

Nonlinear EEG activation evoked by low-strength low-frequency magnetic fields

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Abstract

Recent electrophysiological evidence suggested the existence of a human magnetic sense, but the kind of dynamical law that governed the stimulus–response relationship was not established. We tested the hypothesis that brain potentials evoked by the onset of a weak, low-frequency magnetic field were nonlinearly related to the stimulus. A field of 1 G, 60 Hz was applied for 2 s, with a 5 s inter-stimulus period, and brain potentials were recorded from occipital electrodes in eight subjects, each of whom were measured twice, with at least 1 week between measurements. The recorded signals were subjected to nonlinear (recurrence analysis) and linear (time averaging) analyses. Using recurrence analysis, magnetosensory evoked potentials (MEPs) were detected in each subject in both the initial and replicate studies, with one exception. All MEPs exhibited the expected latency but differed in dynamical characteristics, indicating that they were nonlinearly related to the stimulus. MEPs were not detected using time averaging, thereby further confirming their nonlinearity. Evolutionarily conditioned structures that help mediate linear field-transduction in lower life forms may be expressed and functionally utilized in humans, but in a role where they facilitate vulnerability to man-made environmental fields. © 2007 Elsevier Ireland Ltd. All rights reserved.

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Low-frequency, low-intensity electric and magnetic fields are common in the environment and increasing evidence associates them with various metabolic, behavioral and pathological effects [1]. One possibility is that many of the effects are consequences of sensory transduction of the field [9], and electrophysiological evidence supporting the theory of a human magnetic sense was presented recently [3].

A question raised in that study [3] involved the nature of the relationship between the field stimulus and the evoked response. Field-induced changes in brain electrical activity could be detected only by phase space-based methods intended for the analysis of nonlinear activity, suggesting that the response of the subject was governed by nonlinear laws. If so, the human magnetic sense would be distinguished from the ordinary senses, which are apparently governed by linear laws.

Nonlinear systems do not follow the law of superposition, and therefore their reactions to changes in external conditions cannot be precisely predicted. Thus, under the hypothesis that MEPs are nonlinear, the brain electrical responses exhibited by human subjects would be expected to differ even when the experimental conditions were replicated. Our objective was to test this hypothesis in each of a group of subjects by comparing the subject's response to a specific magnetic stimulus at two times separated by at least 1 week. We expected to observe intra-subject differences of the type that could be manifested only by nonlinear systems.

Eight clinically normal subjects were studied: two males (ages 30 and 45 years) and six females (age range 18–65 years). They were informed of the goals, methods, and general design of the investigation, and a written informed consent was obtained prior to participation in the study. The Institutional Review Board at the LSU Health Science Center approved all experimental procedures.

A 60 Hz uniaxial magnetic field of 1 G (100 μ T) was applied in the coronal plane by means of coaxial coils; details of the exposure system are given elsewhere [2]. The field was applied

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for 2 s, with a 5 s inter-stimulus period. Field onset produced a 30 ms voltage spike in the EEG signal (because of faradic induction) [2], which was deleted prior to all analyses. The subjects did not consciously perceive the field because 1 G, 60 Hz is below the threshold of awareness in humans. Care was taken to insure that the coil power supply and EEG measuring equipment did not provide auditory or visual cues. The absence of sensory cues associated with the field stimulus was verified by interviewing each subject after the experimental session.

EEGs were recorded from O₁ and O₂ (International 10–20 system) referenced to linked ears, using gold-plated electrodes attached to the scalp with conductive paste. Previous studies demonstrated that MEPs were more readily detected in occipital derivations [2,3]. Electrode impedances (measured before and after each experiment) were 3–5 k Ω . Each subject was measured twice, with at least 1 week between the measurements. The signal, $V(t)$, was amplified (Nihon Kohden, Irvine, CA), analog-filtered to pass 0.5–35 Hz, sampled at 300 Hz (National Instruments, Austin, TX) and analyzed offline. For analysis, $V(t)$ was divided into consecutive 7 s trials (onset at $t=0$, offset at $t=2$ s). Trials that contained artifacts (assessed by visual inspection) were discarded, the epochs of interest in each trial ($t=0.03$ –1 s and 5.03–6 s, corresponding to onset and control epochs, respectively) were digitally filtered to pass 0.5–35 Hz and analyzed offline using nonlinear (recurrence analysis) and linear (time averaging) methods. All results were based on data from at least 50 trials.

