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ORIGINAL ARTICLE

Short-term effects of pulsed electromagnetic fields after physical exercise are dependent on autonomic tone before exposure

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Abstract The therapeutic application of pulsed electromagnetic fields (PEMFs) can accelerate healing after bone fractures and also alleviate pain according to several studies. However, no objective criteria have been available to ensure appropriate magnetic field strength or type of electromagnetic field. Moreover, few studies so far have investigated the physical principles responsible for the impact of electromagnetic fields on the human body. Existing studies have shown that PEMFs influence cell activity, the autonomic nervous system and the blood flow. The aim of this study is to examine the instantaneous and short-term effects of a PEMF therapy and to measure the impact of different electromagnetic field strengths on a range of physiological parameters, especially the autonomic nervous systems, determined by heart rate variability (HRV) as well as their influence on subjects' general feeling of well-being. The study comprised experimental, double-blind laboratory tests during which 32 healthy male adults (age: 38.4 ± 6.5 years) underwent four physical stress tests at standardised times followed by exposure to pulsed magnetic fields of varying intensity [HPM, High Performance magnetic field; Leotec; pulsed signal; mean intensity increase: zero (placebo), 0.005, 0.03 and 0.09 T/s]. Exposure to electromagnetic fields after standardised physical effort significantly affected the very low frequency power spectral components of HRV (VLF; an indicator for sympathetically controlled blood flow rhythms). Compared to placebo treatment, exposure to 0.005 T/s resulted in accelerated recovery after physical strain. Subjects with lower baseline VLF power recovered more quickly than subjects with higher VLF when exposed to higher magnetic field strengths. The application of electromagnetic fields had no effect on subjects' general feeling of well-being. Once the magnetic field exposure was stopped, the described effects quickly subsided. PEMF exposure has a short-term dosage-dependent impact on healthy subjects. Exposure to PEMF for 20 min resulted in more rapid recovery of heart rate variability, especially in the very low frequency range after physical strain. The study also showed the moderating influence of the subjects' constitutional VLF power on their response to PEMF treatment. These findings have since been replicated in a clinical study and should be taken into consideration when PEMF treatment is chosen.

Keywords Magnetic field effects · PEMF · Heart rate variability · Very-low-frequency · Recovery

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Introduction

Medical literature includes numerous studies showing that the therapeutic application of pulsed electro-magnetic fields (PEMFs) can accelerate healing after bone fractures (e.g. Icaro Cornaglia et al. 2006; Cheing et al. 2005) and also alleviate pain (e.g. Shupak et al. 2006; Lyskov et al. 2005).

Several studies examined the effects of PEMFs on other medical conditions, including inflammatory or degenerative diseases of the locomotory system, wound healing, depression and tinnitus (e.g. Dortch and Johnson 2006; Owegi and Johnson 2006). However, some of these studies yielded contradictory results. The studies suggest that the effect of magnetic field exposure is dependent on the applied magnetic field strength and also the frequency of the magnetic field (e.g. Markov and Colbert 2000; Stepansky et al. 2000).

If magnetic fields are to become an effective and non-invasive treatment alternative for a wide range of disorders it is desirable, therefore, to have rigorous scientific studies that examine and describe how magnetic fields affect living tissue in order to ensure the selection of the correct dosage and also type of exposure.

The results of studies described in the medical literature show significant variations with regard to the chosen magnetic field strength (amplitude and frequency), signal forms and also duration of exposure and treatment, which are typically linked to the treated disorder (e.g. Quittan et al. 2000).

Pulsed electro-magnetic fields induce electric currents in biological tissue, which is a relatively good conductor. It is not possible to measure the magnitude of the electric current induced by PEMF in living tissue directly, but it can be estimated using the Maxwell equation[1] (e.g. Bassett 1989) or more complex models (e.g. Pilla 2006).

