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Review

Do People With Idiopathic Environmental Intolerance Attributed to Electromagnetic Fields Display Physiological Effects When Exposed to Electromagnetic Fields? A Systematic Review of Provocation Studies

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Idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF) is a controversial illness in which people report symptoms that they believe are triggered by exposure to EMF. Double-blind experiments have found no association between the presence of EMF and self-reported outcomes in people with IEI-EMF. No systematic review has assessed whether EMF exposure triggers physiological or cognitive changes in this group. Using a systematic literature search, we identified 29 single or double-blind experiments in which participants with IEI-EMF were exposed to different EMF levels and in which objectively measured outcomes were assessed. Five studies identified significant effects of exposure such as reduced heart rate and blood pressure, altered pupillary light reflex, reduced visual attention and perception, improved spatial memory, movement away from an EMF source during sleep and altered EEG during sleep. In most cases, these were isolated results that other studies failed to replicate. For the sleep EEG findings, the results reflected similar changes in the IEI-EMF participants and a non-IEI-EMF control group. At present, there is no reliable evidence to suggest that people with IEI-EMF experience unusual physiological reactions as a result of exposure to EMF. This supports suggestions that EMF is not the main cause of their ill health. Bioelectromagnetics 32:593–609, 2011.

Key words: electromagnetic fields; cellular phone; electroencephalography; autonomic nervous system; psychophysiology

INTRODUCTION

Idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF) is a controversial condition in which sufferers experience symptoms that they believe are caused by exposure to weak electromagnetic fields [Bergqvist et al., 1997]. Based on this belief the term ''electromagnetic hypersensitivity'' (EHS) was coined. The more neutral term IEI-EMF is preferred, however, since a hypersensitivity to EMF has not been proven [Rubin et al., 2005, 2010; Röösli, 2008]. Sources of EMF that are reported to trigger symptoms vary and may include mobile phones, computer equipment, overhead powerlines, and domestic appliances [Röösli et al., 2004]. As well as being associated with unpleasant physical symptoms, IEI-EMF can lead to high levels of distress for sufferers and impair their ability to work and maintain normal social and family contacts

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[Röösli et al., 2004; Carlsson et al., 2005; Osterberg et al., 2007; Rubin et al., 2008]. The World Health Organization's (WHO) factsheet about IEI-EMF notes that ''EHS is characterized by a variety of non-specific symptoms that differ from individual to individual. The symptoms are certainly real and can vary widely in their severity. Whatever its cause, EHS can be a disabling problem for the affected individual. EHS has no clear diagnostic criteria and there is no scientific basis to link EHS symptoms to EMF exposure. Further, EHS is not a medical diagnosis, nor is it clear that it represents a single medical problem'' [WHO, 2005].

Because no widely accepted physiological mechanism exists to explain how exposure to electrical devices might cause the symptoms reported by people with IEI-EMF, numerous double-blind experimental provocation studies have been conducted to test the role of EMF in causing these symptoms [Rubin et al., 2005, 2010; Wallace et al., 2010; Nieto-Hernandez et al., 2011]. These studies have typically demonstrated that sham exposure is as likely to trigger symptoms as genuine exposure to electromagnetic fields. This has led some authors to suggest that psychological factors may play an important role in causing or perpetuating the condition [Rubin et al., 2008; Stovner et al., 2008] and that sufferers may therefore respond better to treatments based on cognitive behavior therapy than to interventions involving avoidance of electrical equipment or reduction of exposure [Rubin et al., 2006]. It is possible, however, that exposure to electromagnetic fields might trigger biological effects that may lead to the experience of symptoms in people with IEI-EMF that are too subtle to detect using self-reported measures, but which might be observable by studying physiological changes. While recent review articles have assessed whether RF fields trigger physiological changes in healthy volunteers [Valentini et al., 2007; van Rongen et al., 2009] or whether the presence of electromagnetic fields triggers symptoms in people with IEI-EMF [Rubin et al., 2005, 2010; Röösli, 2008; Marc-Vergnes, 2011], as yet there has been no systematic review as to whether the presence of electromagnetic fields is specifically associated with physiological changes in people with IEI-EMF.

In this article, we conducted a systematic review of blind or double-blind provocation studies in order to determine whether exposure to EMF causes changes in any objectively measured endpoints among people who attribute symptoms to EMF. Because we have previously raised concerns about the quality of some experimental studies in this area [Hillert et al., 1999; Rubin et al., 2005], we used the same review to identify if common methodological flaws exist within this literature.

This review was one of the prioritized activities of the European Cooperation in the Field of Scientific and Technical Research (COST) action BM0704, ''Emerging EMF Technologies and Health Risk Management,'' accomplished as part of Working Group (WG) 3 ''Epidemiology and Human Studies.'' WG members were recruited from the action's Management Committee members and other experts in the relevant area. For this review, individuals were invited who had different backgrounds with respect to disciplines of training (psychology, medicine, biology, and biophysics), and all had experience with scientific studies concerning IEI-EMF.

METHODS

Identification of Studies

The following databases were searched for potentially relevant studies: Amed (up to 2008), Embase, Medline, Psychinfo, Scopus, the Web of Knowledge, the World Health Organization's EMF database and citation list, and the EMF-Portal database. These databases were searched for terms relating to IEI-EMF such as ''electrosensitivity'' or ''electromagnetic hypersensitivity.'' Amed, Embase, Medline, and Psychinfo were also searched for articles which included a keyword relating to an electromagnetic stimulus (e.g., ''cell phone'' or ''visual display unit'') in addition to a keyword relating to a symptom (e.g., ''headache'' or ''symptom''). The reference sections of included studies were examined for further citations, and related article searches were run for included studies. Finally, we publicized our review at international scientific meetings and asked colleagues to send us any additional articles or reports that we may not have been aware of. Searches were conducted for any articles published up until May 2010.

