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The electric field is a sufficient physical determinant of the human magnetic sense

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Abstract

Purpose: The onset and offset of weak low-frequency magnetic fields triggered evoked potentials in human subjects that could be detected using nonlinear analysis, but not by means of time averaging. Because the magnetic fields and their induced electric fields were both present in the brain, their respective role in producing the effect on brain activity could not be ascertained. We inquired whether a biophysical coupling mechanism involving only the electric field could explain the occurrence of the brain potentials.

Materials and methods: An external electric field capable of producing a brain electric field comparable to that induced by the magnetic stimuli was identified by finite-element analysis. The electroencephalogram from 23 subjects was measured from six scalp derivations in the presence and absence of the external electric field, and the presence of evoked potentials was assessed using nonlinear and linear analyses.

Results: Evoked potentials were observed in all but one subject ($p < 0.05$ in each subject); the potentials had the same latency, duration, and distribution of magnitudes as seen in the earlier studies, and were detectable only by means of nonlinear analysis. Using a realistic physical model of an ion channel, we showed that transduction of an electric field could be explained by assuming that the field exerted a force on glycocalyx molecules attached to a channel gate.

Conclusion: The evoked potentials described here, as well as those observed previously in response to magnetic stimuli, were probably triggered by the induced electric field.

Keywords: *Evoked potentials, nonlinearity, electroencephalogram, recurrence analysis, transduction*

Introduction

Natural and artificial nonionising electromagnetic fields (EMF) are ubiquitous in the environment (World Health Organisation). Some animals can detect fields by means of known sensory systems (Wachtel and Szamier 1969, Pettigrew 1999). In other instances where sensory transduction of EMF is known or suspected (Carrubba and Marino 2008), the electroreceptor cell and its afferent innervation have not been identified. In all cases of EMF sensitivity, the way EMF produce changes in mean conductance of ion channels, the process comparable to changes in rhodopsin conformation after photon absorption or to mechanical deformation of stereocilia by sound waves, remains unelucidated.

The electric and magnetic components of EMF are often inextricably linked (Feynman et al. 1965). For example, when low-frequency magnetic fields triggered evoked potentials (Carrubba et al. 2007a, 2007b), electric fields were also present in the brain because time-varying magnetic fields produce electric fields by means of magnetic induction; consequently either field (or both) could have triggered the evoked potentials. High-frequency waves, which have simultaneous electric and magnetic components, also caused changes in brain electrical activity (Eulitz et al. 1998, Borbély et al. 1999, Krause et al. 2006). In instances of magnetic induction or propagating waves, the actual biological stimulus cannot be pinpointed because the electric and magnetic fields occur together in the tissue. The

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uncertainty regarding the biophysical determinant of the electroreceptor response is a major factor accounting for why the transduction mechanism for electromagnetic fields remains unknown.

We addressed the question whether the brain potentials evoked by magnetic stimuli (Carrubba et al. 2007a, 2007b, 2008) could have been mediated by a biophysical coupling mechanism involving only the induced electric field. Our primary goal was to test the hypothesis that the induced electric field was sufficient to explain the evoked potentials. This was accomplished by applying electric fields whose strength was capable of producing brain electric fields comparable to those produced by magnetic induction. After we found that the electric field was sufficient to trigger evoked potentials, our second goal was to examine the sensitivity of the electric-field-governed detection process, which we did by systematically reducing the strength of the applied electric field. Our third goal was to provide a possible mechanistic explanation for how induced electric fields, which were extraordinarily weak, could trigger a deterministic cellular response despite the randomising influence of thermal noise.

Materials and methods

Subjects

Twenty-three clinically normal subjects were studied: six males (age range 23–49 years) and 17 females (21–73 years). The subjects were informed of the goals, methods, and general design of the investigation, but were not told exactly when or for how long the field would be applied. Written informed consent was obtained from each subject prior to participation in the study. The institutional review board at the LSU Health Sciences Center approved all experimental procedures.

External electric field

Uniaxial sinusoidal 60-Hz electric fields were generated by applying a voltage, V_{AC} (801RP, California Instruments, San Diego, CA, USA), to parallel plates 76 cm square, separated by 65 cm (Figure 1A). The plate voltage (6–225 volts) was regulated by a microcontroller programmed to produce the desired repetitive stimulus and inter-stimulus intervals. Field exposure took place in a

