FCC 09-31

Before the
Federal Communications Commission

In the Matter of	)	
	)	
A National Broadband Policy for Our Future	)	GN Docket No. 09-51

To: Office of the Secretary
Federal Communications Commission
Washington, DC 20554

Comment Filed by Cindy Sage, MA

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June 16, 2009

Exhibit 53

AFFIDAVIT OF CINDY SAGE

State of CALIFORNIA]
ss.
County of Santa Barbara]

CINDY SAGE being duly sworn deposes and says:

Reply Comment: FCC GN Docket No. 09-51 A National Broadband Plan for Our Future. Filed in support of The EMR Policy Institute Comment dated June 7, 2009

1. My name is Cindy Sage. I am the owner of Sage Associates, an environmental consulting firm. My business address is 1396 Danielson Road, Montecito, California, 93108

2. I have been a professional environmental consultant since 1972. I hold an M.A. degree in Geology, and a B.A. in Biology from the University of California, Santa Barbara. I am a Senior Fellow, Department of Oncology, School of Health and Medical Sciences, Orebro University, Orebro, Sweden (2008-2010).

3. I am the co-editor of the BioInitiative Report: A Rationale for a Biologically-based Public Exposure Standard for Electromagnetic Fields (ELF and RF). References for my publications are attached. I served as a member of the California Public Utilities Commission EMF Consensus Group, the Keystone Center Dialogue for Transmission Line Siting (a national group developing EMF Policy), and of the International Electric Transmission Perception Project. I am a full member of the Bioelectromagnetics Society.

4. My professional involvement in this area includes constraint analysis, environmental planning, and impact assessment on EMF issues for more than 20 years. My company has provided professional consulting services to city and county planners, private developers, state agencies and schools with respect to measurement and assessment of EMF as a part of land planning and environmental constraints analysis since 1972. I have been an expert witness on

EMF policy. public perception and land use issues, and have qualified both in state and in federal court proceedings as an expert witness in this area.

5. Factors or conditions that can affect the use or development suitability for land development require assessment under both the National Environmental Policy Act and state environmental quality acts.

6. The presence of wireless emissions may have negative impacts on the value and utility of land, may pose potential health risks, may result in loss of property value, and in general may be a negative effect on public perception.

7. Land that is affected can be more speculative and risky to sell and develop; it is considered environmentally flawed.

8. Wise land use requires that homes and other sensitive receptors (schools, day-care, pre-schools) are at levels below those associated with increased risk of cancer and neurological diseases that have been reported with chronic, low-intensity NIER.

9. BPL has the potential to expose entire communities to a new, continuous, involuntary source of RF radiation. The RF signal will be carried on everyone's home wiring, even in the homes of those who do not wish to subscribe.

10. American families cannot 'opt out' of blanket wireless broadband and BPL exposures.

11. There are legitimate health concerns regarding exposure to radiofrequency radiation (RF), which has rapidly become one of the most pervasive environmental exposures in modern life.

12. There are hundreds of studies on adults in high quality, peer-reviewed scientific and public health journals that report health impacts from exposure to radiofrequency radiation (RF) at levels far below existing public safety limits.

13. The existence of low-intensity (non-thermal) effects from wireless technologies is established.

14. Existing FCC uncontrolled public safety limits are inadequate to protect public health.

15. New, biologically-based public exposure standards are needed for NIER.

16. It is not in the public interest to wait.

17. There are very few studies on the impact on childrens' health from RF.

18. Children are more vulnerable to environmental toxins and carcinogens than adults.

19. Children cannot remove themselves from potentially harmful wireless exposures.

20. The US government has a duty to protect the health and welfare of children.

21. Health care costs that will be associated with widespread and unavoidable exposures to low-intensity radiofrequency radiation from wireless broadband and BPL will have a negative economic impact on the American economy.

22. There is no informed consent by the American public about wireless health risks.

23. Prudent public health actions are warranted now that are proportionate to the potential health risks and enormous populations at possible risk.

24. Alternatives to wireless broadband and BPL are available for internet connectivity.

25. The US should implement fiber optic, cable and other wired solutions for internet connectivity and SmartGrid technology instead of wireless broadband and BPL.

26. The NTP has begun but not completed a study of the potential carcinogenicity of radiofrequency radiation.

27. The NTP assessment of the carcinogenicity of radiofrequency radiation should be completed, and a full discussion by stakeholders conducted prior to deployment of wireless broadband and/or BPL.

28. New, biologically-based public exposure standards for low-intensity, chronic exposure to NIER should be developed by individuals competent in human biology and in NIER bioelectromagnetics, independent of agencies that promulgate sales of airwaves for commercial purposes, before a federal commitment is made to deploy wireless broadband and BPL technologies.

29. The unwise, premature and irretrievable commitment of resources to further deployment of wireless technologies, including wireless broadband, BPL and SmartGrid technologies should be avoided until new, biologically-based safety standards are in place.

30. Precautionary, interim RF safety limits should be set in accordance with those recommended in the BioInitiative Report.

Respectfully submitted by:

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Bioelectromagnetics 30:299–306 (2009)

Blood Laboratory Findings in Patients Suffering From Self-Perceived Electromagnetic Hypersensitivity (EHS)

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Risks from electromagnetic devices are of considerable concern. Electrohypersensitive (EHS) persons attribute a variety of rather unspecific symptoms to exposure to electromagnetic fields. The pathophysiology of EHS is unknown and therapy remains a challenge. We hypothesized that some electrosensitive individuals are suffering from common somatic health problems. Toward this end we analysed clinical laboratory parameters including thyroid-stimulating hormone (TSH), alanine transaminase (ALT), aspartate transaminase (AST), creatinine, hemoglobine, hematocrit and c-reactive protein (CRP) in subjects suffering from EHS and in controls that are routinely used in clinical medicine to identify or screen for common somatic disorders. One hundred thirty-two patients ($n = 42$ males and $n = 90$ females) and 101 controls ($n = 34$ males and $n = 67$ females) were recruited. Our results identified laboratory signs of thyroid dysfunction, liver dysfunction and chronic inflammatory processes in small but remarkable fractions of EHS sufferers as potential sources of symptoms that merit further investigation in future studies. In the cases of TSH and ALT/AST there were significant differences between cases and controls. The hypotheses of anaemia or kidney dysfunction playing a major role in EHS could be unambiguously refuted. Clinically it is recommended to check for signs of treatable somatic conditions when caring for individuals suffering from self-proclaimed EHS. Bioelectromagnetics 30:299–306, 2009. © 2009 Wiley-Liss, Inc.

Key words: electromagnetic hypersensitivity (EHS); blood laboratory; TSH; CRP; anaemia; creatinine

INTRODUCTION

Electromagnetic fields are considered by some a source of potential health risks [WHO, 2004; Carpenter and Sage, 2008]. The discussion ranges from impaired well-being to carcinogenic effects and also touches regulatory issues. Individuals with electromagnetic hypersensitivity (EHS) or, synonymously, hypersensitivity to electric and magnetic fields (HSEMF) describe adverse health effects while using or being in the vicinity of devices emanating electric and/or magnetic fields of low intensity [Hillert et al., 1999]. Complaints are usually present without indication of organic lesion. Nevertheless, the health complaints related to EHS result in considerable psychological stress in these patients [Seitz et al., 2005]. Complainants relate their symptoms most frequently to exposure to mobile phone base stations, mobile phones, cordless phones and power lines [Hillert et al., 2002; Röösli et al., 2004] although there is apparently no strong link between field exposure and complaints [Lonne-Rahm et al., 2000; Röösli, 2008]. The group of symptoms usually appears or worsens during perceived exposure to a specific source of electromagnetic fields (EMFs), and they are reported to diminish when patients are distant from the EMF-sources.

An additional phenomenon in this context is the proclaimed ability to perceive electromagnetic fields at a much lower threshold than the general population without necessarily developing health symptoms: electromagnetic sensibility [Leitgeb and Schröttner, 2003]. The decreased perception and the attribution of health symptoms to EMF exposure can be considered as two independent phenomena. Nevertheless, in a survey among self-declared EHS individuals, 56% declared

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their ability to perceive electromagnetic fields [Röösli et al., 2004].

Early reports stress the occurrence of dermatological symptoms (facial dermatosis such as seborrheic eczema, acne vulgaris, mild rosacea, and atopic dermatitis) which are mainly related to exposure to video display units (VDUs) and mostly have a good prognosis [Lindén, 1981; Nilsen, 1982; Berg, 1988; Berg et al., 1990; Bergqvist and Wahlberg, 1994; Bergqvist and Vogel, 1997]. In more recent reports, patients show multiple non-specific health complaints such as sleep disturbances, headache, nervousness or distress, general anxiety, depression, fatigue or problems in concentrating, memory problems, respiratory problems (difficulty breathing), gastrointestinal symptoms, dry eyes, photosensitivity, palpitations, loss of weight, increased sweating and heat intolerance [Bergdahl, 1995; Knave, 2001; Hietanen et al., 2002; Röösli et al., 2004; Silny et al., 2004].

So far a commonly accepted pathophysiological basis for the symptoms presented by EHS sufferers has not been reported. Due to the lack of knowledge of the EHS pathophysiology, adequate medical treatment for these patients remains a challenge. Several authors have concluded that EHS in most cases can be considered a somatoform disorder. It is well conceivable that EHS is not a homogeneous entity but rather a heterogeneous mixture of a whole variety of disorders ranging from delusional disorders to severe somatic disorders. Many of the symptoms can be found in disorders quite common in the general population such as thyroid dysfunction, chronic liver disease, anaemia, chronic kidney disease and chronic inflammatory processes (see Table 1).

Therefore, we hypothesized that there might be a large fraction of electrosensitive individuals who are in essence suffering from common somatic health problems secondarily ill-attributed to EMF. Toward this end we analysed clinical laboratory findings in subjects suffering from EHS and in controls that are routinely used in clinical medicine to identify or screen for common somatic disorders.

SUBJECTS AND METHODS

Patients

This study is part of a broader effort to clinically characterize EHS patients within the framework of the German Mobile Telecommunication Research Program (DMF) [www.emf-forschungsprogramm.de]. For the present analysis, 132 patients ($n = 42$ males and $n = 90$ females) and 101 controls ($n = 34$ males and $n = 67$ females) were recruited. Patients were from German EMF self-help groups, the 'Mainzer EMF-Wachhund', an Internet watchdog project [Schüz et al., 2006] or by local advertisement in Mainz and Regensburg. Inclusion criteria for electromagnetic hypersensitive patients were: (1) an EMF-related symptom load of at least 14 points on a modified 'Regensburger EMF-complaint list' [Frick et al., 2002]; (2) attribution of the health symptoms experienced to named electromagnetic emission sources (e.g., mobile phone base stations, wireless routers for internet access, etc.); (3) aged 18–65 years. Exclusion criteria were acute psychiatric disorders such as acute depressive or paranoid psychosis. All subjects were seen by an experienced psychiatrist (ND). In addition, the standardized interview for the detection of psychiatric disorders 'Mini-DIPS' was used [Markgraf, 1994].

Patients and controls were matched for age, sex and BMI (Table 2). All participants gave written, informed consent to the study. The study protocol was approved by the ethic committee of the medical association of Rhineland-Palatinate that is responsible for all clinical studies of the University of Mainz.

Measurements

The blood chemistry parameters were measured with a Roche Hitachi 917 Analyzer (Roche Diagnostic,

TABLE 1. Comparison of EHS Symptoms With Symptom of Disorders Common in the General Population

Symptoms	EHS	Thyroid dysfunction	Liver disease	Anaemia	Kidney disease	Chronic Inflammation
Sleep disorder	+++	++	+	++	+	+
Fatigue	+++	+++	+++	+++	++	+++
Skin problems	+++	++	++	+	+	++
Headache	+++	++	++	++	++	+++
Nervousness/distress	++	++	++	+	+	+
Difficulty in concentrating	+	++	+	+	+	++
Nausea or dizziness	+	+	+	++	+	+
Unspecific symptoms like coughing, eye irritation, hoarse or dry throat, runny or stuffy nose	++	+	−	−	+	++

Modified according to Harrison's Principles of Internal Medicine 16th edition [Hillert et al., 2002; Röösli et al., 2004].

TABLE 2. Characterization of Cases and Controls

Characteristics	EHS cases	Controls	*P*-values
n	132	101	
Males	42 (31.8%)	34 (33.7%)	
Females	90 (68.2%)	67 (66.3%)	
Age (years)	51.5 ± 13.3	49.7 ± 12.6	0.263
Males	53.7 ± 12.8	52.4 ± 11.0	
Females	50.5 ± 13.5	48.3 ± 13.2	
BMI (kg/m^2)	24.6 ± 4.5	24.7 ± 3.5	0.669
Males	25.9 ± 3.9	25.0 ± 2.8	
Females	24.0 ± 4.7	24.6 ± 3.9	
Symptoms most frequently attributed to EMF			
Sleep disturbances	101 (77%)	2 (2%)	<0.001
Fatigue	101 (77%)	2 (2%)	<0.001
Difficulty in concentrating	93 (70%)	1 (1%)	<0.001
Duration of disease (years)	9.10 ± 8.05		
Males	9.08 ± 4.63		
Females	9.11 ± 9.23		
Age of onset (years)	42.8 ± 12.5		
Males	43.5 ± 12.8		
Females	42.4 ± 12.4		

Only symptoms attributed to EMF are given.

Mannheim, Germany) and the parameters of the red blood count were detected with the Coulter LH-750 Hematology Analyzer (Fa. Beckmann/Coulter, Krefeld, Germany) at the Institute of Clinical Chemistry and Laboratory Medicine of the University of Mainz Hospital.

Statistical Analysis

All statistical analyses were performed using SPSS v12 (SPSS, Chicago, IL). Descriptive results of continuous variables are expressed as means ± SD. Group differences were tested with the Student's *t*- or Mann–Whitney *U*-test. For the assessment of correlations, Spearman correlation coefficients were calculated. *P*-values of <0.05 were considered to be statistically significant.

RESULTS

Thyroid (TSH)

More patients than controls had TSH levels below the reference value of 0.3 mU/L (6.1% vs. 0.9%; $P = 0.042$).

Liver (ALT, AST)

Mean ALT and AST levels were significantly higher in the group of EHS affected individuals. In the analysis of the male and female subgroup, this difference was only significant in the females (see Table 2). Elevated ALT (ALT ≥ 35 U/L) was found in 27 (20.9%) EHS affected persons and in 11 (11%) of the controls ($P = 0.045$). Elevated AST (AST ≥ 35 U/L) was found in 16 (12.4%) affected persons and 6 (5.9%) of the controls ($P = 0.098$). Three persons in the EHS group had ALT > 70 U/L and only one person in the EHS group had AST > 70 U/L. None of the ALT or AST levels exceeded 120 U/L. As expected, ALT and AST were significantly higher in males (ALT: 30.03 ± 14.2 U/L; AST: 30.03 ± 14.2 U/L) than in females (ALT: 24.52 ± 8.86 U/L, $P = 0.001$; AST: 25.78 ± 9.4 U/L, $P < 0.001$).