Inclusion Criteria

We included studies in this review if they: included a discrete set of participants who reported symptoms that were explicitly attributed to the presence of electromagnetic fields or proximity to electrical equipment; deliberately exposed the participants to two or more conditions involving different low levels of electromagnetic fields; conducted the exposures single or double-blind; and used one or more objective outcome measures during or after each of the exposures. Studies published in any language were eligible for the review, as were non-peer-reviewed studies.

Data Extraction

For each study that we included in our review, we extracted details relating to 39 methodological issues using a standardized spreadsheet. In summary, these variables related to: the hypotheses given by the authors; demographic details of the IEI-EMF participants and any non-IEI-EMF participants; the type of electrical devices reported as triggering symptoms by the participants; the symptoms described by the participants as resulting from these exposures; the general health of the participants; the inclusion criteria and selection procedures used by the study; how many participants withdrew from the study after their first exposure session and for what reasons; the type and levels of electromagnetic fields used; the number, length and timing of exposure conditions; whether the study was double or single-blind; whether condition order was randomized; whether condition order was counterbalanced; whether other factors that might have influenced the endpoint had been controlled or registered; whether a sample size calculation had been reported; whether a procedure was used to allow participants to habituate to the experimental setting prior to their first exposure session; and how relevant the exposure was in relation to the participants' self-reported sensitivity. For this last point, an experimental exposure was categorized as "high" relevance if all or most of the IEI-EMF participants in that study attributed their day-to-day symptoms to a trigger that was of the same type as that used in the study (e.g., day-to-day symptoms attributed to mobile phones, and experimental exposure emulated that from a mobile phone); "medium" if all or most of the IEI-EMF participants attributed their symptoms to a trigger in the same frequency range as that used in the study (e.g., day-to-day symptoms attributed to mobile phones, and experimental exposure emulated that from a mobile phone base station); and "low" if the participants attributed their symptoms to an electrical trigger that was not in the same frequency range as that used in the study.

We also extracted data relating to the results of each study. More specifically, we extracted data on the objective outcomes that were measured in the study; the times at which these outcomes were measured; the results reported for these outcomes; and whether self-reported outcomes were also measured and, if so, whether a correlation analysis was performed for the subjective and objective outcomes.

Review Process

RN-H and GJR conducted the database searches, while LH, GO, and EvR searched conference proceedings, journals, and other websites. A single reviewer performed the initial screening of the titles and abstracts of articles found via these searches in order to assess their potential relevance. Individual reviewers then obtained the full articles for those citations that appeared potentially relevant and checked them against our inclusion criteria. If it was unclear whether an article met our inclusion criteria or not, consensus was sought from all five reviewers. At least two reviewers then independently extracted data for each included study with any disagreements resolved through discussion. Where necessary, we sought additional information from the original authors of a study in order to assess their eligibility or to clarify their methods and results.

RESULTS

Search Results

Our database searches retrieved 3971 citations; 122 articles relating to 84 studies appeared potentially relevant and were examined in full. Nineteen studies were excluded for not using an objective outcome measure, 15 for not having a discrete sample of IEI-EMF participants, 11 for not experimentally exposing participants to low-level electromagnetic fields and 10 because they were not blinded. Twenty-nine studies met our inclusion criteria. One of the included studies was described in three articles and one meeting abstract, each broadly relating to a different set of endpoints [Arnetz et al., 2007; Hillert et al., 2007, 2008; Wiholm et al., 2009]. For ease of reference, we describe this study in our text by the study's acronym, "MPDHE" (Mobile Phones and Direct Health Effects), together with the specific citation containing relevant data. Two other articles reported the results of two separate experiments [Lonne-Rahm et al., 2000; Kaul, 2009]. We have counted these as separate studies for the purposes of our review, and refer to them as "study 1" or "study 2" where necessary.

The Methodology and Quality of Included Studies

Table 1 shows a summary of the methods used by each study. More detailed methods tables and a table providing summary statistics concerning the recruitment and selection of IEI-EMF participants are available in the online supporting information. The statistics provided in these tables were derived from the details that were given or could be inferred from the original publications. However, many

TABLE 1. Summary of the Methods of the Studies With Information of Samples, Type of Attributed EMF Sources, Exposure Type Used in Experimental Studies and Details of Each Study Design