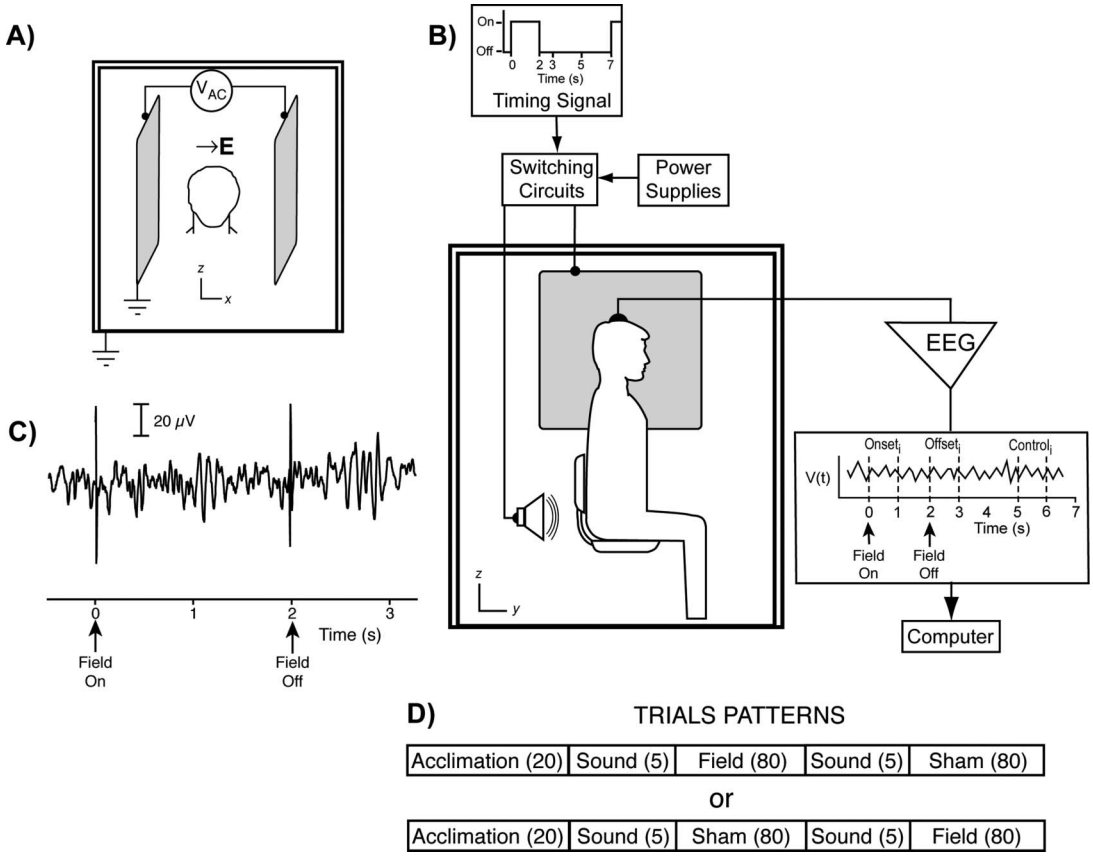

Figure 1. External electric fields. (A) Electric field (E) generated by applying a voltage (V_{AC}) to parallel metal plates in an electrically grounded room. (B) Schematic diagram of the exposure and EEG-detection systems (mid-sagittal view). (C) Spike artifacts in the EEG produced by the onset and offset of the electric field. (D) Organisation of trials in the experimental session; number of 7-s trials shown in parentheses.

darkened isolation room that reduced the potential impact of random ambient stimuli (Figure 1B). The subjects sat in a comfortable wooden chair with their eyes closed; the field was applied perpendicularly to the sagittal plane. The equipment that controlled the voltage and recorded the electroencephalogram (EEG) was located outside the room; the absence of sensory cues was verified by interviewing each subject at the end of the experimental session. The field strength was below the threshold for awareness and was therefore not consciously perceived by any subject. The background 60-Hz electric field (the field present irrespective of whether or not a voltage was applied to the parallel plates) was about 1 V/m throughout the region occupied by the subject (HI-3603, Holaday, Eden Prairie, MN, USA). As previously (Carrubba et al. 2007a), the background 60-Hz magnetic field was 0.1 mG, and the geomagnetic field was 599.8 mG, 68.4° below the horizontal component (component along the direction of the applied field, 360.5 mG) (MAG-03, Bartington, GMW, Redwood City, CA, USA).

The field was applied for 2-s intervals (5 ms onset, 15 ms offset, with a period of 5 s between each interval; the EEG, V(t), was recorded continuously (Figure 1B). The onset and offset of the field each produced a spike in V(t) that was broadened to 30 ms by the time-constant of the EEG amplifier (Figure 1C). In preliminary studies using electrical phantoms of the human head, we established that the spikes arose from a direct interaction of the field and the metallic electrodes. Prior to analysing V(t), the spikes were removed by deleting the first 30 ms of data (10 points, see below) after presentation of the stimulus.

Each subject underwent 2 blocks of 80 trials (Figure 1D); the electric field was applied in either the earlier or later block, as determined randomly from subject to subject. In the block where the field was not applied, the data was analysed as a negative control (sham exposure). To help maintain alertness, five binaural 2-s 424-Hz tones were presented prior to each field or sham session.

Field strength

We sought to apply an electric field that would induce brain electric fields comparable in strength to that induced by 100–200 μT, 60 Hz (Carrubba et al. 2007a, 2007b, 2008). A determination of the comparability of the two types of applied fields depended on the assumptions used in the calculations of the induced fields. However, within an order of magnitude, at 60 Hz, an applied electric field of 1000 V/m and an applied magnetic field of 100 μT each induce a brain electric field of about 1 mV/m (Hart 1992, Dawson et al. 1997). Although the calculations were model-dependent, and the equivalence they established took no account of field direction, the calculations were reasonably suitable for comparing the strength of the induced electric fields.

We calculated the applied electric field (Figure 1A) from Maxwell's laws. A seated subject was modeled as an electrically isolated composite of rectangular solids representing the trunk and extremities, and an ellipsoid representing the head; the assumed conductivity was 1 S/m. One plate was grounded and the other was held at the voltage V_{AC} (Figure 1A); the walls, floor, and ceiling of the room were grounded. The total electric field at every point in the room was determined as a function of V_{AC} using finite-element analysis consisting of approximately 10^6 elements; a more detailed mesh was automatically generated in the head region (Multiphysics, Comsol, Los Angeles, CA, USA) (Figure 2).

At $V_{AC} = 225$ volts, the peak electric field was about 1000 V/m (Figure 2). We therefore regarded the corresponding induced brain electric field (1 mV/m) as roughly equivalent to that induced by exposure to 100 μT, 60 Hz. Other desired strengths of the applied electric field (and its corresponding brain electric field) were produced by utilising proportional changes in V_{AC}.

EEG recording

Electroencephalograms were recorded from scalp locations O_1, O_2, C_3, C_4, P_3, and P_4 (International 10–20 system) (Niedermeyer and Lopes da Silva 2004) referenced to linked ears, using gold-plated electrodes attached to the scalp with conductive paste. Electrode impedances (measured before and after each experiment) were < 10 kΩ in all subjects.

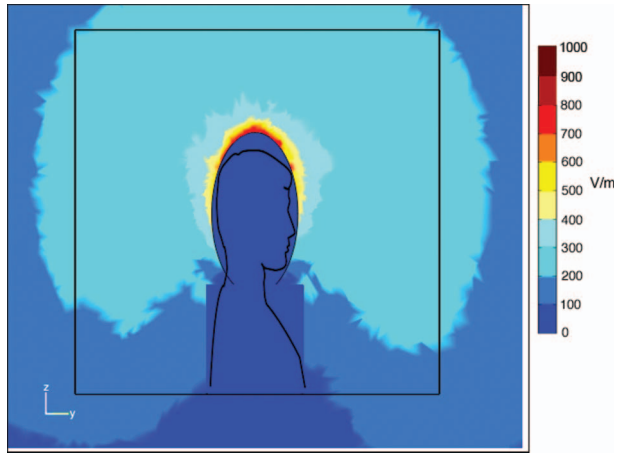

Figure 2. Calculated electric field in the mid-sagittal plane of a subject seated between parallel plates, with $V_{AC} = 225$ volts (see Figure 1A). The average electric field (±SD) surrounding the head was 430 ± 308 V/m.

