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**Hypersensitivity to electricity;
symptoms, risk factors and
therapeutic interventions**

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ABSTRACT

Persons reporting nonspecific health complaints attributed to activated electrical equipment have been a growing concern in Sweden in the last decades. The aims of this thesis were to investigate possible risk factors (personal and work-related), symptoms, and complaints associated with reported hypersensitivity to electricity (HE) and to test hypotheses concerning possible biological mechanisms and effective treatments.

In a survey of an unselected population in Stockholm County, 1.5% of the respondents reported hypersensitivity to electric or magnetic fields. In selected populations, for example, IT companies, the proportion who reports HE may be substantially higher.

Reported HE is associated with higher prevalence of complaints with regard to symptoms, other hypersensitivities and traditional allergies and disturbances from different environmental factors, compared to groups not reporting HE. Reported asthma and hay fever were also more common in the HE group. No specific symptom constellation was identified. Persons who report HE seem to be characterized, at least in early stages, by skin complaints.

Fatigue was, except for skin complaints in the group that reported HE, the most commonly reported complaint in the HE group and in referents who did not report this syndrome. General but not physical fatigue was associated with the perceived influence of electromagnetic fields. Scores on sleep indices and sleep quality were similar in cases of HE and referents. The hypothesis that fatigue in HE might be due to a decrease in cholinesterase activity wasn't confirmed.

Persons who reported HE did not differ from referents with regard to mental well being, personal traits, anxiety or psychosocial work characteristics. Patients who reported HE scored within the normal range in questionnaires on symptom dimensions (SCL-90), alexithymia (TAS-20), attributional style (ASQ) and sense of coherence (SOC) according to the evaluation guidelines for these respective instruments.

Two interventions were evaluated. In a randomized controlled clinical trial, antioxidant supplementation wasn't shown to reduce symptoms and ill health in HE. Cognitive therapy was offered as part of a multidisciplinary team program. The prognosis of HE seems to be good in most cases, at least in case of early intervention based on a broad approach. Cognitive therapy may further reduce perceived hypersensitivity to electricity.

Clinical studies on HE have revealed that the group of persons reporting this syndrome is very heterogeneous. A multidimensional characterization (including symptom indices, belief, reported triggering factors, temporal aspects and behavior) is proposed to facilitate comparisons between study groups. Individuals who report HE seem to be suffering from an increase in ill health and report a wide range of complaints. The nature of associations and interactions between different observations and complaints isn't known. Some observations may represent risk indicators for a vulnerable group, while others may be consequences of long time suffering from ill health. Individually determined response to different kinds of stressors in everyday life is discussed. Medical, psychosocial and environmental factors of possible importance should be considered in the investigation of patients who report HE. In case of persisting symptoms, individual recommendations should be given based on this broad evaluation. More research is motivated to increase our knowledge on the background for the reported complaints and ill health.

LIST OF PUBLICATIONS

This thesis is based on the following original publications, which will be referred to by their Roman numerals (the papers are presented in logical rather than chronological order):

- I. **Hillert L**, Berglind N, Arnetz BB, Bellander T. Prevalence of self-reported hypersensitivity to electric or magnetic fields in a population-based questionnaire survey. Manuscript submitted (2001).
- II. **Hillert L**, Kolmodin Hedman B, Söderman E, Arnetz BB. Hypersensitivity to electricity: working definition and additional characterization of the syndrome. *J Psychosom Res* 1999;47:429-438.
- III. **Hillert L**, Flato S, Georgellis A, Arnetz BB, Kolmodin-Hedman B. Environmental illness: fatigue and cholinesterase activity in patients reporting hypersensitivity to electricity. *Environ Res* 2001;85:200-206.
- IV. **Hillert L**, Komodin-Hedman B, Eneroth P, Arnetz BB. The effect of supplementary antioxidant therapy in patients who report hypersensitivity to electricity: a randomized controlled trial. *MedGenMed*, March 23, 2001. Available from: URL: <http://www.medscape.com/Medscape/GeneralMedicine/journal/2001/v03.n02/mgm0323.01.hill/mgm0323.01.hill-01.html>
- V. **Hillert L**, Kolmodin Hedman B, Dölling BF, Arnetz BB. Cognitive behavioural therapy for patients with electric sensitivity - a multidisciplinary approach in a controlled study. *Psychother Psychosom* 1998;67:302-10.

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DEFINITIONS AND ABBREVIATIONS

Allergy	Hypersensitivity caused by exposure to a particular antigen (allergen) resulting in a marked increase in reactivity to that antigen upon subsequent exposure, sometimes resulting in harmful immunologic consequences.*
Bias	Deviation of results or inferences from the truth, or processes leading to such deviation.†
CI	Confidence interval (the computed interval with a given probability, e.g., 95%, that the true value of a variable such as a mean, proportion, or rate is contained within the interval).†
Disability	Any restriction or lack (resulting from an impairment) of ability to perform an activity in a manner or within the range considered normal for a human being. The term disability reflects the consequences of impairment in terms of functional performance and activity by the individual; disabilities thus represent disturbances at the level of the person.†
Disease	A disease is a disorder that can be assigned to a diagnostic category; it usually has a distinct clinical course and often a distinct etiology.†
Disorder	A disorder is a disturbance or departure from normal healthy function, e.g. of an organ or body system, i.e., an impairment.†
Handicap	A disadvantage for a given individual, resulting from an impairment or a disability, that limits or prevents the fulfillment of a role that is normal (depending on age, sex, and social and cultural practice) for that individual. The term handicap thus reflects interaction with and adaptation to the individual's surroundings.†
HE	Hypersensitivity to electricity (for further definition see section 2.2 Operational definition).
Hypersensitivity	Abnormal sensitivity, a condition in which there is an exaggerated response by the body to the stimulus of a foreign agent.*
Illness	A subjective state of the person who feels aware of not being well. †‡
N.S. (n.s.)	Not statistically significant.
Risk factor	An attribute or exposure that is associated with an increased probability of a specified outcome, such as the occurrence of a disease. Not necessarily a causal factor. A risk marker.†
SD	Standard deviation. A measure of dispersion, or variation. The mean tells where the values for a group are centered. The standard deviation is a summary of how widely dispersed the values are around this center.†
Syndrome	The aggregate of signs and symptoms considered to constitute the characteristics of a morbid entity: used especially when the cause of the condition is unknown.§

Validity	<p>V., measurements: An expression of the degree to which a measurement measures what it purports to measure. †</p> <p>V., study:</p> <p>Internal validity: The index and comparison groups are selected and compared in such a manner that the observed differences between them on the dependent variables under study may, apart from sampling error, be attributed only to the hypothesized effect under investigation. †</p> <p>External validity: A study is externally valid, or generalizable, if it can produce unbiased inferences regarding a target population (beyond the subjects in the study). †</p>
VDT	Visual display terminal (or video display terminal)
VDU	Visual display unit (or video display unit)

Cited from:

*Stedman's Medical Dictionary. 27th edition. Baltimore: Lippincott Williams & Wilkins; 2000.

†Last JM, ed. A Dictionary of Epidemiology. 4th edition. New York: Oxford University Press; 2001.

‡Susser MW. Causal thinking in the health sciences. New York: Oxford University Press, 1973.

§International Dictionary of Medicine and Biology. Vol III. New York: John Wiley & Sons; 1986.

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1 INTRODUCTION

In the beginning there was the patient. The patient who presented symptoms and complaints that he or she had come to attribute to activated electrical equipment. This patient is the background and focus of my thesis in which I have explored what might characterize this syndrome and evaluated different possible interventions to reduce ill health and functional handicap.

2 BACKGROUND

In the early 1980s reports were being published on symptoms, primarily from the skin, occurring in relation to work with visual display units (VDUs) (Lindén and Rolfsen 1981; Nilsen 1982). An epidemiological study demonstrated an increase in reported skin disorders among VDU workers (Knave 1985), but no specific skin disease or histological changes were identified (Berg et al. 1990a; Berg et al. 1990b). One research group later reported results indicating that persons with skin problems that they related to VDU work differed from healthy controls in analyses of biological markers in biopsies taken from facial skin (Johansson et al. 1996). But this study did not permit conclusions on the cause of the observed differences. A possible role of mast cells has also been discussed, but no conclusive evidence has been presented (Berg et al. 1990b; Gangi and Johansson 2000).

During the second half of the 1980s, focus was turned to a group of people who reported reactions to activated electrical equipment in general. In this group so called neurovegetative symptoms like fatigue, difficulties concentrating and headache were more pronounced (Knave et al. 1989). A self-help group was formed in Sweden and it soon grew to have some 2000 members. Surveys from labor unions later indicated that there might be more than 20 000 people suffering from hypersensitivity to electricity in Sweden (Fransson 1996). A European group of experts reported that the phenomenon was known in many countries, not only Sweden, but geographical differences were recognized in prevalence as well as in reported symptoms and attributions (Bergqvist and Vogel 1997). But no specific causal factor was identified and the condition remained a medical problem of uncertain etiology.

2.1 TERMINOLOGY

2.1.1 Hypersensitivity to electricity

The afflicted persons, based on their experience that being in the vicinity to activated electrical equipment triggered symptoms, introduced the term hypersensitivity to electricity (HE). Alternative terms have also been proposed and discussed. In Sweden, allergy to electricity, electrosensitivity and electrical sensitivity are some examples. The term allergy is not desired since it refers to specific immunological mechanisms, which, as of yet, have not been shown in HE. Hypersensitivity to electricity and electrosensitivity are used by and preferred in different groups.

The Swedish National Board of Health and Welfare suggested, in the report on health effects of electromagnetic fields from 1995, the term electrical sensitivity (“elkänslighet” in Swedish) (Socialstyrelsen 1995). The argument was that the term hyper-sensitivity implies an observed and detectable increase in sensitivity, i.e. that a person reacts to a condition or exposure that does not cause any reaction in the majority of persons. This has not been shown in controlled studies with regard to HE and electric or magnetic fields. The Swedish self-help group, the Swedish Association for the ElectroSensitive (“Elöverkänsligas Förbund” in Swedish, previously The Swedish Association for the Electrically and VDT-injured/ “Föreningen för El- och Bildskärmskadade” in Swedish) and most researchers in the field of HE have argued that “hypersensitivity” (“överkänslighet” in Swedish) is a logical choice since these people report

reactions in situations, or to exposures, which leave most people unaffected (Bergqvist et al. 2000).

Also in English speaking countries several syndrome labels are used: electrical sensitivity (Smith 1997), sensitive to electromagnetic fields (Wang et al. 1994) and electromagnetic field sensitivity (Rea et al. 1991.). The European group of experts chose the term “electromagnetic hypersensitivity” (Bergqvist and Vogel 1997).

2.1.2 Idiopathic environmental intolerances

In 1996, experts in a workshop organized by the International Programme on Chemical Safety of the World Health Organization and other organizations recommended that the name idiopathic environmental intolerances (IEI) be used to describe subjective illness attributed by the afflicted persons to numerous and varied environmental exposures (Conclusions and recommendations of a workshop on multiple chemical sensitivities (MCS) 1996). Typically these conditions lack objective diagnostic physical findings or laboratory test abnormalities that can define the illness. Multiple chemical sensitivity is one example where symptoms from several organ systems are attributed to exposure to very low doses of chemicals, far below existing reference levels. Other terms used are 20th-century disease and total allergy syndrome. Hypersensitivity to electricity may also be regarded as an example of IEI. The term idiopathic environmental intolerances was preferred since it does not make an unsupported judgement on causation.

The proposed working definition for IEI (chemical) was:

- an acquired disorder with multiple recurrent symptoms
- associated with diverse environmental factors tolerated by the majority of people
- not explained by any known medical or psychiatric/psychologic disorder.

The disease entity of IEI, or subgroups of different attributions and inflicted causal factors are still under debate (AAAAI 1999). The subjective nature of the illness does not allow an objective case definition.

2.1.3 Medically unexplained symptoms

A noncommittal descriptive name such as medically unexplained symptoms has also been suggested (Mayou 1993.). This term refers to symptoms only and does not, contrary to IEI or HE take any possible attribution made by the afflicted individuals into consideration. The term medically unexplained symptoms is neutral with regard to the origin of the symptoms as organic or psychogenic. Wessely and co-authors suggested the syndrome label functional somatic syndromes, defining a functional somatic symptom as one that, after appropriate medical assessment, cannot be explained in terms of a conventionally defined medical disease (Wessely et al. 1999). Hodgson and Kipen also pointed out the apparent resemblance among different disorders, like multiple chemical sensitivity, chronic fatigue syndrome and fibromyalgia, using the term emerging overlap syndromes (Hodgson and Kipen 1999).

Arguments can be made for all these terms. Different terms may be preferred depending on the actual situation and context, inferring a broader or more narrow definition, for example:

<i>Medically unexplained symptom</i>	all medically unexplained symptoms.
<i>IEI</i>	all medically unexplained symptoms attributed by the afflicted individuals to environmental exposure.
<i>HE</i>	all medically unexplained symptoms attributed by the afflicted individuals to environmental exposure to electric or magnetic fields or situations associated with proximity to activated electrical equipment.

As discussed above, terms including a non-proven causal factor have been criticized. One alternative would be to use IEI together with additional information on attributions that characterize certain subgroups. This is further discussed in section 7 (DISCUSSION). Since the background for this thesis is patients reporting HE the term hypersensitivity to electricity has been used in the studies (with the exception of study V) and will be used in this thesis.

2.1.4 Undifferentiated Somatoform Disorder

Theoretically, most cases of reported IEI or HE meet the criteria of undifferentiated somatoform disorder. The diagnostic criteria for undifferentiated somatoform disorder published by the American Psychiatric Association in 1994 (American Psychiatric Association [APA] 1994) are:

- A. One or more physical complaints (e.g. fatigue, loss of appetite, gastrointestinal or urinary complaints).
- B. Either (1) or (2):
 1. after appropriate investigation, the symptoms cannot be fully explained by a known general medical condition or the direct effects of a substance (e.g., a drug of abuse, a medication);
 2. when there is a related general medical condition, the physical complaints or resulting social or occupational impairment is in excess of what would be expected from the history, physical examination, or laboratory findings.
- C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- D. The duration of the disturbance is at least 6 months.
- E. The disturbance is not better accounted for by another mental disorder (e.g. another Somatoform Disorder, Sexual Dysfunction, Mood Disorder, Anxiety Disorder, Sleep Disorder, or Psychotic Disorder).
- F. The symptom is not intentionally produced or feigned (as in Factitious Disorder or Malingering).

