ELSEVIER

Clinical Neurophysiology 111 (2000) 1942–1948

www.elsevier.com/locate/clinph

Brain frequency magnetic fields alter cardiac autonomic control mechanisms

Antonio Sastre*, Charles Graham, Mary R. Cook

Midwest Research Institute, 425 Volker Boulevard, Kansas City, MO 64110, USA

Accepted 7 August 2000

Abstract

Objective: Heart rate variability (HRV) is a noninvasive indicator of sympathetic and vagal cardiovascular control known to be tightly correlated with sleep stages. Recent studies indicate that HRV in humans is altered by nocturnal exposure to power-frequency (60 Hz) magnetic fields. Given the central origin of autonomic cardiac control, we determined if field exposure in the $beta_1$ EEG/MEG frequency range was a more effective stimulus for HRV alteration than 60 Hz fields, and explored the mechanisms involved.

Methods: Healthy young men were exposed ($n = 9$) overnight to an intermittent magnetic field (16 Hz, 28.3 microTesla, μT), or sham exposed ($n = 9$), under blind test conditions in a laboratory exposure facility.

Results: Field exposure was associated ($P < 0.05$) with reduced power in the low band of the HRV frequency spectrum, and with decreases in mean heart rate. Analysis of the timing of the R waves surrounding each on-off transition of the intermittent field revealed no evidence for a direct effect on the cardiac pacemaker.

Conclusions: Magnetic field exposure in the EEG/MEG $beta_1$ frequency range alters HRV via a CNS effect. Phase-resetting experiments rule out a direct effect on the cardiac pacemaker. Biophysical calculations of the intensity of the electric fields induced in brain versus heart under the present exposure conditions are also consistent with and support a central rather than a peripheral site of action.

Keywords: Heart rate; Heart rate variability; Phase resetting; EEG; Sleep

1. Introduction

Beat-to-beat heart rate variability (HRV) in humans has been shown to be a noninvasive indicator of sympathetic and vagal cardiovascular control (Kamath and Fallen, 1993). Reductions in HRV are recognized as predictive indices of long-term cardiac morbidity and mortality (Bigger et al., 1993; Tsuji et al., 1996). HRV displays a number of periodic and nonlinear components. Spectral or autoregressive methods (Malik and Camm, 1995; Anonymous, 1996; Braun et al., 1998; Otzenberger et al., 1998; Roach and Sheldon, 1998) yield two main spectral components: a low-frequency (LF; 0.04–0.15 Hz) periodic component that reflects sympathetic baroreceptor and thermoregulatory influences (Fleisher et al., 1996) combined with some parasympathetic effects (Malik and Camm, 1995), and a high-frequency (HF; 0.15–0.40 Hz) periodic component that reflects primarily parasympathetic tone. The LF/HF ratio is widely used as an indicator of overall sympathovagal balance (Malik and Camm, 1995; Anonymous, 1996).

Human HRV during sleep is tightly associated with electroencephalographic (EEG) and magnetoencephalographic (MEG) spectral changes and sleep stages. LF power, and the LF/HF ratio decrease from wakefulness to non-REM (NREM) sleep; both of these parameters increase during epochs of REM sleep (Vaughn et al., 1995; Bonnet and Arand, 1997; Roach and Sheldon, 1998). HF increases with sleep onset, reaches maximal values during slow-wave sleep, and often behaves as a mirror image of LF (Baharav et al., 1995). These associations cannot be explained simply by changes in respiratory patterns during sleep (Van de Borne et al., 1995), nor are they dependent on the coincidence of conventional wake-sleep cycles with light-dark cycles (Freitas et al., 1997). The association between certain patterns of HRV and sleep states is sufficiently tight that some sleep disorders, like apnea, can be reliably screened by HRV analyses in the absence of conventional polysomnography (Roche et al., 1999).

HRV can be altered by nocturnal exposure to exogenous extremely low frequency (ELF) magnetic fields of sufficient

* Corresponding author. Tel.: +1-816-753-7600 ext. 1157; fax: +1-816-753-7380.

E-mail address: asastre@mriresearch.org (A. Sastre).

1388-2457/00/$ - see front matter CLINPH 2000050

PII: S1388-2457(00)00438-7

intensity. Previous studies from our laboratory demonstrate that acute exposure of healthy human volunteers to a sinusoidal 60 Hz magnetic field at a resultant intensity of 28.3 microTesla (μT) during sleep produces significant reductions in LF power, while exposure to a similar field at a much lower intensity (1.4 μT) has no effect (Sastre et al., 1998). Sinusoidal 60 Hz magnetic field exposure at 28.3 μT has also been found to produce significant reductions in total sleep time, sleep efficiency and REM sleep, and increased duration of Stage 2 sleep (Graham and Cook, 1999). These results have been interpreted as evidence that exposure to ELF magnetic fields of sufficient magnitude alters neuronal activity in the central nervous system (CNS), resulting in sleep alterations and related changes in HRV. The internal electric field induced by the magnetic field in the brain is believed to be the causative physiological stimulus that leads to alterations in sympathovagal balance and perturbations of the normal sleep architecture.

