The use of low-level electromagnetic fields to suppress atrial fibrillation

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BACKGROUND Extremely low-level electromagnetic fields have been proposed to cause significant changes in neural networks.

OBJECTIVE We sought to investigate whether low-level electromagnetic fields can suppress atrial fibrillation (AF).

METHODS In 17 pentobarbital anesthetized dogs, bilateral thoracotomies allowed the placement of multielectrode catheters in both atria and at all pulmonary veins. AF was induced by rapid atrial pacing (RAP) or programmed atrial extrastimulation. At baseline and end of each hour of RAP, during sinus rhythm, atrial programmed stimulation gave both the effective refractory period (ERP) and the width of the window of vulnerability. The latter was a measure of AF inducibility. Microelectrodes inserted into the anterior right ganglionated plexi recorded neural firing. Helmholtz coils were powered by a function generator inducing an electromagnetic field (EMF; 0.034 μG, 0.952 Hz). The study sample was divided into 2 groups: group 1 (n = 7)—application of EMF to both cervical vagal trunks; group 2 (n = 10)—application of EMF across the chest so that the heart was located in the center of the coil.

RESULTS In group 1, EMF induced a progressive increase in AF threshold at all pulmonary vein and atrial sites (all $P < .05$). In group 2, the atrial ERP progressively shortened and ERP dispersion and window of vulnerability progressively increased ($P < .05$ compared to baseline values) during 3 hours of RAP and then returned to baseline values during 3 hours of combined application of RAP and EMF ($P < .05$ compared to the end of the third hour of RAP). The frequency and amplitude of the neural activity recorded from the anterior right ganglionated plexi were markedly suppressed by EMF in both groups.

CONCLUSION Pulsed EMF applied to the vagal trunks or noninvasively across the chest can significantly reverse AF inducibility.

KEYWORDS Electromagnetic field; Atrial fibrillation; Autonomic nervous system

ABBREVIATIONS **AF** = atrial fibrillation; **ARGP** = anterior right ganglionated plexi; **CANS** = cardiac autonomic nervous system; **EMF** = electromagnetic field; **ERP** = effective refractory period; **GP** = ganglionated plexi; **LL-EMFs** = low-level electromagnetic fields; **LL-VNS** = low-level vagal stimulation; **PV** = pulmonary vein; **RAP** = rapid atrial pacing; **RSG** = right stellate ganglion; **WOV** = window of vulnerability

(Heart Rhythm 2015;12:809–817)

Introduction

Extremely low-frequency (<50–60 Hz) electromagnetic fields (EMFs) have been proposed to cause subtle changes in the excitability of tissues but can potentially lead to significant physiological changes because neural networks exhibit complex nonlinear dynamics to small changes in ionic flux.[1,2] Small changes in the neural signals can be amplified at sites with a high density of ion channels, for example, Ca^{2+} channels at the synaptic junctions.[3]

Recent reports from our laboratories and others have found that vagal stimulation at levels 10% or even 80% below that which slowed the sinus rate or atrioventricular conduction could markedly suppress or reverse atrial fibrillation (AF) inducibility as well as reduce the AF duration in several experimental models of AF.[4–6] Although the mechanisms of action are not well understood, modulation of afferent as well as efferent vagal synaptic transmission was proposed to account, at least partially, for these effects. In search of a noninvasive therapy to suppress AF, we performed the present study based on previous reports showing that low-level electromagnetic fields (LL-EMFs) in the microgauss (picotesla) range could alter cardiovascular physiology at the cellular and organ levels.[7,8] In the present

The first 2 authors contributed equally to this work. This work was supported by the Heart Rhythm Institute of the University of Oklahoma (to Dr Po) and by the Helen and Will Webster Arrhythmia Research Fund (to Dr Scherlag). **Address reprint requests and correspondence:** Dr Sunny S. Po, Heart Rhythm Institute, University of Oklahoma Health Sciences Center, 1200 Everett Dr (6E103), Oklahoma City, OK 73104. E-mail address: sunny-po@ouhsc.edu.

1547-5271/$-see front matter http://dx.doi.org/10.1016/j.hrthm.2014.12.022

study, we applied LL-EMFs to both cervical vagal trunks and across the chest wall to suppress AF inducibility as well as to determine the effects of LL-EMFs on autonomic control of cardiac arrhythmias.

Methods

All animal studies were reviewed and approved by the Institutional Animal Care and Use Committee of the University of Oklahoma Health Sciences Center. Seventeen adult mongrel dogs weighing 20–25 kg were anesthetized with Na-pentobarbital (50 mg/kg) and ventilated with room air by a positive pressure respirator. The core body temperature was maintained at (36.5 ± 1.5)°C. Standard electrocardiograms and blood pressure were continuously recorded.

Bilateral thoracotomy was performed at the fourth intercostal space. Multielectrode catheters were sutured to both atria and all pulmonary veins (PVs) as described in previous studies.[4,5] An octapolar electrode catheter was inserted through a small opening in the parietal pleura at the junction of the second and third rib and the vertebral column. The catheter was positioned adjacent to the right stellate ganglion (RSG), verified by the response of increased heart rate induced by RSG stimulation (frequency 20 Hz, duration 0.1 ms, voltage 4.5 V). The catheter was then sutured in place for stability.

