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Holter ECG monitoring in patients with perceived electrical hypersensitivity

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Abstract

Earlier studies have indicated that patients claiming to be sensitive to electromagnetic fields, so-called electrical hypersensitivity (EHS), have a dysbalance of the autonomic nervous system (ANS) regulation. This paper focuses on a possible dysbalance in the ANS among EHS patients by the use of long-term monitoring of electrocardiogram (ECG) in both a patient and a matched control group. At the same time, the environmental power frequency magnetic field was recorded for both groups in order to see if there was any difference in exposure between the groups. ECG, heart rate (HR) and heart rate variability (HRV) as well as the magnetic field exposure were monitored for 24 h. Fourteen patients with perceived EHS symptoms were selected from the University Hospital, Umeå, Sweden. Symptoms indicating autonomic nervous dysregulation were not part of the inclusion criteria of the patient group. Age and sex matched healthy subjects were used as controls. No differences were found between the groups regarding magnetic field exposure or the mean HR for 24 h. The HRV analyses showed that the high-frequency (HF) component did not have the expected increase with sleep onset and during nighttime in the EHS group. When separating the sleeping and awake time even less differences between the two conditions in the EHS patients, both for the low-frequency and HF components in the HRV spectrum, were seen. EHS patients had a disturbed pattern of circadian rhythms of HRV and showed a relatively 'flat' representation of hourly-recorded spectral power of the HF component of HRV.

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Keywords: Autonomic nervous system; Heart rate; Heart rate variability

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1. Introduction

A significant number of persons are claiming to be sensitive to electromagnetic fields (EMF) with facial skin symptoms, neurovegetative and sometimes ocular symptoms. The phenomenon called electrical hypersensitivity (EHS) has been discussed and investigated for several years in Sweden and some other countries (Bergqvist and Vogel, 1997; Hillert et al., 1999; Rea et al., 1991). An increasing concern has followed the installation of new wireless technologies and rapidly increased exposure to other sources of EMF. The management of EHS and other forms of idiopathic environmental intolerance is problematic since no consistent diagnostic criteria exist. The combination of general neurasthenic complaints and somatic symptoms are unspecific and overlap with many other syndromes like multiple chemical sensitivity, sick building syndrome, fibromyalgia and gulf syndrome (Barsky and Borus, 1999; Sparks, 2000).

Different research approaches to this issue have been tried. Previously we have shown that EHS patients have a dysbalance of the autonomic nervous system (ANS) regulation with a trend to hyper-sympathotonia, as measured by heart rate (HR) and electrodermal activity, and a hyperreactivity to different external physical factors, as measured by brain evoked potentials and sympathetic skin responses to visual and audio stimulation (Lyskov et al., 2001a,b; Sandström et al., 1997). These data are in agreement with the physiological findings from other studies on persons with perceived EHS (Rea et al., 1991; Wang et al., 1994; Wibom et al., 1995). These observations indicate a deficiency in adaptive resources and possible predisposition to environmental maladaptation. Provocation studies of these patients have not revealed any worsening of symptoms or physiological reactions related to laboratory exposure to EMF (Lyskov et al., 2001b; Sandström et al., 1993; Swanbeck and Bleeker, 1989). Analysis of heart rate variability (HRV) has become a useful non-invasive tool in the assessment of ANS functions. The balance of sympathetic and parasympathetic activity can be

evaluated in several quantitative characteristics of the time and frequency domains. It has been established that the high-frequency (HF) oscillations reflect predominantly parasympathetic influences, but other non-neural mechanisms such as respiratory capacity may also be reflected in these oscillations (Malpas, 2002).

The spectral power of the low-frequency (LF) component is considered to be related to baroreceptor mediated blood-pressure control, and its magnitude (in normalized units) after postural change has been regarded as a marker of sympathetic activity. In general, however, the LF component is assumed to reflect both sympathetic and parasympathetic modulations of the cardiovascular system (Malliani et al., 1991; Task Force of the European Society of Cardiology and North American Society for Pacing and Electrophysiology, 1996). Characteristics of HRV can be used as predictors of cardiac morbidity and mortality (Dekker et al., 1997; Vein, 2000), or influence of occupational stressors (van Amelsvoort et al., 2000).