The above results together with the evidence for central control of HRV (e.g. Cooley et al., 1998) led us to test the hypothesis that magnetic field exposure at a lower frequency, where there is considerably more power in the human EEG and MEG, would provide a more effective stimulus for altering HRV, and possibly also mean heart rate (HR). MEG recordings, which are not subject to the low-pass filtering artifacts of the scalp EEG, indicate that over 85% of the MEG power during sleep is below 30 Hz (Simon et al., 2000; see their Fig. 2a,b). We chose to examine 16 Hz, a frequency within the $beta_1$ band of the EEG/MEG, since that band exhibits a close temporal association with epochs of REM sleep, and has a reciprocal relationship with delta activity during NREM sleep (Merica and Blois, 1997). To explore the physiological mechanisms involved, we performed a detailed analysis of electrocardiographic (ECG) activity surrounding each on-off transition of the magnetic field during intermittent exposure to determine if phase resetting, a known physiological mechanism acting directly on the heart itself, was responsible for the observed alterations in HRV. Previous research using a variety of cellular and tissue preparations has demonstrated that when a stimulus occurs at selected time points within the cardiac cycle, this can either delay or accelerate the timing of subsequent cardiac impulses (Anumonwo et al., 1991; Chay and Lee, 1985; Clay et al., 1984, 1990; Demir et al., 1999). Evidence for this phenomenon, generally referred to as phase-resetting behavior, in our data would indicate that the internal electric field induced by the exogenous magnetic field was acting directly on cardiac electrical activity to alter pacemaker function.

2. Methods

2.1. Subjects

The study group consisted of 18 healthy, male volunteers (mean age 21 years, range 18–33 years) recruited from the local community who were not currently taking medication, had normal sinus rhythm, and regular sleep and dietary habits. On study entry, the subjects were randomly assigned to either a no-exposure, sham control group ($n = 9$) or to a magnetic field exposure test group ($n = 9$). The study protocol was approved by the Midwest Research Institute (MRI) Institutional Review Board for Human Studies, and written informed consent was obtained prior to participation.

2.2. Procedures

Characteristics of the magnetic field exposure test facility in which the study was performed have been documented by the U.S. Department of Energy as part of the EMF-RAPID national research program directed by the National Institute of Environmental Health Sciences (NIEHS: Olden, 1999). This facility is described in detail in Doynov et al. (1999). Each subject slept overnight on a bed in a sound-attenuated and air-conditioned exposure test room (a cube about 2.4 m on each side). Lights were switched off at 23:00 h and subjects were awakened at 07:00 h. During the night, the men were monitored via infrared, closed-circuit TV, open audio intercom, and the physiological recording system. Subjects in the no-exposure, sham control group were exposed only to the ambient, background 60 Hz magnetic field measured in the laboratory (<0.2 μT). This intensity is typical of everyday residential exposures. Subjects in the test group were exposed to a circularly-polarized, sinusoidal 16 Hz magnetic field at the same resultant flux density (28.3 μT) used previously (Sastre et al., 1998). This intensity is within the range of exposures often associated with electric utility operations and the use of industrial machinery or power equipment. Magnetic field generation at the selected frequency, intensity, waveform, and duration was controlled by software operating in conjunction with a function/waveform generator (Model 33120A, Hewlett Packard, Palo Alto, CA). The generator drove current from two power amplifiers (Model 7571, 1350 W into 4 Ω; Techron, Elkhart, IN) through the horizontal and vertical concentric coil systems surrounding the exposure room. To produce the circularly-polarized field, one axis of the field was phase-shifted 90° with respect to the other axis. The Merritt-type concentric coil systems were located out of the subject's sight behind the walls, ceiling, and floor of the exposure room. For additional details, see Doynov et al. (1999).

The magnetic field was presented intermittently over the night according to the protocol described by Sastre et al. (1998). This consisted of alternating 1 h field-on and field-off periods. During field-off hours, the field generation coils were not energized. During field-on hours, the field cycled on and off at 15 s intervals. A zero-current crossing technique allowed the magnetic fields to be switched without introducing artifacts due to the generation of high frequency magnetic field transients at the switch points. The decision to use circularly-polarized fields, and to present them inter-

mittently, was based on previous reports (Cook et al., 1992; Graham et al., 1994; Sastre et al., 1998) indicating that such exposures at 60 Hz are associated with alterations in cardiac parameters.