Rapid atrial pacing and electrophysiological studies

The left atrial appendage was paced at 1200 beats/min (2× threshold) to simulate AF, leading to electrophysiological remodeling. After each hour of pacing, rapid atrial pacing (RAP) was temporarily stopped for 5–10 minutes, allowing sinus rhythm to return, so that the atrial effective refractory period (ERP) and AF inducibility could be measured. The ERP at atrial and PV sites was determined by programmed stimulation (S1–S1 interval 330 ms, 8 beats, 10× diastolic threshold). The S1-S2 intervals were decreased from 150 ms initially by decrements of 10 ms and then 1 ms when approaching the ERP.[5] The difference between the longest and the shortest S1–S2 interval (in ms) at which AF was induced was defined as the window of vulnerability (WOV), which served as a quantitative measurement of AF inducibility. $\sum$WOV was the sum of WOVs at all sites in each dog.[4,5,8–10] ERP dispersion was calculated off-line as the coefficient of variation (SD/mean) of the ERP at all recording sites.[5,10]

LL-EMFs

Two sets of Helmholtz coil arrangements with different diameters were used to generate EMFs at different anatomical sites. One Helmholtz coil had a diameter of 1.5 cm, while the other coil had a diameter of 45.7 cm. The Helmholtz coils were made of an insulated copper wire. In each case, the separation between the coils was equal to the radius of each coil to provide a homogeneous EMFs. Each Helmholtz coil configuration was calibrated using Faraday's law and a computer-generated map that displays the flux density field. The electrical source that induced the EMFs was a Stanford adjustable amplitude-frequency generator (Standard Research Systems, Sunnyvale, CA). The frequency and amplitude of LL-EMFs were calculated using Equations 1 and 2 (see the Appendix for details) as well as the results of our previous experiments.[8–10] The sinus rate and atrioventricular conduction (AH interval) were monitored throughout each experiment to ensure that they were not affected by LL-EMFs.

Neural recordings of the ganglionated plexi

Neural recordings were obtained from the anterior right ganglionated plexi (ARGP) at the junction of the atrium and right superior PV, as described previously.[9,10] In brief, a coated tungsten microelectrode (9–12 MΩ at 1000 Hz) was inserted into the ARGP. Electrical signals generated by the ARGP were amplified (Amplifier Model 113, Princeton Applied Research, Princeton, NJ) with band-pass filters set at 300 Hz to 1 kHz and with an amplification range of 30–50 times.[9] Neural recordings from the ganglionated plexi (GP) were acquired with a computer-based analog-to-digital converter (Spike 2, Cambridge Electronic Design Limited, Cambridge, England, UK). The neural activity recorded from the GP, characterized by its amplitude and frequency, was continuously acquired throughout the entire experimental period. Neural activity was defined as deflections with a signal-to-noise ratio greater than 3:1. At the end of each hour of intervention, a 2-minute period was randomly selected during sinus rhythm and the amplitude and frequency were manually determined as described previously.[9]

Group 1: LL-EMF applied to both cervical vagal trunks (n = 7) in an animal model in which AF was induced by delivering high-frequency stimulation to the autonomic nerves

The right and left carotid sheaths were dissected to separate both vagal trunks. For the delivery of EMFs to the vagal trunks, a pair of Helmholtz coils (1.5 cm in diameter) was placed to encompass a portion of each vagal trunk (Figure 1). The Helmholtz coils were energized using a sinusoidal waveform creating an oscillating magnetic field with a strength of 0.034 μG and a frequency of 0.952 Hz (see the Appendix for details). Atrial pacing (at 2× diastolic threshold) was performed at cycle lengths of 330 ms. In 4 animals, a 40-ms train of stimuli (200 Hz, stimulus duration 0.1–1.0 ms) was delivered 5 ms after the atrial pacing stimulus via a Grass S88 stimulator to stimulate local nerves but not PV or atrial myocardium.[4,10] In 3 other animals, no EMF was delivered to the cervical vagal trunks. None of the 7 animals received RAP. The lowest voltage of high-frequency stimulation that induced AF was defined as the AF threshold. AF was defined as irregular atrial rates >500 beats/min and a duration >5 seconds, associated with irregular atrioventricular conduction.

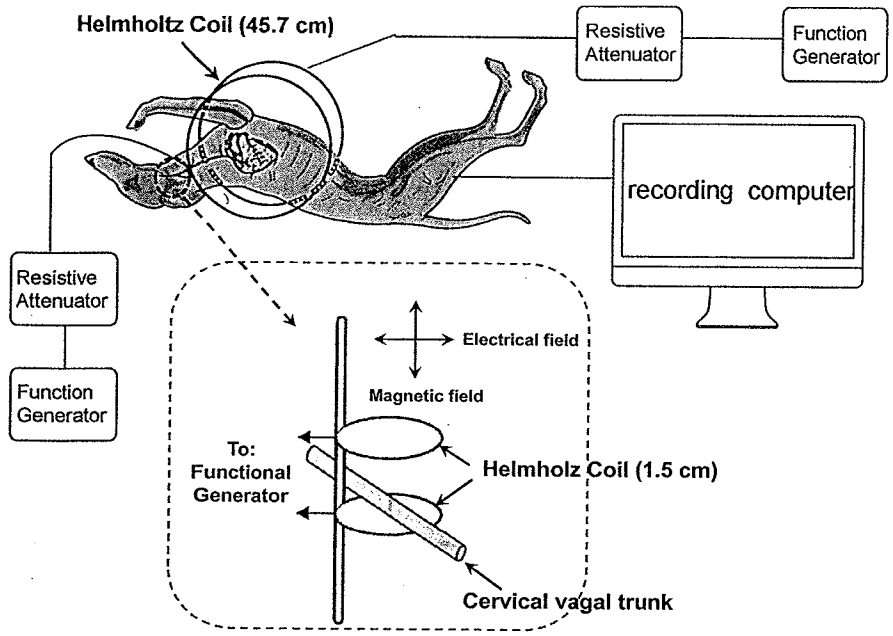

Figure 1 Schematic representation of the experimental setup. The placement of the small Helmholtz coils (1.5 cm in diameter) at both vagal trunks is shown (inset). Each vagal trunk was positioned in the center of the 2 coils. The larger coil (45.7 cm in diameter) was positioned across the chest of the anesthetized dog.

