OR for MF exposure > 0.2 µT, of 1.3 (95% CI: 0.7 – 2.5). The latter assessed household distance to the closest TL and evidenced augmented risk among people who lived within a distance of up to 50 m from TL in comparison with those that always lived more than 300 m away (OR*:* 2.1; 95% CI: 0.9 - 4.9). Risk was also augmented for those that had already lived within a distance range from 50 to 300 m (OR*:* 1.3; 95% CI: 0.9 - 1.9).

Studies assessing occupational exposure did not reach such consistent results. A case-control study conducted in New Zealand[65] used an occupational exposure matrix, and found augmented risk, with OR of 1.9 (95% CI: 1.0 – 3.8) among the workers exposed.

A cohort among electricity utility workers in Denmark, on the other hand, did not detect augmented risk for the occurrence of leukemia, not even when subgroups like 'acute', 'chronic lymphocytic', 'chronic myeloblastic' and 'other non-specified types' were analyzed in separate[66,67].

Hakansson et al.[68] published results of a cohort study assessing the incidence of several types of cancers among workers. Among men with higher exposure, there was no augmented risk for leukemia—neither when all types of leukemia were analyzed jointly, nor when the 22 cases of ALL were assessed separately (OR*:* 0.7; 95% CI: 0.1 – 3.6). Among women, 41 cases of leukemia were included, in that only 2 were in the higher exposure category. For this group, augmented risk was found, with OR of 1.8 (95% CI: 0.4 - 8.5).

Likewise, case control studies conducted by Willet et al.[69] and the case-cohort study conducted by Savitz et al.[70] did not suggest augmented risk of leukemia among workers with higher occupational exposure to MF.

Table 2 provides a summary of the epidemiological studies assessing occurrence of adult leukemia based on MF exposure

Childhood brain tumors

The historical 1979 paper of Wertheimer and Leeper[2] used the wire code system to assess relationship of childhood brain tumors and residential exposure to MF, finding augmented relative risk (RR) among children with higher exposure.

Later studies, however, did not find any risks or found minimum risks and confidence intervals encompassing null risk[37,60]. In 2002, IARC review stated that evidences at the time were unsuitable to show association between MF and the risk of brain cancer [18].

After IARC[18] publication, a case-control study was conducted in Great Britain[29]. The authors did not find augmented risk for brain tumors among children that lived closer to TL.

Table 3 brings a summary of the epidemiological studies assessing the occurrence brain tumors in children exposed to MF.

Tabela 1: Estudos avaliando a associação entre leucemia em crianças e exposição a campos magnéticos, publicados após a monografia da IARC (2002)[18]

Table 1: Studies assessing association between childhood leukemia and exposure to magnetic fields published after the IARC (2002)[18] risk assessment

Author (year)	Type of Study	Population	Definition of exposure	RR **(95% CI)**
Infante-Rivard et al. (2003)[61]	Case-control	491 cases/491 controls	Maternal exposure during pregnancy based on occupational exposure matrix.	2.5 (1.2–5,0)
Draper et al. (2005)[29]	Case-control	6,605 cases/6,605 controls	Distance of household from closest TL	1.7 (1.1-2.5)
Kabuto et al. (2006)[40]	Case-control	312 cases/603 controls	Focal measurement in child bedroom	2.6 (0.8-8,6)
Pearce et al. (2007)[62]	Case-control	4,723 cases/ 100 controls per case	Parents exposure based on occupational exposure matrix.	1.4 (1.1-1.8)
Mejia-Arangure et al. (2007)[39]	Case-control	42 cases/124 controls (cases and controls were children with Down Syndrome)	Focal measurements at entrance door of household	3.7 (1.1-13.1)

Adult brain tumors

The first investigations involving MF as a possible risk factor for adult brain tumors assessed occupational exposure, and this is the focus of most studies on the theme to today.