The signals were amplified (Nihon Kohden, Irvine, CA, USA), filtered to pass 0.5–35 Hz, sampled at 300 Hz using a 12-bit analog-to-digital converter (National Instruments, Austin, TX, USA), and analysed offline. Each signal was divided into consecutive 7-second intervals (trials), with field onset at $t = 0$, field offset at $t = 2$ seconds, and the interval $2 < t \leq 7$ s during which there was no applied field (Figure 1B). Trials containing movement artifacts as assessed by visual inspection were discarded ($<5\%$ of all trials), and the artifact-free trials were digitally filtered between 0.5–35 Hz. All results were based on data from at least 50 trials.

Nonlinear and linear analysis

Details of our nonlinear method were given elsewhere (Carrubba et al. 2006). Briefly, the first 100 ms of each of the epochs of interest in V(t) ($t = 0.03$–1 s, 2.03–3 s, and 5.03–6 s, corresponding to onset, offset, and control intervals, respectively) (Figure 1B) were embedded in five-dimensional phase space, using a time delay of 5 points (17 ms), and the resulting trajectory was mapped to a two-dimensional recurrence plot by placing a point at (i,j) whenever the i^{th} and j^{th} state vectors in the trajectory were near (defined as within 15% of the maximum distance between any two states) (Eckmann et al. 1987). We used the Euclidean norm for calculating the distances. The plots were quantified using two recurrence variables (Zbilut and Webber 2006): (i) Percent recurrence (%R), defined as the ratio of the number of points in the plot to the total number of points in the recurrence matrix; and (ii) percent determinism (%D), defined as the fraction of points in the plot that formed diagonal lines consisting of at least two adjacent points. The process was repeated using a sliding window of 1 point in V(t), yielding the time series %R(t), which was smoothed using a 100-ms, step-1 averaging window. The resulting time series, $\overline{\%R(t)}$ and $\overline{\%D(t)}$, were analysed for the presence of evoked potentials. All calculations were performed using publicly available software (Webber 2007), and verified using a custom Matlab code (Mathworks, Natick, MA, USA).

Linear analysis was also performed for each subject; V(t) was averaged and examined for the presence of evoked potentials (Ruchkin 1988).

Experimental design and statistics

Onset and offset of a magnetic field each triggered evoked potentials (Carrubba et al. 2007a); we examined the same latency range to detect putative evoked potentials due to the electric field. Each of the 60 points in $\overline{\%R(t)}$ and in $\overline{\%D(t)}$ between 209–404 ms (which described the dynamical activity in V(t) at 109–504 ms) were compared individually with the corresponding points in the control epochs using the paired *t*-test at a pair-wise significance level of $p < 0.05$ (identical results were found using the Wilcoxon signed rank test). In preliminary studies on baseline EEG (no field) consisting of 2048 sets of 50 sham-field versus control comparisons, we found that the probability of observing ≥ 10 significant tests (out of 60) due to chance was about 0.04. We therefore planned to regard a comparison of a set of evoked-potential and control epochs from any particular electrode as significant if ≥ 10 tests were pair-wise significant at $p < 0.05$.

Filtering the EEG in the alpha band facilitated detection of magnetosensory evoked potentials; sometimes filtering 9–12 Hz but not 8–10 Hz was effective, and sometimes conversely (Carrubba et al. 2007a, 2007b, 2008). Use of $\overline{\%R}$ and $\overline{\%D}$ often give the same result, but there were instances where only one of them revealed a field-induced change in the EEG (Carrubba et al. 2008). Based on these prior observations, we systematically considered all conditions of analysis previously shown capable of revealing a magnetosensory evoked potential (Carrubba et al. 2008). First, we analysed $\overline{\%R(t)}$ in all six electrodes. If we found an evoked potential (≥ 10 pair-wise significant tests within the expected latency interval) in at least three electrodes, no further analyses were conducted. If fewer than three evoked potentials were found, we analysed $\overline{\%D(t)}$. If a total of three evoked potentials were still not detected, we filtered V(t) prior to calculating $\overline{\%R(t)}$ and $\overline{\%D(t)}$ and continued the analysis until either three evoked potentials were detected or all the six predetermined conditions (combinations of recurrence variable and filtering conditions) were considered. The overall results did not depend on the order; for presentation, we chose the sequence $\overline{\%R(t)}$, $\overline{\%D(t)}$, $\overline{\%R(t)}$ after filtering the EEG at 8–10 Hz, $\overline{\%D(t)}$ after filtering at 8–10 Hz, $\overline{\%R(t)}$ after filtering at 9–12 Hz, $\overline{\%D(t)}$ after filtering at 9–12 Hz. Whenever tests were done to compare evoked-potential and control epochs, the conditions being evaluated were also applied to the sham data (sham-evoked potential vs. sham control). Thus, for example, when the experimental data was filtered at 8–10 Hz, so was the sham data. At the conclusion of the study we calculated the *a posteriori* false-positive rate (number of false-positive effects in the sham data divided by the total number of tests performed), and used that error rate to estimate the family-wise error (P_{FW}) for the decision that a subject had exhibited field-induced evoked potentials.

Prior to the study we were unaware of whether the probability of detection of evoked potentials would depend on the electrode derivation. We therefore

computed the contributions to P_{FW} separately for the central, occipital, and parietal electrodes using the binomial formula, and the overall family-wise error rate for the occurrence of evoked potentials in each experiment was determined by the law of compound probability.

V(t) was also evaluated directly (no unfolding in phase space) by time averaging to detect linear evoked potentials, should they occur. The estimation of the *a posteriori* false-positive rate and the family-wise error for each of the two experiments in each subject was identical to the analysis used to evaluate the recurrence time series.

We regarded a potential as nonlinear if it was detected by recurrence analysis but not by time averaging.