Group 2: LL-EMF applied by a 45.7-cm Helmholtz coil positioned across the chest (n = 10) in an animal model in which AF was simulated by 6 hours of RAP

After observing a striking antiarrhythmic effect in group 1 animals, we moved forward to a completely noninvasive approach and chose the most established animal model of AF (RAP) to test the effects of LL-EMFs. Of note, experiments for group 2 animals were not designed to compare with the results for group 1. The 45.7-cm Helmholtz coil was fixed in a position that encompassed the dog chest noninvasively with the heart approximately located in the center of the coil axis. The sinusoidal waveform exciting the coil was adjusted to ensure that the magnetic field strength and frequency remained at 0.034 μG and 0.952 Hz, respectively. After 3 hours of RAP, LL-EMF was applied to the dog chest through the 45.7-cm Helmholtz coils for 3 hours. At the end of each hour, programmed stimulation as described above was performed to determine the ERP and WOV at all sites during sinus rhythm.

Statistical analysis

All data are presented as mean ± standard error. The changes in parameters at each hour were evaluated by using an analysis of variance test for comparisons between baseline and LL-EMF treatment. A P value of $<.05$ is considered statistically significant.

Results

Group 1

Effects of LL-EMF on the AF threshold

Figure 2 demonstrates that after 2 hours of LL-EMF application, there was a significant increase in the AF threshold voltage at all sites (dark bars). No change in the AF threshold was noted in the 3 control animals without LL-EMFs (open bars).

Effects of LL-EMF on the RSG and ARGP function

The tachycardia response and bradycardia response induced by stimulating the RSG and ARGP were used as surrogates for the sympathetic and parasympathetic activity, respectively. Figure 3A shows the effects of 3-hour LL-EMFs on the voltage-response curves of sinus rate acceleration due to incremental RSG stimulation (left panel) and sinus rate slowing due to incremental ARGP stimulation (right panel). Both responses were markedly attenuated by LL-EMFs.

Effects of LL-EMF on the neural activity recorded from the ARGP

Figures 3B and 3C illustrate that both the frequency and amplitude of the neural activity (with RAP) recorded from the ARGP were markedly suppressed after 3 hours of LL-EMFs (n = 6 for RAP and LL-EMF combination; n = 4 for RAP alone). The mean values of frequency and amplitude of the neural activity recorded from the ARGP at baseline were 60 ± 8 impulses/min and 0.46 ± 0.07 mV, which were steadily decreased to 17 ± 4 impulses/min ($P < .01$) and 0.11 ± 0.02 mV ($P < .01$) after 3 hours of LL-EMFs. While in the control group (without LL-EMFs), there was no change in the neural activity over the 3-hour period (baseline: 56 ± 10 impulses/min and 0.51 ± 0.09 mV; over the 3-hour period: 59 ± 9 impulses/min and 0.52 ± 0.10 mV).

Group 2

Effects of LL-EMF on the ERP and ERP dispersion during RAP

During the first 3 hours of RAP, there was a progressive decrease in the ERP at all recording sites (Figure 4) and increase in ERP dispersion (Figure 5A). These changes returned to the baseline levels after 3 hours of LL-EMFs. Of note, a control group (without LL-EMF) in which RAP was applied for 6 hours was not included in the present study because of a previous