The general properties of recurrence analysis have been described [4,5,12,13,15], as have its uses for evaluating brain potentials [2,3]. For detection of MEPs in each subject due to field onset, $V(t)$ corresponding to the onset ($t=0.03$ –1 s) and control ($t=5.03$ –6 s) epochs was embedded in phase space and recurrence plots were generated and quantitated. Briefly, the first 100 ms of each $V(t)$ epoch (30 points) was embedded in a five-dimensional phase space using a time delay of 5 points (17 ms), and the corresponding recurrence plot was generated. Points in phase space are said to be recurrent if the distance between them is less than an adjustable parameter (here, chosen to be 15% of the maximum distance). For calculating the distances we used the Euclidean norm [15]. A recurrence plot is a useful device for revealing patterns of dynamical (time-related) activity not detectable by eye or by conventional analysis. We quantified the plot using percent recurrence, $\%R$, defined as the number of recurrent points in the plot divided by the total number of points in the recurrence matrix. The computational process was iterated 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, $\overline{\%R(t)}$, was analyzed for the presence of evoked potentials. The advantage of $\overline{\%R(t)}$ is that it is useful for detecting nonlinear stimulus-induced changes in brain electrical activity. The disadvantage is that the time series does not provide direct insight into the physiological basis of the EEG or the MEPs. All adjustable parameters used in the analysis, including those listed above and alpha filtering (see below), were ascertained by trial and error in earlier studies [2,3].

Quantifiers other than $\%R$, each of which has a different theoretical significance, can be used to characterize a recurrence

plot [13]. We chose $\%R$ because it required one less adjustable parameter (line parameter not required) and was effective in revealing the presence of MEPs.

To synchronize the graphical representation of $V(t)$ and $\overline{\%R(t)}$, we adopted the convention that each point in $\overline{\%R(t)}$ was plotted at the time corresponding to the middle of the interval in $V(t)$ from which it was computed. For example, the value of $\overline{\%R(t)}$ calculated from the 100 ms interval in $V(t)$ beginning at $t=30$ ms appeared in a plot of $\overline{\%R(t)}$ at $t=80$ ms; when that point was the first in the 100 ms averaging window for $\overline{\%R(t)}$, it was plotted at $t=130$ ms. Thus, $\overline{\%R(130)}$ reflected the activity in $V(t)$ between 30 and 230 ms. The convention was chosen because it results in an alignment of the probability curve ($P(t)$) with the visually observable difference in the average $\overline{\%R(t)}$ curves for the onset and control epochs (see below).

The subject underwent a block of trials in which the magnetic field was applied and another block where the field was not applied (sham exposure); the sequence of the blocks for a particular subject was chosen randomly. The data from the sham block were analyzed as a negative control.

When the relative alpha power (8–13 Hz) was $\geq 30\%$, $V(t)$ was digitally filtered to remove some or all of the 9–12 Hz power prior to computing $\overline{\%R(t)}$; this procedure was previously found to increase sensitivity for detection of MEPs [3,6].

Brain potentials triggered by the stimulus used in this study occur with a latency of 109–454 ms [3]; our experimental design was therefore based on detecting MEPs in this interval. First, we produced probability curves, $P(t)$, by computing the comparison-wise probability of a difference between each point in the interval 0.03–1 s, and its corresponding point in the control epoch (5.03–6 s). Then, to detect the potentials, each of the 45 points in $\overline{\%R(t)}$ between 209 and 354 ms (which quantitates the regularity of the activity in $V(t)$ at 109–454 ms that was reflected in the recurrence plot) was compared with the corresponding point in the control epochs (5.209–5.354 s) using the paired t -test (pair-wise significance level, $p < 0.05$). The probability of observing ≥ 6 pair-wise significant differences by chance in 45 tests is 0.024. We planned to conclude that an MEP had been observed from a given electrode if ≥ 6 tests were pair-wise significant. The reliability of this statistical design was evaluated experimentally by computing the *a posteriori* probability of a false-positive result, P_a , defined as the number of significant differences found in the sham data divided by the number of tests performed.

Linear analysis was also performed in each subject. $V(t)$ from each derivation was smoothed (100 ms step-1 averaging window) and the onset and control epochs were compared for the presence of evoked potentials, as described for $\overline{\%R(t)}$.