2.3. Measures

The ECG (Lead II) was recorded throughout each session using a Neurodata Physiological Data Acquisition System (Model 15, Astro-Med, Inc., West Warwick, RI). The recording system utilized optically isolated amplifiers with high common mode rejection, high input impedances, and isolated power supplies. The analog signals were digitized at 256 Hz via special-purpose data acquisition and control programs operating through personal computers. The fiducial point of the R-wave was identified using custom software, which permitted expert operator review. ECG data were stored off line for later use in the statistical analysis of group differences in mean HR (expressed in beats/min) and HRV, and for the examination of possible phase-resetting of the cardiac rhythm during intermittent field exposure.

For quantitative analysis of HRV, the R-R interval data were first converted to instantaneous HR to provide a regularly spaced time series with a 1 s resolution. Since our healthy volunteers did not exhibit premature ventricular contractions or other forms of ectopy, and our recording conditions had extremely low noise, there was no need to correct the records for ectopy-containing segments. The time period selected for analysis was midnight to 06:00 h. Each hour was divided into 3 equal periods containing 1024 points. After de-trending and applying a Hamming window, a digital Fourier transform was performed on each period. Results were expressed as the power spectrum in the 0.0–0.5 Hz range. Analyses were performed for total power in all frequency bands of the HRV spectrum, absolute and percent power in the LF and HF bands, and for the power ratio between bands (LF/HF) following consensus guidelines (Anonymous, 1996). HRV spectral data were submitted to analysis of variance (ANOVA) for repeated measures. Exposure Type (control, exposed) was the between-subjects variable. Field-on/Field-off, Hour (midnight to 06:00 h), and Period (1–3 in each hour) were the within-subject variables. Results were considered statistically significant if $P \leq 0.05$. Probability values were corrected for lack of sphericity using the Huynh-Feldt epsilon technique. Significant main effects or interactions were followed up with simple effects analyses.

2.4. Phase-resetting design

In the 3 field-on hours between midnight and 06:00 h, each of the 9 subjects in the intermittent exposure test group was exposed to a magnetic field that changed in intensity (from 0.0 to 28.3 μT) 360 times as it was switched from off to on, and another 360 times (from 28.3 to 0.0 μT) as the field changed from on to off. Since these field transitions occurred on a fixed time schedule unsynchronized with the heart rhythm, each transition happened at a random time within the cardiac cycle. The waveform of the intermittent magnetic field (recorded from a standard pick-up coil placed in the exposure system) and the ECG were simultaneously digitized at 256 Hz. This allowed the exact time of each field transition, and also of any point within the cardiac cycle, to be resolved with an error of measurement of 3.9 ms. Since the mean cardiac cycle duration of our volunteers during the night ranged from 925 to 1200 ms, this level of accuracy was adequate to test whether there were differences in R-R interval duration as a result of a field transition, and whether alterations in R-R interval depended on when in the cardiac cycle the field transition occurred.

Custom software first selected the time of each field transition (in ms from midnight), and then determined the time of occurrence of the R-waves in the ECG for the 5 heart beats that preceded each field transition and the 5 heart beats that followed each transition. Analysis terms were operationally defined as follows. The time of each field transition within a cardiac cycle was expressed as a percentage of the elapsed time between successive R waves ($T_{\%}$); for example, a value of T_{50} represented a field transition that happened exactly halfway between two consecutive R waves. The quantity Delta_n was used to identify the duration in seconds of the nth cardiac cycle after the field transition, minus the duration of the corresponding cardiac cycle before the field transition. Thus, Delta_1 through Delta_5 represented the timing differences associated respectively with the 5 pairs of heart beats surrounding each field transition. In a similar fashion, the quantity Delta_{m-n} was used to identify the duration in seconds of the average of mth through nth cardiac cycles after the field transition, minus the duration of the corresponding average of cardiac cycles before the field transition. Thus, Delta_{1-2} represented the average of the first two cardiac cycles after a field transition minus the average of the corresponding two cardiac cycles just before a field transition.