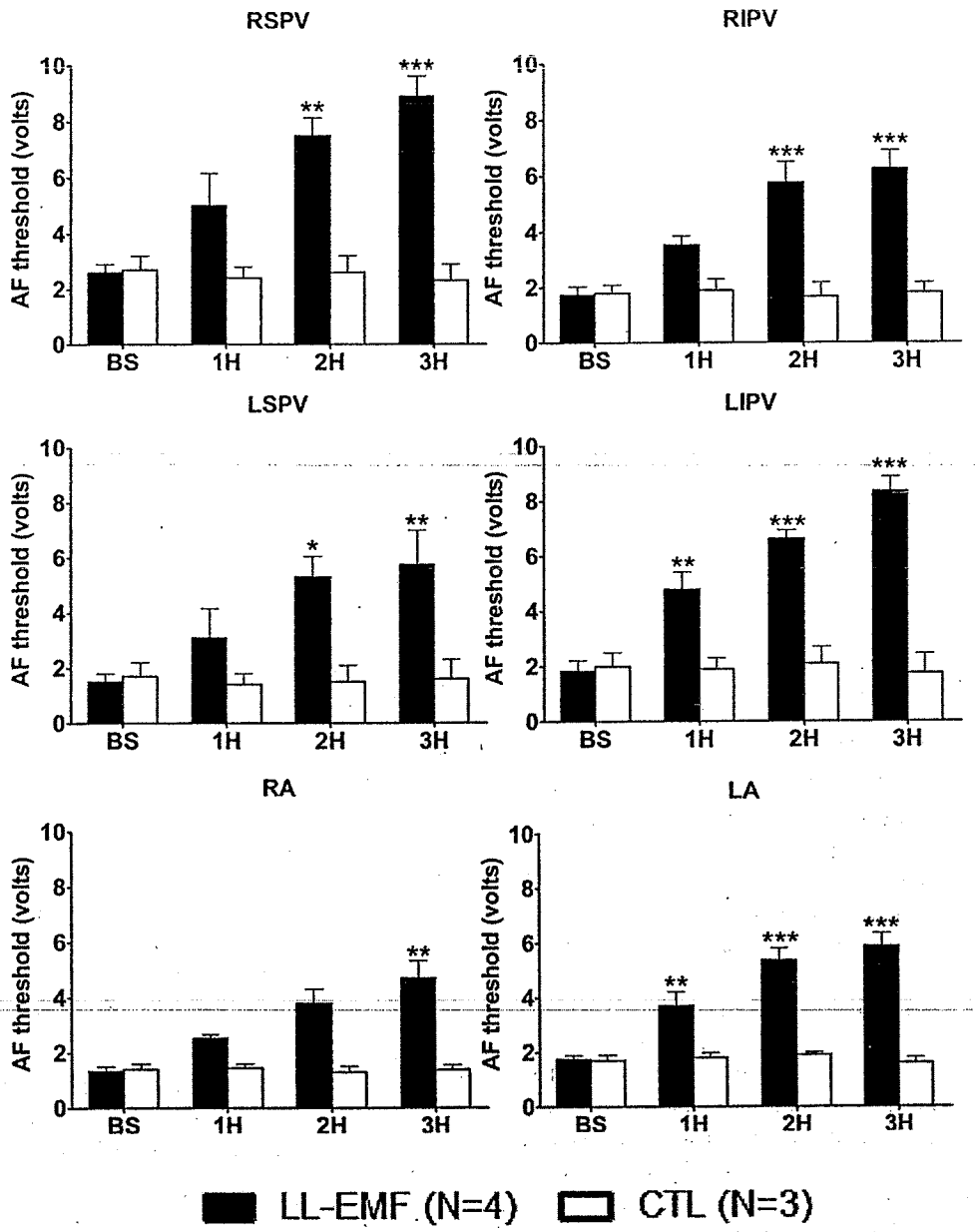

Figure 2 AF threshold at multiple PV and atrial sites with LL-EMF applied for 3 hours (solid bars; n = 4) and without LL-EMF (open bars; n = 3). At each site, there was a progressive and significant increase in the AF threshold, whereas the control animals showed no change over the same time period. Of note, none of these 7 animals received rapid atrial pacing. $^{*}P < .05$, $^{**}P < .01$, $^{***}P < .001$ compared to baseline. AF = atrial fibrillation; BS = baseline; CTL = control; LA = left atrium; LIPV = left inferior pulmonary vein; LL-EMF = low-level electromagnetic field; LSPV = left superior pulmonary vein; PV = pulmonary vein; RA =right atrium; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

study from our group which showed that ERP shortening persisted during 6 hours of RAP.[10]

Effects of LL-EMF on ∑WOV during RAP

There was a progressive and significant increase in the WOV during the first 3 hours of RAP, and it returned to baseline values when RAP and LL-EMFs were simultaneously applied during the last 3 hours (Figure 5B).

Effects of LL-EMF on the neural activity recorded from the ARGP during RAP (n = 4)

Figure 6A illustrates a typical recording of the increase in neural activity recorded from the ARGP after 3 hours of RAP. From the fourth to the sixth hour, concomitant LL-EMFs and RAP were applied (top panel). These neural recordings were made in sinus rhythm shortly after RAP was stopped at the end of each hour. Note the reversal of the frequency and amplitude of the neural activity at the sixth hour. In contrast, the neural activity recorded from the ARGP of the control group progressively increased over the 6 hours of RAP alone (bottom panel).

The bar graph (Figure 6B, top panel) shows the changes in the mean values of frequency and amplitude of the recorded neural activity at baseline (55 ± 7 impulses/min, 0.38 ± 0.05 mV), after 3 hours of RAP (162 ± 11 impulses/min, 0.91 ± 0.08 mV; $^{***}P < .001$ compared to baseline),