There is conclusive evidence that PEMF treatment affects cell growth especially of osteoblasts (e.g. Fassina et al. 2006; Yuge et al. 2003; Diniz et al. 2002; Lee and McLeod 2000; De Mattei et al. 1999; Heermeier et al. 1998; Fitzsimmons et al. 1994). Some studies suggest that PEMFs might also have an impact on the autonomic nervous system, which is anatomically located in the human organism similar to an electromagnetic aerial. The effects on blood flow described in the literature (e.g. McKay et al. 2006; Kanai et al. 2004; Ichioka et al. 1998) may also be explained by sympathetic nervous system involvement.

Several studies have examined the effects of PEMFs on the autonomic nervous system and heart rate variability (HRV):

Tabor et al. (2004) investigated the impact of exposure to 50 Hz PEMF on the heart rate variability in human subjects and found a marked decrease in the heart rate and increase in SDNN (standard deviation of normal to normal interval within a 15-min period) in the PEMF group. Exposure protocols were either "half-hour PEMF-off/half-hour PEMF-on" or "half-hour PEMF-off/half-hour PEMF-off", whereas the field strength was 500 microT at the centre of the coil, 150–200 microT at the human subject's heart and 20–30 microT at the subject's head.

Similar results were reported by Sait et al. (1999) who found that exposure to PEMF (28 microT at 50 Hz for 100 or 150 s) decreased the heart rate while the vagal tone [high frequency (HF) band of the HRV spectrum] increased, as compared to a similar period of sham-exposure.

The effects of nocturnal exposure to magnetic fields on heart rate variability were investigated by Sastre et al. (1998) and Graham et al. (2000). Both studies reported a reduction in the low frequency (LF) band of HRV, which is associated with heart rate synchronous blood pressure rhythm. The applied field strength in these double-blind studies was 200 mG resp. 28.3 microT.

The main aim of this study was to examine the instantaneous and short-term effects of exposure to electromagnetic fields of different strengths on the psycho-physiological recovery of humans. The study assessed the effects on physiological and psychological parameters especially of the autonomic nervous system, as well as the subjects' general feeling of well-being. It was hypothesized that the beneficial effects of electromagnetic fields on recovery and pain relief described in the literature are due to the response of the autonomic nervous system to the stimulation, which should result in measurable influences on parameters of HRV. We focused on the effects on the autonomic balance and the response of the autonomic nervous system.

Methods

Design

The study employed a single-factor repeated measurement design, comprising experimental, double-blind laboratory tests and exposure to varying magnetic field strengths. Four magnetic field strengths were employed. A pulsed signal was used (HPM, High Performance Magnetic field, produced by LEOTEC Technische Handels- und Produktionsges.m.b.H; standard: EN 60601). The mean magnetic pulse increase was 0 T/s (placebo), 0.005, 0.03 and 0.09 T/s. The order of the testing procedures were partially varied between the subjects.

Subjects

Thirty-two healthy male adults were accepted for the study. The average age of the subjects was 38.4 years, with a range of 30–56 years (Weight: mean = 84.2 kg, range: 68–105 kg;

[1] According to the Maxwell equation, we induced three different field strengths (E; mV/cm) and current densities (J; mA/mm^2) in the tissue of our subjects: 0.005 T/s: $E = 3.75$, $J = 0.0039$; 0.03 T/s: $E = 22.5$, $J = 0.0233$ and 0.09 T/s: $E = 67.5$, $J = 0.0700$; To estimate the induced field strengths and current densities we used the properties of the medulla with a specific conductivity of 0.10375 S/m and a diameter of 3 cm. Furthermore, we assumed that the flux densities as well as the conductivity of the living tissue is homogeneous, which is not completely accurate for real tissue.

height: mean = 182 cm; range: 172–196 cm; BMI: mean = 25.4 kg/m^2, range: 21–31 kg/m^2). Three of the subjects had to be excluded because of unexpected health problems (frontal aneurysm, prolapsed disc and high blood pressure) not connected to the interventions. The test persons had received oral and written information about the tests and the proposed procedure. They gave their written consent and received a payment of € 70 as well as comprehensive feedback on the results after completion of the study.