A lightweight, non-invasive electrocardiogram (ECG) Holter recorder does not limit daily life activity and is easily tolerated by the subjects. It can be used in combination with portable devices for monitoring individual magnetic field exposure. Such a tandem of methods is informative in the study of possible relationships between particular characteristics of magnetic field exposure and ANS functioning.

This paper focuses on ANS characteristics in EHS patients by the use of long-term monitoring of ECG in both a patient and a matched control group. The groups were also monitored for LF magnetic field exposure in their environment.

2. Methods

2.1. Study group

All subjects but one were recruited from patients registered at the Departments of Dermatology and Occupational and Environmental Medicine, University Hospital in Northern Sweden, Umeå, Sweden. To be included, subjects should perceive that exposure to video display terminals (VDT), fluo-

rescent tube light and TV set or other electrical sources induced symptoms within 24 h from exposure. The second criterion was that this possible association could not be ruled out or given an indisputable alternative explanation at the primary medical investigation. The subjects should either have VDT-related skin symptoms in whom facial skin symptoms dominate and VDT, TV set and fluorescent tube light were major aggravating factors, or suffer from perceived hypersensitivity to electricity for whom general/neurological/cognitive symptoms dominate and are aggravated by non-light emitting sources. Symptoms indicating autonomic nervous dysregulation were not part of the inclusion criteria of the patient group. The selection criteria excluded persons undergoing hormonal or hypotensive therapy. Since the HRV measures variations in RR intervals as a substitute for variations in PP intervals during sinus rhythm, the sinus node and thereby the HRV are influenced by the autonomic balance, and the method is, therefore, not applicable in patients with frequent supraventricular or extrasystoles (ES), so those had to be excluded.

Age and sex matched 'office' workers free from such symptoms were used as controls.

A total of 18 patients and 23 controls were included, but due to the selection criteria (medication, age matching, having arrhythmia, due to frequent non-sinus beats or severe cardiac conduction disturbances) and technical reasons in the recordings, 4 of the patients and 9 of the controls were excluded, leaving two groups of subjects (14 persons in each: 5 males and 9 females) in the investigation. The mean age of the patient group was 48.9 ± 9.2 years and for the control group the corresponding figure was 49.6 ± 10.6 years.

The study was approved by the local ethics committee.

2.2. ECG recording

Continuous ambulatory ECG monitoring was recorded over a 24-h period, using a two channels 24 h ambulatory tape recorder (Tracker 2, Reynolds Medical Ltd, UK). Two channels record

prevented possible artifact contamination in the HR and HRV analysis.

Four electrodes were attached: one in the V2 position, one in the V5 position and two as references underneath the right clavicle.

After visual examination for arrhythmia and ES, the ECG data were digitized and transferred to a computer for analysis. A standard program (Danica Holter Replay Unit, Danica Biomedical, Sweden) detected and calculated pathological events as well as dynamics of HR and HRV as measured in time domain: the average RR interval value calculated from accepted beats (mean RR), the standard deviation of the all NN (normal-to-normal) RR intervals (SDNN), square root of the mean squared differences of successive NN intervals (RMSSD), and ratio of NN intervals greater than 50 ms to total number of NN intervals (pNN50%), baseline width of the minimum square difference triangular interpolation of the highest peak of the histogram of NN intervals (TINN), mean of the standard deviation of all NN intervals for all 5 min segments of entire recordings (SDNN index).

In the frequency domain, only RR intervals related to normal beats were analyzed. Power spectral analysis was performed on the corresponding HR data by means of Fast Fourier Transformation. Total power in frequency band 0.003–0.4 Hz, as well as the power of the very low-frequency (VLF; 0.003–0.05 Hz), LF (0.05–0.15 Hz) and HF (above 0.15 Hz) components were calculated for each hour, as well as average data over the sleep and awake periods (see below). We also calculated the LF/HF-ratio and the normalized LFn [$LF/(tot - VLF)$] and HFn [$HF/(tot - VLF)$] values.

The ECG recording was also analyzed for underlying rhythm, frequency of atrial and ventricular ES. All data were reviewed and edited by the same technician.

2.3. Magnetic field monitoring

The monitoring of the power frequency magnetic field exposure for the patients and the controls during the 24-h period was done by an EMDEX II instrument (EnerTech Inc., USA). The instrument measures the magnetic field in the

frequency range 40–800 Hz, and the instrument can display values with different frequency bandwidth. In this paper we have used the broadband (BB) display of the resultant magnetic field.