Refs.	IEI-EMF (n)	Control (n)	Attributed EMF trigger/s	Exposure type	Study design
Andersson et al. [1996]	17	None	Electrical environment, VDU	Cathode ray tube-type VDU	DB, R
Bamiou et al. [2008]	9	21	MP	GSM 900 MP-like EMF and continuous 882 MHz	DB, R
Eltiti et al. [2009]	44	114	EMF (MP and MP base station)	GSM 900, GSM 1800, and UMTS base-like station RF	DB
Furubayashi et al. [2009]	11	43	MP and MP base station	W-CDMA (UMTS) base station-like RF EMFs	DB, R
Hamnerius et al. [1993]	30	None	VDU	Simulated cathode ray tube-type VDU, low frequency and RF EMFs	DB, R
Hietanen et al. [2002]	20	None	MP and other EMF sources	Analogue NMT 900, GSM 900 and GSM 1800	SB, R, C
Kaul [2009]	(S1) 24 (S2) 24	(S1) 96 (S2) None	(S1) At least low frequency EMF (S2) At least RF EMF	(S1) 50 Hz coil (S2) GSM 916.2 MHz	(S1 and S2) DB, R, C
Leitgeb et al. [2008]	43	None	Environmental RF EMF sources (broadcasting, MP base stations)	Environmental sources—at least ∼400–2500 MHz	SB, R
Lonne-Rahm et al. [2000]	(S1 and S2) 24	(S1 and S2) none	(S1 and S2) VDU	(S1 and S2) Cathode ray tube-type VDU	(S1 and S2) DB
Lyskov et al. [2001]	20	20	None stated	Intermittent (5 s on, 15 s off) 60 Hz sine wave magnetic field	SB, C
Mueller and Schierz [2004]	54	None	EMF 50-Hz sources	50 Hz sine wave electric/magnetic field	DB, R
Nam et al. [2009]	18	19	CDMA phones	CDMA MP-like RF EMFs (835 MHz)	SB, R
Nilsen [1982]	5	None	VDU	Cathode ray tube-type VDU	SB
Oftedal et al. [1995]	20	None	VDU	Cathode ray tube-type VDU	DB, R, C
Oftedal et al. [2007]	17	None	MP	GSM 900 MP-like RF EMFs	DB, R, C
Rea et al. [1991]	100	25	EMF in general	Square waves between 0.1 Hz and 0.5 MHz	DB, C (some)
Regel et al. [2006]	14/19	84	Any source of RF	UMTS base station-like RF EMFs	DB, R, C
Sjöberg and Hamnerius [1995]	7	None	VDU	Cathode ray tube-type VDU	DB, R
Swanbeck and Bleeker, 1989	30	None	VDU	Cathode ray tube-type VDU	DB, R
Trimmel and Schweiger [1998]	36	30	Sensitivity to EMF	50 Hz sine wave magnetic field	DB, R
Wallace et al. [2010]	51	143	EMF (MPs and base stations)	TETRA base station-like RF EMFs	DB, R, C
Wang [1995]	19	34 + 28[d]	EMF and chemicals	10, 50, 60, 100, 200, 300 Hz sine wave magnetic fields	SB, R
Wennberg et al. [1994]	5	5	Electrical equipment, VDU	Simulated cathode ray tube-type electric fields	SB, R
Wenzel et al. [2005]	3	7	Mainly VDUs	50 Hz magnetic field	DB (some)
Wiholm et al. [2009][a]	23–38[c]	19–33	MP only	GSM 900 MP-like RF EMFs	DB, R
Wilén et al. [2006]	20	20	MP only	GSM 900 MP-like RF EMFs	SB, R, C
Zwamborn et al. [2003][b]	36	36	GSM antennae	GMS 900 or 1800 base station-like RF, UMTS MHz base station-like RF (2140 MHz)	DB, R, C

S1, Study 1; S2, Study 2; EMF, electromagnetic fields (in general); ELF, extremely low frequency; RF, radio frequency; VDU, visual display unit; MP, mobile phone; GSM, Global System for Mobile Communications; UMTS, Universal Mobile Telecommunications System; CDMA, Code Division Multiple Access; TETRA, Terrestrial Trunked Radio; DB, double blinded; SB, single blinded; R, randomized; C, counterbalanced design.

[a]This study has information from different articles [Arnetz et al., 2007; Hillert et al., 2007, 2008; Wiholm et al., 2009].

[b]Data from this study were re-analyzed in the report by HCN [2004] and these results have been applied for this review.

[c]Different samples sizes for each test.

[d]Chemical sensitivity sample.

publications did not provide the necessary information, particularly in terms of how EMF exposure was controlled for prior to a participant's arrival at the laboratory, what symptoms participants attributed to EMF exposure, how severe their symptoms typically were, and who funded the study.

In 19 studies IEI-EMF participants were recruited from the general population by invitations published in the media, or were employees, students or military personnel. Three of these studies also invited patients who had been registered by physicians as having or possibly having ''electromagnetic hypersensitivity'' or EMF-attributed complaints. Six studies included only patients selected via this route.

For issues other than recruitment and selection of IEI-EMF participants, quality of the studies is summarized in Table 2. Particularly notable was that the order of real and sham exposures was explicitly counter-balanced in only nine studies; only six controlled or assessed the EMF exposure of subjects before their arrival at the test laboratory; only 15 studies provided a habituation session similar to the test sessions for the participants; and only four studies reported having conducted a sample size calculation.

Effects of EMF Exposure

Twenty of the included studies used outcomes relating to the autonomic nervous system; four assessed blood biochemistry variables; three assessed brain physiology or the sensory system; seven used objective measures of cognitive function; five measured the effects of electromagnetic fields on skin or the immune system; and three used objective sleep measurements. Tables 3–8 summarize the effects of EMF exposure for the various groups of outcome variables and provide references to the relevant studies.

Autonomic Nervous System

Among the 20 studies that tested endpoints influenced by the autonomic nervous system (Table 3), two observed a significant effect of EMF [Rea et al., 1991; Hietanen et al., 2002]. In the study by Hietanen et al. [2002], IEI-EMF participants experienced reduced heart rate and diastolic and systolic blood pressure changes during some of their exposures to mobile phone handset signals. These results, consistent with reduced stress during the EMF exposures, might have been influenced by an unbalanced order of exposures, in which sham exposure was always first or second in a series of three or four consecutive exposures. None of the other 12 studies in which heart rate was recorded observed any effect on this endpoint for IEI-EMF participants. Likewise, six other studies did not give rise to any change in blood pressure for the participants with IEI-EMF.

Rea et al. [1991] exposed subjects to magnetic fields from a coil fed with square waves with frequencies ranging from 0.1 Hz to 5 MHz during three study phases. While most of the physiological endpoints were not quantified, the authors reported that the magnetic fields in the last phase of the study always caused a change in the pupilary light reflex, while no change was recorded during sham exposures. In this last phase, people with IEI-EMF only participated if they had reacted to at least some of the frequencies and not to sham in the previous phases. The magnetic flux density measured at floor level (i.e., close to the magnetic coil) was 2900 μT, at chair level it was 350 μT, and at hand level it was 7 μT. This indicates that the values at the head level (presumably some 30–40 cm above hand level) most likely were in the range of the background field, which was recorded to be 0.02–0.2 μT. Only one other study tested pupilary light reflexes [Wang, 1995]. In the IEI-EMF participants, no effect of the low frequency exposure was observed.