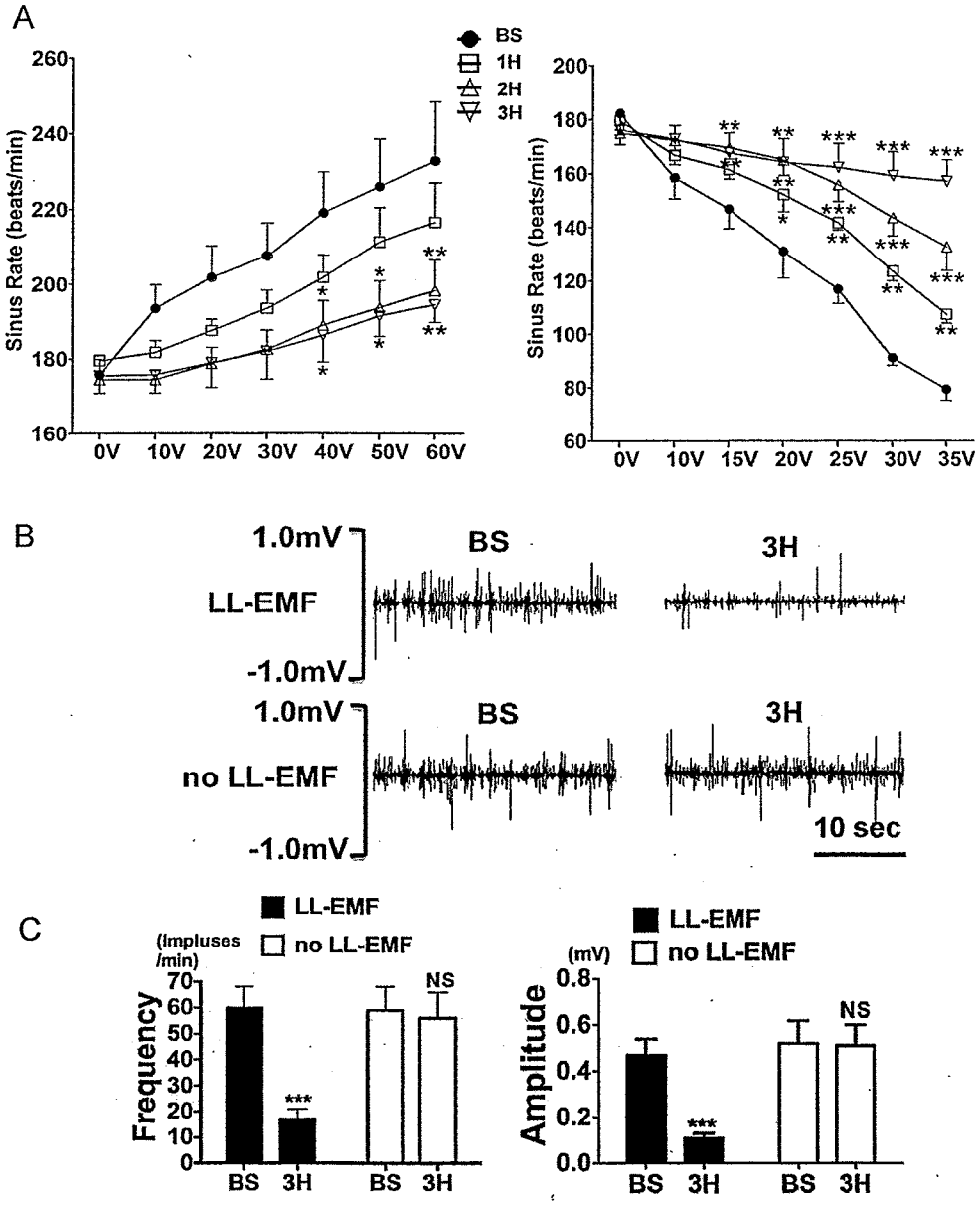

Figure 3 **A:** Effects of LL-EMF on ARGP and RSG function (n = 4). LL-EMF induced a progressive suppression of the sinus rate acceleration response induced by RSG stimulation (left panel) and sinus rate slowing response induced by ARGP stimulation (right panel). **B:** Typical examples of neural recordings from the ARGP at baseline (BS) and after 3 hours of LL-EMF applied to bilateral vagal trunks. **C:** Quantitative measurement of a decrease in both the frequency (left panel) and the amplitude (right panel) of neural activity induced by LL-EMF for 3 hours. $^{*}P < .05$, $^{**}P < .01$, $^{***}P < .001$ compared to baseline. ARGP = anterior right ganglionated plexi; LL-EMF = low-level electromagnetic field; RSG = right stellate ganglion.

and after 6 hours of combined application of RAP and LL-EMFs (solid bars; 50 ± 9 impulses/min, 0.4 ± 0.07 mV, $^{\Delta\Delta\Delta}P < .001$ compared to the end of the third hour of RAP; P = not significant compared to baseline). In contrast, without LL-EMFs, RAP alone showed a progressive and significant increase in neural activity (open bars).

Discussion

Major findings

In this study, we applied a LL-EMF that was focused at different levels of the cardiac autonomic nervous system (CANS): the extrinsic CANS (vagal trunks) and both the extrinsic and intrinsic CANS (across the chest wall). When LL-EMF was applied to vagal trunks, AF thresholds at multiple PV and atrial sites were significantly and progressively increased. Moreover, the sympathetic activity measured by the sinus rate acceleration response induced by RSG stimulation was significantly suppressed by LL-EMFs as was the parasympathetic activity measured by the sinus rate slowing response induced by ARGP (Figure 3A). These findings suggest that LL-EMFs may mitigate both the sympathetic and parasympathetic inputs to the heart and may be used to treat a variety of arrhythmias. The anti-fibrillatory effects of EMFs are similar to those observed during low-level vagal stimulation (LL-VNS), which were also shown to be antisympathetic and anticholinergic.[4–6,9,10] While moving toward a completely noninvasive approach by