Undifferentiated somatoform disorder is thus used for classifying patients suffering from symptoms that are not explained by any pathophysiological markers. The term undifferentiated somatoform disorder is however generally understood to imply an interpretation of the illness to be mental in the absence of signs of bodily illness. This makes the term less appropriate as a name for a proposed syndrome, which is still under debate and investigation. Reported symptoms may be either an indication of new diseases or physiological reactions triggered or

interpreted in a new way. The diagnoses of somatoform disorders have also been criticized as still lacking definite clinical validity and mostly being based on the exclusion of other diagnoses (Peveler 1998).

2.2 OPERATIONAL DEFINITION

A diagnosis needs clinical validity in order to be accepted. It should encompass a clinical entity that can be identified and separated from other medical conditions on the basis of assessed objective findings or at least a set of criteria based on self-reported consistent characteristics that distinguishes it from other illnesses. A diagnosis should also have valid implications on the clinical course and response to treatment (Kendell 1989). If these requirements are not met, we will have to create an operational definition to be used in further research. The operational definition may vary depending on the purpose of the study. Possible overlap between different operational definitions and diagnoses may be presented.

To date, there is no universal consensus on an operational definition of HE. Most studies use the criterion that a person should report being hypersensitive to electricity (or electric or magnetic fields).

The Swedish association for the electrosensitive presents HE in the following way at their web site (Available from: URL: www.feb.se/FEB/feb_info.html, 2001-05-21):

“When the symptoms have become this severe* at the VDT**, the same symptoms appear at other times as well. The injured soon realise that there is a relationship between different kinds of electrical apparatus and the severity and duration of the symptoms. Both domestic TV-receivers and fluorescent light (strip lights) generally cause intense symptoms.

A person with these symptoms has developed a general oversensitivity to electricity. Those who are extremely oversensitive can also react adversely to daylight and must stay indoors in darkness during daylight hours.”

*”The whole body is affected including the nervous system. This might include:

- difficulties in concentration
- dizziness
- headache and nausea
- teeth and jaw pains
- ache in muscles and joints and
- cardiac palpitations.”

** Visual display terminal

The Swedish Council for Work Life Research was in 1997 commissioned by the Swedish government to present a research review and evaluation of the results of Swedish as well as international research into electromagnetic hypersensitivity and the health risks posed by electric and magnetic fields (EMF). The working group arranged three workshops with invited experts (including the self-help group) to discuss different aspects of HE. Based on the discussions in these workshops, an open hearing and a further meeting to discuss what

statements on HE the experts could reach an agreement on, consensus for the following definition for HE was presented (Bergqvist et al. 2000):

“Electromagnetic hypersensitivity is defined as those symptoms that are experienced in the proximity to, or during use of electrical equipment, and which result in varying degrees of discomfort or ill health in the individual, and which the individual attributes to the activation of the electrical equipment.”

It is apparent that the interpretation of the nature of the condition by the person himself is essential. HE might be regarded as a subgroup of IEL distinguished by the reported temporal relationship between symptoms and being in the proximity to electrical equipment and symptom attribution to this situation.

The use of the term HE in this thesis is based on the definition above (Bergqvist et al. 2000) and does not imply an established causal relationship between electric or magnetic fields and reported health complaints.

2.3 ELECTRIC AND MAGNETIC FIELDS

New technologies and our use of electrical equipment has led to a dramatic increase in the number of sources of electric and magnetic fields in our everyday environment. Negative health effects from new exposure situations are discussed. Scientific investigations are initiated to increase our knowledge of possible biological effects and health implications. Evaluations of the current state of the art are continuously performed by international groups of experts. Recently an expert scientific working group of the Monographs Programme of the International Agency for Research on Cancer (IARC) evaluated extremely low frequency magnetic fields as possibly carcinogenic to humans (Group 2B) (IARC 2001). Other expert working groups have come to similar conclusions (Kriteriegruppen för fysikaliska riskfaktorer 1995; NIEHS 1999). Other health effects as neurological diseases have also been discussed. These possible health effects are today not considered to have enough scientific support to motivate other risk reducing strategies than precautionary approaches. Current recommended exposure restrictions are based on established acute health effects from exposures to electric and magnetic fields (ICNIRP 1998). But some persons, for example, many persons reporting HE, do not consider these reference levels as adequate and sufficient for the prevention of health effects.

In Sweden, guidelines for decision-makers regarding low-frequency electrical and magnetic fields were issued in 1996 by five Swedish authorities (the Swedish National Board of Occupational Safety and Health, National Board of Housing, Building and Planning, National Electrical Safety Board, National Board of Health and Welfare and Radiation Protection Institute 1996). The guidelines recommended a precautionary approach based primarily on non-discountable cancer risks¹⁾. The document stated that a similar precautionary approach should also be applied to other suspected effects on health, but at the same time it said that, due to the lack of knowledge, the authorities refrained for the time being from issuing any joint, general recommendations with concern to electrical hypersensitivity.

¹⁾ The precautionary principle stated that “if measures generally reducing exposure can be taken at reasonable expense and with reasonable consequences in all other respects,

an effort should be made to reduce fields radically deviating from what could be deemed normal in the environment concerned. Where new electrical installations and buildings are concerned, efforts should be made already at the planning stage to design and position them in such a way that exposure is limited.”

A relationship between symptoms and exposure to electric or magnetic fields has been investigated with regard to VDU related skin symptoms as well as reported HE. The two groups partly overlap each other. Some persons experiencing skin symptoms during VDU work interpret this as HE and the majority of – but not all – persons reporting HE has a history of VDU work as the initial triggering situation for skin, and possibly other, symptoms. It should however be noted that the majority of persons with VDU-related skin symptoms experiences a complete or partial recovery (Bergqvist et al. 1998). For clarity, references referring to studies focused on VDU related skin symptoms will be marked by “^{vd}” in chapters 2.3 (Electric and magnetic fields) and 2.4 (Factors associated with hypersensitivity to electricity).

Skin symptoms were in some studies associated with electric fields (Sandström et al. 1995^{vd}, Oftedal et al. 1995^{vd}). The symptom “tingling, pricking or itching” was significantly reduced during the period of active filter in the study by Oftedal and co-workers from 1995 (Oftedal et al. 1995^{vd}). However, a second study by the same research team did not confirm the results in the first study (Oftedal et al. 1999^{vd}). Other studies did not report any clear association between fields and symptoms or signs (Bergqvist and Wahlberg 1994^{vd}, Stenberg et al. 1995a^{vd}). Initially observed associations between fields and symptoms were in many cases reduced after adjustments for other factors. Accumulated field exposure was, for example, interpreted to be an indicator of the amount of VDU work (Bergqvist and Wahlberg 1994^{vd}). Situations reported to trigger symptoms (for example, VDU work) are not in general characterized by high exposure to electric or magnetic fields (Bergqvist et al. 1998; Bergqvist et al. 2000). Some support for an influence of static electric fields on skin symptoms was reported in an intervention study, but only in offices with high dust concentrations (Skulberg et al. 2001^{vd}). Lowering the VDU related static electric fields had no effect on general symptoms as fatigue, headache etc.

Controlled experimental studies have, with some few exceptions (see below), to date failed to provide support for the hypothesized causal relationship between fields and symptoms, or to show that subjects can detect the presence of fields (Bergqvist and Vogel 1997; Bergqvist et al. 1998; Bergqvist et al. 2000). Subjects have reported symptoms, but not to a higher degree during actual exposure than during sham exposure (Hellbom 1993; Andersson et al. 1996; Lonne-Rahm et al. 2000; Flodin et al. 2000). One exception is an American study on persons that, apart from reporting sensitivity to chemicals (multiple chemical sensitivity, MCS) also reported HE (Rea et al. 1991). Sixteen persons, who in a previous part of the study had reacted to certain frequencies, were tested in a double-blind provocation study with an individual choice of frequency (i.e. the frequency that previously had caused the greatest increase in symptoms). Symptoms were provoked during all actual exposure sessions, but not during sham exposure. Reactions in the autonomic nervous system were reported. The reported symptoms are not described, nor the temporal relationship to the exposure, except for the information that symptoms lasted from five hours to three days. A comment is made that two patients had delayed reactions and gradually became depressed and finally unconscious. They awoke without treatment.

In a Swedish study, one of seven persons (who all reported HE) experienced symptoms only during and after the five times a mobile phone was present and not during the four sham exposures (a fake mobile phone) (Johansson 1995). The mobile phones (in some cases a GSM phone and in some cases a NMT) in this study were turned on and in stand by, but not actively transmitting. The actual exposure with regard to EMF is not described. Johansson and co-authors also reported an open provocation study of two persons who reported VDU related skin symptoms (“screen dermatitis”) where the number of somatostatin immunoreactive dendritic cells were drastically decreased after the persons had been exposed to a television set (Johansson et al. 1994^{VDU}).

A weakness of the experimental situation in many controlled provocation studies might be the relevance of the actual field exposure as compared to everyday life situations. A study by Flodin and co-workers tried to handle this problem by choosing the actual electrical apparatuses that had been reported to provoke symptoms for the provocations and to test these in the homes or workplaces of the subjects (Flodin et al. 2000). Due to practical reasons provocations with the participants’ own appliances were not possible in all cases and a VDU was used as a substitute in most of cases. There were no differences between the group reporting HE and the control group in ability to decide on whether or not they were exposed to electric and magnetic fields.

Based on the results in presented studies, an argument can be made that neither electric fields nor magnetic fields are sufficient or necessary causes of the reported complaints:

- Symptoms can appear in the absence of EMF (for example, during sham exposures in provocation studies) and might be manifestations of organic disease, i.e. EMF is not a necessary cause for the symptoms (Rea et al. 1991; Hellbom 1993; Wennberg et al. 1994; Andersson et al. 1996).
- EMF (*nota bene* that this conclusion is restricted to the aspects of EMF thus far investigated) do not always provoke symptoms during provocation studies, i.e. EMF is not a sufficient cause of the symptoms (e.g. Hellbom 1993).

If electric or magnetic fields, under some conditions, may act as contributing factors is still an open question. The number of possible combinations of factors that might be of importance makes it hard to test all possible hypotheses. Individual and environmental factors might interact with electric and magnetic fields, and possibly differ from time to time and from individual to individual. Besides, fields may be characterized by a large number of different parameters such as frequency, intensity, intermittency etc., and an almost infinitive number of combinations of these parameters can be hypothesized to be of causal importance.

The question of electric or magnetic fields’ possible role as a causal factor was not the primary focus in this thesis.

2.4 FACTORS ASSOCIATED WITH HYPERSENSITIVITY TO ELECTRICITY

There are indications that other factors than EMF may be of importance with regard to maintenance of illness and improvement in health in persons who report HE:

- Alternative medical conditions are found in a substantial number of persons who report HE (table 1).
- Alternative contributing factors have been indicated in several studies (Socialstyrelsen 1995; Bergqvist and Vogel 1997; Bergqvist et al. 1998).
- There are indications that certain situations/appliances (for example, a VDU) might act as conditioned stimuli, for example, symptoms are triggered in open but not in blind provocations (Hellbom 1993; Andersson et al. 1996; Lonne-Rahm et al. 2000).
- Improvement in health has been shown to occur without an increase in avoidance to EMF and/or VDU work (Andersson et al. 1996; Eriksson et al. 1997a^{VDU}; study V).

For example, a follow-up study showed that the group of VDU workers who got well, or significantly improved, from skin symptoms had continued to work with VDU to a higher degree than the group with persisting skin symptoms (Eriksson et al. 1997a^{VDU}). It must however be kept in mind that it is usually not possible to control for all possible actions taken by the afflicted individuals during the time of a follow-up or treatment study.

Examples of contributing factors indicated in studies are:

- High work pace or high work load (Bergqvist and Wahlberg 1994^{VDU}; Stenberg et al. 1995a^{VDU})
- Lack of support from co-workers (Eriksson et al. 1997b^{VDU})
- High temperature and/or low relative humidity indoors (Bergqvist et al. 1998)
- Personal factors as gender (HE is more common in women) and age (neurovegetative symptoms are more pronounced in older persons with HE) (Klave et al. 1989; Wadman et al. 1996).

Table 1. Medical diagnoses in patients referred to specialists because of hypersensitivity to electricity (Presented at the International Workshop on Electromagnetic Fields and Non-Specific Health Symptoms, Graz, Austria; September 19-20, 1998).

<i>Author(s)</i>	<i>Investigated group</i>	<i>Proportion of patients where possible alternative medical causes of symptoms were found</i>
Hillert et al. 1998	63 patients referred to a center of occupational medicine	16 % somatic diagnoses, 15 % psychological conditions of importance
Harlacher 1998	80 patients referred to a department of dermatology	56 % received a diagnosis of a skin disease (66% of which previously undiagnosed)
Ahlborg and Gunnarsson 1998	65 patients referred to a centre for environmental sensitivity at a department of occupational and environmental medicine	14 % somatic diagnoses and 5 % psychiatric diagnoses

Taken together, these observations indicate that a focus on only one factor should be avoided. It seems that if all persons who report HE should change their lifestyles and start avoiding EMF and VDU work immediately after the first experience of symptoms, this would, at least in some

cases, be an unnecessary action. This conclusion is a strong argument for primarily trying other actions and interventions. The non-specific symptoms, which might be provoked by many factors, and the ubiquity of the proposed causal factor EMF (which might lead to extreme social withdrawal and handicap if complete avoidance of EMF is sought), constitutes additional arguments for other interventions than avoidance of EMF.

2.5 INTERVENTIONS

Different interventions have been tried. The choice of factor as the prime target for intervention depends on several aspects:

- The appreciated relative influence of the factor on the condition
- If the factor is perceived as familiar or new and unfamiliar
- If the factor is open for intervention
- Who is considered to be responsible for taking action
- The cost and other possible undesirable side effects of a certain intervention

Different groups might, based on different evaluations of the five points presented above, come to different conclusions regarding the priority of different interventions. Most people who report HE are, based on their own experience, convinced that electric and/or magnetic fields are the main contributing factors (and possibly even a sufficient cause) for the symptoms. Stakeholders as the standard health care system and employers are asked by afflicted individuals and self-help groups to act to reduce these exposures. Side effects as costs, the possibility of restrained living conditions and consequences for other persons are downplayed in order to achieve the desired reduction in field exposure.

But no causal relationship has, as of yet, been proven and there is at present no scientific basis for guidance as to which parameter of the fields that might be of relevance. Scientific studies have not demonstrated any dose-response relationship. The ubiquitous nature of electric and magnetic fields also raises the question if a reduction in exposure in some situations will lead to a significant reduction in the total exposure of the individual. It is not possible, by measuring electric or magnetic fields, to predict if a situation or an environment will trigger symptoms in a person who reports HE (Bergqvist and Vogel 1997).