Other endpoints related to the autonomic nervous system were tested in several studies without demonstrating any effect of exposures (Table 3). These were heart rate variability (5 studies), local blood flow (3 studies), skin temperature (5 studies), skin conductance (6 studies), skin response to sound/galvanic skin response (3 studies), respiratory rate (5 studies) and arterial oxygen saturation (1 study). Radiofrequency exposure was used in half of the autonomic nervous system-related studies.

Blood Chemistry

Various blood compounds such as electrolytes, hormones and others were tested in four studies [Andersson et al., 1996; Lonne-Rahm et al., 2000 (studies 1 and 2); Hillert et al., 2007] (Table 4). No effect of exposure was found. In three of these studies the subjects were exposed to fields from video display units (VDU) and in one study mobile phone-like exposure was used.

Skin and Immune System

Assessment of visible skin changes was done in three studies [Nilsen, 1982; Swanbeck and Bleeker, 1989; Oftedal et al., 1995], while skin biopsy for immune system assessment was done in two studies and presented in one article [Lonne-Rahm et al., 2000]. In all of these studies (Table 5), participants were only exposed to EMF from VDUs. EMF

TABLE 2. Summary of Qualities of All Studies, Including Studies With Negative Findings Only and Studies With At Least One Positive Finding

	All studies (n = 29)		Negative studies (n = 24)		Positive studies (n = 5[a])	
	Number of studies	% of studies[b]	Number of studies	% of studies	Number of studies	% of studies
Number of IEI-EMF participants						
1–20	17	59	16	67	1	20
21–30	5	17	4	17	1	20
31 or more	7	24	4	17	3	60
Attributed symptoms						
Info provided	19	66	18	75	1	20
Not stated	10	34	6	25	4	80
Severity of attributed symptoms						
Info provided	18	62	17	71	1	20
Not stated	11	38	7	29	4	80
Drop-outs (after first provocation)						
Yes	9	31	7	29	2	40
None	16	55	13	54	3	60
Not stated	4	14	4	17	0	0
Randomization						
Yes	22	76	18	75	4	80
No/not stated	7	24	6	25	1	20
Counterbalanced						
Yes	9	31	8	33	1	20
No/not stated	20	69	16	67	4	80
Blinding						
Double (D)	20	69	16	67	4	80
Single (S)	8	28	7	29	1	20
Partly D and S	1	3	1	4	0	0
Exposure duration[c]						
3–10 min	5	17	4	17	1	20
25–60 min	19	66	17	71	2	40
>180 min	5	17	3	13	2	40
Interval between exposures						
<2 h	10	34	8	33	2	40
16 h to 2 days	12	41	10	42	2	40
>2 days	6	21	6	25	0	0
Not stated	1	3	0	0	1	20
Relevance of type of exposure[d]						
High	22	76	19	79	3	60
Medium	3	10	3	13	0	0
Low	0	0	0	0	0	0
Unclear	4	14	2	8	2	40
Background/sham level given						
Yes	25	86	21	88	4	80
No	4	14	3	13	1	20
Pre-exposure control of EMF						
Yes	6	21	4	17	2	40
Not stated	23	79	20	83	3	60
Control of other factors						
Yes	20	69	16	67	4	80
Not stated	9	31	8	33	1	20
Habituation session						
Yes	15	52	14	58	1	20
Not stated	14	48	10	42	4	80
Power calculation						
Yes	4	14	4	17	0	0
Not stated	25	86	20	83	5	100
Industry funding						
No	7	24	7	29	0	0
Partly	9	31	8	33	1	20
Yes	1	3	0	0	1	20
Not stated	12	41	9	38	3	60

[a]Hietanen et al. [2002], Mueller and Schierz [2004], Rea et al. [1991], Trimmel and Schweiger [1998], MPDHE study [Arnetz et al., 2007; Hillert et al., 2007, 2008; Wiholm et al., 2009].
[b]Some totals do not add to 100 % because of rounding.
[c]Two different exposure durations were used in one study [Wenzel et al., 2005]; the longest duration is included here.
[d]See Methods Section for the rationale used to assess the relevance of type of exposure for each study.

TABLE 3. Summary of Autonomic Nervous System Findings

Refs.	Endpoints	Assessment times	Results (effect of EMF exposure)
Eltiti et al. [2009]	Blood volume pulse, heart rate, skin conductance	Continuously during exposure	Cases and controls: no effect
Furubayashi et al. [2009]	Heart rate, skin surface temperature, local blood flow	Continuously during 0–5, 12–17, and 25–30 min of exposure	Cases and controls: no effect
Hamnerius et al. [1993]	Skin surface temperature, capillary blood flow, galvanic skin response, heart rate	20 s intervals throughout exposure	Cases: no effect
Hietanen et al. [2002]	Systolic and diastolic blood pressure, heart rate, breathing frequency	Every 5 min during exposure	Cases: systolic blood pressure lower during NMT and GSM 1800 exposures than sham ($P < 0.05$); heart rate lower during GSM 900 exposure than sham ($P < 0.05$). No result provided for breathing frequency
Kaul [2009]	Studies 1 and 2: skin conductance	Studies 1 and 2: continuously recorded during exposure (results averaged for whole exposure period and last minute)	Studies 1 and 2: cases and controls: no effect
Leitgeb et al. [2008]	Heart rate, heart rate variability	When in bed during night	Not reported
Lonne-Rahm et al. [2000]	Studies 1 and 2: heart rate, heart rate variability	Study 1: immediately before and after exposure. Study 2: immediately before and after exposure and 30 min after exposure	Studies 1 and 2: Cases: no effect
Lyskov et al. [2001]	Systolic, diastolic blood pressure and heart rate in reclining position. Heart rate and heart rate variability	Immediately before and after exposure	Cases and controls: no effect
	Spontaneous electrodermal activity and sympathetic skin response to sound	Before and 40 min during exposure	Cases and controls: no effect
Mueller and Schierz [2004]	Heart rate, interbeat interval, heart rate variability, breathing frequency	When in bed during night	Cases: no effect
Nam et al. [2009]	Heart rate, heart rate variability, respiratory rate, skin conductance	5 min before exposure, after 15 and 31 min of exposure, 10 min post-exposure	Cases and controls: no effect. Skin conductance not analyzed due to unstable recordings
Oftedal et al. [2007]	Heart rate, systolic and diastolic blood pressure	Continuous from 10 min before to 5 min after exposure	Cases: no effect
Rea et al. [1991]	Pupillary light reflex (time and rate of pupil constriction/dilation)	In phases 2–4 (not further specified)	Cases: phase 2 and 3: effect of exposure cannot be derived from provided results. Phase 4: all 16 cases showed reactions (change more than 2 standard deviations from baseline results) to magnetic field exposures and not to sham. Controls: Phase 3: no effect of exposure
	Blood pressure, heart rate, respiratory rate, temperature	Heart rate and pulmonary function at least in phase 4	Examples of individual results given
Sjöberg and Hamnerius [1995]	Facial skin temperature distribution	Not given	Cases: no effect
Wallace et al. [2010]	Heart rate, blood volume pulse, skin conductance	Continuously during exposure	Cases and controls: no effect