Test protocol

Each subject participated four times in the test protocol (see Fig. 1), which was conducted on the same days of the week and at the same time in the morning using standardised test conditions. At the beginning of the test, a single-channel high-speed ECG monitor (HeartMan, Graz, Austria; sample rate: 4,000 Hz, resolution: 16 bit; Moser et al. 1992) was fitted and the subjects filled in a questionnaire on their well-being (Basler Befindlichkeits-Skala; Hobi 1985). This was followed by a 15-min rest period ('pre-strain') during which the subjects lay down with their eyes closed so as to permit the determination of the physiological resting state for each participant. The subjects were then instructed to stand upright before they completed a physical stress test ('strain'; Harvard Step Test; Keen and Sloan 1958). During this test the subjects had to step for 4-min with a stepping rate of 0.5 Hz.[2] This was followed by a 30-min supine phase. During the first 20 min the test persons were treated with a pulsed magnetic field or received placebo treatment ('exposure-rest'). The subjects did not know the duration of the exposure. After the tests, the subjects again answered questions on their feeling of well-being and their opinion of electromagnetic field therapy. The ECG recording (HRV assessment) was acquired during the whole test-procedure.

Biometric measurements

The HRV parameters[3] were calculated for 5-min sequences according to the standards of Task Force (Moser et al. 1994; Task Force 1996; http://www.heartbalance.com). For statistical analyses the last 5 min of each test-phase was used, whereas the transitions between the different test phases were excluded from the computations.

The mean pre-strain values of each test person were used to estimate autonomic tone, which can be seen as a constitutional factor.

All HRVs were computed from the RR intervals of heartbeat and the natural logarithm was used to avoid problems of logarithmic distribution of the data. Artefact-related data (containing less than 95% of valid data for a given sequence) also excluded after automatic and visual checks. An error probability (α) of 0.05 and a test strength (1-ß) of 0.80, considering an average effect size (d) of 0.5, resulted in an optimum random sample size of 23. The correlations of the measured physiological parameters ranged between $r = 0.45$ and $r = 0.90$. The sample sizes were computed using nQuery Adviser® (5.0).

A two-sided test statistic without alpha adjustments was applied as well as single factor variance analysis for repeated measurements.

Ethical issues

The proposed test procedures were submitted to an ethics committee [*Österreichische Arbeitsgemeinschaft für klinische Pharmakologie* (Austrian Working Group on Clinical Pharmacology), *Institut für Hypertoniker*; Protocol 10/04; registration number of the clinical evaluation in the Federal Ministry: No 20040031]. The proposed tests were approved.

This study was commissioned by LEOTEC Technische Handels- und Produktionsges.m.b.H. (LEOMED Medical Systems GmbH; 4030 Linz, Neubauzeile 101, Austria) as a Phase IV study.

Results

After completion of the tests and collection and archiving of all the data, the key identifying the subjects and to which group they belonged was submitted to the researchers by the sponsor to process and evaluate the data. The data (metric data, normal distribution, homogeneous variances; cf. Kuo et al. 1999) were examined for consistency and suitability for statistical evaluation and approved. The results for five subjects had to be excluded owing to unexpected events not related to the treatment ($n = 3$), technical problems problems during ECG monitoring ($n = 1$), or artefacts ($n = 1$). Only those subjects were included in the statistical analysis for whom valid data had been recorded under all four-test conditions ($n = 27$).

The heart rate was on average 12.7 ± 6.8 bpm higher during the recovery phase after physical strain (last 5 min of 'exposure-rest'; see Fig. 1) than during the 'pre-strain' phase. The return of the heart rate to the 'pre-strain' level following exercise took longest after placebo treatment. The fastest return to the pre-strain level was recorded after

[2] The height of the platform was adjusted to the size of each test person followed by a short test trial to get used to the physical stress test before starting the test protocol. Subjects showed an average heart rate of 155 beats per minute (bpm; range: 116–192 bpm).

[3] HRV values are depending on the age and decline with aging (e.g. O'Brien et al. 1986; Moser et al., 1998; Umetani et al. 1998), but this is not important for a test protocol with repeated measurements (cross-over design). In this study, age is not significantly associated with the reported dependent variables and their changes during exposure.