Anaemia (Hb, MCV, MCHC, Hct, Iron, Ferritin, ZPP)

No pathological Hb concentration or Hct levels were found in the EHS group.

Kidney (Creatinine and Electrolytes)

Twenty-eight percent of the EHS group and 32% of the controls had creatinin levels above 0.9 mg/dl ($P = 0.706$). Only one individual in the EHS group had a serum creatinin level above the more stringent reference value of 1.4 mg/dl and none above 1.7 mg/dl. The mean sodium level in the EHS group was slightly higher than in the control group (140.34 ± 3.28 vs. 139.87 ± 2.48; $P = 0.042$), especially within the female subgroups (140.53 ± 3.27 vs. 139.40 ± 2.36; $P = 0.001$). The male groups showed no significant difference ($P = 0.312$). Within the EHS group were six cases of hypernatraemia; the maximum sodium concentration was 148 mmol/L, well below the threshold for severe hypernatraemia of 160 mmol/L. Hyponatraemia was detected in four EHS individuals.

The minimal sodium concentration was 119 mmol/L. Hyperchloremia was found in five EHS individuals. Hypochloremia was noted in 4 EHS patients. The maximum chloride concentration was 111 mmol/L, the minimum was 86 mmol/L.

Inflammation (CRP, Leucocytes, Thrombocytes, MPV)

Increased CRP levels (>5 mg/L) were found in both groups, with 10 samples in each. Three values in the EHS group were above 10 mg/L with two being between 10 and 15 mg/L and the maximum value of 25 mg/L. In the control group, platelet count above the reference range was found in six controls whereas only one pathological value was found in the EHS group ($P = 0.024$). There were no significant differences in MPV between patients and controls ($P = 0.332$), only the female subgroup showed a significant difference (9.53 ± 0.96 vs. 9.09 ± 1.04; $P = 0.012$).

The complete data set is given in Table 3 (mean values) and Table 4 (number of individuals outside of reference values). There were no correlations between laboratory data and number or intensity of symptoms (data not shown).

DISCUSSION

Symptoms presented by individuals suffering from EHS resemble symptoms from individuals suffering from common conditions such as hypo- or hyperthyroidism, liver disorders, anaemia, kidney disorders or chronic inflammations (Table 1). By analysing a range of blood chemistry parameters we were able to test the hypothesis that EHS symptoms are caused by detectable common disorders.

Thyroid Dysfunction (TSH)

The prevalence of hyperthyroidism in Germany is 2–5% in women and 0.2–0.7% in men. Main symptoms are nervousness or distress, loss of weight, heat intolerance, sweating, fatigue, headache and eye and vision symptoms. Additional symptoms include the sense of not feeling well, emotional irritability, a tendency towards depressiveness and an increased lack of vitality and activity [Suwalska et al., 2005]. Although overt hyper- and hypothyroidism individuals show the most symptoms, subclinical hyperthyroidism may also cause symptoms [Gulseren et al., 2006]. TSH is an effective screening instrument for the detection of thyroid dysfunctions [Spencer et al., 1987].

The finding of an enlarged fraction of persons showing TSH levels below the reference value raises two questions: (1) Does a fraction of EHS patients truly suffer from thyroid gland dysfunction? (2) Is there a link between thyroid function and EMF exposure? To answer the first question a well-designed replication study would be necessary. The replication should also comprise the measurement of the thyroid hormones T3 and T4. Currently we consider our result a 'signal' awaiting replication. In any case, the fraction of persons

TABLE 3. Mean Values ± Standard Deviation of Measured Blood Parameters

	All			Males			Females		
	Patients ($n = 132$)	Controls ($n = 101$)	P	Patients ($n = 42$)	Controls ($n = 34$)	P	Patients ($n = 90$)	Controls ($n = 67$)	P
TSH[a] (mU/L)	1.35 ± 0.98	1.34 ± 1.13	0.334	1.38 ± 0.90	1.20 ± 0.68	0.461	1.34 ± 1.02	1.40 ± 1.30	0.531
ALT[a] (U/L)	26.54 ± 15.66	22.50 ± 13.65	**0.007**	33.40 ± 19.25	31.76 ± 18.37	0.54	23.23 ± 12.43	17.73 ± 6.66	**0.001**
AST[a] (U/L)	26.88 ± 9.09	25.64 ± 13.42	**0.003**	29.17 ± 8.05	31.09 ± 19.38	0.405	25.78 ± 9.40	22.88 ± 7.87	**0.002**
Iron (μg/dl)	94.63 ± 34.71	95.10 ± 34.36	0.919	98.67 ± 32.70	100.52 ± 26.31	0.792	92.66 ± 35.67	92.43 ± 37.60	0.969
Ferritin[a] (ng/ml)	97.59 ± 93.74	93.16 ± 106.96	0.192	155.84 ± 110.71	167.10 ± 141.41	0.965	70.86 ± 70.88	55.63 ± 55.57	0.101
ZPP[a] (mmol/molHb)	58.99 ± 24.05	61.58 ± 22.41	0.393	50.13 ± 22.69	57.21 ± 22.98	0.246	63.15 ± 23.67	63.87 ± 21.95	0.602
Erythrocyte (per pl)	4.63 ± 0.40	4.59 ± 0.40	0.464	4.87 ± 0.36	4.88 ± 0.36	0.926	4.52 ± 0.33	4.45 ± 0.34	0.235
Haemoglobin (g/dl)	14.28 ± 1.20	14.16 ± 1.22	0.489	15.24 ± 1.03	15.14 ± 1.05	0.649	13.80 ± 0.97	13.67 ± 0.99	0.413
Hematokrit (%)	41.57 ± 3.32	41.17 ± 3.66	0.395	44.15 ± 2.69	43.94 ± 3.38	0.771	40.31 ± 2.85	39.77 ± 2.95	0.253
MCH (pg)	30.83 ± 1.76	30.84 ± 1.44	0.973	31.31 ± 1.73	31.07 ± 1.36	0.505	30.60 ± 1.74	30.72 ± 1.48	0.638
MCV (fl)	89.68 ± 4.47	89.64 ± 4.09	0.935	90.65 ± 5.02	90.16 ± 4.43	0.657	89.21 ± 4.13	89.37 ± 3.92	0.809
MCHC[a] (g/dl)	34.39 ± 1.15	34.42 ± 1.01	0.546	34.57 ± 0.85	34.49 ± 1.12	0.727	34.30 ± 1.26	34.38 ± 0.95	0.293
Creatinin[a] (mg/dl)	0.84 ± 0.17	0.85 ± 0.19	0.84	0.94 ± 0.16	0.98 ± 0.19	0.565	0.79 ± 0.15	0.78 ± 0.15	0.684
Sodium[a] (mmol/L)	140.34 ± 3.28	139.87± 2.48	**0.042**	139.95 ± 3.29	140.79 ± 2.50	0.312	140.53 ± 3.27	139.40 ± 2.36	**0.001**
Chloride[a] (mmol/L)	103.12 ± 3.45	102.49 ± 2.68	**0.041**	102.98 ± 3.52	103.35 ± 2.97	0.773	103.18 ± 3.44	102.05 ± 2.41	**0.006**
Potassium[a] (mmol/L)	4.24 ± 0.53	4.18 ± 0.47	0.452	4.27 ± 0.50	4.23 ± 0.35	0.821	4.22 ± 0.55	4.15 ± 0.52	0.275
CRP[a] (mg/L)	1.83 ± 2.90	2.20 ± 3.51	0.601	1.23 ± 1.41	1.47 ± 1.83	0.393	2.11 ± 3.38	2.56 ± 4.07	0.899
Leukocyte (per nl)	6.48 ± 1.65	6.62 ± 2.05	0.541	6.44 ± 1.67	6.14 ± 2.06	0.477	6.49 ± 1.64	6.87 ± 2.01	0.198
Thrombocyte (per nl)	264.04 ± 64.29	267.36 ± 68.25	0.706	254.19 ± 59.65	233.59 ± 57.60	0.133	268.85 ± 66.25	284.49 ± 67.19	0.152
MPV (fl)	9.41 ± 0.97	9.27 ± 1.10	0.332	9.14 ± 0.97	9.61 ± 1.16	0.086	9.53 ± 0.96	9.09 ± 1.04	**0.012**

[a]Non-Gaussian variables.
Significant differences in bold.

TABLE 4. Number of Individuals Outside the Reference Values

		<Ref. range			>Ref. range		
	Reference range	Patients ($n = 132$)	Controls ($n = 101$)	P	Patients ($n = 132$)	Controls ($n = 101$)	P
TSH (mU/L)	0.3–4.2	8 (6.1%)	1 (0.9%)	**0.042**	2 (1.5%)	3 (2.9%)	0.514
ALT (U/L)	<35 U/L				27 (20.5%)	11 (10.8%)	0.045
AST (U/L)	<35 U/L				16 (12.1%)	6 (5.9%)	0.098
Iron (μg/dl)	37–145	2 (1.5%)	2 (1.9%)	0.860	13 (9.8%)	7 (6.9%)	0.403
Ferritin (ng/ml)	30–320	24 (18.2%)	32 (31.7%)	**0.028**	0 (0%)	1 (0.9%)	0.263
ZPP (mmol/molHb)	<40				105 (79.5%)	90 (89.1%)	0.126
Erythrocyte (per pl)	4.1–5.1	10 (7.6%)	9 (8.9%)	0.765	12 (9.1%)	14 (13.8%)	0.288
Haemoglobin (g/dl)	12.1–16.1	0 (0%)	3 (2.9%)	**0.049**	11 (8.3%)	7 (6.9%)	0.642
Hematokrit (%)	35–47	0 (0%)	4 (3.9%)	**0.023**	8 (6.1%)	3 (2.9%)	0.249
MCH (pg)	27–34	0 (0%)	1 (0.9%)	0.259	5 (3.8%)	0 (0%)	**0.045**
MCV (fl)	80–100	2 (1.5%)	0 (0%)	0.207	0 (0%)	1 (0.9%)	0.259
MCHC (g/dl)	31.5–36	0 (0%)	1 (0.9%)	0.259	4 (3.1%)	5 (4.9%)	0.450
Creatinin (mg/dl)	0.5–0.9	0 (0%)	1 (1%)	0.259	37 (28%)	32 (31.7%)	0.706
Sodium (mmol/L)	135–144	4 (3.1%)	2 (1.9%)	0.597	6 (4.5%)	3 (2.9%)	0.514
Chloride (mmol/L)	97–108	4 (3.1%)	1 (0.9%)	0,282	5 (3.8%)	1 (0.9%)	0.177
Potassium (mmol/L)	3.6–4.8	5 (3.8%)	2 (1.9%)	0.460	8 (6.1%)	5 (4.9%)	0.683
CRP (mg/L)	<5				10 (7.6%)	10 (9.9%)	0.530
Leukocyte (per nl)	3.9–10.0	6 (4.5%)	8 (7.9%)	0.311	4 (3.1%)	6 (5.9%)	0.301
Thrombocyte (per nl)	150–400	5 (3.8%)	2 (1.9%)	0.401	1 (0.8%)	6 (5.9%)	**0.024**
MPV (fl)	7.6–11.2	2 (1.5%)	3 (2.9%)	0.544	3 (2.3%)	7 (6.9%)	0.134

showing noteworthy TSH values was below 10%. Therefore, our result points towards the hypothesis of EHS being a heterogeneous mixture of conditions rather than reflecting a single pathophysiology. The link between EMF and thyroid function has been poorly explored so far and the few publications fall into either of the two categories positive reports without replication or negative reports. In the largest study involving humans Bergamaschi et al. [2004] studied TSH values in 2,598 employees grouped according to the extent of mobile phone use. No statistically significant difference regarding TSH values below 0.4 UI/L was observed but there was a greater prevalence of subjects with low TSH values among 192 employees with more than 33 h/month conversation time. Djeridane et al. [2008] studied TSH levels in 20 healthy young men in an experimental design with the pre-exposure levels as controls and found no effect of 900 MHz EMF exposure on TSH profiles.

Liver Disease (ALT, AST)

In liver diseases fatigue is a major symptom and at times the presenting symptom [Kumar and Tandon, 2002]. In addition malaise, lethargy, anorexia, listlessness, loss of social interest and inability to concentrate are commonly associated with liver affectations. Cauch-Dudek et al. [1998] and Swain [2006] showed that the genesis of the symptom of fatigue in chronic disease is complex and poorly understood, although the cause of fatigue could be multifactorial. Depression is also common in fatigued patients whereas it is unclear whether fatigue leads to depression or vice versa. Serum alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST) levels are the most common screening tests as part of a routine evaluation of liver damage [Leclercq et al., 1999] with ALT being the most specific marker of liver cell damage.

The vast majority of the ALT and AST values were within the narrowly defined normal range < 35 U/L and only three ALT-values were above 70 U/L in the EHS group. None was above 120 U/L. This result shows that liver affectations might play a role in a small minority of patients but are of no concern in most cases of EHS.

Anaemia (Hb, MCV, MCHC, Hct, Iron, Ferritin, ZPP)

Anaemia is a condition in which the haemoglobin concentration in the blood is below the reference level, resulting in a reduced oxygen-carrying capacity of red blood cells. About half of all cases of anaemia can be attributed to iron deficiency; other common causes include infections and genetic factors. In its severe form, anaemia is associated with fatigue, weakness, dizziness and drowsiness. Pregnant women and children are particularly vulnerable. It is well known that normal haemoglobin distributions vary with age and gender, at different stages of pregnancy, and with altitude and smoking. The main indicators of anaemia

are haemoglobin level (Hb) and haematocrit (Hct). Severe anaemia is defined as haemoglobin < 7 g/dl and requires medical treatment. Among all the red cell indices measured by electronic blood counters, mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) are the two most sensitive indices of iron deficiency. Reduction in mean corpuscular volume (MCV) occurring in parallel with anaemia is a late phenomenon in the development of iron deficiency [WHO, 2006]. Low serum iron by itself is no proof of iron deficiency as it also occurs in inflammatory disorder [Cartwright, 1966] and malignancies [Banerjee and Narang, 1967]. Ferritin is an established additional parameter with which to evaluate endogenous iron availability [Wish, 2006].

No pathological Hb concentration or Hct levels were found in the EHS group. Fatigue and related symptoms caused by anaemia do not appear to be of particular relevance in EHS. This result is in line with human data on the EMF effects on blood parameters although highly speculative reports on the potential link between EMF and iron metabolism also exist [Hachulla et al., 2000]. For example, the results of Dasdag et al. [2002] suggest that electromagnetic fields did not affect the haematological and immunologic parameters of welders. Likewise, the results of Selmaoui et al. [1996] and Akdag et al. [2006] indicated that both continuous and intermittent 50 Hz MFs had no effects on the iron levels, electrolytes, liver enzymes or lipids.