Brain potentials evoked by field onset were detected by recurrence analysis but not by time averaging; typical results are shown in Figs. 1 and 2 (subject S1). When the activity in $V(t)$ from O₂ was captured using $\overline{\%R(t)}$, potentials in the expected latency range occurred in both the initial study and the replicate, evidenced by point-wise differences at 204–279 ms (22 points) in the initial study (Fig. 1a, left panel) and 229–275 ms (15 points) in the replicate (Fig. 1b, left panel). No differences in $\overline{\%R(t)}$ occurred in the sham-field onset epochs (Fig. 1a and

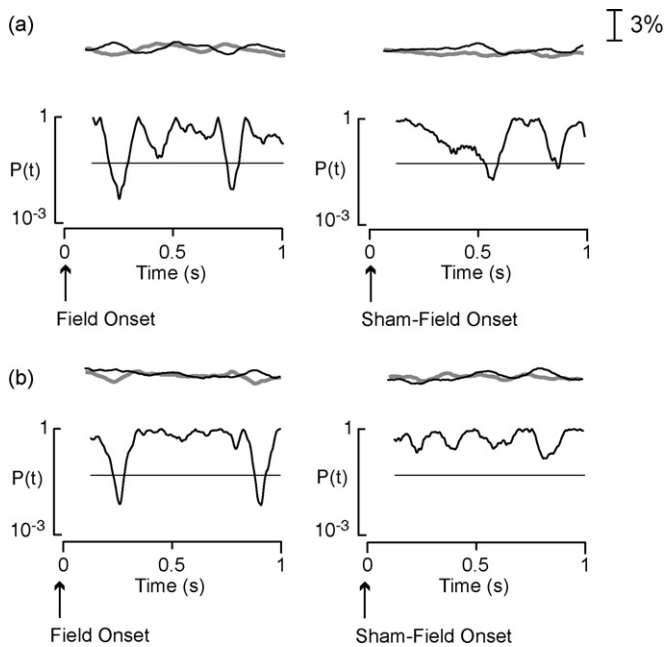


Fig. 1. Detection of magnetosensory evoked potentials having the predicted latency using recurrence analysis; O₂ derivation (S1). (a) Initial study and (b) replicate study. Upper curves (a and b), $\%R(t)$ averaged over ≥ 50 trials. Lower curves, point-wise probability (t -test) of a difference between onset (black) and control (gray) curves. $\%R(t)$ was plotted such that each point corresponded to the middle of the EEG time interval from which it was computed [5]. Thus, $\%R(133)$ reflected the determinism that occurred in $V(t)$ within 33–233 ms. $P(t)$, probability of a point-wise difference in the t -tests between the exposed and control epochs of $\%R$.

b, right panels). MEPs were not detected in $V(t)$ in either study (Fig. 2).

Using recurrence analysis, MEPs were detected in all subjects in the initial series of studies, and in all but 1 subject in the replicate studies (Fig. 3). One false-positive result was found in the sham exposures in the initial and in the replicate studies. Using linear analysis, no MEPs were detected, but 1 false-positive result was found in the sham.

The average effect (difference between stimulus and control epochs in bar graphs in Fig. 3, expressed as a percent of the mean of the stimulus and control epochs) was essentially identical in the two series of experiments (Table 1).

When a visual or auditory stimulus is repeated, the evoked potentials are usually sufficiently similar that they can be detected by time averaging, and the transduced signal is perceived in more or less the same way. These characteristic

Table 1
Effect of stimulus on the average percent change ($\% \Delta$) in $\%R(t)$ averaged over the duration of the MEPs

Field (G)	Initial study			Replicate		
	<i>N</i>	<i>n</i>	$\% \Delta$	<i>N</i>	<i>n</i>	$\% \Delta$
1	8	11	22.6 ± 4.6	7	9	25.0 ± 4.0
2	17	42	25.1 ± 8.4	–	–	–

N, number of subjects; *n*, number of electrodes. $\% \Delta \equiv \sum_{i=1}^n 200|E - C|/(E_i + C_i)$, where *E* and *C* are the average $\%R(t)$ of the stimulus and control epochs (for 1 G, bar graphs in Fig. 3; for 2 G, from Ref. [1]).