Results

Evoked potentials

Using the nonlinear variable $\overline{\%R(t)}$, brain potentials evoked by an electric field of peak strength 1000 V/m were found in seven of eight subjects (Table I, first data column). In subject S8 for example, potentials were found at O_1 and C_3 due to field onset, and at O_1, C_3, and P_3 due to field offset; the offset results are shown in detail in Figure 3. When $\overline{\%R(t)}$ was used to compare the offset and control epochs (2–3 s and 5–6 s, respectively) point by point, an evoked potential (>10 pair-wise significant tests between the offset and control epochs) having the expected latency was detected from each of three derivations (Figure 3, left panels); sham-field exposure (the negative control procedure) yielded no false-positive results (<10 significant tests in each derivation) (Figure 3, right panels). A total of 96 statistical tests involving the $\overline{\%R(t)}$ time series were performed to evaluate the effect of the electric field (2 stimuli $\times$ 6 derivations $\times$ 8 subjects) resulting in 18 evoked potentials (Table I, first data column).

When a subject exhibited fewer than three evoked potentials in response to either the onset or offset of the field, $\overline{\%D(t)}$ was computed and analysed; evoked potentials were found in S3 and S5 that had not been detected with $\overline{\%R(t)}$ (Table I, second data column). Filtering the EEG to remove 8–10 Hz or 9–12 Hz prior to computing $\overline{\%R(t)}$ or $\overline{\%D(t)}$ revealed additional potentials; for example, when the 8–10-Hz energy was removed from the EEG signals prior to computing $\overline{\%R(t)}$, previously undetected potentials were found in all subjects (S6 and S8 were not examined because they had already met the subject-based criterion (three evoked potentials) for exhibiting a response to the field). We used the overall *a posteriori* error rate (43 false-positive tests $\div$ 1040 total tests $= 0.0413$) (see *Methods*) to compute the family-wise error rate. Each subject detected the electric field ($P_{FW} < 0.05$ for either onset or offset); detection occurred in all 16 experiments except S4 (offset) and S7 (onset).

When the strength of the applied electric field was halved in two successive groups of subjects, the field was transduced in both groups, as evidenced by observations of evoked potentials. At 500 V/m, all subjects detected the field; three of the five subjects detected both the onset and offset of the field (Table II). At 250 V/m, all subjects detected either

Table I. Evoked potentials in subjects exposed to a peak electric field of 1000 V/m (430 V/m averaged over the head). At 1000 V/m, the brain electric field was estimated at 1 mV/m (equivalent to a magnetic field of 100 μT). Column heads indicate conditions of analysis. Effects in $\overline{\%D(t)}$ are shown in bold. X, evoked potentials not detected. Dashes indicate conditions not analysed. P_{FW}, family-wise error for the decision that the subject exhibited evoked potentials.

Subject	EEP	$\overline{\%R}$	$\overline{\%D}$	$\overline{\%R}$ (8–10 Hz)	$\overline{\%D}$ (8–10 Hz)	$\overline{\%R}$ (9–12 Hz)	$\overline{\%D}$ (9–12 Hz)	All effects	No. tests	P_{FW}
S1	Onset	C3	X	O2	**O2**	–	–	C3 O2 **O2**	23	0.027
	Offset	X	X	X	**C4 P3**	X	**C3**	**C3 C4 P3**	34	0.072
S2	Onset	C3	C3	O2 P4	–	–	–	O2 C3 **C3** P4	17	0.001
	Offset	C4	C4	X	X	P4	–	C4 **C4** P4	27	0.037
S3	Onset	X	X	C4	**P3**	O2	–	O2 C4 **P3**	29	0.037
	Offset	X	**P3**	C3 P3	–	–	–	C3 **P3** P3	18	0.014
S4	Onset	C4	**C4**	C3 P3	–	–	–	C3 **C4** C4 P3	17	0.003
	Offset	X	X	X	**P3**	X	X	P3	35	0.775
S5	Onset	C3 C4 P4	–	–	–	–	–	C3 C4 P4	6	0.001
	Offset	P3	**O2**	C4	–	–	–	**O2** C4 P3	17	0.009
S6	Onset	C3 C4	**C3 C4**	–	–	–	–	C3 **C3** C4 **C4**	12	0.001
	Offset	C4 P4	**P4**	–	–	–	–	C4 P4 **P4**	12	0.007
S7	Onset	C3	**C3**	X	X	X	X	C3 **C3**	32	0.345
	Offset	X	X	O2	**O1 O2 C3 P3**	–	–	**O1** O2 **O2 C3 P3**	24	0.000
S8	Onset	O1 C3	**O1**	–	–	–	–	O1 C3 **O1**	12	0.005
	Offset	O1 C3 P3	–	–	–	–	–	O1 C3 P3	6	0.001