There is no controlled study on the effect on reported HE by so called EMF clean-ups, i.e. reduction of exposure to electric or magnetic fields. There have been two retrospective investigations in Sweden of the experience after alterations either at work (29 persons) (Almgren 1996) or at home (36 persons, including two persons where no alterations had been made) (Järvholm and Herloff 1996) in persons reporting HE. The actions taken ranged from single measures like replacement of fluorescent light by light bulbs to very extensive actions and the results are difficult to appraise. No conclusion can be made regarding the effect of separate measures or regarding significant changes in work ability. In general, the interviewed persons reported an experience of a reduction in symptoms but not full recovery. Eight of the 14 persons previously living elsewhere had been able to move back to their homes (Järvholm and Herloff 1996). In the group of 19 persons who had been granted home adaption grants from local authorities, all six persons that prior to the actions lived at other places, including caravans and tents, were able return home.

A lack of improvement after measures to reduce exposure in one, or a few places are in some cases interpreted as a motive for further actions to reduce exposure to an even greater extent or in additional places. This increase in avoidance behavior may be considered an undesired state where the afflicted person has given up control. Arguments for and against actions aimed at electric or magnetic fields must in each case be carefully considered and weighed together.

Arguments for measuring electric or magnetic fields (in individual cases) may, for example, be that it may provide information on whether present reference levels and recommendations are met and that it may form a basis for actions that the individual decides to take by himself. Measuring and initiating actions to reduce field exposure is sometimes stressed as one way of showing that the concerns of the afflicted individual are taken seriously.

Many stakeholders (like the Swedish National Board of Health and Welfare), physicians and psychologists, emphasize the possible importance of other contributing factors than EMF and focus primarily on interventions aimed at these factors (Socialstyrelsen 1998). The uncertain outcome of actions aimed at measuring and reducing the exposure to electric and magnetic fields, as well as possible side effects of such actions, are pointed out. Centers of occupational and environmental medicine in Sweden will usually investigate cases of IEI, like hypersensitivity to electricity, in multidisciplinary teams with the aim to identify medical, psychosocial or environmental conditions of possible importance for the complaints. Results of different interventions are further discussed in section 7 (DISCUSSION) below.

Preventive programs were launched by some, especially larger, companies in Sweden in the beginning of the 1990s. The number of persons who reported HE was starting to be a problem and in the majority of these cases the first symptoms were experienced during VDU work. The preventive strategies applied were based on a broad approach to the problem. They included, for example, optimizing physical and psychosocial factors, as well as introducing an openness about, and readiness to act in response to, the problem. The actions were not primarily aimed at reducing EMF, but to ensure that electrical equipment met present standards and recommendations was often part of the programs. The general approach makes it impossible to evaluate the effect of separate actions taken, but several companies have reported that the programs were effective and that the number of new cases dropped significantly in these places of work (Lidén et al. 1996; Sandell 1993). However, new cases of HE still present themselves and continue to challenge the standard health care system and decision-makers in different authorities.

3 AIMS OF THE THESIS

The overall aim of this thesis was to increase our knowledge on reported hypersensitivity to electricity in order to develop better preventive strategies and improve our ability to offer help and guidance to persons reporting this syndrome.

Research on self-reported illness faces several difficulties. The lack of objective signs and pathophysiological markers leads to a risk of heterogeneous study groups where possible findings in the real target group will elude the investigator. This problem is a strong argument for pursuing the search for specific markers and characteristics of the group of interest, in this case people who report HE. This is the focus in studies I, II and III. In study III, a study on fatigue, one of the most commonly reported complaints and cause of disability in people with HE, a possible biological marker is investigated.

Physicians are faced with the challenge to decide how to best help the afflicted patient in a situation where no specific cause is identified for the present ailment. The patients are often told that there is no proven cure but different strategies to reduce symptoms might be tried. In this situation, it is quite common that patients will look for help from outside the standard health care system. An open mind to new treatments is desired, but the efficacy should be evaluated in scientific studies in order to provide information to physicians for future recommendations to these patients. Paper IV presents a study in which an unconventional treatment, antioxidant supplementation, is tried in a double-blind placebo controlled study.

If the clinical work-up fails to identify any specific disease or medical disorder, intervention should aim at reducing symptoms and functional handicap. Paper V reports a treatment study on cognitive therapy. Cognitive therapy has been shown effective in many diseases and illnesses with persisting symptoms.

3.1 SPECIFIC AIMS

The aims of this thesis were to investigate possible risk factors (for example, personal and work-related factors), symptoms and complaints associated with reported hypersensitivity to electricity (study I and II), to test hypotheses concerning contributing biological mechanisms (study III and IV) and effective treatments (study IV and V) for people reporting this syndrome.

4 MATERIALS AND METHODS

4.1 OBSERVATIONAL STUDIES

4.1.1 Study I

Prevalence of self-reported hypersensitivity to electric or magnetic fields in a population-based questionnaire survey.

A random selection from the population in Stockholm County was investigated in a cross-sectional questionnaire survey, study I. The survey was part of a periodic survey focused on allergies and ill health related to environmental exposures. A questionnaire was mailed to 15 000 men and women in ages 19-80. Subjects were selected from 17 different geographical strata in order to ensure the most reliable information on the distribution of health problems among different areas in Stockholm and areas exposed to airport noise and heavy traffic. After three reminders there were 10 670 respondents (response rate 73% excluding those who were not identified by the postal service).

The questionnaire included 87 questions on symptoms, complaints, allergies, hypersensitivities, education, living arrangements and disturbances from environmental factors. Information on age, gender, income and country of birth was obtained from the national population register. Persons reporting hypersensitivity to electric or magnetic fields were regarded as cases and compared to the rest of the respondents who did not report this form of ill health. Comparisons were also made in some instances to the case subgroup reporting amalgam intolerance as well as HE and the referent subgroup of persons reporting asthma and/or hay fever. Factor analysis was applied to investigate possible underlying symptom constellations in cases and referents.

4.1.2 Study II

Hypersensitivity to electricity: working definition and additional characterization of the syndrome.

A self-administered questionnaire was distributed to employees at a Swedish high-technology, multinational telecommunication corporation (IT-company) as part of a health survey in 1990. Information on individual and occupational factors was attained. The questionnaire was answered by 241 persons, a response rate of 71%. Age and gender did not differ to a statistically significant degree between those who answered the questionnaire and all employees (based on information from other assessments).

The questionnaire contained questions on symptoms, gender, age, education, working conditions, anxiety and sleep quality. The Eysenck Personality Inventory (EPI) (Eysenck 1958) and the General Health Questionnaire (GHQ, version slightly modified) (Goldberg 1972; Banks et al. 1980) were also included. Indices were formed, based on the Karasek Theorell model, regarding mental demand at work, control over the work process and intellectual discretion (Karasek and Theorell 1990). Symptoms were rated on a scale of 0 to 3. The questionnaire choices were 0 for no symptoms, 1 for rarely occurring symptoms (or symptoms once or twice a month), 2 for fairly often (or once or twice a week) and 3 for very often (or daily) symptoms.

Persons reporting hypersensitivity to electricity were regarded as cases and compared to the referent group, i.e. respondents not reporting this illness.

Two symptom scales, based on the experience from a questionnaire applied to patients at our department, were tested. The index for skin symptoms experienced in the face or upper part of the body were based on reported degree of heat or burning sensation, tingling and redness. The neurovegetative index included the reported symptoms difficulties in concentrating, fatigue and headache. Both indices had a range of 0 to 3, based on a mean of the ratings of included symptoms. The Cronbach α was 0.7 for the skin index and 0.6 for the neurovegetative index.

In addition to testing for differences in scores on indices between cases and referents from the IT-company we also made comparisons to a group of twenty-two patients from our department who completed the same questionnaire during 1993 and 1994 at the start of the treatment study on cognitive therapy (study V). Because age and gender are known to influence the degree of reported symptoms we had made an *a priori* decision to adjust for these factors when the group of patients were included in the analyses. The influence of the duration of HE was also investigated.

4.2 CLINICAL STUDY

4.2.1 Study III

Environmental illness: fatigue and cholinesterase activity in patients reporting hypersensitivity to electricity.

Fatigue is one of the most commonly reported reasons for suffering and disability in HE. Fatigue is also a common complaint in the general population (Tibblin et al. 1990; Hyyppä et al. 1993). But the reported variation in the degree of fatigue due to perceived exposure to electric or magnetic fields is characteristic for HE. This offers an opportunity to study possible biological variations during times of severe fatigue or absence of this symptom. The aim of study III was to investigate a possible correlation between the reported degree of fatigue and cholinesterase activity in persons reporting HE.

Cholinesterase inhibition due to exposure to organophosphates has been reported to increase the degree of fatigue (Markowitz 1992; Richter et al. 1992). Symptoms have been suggested to increase even at small changes in cholinesterase activity (near or within normal range or very slight depression of less than 20%) (Gordon and Richter 1991). Muscular weakness as well as symptoms mediated by central receptors may occur.

Ambient and intracellular calcium may influence the impulse transmission from nerve to muscle. Magnetic fields were shown to influence intracellular levels of calcium (Lindström et al. 1993; Ihrig et al. 1997). Hypothetically, a possible mechanism for the experienced fatigue in HE may be a reduction of cholinesterase activity due to altered levels of calcium.

The study group was 14 persons reporting HE and suffering from severe fatigue. Inclusion criteria were reported hypersensitivity to electricity and disabling fatigue that was reported to wax and wane according to perceived exposure to EMF. The selection of subjects for the study and the times for blood sample collections were solely based on the participants reports of

illness since there are currently no biological marker nor diagnostic test for HE. Nine women and five men were recruited from patients referred to the Environmental Illness Research Center, Stockholm County Council. Two persons declined participation. All participants reported some avoidance behavior due to HE.

Cholinesterase activity was estimated according to the method used by Eriksson and Fajersson (Augustinsson et al. 1978; Eriksson and Fajersson 1980). The method has been applied for surveillance of workers exposed to organophosphates in Sweden for more than 30 years. Acetylcholinesterase as well as butyrylcholinesterase is analyzed from capillary blood samples. Intraindividual comparisons is the preferred method since there are large differences in activity levels between individuals. There are also intra-individual variations and changes of less than 20% in plasma enzyme and 15% in erythrocyte enzyme are too small for statistical recognition of abnormal decrease in cholinesterase activity in an individual (Hayes and Laws 1991).

We assessed cholinesterase activity three times: twice based on current degree of fatigue reported by the subjects (severe fatigue attributed to EMF exposure and absence of this symptom) and at a randomly selected time. Blood samples were collected at the home or the place of work of the participants. Routine blood analyses and self-administered questionnaires on present symptoms, avoidance behavior and drug intake were also applied at the same times.

4.3 INTERVENTION STUDIES

4.3.1 Study IV

The effect of supplementary antioxidant therapy in patients who report hypersensitivity to electricity: a randomized controlled trial.

Patients reporting HE often seek to improve their health by different treatments offered by persons practicing complementary medicine. Several persons have testified that they have experienced a reduction in symptoms after antioxidant supplementation. To test the hypothesis that antioxidant therapy reduces symptoms and improves health in patients reporting hypersensitivity to electricity a randomized, double-blind crossover, placebo-controlled study was applied. Sixteen patients (13 women, 3 men) referred to our department due to reported HE were included and entered into the study at three different times. In order to make the group as representative as possible for the majority of people reporting HE inclusion criteria were set to 1) reported HE, 2) reported change in symptoms within 24 hours after a perceived change in exposure to EMF and 3) a history of visual display units or fluorescent lights as the initial triggering factors. Patients with known somatic or psychological disorders that could account for the present symptoms and reported variations in symptoms were excluded (six persons). Four persons did not want to discontinue their own choices of therapies including antioxidants and three persons were too busy at work to participate. Three patients had experienced a complete recovery before the onset of the study.

Antioxidant supplementation was a daily intake of 180 mg vitamin C and 100 mg vitamin E. In addition 120 µg selenium was included. Selenium is an essential trace mineral that affects the antioxidant enzyme activity of glutathion peroxidase. The treatments with antioxidants and placebo were run in parallel during all times with an equal number of patients in each group. A wash-out period of three weeks was scheduled after each treatment period, figure 1.

Antioxidants and placebo were available as pills, identical in appearance, to be swallowed without chewing (Pharmaica & Upjohn, Sweden). The patients, physicians, nurses and laboratory technicians were blinded to the medication code for antioxidants and placebo. The code was broken after the initial statistical analyses.

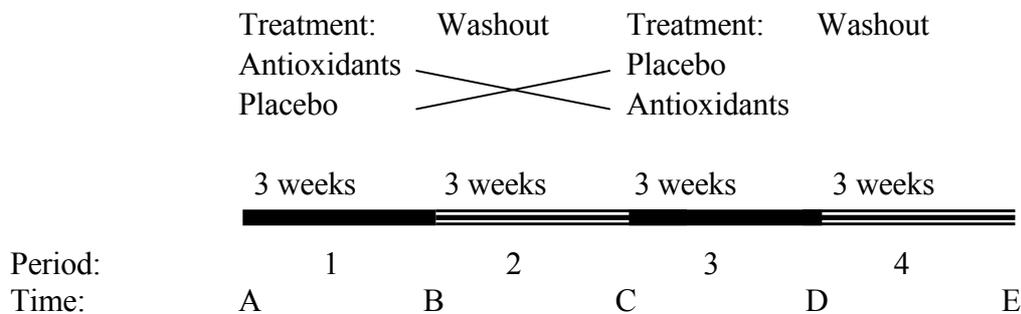


Figure 1. Flow chart of study design (study IV).

The outcome variables are presented in table 2. The primary outcome of interest was a possible reduction in reported symptoms and degree of HE. Blood samples were drawn on three separate days before each treatment period and during the last three days of treatment and washout period, respectively. The mean values of each period of three days were used for the analyses in order to minimize the influence of day to day variations. Diphenylpicrylhydrazyl (DPPH) (Dinis et al. 1994) and uric acid (Ames et al. 1981) in serum were analyzed for detection of change in the oxidative status in the participants' blood. Since antioxidant supplementation theoretically may result in either an increase of other antioxidants in the blood (due to a decrease in the utilization of these) or decrease (due to a reduction in the production) we looked for a possible change in either direction. Any observed change after the treatment period was expected to disappear during the following washout period.

4.3.2 Study V

Cognitive behavioural therapy for patients with electric sensitivity - a multidisciplinary approach in a controlled study.

The source population for the study consisted of patients referred to the Department of Occupational and Environmental Health at Huddinge University Hospital because of perceived hypersensitivity to electricity. The inclusion criteria were that the subjects be Swedish speaking men or women aged 18-65, who had been at work for at least 1 week during the past 3 months (in order to ensure a present place of work to aim at in rehabilitation) and report HE. In addition, symptoms were to vary due to perceived exposure to electric or magnetic fields. Medical or mental disease capable of accounting for the reported symptoms constituted the exclusion criteria. The aim of the study was to evaluate the effect of cognitive behavioral therapy on symptoms and ability to work in patients reporting HE.