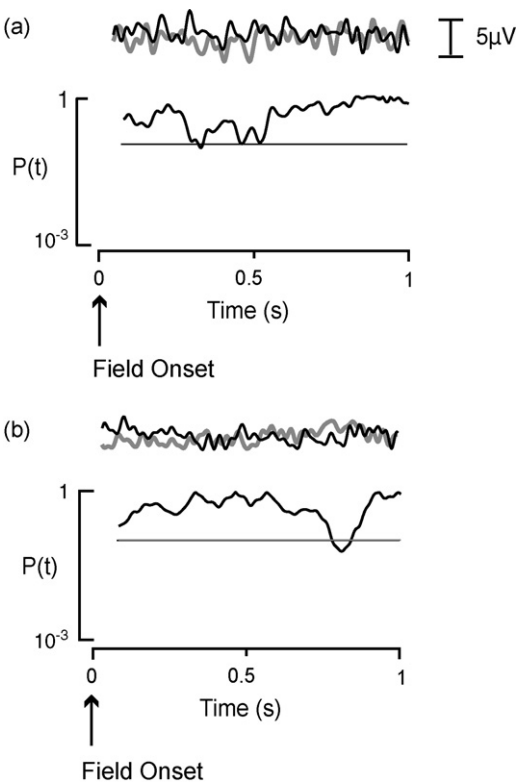


Fig. 2. Linear analysis for magnetosensory evoked potentials; O₂ derivation (S1). (a) Initial study and (b) replicate study. Upper curves (a and b), $V(t)$ averaged over ≥ 50 trials. Lower curves, point-wise probability (t -test) of a difference between onset (black) and control (gray) curves. $P(t)$, probability of a point-wise difference in the t -tests between the exposed and control epochs of $V(t)$.

electrophysiological and subjective behaviors arise because the stimulus–response relationships of sensory systems are governed by linear laws (linear differential equations). Low-intensity, low-frequency magnetic stimuli did not produce conscious sensation and did not produce evoked potentials that were detectable by time averaging [3]. However, when the stimulus–response relationship was analyzed using phase-spaced-based methods, MEPs having latencies of 109–454 ms were detected [3]. We interpreted these results to indicate that MEP production was governed by nonlinear laws, and this study was performed to test that hypothesis.

Nonlinear stimulus–response relationships are not precisely predictable because the principle of superposition does not hold for nonlinear systems, and because biological noise can modify the stimulus–response relationship (rather than functioning simply as an additive factor whose impact can be mitigated by signal averaging). Thus, we expected that replicate experiments on a given subject would produce MEPs within a specific range of latencies [3], but that other characteristics of the MEPs would differ between the independent measurements. In general, the distinctive characteristic of a nonlinear system is its ability to exhibit an inconsistent response, whereas the distinctive characteristic of a linear system is its consistency in response to a stimulus.

With one exception (S6), the MEPs observed in the initial studies were also observed in the replicates. However, the