Intermittency (IM) is a measure of the variation between the different measurement in a data set. It is based on the statistics of the absolute values of the differences between adjacent measurements.

The instrument is set to log and store the resultant flux density every third second. The data were processed by means of the computer program EMCALC.

2.4. Procedures

All participants were informed about the aims, methods and schedule of study and were paid for their participation. After an introductory part, subjects were asked to complete a Profile of Mood States (POMS), questionnaire, intended to assess the participant's mood over the past week (McNair et al., 1981). Then, ECG electrodes were attached, Holter recorder and EMDEX device were switched on. The participant carried the ECG recorder for 24 h during a typical working day and maintained a simple diary of the activities during that time, such as for instance entering and leaving the following places: in bed, at home but not in bed, on way to and from the work place, work hours, none of these places, unusually high physical activity, as well as time spent in front of a computer or TV. After the 24-h measurement period, the participant returned to the laboratory for unattachment of ECG electrodes and EMDEX device.

2.5. Statistical analyses

Analyses were made using SPSS for Windows (SPSS Inc., Chicago, IL). Student's *t*-test was applied to analyze difference between control and patient groups for average ECG and magnetic field data. For hourly calculated data, repeated measurement analysis of covariance (ANCOVA) with adjustment for age was used. The Huynh-Feldt epsilon was used to correct the degrees of freedom

Table 1

Selected time-domain measures of HRV during 24 h

Parameter (units)	Mean	
	Controls	EHS
SDNN (ms)	138 ± 42	151 ± 47
Mean RR (ms)	762 ± 65	780 ± 123
TINN (ms)	577 ± 145	670 ± 179
RMSSD (ms)	34 ± 15	35 ± 24
pNN50%	7.2 ± 6.8	8.6 ± 12.1
SDNN index (ms)	58 ± 18	65 ± 29

SDNN, standard deviation of the averages of RR intervals of the entire recording; Mean RR, RR interval duration; TINN, baseline width of the minimum square difference triangular interpolation of the highest peak of the histogram of NN intervals; RMSSD, root mean square differences of successive NN intervals; pNN50%, number of pairs of adjacent RR intervals differing by > 50 ms divided by the total number of RR intervals; SDNN index, mean of the standard deviation of all NN intervals.

for the interaction between the *Group* (control, EHS) and *Time* (24 levels) factors. The absolute values of HRV indices were log-transformed because of skewed distributions (total power, LF and HF). Data were also separated into 'sleep' and 'wakefulness' according to the subjects' diaries. The effects of the following factors and their interaction on the mean values of HRV indices for each period were tested in a separate ANOVA: *Group* (control, EHS) and *Sleep* (sleep, wakefulness). *P*-values less than 0.05 were considered to indicate statistical significance.

3. Results

There was no different in mood over the past week between the two groups, measured by the POMS test.

All the test persons were in sinus rhythm, and only few numbers of ES were recorded, amounting to a total of 0–130 ES during the 24 h recording period. Two patients and two controls had short series of supraventricular ES (<6 beats after each other).

ECG-data in time domain accumulated from 24 h registration did not show any significant difference between the groups, but the EHS group showed pervading higher values (Table 1).

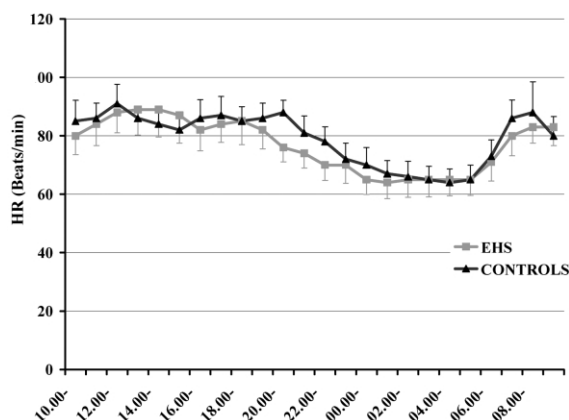


Fig. 1. Twenty-four-hour registration of HR (mean values for each hour) from EHS and controls. In bars the 95% confidence intervals are shown.