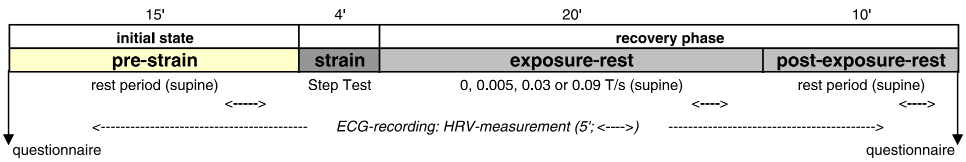

Fig. 1 Test-protocol. At the beginning and the end auf the test-procedure the subjects filled in a questionnaire on their well-being. The HRV measurements started with the 15-min rest period ('pre-strain'; initial state) in supine position. After that they had to complete a 4-min physical stress test ('strain'), which was followed again by a 30-min rest-phase in supine position with their eyes closed. During the first 20 min the test persons were treated with a pulsed magnetic field or received placebo treatment ('exposure-rest'). During the last 10 min of the resting period no magnetic field exposure was applied ('post-exposure-rest'). The volunteers' had no knowledge about the timing of the exposure-protocol (and the treatment condition). The last 5 min sequence (↔) of each test phase was selected for statistical calculations

exposure to a PEMF of 0.09 T/s (mean difference between 0.09 and 0 T/s: 1.85 ± 6.57 bpm; Post-Hoc$_{LSD}$: $P = 0.156$). No significant differences in heart rate responses were found between the four test conditions (GLM: $P = 0.376$).

The statistical analysis of recovery related HRV parameters shows a significant reduction of the vagal tone by around 15% after physical exercise ('exposure-rest') compared to the 'pre-strain' phase, which was not dependent by the strength of the applied electromagnetic field.

Figure 2 shows the values for two parameters of sympathetic and total autonomic nervous system activity (absolute values) under the four test conditions [0 T/s (placebo group), 0.005, 0.03 and 0.09 T/s]. There is a significant dependency between the applied magnetic field strength and the observed sympathetic tone. After exposure to an electromagnetic field of 0.005 T/s the sympathetic tone more rapidly returned to the initial state ('pre-strain') during the recovery phase after physical exercise ('exposure-rest') than after placebo treatment (0 T/s). With higher magnetic field strengths, the effect of accelerated recovery is reduced and no significant short-term effects on the autonomic responses of the body were seen after stop of PEMF exposure ('post-exposure-rest').

Figure 3 shows the values of the sympathetic and total autonomic nervous system activity recorded for all the subjects following exposure to PEMFs of 0.005, 0.03 and 0.09 T/s (ordinate axis) compared with the placebo treatment of 0 T/s (abscissa axis). The resulting regression lines show significant deviations ($P < 0.05$; cf. Kleinbaum 1978) from the line of identity (hatched line). During the subsequent 'post-exposure-rest' phase (instantaneous effect), the effect disappeared.