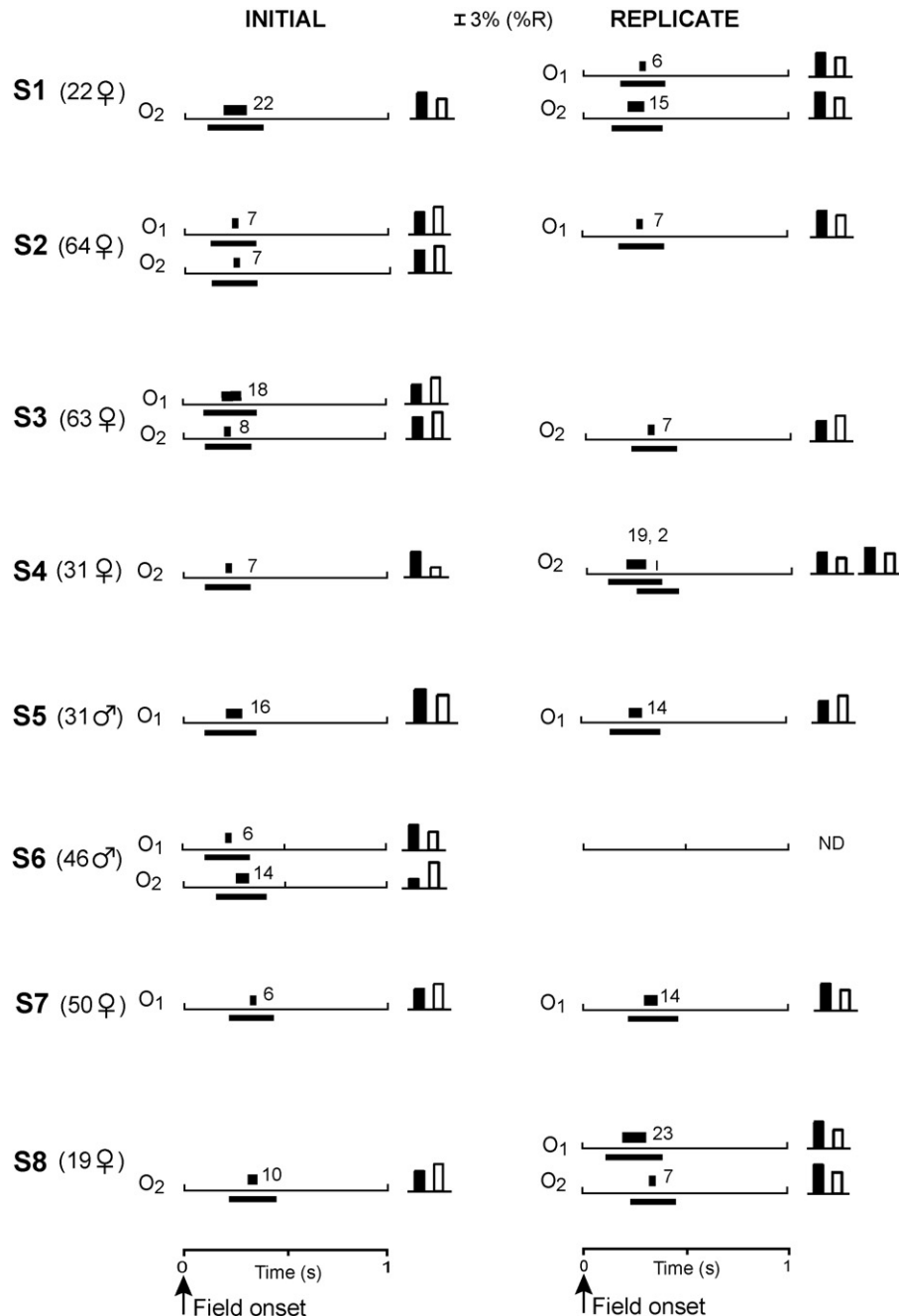


Fig. 3. Detection of magnetosensory evoked potentials (MEP) in initial and replicate studies, using recurrence analysis. Latency and duration in each subject are indicated on the time axis. The location of the points in $\%R(t)$ that differed from the corresponding control and the number of significant points (plotted according to the convention described in the text) are shown above the axis. The corresponding range in $V(t)$ is shown below the axis. Bar graphs indicate the mean of the MEP observed in $\%R(t)$ (average of the significant points); black and white bars correspond to offset and control epochs, respectively (SD not resolved at scale presented); S1–8, subjects 1–8; ND, not detected.

relation of the determinism in the replicate (the law-governed dynamical activity as reflected in pattern formation in the recurrence plot and characterized by the quantifier $\%R$) to that in the original MEP differed widely from subject to subject. The replicate MEP was manifested as a consistent increase in determinism in S1 and S4 (increase in $\%R(t)$), a consistent decrease in S3, and as inconsistent differences in the other subjects which included three subjects who first exhibited a decrease and then an increase (S2, S7, S8) and one subject who responded oppositely

(S5). Thus, the MEPs detected in this study were inconsistent, as predicted. Only a system governed by nonlinear laws can exhibit such a pattern of responses.

The average strength of the applied field was half of that used previously [3], but the magnitude of the effect on brain determinism (as reflected in $\%R(t)$) was essentially identical (Table 1). The absence of proportionality between the strength of the field and the magnitude of the resulting change in brain determinism differed from that found with visual and auditory evoked

potentials, which were both proportional to the magnitude of the stimulus [10,14]. Moreover, as previously [3] the MEPs were observed only when the recorded signals were analyzed using recurrence analysis, which is a technique specifically designed to detect the presence of nonlinear determinism. Both the absence of proportionality (a basic property of a linear system) and the need to use recurrence analysis to detect the MEPs support the inference of a nonlinear stimulus/response relationship.

Questions arise from an evolutionary perspective regarding why and how a nonlinear magnetic sense evolved. Perhaps the structures that mediate linear field-transduction in lower life forms [8,11] are still expressed in humans but play some other role. If so, their reaction to the fields would simply constitute a vulnerability of that system [7]. We did not address this possibility experimentally, but merely observe that it is possible for structures brought about by natural selection to lead to afferent signals that have no identifiable benefits for the subject, and may even be harmful [1].

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