3. Results

3.1. Effects on mean HR

Mean HR was altered by magnetic field exposure compared to no-exposure control conditions. Fig. 1 shows the means for HR for the control and exposed groups computed every 20 min. Shaded areas indicate hours during which the intermittent magnetic field was activated. Both groups had comparable mean rates at midnight just before exposure began (control = 60.9 beats/min, exposed = 61.7 beats/min, $P = 0.85$), and as expected mean HR decreased through the night ($F(2, 32) = 8.5$; $P = 0.001$). The two groups showed different patterns of change, however, and field exposure lowered HR. The decrease in mean HR in the exposed group began during the second 20 min period of

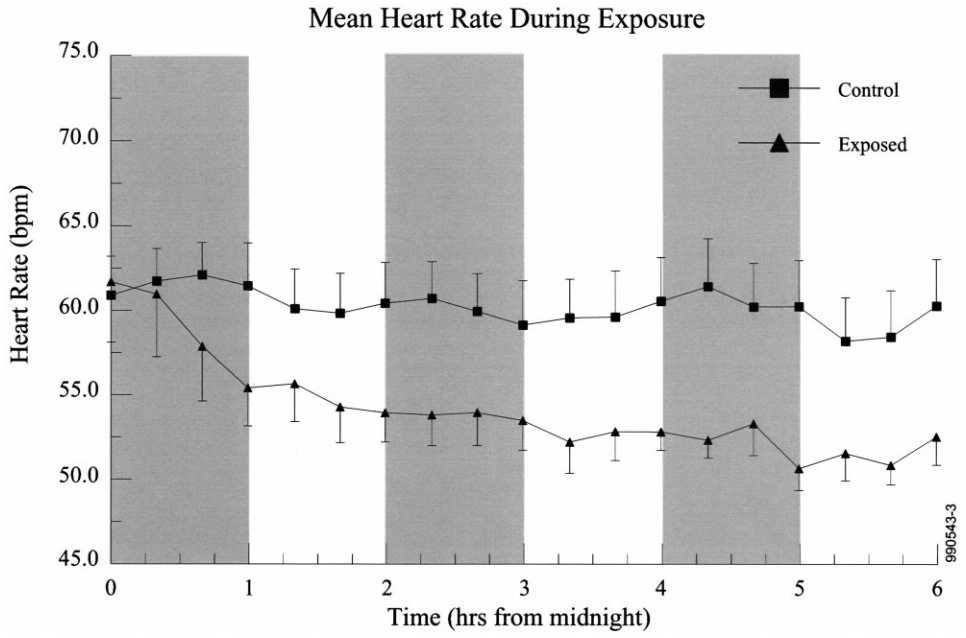

Fig. 1. Exposure-related reduction in heart rate. Group means (±SE) are plotted for heart rate in the control and exposed groups over successive 20 min periods. Value at zero time (i.e. midnight) reflects the mean of the 20 min preceding midnight, and shaded areas indicate hours when the magnetic field was applied.

exposure after midnight, and by the third 20 min period the exposed population mean was 55.4 beats/min, while the mean of the controls was 61.5 beats/min. The decreases during the first hour for the exposed group were significant ($F(2, 32) = 3.9$; $P = 0.04$). The magnitude of the reduction in mean HR in the exposed group increased through the night ($F(1.6) = 5.1$; $P < 0.04$), with a maximal group difference observed between 04:00 h and 05:00 h (control = 60.3 beats/min, exposed = 50.7 beats/min).

3.2. Effects on HRV

Magnetic field exposure selectively affected the LF band, leaving other HRV parameters unchanged. Absolute power in the LF band decreased across the 3 20-min periods of the hour when the field was on, but increased when the field was off ($F(2, 32) = 3.7$; $P = 0.035$). Power in the LF band, expressed as percent of total power, was also reduced in the volunteers exposed to the magnetic field compared to the control group ($F(1, 16) = 4.5$; $P < 0.05$). Both groups had comparable mean percent LF power at midnight just before exposure began (control = 34.0%, exposed = 33.6%; $P = 0.87$). Fig. 2 shows the mean percent power in the LF band plotted in 20 min segments over the night within the exposed and control groups. The shaded areas indicate hours during which the intermittent field was activated. Standard errors ranged from 1.1 to 2.7%. In contrast to the results obtained for mean HR and LF absolute and percent power, field exposure had no effect on HF absolute and percent power, total power or the LF/HF ratio.

It should be noted that the volunteers were unable to judge at better than chance levels whether they were in the exposed or control condition ($\chi^2 = 1.0$; $P = 0.32$); i.e. the blind control procedures used in this study were effective. Thus, the volunteers did not consciously perceive the exposure conditions that resulted in the aforementioned changes in mean HR and LF power.

3.3. Phase-resetting analysis

To determine if the alterations in mean HR and LF power in the field-exposed group were the result of phase resetting of the cardiac pacemaker, the 360 on-to-off and 360 off-to-on field transitions were examined separately for each of the exposed subjects. $Delta_1$ through $Delta_5$ were first plotted against $T_{\%}$. If phase-resetting was operative in the data set, the plot of $Delta_1$ versus $T_{\%}$ should exhibit a markedly non-linear shape. No evidence of phase-resetting was found. Linear regressions were performed separately for each subject and for each transition type, with $T_{\%}$ as the independent variable and each of the $Delta_n$ as the dependent variables. For all subjects the values for $Delta_1$ were uniformly distributed around zero, and all linear regressions had a slope of zero. Similar analyses of the quantities $Delta_2$ through $Delta_5$ did not alter the above results, nor did analyses of the quantities $Delta_{m-n}$, the successive averages for 2, 3, 4 and 5 cardiac cycles before a field transition compared to corresponding averages after a field transition. Table 1 summarizes these results. Finally, examination of individual plots for the 9 exposed men revealed no deviations from linearity. By way of illustration, Fig. 3 provides the $Delta_1$ versus $T_{\%}$ values for a representative subject.