An example of such is the cohort conducted by Johansen and Olsen[66,67], described above. The study did not find higher mortality by CNS neoplasms among male workers in the electric power industry compared to the country's expected mortality rates. For women, augmented risk was observed, although a very small number of cases had occurred during the cohort; neither was there augmented risk among male workers with higher occupational exposure in the cohort conducted by Hakansson et al., in Sweden[68].

A case-cohort study assessed MF exposure among workers of electric power companies in the US, based on an occupational exposure matrix[70]. Augmented risk was found among workers with higher exposure, with an RR of 2.5 (95% CI: 1.0 - 6.3) in cumulative exposure analysis. The cohort conducted by Sorahan et al[71] in England and Wales also found augmented risk, although not statistically significant, among workers with higher MF exposure.

A study using data from the Canadian National Enhanced Cancer Surveillance System—NECSS—compared levels of occupational exposure between cases and controls. Augmented OR was found for brain cancer among men who had jobs with exposure to magnetic fields > 0.6 μT in relation to the group exposed to MF < 0.3 μT[72].

More recently, Karipidis et al.[73] published the results of a population-based case-control type study investigating the risk for gliomas in relation to occupational exposure. Augmented risk was observed for the occurrence of gliomas among workers with higher exposures.

Wrensch et al.[74] assessed the risk of glioma in relation to residential exposure. Exposure was assessed based on the wire

Tabela 2: *Estudos avaliando a associação entre leucemia em adultos e exposição a campos magnéticos*
Table 2: Studies assessing association between adult leukemia and exposure to magnetic fields

Author (year)	Type of Study	Population	Definition of exposure	**RR** (95% CI)
Johansen and Olsen (1998)[66]	Cohort	32,006 workers/60 cases between men and 3 cases between women	Occupational exposure matrix	Men: 0.9 (0.7-1.2) Women: 1.5 (0.1-1.5)
Johansen and Olsen (2007)[67]	Cohort (2nd follow-up)	28,224 workers/70 cases between men	Occupational exposure matrix	1.0 (0.5-2.1)
Savitz et al. (2000)[70]	Case-cohort	164 cases/800 controls	Occupational exposure matrix	1.4 (0.5-3.9)
Bethwaite et al. (2001)[65]	Case-control	110 cases/ 199 controls	Occupational exposure matrix	1.9 (1.0-3.8)
Hankansson et al. (2002)[68]	Cohort	646,694 workers/26cases of men and 2 cases of women in category of higher exposure	Occupational exposure matrix	Men: 0.9 (0.6-1.5) Women: 1.8 (0.4-8.5)
Tynes and Haldorsen (2003)[63]	Case-control	1,068 cases/2,136 controls	Calculation of magnetic induction in households	1.3 (0.7–2.5)
Willet et al. (2003)[69]	Case-control	764 cases/1,510 controls	Occupational exposure matrix	0.7 (0.5-1.1)
Lowenthal et al. (2007)[64]	Case-control	854 cases/854 controls	Household distance from closest TL	2.1 (0.9-4.9)

Tabela 3: *Estudos avaliando a associação entre neoplasias do SNC em crianças e exposição a campos magnéticos*
Table 3: Studies assessing association between childhood CNS tumor and exposure to magnetic fields

Author (year)	Type of Study	Population	Definition of exposure	**RR** (95% CI)
UKCCSI (1999)[37]	Case-control	359 cases/371 controls	Matrix of exposure including: focal measurements in child household and school, measurement of distance from household to closest transmission line and application of questionnaire about the use of electric equipment.	0.5(0.1-1.9)
Feychting et al. (2000)[20]	Cohort	235.635 children	Parents exposure based on occupational exposure matrix.	0.5 (0.3-1.0)
Draper et al. (2005)[29]	Case-control	6605 cases/6605 controls	Distance from household to closest TL	0.4[£]

[£] 95% CI not informed

code system and on focal measurements at the subject's household entrance door. Augmented risk was not found among individuals with higher exposure based on the wire code system (OR: 0.9; 95% CI: 0.7 - 1.3). Based on focal measurements, augmented risk was found for the most exposed category, although not statistically significant

(OR*:* 1.7; 95% CI: 0.8 – 3.6).