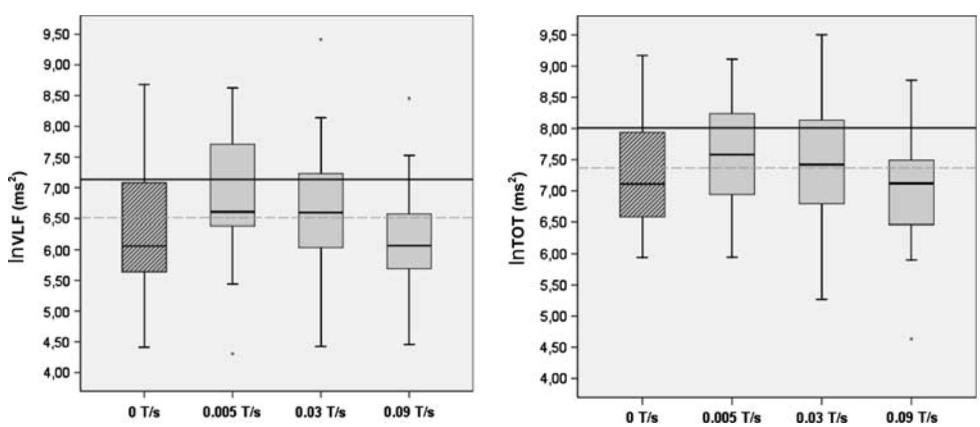

Fig. 2 Instantaneous effect of different magnetic field strengths on VLF and total heart rate variability (*TOT*). Box plots were used to visualise the absolute values recorded during exposure to PEMF or placebo treatment under the four test conditions ($n = 27$). The continuous line indicates the mean 'pre-strain' value before physical exercise; the hatched line represents the average absolute value during exposure for all four test conditions. The 'pre-strain' values are not reached during magnetic field exposure following strain. The values for VLF (*left plot*) differed significantly between the four test conditions [GLM: $df = 3$; $n = 27$; $F = 3.74$, $P = 0.014$ or $p_{quadratic} = 0.001$ ($F = 14.22$); PostHoc$_{LSD}$: 0 vs. 0.005 T/s, $P = 0.017$; 0.005 vs. 0.09 T/s, $P = 0.001$; 0.03 vs. 0.09 T/s, $P = 0.066$]. This was not found in the pre-strain phase (not illustrated here; $F = 0.28$; $P = 0.843$). After the end of exposure these differences subsided ($F = 0.35$, $P = 0.790$; not illustrated here). The results for TOT (total variability in the spectral range, box plot on the right) are comparable although not so significantly different [$P = 0.048$ ($F = 3.02$) or $p_{quadratic} = 0.004$ ($F = 10.29$); 0 vs. 0.005 T/s, $P = 0.013$; 0.005 vs. 0.09 T/s, $P = 0.009$; 0.003 vs. 0.09 T/s, $P = 0.092$; pre-strain: $F = 0.46$; $P = 0.658$; post-rest: $F = 0.89$, $P = 0.451$]. The results for SDNN (total variability in the time range) are not shown here. They show similar trends [$P = 0.151$ ($F = 1.82$) or $p_{quadratic} = 0.019$ ($F = 6.28$); 0.005 vs. 0.09, $P = 0.025$; pre-strain: $F = 0.97$; $P = 0.410$; post-rest: $F = 0.99$, $P = 0.389$]. The computation of HRV parameters follows the criteria of the Task Force (1996). An analysis of the quadratic trend ($p_{quadratic}$) is only useful if the measurement repetition factor is a metric variable and the differences between the factors are the same. It was nevertheless decided to include the exact significance levels in order to illustrate the non-linear dosage–effect relationship.

