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 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. The Helmholtz coils were powered by 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-EMF** = low-level electromagnetic field; **LL-VNS** = low-level vagal stimulation; **PV** = pulmonary vein; **RAP** = rapid atrial pacing; **RSG** = right stellate ganglion; **WOV** = window of vulnerability

Introduction

Extremely low-frequency (<50–60 Hz) electromagnetic fields (EMF) 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-EMF) 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.

study, we applied LL-EMF to both cervical vagal trunks and across the chest wall to suppress AF inducibility as well as to determine the effects of LL-EMF 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 electrocardiogram 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. ∑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-EMF

Two sets of Helmholtz coil arrangements with different diameters were used to generate EMF 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 EMF. Each Helmholtz coil configuration was calibrated using Faraday's law and a computer-generated map that displays the flux density field. The electrical source for inducing the EMFs was delivered from a Stanford adjustable amplitude-frequency generator (Standard Research Systems, Sunnyvale, CA). The frequency and amplitude of LL-EMF 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-EMF.

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 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.