Kidney Disease (Creatinine, Na, K, Cl)

Symptoms of renal diseases such as fatigue/tiredness, pruritus, constipation, anorexia, sleep disturbance, anxiety, dyspnoea, nausea and depression are often underrecognized [Murtagh et al., 2007]. Serum creatinine level is the most commonly used measure of kidney function in clinical practice. Serum creatinine is derived from the metabolism of creatine in muscle and the generation of creatinine tends to be proportional to muscle mass. In addition, associations of higher creatinine with male sex, older age, black race, history of diabetes and cimetidine use have been reported [Salive et al., 1995]. Increased serum creatinine concentrations were also noticed after meals rich in meat.

In our study, there were slightly elevated creatinine levels (>0.9 mg/dl) in almost one third of the probands of both groups. However, in both groups clinically relevant creatinine levels were not observed. Only one individual in the EHS group had a serum creatinine level above the more stringent reference value of 1.4 mg/dl and none were above 1.7 mg/dl. None of the values was of immediate clinical relevance. Thus, it can be safely concluded that kidney dysfunction is not of major concern in EHS.

Inflammation (CRP, Leucocytes, Thrombocytes, MPV)

Chronic inflammation could be a reason for the non-specific symptoms of EHS patients. CRP and leucocytes are reliable and easily accessible biomarkers for clinical use. CRP is the most sensitive of the acute phase reactants. Its concentration increases rapidly during inflammatory processes. In most cases, mild to moderately elevated platelet counts are seen when chronic inflammation is present. Mean platelet volume (MPV) has been proposed as a potential marker of clinical disease activity, being inversely proportional to the levels of classical inflammatory markers such as CRP [Danese et al., 2004].

7.6% of the EHS group displayed elevated (>5 mg/L) CRP levels; three individuals had CRP > 10 mg/dl. Thus, at least three and up to 10 individuals in the EHS group (2.3%) were harbouring an inflammatory process. The potential link between immune function, EMF exposure and EMF effect is unclear and immune suppressive as well as immune stimulatory effects have been reported in addition to the absence of effects. Moreover, in some exposure studies it was impossible to discriminate potential EMF effects, the effects of stress and potential pre-existing abnormalities [review by Boscolo et al., 2007].

In summary, our results identified thyroid dysfunction, liver dysfunction and chronic inflammatory processes in small but remarkable fractions of EHS sufferers as potential sources of symptoms that merit further investigation in future studies. In the cases of TSH and ALT/AST there were significant differences between cases and controls. The hypotheses of anaemia or kidney dysfunction playing a major role in EHS could be unambiguously refuted. The results are compatible with those of Hillert et al. [2002] who measured routine laboratory parameters in 14 EHS patients without detecting a specific pattern of abnormalities. EHS might not be a single disorder with defined pathophysiology but rather a complex mixture of different etiologies held together by the subject's EHS disorder model. Clinically it is recommended to check for signs of treatable somatic conditions when caring for individuals suffering from self-proclaimed EHS.

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Altered cortical excitability in subjectively electrosensitive patients: Results of a pilot study

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Abstract

Objective: Hypersensitivity to electromagnetic fields is frequently claimed to be linked to a variety of unspecific somatic and/or neuropsychological complaints. Whereas provocation studies often failed to demonstrate a causal relationship between electromagnetic field exposure and symptom formation, neurophysiological examinations highlight baseline deviations in people claiming to be electrosensitive. **Methods:** To elucidate a potential role of dysfunctional cortical regulations in mediating hypersensitivity to electromagnetic fields, cortical excitability parameters were measured by transcranial magnetic stimulation in subjectively electrosensitive patients (n=23) and two control groups (n=49) differing in their level of unspecific health complaints. **Results:** Electrosensitive patients showed reduced intracortical facilitation as compared to both control groups, while motor thresholds and intracortical inhibition were unaffected. **Conclusions:** This pilot study gives additional evidence that altered central nervous system function may account for symptom manifestation in subjectively electrosensitive patients as has been postulated for several chronic multisymptom illnesses sharing a similar clustering of symptoms.
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Keywords: Chronic multisymptom illnesses; Electromagnetic hypersensitivity; Intracortical facilitation; Transcranial magnetic stimulation

Introduction

Hypersensitivity to electromagnetic fields as an alleged cause of many unspecific somatic and/or neuropsychological complaints of patients is very common in western communities, with an assumed prevalence of up to 3% [1,2]. However, a clear definition of "electromagnetic hypersensitivity" and its diagnostic criteria is lacking so far [3]. The initial symptoms recognized in association with exposure to electromagnetic fields were dermatologic in nature, such as itching, burning, and various kinds of dermatoses frequently found on the face. This prior symptom constellation extended to a so-called "general syndrome" [4], including neurasthenic and/or somatic symptoms, such as dizziness, fatigue, headache, difficulties in breathing, or palpitations. Despite accumulating experience, a clear relationship between exposure to electromagnetic fields and these symptoms has not yet been established, and a majority of published provocation studies failed to demonstrate this relationship [5–8]. Due to these findings, symptom generation in these patients may be rather based on dysfunctional attributions of somatic symptoms to electromagnetic field exposure than to the exposure itself. The symptoms of subjectively electrosensitive patients are unspecific and overlap with many other syndromes of environmental intolerance, such as multiple chemical sensitivity or sick building syndrome [9,10], suggesting that hypersensitivity to electromagnetic fields should be considered as a form of a more general diagnostic entity labeled as chronic multisymptom illnesses (CMI) [11]. Despite serious scientific problems in definition

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Exhibit 55

and diagnostic criteria, the social impact of these illnesses is considerable, taking into account their high prevalence [1,2,4] and typical course, often ending in disablement [12].

Aggregated research concerning the pathophysiology of CMI has suggested that an aberrant function of centrally mediated processes may play a significant role in initiating and/or perpetuating symptoms [13]. In line with these findings, a growing body of literature reports imbalances in nervous system functions in patients with perceived electrical hypersensitivity [14–16]. To further address this issue, we used transcranial magnetic stimulation (TMS) to measure different parameters of cortical excitability (e.g., resting and active motor threshold, intracortical inhibition, and intracortical facilitation) [17] in patients claiming to be hypersensitive to electromagnetic fields. These parameters are assumed to reflect the integrity of distinct interneuronal circuits [18] and have proven to be sensitive to the detection of dysfunctional cortical regulation associated with different neuropsychiatric diseases or personality traits [19–21]. Here, we investigated whether electrosensitive patients display altered cortical excitability as compared to population controls, indicating a potential contribution of centrally mediated dysfunctional processes to symptom formation.

Materials and methods

Parameters of cortical excitability were measured in a group of people who claim themselves to be sensitive to electromagnetic fields (subjectively electrosensitive patients; n=23) and compared to those of two control groups from a representative sample of the general population in the city of Regensburg. To recruit subjectively electrosensitive patients, an article was published in a local Regensburg newspaper reporting on the study and its objectives. People who perceived themselves as electrosensitive after reading this article were invited to participate in the study. Inclusion criteria for patients with subjective electrohypersensitivity were as follows: age between 18 and 64 years and articulation of serious complaints limiting activities of daily living. Complaints were subjectively interpreted as caused by explicitly named sources of electromagnetic fields (e.g., mobile phone base stations, TV towers, etc.).

Cortical excitability parameters were measured subsequent to initial determination of individual subjective perception levels using magnetic stimuli [22]. For various reasons (e.g., refusal to give informed consent), not all probands participated in the subsequent determination of cortical excitability. Therefore, study groups are slightly smaller in the present study than in a previously published perception experiment [22].

Population controls were recruited according to their level of unspecific health complaints, which they had reported during a prior health survey [23]. In order to maximize differences in the complaint level of the two control groups, they were measured on a Rasch conform list of 36 unspecific health symptoms, which all had been alleged in the literature to be potentially related to electromagnetic field exposure. The most frequently reported symptoms encompassed fatigue, daytime sleepiness, headache, problems in concentrating, and neck pain. Latent class and latent trait analyses revealed that all symptoms, despite their heterogeneity concerning affected organ systems, measured all the same latent psychological traits [24]. Complaint scores range from 0 (*no complaints at all*) to a theoretical maximum of 108 (*all 36 symptoms experienced in maximum intensity*). One control group stemmed from the upper decile of that sample displaying a high symptom load (high complaint level; n=23), whereas the second control group stemmed from the lowest decile with virtually no complaints (low complaint level; n=26; for details in study group recruitment and for a complete list of unspecific health complaints, see Frick et al. [22]). Mean scores in Table 1 reflect the prevalence of symptoms during the last 7 days prior to paired-pulse experiment.

Two population control groups with maximized differences concerning their levels of health complaints were chosen in order to gain maximum statistical power for potential differences in variables causing these

Table 1
Demographic characteristics and cortical excitability parameters

	Subjectively electrosensitive patients (n=23)		High-complaint-level group (n=23)		Low-complaint-level group (n=26)	
Age (years)	41.3±12.1		47.2±13.8		44.4±13.9	
Gender (male/female)	6/17		5/18		20/6	
Major depression	1/23		12/23		0	
Generalized anxiety disorder	1/23		1/23		0	
Somatoform disorder (SOMS)	0		1/23		0	
Complaint score (last 7 days)	10.9 (7.7)		16.7 (6.7)		4.5 (5.6)	
ISI (ms)	Male (n=6)	Female (n=17)	Male (n=5)	Female (n=18)	Male (n=20)	Female (n=6)
2	0.62±0.3	0.77±0.3	0.83±0.3	0.52±0.3	0.70±0.2	0.61±0.3
6	1.10±0.2	1.10±0.2	1.54±0.4	1.13±0.3	1.09±0.2	1.09±0.3
15	1.10±0.2	1.14±0.6	1.61±0.1	1.40±0.4	1.23±0.2	1.46±0.5

Demographic characteristics of subjectively electrosensitive patients and control groups, as well as parameters of cortical excitability, comorbidity rates, and Rasch scores of health complaints. Data are presented as mean±S.D.

health complaints (e.g., degree of electrosensitivity) and to minimize potential confounding factors due to the selection of an artificially "healthy" sample [25]. In order to differentiate electrosensitivity from somatoform disorders, the German standardized interview Screening für somatoforme Störungen (SOMS; screening for somatoform disorders) [26], a validated self-questionnaire, was applied. Major depression and anxiety disorders were assessed with the Composite International Diagnostic Interview, Short Form (CIDI-SF) [27]. The study was approved by the local ethics committee. Written informed consent was obtained from all participants.

Experimental procedure

Resting and active motor thresholds representing parameters of cortical excitability were measured by TMS, according to Rossini et al. [28]. In detail, this procedure was performed using two Magstim 200 stimulators (Magstim Co., Whiteland, Dyfed, UK) connected via a Bistim module to a figure-of-eight coil (a double-circular 70-mm coil). The coil was held in optimal position (i.e., with the junction of two wings tangential to the skull and with the handle pointing backwards and ~45° away from the midline). Thus, induced current in the brain was directed about perpendicular to the assumed line of the central sulcus. We recorded motor-evoked potentials (MEPs) from the right abductor digiti minimi at rest using surface electrodes in a belly-tendon montage (filters, 20 Hz–10 kHz; A/D rate, 5 kHz). MEP amplitudes were measured peak to peak. Fifty milliseconds of prestimulus electromyogram (EMG) were recorded to assess muscle relaxation. With a slightly suprathreshold stimulus intensity, the optimal position for eliciting maximal amplitude MEPs was determined and marked to ensure constant coil placement throughout the experiment.

Reducing the stimulus intensity in steps of 1%, we defined resting motor threshold as the lowest intensity at which at least 5 of 10 consecutive MEPs were ≥50 μV in amplitude while the investigated muscle was at rest. Audiovisual electromyographic feedback was provided to control for muscle relaxation. Active motor threshold was determined as the lowest stimulation intensity that evoked an MEP≥250 μV during voluntary abduction of the small finger in at least 5 of 10 consecutive trials. A constant level of voluntary contraction was maintained by audiovisual feedback of EMG activity. Intracortical inhibition and facilitation were measured with a paired-pulse TMS protocol [17]. The intensity of the first (conditioning) stimulus was 10% below the active motor threshold. The second (test) stimulus was delivered at an intensity that produced MEPs of about 1 mV in the resting adductor digiti minimi muscle. Interstimulus intervals (ISIs) of 1–5 ms allow to measure aspects of intracortical inhibition, while ISIs of 7–30 ms allow to determine aspects of intracortical facilitation. Here, we used ISIs of 2, 6, and 15 ms, with each interval at least 10 times in random order. The interval between sweeps was 4 s. The effect of conditioning stimuli on MEP amplitude at each ISI was determined as the ratio of the average amplitude of conditioned MEP (cMEP) to the average amplitude of unconditioned test MEP (MEP) for each 10-trial block. MEPs were digitally recorded and analyzed with the program Vision Analyzer (Brain Products, Germany).

Statistical analysis

Statistical analyses of recorded MEP ratios were performed by an analysis of covariance model using two between-subjects factors (gender with two levels; group membership with three levels: subjectively electrosensitive patients, controls with low complaint level, and controls with high complaint level) and a within-subject factor for the three ISI times. Additionally, a contrast analysis comparing the subjectively electrosensitive group to the pooled low-complaint-level and high-complaint-level groups (population controls) was planned a priori. Gender was introduced as a between-subjects factor in order to control for uneven gender distribution over comparison groups (with males dominating the low-complaint-level group). Due to the exploratory character of this study, P values are given without adjustment for multiple testing. Calculations were performed with SAS module PROC GLM.

Results

All participants tolerated the study without any side effects. Demographic characteristics of the study population, as well as TMS parameters and Rasch scores of health complaints, are shown in Table 1. Among the low-complaint-level control group, no psychiatric comorbidity could be observed. From the high-complaint-level control group, 12 subjects fulfilled the criteria for major depression, with one subject also qualifying for anxiety disorder and somatoform disorder (according to the SOMS) [29]. With regard to the subjectively electrosensitive group, one subject qualified for generalized anxiety disorder and major depression according to the criteria of the WHO CIDI-SF [27].