During October 1993 to November 1994 63 patients reporting hypersensitivity to electricity were referred to our department. In 21 patients medical illnesses or mental disorders were the reason for exclusion. Eleven patients did not meet the inclusion criteria due to longer periods of

Table 2. Outcome variables in study IV.

Uric acid:	Observed change during the treatment period, such as, difference between the mean of the three days of measurements before and after each treatment. (mg/dl)
DPPH (Diphenylpicrylhydrazyl):	Observed change during the treatment period, such as, difference between the mean of the three days of measurements before and after each treatment. (red/ox equivalent of uric acid, $\mu\text{mol/L}$)
Daily, all:	Mean score of perceived degree of stress and twelve symptoms reported in the daily questionnaire during a treatment period. (100 mm visual analogue scale (VAS), from “not at all” and “to an extreme degree”)
Daily, skin:	Mean score of skin symptoms reported in the daily questionnaire during a treatment period. (VAS, see above)
Daily, not skin:	Mean score of perceived degree of stress and other symptoms than skin symptoms, reported in the daily questionnaire during a treatment period. (VAS, see above)
Daily, HE:	Mean score of degree of perceived HE reported in the daily questionnaire during a treatment period. (VAS, see above)
Daily, avoidance:	Mean score of degree of avoidance reported in the daily questionnaire during a treatment period. (VAS, see above)
After treatment, HE:	Estimated change in the degree of perceived HE during the last treatment period as compared to the three weeks preceding it. (100 mm VAS, from “much worse” to “much better”)
After treatment, skin:	Estimated change in the degree of skin symptoms during the last treatment period compared to the three weeks preceding it. (VAS, see above)
After treatment, not skin:	Estimated change in the degree of other symptoms than skin symptoms during the last treatment period as compared to the three weeks preceding it. (VAS, see above)

sick leave or unemployment. One patient had no longer any complaints related to electromagnetic fields by the time of the first visit to our department. Five patients were satisfied after the initial investigation and information given and declined participation in any study since they did not want to focus on any possible hypersensitivity to electricity any more.

Twenty-five patients entered the study and were randomized to either a therapy or control group. The patients in the control group were offered therapy after the 6-month follow-up. Two patients in the therapy group left the study after the initial one or two meetings with the therapist. In one case the therapist judged that the person was unable to participate in the therapy in the required way, and in the other case it was by request of the patient due to lack of interest in this kind of treatment. Lung cancer was diagnosed in one patient in the control group shortly after the start of the study and this patient was therefore excluded. The final study group thus consisted of ten patients in the therapy group and twelve patients in the control group. For comparisons, the study groups of study III, IV and V are presented in table 3.

All patients in the study received a thorough medical work-up by a physician at the beginning of the study. The patients in both groups were able to contact the physician at any time during the study period, planned visits were booked for the 6- and 12-month assessments. The physician and the industrial hygienist gave information on the present knowledge of electromagnetic fields to all participants. The investigation of the patients' places of work by the industrial hygienist showed overall very good conditions. In one case disturbing light reflection was noted. There were no differences between the groups with regard to the number of electrical equipment in the rooms where the participants worked (or within 5 m from the place of work in case of large shared rooms).

The assessments included self-administered questionnaires for reported symptoms, degree of HE, attribution and avoidance behavior, information on absences from work and biochemical measurements of stress-related variables (thyroxin, prolactin, cortisol, fructosamine, and salivary IgA). Blood samples were collected at standardized times (between 8 and 10 a.m.) at a visit to our department and on another day at the patients place of work. Questionnaires were used for symptom dimensions (SCL-90) (Derogatis et al. 1973; Öhman and Armelius 1989), alexithymia (the 20-item Toronto Alexithymia Scale, TAS-20) (Bagby et al. 1994a; Bagby et al. 1994b), attributional style (Attributional Style Questionnaire, ASQ) (Peterson et al. 1982) and the patients' sense of coherence (SOC) (Antonovsky 1987). The SCL-90 measures nine symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism.

All outcome variables were collected prior to the study, after six months (post-treatment) and after an additional 6-month follow-up, but due to different circumstances concerning the work situation we were not able to collect blood samples from all the participants at their place of work at all times. None of the participants was engaged in any other systematical treatment or therapy due to perceived HE during the study.

Cognitive therapy is a system of psychotherapy that gives primacy to cognitive processing in the development of psychological distress. How a person structures his or her experiences strongly influences his or her feelings and behavior. The therapy offered here was an individual therapy focused on the practical problems and dysfunctional cognitive structures (attitudes and assumptions) made by the patients. We developed a form of cognitive behavioral therapy suitable for patients with HE. In this group of patients it is usually not possible to start out by aiming at re-evaluating the cause of symptoms, but rather to focus on the reactions to the symptoms and coping behavior. The starting point was to find out what the patient's problem

was at that time. The patients, sometimes in collaboration with the therapist, set the goals, and new goals were set as the old ones were attained. Relaxation was used to prevent hyperarousal. The therapy was an active, structured and time-limited therapy with the overall aim of helping the patient find less handicapping and restricting ways to interpret and react to possible symptoms. The maximum number of session was set to 15 within 6 months. The same therapist treated all participants.

Table 3. Baseline assessments of the subjects in study III, IV and V at the start of the respective study.

<i>Study</i>	<i>III</i>	<i>IV</i>	<i>V</i>
Recruitment	Patients	Patients	Patients
Men/women	5/9	3/13	6/16
Age, years (mean, range)	46 (37-57)	39 (21-59)	40 (26-58)
Duration of illness, years (mean, range)	5 (2-10)	<1 year: 4 patients =>1 year: 12 patients	2 (<1-6)
Skin index	1.4	2.1	1.9
Neurovegetative index	1.9	1.2	1.2
Reported triggering factors			
Sources of light	14	15	22
Other sources	14	14	14
Avoidance behavior	14	14	20
On sick leave/ disability pension	7	3	1
Working (part or full time)	6	13	21
Unemployed	1	0	0

5 STATISTICAL METHODS

Wilcoxon's signed rank test for paired observations was used for comparisons of outcome variables in study III and IV. Wilcoxon rank sum test was applied for examination of possible carryover and period effects in study IV.

Spearman's rank test for correlations was used to investigate possible associations among different variables in study III and IV.

Students non-paired t-test and analyses of variance (ANOVA) were used for comparisons of groups and change in groups over time in study II, IV, V and for additional analyses of the influence of treatments, periods and individual variations in study IV. In study II age and gender were used as covariates in the analyses of variance comparing the groups from the health survey to the group of patients from our department of occupational and environmental medicine and the Bonferroni method was used to adjust the observed significance level in the pairwise comparisons of scores on indices.

In the descriptive analyses in study I inverse probability weights based on the stratified sampling method were applied. With the exception of the information on demographic data, prevalence data are presented as standardized rates using the non-hypersensitive group as a standard population regarding the age and gender distribution. Proportions and 95% confidence intervals (CI) are presented. The chi-square test was used to test for independence between discrete variables.

General factorial analysis was used to investigate possible patterns of symptoms in study I. Principal factor analysis with varimax (orthogonal) rotation was applied in the analysis of the referent group and the oblique method of rotation promax was also used for scale evaluation in the group reporting HE. The latter method does not force the factors to independence.

Significance levels were set to $p < 0.05$. In section 6 (RESULTS), all differences presented are statistically significant, unless otherwise stated (n.s. = no statistically significant difference).

SPSS statistical software was used for the analyses. In study IV, part of the analyses was performed in the SAS statistical system.

6 RESULTS

6.1 PREVALENCE OF HYPERSENSITIVITY TO ELECTRIC OR MAGNETIC FIELDS

In the survey of an unselected population in the Stockholm County (study I), 1.5% of the respondents reported hypersensitivity to electric or magnetic fields (167 persons). More women than men reported HE (1.8%, 95% CI 1.4-2.2, as compared to 1.1%, 95% CI 0.8-1.5). There were no statistically significant differences in the prevalence of reported HE in different age groups.

The proportion of persons who reported HE was higher in people not born in a Nordic country (Sweden 1.3%, 95% CI 1.1-1.6, other Nordic country 1.4%, 95% CI 0.7-3.0, EU country besides Nordic countries 2.3%, 95% CI 1.2-4.6, country outside EU 2.8%, 95% CI 1.7-4.8,) and in lower income groups (1.9%, 95% CI 1.5-2.4 in the group with an income of less than \$ 15,000, 1.1%, 95% CI 0.9-1.5 in the group with higher income).

In the health survey in the IT-company 40 out of 241 respondents reported HE, i.e. 17%. There were no differences between the group reporting HE and controls with regard to gender and age.

6.2 CHARACTERISTICS OF HYPERSENSITIVITY TO ELECTRICITY

6.2.1 Personal and work related factors

There was no association in the health survey (study II) between reported HE and mental wellbeing, personal traits assessed as neuroticism and extraversion or scores on the anxiety and sleep indices. The indices for mental demand at work, intellectual discretion and control over the work process did not differ significantly between cases and referents. The two groups were also comparable with regard to marital status, use of cigarette and snuff, and educational level.

In study I the proportion of people on early retirement or disability pension was higher among those who reported hypersensitivity to EMF (7.7%, 95% CI 4.1-14.1) than among all referents (3.8%, 95% CI 3.4-4.3), and also compared to referents reporting asthma and/or hay fever (4.8%, 95% CI 3.9-6.0, n.s.). The differences in distribution of people on sick leave were smaller and not statistically significant (HE 2.5%, 95% CI 0.5-10.4, referents 1.6%, 95% CI 1.4-1.9). A significantly higher proportion of persons were unemployed in the HE group (12.1%, 95% CI 6.8-20.6) than in the referents groups (all referents 4.4%, 95% CI 4.0-4.9, referents with asthma and/or hay fever 4.5%, 95% CI 3.6-5.6).

6.2.2 Symptoms

The HE group in study I reported all included symptoms to a significantly higher degree than the referent group (figure 2). Symptoms were reported as being experienced “often or every week”, “sometimes” or “never”, except for “skin symptoms” which were reported as experienced or not experienced during the last 12 months. Comparing the reported frequency of symptoms in the HE group to the group of referents reporting asthma and/or hay fever we observed significant differences when it came to skin symptoms, eye irritation, impaired sense

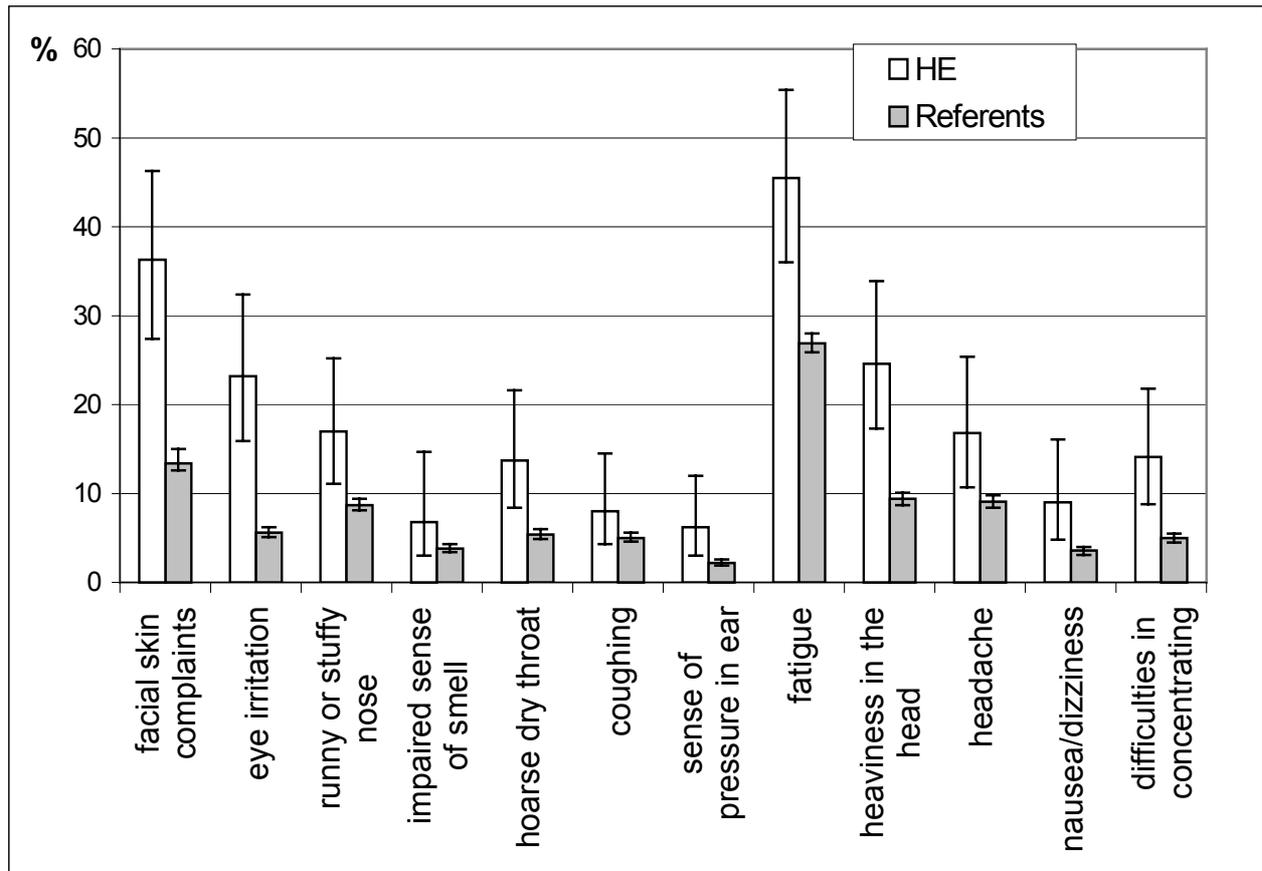


Figure 2. Prevalence of persons who report having complaints at least once a week during the last three months (facial skin complaints represents the percentage who reported having experienced this complaint during the last 12 months) in persons reporting HE and referents not reporting this syndrome (percentage and 95% CI). (*Adjusted for age and gender*)

of smell, feeling of pressure in ear, heaviness in the head, nausea/dizziness and difficulties in concentrating.

Fatigue was the most commonly reported symptom in all groups in study I. In the HE group, 45.5% (95% CI 36.0-55.4) reported suffering from fatigue “often or every week”. The corresponding proportions were 26.9% (95% CI 25.9-28.0) for all referents and 34.8% (95% CI 32.8-37.1) for referents reporting asthma and/or hay fever. The largest difference in proportions was observed with regard to skin symptoms. The percentage that had experienced skin symptoms during the last 12 months was 36.3% (95% CI 27.4-46.3) in the HE group, 13.4% (95% CI 12.6-14.2) in all referents and 19.1% (95% CI 17.3-21.1) in referents reporting asthma and/or hay fever.