The HRV analysis was done on an hour-by-hour basis for 24 h, and since no overall group differences were found, we focused on the interaction between the group- and the time-factors. The HR mean values for every hour of the day are shown in Fig. 1. No difference between the groups was found ($d.f. = 10.8$, $P = 0.15$, $F = 1.46$). However, a slight non-significant lowered HR in the EHS group was noted for the late evening–early night hours. The log-transformed LF component representing the activity in both the sympathetic and parasympathetic branches showed no difference between groups ($d.f. = 13.9$, $F = 0.96$, $P = 0.49$). The same results were found when comparing total power ($d.f. = 14.4$, $F = 0.96$, $P = 0.50$) and VLF ($d.f. = 15.1$, $F = 1.1$, $P = 0.36$). However, the HF component representing the parasympathetic branch did not show the expected increase during nighttime in the EHS group. A significant difference between the groups was found for both the log-transformed and normalized HF component ($d.f. = 9.0$, $F = 2.25$, $P = 0.02$ and $d.f. = 8.6$, $F = 3.40$, $P = 0.001$, respectively) (Fig. 2). In addition, when comparing the log-transformed LF/HF a significant difference between the groups was also found ($d.f. = 9.4$, $F = 3.28$, $P = 0.001$).

Fig. 3 shows examples of power spectra for

both an EHS subject and a gender and age matched control subject, where the lack of increased HF component for the EHS subject during night is clear. However, not every patient showed such a distinct pattern of decreased HF during night. One patient had a pronounced enhancement in respiratory sinus arrhythmia as compared to the other subjects. The P -values reported above remained essentially unchanged when the analysis was repeated without this patient.

Separating the analyses of the relative power spectrum into sleeping and awake time showed differences between the two conditions in the EHS patients both for the LF and HF components (Table 2). The interaction between the sleep/wakefulness and group factor was statistically significant for the normalized HF power as well as for the index LF/HF.

The 24 h mean and median values of the magnetic field recordings for the patient group was 0.10 and 0.05 μT , respectively, and for the control group the corresponding values were 0.11 and 0.06 μT . In Table 3, the mean values of the BB field and the IM are given during sleeping time and when awake. No significant differences in magnetic field values were found between the groups.

4. Discussion

The methods of Holter monitoring provides information on HR and HRV, depending on the

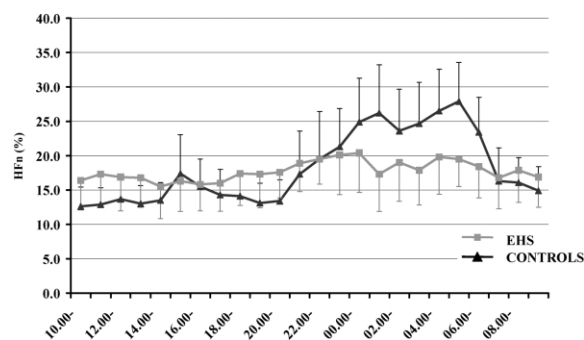


Fig. 2. Twenty-four-hour registration of normalized HF (mean values for each hour) from EHS and controls. In bars the 95% confidence intervals are shown ($F = 3.40$, $P = 0.001$, for group differences).