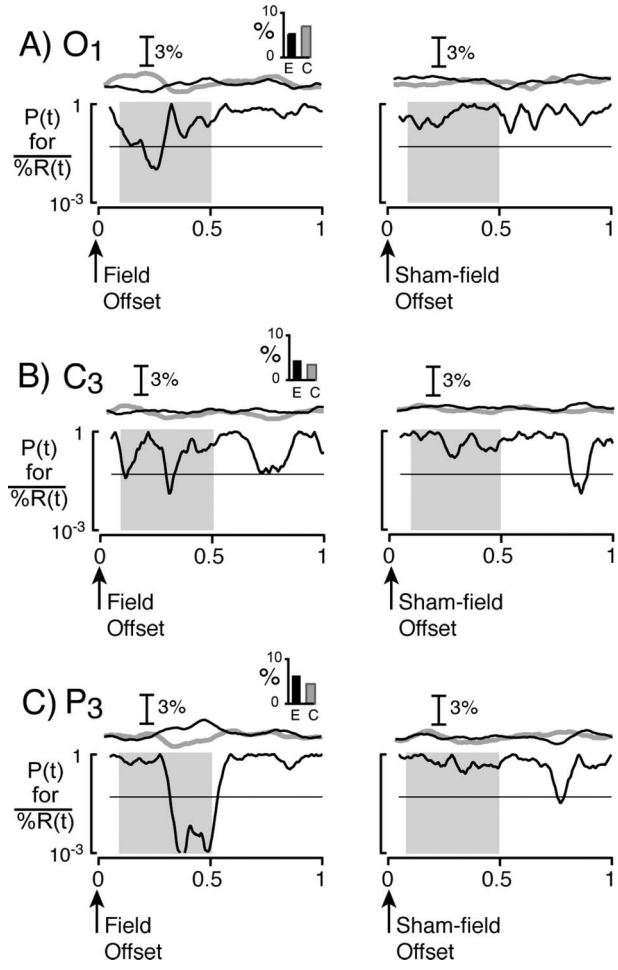

Figure 3. Evoked potentials in subject S8 exposed to 1000 V/m, observed using the recurrence analysis variable $\overline{\%R(t)}$. Potentials from O_1, C_3, P_3 shown in (A)–(C), respectively. Left panels, field offset; right panels, sham-field offset. The curves at the tops of the panels show the average values of the offset (t = 2.03–3 s) (E) and control (t = 5.03–6 s) (C) epochs for the respective $\overline{\%R(t)}$ time series (N ≥ 50 trials). The p(t) curves are the probability that the difference between the means of the offset and control epochs at time t was due to chance. Bar graphs indicate the average value of $\overline{\%R(t)}$ over the latency interval for which $p(t) < 0.05$ (horizontal line); the standard deviations are not resolved at scale shown. The stippled regions show the expected latency intervals.

the onset or the offset of the field (Table III). When we reduced the strength of the applied field by a factor of about 40 below the initial level, we again found that each subject detected either the onset or offset, except for S20 (Table IV). Overall (Tables I–IV), there were two false-positive results (Table III, sham offset in S14, and sham onset in S18).

Neither the latency nor duration of the potentials depended on the stimulus (onset or offset), stimulus strength, gender, or electrode derivation (Table V). When the recurrence variable for each evoked potential (Tables I–IV) was compared with its control (expressed as a percent of the average of the sum), the change was sometimes greater than the control, and sometimes less (Figure 4); the average of the absolute value was 32%.

Evoked potentials were not detected in any subject based on an analysis of the EEG using time averaging. Typical results are shown in Figure 5. Neither time averaging of the EEG nor point by point comparisons (Figures 5A and 5B, left column) provided any evidence of either onset or offset evoked potentials. In contrast, evoked potentials were detected by means of recurrence analysis (Figures 5A and 5B, right column).

Biophysical model

One possibility to account for transduction of the induced electric field is that the process involved forces on ion-channel gates (Figure 6). At normal pH the oligosaccharides in the cell glycocalyx are negatively charged. In the presence of an electric field (**E**) each charge in the system experiences a displacement force $\mathbf{F} = q\mathbf{E}$. A formal condition sufficient for transduction is $|q\mathbf{E}\Delta x| \geq U \geq kT/2$, where q is the negative charge on a portion of the glycocalyx mechanically linked to a channel gate, Δx is the displacement of the channel gate, U is the potential energy barrier between closed and open channel states, k is Boltzmann's constant and T is temperature, and kT/2 is the thermal energy associated with one degree of freedom. If q is taken to be the negative charge per molecule in the glycocalyx, $q = -eZ$, where e is the elementary charge, and Z is the number of charges per molecule. Thus $neZ\mathbf{E}\Delta x \geq kT/2$, where n is the number of molecules necessary to alter the probability of the channel to be in the open state. To estimate the corresponding glycocalyx mass (M), we assume that each oligosaccharide monomer has one negative elementary charge and the same mass, m, taken to be that of a hyaluronan disaccharide (6.7×10^{-25} kg). Then, $M = nZm$, and from the inequality above, $M > kT\,m/2\,e\mathbf{E}\Delta x = 1.4 \times 10^{-18}/\mathbf{E}$. If we assume a height $h = 50$ nm (a common thickness for the glycocalyx), the radius of the mass is $r = (M/\pi h\rho)^{1/2}$, where ρ is the density ($\rho \approx 10^3$ kg/m^3). To detect a field of say 0.1 mV/m, $M \approx 1.4 \times 10^{-18}/10^{-4} \approx 1.4 \times 10^{-14}$ kg, which corresponds to a glycocalyx region with a radius of about 9 μm.

Discussion

Attempts to understand the biophysical basis of biological sensitivity to electromagnetic fields have been hampered by the consistent inconsistency of the results of studies involving the effects on brain electrical activity (Carrubba and Marino 2008, Marino and Carrubba 2008), and by the absence of an understanding of the coupling mechanism

Table II. Evoked potentials in subjects exposed to a peak electric field of 500 V/m (215 V/m, average). The corresponding brain electric field was approximately 0.5 mV/m. Effects in $\overline{\%D(t)}$ are shown in bold. X, evoked potentials not detected. Dashes indicate conditions not analysed. P_{FW}, family-wise error for the decision that the subject exhibited evoked potentials. NE, no effect.

Subject	EEP	$\overline{\%R}$	$\overline{\%D}$	$\overline{\%R}$ (8–10 Hz)	$\overline{\%D}$ (8–10 Hz)	$\overline{\%R}$ (9–12 Hz)	$\overline{\%D}$ (9–12 Hz)	All effects	No. tests	P_{FW}
S9	Onset	X	X	X	X	X	X	–	36	NE
	Offset	O2	**O2**	X	X	X	**P3**	O2 **O2 P3**	32	0.052
S10	Onset	X	X	C3	**O1 C3 P3**	–	–	**O1** C3 **C3 P3**	24	0.003
	Offset	O1 O2 C3 P3 P4	–	–	–	–	–	O1 O2 C3 P3 P4	6	0.000
S11	Onset	O1 P3	**C3**	–	–	–	–	O1 **C3** P3	12	0.004
	Offset	X	X	O1	**O1**	P3	–	O1 **O1** P3	29	0.049
S12	Onset	X	**C4**	O1 O2 C4 P3 P4	–	–	–	O1 O2 **C4** C4 P3 P4	18	0.000
	Offset	C3 P3	**C3 P3**	–	–	–	–	C3 **C3** P3 **P3**	12	0.000
S13	Onset	P4	**P4**	P3	–	–	–	P3 P4 **P4**	17	0.032
	Offset	X	X	X	X	X	X	–	36	NE

Table III. Evoked potentials in subjects exposed to a peak electric field of 250 V/m (107 V/m, average). The corresponding brain electric field was approximately 0.25 mV/m. Column heads indicate conditions of analysis. Effects in $\overline{\%D(t)}$ are shown in bold. X, evoked potentials not detected. Dashes indicate conditions not analysed. P_{FW}, family-wise error for the decision that the subject exhibited evoked potentials. NE, no effect. *False-positive result found in the sham-field analysis.