The factor analyses revealed two similar factors of symptoms in the group of all referents as well as in the HE group. The first factor included so called neurovegetative symptoms (fatigue, heaviness in the head, headache, nausea/dizziness and difficulties in concentrating) and the second factor symptoms from eyes and airways (eye irritation, runny or stuffy nose, impaired

sense of smell, hoarse dry throat and coughing). The Cronbach α coefficients were 0.8 and 0.7 respectively. Skin symptom was not associated to either factor.

In the health survey (study II) several symptoms were significantly more frequently reported in cases: skin symptoms as redness, heat/burning sensation, tingling, smarting pain/soreness, swelling/blisters, dry skin or mucosa and symptoms from other organ systems as myalgia, dizziness or vertigo and nausea. Cases of reported HE were primarily associated with skin symptoms or signs of short duration (for example, temporary redness) while they did not report any medical history of treatment for seborrhoeic eczema, rosacea or any other skin disease to a significantly higher degree than referents.

Headache, palpitations, fatigue, physical or mental exhaustion and difficulties in concentrating or remembering were not significantly more common in persons who reported HE in study II. Fatigue was however, with the exception of dry skin/mucosa in the HE group, the most frequently experienced symptom in cases as well as referents.

Two symptom scales, one for skin symptoms and one for neurovegetative symptoms, were tested in study II. The skin index, but not the neurovegetative index, was significantly increased in the group reporting HE. Longer duration of symptoms was significantly associated with higher score on the skin index but not on the neurovegetative index. When the scores of a group of patients at our department were compared to the scores from the health survey the patients scored significantly higher than both cases and controls from the health survey with regard to the skin index.

6.2.2.1 Fatigue

No significant reduction for individual change in acetylcholinesterase activity was identified in any subject at the time of reported fatigue (study III). As a group, no significant reduction in activity was identified at the time of severe fatigue and no correlation between reported degree of fatigue and cholinesterase activity was observed. A significant individual reduction of butyrylcholinesterase activity was noted in two cases. Two participants had subnormal butyrylcholinesterase activity at one of the sampling times, but no association was observed between low activity and increase in reported fatigue. The biological importance of butyrylcholinesterase is less well known than that of acetylcholinesterase (Goodman Gilman et al. 1990). For the whole study group, there was no significant correlation between change in reported degree of fatigue in the questionnaires and change in acetyl- or butyrylcholinesterase activity at sampling times chosen due to perceived EMF triggered fatigue or absence of this complaint. No time trends for any activity level were observed.

General but not physical fatigue was significantly increased at the times of reported aggravation of illness due to EMF. General fatigue was significantly correlated to difficulties in concentrating. No other symptom showed a consistent correlation to the degree of fatigue across the sampling times. The score on the degree of difficulties falling asleep and feeling refreshed when waking were similar on different sampling occasions. The reported degree of exposure to EMF in the questionnaire was significantly higher at collection times chosen due to reported increase in EMF triggered fatigue, but no difference was observed with regard to avoidance behavior.

All but one subject had one or more results outside the laboratory-established reference interval in at least one of the blood chemistry analyses. Seven participants had at least one pathological finding at all three assessment times. The number of pathological results in the blood chemistry was not related to the reported degree of fatigue and the pathological tests showed great intra- as well as inter-individual variations.

6.2.3 Illness and disease

6.2.3.1 Hypersensitivity and allergy

The question on hypersensitivity and allergy in the survey in Stockholm county included, apart from electric and magnetic fields, furry animal, pollen, dust, mold, mite, food, gluten, amalgam, dental fillings other than amalgam, nickel and cosmetics. The HE group reported all included hypersensitivities and allergies to a significantly higher degree than all referents. The differences in proportions that reported the respective hypersensitivity or allergy ranged from 10.3% to 30.1%. The most commonly reported allergies or hypersensitivities in the HE group were dust (39.9%, 95% CI 30.9-49.8) and cosmetics (39.0%, 95% CI 30.0-48.8). In study II, it was almost twice as common to report having or having had an allergy in the HE group as compared to the reference group, but the difference was not statistically significant ($p < 0.1$).

A substantial overlap between groups reporting HE and amalgam intolerance was observed in study I. Fifty-four persons reported amalgam intolerance as well as HE (altogether 185 persons reported amalgam intolerance). In this subgroup the proportion that reported allergies or hypersensitivities ranged from 24.5% (95% CI 12.8-41.8) for pollen to 62.1% (95% CI 45.0-76.7) with regard to cosmetics. The differences between the HE group and referents are especially remarkable with regard to hypersensitivities that are less common in the population at large. For example, gluten intolerance was reported by 33.2% (95% CI 19.9-49.8) in the HE-amalgam group, by 13.4% (95% CI 8.3-21.0) of all persons reporting HE as compared to 0.5% (95% CI 0.3-0.6) in all referents and 0.9% (95% CI 0.6-1.5) in the referents group with asthma and/or hay fever. The only two allergies more frequently reported in the group of referents with asthma and/or hay fever as compared to the HE group were allergy to pollen and furry animal.

6.2.3.2 Other reported medical conditions

The proportion of respondents in the HE group who reported that they suffered from the common cold at least twice a year was significantly larger than for all referents (HE 33.1%, 95% CI 24.3-43.3, all referents 22.7%, 95% CI 21.8-23.7). The prevalence of physician-diagnosed hypertension was not significantly higher in the HE group as a whole (HE 18.4%, 95% CI 12.3-26.8, all referents 13.1%, 95% CI 12.3-13.9), but in the group that reported both HE and amalgam intolerance a significantly higher prevalence as compared to the referent group was observed (the reported prevalence of physician-diagnosed hypertension in the HE-amalgam group was 35.3% (95% CI 21.3-52.4). In study II, no difference in the prevalence of high blood pressure or the common cold was observed.

The prevalence of reported asthma (HE 20.1%, 95% CI 13.3-29.1, referents 9.5%, 95% CI 8.9-10.2), hay fever (HE 27.4%, 95% CI 19.4-37.2, referents 18.4%, 95% CI 17.5-19.2), and allergic conjunctivitis (HE 31.8%, 95% CI 23.3-41.7, referents 15.3%, 95% CI 14.5-16.2) was significantly higher in the group that reported HE in study I than in the referent group. There

were no statistical significant differences in study II in the comparisons of the HE group to referents with regard to asthma or hay fever, although the prevalence of past or present hay fever was almost twice as high in the HE group.

6.2.4 Complaints related to environmental factors

The group reporting hypersensitivity to electric or magnetic fields were significantly more often disturbed in their homes by noise from neighbors, ventilation system and traffic, from car exhaust, smell from street, soot, dust, stuffy bad air, low room temperature and dry air than the referent group. The proportion that reported being disturbed at least once a week by environmental tobacco smoke (ETS) was similar in the HE and asthma/hay fever groups, 5.3% (95% CI 2.4-11.1) and 5.2% (95% CI 4.2-6.4) respectively. The percentage was somewhat lower for all referents, 3.6% (95% CI 3.2-4.1) (n.s.). But apart from ETS and smell from the street, the HE group seemed to be more disturbed by all other environmental factors than the asthma/hay fever group.

6.3 EFFECTIVENESS OF APPLIED TREATMENTS

6.3.1 Antioxidant therapy

There were no indications of any delayed effect during the treatment periods so the mean of the daily scores for the periods was used in the analyses. With one exception (a decrease in DPPH after the first treatment period and an increase after the second treatment period, regardless of treatment order) no carryover (i.e. treatments followed by control show less of a difference than control followed by treatment) or period effects (changes over time regardless of treatment given) were identified for any outcome parameter.

The results did not show any significant differences in reported symptoms, HE or oxidative status in blood between periods of antioxidant and placebo treatments. Serum levels of DPPH and uric acid showed no correlation to the reported degree of symptoms or HE and were within expected range. Effects of larger doses of antioxidants cannot be ruled out but it seems unlikely that an increase in oxidative stress is a major factor in HE since the offered supplementation did not result in any detectable change.

The daily reports of the degree of symptoms (both skin and neurovegetative symptoms) showed a significant increase during weekdays as compared to weekends during all periods but one. There was also a significant increase in reported perceived relationship between symptoms and exposure to electricity during weekdays, and an increase in avoidance behavior during weekends.

6.3.2 Cognitive behavioral therapy

The ANOVA tests of main effects of, and interactions between time and treatment did not identify any significant effects. However, looking at a more detail level for tendencies in the results, the therapy group rated their hypersensitivity to electricity as significantly lower than the control group at the 6-month follow-up. The reduction over time in self-rated discomfort from triggering factors was significant in the therapy group but not in the control group. Three persons in the therapy group did not regard themselves as being HE at the 6-month follow up, while all participants in the control group still reported being hypersensitive to electricity. Eight

out of 10 in the therapy group and 6 out of 12 in the control group rated their health with regard to HE as improved. No patients in the therapy group but two patients in the control group reported an increase in their health disturbances due to HE. There were no systematic changes in the biochemical variables. The scores on the symptom index (based on the sum of reported degree and frequency of all symptoms) were significantly reduced over time in the therapy as well as the control group. The non-significant tendency of decrease in avoidance behavior in both groups supports the interpretation of a real improvement and not only due to an increase in avoidance of perceived triggering factors or situations.

During the study time small changes were done at the some patients' places of work, for example, change of computers and screens or change of fluorescent light to light bulbs. The therapy group did not differ from the control group in this regard. Due to the inclusion criterion that participants should have been at work for at least 1 week during the last three months the study turned out to be more of an early intervention study than a rehabilitation study. The work ability continued to be good in both groups. Only one person (in the control group) was on full time sick leave at the start of the study. After the treatment period, all participants were working part- or full time.

The scores on the questionnaires concerning symptom dimensions, alexithymia, attributional style and sense of coherence showed no significant changes. The scoring was within the normal range according to the evaluation guidelines. There were no extreme values in the scores for optimism or pessimism. Prior to the study, the factor for somatization in SCL-90 was increased for both groups as compared to the Swedish norm (Öhman and Armelius 1989). The importance of this observation is however difficult to interpret as the factor is based on reported symptoms from different organ systems, and one reason for these patients to identify themselves as HE is in fact various symptoms from different parts of the body.

The concentrations of fructosamine, thyroxin, prolactin and cortisol in blood and salivary IgA showed no systematic changes between the groups or over time. Nor was there any difference observed between free and working time.

In comparing the 14 patients who reported improvement to the other eight patients (regardless of treatment group) significant differences prior to the start of the study were observed for scores on depression and hostility, working climate and levels of cortisol, but not for symptom scores. The improved group were noted to score higher on the factors of depression and hostility, lower on the index for positive working climate and to have a higher mean serum level of cortisol.

The results show that the prognosis of HE is good with regard to reported symptoms and work capacity, at least when early intervention is applied. Although no significant main effects were observed in the ANOVA tests, there are consistent indications in the results that imply that cognitive therapy may be helpful and further reduce the perceived hypersensitivity.

7 DISCUSSION

7.1 VALIDITY AND POTENTIAL BIAS

The population survey in Stockholm County indicates that the equivalent of 16,000-22,000 persons in this region would report HE. This study does not permit any conclusions on possible subgroups such as persons with primarily VDU-related skin symptoms and persons who attribute a wide range of symptoms to electrical equipment in general. We do not know in how many of these cases the reported HE is, due to the ill health or a wish to avoid perceived triggering factors, a cause of disability or social withdrawal in everyday life.

Cross-sectional studies like study I are not a good source of information for conclusions on temporal aspects of different observations. We don't know, for example, whether the perceived HE has been a cause for the observed increase in unemployment, early retirement or disability pension, or if subjects who, for any reason, are not working are at greater risk for developing HE. The association between low income and HE might also be either due to low income being a risk indicator or due to ill health leading to lower income. But the results do indicate a widespread concern in the general population about health risks from electric and magnetic fields. Future studies including questions on more detailed information (for example, on temporal relationships of different complaints and life events, environmental exposures), or in-depth interviews, might increase our knowledge on HE.

The question on electric or magnetic fields (study I) was included in a survey with the main focus on traditional allergies and hypersensitivities and environmental factors. Any possible response bias is therefore most likely to be associated with these diagnoses. The survey was however presented as a survey on allergies and environmental factors and a selection of respondents that are concerned or worried about environmental factors cannot be excluded. A higher percentage of persons reporting HE was observed in immigrants and this might theoretically have been influenced by a lower response rate in this group. The higher frequency of reported HE in women in study I agrees with the results in several other studies and reports on patients referred to departments of occupational and environmental medicine.

The respondents to the health survey in the IT-company seemed to be representative for all employees with regard to age and gender. The survey was however launched at a time when VDU-related illness was very much on the agenda and persons experiencing symptoms during VDU-work might have been more apt to answer the questionnaire. Some of these persons might have come to interpret their symptoms as hypersensitivity to electricity while others had not. This situation would bias the results toward a reduction in the observed difference in symptoms between the HE and control group (as compared to the situation where the control group is interpreted as being without these complaints). Physical symptoms, even symptoms severe enough to cause temporary disruption in activities and prompt medical consultations, are common in the general population (Kroenke and Price 1993). But bearing in mind that the comparison is focused on possible differences between persons reporting HE and those who do not, and that the results are only representative for these groups, the results may still be valid.

Epidemiological investigations on symptoms and self-reported illnesses are often problematic in controlling for potential bias, illness misclassification and chance findings from multiple

comparisons. The results must be interpreted with caution. However, until the conditions under study have been linked to any sign or biological marker this is an inherent problem. Observations from hypothesis generating studies should be tested in subsequent hypothesis driven studies.

Study I is the first reported study on HE in an unselected population in Sweden. The noted prevalence cannot be compared to results in surveys in selected companies, especially since these surveys in many cases were initiated by some kind of concern for a problem. The prevalence of reported HE is also higher, 17%, in the health survey in the IT-company (study II). In a questionnaire survey in four companies Wadman and co-workers found a prevalence of reported HE of 15% (Wadman et al. 1996). We do not know the reason for these observed clusters. Possible contributing factors might be an increased prevalence of any risk factor, either environmental or psychosocial, or an influence of a behavioral epidemic. Patients referred to departments of dermatology or occupational and environmental medicine constitute another source of information on the prevalence of HE. European centers of occupational medicine responding to a questionnaire in 1996 indicated significant geographical differences (Bergqvist and Vogel 1997). The median of all replies from respective country concerning the estimated number of cases of HE ranged from less than 10 in Great Britain to 1000-10 000 cases in Sweden and Germany (no response was attained from centers of occupational medicine in Belgium, Greece, Luxembourg, Portugal and Spain).