A nested case-control study conducted in Norway assessed both the risks of household and occupational exposure[34]. Augmented risk was found in the categories of higher residential exposure, but not for occupational exposure.

Kleinerman et al.[75] investigated the risk of brain tumors related to the use of 14 electric pieces of equipment commonly used close to the head. The use of hair blowers (at least 3 times along life) was associated to increased OR for glioma between women and men (OR: 1.7; 95% CI: 1.1 – 2.5) and among men only (OR: 1.7; 95% CI: 1.1 – 2.7).

Table 4 provides a summary of the epidemiological studies assessing the occurrence of brain tumors in adults exposed to MF.

Analyses of published studies did not show consistent results to support association between MF exposure and the occurrence of brain tumors in adults or children. Study reviews bring to surface the difficulties in assessing risk, due to the rarity of the disease itself. In general, risk definition is based on a very small number of cases, resulting in very broad 95% CI.

Breast cancer

The hypothesis of MF influence on the melatonin system placed breast cancer as a possible outcome associated to MF exposure[9]. Based on this, several Studies assessing association were published.

Some publications assessed the risk of disease associated to MF exposure generated by electric blankets and other household appliances. Results found do not suggest augmented risk among women who use such appliances[76-79]. A study with similar methodology, but which assessed risk among Afro-American women only, found augmented risk among those who used electric blankets (OR: 1.4; 95% CI: 0.9 – 2.2)[80]. In it, the higher the period electric blankets were used, the higher the risk.

Studies investigating the risk of breast cancer associated to residential exposure used several exposure indicators, such as questionnaires, MF measurement at subject households, the wire code system and household distance from closest TL. No augmented risk was found among women with higher exposure[38,81,83].

Occupational exposure risk was also assessed. A cohort conducted in Norway found an RR of 1.1 (95% CI: 1.0 – 1.2) among women with cumulative exposure higher than 3.0 μT-years, compared to those with exposure equal or below 0.8 μT-years[84].

Another study, assessing the risk of breast cancer among post-menopausal women associated to occupational exposure, found increased OR for substantial exposures to MF (for more than 5 years) occurred before 35 years old[85].

Two population-based case-control studies using similar methodologies found no augmented risk in any of the categories of exposure studied. The first assessed women occupationally exposed in the US, and the second, in Sweden[86,87].

A nested case-control study assessed both residential and occupational exposure. Residential exposure was considered by calculating MF in each household. An exposure matrix was used to calculate occupational exposure. Augmented risk was observed among women in the higher category of residential exposure (≥ 0.2 μT), with OR of 1.4 (95% CI: 1.0 – 1.8). Risks were also slightly augmented in the group of higher occupational exposure (OR: 1.1; 95% CI: 0.9 – 1.4)[35].

More recently, results of a population-based case-control study conducted in the US were published[88]. For women with high MF exposure, an OR of 1.2 (95% CI: 0.9 – 1.5) was detected.

Other cancers

Some studies assessed the effect of MF exposure related to the occurrence of other cancer types and sites in children and adults. Lymphomas and myelomas were the outcomes studied most often[63.69,89,90]. Other sites included endometrium[9], melanoma[63], testicle[92,93], acoustic neuroma[94], and prostate cancer [95]. To the moment, these studies so

Tabela 4: Estudos avaliando a associação entre neoplasias do SNC em adultos e exposição a campos magnéticos
Table 4: Studies assessing association between adult CNS tumors and exposure to magnetic fields