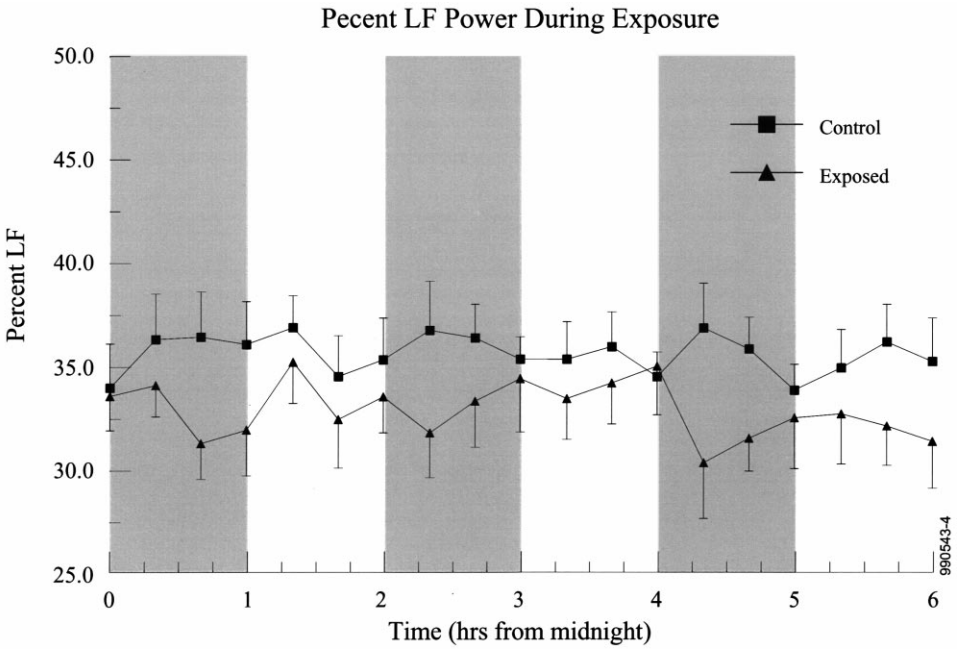

Fig. 2. Exposure-related reduction in percent LF power. Group means (±SE) are plotted for percent power in the LF band for the control and exposed groups over successive 20 min periods. Value at zero time (i.e. midnight) reflects the mean of the 20 min preceding midnight, and shaded areas indicate hours when the magnetic field was applied.

4. Discussion

The present results support the hypothesis that nocturnal magnetic field exposure at a frequency in the $beta_1$ range of the human EEG/MEG provides an effective stimulus for altering HRV. In previous work (Sastre et al., 1998), subjects were exposed to magnetic fields of comparable intensity but at a higher frequency (60 Hz); similar reductions in LF power were observed, but mean HR was not influenced by exposure. The present exposure conditions resulted in reductions in LF power as well as rapid reductions in mean HR, and these effects were sustained through the night. The subjects in this study were unable to detect when they were exposed to the fields, and they did not report any subjective symptoms or cardiac distress. Thus, psychological factors such as anxiety or stress do not provide a likely explanation for the observed cardiovascular changes. The uniformly negative results of the phase-resetting analyses also provide a strong argument against a direct effect of the magnetic field on the normal cardiac pacemaker, the sinoatrial node.

The pattern of results observed suggests that exposure to the 16 Hz magnetic field was associated with a centrally-mediated reduction in sympathetic tone. The HF band, which is principally under the control of the parasympathetic branch of the autonomic nervous system, was not influenced by exposure. The observed reduction in mean HR during field exposure provides additional support for this supposition.