Results in a survey conducted by self-completed questionnaire depend on how the questions are phrased and how the respondents interpret them. The respondent may for example interpret questions on hypersensitivity and allergies either as referring to diagnoses made by a medical doctors or referring to possible medical conditions they suspect that they suffer from. In a population-based survey in California, 6.3% of the respondents reported physician-diagnosed environmental illness or multiple chemical sensitivity (a more common form of IEI than HE in the USA) (Kreutzer et al. 1999). Hypersensitivity to electricity is not used as a diagnosis in Sweden why it is hard to compare the results in the Californian and Swedish studies.

It is interesting to note that in a study on the prevalence of symptoms corresponding to different IEI (sick building syndrome, VDU-related skin symptoms, HE), 2% of the respondents reported symptoms chosen to be typical for HE (Eriksson et al. 2000). Respondents were judged to fulfil the criteria for HE like symptoms if they had reported each of these ten symptoms to be experienced every week or "sometimes" during the last three months. The symptoms were "fatigue", "heaviness in the head", "headache", "difficulties concentrating", "itching, soariness or irritation in the eyes", "dryness in the eyes", "dry skin in the face", "redness in the face", "itching, stinging, tight or burning sensations in facial skin" and "cold hands or feet". The prevalence of HE like symptoms was greater in women (3.1% as compared to 1.1% in men). A dose-response relationship was noted for office work (2.9% in the group working full time in an office, 2.2% part time, 1.2% in persons with mainly other types of work) and VDU work (2.8% in the group reporting VDU work for "more than 4 hours per day", 2.6% "1-4 hours per day", 2.0% "less than one hour per day", and 0.8% in the group that did not report any VDU work). These results are very similar to the results in studies on reported HE. HE like symptoms were most prevalent in the age group 30 to 39 years (3.5%), which is close to the mean age of participants of most studies including persons reporting HE (for example, study IV and V).

The aim to investigate homogenous groups in studies on HE often has a major impact on the final size of the study group. Most studies on HE have enrolled some 20 to 30 subjects, even when the study design planned for larger groups (see table 5 below). Even in these small groups, the difference of illness presentation from person to person in the group reporting HE is often striking. The nature of the study and the type of activities that participants are expected to take part in may influence the selection of subjects. Persons with mild symptoms, who are not on sick leave, may refrain from participation due to the time it would take from their work. A person's own interest in the particular intervention offered might also influence the decision to accept participation. Some persons may find environments, for example, for meetings intolerable or be too ill for engagement in any activity. In study III we tried to avoid some of these problems by taking the blood samples at the participants home or at work. In study IV the approached patients' interest, or lack of interest, to try antioxidant therapy probably influenced the study group. Some patients did not want to discontinue their own therapies and some were not interested in trying this intervention. In some cases patients seemed reluctant to take part in the study because they disliked having repeated blood samples taken. Blood samples were also in this study collected at places chosen by the participants. Bias due to withdrawal can be a problem especially in studies where the participants are expected to take a more active part. In study V on cognitive behavioral therapy two patients left the study after the initial one or two meetings with the therapist, but in study IV on antioxidant supplementation there were no drop-outs. Due to the lack of knowledge on HE it is somewhat difficult to judge in what way these selection mechanisms might have influenced the results and the external validity of the studies. The problem is, at least to some extent, overcome by a multidimensional characterization of the study groups.

Depending on the primary aim of the study – to investigate the cause of ill health in general in groups reporting HE, to test different interventions or to test the proposed causal relationship to EMF – heterogeneous groups may impose more or less of a problem.

If the main purpose is to describe the group of persons reporting HE, the inclusion criteria should be that the subjects report HE. In this broad general approach the heterogeneity of the group is a possible main outcome. If further investigation of possible sub-groups (that might share a common background) is desired, additional criteria have to be applied. The basic inclusion criterion of persons reporting HE was used in our cross-sectional studies. In spite of the fact that HE was reported by 1.5% respondents in the survey in Stockholm County and 17% in the IT-company health survey, the groups (157 and 40 persons respectively) are too small to allow any conclusions on subgroups. But it may still be of interest to explore the nature of smaller groups in a hypothesis generating way. This was, for example, done with regard to the subgroup reporting amalgam intolerance in addition to HE in study I.

In the evaluation of an intervention, the heterogeneity of the group reporting HE might pose a problem with regard to the external validity of the results. It may also have implications on the results. A possible positive effect in one subgroup may be diluted by the lack of an effect for other participants. In study IV we defined the inclusion criteria in such a way that the study group was to be as representative as possible for most typical presentation of HE. We also presented further characterization of the subjects included in the studies.

In study V, which meant to evaluate a possible improved rehabilitation for afflicted individuals, a criterion of having been working for at least one week during the last three months was included. This decision was based on our experience that secondary effects of longer absence from work were to reduce our chances to demonstrate a possible success in the rehabilitation of the subjects due to our intervention. This criterion did however have the effect that most participants were still working and the study turned out to be more of an early intervention study than a rehabilitation study.

The decision on whether or not to exclude subjects with known medical disorders may be discussed. If subjects with medical diagnoses are included there is a risk that the study group will be obscured by persons with a different etiology for their ill health. An exclusion of subjects with known medical or psychological disorders may on the other hand mean that possibly more sensitive groups are omitted. There is also a theoretical possibility of these diagnoses being additional effects of a common causal factor. In study III, IV and V we chose to exclude subjects where the reported presentation of symptoms were judged to be fully explained by a known medical condition, i.e. the mere fact that the subject had a diagnosis was not enough ground for exclusion.

7.1.1 Multidimensional characterization

The heterogeneity of the group of persons reporting hypersensitivity to electricity makes it very hard to compare the results in different studies. Studies should include information on reported symptoms, duration of symptoms, attribution, triggering factors and behavior including work ability in order to facilitate comparisons of results (table 4).

Knave and co-workers described two groups of persons reporting HE (Knave et al. 1989):

- Predominantly redness and sensory skin symptom in the face, mainly in relation to VDU-work. The prognosis seemed to be good and different interventions effective.
- Predominantly symptoms from the nervous system like vertigo, headache, fatigue, etc (in many cases in addition to skin complaints), several types of electrical equipment were reported to trigger symptoms. In this group applied interventions were less successful.

Bergdahl also made similar distinction between a group of person reporting VDUs, television sets and fluorescent lights to trigger symptoms and a group relating their symptoms also to electrical equipment with no visible light (Bergdahl 1995). Persons with mainly skin symptoms were shown to differ from those where neurovegetative symptoms are more pronounced and persons where symptoms are triggered mainly during VDU work differ from those who attribute symptoms to activated electrical equipment in general (Knave et al. 1989; Bergdahl 1995; Wadman et al. 1996). The differences include age, personality and prognosis.

Information on reported symptoms and triggering factors in accordance to this is included in the proposed multidimensional characterization proposed in study II, table 4. The presented indices of skin and neurovegetative symptoms provide a possibility to estimate the relative importance of these groups of symptoms. Additional information may be added, as for example, environmental exposure.

Table 4. Dimensions for characterization of the clinical picture of and consequences for persons who report hypersensitivity to electricity. (From study II)

<u>Dimension</u>	<u>Variables</u>
Symptoms	Skin index* Neurovegetative index
Belief	Hypersensitivity to electricity**
Triggering factors	VDU and/or fluorescent lighting Other sources/situations than above
Temporal aspects	Duration of symptoms Recurrent acute or chronic symptoms
Behavior	Avoidance of triggering factors*** On sick leave

If adapted to other idiopathic environmental intolerance:

*or other relevant symptom scales

**or other attribution made

***or, for example, removal of dental amalgam

7.2 SYMPTOMS IN HYPERSENSITIVITY TO ELECTRICITY

All symptoms were reported to be more frequently experienced in the HE group as compared to the rest of the respondents in study I. A similar result was indicated in study II (the health survey in the IT-company), but in many cases the difference was not statistically significant. With the exception of some skin symptoms (dry skin/mucosa), there was a great consistency between cases and referents with regard to which symptoms that were most commonly reported. Fatigue, mental and physical exhaustion was most common followed by difficulties concentrating and headache in both cases and referents. No specific symptom constellation was identified in the HE group in based on the results of the population survey.

These results are in agreement with other studies. Wadman and co-worker studied 731 office workers including 111 who reported hypersensitivity to electricity (Wadman et al. 1996). The results from this questionnaire survey showed that the HE group reported most symptoms more frequently than the rest of the employees. For example, 57 % of persons reporting HE reported one or more skin symptoms as compared to 25% in the rest of the respondents. The corresponding prevalence of neurovegetative symptoms was 36 and 20%. Persons who reported HE tended to report more symptoms than the rest of the respondents, especially with regard to skin symptoms where the most common number of reported symptoms in the HE group was five as compared to one in the non-HE group. In an American study on multiple chemical sensitivity all categories of symptoms and complaints included (eye, nose, throat, gastrointestinal, systemic, musculoskeletal, central nervous system, headaches, dermatological, lower respiratory, genitourinary, and circulatory) were reported to a significantly higher degree by the sensitive group as compared to referents (Davidoff and Keyl 1996).

In study II, the HE group reported myalgia, dizziness and nausea to a significantly higher degree than referents. These symptoms had at that time not been commonly reported by patients at our department, and were, as described in the paragraph above, not among the three most commonly reported symptoms in the HE group. Dizziness, together with fatigue and difficulties concentrating, was however among the most commonly reported symptoms in a report from the western branch of the Swedish self-help group the Swedish Association for the Electrically and VDT-injured (Rosell 1994). The somewhat unexpected finding of an increase in myalgia in the health survey (study II) may have several explanations. It is not possible to determine if reported myalgia was caused by ergonomic factors related to VDU-work or represents more nonspecific pains in different parts of the body. We did not ask which symptoms that were attributed to electric or magnetic fields.

The group of persons reporting HE in study II were characterized by an increase in skin symptoms and most likely represents early-phase or mild cases with mainly VDU-related symptoms. It must be kept in mind that the survey was conducted at a place of work, which meant that all participants had a fairly good work capacity and were not on long term sick leaves. The health survey was launched in 1990 and a change in symptom profile over time for persons reporting HE might have occurred. Little is known about possible change over the last one or two decades regarding symptom constellation and reported triggering factors in people who report HE. Comparisons of different studies are often, due to, for example, different selection criteria, not a good source of information in this matter. But the largest difference in prevalence between cases of HE and referents was observed for skin symptoms also in study I from 1997.

As a group, persons reporting HE group in study II tended to report their health as poorer than referents (2.5, SD 1.0, as compared to 2.0, SD 1.1 for referents, on a five step scale where 1 was very good and 5 was poor), but the difference was not statistically significant ($p=0.06$). The group of patients from our department who were compared to the employees at the IT-company regarding the indices had a mean rating of their health as 2.4 (SD 0.9). This indicates that this group probably consisted of comparably mild cases (which is also indicated by the comparison of the neurovegetative index), in spite of the fact that they had sought medical advice.

Fatigue was more common in the HE group as compared to referents in the population study but not in the health survey in the IT company. The results in study III indicated that HE was associated with general but not physical fatigue. This observation has gained further support in an intervention program that was implemented at our department during 1997 and 1998. A physical fitness test showed that the participants, 22 persons reporting HE, had an overall good physical fitness (Hillert et al. In press). Even though many persons reporting HE suffer from severe fatigue, outdoor activities and environments are often preferred as they are perceived as less triggering of symptoms. This might prevent deterioration in physical fitness.

Sleep disturbances have been reported during nights with exposure to magnetic fields (Åkerstedt et al. 1999). In a study on healthy volunteers exposure to 50 Hz magnetic fields seemed to shorten the time of sleep and to reduce the estimated depth of sleep. These early results need to be reproduced in independent laboratories prior to drawing any firmer conclusions. Until then, the results should be considered tentative. The sleep quality index did

not differ between persons reporting and not reporting HE in the health survey (study II). There was no indication in study III of sleep disturbances at the times of increased fatigue attributed to EMF. The score on the degree of difficulties falling asleep or feeling refreshed when waking was not associated to reported degree of fatigue due to HE. No association to cholinesterase activity was proven.

Fatigue is common in the general population. Stenberg reported that the sensitivity of fatigue for diagnosing sick building syndrome was 97.5%, but the specificity only 22.3% (Stenberg 1994). The prevalence of reported fatigue depends on age and gender (Tibblin et al. 1990; Kroencke and Price 1993). If groups under study are not comparable with regard to age and gender these factors might influence observed differences in reported fatigue. The significantly higher prevalence in the HE group in study I remained after adjustment for age and gender.

7.2.1 Individually determined response

One may speculate on the reason for the failure to identify any specific symptom constellations and exposure factors in cases of HE. One possibility is that physical factors might interact with psychological factors and a susceptibility of the individual to develop a certain clinical picture. Individually determined response (i.e. a response to an external stimulus that is not uniform in all individuals and depends on the response of the individual to the stressor) has been discussed for multiple chemical sensitivity (another form of IEL) as a main determinant of the ill health or as a modifier of an organic effect caused by some other agent (Gots 1996). Some individuals may also be more prone to produce specific physiological responses to many different stressors. This tendency has been called individual response stereotypy (Lehrer 1997). This would account for similar reactions triggered by different factors at different times. The reactions may differ between individuals, one person might experience mainly skin sensations and another palpitations and dizziness. Individual response stereotypy has been suggested to predispose for medically unexplained symptoms (Lehrer 1997, Engel and Moos 1967).

Coping has been indicated to influence physiological response to stressors (Lazarus 1966; Lehrer 1997). Passive coping was associated with more alpha sympathetic activation including constriction of peripheral vessels, bronchconstriction and a parasympathetic influence of the heart rate. More active coping seems to trigger more of a beta sympathetic response of increase in systolic blood pressure, heart and ventilation.

Arnetz described a model where psychophysiological reactions interact with environmental stressors (Arnetz 1999). Environmental stressors, interacting with genetic and environmental modifiers, will induce sensitization and hyperreactivity in the limbic system and other parts of the brain. This will influence future reactions to different stressors and a lower tolerance may be expected. Triggering factors might include chemical, physical as well as psychosocial stressors.

7.3 CLINICAL COURSE AND INTERVENTIONS

As in all cases of ill health, a medical work-up is motivated for patients reporting HE. Other medical conditions of importance, possibly requiring specific treatments, must not be overlooked. In the primary medical work-up of persons reporting HE medical conditions of importance are quite often identified, see table 1 above.

A clinical investigation of 201 patients with skin problems attributed to VDU work revealed 93 cases of rosacea, 28 cases of seborrhoeic eczema, 21 cases of atopic eczema, 13 cases of acne vulgaris and 25 cases of other diagnoses (Berg 1988). No cases of malignant or pre-malignant changes were found. 36 patients had non-specific symptoms or signs. The prevalence of skin diseases might seem high in this group of VDU workers, but skin problems are common in the general population and objective facial signs in the skin were not shown to be more common among persons with VDU work than among those who did not report working with VDUs (Berg et al. 1990a).