(*Continued*)

TABLE 3. (*Continued*)

Refs.	Endpoints	Assessment times	Results (effect of EMF exposure)
Wang [1995]	Systolic and diastolic blood pressure and pulse rate	After each exposure	Cases: no effect. Chemical sensitive: lower systolic blood pressure for 50 Hz ($P \leq 0.05$). Controls: higher diastolic blood pressure for 50 Hz compared to sham ($P \leq 0.05$)
	Pupillary light reflex	After each exposure	Cases: no effect. Chemical sensitive: shorter time for half contraction for 200 and 300 Hz (both $P \leq 0.01$), longer time for total contraction for 10 Hz ($P \leq 0.05$), higher max contraction velocity for 200 and 300 Hz (both $P \leq 0.01$), higher max acceleration of contraction for 300 Hz ($P \leq 0.05$); higher max dilation velocity for 10 Hz ($P \leq 0.05$). Controls: shorter time for half contraction for 60 ($P \leq 0.05$), 100, 200, and 300 Hz (all $P \leq 0.01$); higher max contraction velocity for 50 ($P \leq 0.05$), 100 and 200 Hz (both $P \leq 0.01$)
Wennberg et al. [1994]	Difference in skin temperature (cheek and nose tip) between exposed and non-exposed side	Every 5 min	Cases and controls: no effect
Wenzel et al. [2005]	Cutaneous blood flow variations in the thumb fingerprint area, blood pressure, heart rate, arterial oxygen saturation	Protocol 1: Cutaneous blood flow recorded during exposure. Protocol 2: Cutaneous blood flow recorded after tests. Blood pressure saturation recorded during any test sequence. Heart rate and arterial oxygen recorded during exposure	Cases and controls: no effect
Wilén et al. [2006]	Heart rate, heart rate variability, respiratory rate, electrodermal response to sound	Continuously from 10 min before until 10 min after exposure	Cases and controls: no effect

TABLE 4. Summary of Blood Biochemistry Findings

Refs.	Endpoints	Assessment times	Results (effect of EMF exposure)
Andersson et al. [1996]	Electrolytes, transaminases, fibrinogen, cholesterol, apolipoproteins, prolactin, testosterone, dehydroepiandrosterone, cortisol	Immediately before and after exposure	Cases: no effect
Lonne-Rahm et al. [2000]	Blood tests: Studies 1 and 2: prolactine, adrenocorticotrophic hormone, growth hormone. Study 1: melatonin, neuropeptide Y	Study 1: immediately before and after exposure. Study 2: immediately before and 30 min after exposure	Study 1 and 2: cases: no effect
Hillert et al. [2007]	C-reactive protein, prolactin, cortisol, growth hormone, thyroid-stimulating hormone, free thyroxin, dehydroepiandrosterone, neuropeptide Y	Before, 1.5 h after start and at end of exposure	Cases and controls: no effect

TABLE 5. Summary of Skin and Immune System Findings

Refs.	Endpoints	Assessment times	Results (effect of EMF exposure)
Lonne-Rahm et al. [2000]	Studies 1 and 2: skin biopsies: mast cells, cytotoxines (somatostatin, CD1a, factor XIIIa, tumor necrosis factor-[alpha]) by immunohistochemestry	Study 1: immediately before and after exposure. Study 2: immediately before and 30 min after exposure	Studies 1 and 2, cases: no effect
Nilsen [1982]	Facial skin evaluation by comparing photographs	At the beginning and at the end of test days	Cases: no effect
Oftedal et al. [1995]	Facial skin evaluation by dermatologist who visually inspected eight defined facial regions	At the end of each 2-week exposure period	Cases: no effect
Swanbeck et al. [1989]	Facial skin evaluation by comparing colors of photographs	Before, immediately after, 30 min and 4–20 h after exposure	Cases: no effect

exposure gave rise to findings that were significantly different from those observed after sham exposure in none of the studies.

Brain Physiology and the Sensory System

In three studies, one using 60 Hz exposure [Lyskov et al., 2001] and two using mobile phone-like exposure [Wilén et al., 2006; Bamiou et al., 2008], no effects of EMF exposure were detected on brain physiology, and the visual, auditory and balance systems (Table 6). With the exception of critical flicker fusion frequency, which was recorded in two studies, each of the other endpoints was tested in only one study.