Author (year)	Type of Study	Population	Definition of exposure	RR (95% CI)
Johansen and Olsen (1998)[66]	Cohort	32,006 workers/57 cases between men and 15 cases between women	Occupational exposure matrix	Men: 0.8 (0.6-1.0) Women: 1.3 (0.7-2.2)
Johansen and Olsen (2007)[67]	Cohort (2nd follow-up)	28,224 workers/24 cases between men and 20 cases between women	Occupational exposure matrix	Men: 0.7 (0.4-1.3) Women: 1.4 (0.5-3.7)
Wrensch et al. (1999)[74]	Case-control	492 cases of glioma/462 controls	Focal measurement at household entrance door + wire code classification	*Focal measurement:* 1.7 (0.8-3.6) *Wire code:* 0.9 (0.7-1.3)
Savitz et al. (2000)[70]	Case-cohort	145 cases/800 controls	Occupational exposure matrix	2.5 (1.0-6,3)
Sorahan et al. (2001)[71]	Cohort	83,997/158 cases	Occupational exposure matrix	1.1(0.9-1.3)*
Hankansson et al. (2002)[68]	Cohort	646,694 workers/47 cases of men and 9 cases of women in category of higher exposure	Occupational exposure matrix	Men: 0.8 (0.5-1.1) Women: 1.9 (0.9-3.9)
Villeneuve et al. (2002)[72]	Case-control	543 cases/543 controls	Occupational exposure matrix	1.3 (0.8-2.4)
Klaeboe et al. (2005)[34]	Case-control	454 cases/908 controls	Occupational exposure matrix + household distance to closest TL	*Occupational:* 0.6 (0.3-0.9) *Household:* 1.3 (0.7-2.3)
Kleinerman et al. (2005)[75]	Case-control	410 cases of glioma, 178 cases of meningioma, 90 cases of acoustic neuroma/686 controls	Use of electric appliances	*Use of hair blowers and glioma:* 1.7 (1.1-2.5) *Microwaves and meningioma: 1.5 (0.5-4,7); Glioma and microwaves: 2.0 (0.9-4,8).*
Karipidis et al. (2007)[73]	Case-control	414 cases of glioma/421 controls	Occupational exposure matrix	1.4 (0.9-2.3)

* SMR (standardized mortality ratio)

not comprise a sufficient set of information to suspect risk associated to MF exposure.

Neurodegenerative diseases

Several epidemiological studies assessed the risk of occurrence of neurodegenerative diseases, such as Parkinson's Disease, Alzheimer's Disease and Amyotrophic Lateral Sclerosis (ALS), associated to MF exposure. Although these conditions have different locations and pathogenesis, they were typically assessed as a group, since they all involve death of a specific group of neurons. Among these, ALS was the diagnosis most studied.

Neurons are directly activated by electric current stimulation. Evidences suggest that exposure to extremely low-frequency MF may modulate functional electric activity in the CNS. Although these effects apparently do not cause damage to the nervous tissue, it is possible that prolonged exposure may interfere in neurons with higher sensitivity to fields, possibly changing the physiology of calcium channels. It is also possible that small effects caused by low-frequency fields may exacerbate a pathologic condition in already compromised neurons [15].

Amyotrophic Lateral Sclerosis

To the present, all epidemiological studies analyzing ALS risk relative to MFs were job-related. The first was published in Germany, in 1964. As of then, new studies were conducted, some finding augmented risk of ALS among people with higher occupational exposure to MF[50.96,97]. Table 5 brings a summary of the epidemiological studies assessing association between ALS and MF exposure.

Alzheimer's disease

Studies investigating the risk for Alzheimer's disease and MF assessed mainly occupational exposure and typically found augmented risk among workers with higher levels of exposure. In 1998, the case-control study conducted by Savitz et al.[96] found the OR of 1.2 (95% CI: 1.0 – 1.4) among electric utility workers.

More recently, results of three cohort studies showed augmented risk for workers with higher level of exposure[49-51]. In two of them[49,51], risk was just higher when analysis was restricted to men, with RR of 2.3 (95% CI: 1.6 – 3.3) and 2.4 (95% CI: 1.1 – 5.2), respectively. In the third, augmented risk was found among men and women, with RR of 4.0 (95% CI: 1.4 - 11.7) for the category of higher exposure (> 0.53 μT)[50].

A recently published meta-analysis included results of 14 studies that assessed risk of disease relative to occupational exposure, and found augmented risk among workers with higher exposure both when analyzing case-control type studies alone (OR: 2.0; 95% CI: 1.4 – 3.0) and with cohort studies (OR: 1.6; 95% CI: 1.2 – 2.3)[98].