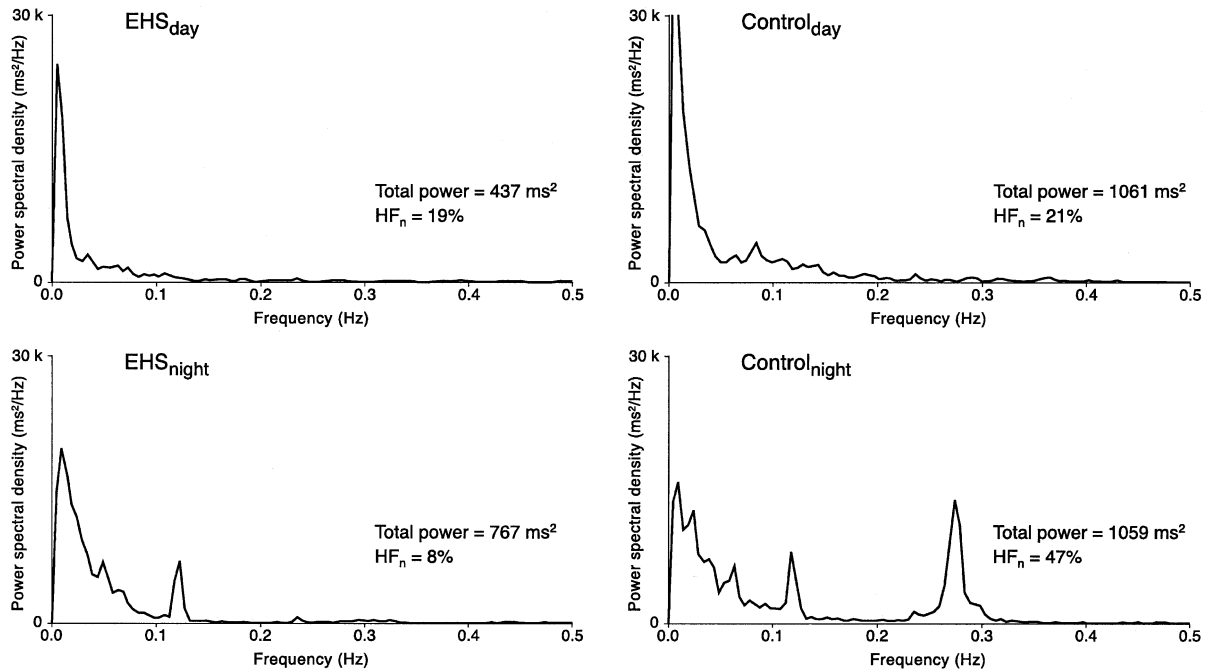


Fig. 3. Examples of power spectra for both an EHS subject and a gender and age matched control subject. The recordings are done during the night (01.00–02.00 h) and day (14.00–15.00 h). Total power as well as the relative power of the high-frequency component (HF_n) is noted for each recorded hour.

influence of sympathetic and parasympathetic activity on the sinus node and, therefore, reflect changes in balance of autonomic regulation during the 'real life' circumstances. Such examinations have not been carried out previously in patients with perceived EHS.

The major finding of the present study is that patients with perceived EHS had disturbed patterns

of circadian rhythms of HRV. In healthy subjects the autonomic activity shows a circadian rhythm with a domination of sympathetic tone during the day and typical considerable increase in parasympathetic tone during the night (Ito et al., 2001), a cycle clearly presented in our control group. In contrast, EHS patients showed a relatively 'flat' representation of hourly-recorded spectral power

Table 2

Mean values and standard deviation of HR, logarithm of total power (log tot), logarithm of absolute values and relative power of the LF and HF components and the index of sympathetic outflow (LF/HF) during sleep and when awake in control and EHS groups

Group	Log tot (ms ²)	Log LF	LFn (%)	Log HF	HF _n (%)	LF/HF	HR (beats/min)
Controls sleep	3.41 ± 0.35	2.83 ± 0.38	57.6 ± 7.0	2.43 ± 0.50	25.3 ± 8.8	0.40 ± 0.22	67.1 ± 9.4
EHS sleep	3.47 ± 0.35	2.87 ± 0.38	62.5 ± 7.0	2.31 ± 0.50	19.0 ± 8.7	0.56 ± 0.27	65.2 ± 9.6
Controls awake	3.30 ± 0.25	2.77 ± 0.33	69.4 ± 5.6	2.05 ± 0.37	14.7 ± 5.2	0.71 ± 0.18	84.1 ± 6.6
EHS awake	3.37 ± 0.34	2.84 ± 0.34	67.0 ± 8.2	2.21 ± 0.47	17.1 ± 7.1	0.63 ± 0.22	82.4 ± 10.7
Group × sleep/awake	<i>F</i> = 0.01 <i>P</i> = 0.94	<i>F</i> = 0.02 <i>P</i> = 0.89	<i>F</i> = 3.36 <i>P</i> = 0.06	<i>F</i> = 1.78 <i>P</i> = 0.19	<i>F</i> = 4.55 <i>P</i> = 0.04	<i>F</i> = 4.40 <i>P</i> = 0.04	<i>F</i> = 0.02 <i>P</i> = 0.90

F and *P* values from the ANOVA tests are shown (d.f. = 1).