No medical disease is known to predispose for HE or to be part of the clinical picture in later stages. In study I, reported HE was associated with more reported episodes of the common cold, and the subgroup who reported amalgam intolerance as well as HE had a significantly higher prevalence of physician diagnosed hypertension. In a study on persons with VDU related skin problems, 40% reported migraine-like headaches (Berg M, 1988). The incidence of migraine in the general population is estimated to 15-25%. Migraine, as well as rosacea, is associated with reactions in regulatory mechanisms in the blood vessels.

Asthma, hay fever, allergic conjunctivitis and all allergies and hypersensitivities included in the questionnaire were significantly more often reported in the HE group as compared to referents. In an American study on multiple chemical sensitivity the proportion of respondents who reported a change in tolerance for allergens and foods, was more than twice as high in the group that reported chemical odor intolerance than in the control group (Davidoff and Keyl 1996). In another American study persons with chemical odor intolerance were four times more likely to report asthma and 72% more likely to report a history of hay fever than persons without odor sensitivity (Baldwin et al. 1999). In contrast to these studies, the two Swedish company based studies did not find any association between reported HE and allergies (Wadman et al. 1996, study II). In the health survey in the IT-company there was no statistically significant difference with regard to the prevalence of allergies in cases and referents, but the tendency was that of a higher prevalence in the HE group.

The commonplace of results in the biochemical analyses outside the laboratory establish reference values in study III provides further support that this group with predominantly neurovegetative symptoms (in this case disabling fatigue) distinguishes itself from the group with mainly skin complaints. In study groups that are characterized by VDU-related skin symptoms it is quite rare to find results in the blood chemistry that are outside the reference values (Hansson Mild et al. 1998). The nature of the pathological laboratory findings in study III did not however give any indication of specific disease or disorders. Great inter- as well as intra-individual variations were observed. One must also keep in mind that the chance for random results outside reference values increase with the number of performed analyses.

In a questionnaire survey of office workers, 69% in the HE group described skin symptoms to be the initial symptoms at the start of their hypersensitivity and 31% reported symptoms from the eyes as the first symptoms (Wadman et al. 1996). Thirteen percent reported some neurovegetative symptom, mostly vertigo and headache. In a survey to the members of the Swedish Confederation of Professional Employees (TCO), skin and eye symptoms were common early symptoms (Fransson 1996). But reported eye symptoms seemed less common in persons with longer illness duration. In the report from the survey of members of the self- help

group, symptoms from the eyes were not among the most commonly reported symptoms (Rosell 1994). Factors related to vision ergonomics and flickering light might be of importance in eye symptoms. Taken together these results might indicate either that eye symptoms decrease with longer duration of illness, or alternatively, that symptoms from the eyes are less predicative of progression in illness. Neurovegetative symptoms on the other hand were associated with poor prognosis (Knave et al, 1989). In a study on persons with VDU work, the coexistence of other symptoms than from the skin was associated with persisting complaints in a follow-up study after five years (Eriksson et al. 1997a).

In study V improvement was associated with higher scores on depression and hostility in SCL-90 prior to the intervention. The improved group also scored significantly lower on the index representing positive work climate at the pre-treatment assessment. It may be that the group that benefited the most from early intervention and a caring environment was the group who had experienced a sense of helplessness and lack of positive working climate. VDU related skin symptoms were shown to be influenced by the psychosocial work environment (Stenberg et al. 1995a, Eriksson et al. 1997b). A correlation between anxiety and depression and the number and severity of somatic symptoms has also been observed (Kellner R, 1994). An increase in cortisol was seen in the improved group prior to the study. Real-life stressors, like, for example unemployment, have in some studies been associated with increased levels of plasma cortisol (Biondi and Picardi 1999). But it seems apparent that there are great individual differences in the subjective perception of stress in a certain situation as well as extensive interactions between different neuroendocrine axes, which may explain observed variations in assessed biological markers. There has been an increasing interest during the last decades in psychoneuroimmunology and the complex processes and interaction among the behavioral, neural, endocrine and immune systems (Ader et al. 1995).

The result in several studies, including study V, indicates that several treatments and interventions may improve the well being in persons reporting HE (table 5). In many cases, there is improvement over time also in subjects where no specific intervention was applied. In a study on VDU-related skin complaints, 75% of 201 persons were followed 8 months (Berg 1988). Fourteen percent of these persons no longer had any VDU-related complaints after 8 months, 52% reported less problems and 28% had not experienced any change. In 6% the complaints had increased. A so-called spontaneous recovery (partial or complete) cannot be ruled out, nor the positive effect of a caring environment in general. An improvement was indicated in the control groups in the study on acupuncture (Arnetz B et al. 1995) as well as in study V. In study V the cognitive therapy was part of a multidisciplinary treatment package including an evaluation of the work place by an occupational hygienist and medical work-up and repeated visits to a physician. Perhaps the success of different interventions illustrates that a caring environment is of more importance than a specific treatment. An observation of an improvement in a group after the initial contact may also be an effect of regression to the mean, i.e. patients often seek help at a time when they felt at worst. An additional problem in evaluating results of specific actions is that several actions are often taken simultaneously.

Three persons have been reported to have improved after low doses of antidepressant and neuroleptic drug treatment (Jansson 1993). Persons reporting HE have reported that supplementation of vitamins, minerals and antioxidants has improved their health (Hillert 1993). But, in a randomized controlled clinical trial we did not observe any positive effect with

Table 5. Follow-up results from different interventions in groups reporting HE (presented in order based on type of intervention).

Project leader/author(s)	No of patients	Therapy/Intervention	Follow-up time	Results
Gustavsson and Ekenwall 1992	24	Investigation by a specialist in occupational medicine	4-33 months	11/24 improved, (reduced time of VDU work seemed to facilitate)
Hillert 1993	18	Investigation by a specialist in occupational medicine	25 months (mean)	10/18 improved, but all but one with some avoidance behavior
Lidén et al. 1996	220	Multidisciplinary intervention program (company based occupational health service)	Approx. two years	60 % had no symptoms (in full time work with VDU), 30 % improved
Harlacher 1998	80	Investigation by a dermatologist (extra time, special interest given to psychosocial factors)	0-24 months	30/80 recovered
Andersson et al. 1996	17 (9 treated, 8 controls)	Cognitive behavioral therapy	6 months	Significant reduction of estimated disability due to HE in the treated group.
Harlacher 1998	26 (13 pairs, 13 patients initially in a waiting group)	Cognitive behavioral therapy	9-12 month, incl. 3-5 months treatment	50 % improved or recovered, sign. reduction of complaints after therapy as compared to control group
Hillert et al. 1998 (Study V)	22 (10 treated and 12 controls)	Cognitive behavioral therapy	12 month (incl. 2-5 months treatment)	No difference between groups. Significant reduction of symptoms in both groups, significant reduction of complaints from HE in the treated group.
Arnetz et al. 1995	20 (13 deep, 7 superficial)	Acupuncture	7-8 months	Significant reduction of health problems in both groups, no significant difference between groups
Eliasch 1996 (personal communication*)	36	Shiatsu, offered to persons on sick leave because of HE	12-18 months	78 % were very satisfied 12 months after treatment, 47 % in work
Hillert et al. 2001 (Study IV)	16	Antioxidant supplementation	3 weeks treatment period	No effect of antioxidant supplementation on symptoms or reported HE

*The National Board of Health and Welfare (Message No 22/97) 1997.

regard to symptoms and perceived HE (study IV). Compliance seemed to have been good in the study, but the supplementation therapy did not produce any change in the biophysiological outcome parameters. There may be several explanations for this. The supplementation was within range of the recommended daily intake. The dose may have been too low in an absolute sense or relative to the participants' intake of antioxidants from their ordinary diet. The group reporting HE seems to be health conscious and may have a sufficient basic intake of antioxidants. A low antioxidant level was not indicated in any subject. In many cases the patients report taking higher doses on their own initiative and an effect of higher doses cannot be ruled out. There is in general limited evidence from prospective controlled studies that antioxidant supplementation has positive health effects (SBU 1997).

The prognosis appears to be very much dependent on how far the syndrome have progressed, see figure 3. Early handling has been associated with better prognosis (Harlacher 1998; Ahlborg and Gunnarsson 1998). It is our clinical experience that the risk for progress is increased in patients with several identified problematic factors (for example, medical diseases, problems at work and at home). The choice of therapy or intervention should be based on the clinical presentation of the syndrome, a broad-based investigation of environmental factors as well as the patient's point of view. Persons with long histories of illness, sick leaves or disability pensions usually have a need for a long rehabilitation period. In many cases, we find a need to start by offering these people supportive therapy to improve their quality of life.

In study IV a significant increase in symptoms and perceived HE was observed during weekdays. A decrease in avoidance behavior was also noted as compared to week-ends. The experience of a relationship between symptoms and work is a risk factor for an inability to work. A lower proportion was working in the HE group than in the referent group in study I (n.s.). In some cases, interventions aimed at reducing the exposure to electric and/or magnetic fields at work are successful and the afflicted person reports a reduction in symptoms. But in some cases we have observed an increase in symptoms in other situations and environments, for example, in the home environment, shortly after the interventions at work. The reason for this observation might be a true increase in sensitivity. Another possibility is that the experience of improvement at work after the intervention is taken as proof of causal relationship, which might induce a wish to avoid EMF exposure also in other places in order to prevent a deterioration in health. This may lead to an increase in worry and apprehension for experiencing symptoms in other situations, a state that may in itself influence the persons' well being.

7.3.1 Cognitive therapy

Regardless of the initial origin of the ill health in HE, there are strong indications that cognitive therapy may increase the chance of an improvement in health. Cognitive therapy may be introduced as one way to reduce symptoms and improve health, and the patients do not have to commit themselves to accepting alternative explanations for HE.

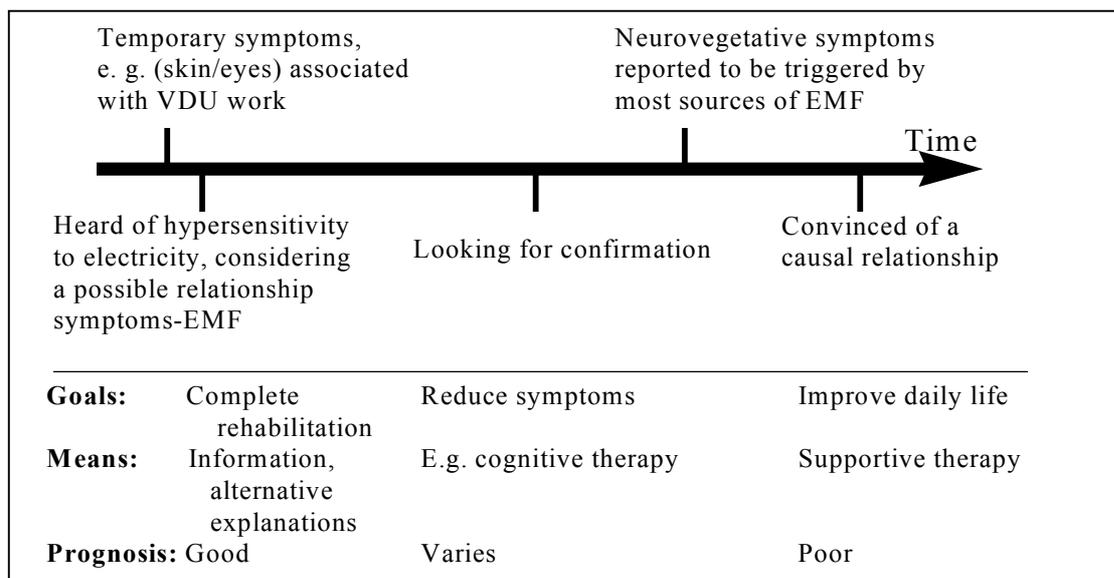


Figure 3. A proposed time axis of symptoms, attributions, interventions and prognosis for persons with medically unexplained symptoms that they suspect or believe to be cause by hypersensitivity to electricity.

Cognitive behavioral therapy has been evaluated in several studies, see table 5. The therapy often initially focuses on helping the patient find alternative, and better, ways to cope with the symptoms and thus reducing disability. The patients' interpretation of the symptoms as hypersensitivity to electricity might be questioned and tested in therapy. The therapist may then suggest alternative mechanisms behind symptoms and interpretations. The possibility of confirmation bias, i.e. a favoring information that supports a certain belief, may be pointed out. It is the experience of most therapists who have worked with this group of patients that an individual approach is necessary. The mean number of therapy sessions did not differ much among the three studies on cognitive therapy. Harlacher reported a mean of 8 sessions (range 3 to 16) (Harlacher 1998), Andersson and co-workers 7.4 sessions (range 4 to 10) (Andersson et al. 1996) and Hillert and co-workers (study V) 6.5 sessions (range 3 to 12).

The results in study V point in the same direction as the results in the study of Andersson and co-workers. Andersson and co-workers reported a decrease in reported disability caused by HE after therapy as compared to the waiting group (Andersson et al. 1996). Harlacher found a significant reduction in rated suffering from HE after treatment with cognitive behavior therapy (Harlacher 1998). Cognitive behavior therapy has also been shown effective in, for example, chronic fatigue syndrome. In a randomized controlled trial, significantly more patients in the therapy group improved their daily functioning as compared to the control group (Sharpe et al. 1996). In a similar study, cognitive behavioral therapy was associated with improvement in functional impairment and fatigue, although causal attributions were not challenged and did not change during the therapy (Deale et al. 1998).

The patient should understand that the introduction of psychological approaches to a problem is not equivalent to regarding symptoms as being of psychogenic origin or “fictitious”. Medically unexplained syndromes included in IEI do not as a rule qualify as psychiatric or mental disorders, but are according to the present knowledge not strictly somatic states either. The condition might be regarded as a psychobiological phenomenon (Ursin 1997). Body and mind should not be conceptualized as two separate entities (van der Feltz-Cornelis and van Dyck 1997). Reactions and changes in one necessarily lead to reactions in the other. One obvious example of this is the suffering and stress caused by any chronic disabling illness including the ill health in many persons reporting hypersensitivity to electricity, regardless of the initial cause of ill health. The need for improved models based on a biopsychosocial perspective has been pointed out (Arnetz 1996). Both somatic and psychological approaches may accordingly be applied as interventions. Drugs, physical training, psychological therapies can all influence the psychobiological balance. This is not exclusive for HE, the same principles apply for other conditions and diseases. Cognitive therapy has been demonstrated to improve the well-being in patients suffering from persisting symptoms in a variety of conditions including chronic cancer pain (Thomas and Weiss 2000) and persistent neck and back pain (Linton and Ryberg 2001).