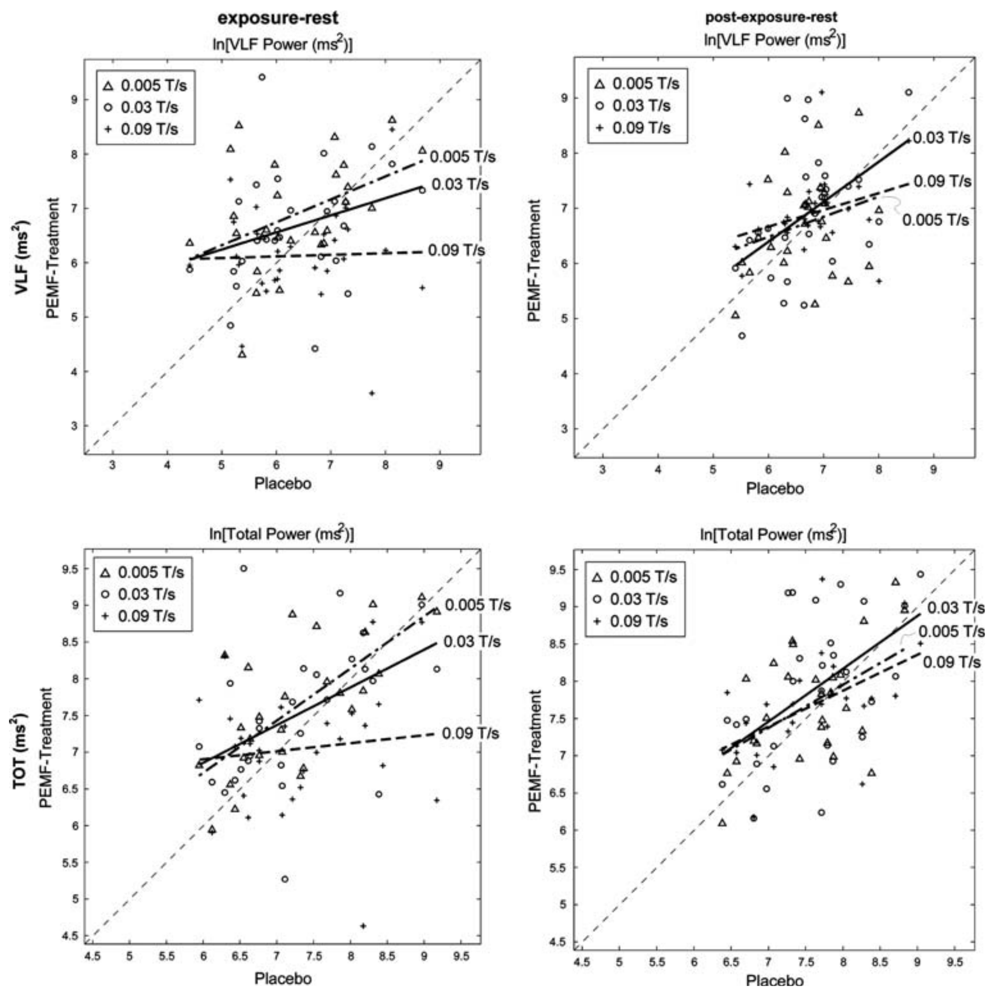

Fig. 3 Short-term effects on VLF and Total Variability. Figure uses scatter plots to compare the results obtained during exposure to PEMFs [0.005 (*triangle*, *dash dotted line*), 0.03 (*circle*, *solid line*) and 0.09 (*plus*, *dashed line*) T/s; ordinate] and during placebo treatment (0 T/s; abscissa) for each subject ($n = 27$). If no differences were found between PEMF exposure and placebo treatment then the resulting regression line would be accurately 45 degrees (hatched line through the origin; equivalent placebo vs. placebo). The *left column* includes the scatter plots during exposure; the *right column* shows the absolute values after exposure. During exposure (column on the left) the regression lines during PEMF treatment were markedly different from the one expected from the placebo treatment. These differences disappeared during the post-exposure rest phase (column on the right). The following table shows the statistical analysis of the regression lines (cf. Kleinbaum 1978) for the rest during PEMF treatment ("exposure-rest")

Table 1

	VLF: rest during PEMF treatment (*P* values)					TOT: rest during PEMF treatment (*P* values)				
PEMF	Linear regression (r^2)	0	0.005	0.03	0.09	Linear regression (r^2)	0	0.005	0.03	0.09
0	$y = x$ (1)	_	0.048*	0.014*	0.000**	$y = x$ (1)	_	0.001**	0.000**	0.000**
0.005	$y = 0.42x + 4.2$ (0.18)		_	0.426	0.019*	$y = 0.71\,x + 2.5$ (0.48)		_	0.690	0.121
0.03	$y = 0.31x + 4.7$ (0.10)			_	0.172	$y = 0.51\,x + 3.8$ (0.21)			_	0.281
0.09	$y = 0.029\,x + 5.9$ (0.00)				_	$y = 0.11\,x + 6.3$ (0.01)				_

If the influence of constitutional autonomic factors is considered in the analysis, then the obtained results suggest that the optimal magnetic field strength is linked to individuals' physical characteristics (see Fig. 4). The categorisation of the subjects was based on the average results obtained for the autonomous parameters during the 'pre-strain' phase under laboratory conditions.