Subject	EEP	$\overline{\%R}$	$\overline{\%D}$	$\overline{\%R}$ (8–10 Hz)	$\overline{\%D}$ (8–10 Hz)	$\overline{\%R}$ (9–12 Hz)	$\overline{\%D}$ (9–12 Hz)	All effects	No. tests	P_{FW}
S14	Onset	O1 C3 C4 P4	–	–	–	–	–	O1 C3 C4 P4	6	0.000
	Offset*	X	**P4**	X	X	X	X	**P4**	34	0.765
S15	Onset	P3	X	O1	X	C3	–	O1 C3 P3	27	0.031
	Offset	X	X	X	X	X	X	–	36	NE
S16	Onset	C4	X	C3	**C3 C4**	–	–	C3 **C3** C4 **C4**	23	0.014
	Offset	X	X	X	X	C3	X	C3	36	0.774
S17	Onset	X	X	X	X	O1 O2	**O2**	O1 O2 **O2**	36	0.189
	Offset	O1 P3	**O1**	–	–	–	–	O1 **O1** P3	12	0.005
S18	Onset*	C3 P3	X	X	X	X	X	C3 P3	32	0.208
	Offset	C3 C4 P3	–	–	–	–	–	C3 C4 P3	6	0.000

Table IV. Evoked potentials in subjects exposed to a peak electric field of 27 V/m (13 V/m, average). The corresponding brain electric field was approximately 0.01 mV/m. Column heads indicate conditions of analysis. Effects in $\overline{\%D(t)}$ are shown in bold. X, evoked potentials not detected. Dashes indicate conditions not analysed. P_{FW}, family-wise error for the decision that the subject exhibited evoked potentials. NE, no effect.

Subject	EEP	$\overline{\%R}$	$\overline{\%D}$	$\overline{\%R}$ (8–10 Hz)	$\overline{\%D}$ (8–10 Hz)	$\overline{\%R}$ (9–12 Hz)	$\overline{\%D}$ (9–12 Hz)	All effects	No. tests	P_{FW}
S19	Onset	O2 C3	**O2 C3**	–	–	–	–	O2 **O2** C3 **C3**	12	0.000
	Offset	C3	**C3 P4**	–	–	–	–	C3 **C3 P4**	12	0.001
S20	Onset	X	X	X	X	X	X	–	36	NE
	Offset	X	X	O1 C3	X	X	X	O1 C3	34	0.233
S21	Onset	C4	**C4**	O2	–	–	–	C4 **C4** O2	17	0.011
	Offset	C4 P4	**C4 P4**	–	–	–	–	C4 **C4** P4 **P4**	12	0.000
S22	Onset	P4	**C3 C4 P4**	–	–	–	–	**C3 C4** P4 **P4**	12	0.040
	Offset	X	X	X	X	X	X	–	–	NE
S23	Onset	X	**O2**	P3	X	X	X	**O2** P3	33	0.217
	Offset	C4	**P4**	X	X	C3	–	C3 C4 **P4**	32	0.019

between fields and tissue (Blank and Findl 1987). Inconspicuous experimental errors or hidden variables such as personality or laterality could account for inconsistencies in particular brain-wave studies, but we showed a more global explanation was the common use of methods of analysis which were unable to capture the nonlinear deterministic changes induced by the fields. Using recurrence analysis (Zbilut and Webber 2006), we found that evoked potentials could be consistently and reliably

Table V. Latency and duration of evoked potentials stratified by stimulus (onset or offset), gender, and electrode derivation. Mean ± SD. *n*, number of evoked potentials (from Tables I–IV). Neither the latency nor duration in any subset depended on electric field strength in the range 10–1000 V/m.

	Stimulus		Gender		Electrode		
	Onset	Offset	Male	Female	Occipital	Central	Parietal
Latency (ms)	314 ± 54	303 ± 66	305 ± 65	311 ± 58	312 ± 64	310 ± 53	306 ± 66
Duration (ms)	264 ± 30	256 ± 28	253 ± 23	263 ± 31	264 ± 31	262 ± 25	256 ± 33
n	72	59	31	100	42	57	32

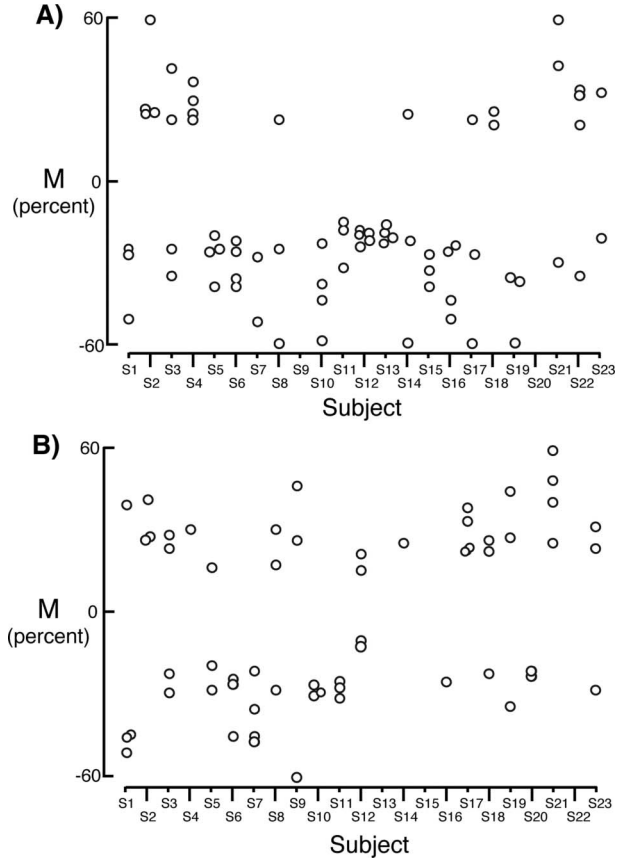

Figure 4. Relative magnitude (M) of each evoked potential (expressed in percent) from each subject (23 subjects), as determined by recurrence analysis (Tables 1–4). (A), (B), onset and offset responses, respectively. For each potential, $M = 100(E - C)/0.5(E + C)$, where E was the average of the recurrence variable over the statistically significant latency interval, and C was the corresponding average in the control epoch. Similar values from different electrodes in a given subject are shown with an offset to improve resolution. Values greater than 60% are shown as 60%.