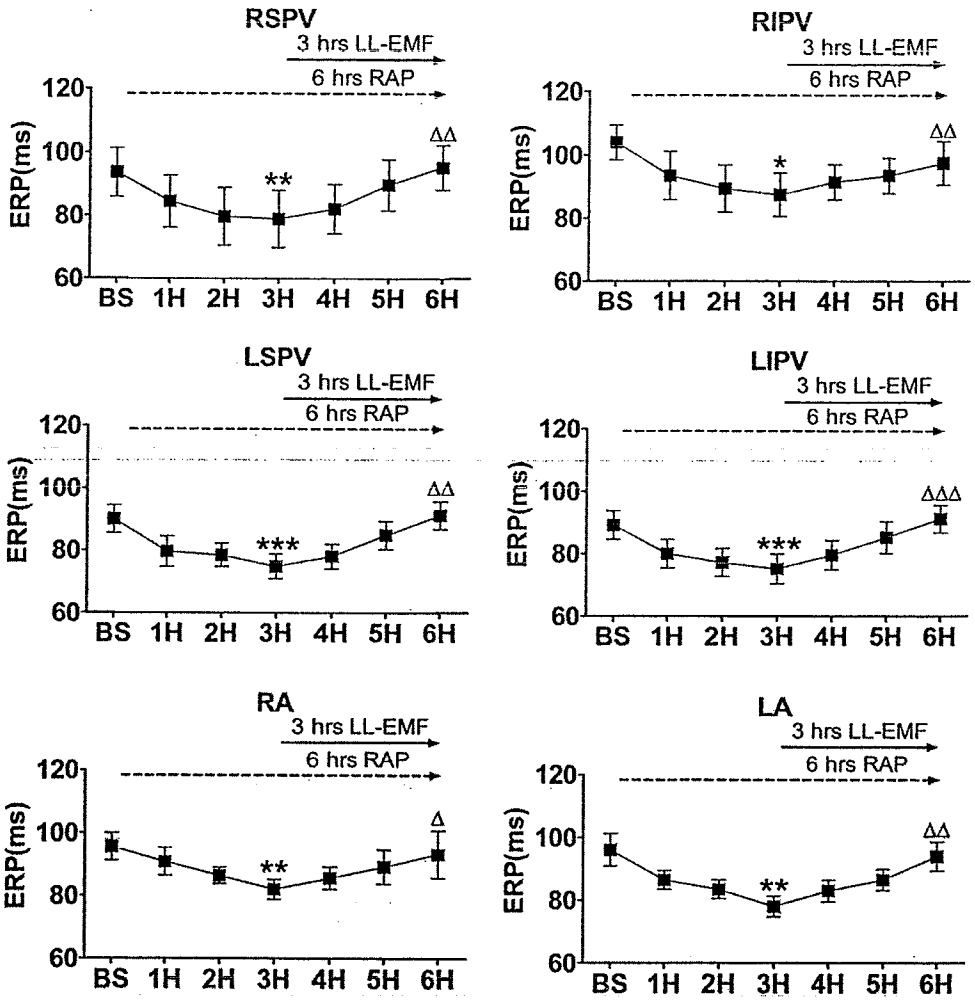

Figure 4 Effects of LL-EMF on the mean ERP during 6 hours of RAP (n = 6). There was a significant decrease in the ERP in the first 3 hours of RAP and a reversal to baseline values with the application of LL-EMF from the fourth to the sixth hour while RAP continued. $^{*}P < .05$, $^{**}P < .01$, $^{***}P < .001$ compared to baseline; $^{\Delta}P \leq .05$, $^{\Delta\Delta}P < .01$, $^{\Delta\Delta\Delta}P < .001$ compared to the end of the third hour of RAP. BS = baseline; ERP = effective refractory period; LA = left atrium; LIPV = left inferior pulmonary vein; LL-EMF = low-level electromagnetic field; LSPV = left superior pulmonary vein; RA = right atrium; RAP = rapid atrial pacing; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

applying LL-EMFs across the chest, the changes in ERP, ERP dispersion, and AF inducibility ($\sum$WOV) were all markedly suppressed. We also provided direct evidence that LL-EMF exerts its antifibrillatory effects by inhibiting neural firing within the intrinsic central nervous system, specifically the ARGP (Figures 3 and 6).

Effects of LL-EMF on other biological systems

The present study clearly demonstrates that an alternating magnetic field around the target organism produced a significant change in AF inducibility. However, the exact mechanism of action in this study is not currently known but may be related to some form of subtle resonance related to neurotransmitters. Earlier clinical studies using extremely low-intensity fields, for example, picotesla, similar to the present study, and low-frequency (<300 Hz) EMFs demonstrated improvement in the brainstem evoked potentials and cognitive responses in multiple sclerosis patients, possibly by modulating axonal and synaptic transmission as well as molecules crucial for immune responses[1]. Bassett et al[11] found that continuous exposure to a pulsed EMFs promoted bone repair in a fracture by using a beagle model. Weinbraub et al[12] found a therapeutic result in symptomatic diabetic neuropathy with a static magnetic field. Byers et al[13] found that sine-wave electromagnetic stimulation enhanced transected nerve regeneration in rats. The recent revival of the interest in the effects of LL-EMFs on biological systems has been based on the calculated cyclotron resonance of the molecule of interest.[7] For example, Ca^{2+} homeostasis is known to regulate membrane excitability and modulate second messengers related to multiple receptors and signal transduction pathways.[14] When Ca^{2+} cyclotron resonance (7 Hz), calculated by using Equation 2 (see the Appendix), was applied to human cardiac stem cells continuously for 5 days, the level of transcription and translation of the cardiosphere was significantly increased.[15] In contrast, when the same intensity but a different frequency of EMF was applied to the same stem cells, it failed to induce the aforementioned effects, stressing the importance of the frequency of LL-EMF that resonates with the target molecule.

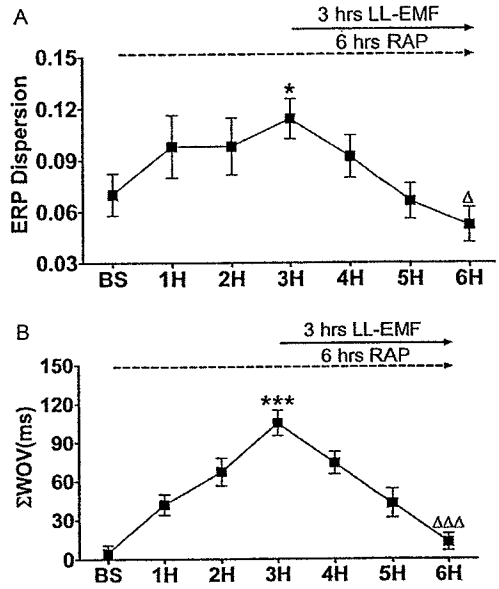

Figure 5 Effects of LL-EMF on ERP dispersion and WOV during 6 hours of RAP, accompanied by LL-EMF in the last 3 hours. **A:** In the first 3 hours, there was a significant increase in ERP dispersion followed by a return to the baseline value during combined application of RAP and LL-EMF. **B:** Similarly, AF inducibility measured by the WOV showed the same pattern of significant changes. $^{*}P < .05$, $^{***}P < .001$ compared to baseline; $^{\Delta}P \leq .05$, $^{\Delta\Delta\Delta}P < .001$ compared to the end of the third hour of RAP. AF = atrial fibrillation; BS = baseline; ERP = effective refractory period; LL-EMF = low-level electromagnetic field; RAP = rapid atrial pacing; WOV = window of vulnerability.