Cognitive Function

Cognitive functions were tested in seven studies, in which all but one used mobile phone-related exposures (Table 7). Two studies resulted in at least one positive finding for IEI-EMF participants [Trimmel and Schweiger, 1998; Wiholm et al., 2009].

Trimmel and Schweiger [1998] observed reduced performance of visual attention and perception by combining a 50 Hz magnetic field with acoustic noise exposure, compared to the effects of noise only. A different visual attention test was used in two other studies employing mobile phone base station-like fields [Zwamborn et al., 2003; Health Council of the Netherlands (HCN), 2004; Regel et al., 2006], with no indication of a significant effect of exposure.

In the MPDHE study, spatial memory was improved in participants with IEI-EMF when they were exposed to mobile phone-like EMF [Wiholm et al., 2009], while in another study only the control group improved in a memory test during base station-relevant exposure [Zwamborn et al., 2003; HCN, 2004]. Different aspects of memory were also tested in four other studies with no significant findings [Trimmel and Schweiger, 1998; Regel et al., 2006; Wilén et al., 2006; Eltiti et al., 2009].

In four studies reaction time tests were performed without any significant influence of EMF exposure [Zwamborn et al., 2003; HCN, 2004; Regel et al., 2006; Wilén et al., 2006; Furubayashi et al., 2009].

Sleep Measurements

In three studies various aspects of sleep quality were measured (Table 8). In two of these some test parameters indicated an effect of EMF exposure [Mueller and Schierz, 2004; Arnetz et al., 2007]. In the study by Mueller and Schierz [2004], participants with IEI-EMF positioned themselves away from the side of their bed below where the sources generating

TABLE 6. Summary of Brain Physiology and Sensory System Findings

Refs.	Endpoints	Assessment times	Results (effect of EMF exposure)
Bamiou et al. [2008]	Transient evoked otoacoustic emission; video-oculography: presence of nystagmus, velocity of nystagmus and drift of gaze	Before and after exposures	Cases and controls: no effect
Lyskov et al. [2001]	EEG	Before and 40 min during exposure	Cases and controls: no effect
	Visual evoked potential, critical flicker fusion frequency threshold	Immediately before and after exposure	Cases and controls: no effect
Wilén et al. [2006]	Critical flicker fusion frequency	After exposure	Cases and controls: no effect

TABLE 7. Summary of Cognitive Function Findings

Refs.	Endpoints	Assessment times	Results (effect of EMF exposure)
Eltiti et al. [2009]	Working memory by mental arithmetic task (MA), attention and perceptual-motor speed by digit symbol substitution task (DSST), immediate memory by digit span task (DS)	MA during first or second 20 min of exposure (counterbalanced across participants), DSST and DS for 8 min after 40 min of exposure (counterbalanced)	Cases and controls: no effect
Furubayashi et al. [2009]	Pre-cued choice reaction time task	5 min before and 5 min after exposure	Cases and controls: no effect
Regel et al. [2006]	Simple reaction time, two-choice reaction time, n-back, visual selective attention	At the beginning of and 22 min after exposure	Cases and controls: no effect after multiple end point correction
Trimmel and Schweiger [1998]	Concentration and endurance under pressure: visual attention, precise visual processing, unsuccessful visual processing; speed and precision of perception; verbal memory performance	During exposure	Difference between ''EMF+ Noise'' and sham compared to the difference between Noise and sham. Cases: reduced scores ($P < 0.05$) for visual attention and for precise visual processing. Controls: no effect
Wiholm et al. [2009]	Spatial memory	Before and after 2.5 h exposure	Cases and controls: better performance after 2.5 h EMF exposure ($P < 0.026$) due to improved performance in cases (exposure by group effect $P < 0.025$); that is, no effect for controls
Wilén et al. [2006]	Short term memory, reaction time	Prior to exposure and after 30 min of exposure	Cases and controls: no effect
HCN [2004]	Reaction time, memory comparison, visual selective attention, dual tasking, filtering irrelevant info	During exposure	Cases: no effect. Controls: improved memory comparison times in UMTS condition ($P = 0.003$)

TABLE 8. Summary of Sleep Measurement Findings

Refs.	Endpoints	Assessment times	Results (effect of EMF exposure)
Leitgeb et al. [2008]	Sleep onset, latencies between sleep stages, percentage of sleep stages, sleep efficiency, number of awakenings, body position changes	When in bed during night	Cases: no effect for pooled analysis. From individual analyses: 5 positive effects of true shield, 10 negative effects of true shield, 1 placebo effect, 5 negative effects of both true and placebo shield
Mueller and Schierz [2004]	Movements, center of gravity (position in bed)	When in bed during night	Cases: moved away from area with maximum field intensity ($P = 0.007$)
Arnetz et al. [2007]	Sleep EEG	Immediately after exposure during sleep	Cases and controls: compared to sham, MP exposure caused longer latency to deep sleep (stage 3) from sleep onset ($P = 0.002$) and reduced amount of slow wave sleep (stages 3 + 4; $P = 0.014$)

50 Hz electric and magnetic fields were placed. In the morning after EMF exposures, participants with IEI-EMF scored higher for pleasure and arousal and more often believed that they had not been exposed, compared to nights with sham exposure.

The other sleep studies tested effects of radiofrequency fields [Arnetz et al., 2007; Leitgeb et al., 2008]. The MPDHE study, using mobile phone-like exposure, observed changes in both participants with and without IEI-EMF in three endpoints involving the recording of EEG during sleep, including shorter time of deep sleep [Arnetz et al., 2007]. Similar changes were not observed by Leitgeb et al. [2008], who tested the effect of shielding of the environmental RF exposure in a field study.