The observed effects of magnetic field exposure showed significant interrelations with the very-low-frequency power spectral components of HRV (VLF). After placebo treatment, the fastest return to the 'pre-strain' values of VLF was recorded for subjects with high very-low-frequency power components (VLF), while for subjects with higher VLF levels the fastest recovery rates and return to initial values were recorded after exposure to magnetic fields.

Psychometric measurements were used to evaluate the subjects' perception of the effect of the different magnetic field strengths during therapy:

The test persons were asked to fill in a standardised questionnaire on their well-being (Basler Befindlichkeits-Questionnaire; Hobi 1985) before and after the tests. The analysis used the differences in order to identify changes in the subjects' perception of well-being following PEMF treatment. The results show no significant effect of the applied magnetic field strengths on the subjects' perception of global well-being.

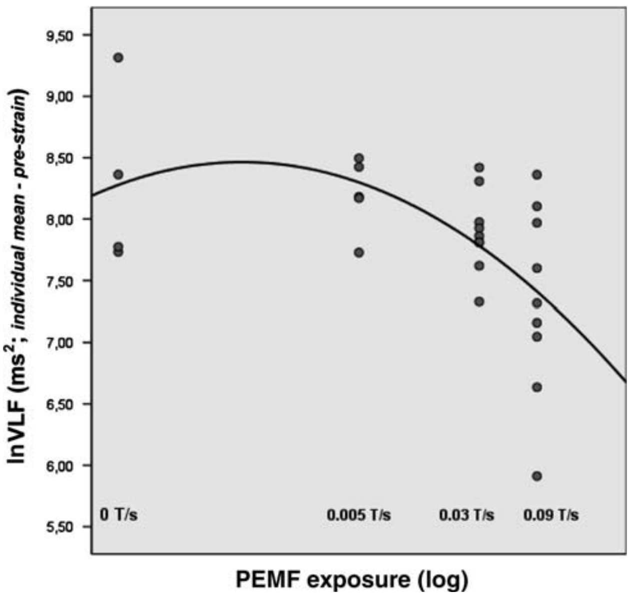

Fig. 4 Moderating influence of constitutional VLF power. For each subject the test condition showing the most complete recovery after strain during the exposure rest phase was selected for this plot ($n = 27$). The corresponding VLF pre-strain values were plotted against the respective magnetic field exposure strength. The graph shows that subjects with low constitutional VLF power (mean absolute value during 'pre-strain' phase; ordinate) show a faster recovery and more rapid return to the initial pre-strain state at higher PEMF exposure levels [abscissa (log)]. Test persons with a high VLF power recover most quickly after placebo treatment ($r^2 = 0.31$). A three-level categorisation of mean VLF 'pre-strain' values (VLF-Cat.) shows significant interactions in a GLM (PEMF × VLF-Cat.: $F = 2.30$; $P = 0.044$) and emphasizes the importance of VLF categorisation

The results of a questionnaire which was filled in after each of the tests to measure the subjects' general attitude to magnetic field therapy and which used a 5-point rating scale (0 = 'I don't agree' up to 4 = 'I agree') showed that all subjects had a positive attitude to PEMF therapy (2.9 ± 0.7) and said that they would also recommend it to other people (2.9 ± 0.6). The majority said that PEMF treatment (including placebo treatment) had been comfortable (3.1 ± 0.6), although they were not sure if they had actually felt an effect (2.4 ± 0.6). No significant differences between the four different laboratory conditions were found.

Discussion

The aim of this double-blind study was to examine the instantaneous and short-term effects of exposure to different magnetic field strengths on the recovery of heart rate variability after physical exercise. Additionally, the subjects' feelings of well-being during treatment should be investigated.

The analysis showed different physiological recovery responses to magnetic field exposure after physical stress dependent on the magnetic field strength. Significant changes of the sympathetic and total HRV parameters (VLF, TOT; Fig. 2) were found, with the magnitude of the changes correlating with the applied magnetic field strength. A non-linear dosage-effect relation between applied magnetic field strength and physiological parameters of the HRV was observed. After the PEMF exposure was stopped, the effects rapidly subsided (Fig. 3; Table 1).