triggered by low-strength magnetic fields (Carrubba et al. 2007a, 2007b, 2008). The magnetic field induced an electric field in the brain of each subject in those studies. Our main purpose here was to test the hypothesis that the induced electric field could explain the evoked potentials. This was accomplished by creating an equivalent brain electric field in the absence of a magnetic field, and determining whether evoked potentials occurred that had characteristics similar to the magnetosensory evoked potentials observed in the earlier studies.

The calculations used to establish an equivalence between the electric and magnetic fields depend on the details of the model adopted for the brain (Hart 1992, Dawson et al. 1997). Another limitation regarding the calculations is that they took no account of differences in the direction of the fields at any particular brain location. Even so, the calculations were sufficient to show that 1000 V/m induced a brain electric field of about 1 mG/m, and that 100 μT induced a comparable brain electric field. Application of 1000 V/m resulted in changes in brain electrical activity in each subject (Table I). Several considerations indicated that the observed changes were true evoked potentials. First, the analysis incorporated protection against family-wise error, which obviated an explanation based on chance. Second, comparable changes were not observed in the sham data. Third, the changes occurred several hundred milliseconds after the field had been switched off; the latency of the changes ruled out the possibility that they could have been generated by a field-electrode interaction (a process that has no latency), but the latency was consistent with the inference that the changes arose from brain processing of afferent signals that resulted from transduction of the field. Fourth, studies using phantoms of the human head verified the absence of electrode signals within the expected latency range.

In additional independent experiments, the applied field was systematically reduced and we consistently found that the subjects exhibited evoked potentials (Tables II–IV). In 10 subjects exposed to 250–500 V/m (induced brain electric field, 0.25–0.50 mV/m) onset evoked potentials were detected in seven subjects and offset evoked potentials were detected in five subjects; at least one stimulus produced a response in every subject. Similar results were found at 10 V/m (0.01 mV/m in the brain); only S20 did not exhibit an evoked potential (Table IV).

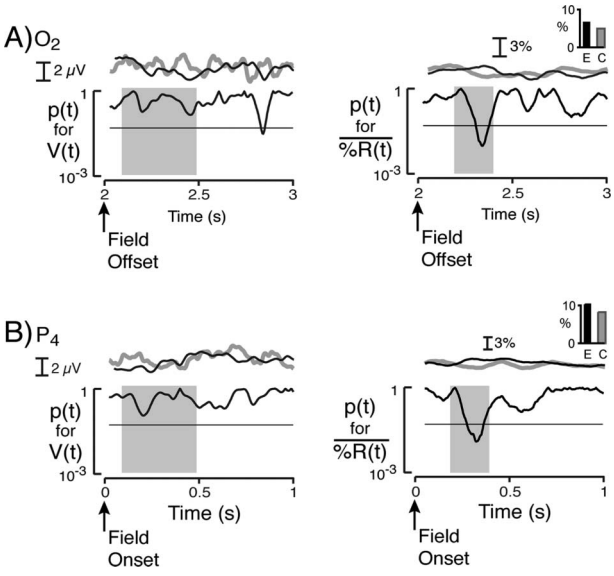

Figure 5. Linear and nonlinear analysis of evoked potentials. (A) O_2 offset from subject S9 (215 V/m). (B) P_4 offset from subject S22 (11 V/m). First column, comparison of the stimulus and control epochs in the EEG (method of time averaging). Second column, comparison of the epochs using $\overline{\%R(t)}$ computed from the EEG. The curves at the tops of the panels show the average values of the stimulus (E) and control (C) epochs for the respective time series ($N \geq 50$ trials). The p(t) curves are the probability that the difference in means at time t was due to chance. Bar graphs indicate the average value of $\overline{\%R(t)}$ over the latency interval for which $p(t) < 0.05$ (horizontal line); the standard deviations are not resolved at scale shown. The stippled regions show the expected latency interval.

Overall, 22 of 23 subjects exhibited evoked potentials in response to electric fields in the range 10–1000 V/m (peak fields) that could only have been caused by the applied electric field. The latency and duration (Table V) of the potentials, and the distribution of their magnitude and direction (Figure 4), were essentially identical to the corresponding values of the potentials triggered by magnetic stimuli (Carrubba et al. 2007a, 2007b, 2008). Because the potentials produced by applied electric fields were indistinguishable (in the respects considered) from those produced by applied magnetic fields, we conclude that the electric field was a sufficient biophysical determinant of the evoked potentials in the present study, as well as in the earlier studies.

We could not establish an effects threshold because the background electric field was about 1 V/m, and the spatial variations of the applied electric field (and its perturbations due to the presence of the subject) prevented us from reliably characterising an average field below about 5 V/m. The important issue of the threshold could be approached experimentally by applying magnetic fields, because they can be used to induce electric fields at least an order of magnitude below our present limit when applying an electric field. We suspect that the threshold is not a discrete level, but rather a probability function that describes the fraction of the study group who exhibit altered brain activity for a given level of the induced electric field.