The antiarrhythmic effect of LL-EMFs shares great resemblance with that of LL-VNS.[4–6,9,16] Within 2 hours, both approaches substantially lengthen the ERP, reduce ERP dispersion, suppress AF inducibility, shorten AF duration, and inhibit neural activity in the intrinsic CANS. A previous study from our group demonstrated that autonomic remodeling and AF form a vicious cycle that can be interrupted by the inhibition of the CANS by LL-VNS.[16] We therefore hypothesize that LL-EMFs and LL-VNS exert their antiarrhythmic effects by suppressing the activity of the CANS.

Study limitations and questions to be answered

Similar to the striking results reported by Lisi et al[15] using Equation 2 (see the Appendix), we observed profound antiarrhythmic effects based on the frequency and amplitude of LL-EMFs calculated by using Equations 1 and 2 (see the Appendix). However, the physiological meaning of the 2 equations and how the parameters of LL-EMF were calculated are based on several assumptions and hypotheses, and they remain to be confirmed. A key element in Equation 1 is the linear dimension (L) of the biological system. Induction by a magnetic field occurs only in the region exposed to the magnetic field, which was circumscribed by the Helmholtz coils. In the present study, we arbitrarily chose the average length of the animal (100 cm) as the L value. Despite the substantial difference in the size of the EMF covering the vagal trunks and the entire chest, the frequency and

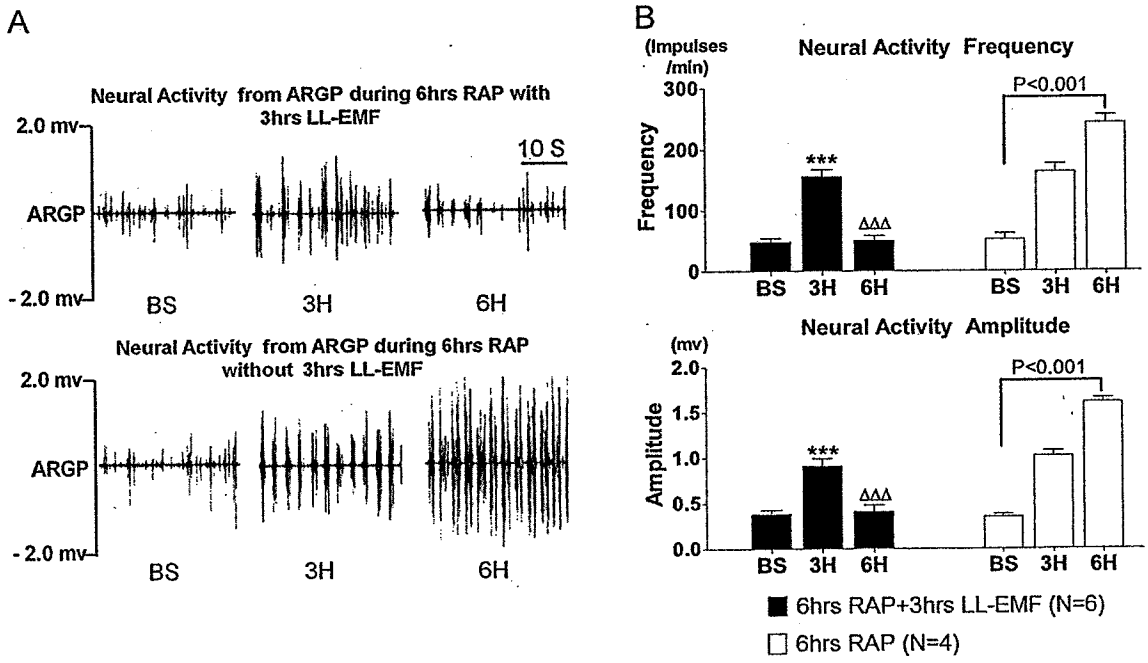

Figure 6 **A:** Typical examples of neural recordings from the ARGP at baseline (BS), after 3 hours of RAP, and after 6 hours of RAP. It illustrates an initial increase in neural activity, which was returned toward the baseline level by LL-EMFs applied from the fourth to the sixth hour while RAP continued (top panel; n = 6). With RAP for the entire 6-hour period, without LL-EMF, there was a progressive increase in the level of neural firing (bottom panel; n = 4). **B:** Quantitative assessment of the frequency (upper panel) and amplitude (lower panel) of neural activity during the first 3 hours of RAP and combined application of RAP and LL-EMF from the fourth to the sixth hour (solid bars). In contrast, there was a significant increase ($P \leq .001$ compared to BS) in frequency and amplitude during 6 hours of RAP alone. ARGP = anterior right ganglionated plexi; RAP = rapid atrial pacing; LL-EMF = low-level electromagnetic field.

amplitude of the EMF worked equally well, indicating multiple mechanisms of action.