Our study has some limitations. Our study population consisted of 18 healthy male volunteers aged 18–33 years, so that extrapolation of our results to other populations may not be warranted. While the sample size may appear small, the results were consistent and statistically highly significant. This is not surprising in light of the recent findings

Table 1
Regression analysis of $Delta_n$ and $Delta_{m-n}$[a]

	Transition type	Intercept	Slope
$Delta_1$	On	−0.004 ± 0.005	0.006 ± 0.007
	Off	0.005 ± 0.004	−0.005 ± 0.007
$Delta_2$	On	−0.004 ± 0.004	0.010 ± 0.006
	Off	−0.007 ± 0.002	0.0 10 ± 0.006
$Delta_3$	On	0.002 ± 0.004	0.001 ± 0.004
	Off	−0.001 ± 0.004	−0.003 ± 0.007
$Delta_4$	On	0.004 ± 0.005	−0.007 ± 0.008
	Off	−0.002 ± 0.004	−0.002 ± 0.008
$Delta_5$	On	0.008 ± 0.005	−0.017 ± 0.008
	Off	0.003 ± 0.004	0.006 ± 0.011
$Delta_{1-2}$	On	−0.004 ± 0.003	0.008 ± 0.005
	Off	−0.001 ± 0.002	0.002 ± 0.005
$Delta_{1-3}$	On	−0.002 ± 0.003	0.006 ± 0.004
	Off	−0.001 ± 0.002	0.001 ± 0.003
$Delta_{1-4}$	On	−0.0004 ± 0.003	0.002 ± 0.005
	Off	−0.001 ± 0.002	0.0002 ± 0.003
$Delta_{1-5}$	On	0.001 ± 0.003	−0.001 ± 0.005
	Off	−0.0005 ± 0.002	0.001 ± 0.004

[a] Linear regressions were performed separately for each subject ($n = 9$) and for each transition type (on or off), with $T_{\%}$ as the independent variable and each of the quantities $Delta_n$ and $Delta_{m-n}$, as the dependent variables. The table provides the mean ± standard error of the mean for the slope and intercept for the 9 linear regressions performed for each of the dependent variables. In all cases the linear regressions had slopes and intercepts of zero.