Average resting and active motor thresholds did not show significant differences between the three study groups, as has been reported elsewhere [22]. With regard to measures of intracortical inhibition, mean levels of inhibition and facilitation were found to be very similar at ISI times of 2 and 6 ms over all three groups. All three groups displayed the typical gradient of increasing facilitation with prolonged ISI intervals. But at an ISI time of 15 ms, there was significantly reduced facilitation, especially for the group of subjectively electrosensitive patients (Group×ISI Time interaction: F=2.48; df=4, 128; P=.047; Table 1 and Fig. 1). Further comparison of this effect by means of a t test contrasting the high-complaint-level group plus the low-complaint-level

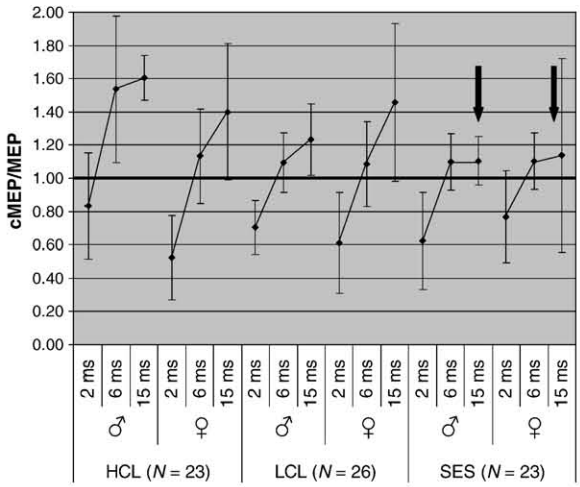

Fig. 1. Cortical excitability according to study group and gender. Note that, in the group of subjectively electrosensitive patients (SES), intracortical facilitation given as the cMEP/unconditioned MEP ratio at an ISI of 15 ms is significantly reduced compared to that in both control groups (HCL=high complaint level; LCL=low complaint level). Arrows indicate significantly decreased intracortical facilitation of SES compared to that in control groups. Values are given as mean±S.D.

group with the subjectively electrosensitive group revealed that the ISI time of 15 ms remained statistically significant, resulting in a t value of 2.38 (df=70; P=.0255). Statistical differences were more pronounced between the high-complaint-level group and the subjectively electrosensitive group than between the low-complaint-level group and the subjectively electrosensitive group.

Gender did not directly influence intracortical excitability but could be shown to interact with group membership (interaction: F=6.54; df=1, 64; P=.003). In the low-complaint-level group and the subjectively electrosensitive group, both genders displayed a very similar gradient of their ISI Time×Facilitation Gradient, but in the high-complaint-level group, this gradient differed somewhat between males and females. As this effect was not a priori in the center of our study design and might be associated with gender-specific illnesses causing the high-complaint-level in this special group, it will not be further discussed and will only be regarded as a statistical adjustment procedure to control for gender-specific influences on the diminished facilitation observed in subjectively electrosensitive patients.

Discussion

To the best of our knowledge, the results of this study give initial evidence that subjectively electrosensitive patients differ from the general population in terms of their cortical excitability parameters. In detail, the main finding is that patients with perceived electromagnetic hypersensitivity displayed an altered cortical excitability indexed by a significantly reduced intracortical facilitation as compared to two control groups, while all other measured parameters of cortical excitability (i.e., resting and active motor threshold, intracortical inhibition) remained unaffected. Comparing patients with two distinct control groups differing in their levels of unspecific health complaints is thought to minimize potential sources of sampling bias due to a rigorous screening process focusing on artificially "healthy" control samples [21,25].

Aspects of cortical excitability are reflected by distinct electrophysiological parameters, such as motor threshold, intracortical inhibition, or intracortical facilitation. Each of these parameters can be attributed to different neuronal circuits and neurotransmitter systems and is modulated in a distinct way by various neuropsychiatric diseases [19,20]. Here we exclusively found changes in intracortical facilitation in subjectively electrosensitive patients, while all other measured parameters of cortical excitability were unaffected. Intracortical facilitation reflects the involvement of intracortical mechanisms and can be modulated by a variety of central-acting agents affecting distinct neurotransmitter systems, preferentially including glutamatergic ones [30,31]. Accumulating data based on a growing body of literature suggest that increase in intracortical facilitation may be associated with an increase in neuroplasticity, whereas lower neuronal excitability as reflected by reduced intracortical facilitation results in attenuation of neuroplastic changes and adaptation abilities [32,33]. Due to these findings, it is tempting to hypothesize that diminished intracortical facilitation, as demonstrated in our sample of subjectively electrosensitive patients, may reflect dysfunctional cortical regulation related to a deficiency in adaptive resources, which might account for a higher vulnerability of these patients to environmental influences. In line with our findings, predisposition to environmental maladaptation has been postulated by several studies as a characteristic feature of subjectively electrosensitive patients [14–16]. Part of this centrally mediated predisposition, as indicated by our TMS measures, might also contribute to an impaired ability of subjectively electrosensitive patients to discriminate exteroceptive sensory inputs from internal perceptions, finally leading to false-positive results in perception experiments [22]. Based on our results, we cannot postulate a causal relationship between alterations of cortical excitability (i.e., reduced intracortical facilitation) and symptom formation. However, considering that our neurobiological findings suggest attenuation of neuroplastic changes and adaptation, these data may indicate a neurobiological predisposition to higher vulnerability for environmental influences. In analogy to current neurobiological conceptualizations with regard to the pathophysiology of somatoform pain symptoms [34], neurobiological predisposition, together with miscellaneous intrapersonal and external factors, may contribute to symptom formation in electrosensitive patients. Assuming that reduced adaptive capacities may play a pivotal role in electrosensitivity, as suggested by our neurophysiological data, cognitive–behavioral therapy may increase the amount of adaptive resources, thus enabling

patients to better deal with environmental stressors. This hypothesis is in line with findings demonstrating that cognitive–behavioral therapy leads to substantial clinical improvement in these patients [35–37].

Moreover, we do not know whether changes in cortical excitability reflect a genuine unspecific dysfunctional processing that is potentially associated with diminished adaptive capacities or reflect a specific vulnerability to the exposition of electromagnetic fields produced by devices such as mobile phones. This issue should be addressed in further studies investigating whether cortical excitability is differently modulated by electromagnetic field exposure in subjectively electrosensitive patients as compared to healthy controls. Interestingly, electromagnetic field exposure has recently been shown to modulate cortical excitability in healthy volunteers as measured by TMS [38].

Previous studies demonstrated that cortical excitability, as detected by TMS, correlates with cortical regulation and specific behavioral traits [21]. In line with these findings, our results suggest that subjectively electrosensitive patients are characterized by a distinct neurophysiological pattern, which is quite different from that of subjects with anxiety-related personality traits [21]. Additional support for this finding comes from recent studies demonstrating that diseases primarily related to CMI and probably encompassing syndromes such as subjective electrosensitivity only show a modest link to classical psychiatric disorders [11]. With regard to our study, only two subjects fulfilled the criteria of major depression or anxiety disorder, strongly suggesting that alterations in cortical excitability in subjectively electrosensitive patients do not result from the additive presence of psychiatric diseases. These findings further point to the limits of clinically and phenomenologically based classification strategies in recruiting homogenous samples of subjectively electrosensitive patients and may also explain why most provocation studies failed to demonstrate any consistent results (for recent reviews, see Rubin et al. [8] and Seitz et al. [39]).

Nevertheless, the results of our study have still to be interpreted with caution since the sample size is limited and, as a consequence, the potential effect size might not be estimated very precisely. Potential confounding effects of gender differences between study groups have been adjusted for in the analysis of variance model. However, to overcome aforementioned limitations, replication in a larger sample is necessary in order to confirm these preliminary results. Moreover, in future studies, functional imaging may help to visualize our neurophysiological data and may contribute to further investigation of which specific brain areas are engaged in mediating vulnerability to electromagnetic fields.

Taken together, our study gives further evidence that TMS is a useful tool to elucidate alterations in cortical processing underlying different diseases and behavioral traits. In this context, we could demonstrate for the first time that subjectively electrosensitive patients display changes of centrally mediated processes indicated by reduced intracortical facilitation, which may contribute to symptom manifestation.

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ORIGINAL ARTICLE

Cognitive and neurobiological alterations in electromagnetic hypersensitive patients: results of a case-control study

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Background. Hypersensitivity to electromagnetic fields (EMF) is frequently claimed to be linked to a variety of non-specific somatic and neuropsychological complaints. Whereas provocation studies often failed to demonstrate a causal relationship between EMF exposure and symptom formation, recent studies point to a complex interplay of neurophysiological and cognitive alterations contributing to symptom manifestation in electromagnetic hypersensitive patients (EHS). However, these studies have examined only small sample sizes or have focused on selected aspects. Therefore this study examined in the largest sample of EHS EMF-specific cognitive correlates, discrimination ability and neurobiological parameters in order to get further insight into the pathophysiology of electromagnetic hypersensitivity.

Method. In a case-control design 89 EHS and 107 age- and gender-matched controls were included in the study. Health status and EMF-specific cognitions were evaluated using standardized questionnaires. Perception thresholds following single transcranial magnetic stimulation (TMS) pulses to the dorsolateral prefrontal cortex were determined using a standardized blinded measurement protocol. Cortical excitability parameters were measured by TMS.

Results. Discrimination ability was significantly reduced in EHS (only 40% of the EHS but 60% of the controls felt no sensation under sham stimulation during the complete series), whereas the perception thresholds for real magnetic pulses were comparable in both groups (median 21% *versus* 24% of maximum pulse intensity). Intra-cortical facilitation was decreased in younger and increased in older EHS. In addition, typical EMF-related cognitions (aspects of rumination, symptom intolerance, vulnerability and stabilizing self-esteem) specifically differentiated EHS from their controls.

Conclusions. These results demonstrate significant cognitive and neurobiological alterations pointing to a higher genuine individual vulnerability of electromagnetic hypersensitive patients.

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Key words: Chronic multisymptom illnesses, dysfunctional cognitions, electromagnetic hypersensitivity, intra-cortical facilitation, transcranial magnetic stimulation.

Introduction

Due to the use of diverse electronic equipment, electromagnetic fields (EMF) have become almost omnipresent in modern societies. In recent years, a variety of unspecific health complaints has been reported by patients alleged to be caused by exposure to EMF. These complaints encompass somatic (e.g. skin or gastrointestinal disturbances) and neurasthenic (e.g. fatigue, concentration difficulties, sleep disturbances) symptoms (Levallois, 2002). Especially radiation from mobile phones and their base stations are frequently thought to cause these complaints and are suspected to be harmful. In contrast, a considerable body of epidemiological (Feychting *et al.* 2005) as well as experimental studies (Rubin *et al.* 2005) have not been able to establish a clear causal relationship between these symptoms and the exposure. The use of the term 'electromagnetic hypersensitivity' for this syndrome is widespread despite its lacking nosological substantiation. The importance of this syndrome is reflected by its considerable prevalence in western communities, which has been estimated at up to 3% (Hillert *et al.* 2002; Levallois *et al.* 2002) with a high rate of disablement among affected patients (Stenberg *et al.* 2002).

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Exhibit 56

Hence, better understanding of the pathophysiology of this syndrome should help to identify the underlying processes.

From a clinical point of view, many features of electromagnetic hypersensitive patients resemble and overlap with chronic fatigue or other syndromes of environmental intolerances such as 'multiple chemical sensitivity' or 'sick building syndrome' (Barsky & Borus, 1999). Symptoms are unspecific, fluctuating and no clear trigger can be found. Higher dysfunctional cognitive processes such as anticipation and mis-attribution seem to play important roles in symptom generation and maintenance in these diseases (Harlacher & Schahn, 1998; Barsky & Borus, 1999). In a number of other psychiatric diseases such as major depression or somatoform disorders, specific cognitive correlates have already been identified and were successfully incorporated in respective psychotherapy models for these disorders. Based on these findings, the first intervention studies using cognitive behavioural therapy were able to show clinical improvement in patients with electromagnetic hypersensitivity (Hillert *et al*. 1998). Detecting the neurobiological correlates of cognitive disturbances linked to electromagnetic hypersensitivity may improve therapeutic interventions.

On a neurobiological level, the first evidence for an alteration of cortical functioning as one potential neurobiological correlate of symptom manifestation in these patients has been found recently by measuring cortical excitability using transcranial magnetic stimulation (TMS; Landgrebe *et al*. 2007). These data point to deficiencies in adaptive abilities due to alterations of glutamatergic neurotransmission via *N*-methyl-D-aspartic acid (NMDA) receptors. In close accordance with these findings, recent work has emphasized high vulnerability against environmental stressors, especially affecting the autonomous nervous system in patients with electromagnetic hypersensitivity (Lyskov *et al*. 2001; Sandstrom *et al*. 2003).

Taken together, the pathophysiology of electromagnetic hypersensitivity seems to be much more complex than a simple somatic reaction to exposure to EMF. Instead, it appears that symptom generation might result from a complex interplay of intra-individual factors (e.g. behavioural traits, cognitive strategies, vulnerability of the nervous system function, genetic background) and environmental factors (e.g. stress, EMF exposure). However, the extent to which these factors are involved in the pathogenesis of electromagnetic hypersensitivity remains largely unknown. Therefore, this study combines for the first time the assessment of individual cognitive strategies, the ability to perceive EMF, the level of complaints, as well as the neurobiological characterization with TMS in order to achieve further insights into the complex pathophysiology of electromagnetic hypersensitivity.

Method

Study design and population sample

This study used a case-control design comparing subjects claiming to be electromagnetic hypersensitive with a sample of age- and gender-matched controls who were living in the same close vicinity or working at the same workplace in a comparable position (1:2 matching if the patient was working, 1:1 if not working). Matching location of private domicile and workplace should minimize potential influences of environmental physical and social stressors.

Inclusion criteria for electromagnetic hypersensitive patients were: (1) a symptom load of at least 19 points on the 'Regensburger EMF-complaint list' (Frick *et al*. 2006) which corresponds to the 4-weeks complaint level of the upper one-third in the general population; (2) attribution of the health symptoms experienced to named electromagnetic emission sources (e.g. mobile phone base stations, hotspots, etc); (3) aged 18–75 years. Exclusion criteria encompassed all obstacles for TMS measurements (e.g. cranial metal implants, cardiac pacemakers, etc.). No further exclusion criteria were used. Subjects with concomitant psychiatric or internal diseases were not excluded from the study except in the case of an unstable medical condition.

Patients were recruited by newspaper announcements or informative events at various public locations such as public health offices, university buildings, etc. Altogether, a total of 135 patients were interested in participating, of which 101 patients were eligible according to the above-mentioned criteria. Twelve subjects withdrew from the study, when informed about the measurement procedures. Thus, 89 cases and 107 controls (living place 65 subjects, workplace 42 subjects) were enrolled into the study. Patients and controls stemmed from small-sized Bavarian cities (Regensburg, Weiden, Straubing, Neumarkt, Landshut, Kempten) and Austrian cities (Feldkirchen, Klagenfurt). Due to mostly technical reasons (e.g. patient living without comparable neighbours or lacking a colleague of the same gender and age), no regular matching pattern could be realized and two employed and six unemployed patients remained without a control subject. Therefore the statistical approach treated cases and controls as independent samples, which means a more conservative approach to detect differences between the two groups. As age and gender were not exactly balanced,

these two variables were introduced as statistical covariates for most of the analyses.

Before starting the study, sample-size calculations (nQuery 3.0 software; Statistical Solutions, Saugus, MA, USA) using data from a pilot study (Landgrebe *et al*. 2007) had revealed that to detect a difference of 9 points on the major study endpoint (discriminative ability) with a power of 90% and restricting type I error risk to 5% required the enrolment of two study groups of 90 subjects each.