The calculation of the strength and frequency of the EMF was based on the characteristics of vasostatin-1. It is possible that other molecules with molecular weights similar to vasostatin-1 may also be responsible for the observed effects. It is also possible that LL-EMFs may induce resonance of other molecules and inadvertently induce other effects not measured by the present study. Future studies that systematically test a series of excitatory and inhibitory molecules will help validate the 2 equations described in this study.

The experiments in the present study were not conducted in a magnetically shielded room. It is possible that the background environmental EMF might have influenced the results. However, all the experiments before and after applying LL-EMFs were conducted in the same environment, neutralizing the potential effects of the environmental EMFs.

Conclusion

Although the exact mechanism of action remains undetermined at present, the LL-EMF is capable of suppressing AF by inhibiting the activity of the CANS. This may be the first step toward a completely noninvasive therapy used to treat drug-refractory AF, particularly in the paroxysmal stage. Further basic and clinical studies would be required to elucidate the mechanism(s) of action and to determine the optimal parameters of LL-EMF to suppress various cardiac arrhythmias.

Appendix

Hypotheses and assumptions used for LL-EMF calculation

The calculation of the amplitude and frequency of LL-EMF was based on several assumptions and hypotheses described below. Jacobson derived the following equation[18,19]:

$$mc^2 = q_j vBL \quad (1)$$

Essentially, this equation states that the amplitude B of the magnetic component of an externally applied EMF can be specified for a target molecule of interest (eg, vasostatin-1 for the present study) with mass m. In Equation 1, c^2 is the velocity of light squared and mc^2 is the intrinsic energy of the target mass. q_J is the electromotive force, which represents energy per unit charge (=1 abcoulomb). v is the velocity of the carrier in which the particle exists, for example, earth's orbital velocity. The velocity of electromagnetic radiant energy is the velocity of light, independent of their inertial frame of reference, that is, the source of EMF. L is defined in references 11 and 12 as the linear dimension of the biological system in which the target mass exists. Using Jacobson's proposed method and selecting m on the basis of the target molecule and L on the basis of the biological system, Equation 1 is solved for the amplitude (B) of the magnetic component of the EMF.

In the present study, we chose vasostatin-1 as the target molecule for its inhibitory effects on the CANS, particularly its antiadrenergic action.[20–22] The average length of an adult dog is 100 cm, and the molecular weight of vasostain-1 is 7 kd ($7000 \times 1.67 \times 10^{-24} = 1.169 \times 10^{-20}$ g). The value of B (0.034 μG) can be derived as follows:

(m) (c^2) (B) (v) (L) (q_r)

$$\left(1.169 \times 10^{-20}\text{g}\right) \times \left(3 \times 10^{10} \frac{\text{cm}}{s}\right)^2 = \left(3.4 \times 10^{-8}\text{G}\right) \times \left(3 \times 10^{6} \frac{\text{cm}}{s}\right) \times (100\ \text{cm}) \times (1\ \text{abcoulomb})$$

On the basis of the aforementioned assumptions and hypotheses, Jacobson then derived the desired frequency of the applied EMFs by using the following cyclotron resonance equation:

$$f = \frac{qB}{2\pi m} \quad (2)$$

The frequency can be calculated if the derived amplitude (B) is known. In Equation 2, q and m are the normalized charge (1.602×10^{-19} abcoulomb) and mass (9.1095×10^{-28} g) of an electron, respectively. The cyclotron resonance frequency can be derived as follows:

$$0.952\ \text{Hz} = \frac{\left(1.602 \times 10^{-19}\text{abcoulomb}\right)\left(3.4 \times 10^{-8}\text{G}\right)}{(6.28)\left(9.1095 \times 10^{-28}\text{g}\right)}$$

Theoretically, each molecule and tissue may respond to EMF with a specific amplitude and frequency. In the present study, we hypothesized that vasostatin-1 is a critical element in suppressing the activity of the intrinsic CANS, on the basis of our previous study.[21] Therefore, the intensity and frequency of the EMF were calculated on the basis of the characteristics of vasostatin-1. In a previous study,[8] we empirically selected a different EMF (0.34 μG, 2 kHz) applied to the vagosympathetic trunks, which markedly *augmented* AF inducibility and the cholinergic effects (slowing of atrioventricular conduction) induced by vagal stimulation. In the present study, we demonstrated an opposite effect of AF *suppression* by inhibiting the activity of the intrinsic CANS (ganglionated plexi), indicating that the effects of LL-EMFs on cardiac electrophysiology depend greatly on the physical characteristics of LL-EMFs and suggesting that LL-EMFs may be customized to resonate different molecules to treat various diseases.

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CLINICAL PERSPECTIVES

Despite the superiority of catheter ablation to drug therapy, recurrence of atrial fibrillation (AF) or atrial tachycardia is still common for patients with paroxysmal AF who underwent AF ablation.[17] The present study described a noninvasive therapy to treat AF in a canine model of AF. When an extremely low-level electromagnetic field (LL-EMFs; 0.034 μG, 0.095 Hz) was applied through a pair of Helmholtz coils across the canine chest wall, the atrial effective refractory period was prolonged, AF inducibility was reduced, and the neural activity in the ganglionated plexi was suppressed. The present study demonstrates that AF can be potentially controlled noninvasively by LL-EMFs within 2–3 hours after it was initiated. Early termination of AF by LL-EMFs, if proven by clinical studies, will have a significantly positive impact on the use of antiarrhythmic drugs and oral anticoagulation therapy, particularly for patients in the earlier stage of paroxysmal AF. This approach, if effective, has a unique advantage that will not destroy any myocardium and perhaps avoid introducing iatrogenic atrial tachycardias.