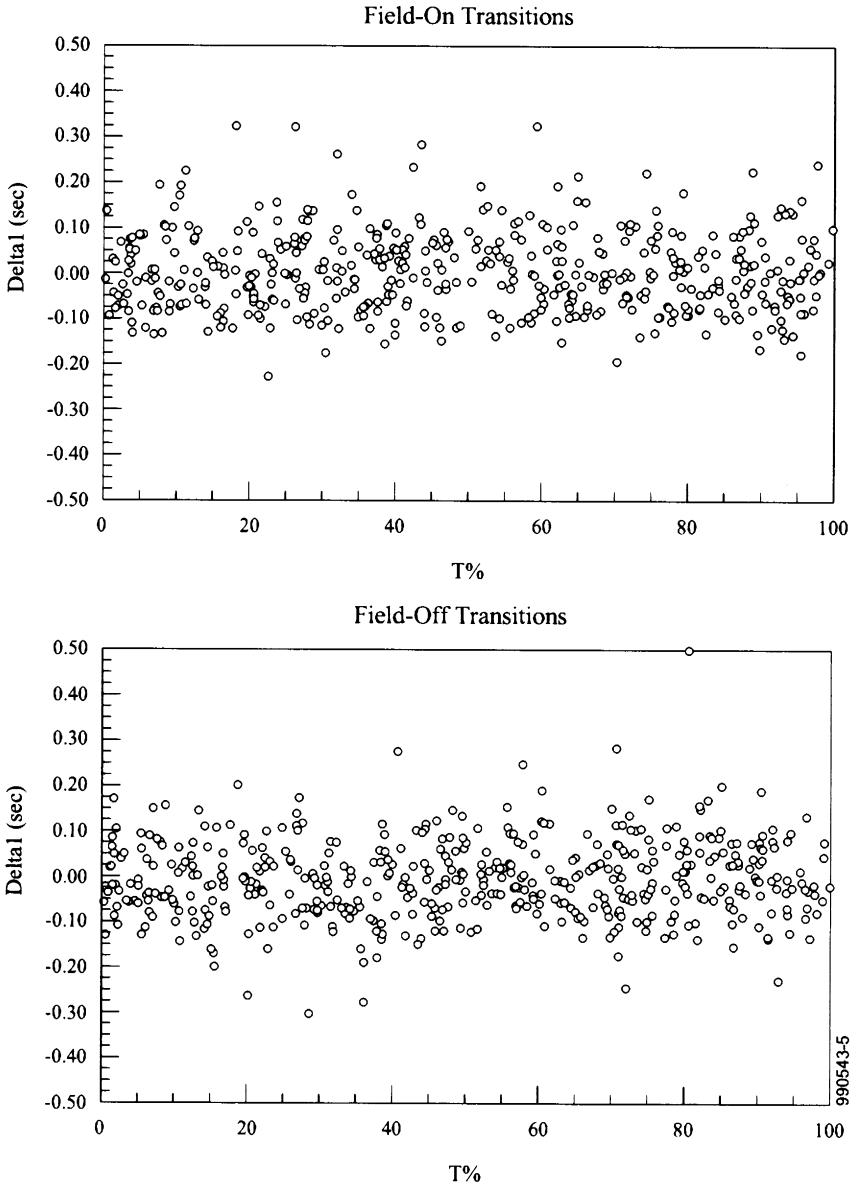

Fig. 3. Magnetic field-on and field-off transitions do not induce cardiac phase-resetting behavior. $Delta_1$ (the time difference between the R-R interval immediately before and after a field transition) is plotted in seconds for a representative subject as a function of $T_{\%}$ (the point in the cardiac cycle when a field transition occurred, expressed as a percentage of the elapsed time between successive R waves). Data from 360 field-on (top panel) and 360 field-off (bottom panel) transitions are presented. $Delta_1$ is uniformly distributed around zero, and fits the $T_{\%}$ line with a slope of zero.

from a multi-study analysis of HRV in 172 healthy volunteers (Graham et al., 2000) which found that under no-exposure baseline conditions HRV measures were consistent and reproducible within individuals, thus enabling the detection of significant field-induced changes with relatively few volunteers. Finally, we only examined magnetic field exposures at 16 Hz, and we cannot exclude the possibility that magnetic field frequencies below 16 Hz may be even more effective in altering HRV and mean HR.

While our data cannot unambiguously identify the anatomical locations affected by magnetic field exposure, biophysical considerations argue for a central nervous system site of action rather than a cardiac one. By Faraday's law, exposure to a time-varying magnetic field induces an electric field inside a conducting body, and the induced electric field is the putative mediator of alterations in cellular activity. Detailed dosimetric analyses with anatomically-correct models (Dawson et al., 1997) indicate that our present exposure conditions are capable of inducing electric fields in cortical, thalamic and subthalamic areas in the CNS in the order of 0.5 mV/m. These are of comparable magnitude to the documented thresholds for electric-field induced alterations in neuronal activity; the extensive primary peer-reviewed literature on this topic is critically analyzed in Portier and Wolfe (1998). In contrast, these conditions would induce an electric field in pontine and medullary

centers well below the documented thresholds (Dawson et al., 1997). Likewise, our exposure conditions would induce electric fields in cardiac tissue of less than 0.1 mV/m (Dawson et al., 1999), which is considerably less than the competing endogenous surface cardiac electric fields at frequencies below 40 Hz of 160 mV/m (Hart and Gandhi, 1998). These biophysical expectations are also consistent with the negative results of the cardiac phase resetting analyses. Further research to elucidate the precise mechanisms and anatomic loci responsible for the observed effects on mean HR and HRV appears warranted.

Acknowledgements

This research was funded by the U.S. Department of Energy/Oak Ridge National Laboratory (Contract No. 85X-SN602C). We wish to thank Donald W. Riffle (night supervisor), Mary M. Gerkovich (biostatistics), Richard M. Ulrich (programming), Jeffrey L. Hackman (ECG signal processing), and Brian E. Peterson (data management). We are grateful to Dr Paul Gailey (Ohio University, Athens) for encouraging us to examine phase-resetting behavior in the SA node.

References

Anonymous. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Special report, Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation 1996;93:1043–1065.

Anumonwo JM, Delmar M, Vinet A, Michaels DC, Jalife J. Phase resetting and entrainment of pacemaker activity in single sinus nodal cells. Circ Res 1991;68:1138–1153.

Baharav A, Kotagal S, Gibbons V, Rubin BK, Pratt G, Karin J, Akselrod S. Fluctuations in autonomic nervous activity during sleep displayed by power spectrum analysis of heart rate variability. Neurology 1995;45:11831187.

Bigger JT, Fleiss JL, Rolnitzky LM, Steinman RC. Frequency domain measures of heart rate variability to assess risk late after myocardial infarction. Circ 1993;88:927–934.

Bonnet MH, Arand DL. Heart rate variability: sleep stage, time of night, and arousal influences. Electroencephalogr Clin Neurophysiol 1997;102:390–396.

Braun C, Kowallik P, Freking A, Hadeler D, Kniffki KD, Meesmann M. Demonstration of nonlinear components in heart rate variability of healthy persons. Am J Physiol 1998;275:H1577–HH584.

Chay TR, Lee YS. Phase resetting and bifurcation in the ventricular myocardium. Biophys J 1985;47:641–651.

Clay JR, Guevara MR, Shrier A. Phase resetting of the rhythmic activity of embryonic heart cell aggregates. Experiment and theory. Biophys J 1984;45:699–714.

Clay JR, Brochu RM, Shrier A. Phase resetting of embryonic chick atrial heart cell aggregates. Experiment and theory. Biophys J 1990;58:609–621.