Assessment of sociodemographic data, medical history and EMF-specific cognitive strategies

Sociodemographic data and medical history of all study participants were collected using a structured interview. Sleep quality was measured with the Pittsburgh Sleep Quality Index (PSQI; Buysse *et al*. 1989). In order to distinguish electromagnetic hypersensitivity from somatoform disorders, the German standardized interview Screening For Somatoform Disorders (SOMS; Rief *et al*. 1997) was applied. Major depression and anxiety disorders were assessed using the short-form of the World Health Organization Composite International Diagnostic Interview (CIDI-SF; Nelson *et al*. 2001). Qualitative interviews with electromagnetic hypersensitive patients from an earlier pilot study (Frick *et al*. 2004) on subjects' self-experience as 'electromagnetic hypersensitives' were used to construct a 42-item questionnaire assessing cognitive aspects of their health status. Items among others covered aspects of rumination, tendency to externalize potential causes of bodily sensations, symptom catastrophizing, distrust in orthodox medicine, stabilizing self-esteem from the symptoms experienced, perceived vulnerability, and intolerance of bodily complaints.

Determination of perception thresholds and cortical excitability by TMS

Individual perception thresholds were determined according to Frick *et al*. (2005). In order to enrol patients and controls from a larger regional background, transportable TMS equipment was used (MagPro magnetic stimulator X100 including MagOption; Medtronic, Copenhagen, Denmark). The perception experiment was conducted with both the test person and the rater, who gave all instructions and was kept blind with respect to the stimulus protocol throughout the experiment. The stimulating physician used two optically identical stimulation coils (real: MCF-B65; sham: MCF-P-B65) placed over the left dorsolateral prefrontal cortex, stood behind the test person and therefore could not be seen by the test person. The rater increased stimulating intensities in steps of 3%, ranging from 0% to 57% of the maximum stimulator output (~1.8 T). Test persons were not informed about the increasing pulse intensities, but knew that each pulse had a 50% probability of representing a real magnetic stimulus or to be only an acoustic click without an accompanying magnetic pulse. After each applied stimulus the participants were asked whether they felt any kind of sensation. After two consecutive positive responses the lower value was recorded as the perception threshold of this series and the stimulation condition was changed without informing the test person on the altered mode of stimulation. In the case of no sensory perception during the whole series of 19 pulses with the same coil, a right-censored threshold value of 57% was recorded. Four series of real and sham stimulation were applied in individually randomized ABAB *versus* BABA design. All test persons (except one from the electromagnetic hypersensitive group who withdrew his informed consent after the structured interview before beginning the perception experiment) completed the whole perception experiment.

Following the perception experiment, parameters of cortical excitability [i.e. active and resting motor thresholds (RMT), intra-cortical inhibition (ICI) and intra-cortical facilitation (ICF) and cortical silent period] were determined according to Rossini *et al*. (1994). In brief, motor-evoked potentials (MEP) were measured from the right abductor digiti minimi muscle (ADM) using surface electrodes in a belly-tendon-montage connected to an EMG (filters: 20 Hz to 3 kHz; Keypoint, Medtronic, Copenhagen, Denmark). MEP amplitudes were measured peak to peak. To assess muscle relaxation, 50 ms of prestimulus EMG were recorded. With a slightly suprathreshold stimulus intensity, the optimal position for eliciting maximal amplitude MEP was determined and marked to ensure constant coil placement throughout the experiment. Reducing the stimulus intensity in steps of 1%, we defined the RMT as the lowest intensity at which at least five of 10 consecutive MEP were $\geqslant 50\,\mu$V in amplitude while the investigated muscle was at rest. Audio-visual electromyographic feedback was provided to control for muscle relaxation. Active motor threshold was determined as the lowest stimulation intensity that evoked an MEP $\geqslant 250\,\mu$V in at least five of 10 consecutive trials during voluntary abduction of the ADM muscle.

ICI and ICF were measured using the paired-pulse TMS protocol (Kujirai *et al*. 1993; Ziemann *et al*. 1996). The intensity of the first (conditioning) stimulus was set at 80% of RMT. The second (test) stimulus was delivered at an intensity that produced MEP of ~1 mV in the resting ADM. Interstimulus intervals of 2 and 15 ms were tested, each interval at least 10 times.

The interval between sweeps was 4 s. The effect of conditioning stimuli on MEP amplitude at each interstimulus interval was determined as the ratio of the average amplitude of the conditioned MEP to the average amplitude of the unconditioned test MEP (cMEP : MEP) for each 10-trial block. MEP were digitally recorded and analysed with the software VISION ANALYSER (Brain Products GmbH, Gilching, Germany). The cortical silent period was recorded according to Moll *et al*. (2001) using a stimulation intensity of 150% RMT.

The study protocol was approved by the local ethics committee. Written informed consent was obtained from every subject prior to study enrolment.

Statistical analysis

The major study endpoint for the perception experiment was the ability of the subjects to discriminate between a real magnetic stimulation and a sham condition. This was measured by subtracting the recorded threshold of the real magnetic pulse condition from the threshold of the sham condition in the original series 1 and 2 and in the repeating conditions 3 and 4. Higher values of the δ variables indicate a better competence of differentiating between both conditions. Using right-censored thresholds (e.g. in the sham condition, when a subject expressed no sensation throughout the whole series) to calculate the signal–noise distance gives a lower limit for the ability of the respective subject to differentiate between the two conditions. The procedure chosen thus is conservative for detecting group differences.

The statistical analysis was *a priori* defined as an analysis of covariance (ANCOVA) with two between-subjects factors: grouping factor 1 represents the differences between electromagnetic hypersensitive subjects and their controls; grouping factor 2 represents the randomization scheme ABAB or BABA for applying the real and sham coil (two levels). Female gender (0/1) and age were introduced as linear covariates. A repeated-measurement factor (signal–noise distance in the first two series *versus* the last two series) controls for potential learning effects throughout the experiment: did subjects profit during series 3 and 4 from their experiences during the first two series? The statistical test for the between-subjects factor 'electromagnetic hypersensitives *versus* controls' was considered the confirmatory test of the experiment. All analyses of variance were performed using SAS procedure GLM (SAS Institute Inc., Cary, NC, USA).

Differences between electromagnetic hypersensitive subjects and controls with respect to dysfunctional cognitions could have been assessed using a series of *t* tests with group membership as the classifying variable and each of the 37 items as a separate dependent variable. Beside from problems due to inflation of type I error risk, this approach would also not contribute to restrict the interpretation of potential cognitive differences to the most important aspects, because intercorrelations of items are not adjusted for. Therefore we chose a multivariate logistic regression approach with group membership as the dichotomously measured 'dependent' variable and items of the questionnaire as potential predictor variables. Logistic regression was favoured over discriminant analysis (which offers an alternative) because of fewer statistical assumptions and (in our case) a better misclassification behaviour of the approach.

Group differences in health status variables with heavily skewed distribution (e.g. sick days) were tested using the non-parametric Mann–Whitney *U* test. Comparison of rates in cross-tabulations was accomplished using χ^2 tests or, in case of cells with expected frequencies below value 5, using Fisher's exact test.

Results

Sociodemographic description of study groups

Details of sociodemographic characteristics are shown in Table 1. The study groups did not differ with respect to age and education. Due to the matching rule of this study (one control from the surroundings of the private domicile, irrespective of the control's employment situation, and one additional and necessarily employed control from the working situation, if the index person was employed his/herself), clearly the proportion of employed controls was higher than that of electromagnetic hypersensitives.

No significant differences were found in body mass index and smoking behaviour. Perceived health status, sick days and doctoral visits during the last year, as well as subjective sleep quality measured by the PSQI, were all less favourably reported by the electromagnetic hypersensitive group. The EMF-specific health complaint score was about three times higher in the group of electromagnetic hypersensitive patients, and psychiatric co-morbidity could be shown to be more prevalent in the same group with regard to major depression, generalized anxiety disorder and somatoform disorder. Concomitant internal medical conditions were rare and comparable in both groups (five subjects in the electromagnetic hypersensitive group and three subjects in the control group). Taken together, data indicate poorer health conditions in the group of electromagnetic hypersensitive patients as compared with controls.

Table 1. *Sociodemographic data and psychiatric co-morbidity of EHS and controls*

	EHS ($n=89$)	Controls ($n=107$)	Differences	
			Statistical test	p
Age (years)	50.5(10.9)	49.0(11.1)		
Proportion females (%)	58.4	62.6		
Education (%)				
Elementary	31.5	42.1	χ^2	0.322
Medium	32.6	26.2		
Highest	34.8	31.8		
Others	1.1	0		
Employment situation (%)				
Full time	37.1	46.7	χ^2	0.047
Part time work	18.0	25.2		
No paid work	44.9	28.0		
Body mass index (kg/m²)	24.8 (4.0)	25.1 (3.9)	Mann–Whitney	N.S.
Perceived health status (1 = excellent; 5 = bad)	3.3 (0.8)	2.7 (0.8)	Mann–Whitney	<0.001
Time sick last year (days)	21.7 (44.4)	11.9 (37.0)	Mann–Whitney	0.013
Doctoral visits last year	18.6 (16.0)	9.4 (10.5)	t test	<0.0001
Subjective sleep quality (PSQI)	9.1 (3.2)	6.6 (2.4)	Mann–Whitney	<0.001
EMF complaint score	47.5 (21.0)	15.6 (15.0)	Mann–Whitney	<0.001
Non-smoker (%)	52.8	53.3	χ^2	N.S.
Major depression (%)	23.6	8.4	χ^2	0.0033
Generalized anxiety disorder (%)	5.6	0	Fisher's exact test	0.0181
Somatoform disorder (%)	10.1	0	Fisher's exact test	<0.001

EHS, Electromagnetic hypersensitive patients; N.S., non-significant; PSQI, Pittsburgh Sleep Quality Index; EMF, electromagnetic fields.

Values are given as mean (standard deviation) or proportion.

Assessment of cognitive strategies

Five items of the questionnaire on cognitions assess potential advantages drawn from the self-characterizationas being 'electromagnetic hypersensitive'. For the obvious reason that the 'non-electromagnetic hypersensitives' could not answer those items, no comparisons could be made for this subscale. Thus in a first step the remaining 37 items were explored by univariate t tests for differences between electromagnetic hypersensitives and controls. All items covering aspects of perceived vulnerability, of rumination with health complaints, and distrust in orthodox medicine were found to differ between the two groups. None of the items assessing the tendency to externalize potential causes of bodily complaints or symptom catastrophizing, and only one item of 14 covering a broad range of cognitions related to stabilizing one's self-esteem from being electromagnetic hypersensitive could be shown to differ between the two groups (not shown).

In a second step of analysis, a stepwise logistic regression procedure was performed on the group membership exploring all 37 items and additionally the time (in min) that it had taken the respondents to fill out the screening instrument (Regensburg EMF-complaint list). Table 2 summarizes the six items that significantly predicted group membership in a parsimonious statistical model with a sensitivity of 84% and a specificity of 70% at the function value = 0.5 of the logistic regression function variable.

Determination of perception thresholds

After the structured interview, one electromagnetic hypersensitive patient withdrew his informed consent. Therefore, only 88 patients underwent TMS measurements. Table 3 summarizes the results of the perception experiment of all four series by group and experimental condition. Fig. 1 illustrates the proportion of subjects (pooled over four series) not experiencing a sensation throughout the experiment as a function of the increasing pulse intensity (i.e. as a function of waiting time in the case of sham exposure). As censored data occurred, a Kaplan–Meier estimate

Table 2. *Cognitions separating 'electromagnetic hypersensitives' from controls*[a]

	Estimate	Error	χ^2	p (χ^2)[b]	Odds ratio
Intercept	6.8595	1.3012	27.79	<0.0001	
Time (min) for completing the EMF-complaint questionnaire	−0.5190	0.1457	12.6880	<0.001	
Variable[c]					
Stabilizing self-esteem					
To be electrosensitive, for me has the implication that:					
I'm different from others	−0.7821	0.2331	11.2524	<0.001	0.457
I'm sharing a big portion of burden	0.6617	0.2351	7.9230	0.0049	1.938
I have to care for myself more intensively than others	0.4785	0.2269	4.4491	0.0349	1.614
Rumination					
I'm reflecting quite a lot on (my) electrosensitivity	−1.2076	0.2332	26.8157	<0.0001	0.299
Intolerance against physical symptoms; vulnerability					
Suffering from unexpected complaints, I usually observe them for a while before I react	−0.4710	0.2300	4.1924	0.0406	0.624
I avoid heavier duties to save my strength	−0.8569	0.3133	7.4811	0.0062	0.424

EMF, Electromagnetic fields.

[a] Together with the time to complete the questionnaire, the shown six items (variables) from a 37-item questionnaire give the most parsimonious statistical model to separate 'electromagnetic hypersensitives' from controls.

[b] The probability modelled is that for membership in the control group.

[c] All items were coded from 1 (=disagree) to 4 (=strongly agree).

Table 3. *Measured perception thresholds*[a] *by group and experimental condition*

Group	n	Experimental condition	Threshold	Experimental condition	Threshold	Discrimination ability
		1st Series		2nd Series		
EHS	46	Real	25.0 (15.8)	Sham	33.1 (21.4)	8.2 (16.8)
	42	Sham	36.4 (22.9)	Real	23.3 (17.3)	13.1 (23.9)
	88	Total	29.8 (19.3)	Total	27.9 (19.3)	10.5 (20.5)
Controls	52	Real	32.0 (16.2)	Sham	39.0 (22.8)	7.0 (23.9)
	53	Sham	49.4 (15.8)	Real	29.3 (16.3)	20.1 (15.9)
	105	Total	39.7 (17.2)	Total	33.3 (19.5)	13.6 (21.2)
Total	98	Real	28.7 (16.3)	Sham	36.2 (22.2)	7.5 (20.8)
	95	Sham	43.6 (20.2)	Real	26.6 (16.9)	17.0 (20.0)
	193	Total	36.1 (19.7)	Total	31.5 (20.3)	12.2 (20.9)
		3rd Series		4th Series		
EHS	46	Real	21.4 (16.4)	Sham	26.7 (24.0)	5.3 (18.2)
	42	Sham	36.5 (23.1)	Real	19.7 (14.2)	16.8 (23.0)
	88	Total	28.0 (20.3)	Total	22.9 (19.3)	10.8 (21.3)
Controls	52	Real	22.7 (16.3)	Sham	36.5 (23.0)	13.8 (20.8)
	53	Sham	46.9 (18.3)	Real	26.8 (14.8)	20.2 (15.0)
	105	Total	33.9 (20.0)	Total	31.0 (19.1)	17.0 (18.3)
Total	98	Real	22.1 (16.3)	Sham	31.9 (23.9)	9.8 (20.0)
	95	Sham	42.3 (21.1)	Real	23.7 (14.9)	18.7 (18.9)
	193	Total	32.1 (21.3)	Total	27.9 (20.3)	14.2 (19.9)

EHS, Electromagnetic hypersensitive patients.

Values are given as mean (standard deviation).

[a] Perception threshold given as % maximum stimulator output.