Table 3

Mean values and standard deviation (μT) of the BB and IM characteristics of EMF exposure during sleep and when awake in control and EHS groups (d.f. = 1)

Group	BB (μT)	IM (μT)
Controls sleep	0.08 ± 0.09	0.04 ± 0.03
EHS sleep	0.07 ± 0.11	0.03 ± 0.03
Controls awake	0.13 ± 0.12	0.18 ± 0.19
EHS awake	0.11 ± 0.13	0.13 ± 0.17
Group $\times$ sleep/awake	$F = 0.11$; $P = 0.92$	$F = 3.66$; $P = 0.06$

of the HF component of HRV, which reflects the respiratory component of sinus arrhythmia and parasympathetic activity. These data might indicate significant parasympathetic withdrawal in EHS group during night hours in comparison with a normal circadian variation. This could lead to a diminished recovery during the night and thereby maybe a greater irritability during daytime. However, since respiration was not recorded, we cannot exclude that the disturbed pattern of HF variability may also be attributed to differences in nighttime breathing patterns. There were no differences in the way the patients and the control group experienced the quality of sleep during night (as read in their diary).

Trend towards parasympathetic reduction over night hours have been observed in patients with fibromyalgia (Martinez-Lavin et al., 1998). The increase of the LF/HF-ratio in the patient group was interpreted as a symptom of sustained sympathetic hyperactivity, which not only is likely to represent an association with typical sleep disturbances but probably also caused them. On the other hand, fibromyalgic patients showed diminished sympathetic responses to laboratory stressors (orthostatic, sensor stimulation, cold water immersion). Summarizing these results the authors concluded that this syndrome dysautonomia is characterized by a baseline circadian sympathetic hyperactivity with lack of additional sympathetic response to stress.

In contrast to this construct proposed for fibromyalgia, laboratory data obtained in EHS patients showed increased sympathetic reactivity to sensoric stimulation and orthostatic tests (Lyskov et al., 2001a,b). Partly a similar interaction of short-term

and long-term characteristics of the autonomic regulation was observed in persons with panic disorders. Reactivity to laboratory stressors such as postural change, emotional challenge and pharmacological probes indicate prevalence of sympathotone and diminished vagal effects (Cohen et al., 2000; Yeragani et al., 1994), whereas 24-h analysis of HRV revealed suppressed baseline sympathetic activity and normal vagal tone under conditions of daily life (McCraty et al., 2001). However, opposite to our findings, patients with panic disorders did not show diminished circadian fluctuations of parasympathetic indices. It seems that involvement of the autonomic system in the genesis of functional syndromes exhibits diverse relationships between baseline sympatho-vagal balance and reactivity to transient stressors and these might have different mechanisms.

Modification of circadian rhythmicity of sympatho-vagal balance without significant changes in general HRV over 24 h have been demonstrated in night shift workers (Ito et al., 2001). Interpretation of these data stress that the autonomic balance largely depends on physical activity levels and sleep–wakefulness cycle. Our study was limited to recording of HRV and diary information about physical activity. However, it seems unlikely that there were any obvious differences between the two groups in posture changes during the sleep hours, contributing to observed shifts in sympatho-vagal balance. Possible interactions with the ‘internal clock’ and circadian fluctuations of hormones and other basic physiological parameters that affect HRV (e.g. breathing patterns and respiratory capacity) need to be further investigated to clarify mechanisms of dysautonomia in these patients. The findings in this study should also be followed up by a thorough clinical investigation of the autonomic system functions including short-term HRV (tilt-table orthostatic challenge and/or cold water immersion) as well as ECG recordings during workload.

We have assumed that persons with dysautonomia might be sensitive to variations of low-level environmental factors. Magnetic field might be such a factor. Sastre et al. (2000) found that reduced power of the LF component of the HRV

spectrum and decreases in mean HR were associated with exposure to intermittent magnetic field.

Although the mean values of recorded 24-h magnetic field (BB or IM recordings) did not differ between patients and controls, EHS patients had in general lower values during the 24-h compared to the control group. Furthermore, the values we found did not differ from what we normally have in our homes (Hansson Mild et al., 1996). However, it is of certain interest to analyse the data on an hourly basis in order to see if there is any correlation between fluctuation in magnetic field and components in HRV. Such analyses are ongoing.

The major finding of the present study is that patients with perceived EHS, as a group, had a disturbed pattern of circadian rhythms of HRV and it seem reasonable to include HRV as part of the clinical investigation.

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