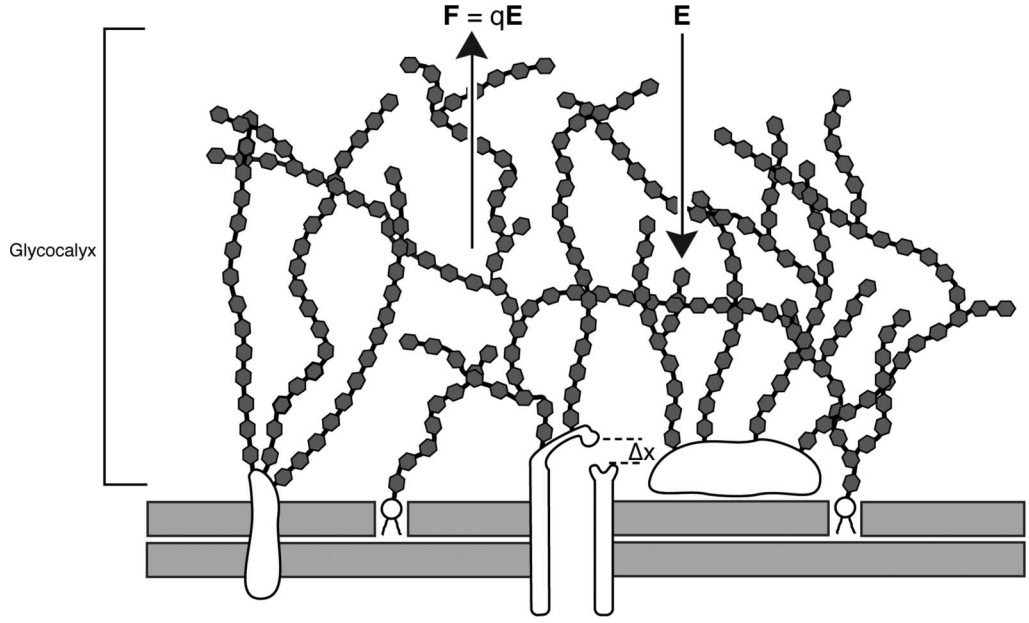

Figure 6. Model for detection of electric fields. The glycocalyx consists of oligosaccharide side chains covalently bound to adsorbed and transmembrane proteins, including ion channels. An applied electric field **E** exerts a force **F** on the negatively charged glycocalyx molecules bound to the gate or interleaved with the bound molecules, thereby mechanically opening the channel gate. It is assumed that the negative charges rotate slightly with respect to the positive counter-ions, which is a reasonable assumption for small displacements. Δx, the channel gate.

Effects of electric fields of about 10 V/m in air on brain activity were reported at least as early as 1968 (reviewed in Adey 1973). Most subsequent work focused on the effect of applied magnetic fields (reviewed in Carrubba et al. 2008).

We found that the induced electric field could explain the effect produced by the magnetic field, but there are biological systems where a magnetic field produced effects that were not associated with the electric field, and other systems where the magnetic and electric field produced different effects (Blackman et al. 1993). There are also reports of dissimilar effects in the same system produced by magnetic and electric fields, but there are no reports involving animals or human subjects where the two fields were equivalent and the geomagnetic field was standardised (see *Methods*).

The question whether the electric field was necessary for the production of evoked potentials cannot be answered empirically because it is not possible to apply a time-varying magnetic field to the brain in the absence of an induced electric field. Nevertheless, based on theoretical considerations, a good argument can be made that the electric field was also a necessary cause of the evoked potentials. There is no published explanation regarding how magnetic fields on the order of 100 μT, 60 Hz could be detected by a sensory cell; the exceedingly small energy of interaction between the field and tissue (compared with thermal energy [kT]) has thus far defeated all proposed models except those that postulate the existence of ferromagnetic structures, which have not been observed in the human brain. On the other hand, it is possible to construct a realistic model to explain detection of induced electric fields comparable to those in the present study (Figure 6).

Filtering within the alpha band was sometimes necessary for detection of the evoked potentials (Tables I–IV), as observed previously (Carrubba et al. 2007a, 2007b, 2008). The rationale for removing alpha energy was that it did not contribute to the response, and therefore that removal of alpha increased sensitivity for detection of the evoked potentials by increasing the signal-to-noise ratio in the system. The increased sensitivity afforded by alpha filtering might mean that the brain region where the alpha activities originate, usually assumed to be the cerebral cortex (Shaw 2003), was not crucial in the brain processing that gave rise to the evoked potentials. This suggestion is consistent with the finding that the subject did not know the electric field was present even though the subject's brain did.

Both %R and %D were used to detect the evoked potentials; whether they actually captured something different from one another about field-induced dynamical changes in brain activity is unknown. It is possible that, in particular cases, one variable or the other was more sensitive because of random fluctuations in the signal. The choice of the phase-space embedding conditions can also affect the sensitivity to detect an evoked potential (Carrubba et al. 2008).

The evoked potentials were not detected when the EEG were analysed by time averaging, indicating that the evoked potentials were nonlinear in origin, as observed previously (Carrubba et al. 2007a, 2007b, 2008). Our observation that the changes in recurrence parameters could be either an increase or a decrease (Figure 5) further confirmed the nonlinearity of the response, because only nonlinear systems can exhibit such behavior.

We did not address the question of the anatomical location of the electroreceptor cell. The observed latencies (Table V) were consistent with any location in the body, however, animal studies suggested the electroreceptor cell was located in the head, possibly the cerebellum (Marino et al. 2003, Frilot II et al. 2008).

The electric field could control several ion channels in a cell by the mechanism illustrated in Figure 6, which would be sufficient to induce a change in membrane potential that could initiate an afferent signal. Even weaker electric fields could be detected if one assumed a higher net charge, greater height for the glycocalyx, a smaller interaction energy (with respect to kT), or a form of cooperativity among ion channels. The model contains several assumptions, and inhomogeneities and anisotropies of the electric fields inside the brain will affect the field strength seen by the protein. Despite these limitations, the calculation shows that electric fields as weak as those induced in the brains of the exposed subjects could result in evoked potentials.

Electric fields greater than 1000 V/m are found in the general and workplace environments such as within about 30 m of high-voltage powerlines, or near (usually less than 1 m) some electrical devices. An electric field of 10 V/m is exceedingly common, and is routinely experienced on a daily basis by most people (World Health Organisation 2002). The public-health significance of the resulting evoked potentials remains to be assessed.

In conclusion, the evoked potentials observed previously in response to the onset and/or offset of a magnetic stimulus were probably triggered by the interaction between the magnetically-induced electric field in the subject's brain and surface charges on the electroreceptor cell.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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