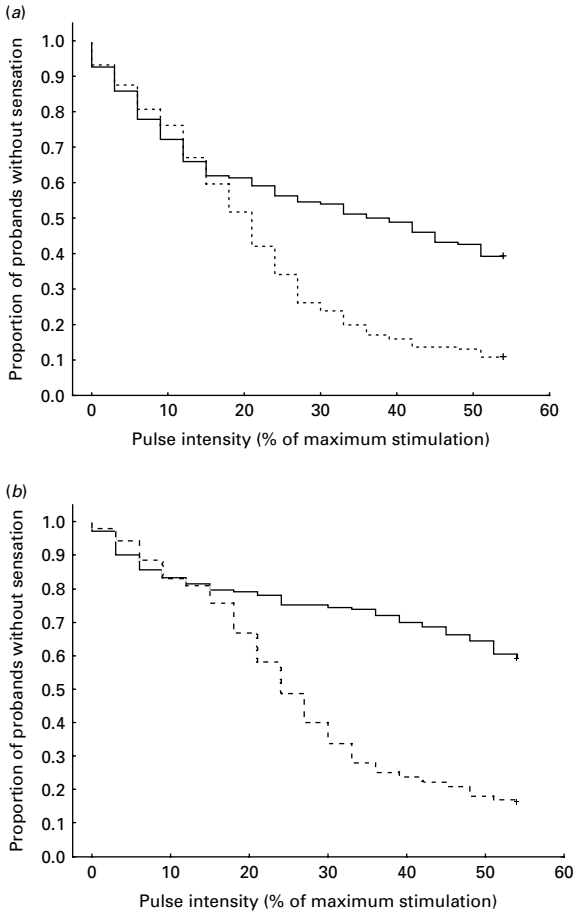

Fig. 1. Sensory perception as a function of pulse intensities. With increasing ordinal number of pulses given, fewer subjects remain who had no sensation. In the case of transcranial magnetic stimulation (- - -), order numbers of pulses correspond to an increase of 3% of the maximum power of the magnetic stimulator. Sham (——) pulses order numbers were projected to the same scale. All four sequential series determining the perception threshold were pooled. (*a*) Electromagnetic hypersensitives (four series pooled) ($n=88$). (*b*) Controls (four series pooled) ($n=107$).

of the survivor function was chosen. As can be seen, only 40% of the electromagnetic hypersensitive group, but more than 60% of the controls felt consistently no sensation throughout the complete sham series of 19 clicks. The median of the perception threshold under transcranial stimulation is comparable between both groups (21% *v.* 24% of the maximum stimulator output).

Electromagnetic hypersensitive patients displayed a diminished ability [$F(1,186)=6.77$, $p=0.01$] to discriminate the two conditions as compared with their controls [$\text{mean}_{\text{series}\,1+2}=10.5$ (S.D. $=20.5$) *v.* 13.6 (S.D. $=21.2$), $\text{mean}_{\text{series}\,3+4}=10.8$ (S.D. $=21.3$) *v.* 17.0 (S.D. 18.3)]. Discriminative ability was also significantly influenced by age ($F=9.25$, $p=0.0027$), gender ($F=7.45$, $p=0.0070$) and sequence (ABAB *versus* BABA) of the four series ($F=13.95$, $p=0.0002$). If the perception experiment started with a series of sham magnetic stimuli, discriminating sham and magnetic pulses was easier for all test persons. Age exerted a negative impact on discriminative ability: the older, the less accurately could subjects discriminate the two experimental conditions. But this effect was partly compensated in the group of electromagnetic hypersensitives (F for interaction $=5.18$, $p=0.024$). Here, older subjects were not worse in discriminating than younger test persons. There were no significant learning effects or interactions of the learning condition with any of the between-subjects variables.

Table 4. *Parameters of cortical excitability of EHS and controls*

	EHS ($n=88$)	Control ($n=105$)
MT (% stimulator output)	38.7 (8.1)	37.4 (7.8)
AT (% stimulator output)	29.5 (7.0)	29.3 (7.3)
ICI (cMEP:MEP ratio)	0.53 (0.35)	0.56 (0.32)
ICF (cMEP:MEP ratio)	1.90 (1.25)	1.96 (1.0)
CSP (ms)	0.139 (0.03)	0.143 (0.037)

EHS, Electromagnetic hypersensitive patients; MT, resting motor threshold; AT, active motor threshold; ICI, intra-cortical inhibition; cMEP, conditioned motor evoked potential; MEP, unconditioned motor evoked potential; ICF, intra-cortical facilitation; CSP, cortical silent period.

Values are given as mean (standard deviation).

Cortical excitability

Parameters of cortical excitability were measured subsequently to the perception experiment and are depicted in Table 4. Resting and active motor thresholds (both F values for group differences <1, N.S.) as well as the cortical silent period ($F=2.62$, $p=0.1075$) did not differ significantly between study groups even after adjusting for age and gender. However, women ($F=4.82$, $p=0.0294$) and older volunteers ($F=4.36$, $p=0.0381$) displayed higher active thresholds in both study groups as compared with men and younger volunteers, respectively.

With respect to ICI and ICF, results of the ANCOVA model were not straightforward, because group differences, age and the intra-individual inhibition–facilitation gradient interacted in a complex manner. There were small but significant differences between study groups (main effect) with less inhibition and more facilitation for controls (ratios below and above 1 are slightly higher in the control group: $F=4.92$, $p=0.0278$, see Table 4). A powerful main effect could

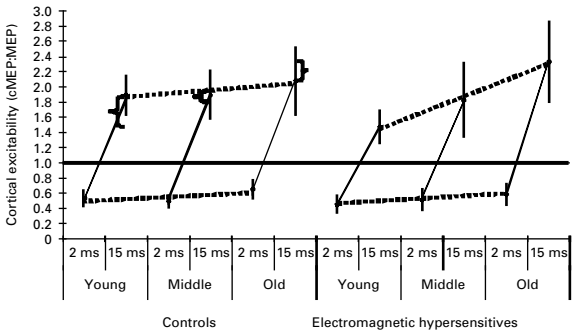

Fig. 2. Cortical excitability of electromagnetic hypersensitive patients (EHS) and controls depicted in equally sized age classes (young, <45 years; middle, 45–54 years; old, ⩾55 years). Intra-cortical inhibition (ICI) results from an interstimulus interval of 2 ms; intra-cortical facilitation (ICF) results from an interstimulus interval of 15 ms. Cortical excitability is expressed as the ratio of conditioned motor-evoked potentials to unconditioned motor-evoked potentials (cMEP:MEP). Age effects on ICI and ICF are shown (- - -). Bracketing indicates significant interaction effects of age and group: ICF is reduced in young and middle-aged EHS and increased in old EHS compared with controls.

be found for age in the form of decreasing inhibition and increasing facilitation in older age groups (see Fig. 2). The intra-individual gradients of inhibition–facilitation as a function of the interstimulus interval were dependent on subjects' ages (F for interaction = 5.09, $p = 0.0253$) and group membership (F for interaction = 4.39, $p = 0.0374$). Age and group as two significant between-subjects main effects also had a two-way interaction ($F = 4.22$, $p = 0.0414$). Finally, a three-way interaction of gradient × group × age proved significant ($F = 4.14$, $p = 0.0433$). Gender had neither a direct nor an indirect impact on this situation. In order to interpret this complex interplay, Fig. 2 visualizes the results with age given in three equally sized classes (<45 years, 45–54 years and ⩾55 years).

Discussion

This study examined a large sample of electromagnetic hypersensitive patients on their individual ability to perceive EMF along with their individual symptom load and possible disposing factors on a cognitive and neurobiological level. Results of a pilot study could be replicated and extended. It could be shown that electromagnetic hypersensitive patients (1) exhibit specific dysfunctional cognitive strategies, (2) do have a lower ability to discriminate real from sham magnetic stimuli as compared with controls, and (3) show alterations in their cortical excitability.

Psychiatric co-morbidity and health status

Major depression, generalized anxiety disorder, and somatoform disorder have been observed significantly more often among electromagnetic hypersensitive patients than controls according to the used screening instruments (CIDI-SF, SOMS). This fact has also been demonstrated in other samples of electromagnetic hypersensitive patients (Bergdahl & Bergdahl, 2001) as well as in other functional somatic syndromes such as multiple chemical sensitivity (Bornschein *et al*. 2002). Although the electromagnetic hypersensitive patients show many characteristics of a somatoform disorder [e.g. chronic disease, many fluctuating symptoms not explained by a physical illness, increased rumination according to the International Classification of Diseases (ICD)-10], interestingly only about 10% fulfilled the criteria of a somatoform disorder according to the SOMS. This fact illustrates the difficulty of standardized diagnosis of these atypical somatoform disorders using operational screening instruments. However, the found neurobiological alterations (see below) can at present not improve differential diagnosis of these diseases.

The significantly worse health status and the higher rate of sick days and doctoral visits during the last year point to the high morbidity of electromagnetic hypersensitives. Furthermore, the high prevalence of electromagnetic hypersensitivity along with increased utilization of the health system underlines the economic impact of this syndrome. Compared with other somatoform disorders, recognizing and effectively treating these patients (e.g. with early interventions with cognitive behavioural therapy) might help to reduce these costs and improve their health status (Hiller *et al*. 2003; Bleichhardt *et al*. 2004).

Dysfunctional cognitions

The structured interview including questionnaires to assess the individual health status and specific beliefs regarding danger and health impact of EMF revealed differences in cognitions between electromagnetic hypersensitive patients and controls. A number of items from the subscale on 'stabilization of self-esteem' contributed significantly to the prediction of group membership. The items describe the feeling of being special because of EMF, and therefore serve to stabilize self-esteem. In addition, corresponding to the findings on somatoform disorders, items covering vulnerability and intolerance against physical symptoms differed between the two groups. This can be explained by 'somatosensory amplification' (Barsky & Borus, 1999) which may play a pivotal role in symptom generation in electromagnetic hypersensitive patients. According to this pathophysiological

concept, the increased awareness of any kind of somatic disturbances may lead to further attention to physiological somatic reactions and increased self-observance. As a consequence, this leads to a hyper-arousal resulting in further enhancement of these physiological reactions, which has been observed with various methods in electromagnetic hypersensitive patients (Lyskov *et al*. 2001; Sandstrom *et al*. 2003). This vicious cycle may finally lead to an impairment of the patient to separate internal perceptions from external stimuli. One may assume that this is one of the potential reasons for the decreased performance of the electromagnetic hypersensitive patients in our perception experiment. As a consequence, cognitive behavioural therapeutic approaches aiming at interfering with these processes should result in both improving health status and better performance in the perception experiment. This fact should be addressed in future studies. Furthermore, the differences reported in our investigation concerning increased rumination, measured by a specific item along with a larger amount of time electromagnetic hypersensitive patients needed to complete the questionnaire, further underline the importance of dysfunctional cognitions for the maintenance of electromagnetic hypersensitivity (Harlacher & Schahn, 1998), which has also been shown in other functional somatic illnesses (Bailer *et al*. 2007). In line with these concepts, especially cognitive behavioural therapeutic approaches appeared to be effective in electromagnetic hypersensitive patients (Hillert *et al*. 1998; Rubin *et al*. 2006).

Alterations of cortical excitability

In agreement with the findings of the pilot study (Landgrebe *et al*. 2007), the paired-pulse experiment again revealed a significant alteration of cortical excitability in electromagnetic hypersensitive patients. In young and middle-aged patients, ICF was significantly reduced compared with controls, thereby confirming our earlier results. All other parameters of cortical excitability as measured by TMS did not differ between both groups. In the elderly patient group, however, ICF was increased compared with controls; this is a new finding that was not observed in the pilot study probably due to a different age range of 18 to 65 years in the former study. Data from other studies yield conflicting results regarding the influence of age on cortical excitability (Peinemann *et al*. 2001; Wassermann, 2002). One potential explanation for these differences may be that the relative amount of ICI and ICF depends on the different physical properties of the used magnetic stimulators (i.e. Medtronic™ *versus* Magstim™; monophasic *versus* biphasic pulses; see Kammer *et al*. 2001; Peinemann *et al*. 2001). Nevertheless, in both our pilot study (using Magstim devices) and the current study (using Medtronic devices), electromagnetic hypersensitive patients differed significantly from healthy controls with respect to ICF.

Until now, the contribution of altered cortical excitability reflected by changes in ICF to symptom generation in people suffering from electromagnetic hypersensitivity is unclear. Possibly, it is just another hint for an increasingly irritable nervous system function in these patients (Lyskov *et al*. 2001; Sandstrom *et al*. 2003). On the other side, alterations in ICF may play a more specific role in symptom generation in this syndrome. ICF measured with TMS mainly reflects intra-cortical, NMDA-glutamatergic neurotransmission and was discussed with regard to adaptation abilities of the individual (Liepert *et al*. 1997; Schwenkreis *et al*. 1999). Based on this theoretical framework, changes in ICF may indicate dysfunctional cortical processes, which may lead to reduced adaptation abilities of these individuals. However, the link between altered neurobiological parameters and dysfunctional cognitive strategies and the health complaints in electromagnetic hypersensitive patients is far from being clear. Furthermore, it remains to be elucidated whether the alterations of cortical excitability reported here represent state or trait characteristics. Intervention studies using cognitive behavioural approaches together with measurement of cortical excitability parameters will be able to answer these questions.

Interestingly, Ferreri *et al*. (2006) recently found significant increases in ICF in young healthy controls during and after 45 min exposure to mobile phone radiation, thereby demonstrating that measuring cortical excitability with TMS seems to be a promising approach to assess the impact of EMF exposure on central nervous system function. However, only healthy test persons and no electromagnetic hypersensitive patients were measured in that study. Although Ferreri *et al*. found the opposite effect as compared with our results (increase of ICF while here we found a decrease in that age group), ICF seems to be a sensitive marker, which is influenced by EMF exposure. The discrepancy with our data is probably due to the differences in the study design with respect to study populations and exposure settings. In the study by Ferreri *et al*. (2006), the effect of an acute exposure (mobile phone exposure for 45 min) on cortical excitability was measured with TMS in a healthy, non-electromagnetic hypersensitive population to test the acute effect of EMF exposure on cortical excitability. In contrast, our study compared cortical excitability of electromagnetic hypersensitive patients with healthy controls without acute, short-time exposure to test whether electromagnetic hypersensitivity is associated

with alterations in cortical excitability. In both studies, long-term exposure levels to EMF have not been assessed and no evidence exists that electromagnetic hypersensitivity is associated with increased long-term exposure. As pointed out, in our study only electromagnetic hypersensitive patients showed changes in ICF, which argues in favour of a possible genuine neurobiological vulnerability of electromagnetic hypersensitive patients for EMF. Owing to our study design, we cannot exclude that long-term exposure to EMF together with an increased individual vulnerability may lead to symptom formation in these patients. Future studies should therefore focus on the topic of whether electromagnetic hypersensitive patients demonstrate differential changes in cortical excitability during acute mobile phone radiation exposure as compared with controls, thereby extending the findings of Ferreri *et al*. (2006). Furthermore, it would be of interest whether other functional somatic diseases such as multichemical sensitivity or other chronic somatoform disorders (e.g. chronic pain) may show changes of cortical excitability similar to changes in our study population. For diagnostic reasons, however, alterations of cortical excitability will be insufficient to distinguish electromagnetic hypersensitivity from other similar conditions, since the pathophysiological relevance of the changes are at present largely unknown. However, corresponding alterations in cortical excitability may further point to common pathophysiological mechanisms of these disease entities and may give further evidence for the 'single syndrome hypothesis' (Ciccone & Natelson, 2003). Including also a control group from this disease entity such as multiple chemical sensitivity into this study was not possible, because the focus of this study was to replicate the initial findings of neurobiological alterations in the pilot study.