Cook MR, Graham C, Cohen HD, Gerkovich MM. A replication study of human exposure to 60Hz Fields: Effects on neurobehavioral measures. Bioelectromagnetics 1992;13:261–285.

Cooley RL, Montano N, Cogliati C, Van de Borne P, Richenbacher W, Oren R, Somers VK. Evidence for a central origin of the low-frequency oscillation in RR-interval variability. Circulation 1998;98:556–561.

Dawson TW, Caputa K, Stuchly MA. Influence of human model resolution on computed currents induced in organs by 60-Hz magnetic fields. Bioelectromagnetics 1997;18:478–490.

Dawson TW, Caputa K, Stuchly MA. Magnetic induction at 60 Hz in the human heart: a comparison between the in situ and isolated scenarios. Bioelectromagnetics 1999;20:233–243.

Demir SS, Clark JW, Giles WR. Parasympathetic modulation of sinoatrial node pacemaker activity in rabbit heart: a unifying model. Am J Physiol 1999;276:H2221–H2244.

Doynov P, Cohen HD, Cook MR, Graham C. Test facility for human exposure to AC and DC magnetic fields. Bioelectromagnetics 1999;20:101–111.

Fleisher LA, Frank SM, Sessler DI, Cheng C, Matsukawa T, Vannier CA. Thermoregulation and heart rate variability. Clin Sci 1996;90:97–103.

Freitas J, Lago P, Puig J, Carvalho MJ, Costa O, Freitas AF. Circadian heart rate variability rhythm in shift workers. J Electrocardiol 1997;30:39–44.

Graham C, Cook MR. Human sleep in 60 Hz magnetic fields. Bioelectromagnetics 1999;20:277–283.

Graham C, Cook MR, Cohen HD, Gerkovich MM. A dose response study of human exposure to 60 Hz electric and magnetic fields. Bioelectromagnetics 1994;15:447463.

Graham C, Cook MR, Sastre A, Gerkovich MM, Kavet R. Cardiac autonomic control mechanisms in power-frequency magnetic fields: a multistudy analysis. Environ Health Perspect 2000;108:737–742.

Hart RA, Gandhi OP. Comparison of cardiac-induced endogenous fields and power-frequency induced exogenous fields in an anatomical model of the human body. Phys Med Biol 1998;43:3083–3099.

Kamath MV, Fallen EL. Power spectral analysis of heart rate variability: a noninvasive signature of cardiac autonomic function. Crit Rev Biomed Eng 1993;21:245–311.

Malik M, Camm AJ. Heart rate variability, Armonk, NY: Futura, 1995.

Merica H, Blois R. Relationship between the time courses of power in the frequency bands of human sleep EEG. Neurophysiol Clin 1997;27:116–128.

Olden K. NIEHS Report on health effects from exposure to power-line frequency electric and magnetic fields, NIH Publication no., 99-4493, 1999.

Otzenberger H, Gronfier C, Simon C, Charloux A, Ehrhart J, Piquard F, Brandenberger G. Dynamic heart rate variability: a tool for exploring sympathovagal balance continuously during sleep in men. Am J Physiol 1998;275:H946–H950.

Portier CJ, Wolfe MS, editors. Assessment of health effects from exposure to power-line frequency electric and magnetic fields: NIEHS working group report NIH Publication no., 98-3981. Washington, DC: National Institutes of Health, 1998.

Roach DE, Sheldon RS. Information scaling properties of heart rate variability. Am J Physiol 1998;274:H1970–H1978.

Roche F, Gaspoz JM, Court-Fortune I, Minini P, Pichot V, Duverney D, Costes F, Lacour JR, Barthelemy JC. Screening of obstructive sleep apnea syndrome by heart rate variability analysis. Circulation 1999;100:1411–1415.

Sastre A, Cook MR, Graham C. Nocturnal exposure to intermittent 60 Hz magnetic fields alters human cardiac rhythm. Bioelectromagnetics 1998;19:98–106.

Simon NR, Manshanden I, Lopes da Silva FH. A MEG study of sleep. Brain Res 2000;860:64–76.

Tsuji H, Martin G, Larson MG, Venditti FJ, Manders ES, Evans JC, Feldman CL, Levy D. Impact of reduced heart rate variability on risk for cardiac events: the Framingham heart study. Circulation 1996;94:2850–2855.

Van de Borne P, Biston P, Paiva M, Nguyen H, Linkowski P, Degaute JP. Cardiorespiratory transfer during sleep: a study in healthy young men. Am J Physiol 1995;269:H952–H958.

Vaughn BV, Quint SR, Messenheimer JA, Robertson KR. Heart period variability in sleep. Electroencephalogr Clin Neurophysiol 1995;94:155–162.