Parkinson's disease

In the case-control study described above, Savitz et al.[96] found a small OR increase among electric utility workers (OR: 1.1; 95% CI: 0.9 – 1.2). Later studies, however, did not replicate the result.

Two cohort studies, one conducted in Denmark[97] and the other in Sweden[50] could not detect augmented risk for Parkinson's

Tabela 5: *Estudos avaliando a associação entre ELA e exposição a campos magnéticos*
Table 5: Studies assessing association between ALS and exposure to magnetic fields

Author (year)	Type of Study	Population	Definition of exposure	RR (95% CI)
Savitz, Loomis, Tse (1998)[96]	Case-control	114 cases 1614 controls	Job based on death certificate	1.3 (1.1-1.6)
Johansen, Olsen (1998)[97]	Cohort	21,236 individuals/14 cases of ALS	Occupational exposure matrix	2.0 (1.1-3.4)**
Feychting *et al* (2003)[49]	Cohort	4,812,646 individuals/1965 cases of ALS	Occupational exposure matrix	0.8 (0.6-1.0) in men 0.8 (0.4-1.4)***
Hakanson *et al* (2003)[50]	Cohort	646,696 individuals/97 cases of ALS	Occupational exposure matrix	2.2 (1.0-4.7)

[£] *apud* WHO,2007[15]
* 95% CI not informed
** SMR (standardized mortality ratio)
*** for category of higher exposure

disease among workers with higher occupational exposure. In the cohort study conducted by Feychting et al.[49], small augmented risk was observed, although not statistically significant, among men in the most exposed categories. When the analysis was performed among women, there was no increase in RR.

Suicide and depression

Studies assessing the risk of suicide and depression associated to MF exposure, to the moment, have not produced consistent results. They all assessed risk associated à occupational exposure.

Cohort studies conducted by Johansen and Olsen[97] and Jarvholm and Stenberg[99] did not show augmented risk among workers exposed to higher MF levels. On the other hand, two case-control studies found augmented risk in suicide among the population with higher exposure[100,101]. A summary of these studies is found in Table 6.

Cardiovascular diseases

Suspicions of possible risks of cardiovascular diseases (CVD) associated to MFs emerged from reports of adverse symptoms occurred among workers with occupational exposure to high MF levels in Russia in the 1960's[9,15].

To support this hypothesis, some experimental studies with humans showed decrease in the heart rate variation after MF exposure[43]. This reduced heartbeat variation was considered a risk factor for CVD in observational studies[9,43].

All studies assessing risk of CVD associated to MF, to the moment, assessed occupational exposure only. Three cohort studies that monitored electric utility workers, one in Denmark, one in the US and another in Great Britain, did not detect augmented risk among workers under higher exposure[44,97,102]. Likewise, a case-control study analyzing the risk of acute myocardial infarction did not detect augmented risk associated to higher MF exposure[45]. On the other hand, Savitz et al.[43] found augmented risk in deaths by arrhythmia (RR: 1.5; 95% CI: 1.0 – 2.2) and ischemic heart disease (RR: 1.4; 95% CI: 1.3 – 1.6) among workers with higher permanence in jobs under high exposure (≥ 20 years).

Reproductive effects

Since the early 1980's, reproductive

Tabela 6: *Estudos avaliando a associação entre suicídio e exposição a campos eletromagnéticos*
Table 6: Studies assessing association between suicide and exposure to magnetic fields

Author (year)	Type of Study	Population	Definition of exposure	RR (95% CI)
Johansen and Olsen (1998)[97]	Cohort	21.236 individuals/133 cases of suicide	Occupational exposure matrix	0.9* £
van Wijngaaarden *et al.* (2000)[100]	Case-control	536 cases 5348 controls	Job category and cumulative exposure based on measurements	1.5 (1.0-2.3)** 2.2 (1.3-3.8)***
Jarvholm and Stenberg (2002)[99]	Cohort	33719 electric utility workers	Occupational exposure matrix	0.6* (0.5-0.7)
van Wijngaaarden (2003)[101]	Case-control	11707 cases 132771 controls	Job title in death certificate	1.3 (1.2-1.4)