Taken together, we found in the up-to-date largest sample of electromagnetic hypersensitive patients significant differences on a cognitive (tendency to increased rumination and intolerance against physical symptoms) and neurobiological (altered ICF) level, pointing to a greater genuine individual vulnerability. This fact along with miscellaneous environmental influences may lead to the generation of symptoms in patients with electromagnetic hypersensitivity. Due to the study design it cannot be ruled out that along with a genuine vulnerability, long-term exposure to EMF may promote the exacerbation of electromagnetic hypersensitivity. But other stressors with ubiquitous prevalence in modern societies could serve as triggers as well. This question should be addressed in future studies. Furthermore, TMS has been proven to be a useful tool in characterizing somatoform disorders on a neurobiological level. The relevance of TMS parameters for diagnosing other somatoform disorders should be proven in the future.

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Declaration of Interest

None.

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Dirty Electricity Elevates Blood Sugar Among Electrically Sensitive Diabetics and May Explain Brittle Diabetes

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Transient electromagnetic fields (dirty electricity), in the kilohertz range on electrical wiring, may be contributing to elevated blood sugar levels among diabetics and pre-diabetics. By closely following plasma glucose levels in four Type 1 and Type 2 diabetics, we find that they responded directly to the amount of dirty electricity in their environment. In an electromagnetically clean environment, Type 1 diabetics require less insulin and Type 2 diabetics have lower levels of plasma glucose. Dirty electricity, generated by electronic equipment and wireless devices, is ubiquitous in the environment. Exercise on a treadmill, which produces dirty electricity, increases plasma glucose. These findings may explain why brittle diabetics have difficulty regulating blood sugar. Based on estimates of people who suffer from symptoms of electrical hypersensitivity (3–35%), as many as 5–60 million diabetics worldwide may be affected. Exposure to electromagnetic pollution in its various forms may account for higher plasma glucose levels and may contribute to the misdiagnosis of diabetes. Reducing exposure to electromagnetic pollution by avoidance or with specially designed GS filters may enable some diabetics to better regulate their blood sugar with less medication and borderline or pre-diabetics to remain non diabetic longer.

Keywords Radio frequency; Transients; Dirty electricity; Power quality; Plasma glucose; Blood sugar; Insulin; GS filters; Electrohypersensitivity; Brittle diabetes; Type 3 diabetes; Type 2 diabetes; Type 1 diabetes.

Introduction

Diabetes mellitus is increasing globally. According to the World Health Organization, in 1985 the global population of diabetics was 30 million (0.6% of the world population). This increased to 171 million (2.8% of the global population) by 2000, and it is expected to more than double to 366 million (4.5% of the global population) by 2030 (Wild et al., 2004; U.S. Census Bureau, 2005). Doctors attribute this rise in diabetes to poor diet and limited exercise, resulting in obesity, and seldom look for causes other than lifestyle and genetics.

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This article presents a paradigm shift in the way we think about diabetes. In addition to Type 1 diabetics, who produce insufficient insulin, and Type 2 diabetics, who are unable to effectively use the insulin they produce, a third type of diabetes may be environmentally exacerbated or induced by exposure to electromagnetic frequencies.

Our increasing reliance on electronic devices and wireless technology is contributing to an unprecedented increase in our exposure to a broad range of electromagnetic frequencies, in urban and rural environments and in both developed and developing countries. This energy is generated within the home by computers, plasma televisions, energy efficient lighting and appliances, dimmer switches, cordless phones, and wireless routers, and it can enter the home and work environment from nearby cell phone and broadcast antennas as well as through ground current.

Although the position of most international health authorities, including the World Health Organization, is that this form of energy is benign as long as levels remain below guidelines, an increasing number of scientific studies report biological and health effects associated with electromagnetic pollution well below these guidelines (Sage and Carpenter, 2007). Epidemiological studies have documented increased risks for childhood leukemia associated with residential magnetic fields exposure (Ahlbom et al., 2000), greater risk for various cancers with occupational exposure to low-frequency electric and magnetic fields (Havas, 2000), miscarriages (Li et al., 2002), Lou Gehrig's disease (Neutra et al., 2002), brain tumors associated with cell phone use (Kundi et al., 2004), as well as cancers and symptoms of electrical hypersensitivity (EHS) for people living near cell phone and broadcast antennas (Altpeter et al., 1995; Michelozzi et al., 2002). Laboratory studies report increased proliferation of human breast cancer cells (Liburdy et al., 1993), single- and double-strand DNA breaks (Lai and Singh, 2005), increased permeability of the blood brain barrier (Royal Society of Canada, 1999), changes in calcium flux (Blackman et al., 1985), and changes in ornithine decarboxylase activity (Salford et al., 1994).

In this article, changes in plasma glucose, in response to electromagnetic pollution, for numerous measurements on four subjects—two with Type 1 diabetes taking insulin and two non medicated with Type 2 diabetes—are described. They include men and women, ranging in age from 12–80, as well as individuals recently diagnosed and those living with the disease for decades.

Case 1: 51-Year Old Male with Type 2 Diabetes

A 51-year old male with Type 2 diabetes, taking no medication, monitored his plasma glucose levels from April 24 to May 30, 2003. He also monitored the dirty electricity in his home using a Protek 506 Digital Multimeter connected to a ubiquitous filter (Graham, 2000) to remove the 60-Hz signal and its harmonics. Measurements were taken in the morning and randomly throughout the day. Low or no readings of dirty electricity were taken in an electromagnetic clean environment far from power lines and cell phone antennas (Fig. 1 upper graph). Three years later, the microsurge meter became available and Case 1 monitored his blood sugar levels once more (Fig. 1 lower graph). This meter provides a digital readout of the absolute changing voltage as a function of time ($|dv/dt|$, expressed as GS units) for the frequency range 4–100 kHz and with an accuracy of $\pm 5\%$ (Graham, 2003).

Figure 1 shows a positive correlation between dirty electricity and plasma glucose levels taken randomly during the day (upper graph) and first thing in the morning (lower graph). His elevated plasma glucose is unrelated to eating. Working

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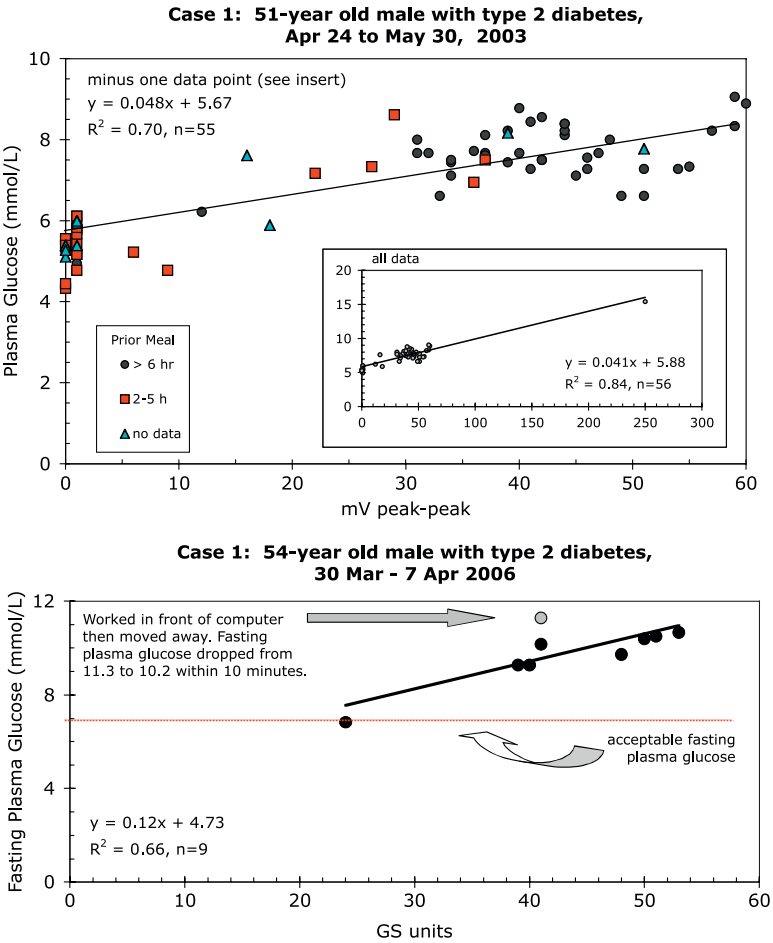

Figure 1. Case 1: *Upper chart*: Plasma glucose levels of a 51-year old male with Type 2 diabetes exposed to different levels of power quality. Insert shows the entire data set with one very high plasma glucose reading that was recorded during a period of high exposure to dirty electricity. *Lower chart*: Three years later, fasting plasma glucose levels correspond to power quality measured in GS units. Time spent in front of computer resulted in higher plasma glucose levels that dropped 1.1 mmol/L [19.8 mg/dL] 10 min after moving away from computer. Note that we have scaled both plots the say way in Fig. 1.

on a computer increases blood sugar, but these values decrease as much as 0.11 mmol/L* [2 mg/dL] per minute after moving away from the computer. Blood viscosity decreased as his plasma glucose levels dropped.

Case 1 also documented rapid changes in blood sugar as he moved from a medical clinic (environment with dirty electricity), to his parked vehicle (no dirty electricity), and back to the medical clinic. His blood sugar levels changed significantly within 20 min. His endocrinologist classified him as *pre-diabetic* when his blood sugar was tested immediately upon entering the medical clinic and as a *Type 2 diabetic* after a 20-min wait in the medical clinic. Measurement of blood sugar needs

*Multiply by 18 to convert to mg/dL.

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to be done in an electromagnetically clean environment to prevent misdiagnosis and to accurately determine the severity of the disease.

Case 2: 57-Year Old Female with Type 2 Diabetes

A 57-year old female with Type 2 diabetes takes no medication and controls her plasma glucose with exercise and a hypoglycemic diet. When she exercised by walking for 20–30 min at a mall after hours, her blood sugar levels dropped from a mean of 11.8 to 7.2 mmol/L [212 to 130 mg/dL] ($p = 0.045$). When she walked on a treadmill, her blood sugar levels increased from 10 to 11.7 mmol/L [180 to 211 mg/dL] ($p = 0.058$) (Fig. 2). Treadmills have variable speed motors and produce dirty electricity.

Doctors recommend exercise for patients with diabetes. However, if that exercise is done in an electromagnetically dirty environment, and if the patient is sensitive to this form of energy, it may increase stress on the body and elevate levels of plasma glucose, as in Case 2.

This subject also measured her plasma glucose as she moved from an environment with dirty electricity to one that was clean, and back again. Her blood sugar in the dirty environment was 12.5 mmol/L [225 mg/dL] and within 20 min in the clean environment dropped to 10.6 mmol/L [191 mg/dL]. Within 5 min after returning to the dirty environment, her blood sugar rose to 10.8 mmol/L [194 mg/dL] and 15 min later to 12.6 mmol/L [227 mg/dL]. She did not eat or exercise during this period. Her elevated plasma glucose levels were associated with headaches, nausea, and joint pain in her home, where she was exposed to both dirty electricity and radio frequency radiation from nearby cell phone antennas. These exposures and symptoms were absent in the clean environment.

Case 3: 80-Year Old Female with Type 1 Diabetes

An 80-year old female with Type 1 diabetes, who takes insulin (Humlin® 70/30) twice daily, documented her blood sugar levels before breakfast and before dinner

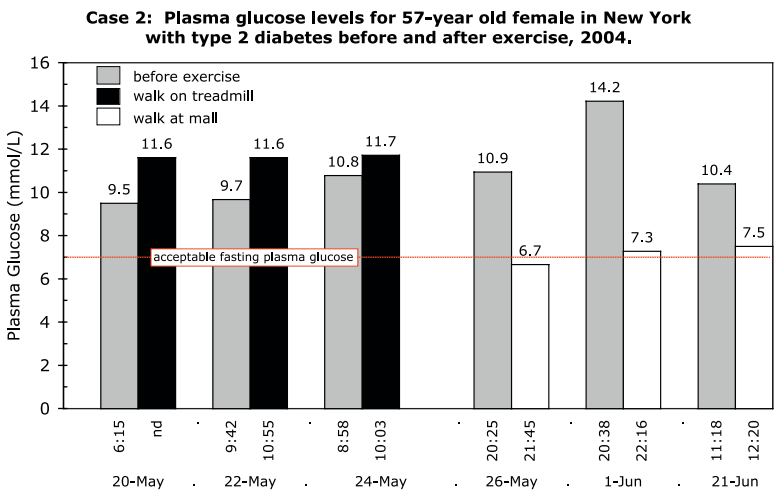

Figure 2. Case 2: Plasma glucose levels for a 57-year old female in New York with Type 2 diabetes, before and after walking for 20–30 min on a treadmill in her home and after hours at a mall.

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for one week. On June 12, 2004, the dirty electricity in her home was reduced from an average of 1,550 GS units (range: 600 to > 2,000) to 13 GS units (range 11 to 22) with Graham/Stetzer filters (GS filters). These filters provide a short to high frequency, and, thus, reduce transients on electrical wiring with an optimal filtering capacity between 4 and 100 kHz (Graham, 2000, 2002, 2003). They are similar to capacitors installed by industry to protect sensitive electronic equipment from power surges and to adjust the power factor. GS units measure the energy associated with dirty electricity (amplitude and frequency) and are a function of changing voltage with time (dv/dt). Dirty electricity can be measured using an oscilloscope or multimeter set for peak-to-peak voltage or a Microsurge meter that provides a digital readout (GS units) and is easily used by non professionals.

Case 3 had mean fasting plasma glucose of 9.5 mmol/L [171 mg/dL] without the GS filters and 6.6 mmol/L [119 mg/dL] with the GS filters ($p = 0.02$) (Table 1). Her evening blood sugar did not change appreciable during this period, although it did differ on days she was away from home. She was able to more than halve her insulin intake ($p = 0.03$) once the GS filters reduced the dirty electricity in her home (Table 1).