Our main finding was that significantly different effects of different magnetic field strengths on the autonomous nervous system and especially on VLF could be observed. The literature suggests that the VLF portion of the HRV is connected to thermoregulation and regulation of the peripheral circulation (Fleisher et al. 1996), showing oscillations similar to that of blood flow. Taylor et al (1998) observed a link between the VLF component and the angiotensin system. Several studies have shown that a reduced VLF component may play a role in depression and increased morbidity (cf. Carney et al. 2005; Hadase et al. 2004).

The VLF portion of the HRV was also shown to be a non-negligible factor concerning the selection of magnetic field strength (Fig. 4). Subjects with low VLF power recovered more quickly at higher magnetic field strengths. These findings have since been replicated in a clinical study of patients receiving in-patient rehabilitation (Fig. 5).

The findings indicate that the initial VLF values of HRV of each subject may be taken into consideration in order to optimize the effect of PEMF treatment on the autonomic parameters.

The subjects reported that they had not felt any difference between the four magnetic field strengths, which they had been exposed to; nor did the PEMF treatment significantly influence their overall feeling of well-being.

Several studies report the beneficial effects of PEMFs in the treatment of inflammatory diseases (e.g. Dortch and Johnson 2006; Owegi and Johnson 2006) and pain (Shupak et al. 2006). There is a large body of literature showing the moderating influence of the autonomic nervous system on healing processes and inflammations (e.g. Shahabi et al. 2006; Miksa et al. 2005; Gaykema et al. 1998). These findings support our conclusion that HRV may play an important role in PEMF therapy evaluation as well as selection of field strengths. VLF and possibly other HRV parameters may be used as an indicator for the reactivity of the autonomic nervous system. Measurement of HRV thus will facilitate the selection of appropriate magnetic field strengths and could also help us understand the potential effects of electromagnetic fields on the body.

The effects of PEMFs on human autonomic nervous system were found to be significant using heart rate variability measurements. The PEMF treatment of healthy individuals shows dosage-dependent effects on the autonomic nervous system. The subjects' constitutional VLF power plays an

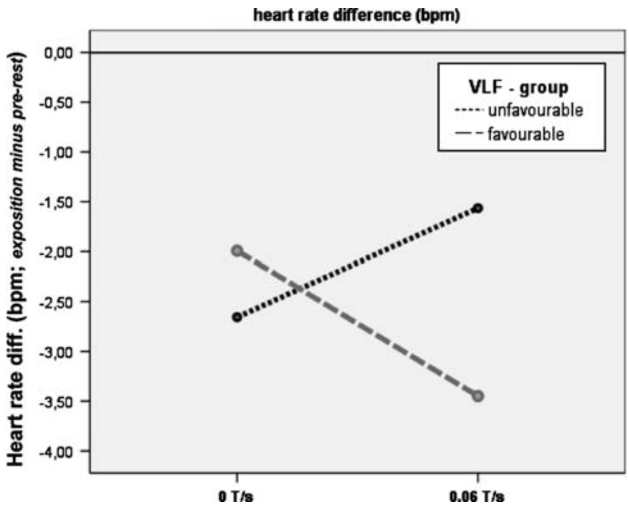

Fig. 5 Impact of VLF-replication in a clinical study ($n = 39$). Instantaneous effect of PEMF treatment on heart rate. A study of patients receiving in-patient rehabilitation who were repeatedly exposed to PEMF while in supine position (0.06 T/s; 'Verum') showed a significantly greater decrease in the heart rate in patients with low ('favourable') VLF compared to patients with high ('unfavourable') VLF in the verum group. Highly significant second-order interaction was observed (GLM: test group × time × VLF-category: $F = 6.378$, $P = 0.001$) as well as significant interrelations between the test group and VLF category ($F = 4.478$, $P = 0.042$). Similar results were found for other HRV components (not illustrated here)

important role on the outcome and is recommended to be taken into account to select field strength in PEMF therapy.

The results of this study do not yet permit us to issue clear recommendations for the selection and use of specific magnetic field strengths in different patient groups as the test persons in this study were healthy males who were subjected to a standardized recovery/stress protocol.

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