DISCUSSION

Out of the 29 studies that met our inclusion criteria, five identified one or more effects of exposure on a physiological or cognitive endpoint in participants with IEI-EMF. These effects consisted of a significant reduction in heart rate and blood pressure [Hietanen et al., 2002], altered pupillary light reflex [Rea et al., 1991], reduced visual attention and perception [Trimmel and Schweiger, 1998], improved spatial memory in the MPDHE study [Wiholm et al., 2009], movement away from an EMF source during sleep [Mueller and Schierz, 2004], and altered EEG during sleep in the MPDHE study [Arnetz et al., 2007]. These findings were equally distributed among 13 studies that focused on exposure in the microwave region (mostly mobile phones or mobile phone base station-like exposures), 15 studies involving sine wave low frequency exposure or VDU/VDU-like exposures and one additional study that used a range of frequencies [Rea et al., 1991].

The cardiovascular effects that were observed were not replicated by numerous other studies included in our review that used similar endpoints. It seems likely that the failure of the original study [Hietanen et al., 2002] to counterbalance the order in which exposures were presented is a sufficient explanation for the apparent effects that were observed.

The findings relating to pupilary reflex in the IEI-EMF group have also not been replicated [Rea et al., 1991], although in this case only one other study had attempted to do so, using a slightly different experimental design [Wang, 1995]. Nonetheless, methodological concerns relating to the original study by Rea et al. [1991] suggest that it would be unwise to place too much weight on its findings. In particular, concerns about the blinding of the exposures in the Rea et al. [1991] study have been expressed [Bergqvist et al., 1997], and it may be inferred from the scant information provided in the article concerning the exposures that the magnetic field strength at head level must have been very low and probably not much different from the background field strength.

With respect to the objective measures of sleep quality, only three studies were included in this review, of which two identified some significant effect of exposure. Mueller and Schierz [2004] found that participants with IEI-EMF moved away from an area of their bed with maximum field strength during the night, while the MPDHE study identified several changes in sleep EEG [Arnetz et al., 2007]. The exact meaning of these changes, should future work be able to replicate them, is unclear. It is notable that the changes observed in these two studies did not appear to coincide with reductions in self-reported sleep quality for the participants. In a recent article describing the MPDHE study in more detail, Lowden et al. [2010] reported that the participants' exposure had no effect on subjectively rated sleep quality. Meanwhile, Mueller and Schierz [2004] showed that the exposure in their study resulted in paradoxically higher levels of pleasure and arousal on awakening compared to sham exposure. Given this lack of association between the objective outcomes and the subjective sensations that define IEI-EMF, it seems unlikely that any such changes would be specific to IEI-EMF sufferers. Indeed, although Mueller and Schierz [2004] did not include a healthy control group in their study, the MPDHE study identified EEG changes in both the IEI-EMF group and control group [Arnetz et al., 2007], while other studies assessing only healthy controls has also occasionally identified small effects of RF on brain electrical activity, especially in the alpha band (frequency range 8–12 Hz) [Valentini et al., 2007; van Rongen et al., 2009]. Lowden et al. [2010] also reported similar findings in the alpha band.

In terms of the effects that have been observed in two studies on visual attention and perception [Trimmel and Schweiger, 1998] and spatial memory [Wiholm et al., 2009], it was notable that five other studies included in our review were unable to demonstrate any cognitive effects resulting from exposure. In addition, the effects that were observed in these two studies are seemingly contradictory, reflecting both impaired and improved performance. Therefore, these findings cannot be taken as indicating a consistently observed effect on cognition.

Finally, it is important to note that 16 of the studies included in our review also included a control group. Two studies identified significant effects for their control participants, which were not apparent for their IEI-EMF participants [Wang, 1995; Zwamborn et al., 2003; HCN, 2004]. Because we did not include studies that assessed the effects of EMF on healthy participants alone, we are unable to comment on the importance of these control group findings in terms of the effects of EMF exposure on the general population (see, e.g., van Rongen et al. [2009] for review). We are, however, able to comment on whether IEI-EMF participants show different responses to non-IEI-EMF participants. There is little evidence that they do. As a general trend, significant effects of exposure were as uncommon among the control groups used in the provocation studies as they were in the IEI-EMF groups.

In summary, our review has identified no consistent pattern of objectively measurable changes resulting from EMF exposure that might be used to characterize or diagnose IEI-EMF.

Quality of the Original Research

There may be several explanations for the absence of any consistent association between EMF exposure and physiological reactions in the reviewed studies. The first and most parsimonious explanation is that there is indeed no association.

An alternative explanation may be that some methodological deficit existed in those studies that failed to report a significant effect. For example, it is possible that EMF does trigger objective changes among a small minority of people who have a genuine sensitivity to EMF, but that the IEI-EMF participants included in the studies we reviewed did not belong to this group. In most respects, the inclusion criteria and the selection procedures for IEI-EMF participants did not differ greatly between those studies with and without significant outcomes (see online Table 3). One possible difference was that none of the eight studies that reported recruiting participants who said that their EMF-associated symptoms typically appeared during or shortly after exposure reported a significant finding. While it seems counterintuitive that only people who fail to react within a short timeframe are genuinely sensitive to EMF, future researchers should ensure that they at least record and report this parameter to enable the detection of any difference between slow and fast responders.

If reactions to EMF are subtle, the number of participants used by each study is also an issue. The average number of participants was lowest in studies where no EMF effects were found (Table 2), and in some of these studies [e.g., Nilsen, 1982; Wennberg et al., 1994; Sjöberg and Hamnerius, 1995; Wenzel et al., 2005], small effect sizes would probably not have been visible. However, half of the studies that observed no reaction to EMF included a similar number of IEI-EMF participants as those in which reactions were observed, or else used repeated tests to increase the chance of detecting an effect.

While other indicators of methodological quality varied substantially between the reviewed studies (see Table 2), for most issues there were no great differences between studies that did and did not find any significant effects of EMF on objectively registered outcomes.