Table 1

Case 3: Plasma glucose levels and daily insulin injections (Humulin® 70/30) for an 80-year old woman with Type 1 diabetes before and while GS filters were installed in her home in Arizona

	Plasma Glucose (mg/dL)		
Date 2004	Morning (7 am)	Evening (5 pm)	Daily Insulin (units)
Without GS Filters: Dirty Electricity 1,550 GS units			
June 5	158	239●	56
June 6	158	167	56
June 7	160	113●	56
June 8	180	104	0
June 9	180	144	56
June 10	151	76	56
June 11	116	229	28
Mean (sd)	171 (20)	153 (63)	44 (22)
With GS Filters: Dirty Electricity 13 GS units (installed June 12)			
June 13	86	194	0
June 14	140	94	25
June 15	115	178	0
June 16	112	135	15
June 17	131	175	20
June 18	167	250●	50
June 19	70	169	22
June 20	133	126	22
Mean (sd)	119 (31)	166 (49)	19 (16)
2-tailed *t*-test	$p = 0.002$**	$p = 0.69$	$p = 0.03$*

●Subject was away from home during the day.

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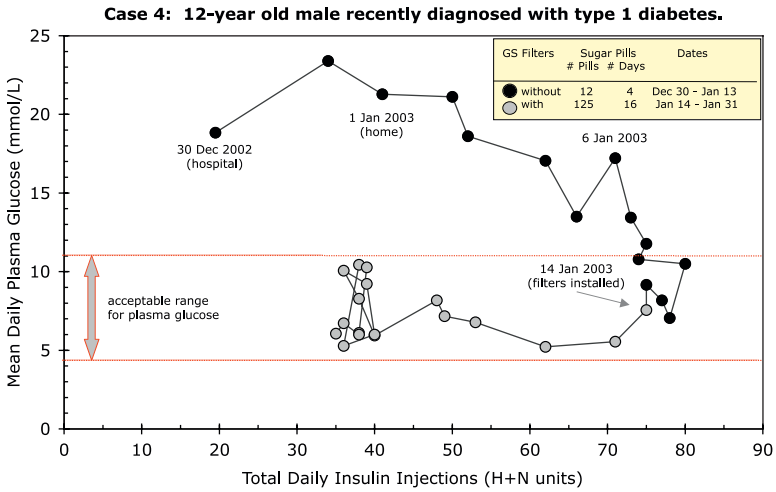

Figure 3. Case 4: Sequence of mean daily plasma glucose levels and total daily insulin injections for 12-year old male with Type 1 diabetes who was admitted to hospital in December 2002 and returned home on January 1, 2003. On January 14, 2003, GS filters were installed in his home to improve power quality.

Case 4: 12-Year Old Male with Type 1 Diabetes

A mother and her 5 children, who were all home schooled, began to develop intermittent, excruciating headaches during the fall of 2002 in rural Wisconsin, shortly after they had a new septic system installed. The headaches continued and a power quality expert measured high levels of dirty electricity and ground current, possibly attributable to the septic system installation.

In December 2002, one child, a 12-year old male, was hospitalized and diagnosed with Type 1 diabetes. His younger sister had been living with diabetes since the age of 3 months and was one of the youngest children diagnosed with diabetes in the United States.

On January 14, 2003, the family installed GS filters to help alleviate their symptoms of electrical hypersensitivity. The headaches disappeared and the family's health began to improve. Shortly after the GS filters were installed, the mother had great difficulty controlling her son's blood sugar. She couldn't reduce the amount of insulin fast enough to keep it within an acceptable range and needed to give him sugar pills to prevent hypoglycemia (Fig. 3). He was taking a combination of Humalog® (H-insulin, a short-acting insulin) and Humulin® NRT (N-insulin, a long-lasting insulin).[1] During this period, her daughter's blood sugar levels began to drop as well.

Doctors attribute the short-term improvement in blood sugar to the "honeymoon period", which is observed among some diabetics shortly after diagnosis and lasts from weeks to months and occasionally for years (Bernstein, 2003). The honeymoon period cannot explain the response of the subject's sister, who had been living with Type 1 diabetes for years, and who also had lower plasma glucose levels

[1]Both the short-acting Humalog® (H-insulin) and the long-lasting Humulin® NPH (N-insulin) are produced by Eli Lilly.

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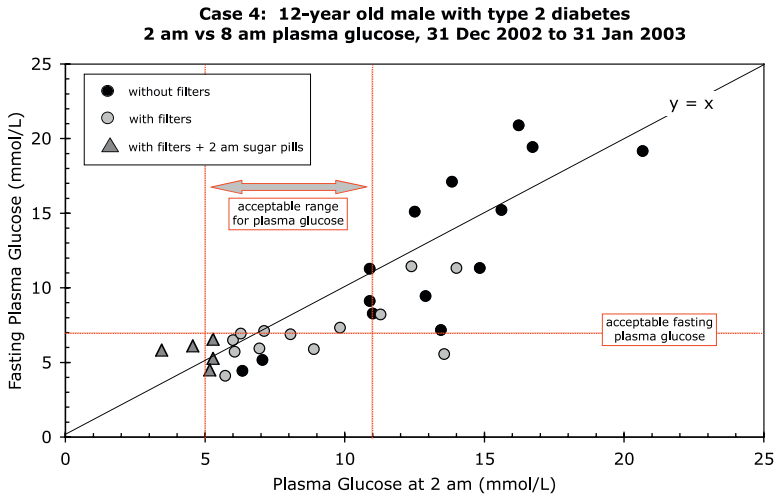

Figure 4. Case 4: Fasting (8 am) and 2 am plasma glucose levels for 12-year old male with Type 1 diabetes with and without GS filters. NOTE: Sugar pills were administered at 2 am for 5 d to prevent hypoglycemia while filters were installed.

and difficulty regulating her insulin within an acceptable range after the GS filters were installed and the dirty electricity was reduced.

Case 4 had higher levels of plasma glucose at 8 am (fasting) than at 2 am on some days before the GS filters were installed. This was not observed with the filters, except when sugar pills were taken at 2 am to deliberately increase blood sugar (Fig. 4). In Wisconsin, dirty electricity often increases in the middle of the night, beginning at 2–3 am and lasting from minutes to hours, as the electric utility makes changes in its system.

Discussion

These results show that plasma glucose levels, in the Type 1 and Type 2 diabetic cases reported, respond to electromagnetic pollution in the form of radio frequencies in the kHz range associated with indoor wiring (dirty electricity). Type 1 diabetics require less insulin in an electromagnetically clean environment and blood sugar levels for Type 2 diabetics increase with increasing exposure to dirty electricity.

In May 2006, a long-term health care facility in Ontario, Canada installed GS filters to reduce dirty electricity. Of the five diabetic residents, for whom data were available, two (aged 87 and 88) were insulin-dependent Type 1 diabetics. Both had significantly lower fasting plasma glucose levels ($p < 0.01$) after the GS filters were installed. Their insulin intake did not change during this period and nursing staff had to give them orange juice on several occasions to prevent hypoglycemia. The levels of plasma glucose of the remaining three, who were Type 2 diabetics, did not change during this period.

The GS filters, used in this study have been tested at the Yoyogi Natural Clinic in Japan (Sogabe, 2006). Three people participated in the study. Three hours after eating, their blood sugar was 6.3, 7.7, 17.9 mmol/L [113, 139, and 322 mg/dL] in an

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environment with more than 2,000 GS units of dirty electricity. GS filters reduced the dirty electricity to 30–35 GS units and, within 30 min, their plasma became less viscous and their blood sugar dropped to 5.6, 6.1, 16.1 mmol/L [101, 110, 290 mg/dL], respectively.

The person with the highest plasma glucose levels was a 28-year old male with Type 2 diabetes and fasting plasma glucose levels of 16.7 mmol/L [300 mg/dL]. Despite taking 250 mg of Glycoran®, 3 times a day, and 12 mg of Amaryl®, spread throughout the day, he still had difficultly regulating his blood sugar. Three days after installing 4 GS filters in his home, his blood sugar dropped to 6.9 mmol/L [124 mg/dL] and he was feeling well. He had been unable to achieve such low values with medication alone.

In this study, we classify diabetics whose blood sugar responds to electromagnetic pollution as Type 3 diabetics. In contrast to true Type 1 diabetics who produce insufficient insulin and true Type 2 diabetics who are unable to effectively use the insulin they produce, Type 3 diabetics are responding to environmental triggers that affect blood sugar readings and blood viscosity. These individuals may be better able to regulate plasma glucose by controlling their exposure to frequencies in the low RF range, and thus differ from true Type 1 and Type 2 diabetics whose blood sugar is not affected by this type of electromagnetic exposure.

The increase in blood viscosity with increasing exposure to dirty electricity is a critical observation. If this turns out to be the case among electrosensitive individuals, it may explain the symptoms of headaches, chest pain, higher blood pressure, blurred vision, and fatigue.

The percentage of diabetics who are likely to be affected by electromagnetic energy is unknown, but if the values are similar to those suffering from symptoms of electromagnetic hypersensitivity (EHS), 3–35% of the population (Philips and Philips, 2006), then globally between 5 and 60 million existing diabetics may have Type 3 diabetes as described in this study.

There is a growing body of *in vivo*, *in vitro*, and epidemiological evidence, which suggests a relationship between plasma glucose levels, insulin secretion, and exposure to electromagnetic energy at frequencies both lower and higher than the ones we tested in this study.

Altpeter et al. (1995) reported that for people living within a 2 km radius of a short-wave transmitter, in Schwarzenburg, Switzerland, the odds ratio (OR) for diabetes was 1.93 when compared with a population further away. There was a significant linear correlation ($R^2 = 0.99$) between daily median RF exposure and incidence of diabetes. The highest RF readings, recorded in the nearest zone (51 mA/m), were well below the International Radiation Protection Agency's 1988 guidelines of 73 mA/m. Those living near the transmitter also had difficulty falling and staying asleep, were restless, experienced weakness and fatigue, and had both limb and joint pain with statistically significant odds ratios between 2.5 and 3.5. These symptoms are typical of radio wave sickness or electrical hypersensitivity (Firstenberg, 2001). Failure of the transmitter for a 3-d period was associated with improved sleep and, hence, these reactions are biological not psychological.

Beale et al. (2001) reported that the prevalence of chronic illness, asthma, and Type 2 diabetes was linearly related to 50-Hz magnetic field exposure for adults living near transmission lines. For Type 2 diabetes, the crude OR was 8.3 (95% CI 1 to 177), but the OR adjusted for possible confounders (age and ethnicity) was reduced to 6.5 and was not statistically significant ($p > 0.05$). Epidemiological

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studies of power lines tend to focus on cancers, rather than diabetes, and, hence, limited information of this type is available.

Litovitz et al. (1994) exposed diabetic subjects to 60-Hz magnetic fields between 0.2–1 μT (2–10 mG) and noticed that blood glucose levels increased above 0.6 μT. No statistical tests were reported and no attempt was made to measure frequencies other than 60 Hz. Magnetic flux densities above 0.6 μT are realistic near transmission lines and overlap with the range documented in the Beale study (2001).

Jolley et al. (1982) exposed islets of Langerhans from rabbits to low-frequency pulsed magnetic fields and noted a reduction in insulin release during glucose stimulation compared with controls ($p < 0.002$). Similarly, Navakatikyan et al. (1994) exposed rats to 50-Hz magnetic fields for 23 h per day for 11 days at 10, 50, and 250 μT. Serum insulin levels decreased at the middle- and high-flux densities, which the authors associated with stress.

Sakurai et al. (2004) measured insulin secretion from an islet derived insulinoma cell line, RIN-m, exposed to low-frequency magnetic fields of 5 mT compared with sham exposure of less than 0.5 μT. Insulin secretion was reduced by approximately 30% when exposed to low-frequency magnetic fields compared to sham exposure. The authors conclude: "it might be desirable for diabetic patients who have insufficient insulin secretion from pancreatic islets to avoid exposure to ELFMF". The magnetic flux density was exceptionally high in this experiment and is unlikely to be encountered in normal daily life. Studies of the incipient level of electromagnetic exposure, at which insulin secretion is reduced, would be useful.

Li et al. (2005) exposed hepatocytes *in vitro* to 50 Hz pulsed electric fields (0.7 V/m) and noted a conformation change in the insulin molecule and an 87% reduction in the binding capacity of insulin to its receptors compared with controls.

Stress often increases plasma glucose levels in diabetics (Hinkle and Wolf, 1950; Jolley et al., 1982). Studies with laboratory animals and *in vitro* studies with human cells show both low-frequency electromagnetic fields and non thermal RF radiation stimulates production of stress proteins, and that the biochemical reactions are the same over a range of frequencies and intensities (Blank and Goodman, 2004). Release of insulin is strongly inhibited by the stress hormone norepinephrine, which leads to increased blood glucose levels during stress. Rajendra et al. (2004) found elevated levels of norepinephrine in the brain of fertilized chick eggs on day 15 following exposure to 5, 50, and 100 μT. The "stress response" to electromagnetic energy may provide, yet, another mechanism that could explain Type 3 diabetes.

Reduced insulin secretion and reduced binding capacity of insulin to its receptors may explain the elevated levels of plasma glucose in Type 3 diabetics exposed to electromagnetic fields. More research on mechanisms is needed.

Conclusions

In addition to lifestyle and genetics, the environment appears to be another factor contributing to high levels of blood sugar. This concept presents a possible paradigm shift in the way we think about diabetes and the consequences may be far reaching. As a result, we have labeled environmental diabetes as Type 3 diabetes.

We recognize that there is, as yet, no accepted definition of Type 3 diabetes and that our definition may be in conflict with others that have been suggested including a combination of Type 1 and Type 2, gestational diabetes, and that Alzheimer's Disease is a form of diabetes (Steen et al., 2005; de la Monte et al., 2006).

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What we describe here is a totally different type in the sense it has an environmental trigger. Doctors have long suspected an environmental component but it has not been until now that one has been found.

The increasing exposure and ubiquitous nature of electromagnetic pollution may be contributing to the increasing incidence of this disease and the escalating cost of medical care. Diagnosis of diabetes needs to be done in an electromagnetically clean environment to prevent misdiagnosis, and to properly assess the severity of this disorder. Most medical centers have electronic equipment and use fluorescent lights that produce dirty electricity, which is likely to cause abnormally high blood sugar readings for those with a combination of diabetes and electrohypersensitivity (Type 3 diabetes). Dirty electricity may also explain why brittle diabetics have difficulty controlling their blood sugar levels.

Type 3 diabetes, as described in this study, is an emerging disease. Unlike true Type 1 and Type 2 diabetics whose blood sugar is not affected by dirty electricity, Type 3 diabetics may be better able to regulate their blood sugar with less medication, and those diagnosed as borderline or pre-diabetic may remain non diabetic longer by reducing their exposure to electromagnetic energy. The GS filters and the microsurge meter provide the tools needed for scientific investigation of dirty electricity and may help diabetics regulate their blood sugar by improving power quality in their home, school, and work environment. Minimizing exposure to radio frequencies (kHz to GHz), flowing along the ground or through the air, also needs to be addressed. Large-scale studies are needed in controlled settings to determine the percentage of the population with Type 3 diabetes.

These results are dramatic and warrant further investigation. If they are representative of what is happening worldwide, then electromagnetic pollution is adversely affecting the lives of millions of people.

Conflict of Interest

Please note that the author has no vested interest, financial or otherwise, in the commercial devices mentioned in this article.

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