7.3.2 Illness behavior

Illness behavior has been described as “the manner in which individuals monitor their bodies, define and interpret their symptoms, take remedial action, and utilize sources of help as well as the more formal health care system” (Mechanic 1986). It also includes how people monitor and respond to symptoms, as well as symptom change over the courses of an illness, and how this affects, for example, their behavior and response to treatment. The cultural context, the individual’s social network, his or her personality and life experience, and the response of the health care system all contribute to the response to symptoms. In a study on patients seeking medical consultation because of fatigue the patients psychological distress as measured with the GHQ was more closely associated with frequent attendance than their level of fatigue (Ridsdale et al. 1999). Patients who acknowledged that a psychological problem might contribute to their fatigue symptoms consulted a doctor significantly less frequently than those who thought the cause was physical or mainly physical.

The persisting conflicting opinions on HE in different groups of stakeholders are likely to influence persons suspecting, or being convinced of, that they are suffering from this syndrome. The conflicting opinions are often most apparent with regard to choices of preferred interventions. This situation might lead to an unfortunate lack of trust and a feeling that different groups try to oppose each other. An open mind is desired from all parties. New information will emerge from future studies, and scientist should take care to make it clear that any conclusions based on the present state of the art may be reevaluated in the future. Mainstream medicine is often perceived as conservative and reluctant to accept new ideas, possibly a side effect of the wish to have conclusive scientific evidence for any opinions expressed. The experiences of individuals should be taken seriously, but it is important to remember that openness to alternative explanations may be advantageous for the afflicted person in order not to overlook alternative causal or contributing factors and effective interventions.

Information from self-help groups that symptoms are to be regarded as warning signals may have important implication on the choice to or not to avoid perceived triggering situations. Improvements – including a possible placebo effect – may provide further support to an interpretation that electric or magnetic fields trigger symptoms. This belief and subsequent expectations of symptoms to be triggered in similar situations as experienced before may influence symptom presentation and prognosis. Confirmation bias may play a part through the tendency to accept and pay attention to experiences that agree with previously held ideas or assumptions. In a study on patients with chronic fatigue syndrome, a persisting belief in avoidance of exercise and activity was associated with lack of improvement (Deale et al. 1998). Media may also play an important part in the formation of risk perception and illness belief system.

Patients who are referred to departments of occupational and environmental medicine may differ with regard to their illness belief system from those afflicted individuals who seek help elsewhere. In a situation where mainstream medicine is perceived to fail to offer any clear explanation or proven cure for the perceived illness, it is not surprising that some afflicted individuals seek help outside the standard health care system. In many cases therapists practicing complementary medicine claim to have identified the cause of reported ill health and to have an effective treatment for the condition. As discussed above, one of these suggested causal theories in Sweden is that patients who experience symptoms attributed to EMF are suffering from oxidative stress even though no deficiency has been proven. People reporting HE often seem to be health conscious, including their diets, and rarely be smokers. Ten of fourteen participants in study III reported self-treatments with vitamins, minerals and/or antioxidants.

7.4 FACTORS ASSOCIATED WITH HYPERSENSITIVITY TO ELECTRICITY

7.4.1 Gender

More women than men reported HE in study I, but no gender difference was observed in the health survey in the IT-company (study II). In another study of employees in four companies, Wadman and co-workers found that reported HE was more common in women (Wadman et al. 1996).

Most other syndromes of unexplained medical symptoms like MCS, chronic fatigue syndrome and fibromyalgia are also more frequently reported by women (Wessely et al. 1999). Women also report most symptoms to a higher degree than men (Tibblin et al. 1990). A study group in primary health care, selected by the criterion that the subjects should present fatigue as their main symptom, turned out to include 75% women and 25% men (Ridsdale et al. 1999).

The influences of hormones, for example in relation to menopause when many of these syndromes seem to peak, have been discussed as a reason for gender differences. The interactions between the hypothalamic-pituitary-gonadal (HPG) and hypothalamic-pituitary-adrenal (HPA) axis have been pointed out (Anderberg 1999). Gender determined response to stress or exposure to different types of stressors might be considered. For example, women were shown to have higher norepinephrine levels than men during as well as after work (Lundberg and Frankenhaeuser 1999).

Observed differences in reported symptoms may represent actual differences in symptoms, due to biological or acquired risks, or an effect of differences in illness perception and reporting behavior. Stenberg and al focused on these alternatives in a study on sick building symptoms. The result did not support the hypothesis that women were more apt to report symptoms (Stenberg and Wall 1995).

7.4.2 Physiology

Physiological differences between persons suffering from HE and healthy controls have been observed. These reported differences include levels of stress-sensitive hormones during VDU work (Berg et al. 1992), heart rate (Wang et al. 1994), difference in skin temperature of left and right cheek at rest (Wennberg et al. 1994), pupil reactions to light (Wang et al. 1994) and EEG (electroencephalogram) registrations during exposure to modulated ("flickering") light (Wibom et al. 1995; Sandström et al. 1997). Studies on persons reporting HE have shown increased cortical response to flickering light as compared to controls (Sandström et al. 1997). In persons reporting HE an increase was found in the α -activity in EEG during exposure to flickering light, which was not the case in the control group (Wibom et al. 1995). An inclusion criterion in this study was however that the person was to have an experience of fluorescent light as a cause of discomfort or symptoms. Exposure to electric and magnetic fields has so far not been shown to produce any altered reactions in persons with HE as compared to controls.

There is substantial overlap between different syndromes of unclear origins. Patients reporting HE report amalgam intolerance to a higher degree than referents (study I). An overlap was also observed by Bergdahl and co-authors (Bergdahl et al. 1994). Overlap between syndromes has been described with regard to, for example, fibromyalgia, irritable bowel syndrome and chronic fatigue (Wessely et al. 1999, Aaron and Buchwald 2001). Observed overlap include case definitions, symptom presentation, non-symptom characteristics like sex and emotional disorders, and similarity in response to treatment. A possible common background may be discussed. In several syndromes, for example, chronic fatigue syndrome and fibromyalgia, focus has moved from discussions on suggested abnormalities in specific organ systems (like muscle dysfunction) to the role of central and neuroendocrine mechanisms (Wessely et al. 1999). The results described in the paragraph above might agree with the hypothesis that persons with environmental hypersensitivities have altered reactions in the autonomic nervous system, possibly due to a sympathetic predominance. Similar observations have been made in studies in patients reporting multiple chemical sensitivity (Wang et al. 1994; Bell et al. 1996; Bell et al. 1997).

Theoretically, the deviations in physiological reactions may be either a common risk factor for the different syndromes, or induced by the initial state of ill health and thereafter predisposing for other functional syndromes. In either case, various treatments are possible, both pharmacologically and psychologically oriented. Interventions that may reset the altered physiological homeostasis are expected to be successful. It may be pointed out that many of the observations and theories discussed above lend strong support to interventions like cognitive therapy or biofeedback, regardless of attribution or reported syndrome.

It is possible that reported possible associations between negative life events (Langworth 1997; Hansson Mild et al. 1998) and syndromes of medically unexplained symptoms may be due to

such a disturbance of the homeostasis by negative stress. If stress responses to maintain or regain the homeostasis are inadequate physical or mental disorders may develop. Negative life events were shown to be associated with increased levels of prolactin in blood (Theorell and Emlund 1993). Other medical disorders may also act as stressors for the individual. This theory is in agreement with the observed higher prevalence of reported HE in immigrants and association between HE and, for example, the common cold and reported allergies. An increase in reported disturbances from environmental factors may also be influenced by an increased reactivity.

Persons with VDU-associated skin complaints were shown to have higher blood levels of thyroxin and prolactin as compared to referents (Berg et al. 1992) – but only during the day of work and not the day of leisure. No association was found between hormone levels and exposure to electromagnetic fields during a provocation study with VDUs (Andersson et al. 1996). We did not observe any changes in stress related hormones in study V.

Rönnbäck and co-workers have hypothesized that neurovegetative symptoms are a result of similar responses in the brain to many different stressors (Rönnbäck et al. 2000; Bergqvist et al. 1998). The theory is based on new knowledge on how different parts of the nervous system communicate. Glutamate is used in signal transmission and glutamate neurons are activated by different kinds of sensory stimuli. In order to maintain an optimal signal-to-noise ratio the level of extra-cellular glutamate and potassium must be kept low (Rönnbäck et al. 2000; Hansson et al. 2000). If astrocytes are depolarized the necessary uptake of glutamate and potassium will decrease. Trauma, infections, cerebrovascular diseases and possibly environmental exposure like flickering light and electromagnetic fields may cause such a depolarization. The subsequently altered signal-to-noise ratio will decrease the ability to take in and process new information leading to difficulties concentrating, headache, fatigue etc. The experience of reduced mental capacity might secondarily lead to worrying, anxiety and stress – a possible vicious circle.

7.4.3 Personality and work related factors

We did not observe any differences in personal traits assessed as neuroticism and extraversion (EPI) in the comparisons between the HE and referent groups in study II. In study V the participants scored within the normal range according to the evaluation guidelines for somatization, alexithymia, attributional style and sense of coherence. Bergdahl reported differences in scores on personality in the HE group as compared to controls (higher scores in the Karolinska Scales of Personality [KSP] for somatic anxiety, muscular tension, psychasthenia and lower scores for socialization) (Bergdahl 1995). In the group that primarily related their symptoms to VDU work, the differences were less pronounced and included only somatic anxiety and muscular tension.

The rapid change in different aspects of office work during the last decades has been discussed as one important factor for the development of medically unexplained symptoms in the office environment. Berg and co-workers suggested the term “techno-stress” (Berg et al. 1992). A possible importance of factors related to the work organization has been suggested. These factors include, for example, lack of performance feedback and discrepancy between mental capacity and goals of the worker. Associations between symptoms and work related factors as

high work load and low social support (Stenberg et al. 1995a), lack of support from co-workers (Eriksson et al. 1997b), perceived higher work load (Arnetz et al. 1997) and observed changes in levels of stress related hormones lend support to this theory. But we did not identify any differences in work characteristics between the HE group and referents in study II. The HE group did not differ from referents with regard to scores on the indices based on the Karasek Theorell model, i.e. mental demand at work, intellectual discretion and control over the work process. Nor did we find any significant differences in levels of stress related hormones in samples taken at our department and samples taken at the participants places of work during workdays.

The differences in results may be due to different assessment instruments applied or study groups selected including their homogeneity. It should be noted that some studies indicating differences were primarily focused on skin symptom related to VDUs or other environmental factors in the work place. As discussed earlier, the exact relationship between groups reporting VDU related skin complaints and groups reporting HE is still unclear. The two groups may have different predisposing and contributing factors. It is difficult to determine if the indication in some studies of an association between HE on one hand and certain personalities and psychosocial factors on the other hand demonstrates a primary risk indicator or an effect of the illness. In the latter case, duration and degree of illness will be of importance regarding these outcomes.

The differences in results may also be an illustration of similar presentations of ill health in spite of different stressors in different individuals and groups as discussed above. The present knowledge on HE may agree with an interpretation of the ill health as an individually determined response to the total sum of different kinds of stressors in everyday life. The stress factors may include psychosocial, biological, physical or any other kind of stressors. Maybe it will not be possible to identify any clearly defined limited group of persons who are at risk of developing HE. Given the right (or wrong) circumstances we might all, more or less, be at risk!

8 CONCLUSIONS

Hypersensitivity to electric or magnetic fields is reported by 1.5% of the respondents in a representative population-based survey, and higher prevalence may be found in selected groups (for example, in work places). These results suggest widespread concern and worry for health effects from electric and magnetic fields in the general population. Hypersensitivity to electricity is more frequently reported by women and immigrants, and in many cases associated with reduced work ability.

Reported HE is associated with a wide range of other complaints and medical conditions, including symptoms from most organ systems, other reported hypersensitivities and traditional allergies, asthma and hay fever, and an increase in perceived disturbances from environmental factors. No specific symptom constellation was identified, but at least early-phase cases seem to be characterized mainly by skin symptoms. Fatigue in HE is reported as general and not physical. No correlation was found between reported degree of fatigue and cholinesterase activity. There is, as of yet, no known biological marker for HE.

Groups formed on the basis of reported HE are very heterogeneous. A multidimensional characterization (including symptom indices, belief, triggering factors, temporal aspects and behavior) is proposed to facilitate comparisons between study groups. Many factors seem to influence the clinical course in cases of reported HE. We did not find any association between personality and work characteristics and reported HE. Individually determined responses to many different kinds of stressors are discussed. The prognosis seems to be good in the majority of cases, at least in case of early intervention and a broad investigation by a multidisciplinary team. Cognitive therapy may further reduce perceived hypersensitivity to electricity. The randomized placebo-controlled study did not confirm the positive effect of antioxidant therapy that has been reported by some persons suffering from symptoms interpreted as HE.

9 FUTURE STUDIES

There are several possible interpretations of the observed higher prevalence of reported hypersensitivities and allergies in the HE group. One possibility is that HE is actually associated with immunologically mediated allergies and hypersensitivities. An alternative explanation would be that persons who report HE interpret their ill health and increased reactivity to different stimuli as allergies and hypersensitivities, even if they have not sought medical advice and had their suspicions confirmed in medical work-ups. It is also possible that persons who report HE suspect that they are (apart from HE) also allergic or hypersensitive to other factors although mainstream medicine isn't able to demonstrate these reactions (in the same way that the health care system has failed to establish HE). Further immunological studies and in-depth interviews may provide answers to these questions.

More information is desired on the most disabled group of persons who report HE. In these cases, social withdrawal is often pronounced. It is possible that qualitative studies are the best choice in the effort to learn more about factors of importance for this extreme progression in illness. The investigations should preferably be made in cooperation with research groups that focus on other forms of medically unexplained symptoms and functional syndromes. Common factors and syndrome-specific factors are of interest.

The possible importance of electric and magnetic fields in reported HE remains a controversial, and as of yet, unsettled question. There is a discrepancy between experiences of afflicted individuals and results in scientific studies. So far, controlled provocation studies have not provided support for a causal relationship or demonstrated an ability of individuals who report HE to detect exposure to EMF. Taken together, the results indicate that EMF is neither a sufficient nor a necessary cause for symptoms interpreted as HE. The possibility that some aspect of electric or magnetic fields under some conditions is a contributing factor isn't possible to test without hypotheses that are more specific. The identification of a biological marker that correlates to reported symptoms would be an advantage.

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ORIGINAL PAPERS

PAPER I

Prevalence of self-reported hypersensitivity to electric or magnetic fields in a population-based questionnaire survey.

PAPER II

Hypersensitivity to electricity: working definition and additional characterization of the syndrome.

PAPER III

Environmental illness: fatigue and cholinesterase activity in patients reporting hypersensitivity to electricity.

PAPER IV

The effect of supplementary antioxidant therapy in patients who report hypersensitivity to electricity: a randomized controlled trial.

PAPER V

Cognitive behavioural therapy for patients with electric sensitivity - a multidisciplinary approach in a controlled study.