* SMR (standardized mortality ratio)
£ 95% CI not informed
** exposure > 0.36 μT in the past 5 years
*** among electric utility workers

health effects associated to MF exposure have been investigated in epidemiological studies and also in laboratory studies[9,15]. Different effects were investigated, such as decreased fertility, spontaneous miscarriage, premature delivery, low birth weight, and congenital malformations.

Shaw et al.[46] and Lee et al.[103] conducted studies assessing the risk relative to the use of electric blankets by pregnant women. The former assessed the risk of occurrence of congenital malformations and the later, of spontaneous miscarriage. There was no augmented risk among women who reported more frequent or longer use of electric blankets.

Blaasaas et al.[33] investigated the risk of congenital malformations relative to MF exposure, based on household distance from the closest TL. Analysis of the total anomalies did not show augmented risk. When defects were divided based on anatomical site, there was augmented risk for esophageal defects (OR: 2.5; 95% CI: 1.0 – 5.9).

De-Kun et al.[42] conducted a cohort study investigating the risk of spontaneous miscarriage. Exposure was assessed based on personal measurements with dosimeters, in addition to focal measurements in the households of each participant. There was augmented risk of miscarriage among women exposed to MF $\geq$ 1.6 µT, with RR of 1.8 (95% CI: 1.2 – 2.7), in comparison to those less exposed.

BRAZILIAN STUDIES

Brazil has very few papers related to the theme. A literature review in Medline and Lilacs database searching for epidemiological studies conducted exclusively in Brazil in the past 10 years, found only three papers published, including a study review[5,104,105].

In 1996, Mattos and Koifman[104] compared the specific mortality from some cancers among electric utility workers of an electric power utility of the State of São Paulo to that of the general population of the city of São Paulo. The study included the 695 deaths by cancer among utility workers that took place between 1975 and 1985. Exposure was determined based on the job of each subject. An augmented standardized mortality ratio (SMR) in deaths related to circulatory system diseases (SMR: 1.1; 95% CI: 1.0 – 1.3) was found among the most exposed workers. An SMR of 1.1 (95% CI: 0.9 – 1.4) was observed for all cancers.

Koifman et al.[105] investigated the occurrence of a cancer cluster occurred in 1992 among Native Indians of a tribe in the Amazon located next to two TLs of 500 kV, built 10 years before. The study describes the comparison between the incidence of cancer observed in the Indian village and the incidence observed in other Brazilian towns. In addition, it reports results of focal measurements during 24 hours in different places of the village, while Natives perform their daily activities. The cluster was defined based on the diagnosis of 3 cancer cases among 306 villagers (leiomyosarcoma in a 22 year-old woman, ALL in a 20 year-old male and a cervical cancer in a 55 year-old woman). Analysis was limited to the first two cases. The probability of random occurrence in the group of cases observed in the village was considered remote ($p < 0.03$ Poisson distribution). Personal cumulative exposure was considered low (< 0.01 µT) in 62% of measurements, and average (0.1 – 0.2 µT) in 33% (7 people, all adults).

FINAL CONSIDERATIONS

Our literature review found considerable bibliographic production on the theme, although we could observe very few studies in Brazil and other countries in South America.

Despite the large number of publications, results about health risks associated to MF exposure have been controversial. The leading outcomes studies were leukemia, brain tumor, breast cancer, and neurodegenerative diseases. Of these, childhood leukemia seems more consistently associated to MF exposure. Adult leukemia and brain tumors also seem to be associated to field exposure, but there are fewer studies that focus on this assessment. Breast cancer, to the contrary, does not seem to show augmented risk due to MF exposure.

Quantification of exposure and lack of a biological mechanism that can explain the interaction among extremely low-frequency MF and health effects are the greatest obstacle in investigating health risks associated to MF.

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