No systematic difference between studies with and without reactions in connection with EMF exposure was detected when comparing studies with the same type of exposure (those with low frequency sine wave magnetic fields and those with mobile phone-like fields). It should also be noted that studies with no observed effects were at least comparable to studies with effects regarding the relevance of similar exposure types or the length of the intervals between exposures, which is important to prevent carryover effects from one exposure to the next. No single methodological factor seemed to differentiate studies that observed a significant effect from those that did not.

In general, studies in this field appeared to be of relatively high quality. It was encouraging that the majority ($n = 20$) were double-rather than single-blind, used some form of randomization to determine the order of exposure ($n = 22$), ensured that the exposure used matched the exposure described by participants as being problematic ($n = 22$), provided information about background or sham EMF levels ($n = 25$), and attempted to reduce the impact that extraneous, non-EMF-related factors such as heat or diet might have had on physiological responses ($n = 20$).

Room for improvement still exists, however. In particular, many studies provided insufficient data about their participants for us to assess the type of symptoms that they normally attribute to EMF sources or the severity of these symptoms. Several studies have demonstrated that IEI-EMF is not a homogenous condition [Rubin et al., 2008; Johansson et al., 2010], yet differences between potential subgroups cannot be assessed unless individual research teams provide sufficient information about their samples using questionnaires such as those used in previous studies [e.g., Eltiti et al., 2007; Rubin et al., 2008; Johansson et al., 2010]. Ideally, the type, severity and chronicity of symptoms, EMF triggers reported as problematic, duration of ill health, and use of coping strategies such as avoidance should be assessed [Hillert et al., 1999]. Where possible, matching IEI-EMF and control participants on demographic or general health-related parameters might also help to identify physiological responses to EMF that are specific to IEI-EMF. Twenty studies either failed to counterbalance the order of their exposures, or provided insufficient information for us to assess whether the order had been successfully counterbalanced; yet order effects are common in this literature, making counterbalancing essential. A related issue concerns the use of a habituation session to prevent anxiety or unfamiliarity with the study's procedures from affecting the results of the first exposure condition for each participant. Fourteen studies either did not use a habituation session or failed to report it if they did. Although habituation sessions add to a study's cost, a strong case can be made to research funders that they are important. Funders themselves should be acknowledged in research articles, not least because a study's funding source has been associated with its outcome [Huss et al., 2007]. It was surprising that sources of funding were unclear in 12 studies. Furthermore, although most studies assessed subjective symptoms or the ability to discriminate active from sham exposures in addition to the objective measures reviewed here, a correlation analysis between these self-reported endpoints and objective physiological measurements was described for only two studies, both reported by Kaul [2009]. Future studies should assess the association between subjective symptoms, physiological variables, and perceived or actual exposure in more detail. Finally, it was disappointing that only four studies mentioned a sample size or power calculation.

Quality of the Review

Our review of this literature used a detailed search strategy in order to identify potentially relevant studies. In addition to searching conventional electronic databases, we used citation analyses of key review articles in this field, examined the reference sections of all included articles, hand-searched our own personal libraries of literature in this area, encouraged other topic experts to provide us with any relevant material, examined conference proceedings, and searched the websites of relevant charities and lobbying groups. Despite this, we cannot be certain that we included every study that meets our inclusion criteria. In particular, studies published in non-European languages may not have been obvious to us, and studies that have not been reported in the conventional peer-reviewed literature are also less likely to have been included. However, because studies that reported a significant effect of exposure are more likely to have been published in easily accessible formats, any missed studies are unlikely to have altered our conclusions.

Because our review aimed to identify every study that has generated data relating to this topic, we deliberately included six studies that were not published in conventional peer-reviewed academic literature [Sjöberg and Hamnerius, 1995; Wang, 1995; Zwamborn et al., 2003; Mueller and Schierz, 2004; Kaul, 2009], together with additional data relating to the MPDHE study that appeared in a conference report [Hillert et al., 2007]. Despite coming from the ‘‘gray literature,’’ these studies all met the basic quality criteria that we set. Importantly, they also produced almost entirely negative findings. As with systematic reviews of healthcare interventions [Hopewell et al., 2007], the exclusion of studies published in the gray literature would therefore have systematically biased our findings. We recommend that future reviewers in the field of bioelectromagnetics consider this problem of publication bias when deciding which studies to include.

For pragmatic reasons, our literature search applied a cut-off point of May 2010. Since then, we have become aware of one additional report that presents more detail about the MPDHE study [Lowden et al., 2010], but which does not alter our conclusions. We have also become aware of a new pilot study by Havas et al. [2010]. This team tested autonomic nervous system responses during exposure to microwaves from a digital cordless phone base station. Of the 25 people tested, 15 (9 with IEI-EMF, 6 without) were described as showing no physiological responses during the course of the experiment, which involved multiple 3 min exposures to real and sham signals. Although the authors reported being able to identify when exposure had been present for some participants by examining the results regarding heart rate variability during active and sham exposures, the manual for the heart rate monitoring equipment used in the study specifically warns that users should ‘‘avoid nearby electromagnetic noise sources’’ [Heart Rhythm Instruments, 2002]. Interference caused by the active exposure may explain this study's results [Trottier and Kofsky, 2010]. In addition to this, the absence of information within the article, including the lack of statistical analyses, makes it difficult to assess the quality of the study. Again, this new study does not affect our conclusions.

CONCLUSIONS

This review found no reliable and consistent evidence to suggest that people with IEI-EMF experience any unusual physiological reactions as a result of exposure to EMF. The findings of this review are therefore in line with the results of previous reviews that have found no robust evidence to support a link between acute EMF exposures and symptom reporting in people with IEI-EMF [Rubin et al., 2005, 2010; Röösli, 2008]. Future studies should take care to include larger, well-characterized study groups that will enable possible differences between subgroups to be investigated. Power calculations should be presented based on hypothesized effects. The study design should include a habituation session and double-blind exposure conditions in a randomized and balanced order.

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