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Nonlinear Changes in Brain Electrical Activity Due to Cell Phone Radiation

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We studied the effect of an electromagnetic field from a cellular telephone on brain electrical activity, using a novel analytical method based on a nonlinear model. The electroencephalogram (EEG) from rabbits was embedded in phase space and local recurrence plots were calculated and quantified using recurrence quantitation analysis to permit statistical comparisons between filtered segments of exposed and control epochs from individual rabbits. When the rabbits were exposed to the radiation from a standard cellular telephone (800 MHz band, 600 mW maximum radiated power) under conditions that simulated normal human use, the EEG was significantly affected in nine of ten animals studied. The effect occurred beginning about 100 ms after initiation of application of the field and lasted ~300 ms. In each case, the fields increased the randomness in the EEG. A control procedure ruled out the possibility that the observations were a product of the method of analysis. No differences were found between exposed and control epochs in any animal when the experiment was repeated after the rabbits had been sacrificed, indicating that absorption of radiation by the EEG electrodes could not account for the observed effect. No effect was seen when deposition of energy in the brain was minimized by repositioning the radiating antenna from the head to the chest, showing that the type of tissue that absorbed the energy determined the observed changes in the EEG. We conclude that, in normal use, the fields from a standard cellular telephone can alter brain function as a consequence of absorption of energy by the brain. Bioelectromagnetics 24:339–346, 2003. © 2003 Wiley-Liss, Inc.

Key words: recurrence quantification analysis; phase space; electroencephalogram

INTRODUCTION

Some of the energy radiated by a cellular telephone is absorbed in the head of the user [Schonborn et al., 1998], thereby giving rise to concerns regarding potential public health implications. Recent reports suggested that cell phone fields could alter brain electrical activity, but other seemingly similar studies were negative [Reiser et al., 1995; Mann and Roschke, 1996; Röschke and Mann, 1997; Vorobyov et al., 1997; Eulitz et al., 1998; Freude et al., 1998; Wagner et al., 1998; Borbély et al., 1999; Krause et al., 2000; Wagner et al., 2000].

We previously pointed out that the pattern of positive and negative reports is pervasive throughout all of EMF biology, as evidenced by the fact that no specific putative EMF induced bioeffect has been conclusively proved or disproved [Marino et al., 2001]. We addressed the problem and concluded that, at least in the context of effects on the immune system, the pattern exhibited by the EMF reports could be understood as resulting from the use of linear methods to analyze activity governed by nonlinear laws. It occurred to us that a similar mismatch between the dynamical activity of the system and the method used to analyze it might account for the lack of consensus regarding the effects of cell phone fields on the electroencephalogram (EEG).

The previous reports were mostly based on use of the Fourier transform to ascertain and compare the frequency components of the EEG. A major difficulty

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with the method of spectral analysis is that it averages away dynamical changes that might have occurred during part of the period for which the transform was calculated and replaces them with fictional frequencies, amplitudes, and phases that are assumed constant throughout the period. Field induced changes may or may not survive the averaging process. Consequently, when frequencies or bands of frequencies are compared, true differences may go unrecognized. For example, low dimensional chaotic systems can differ even though their spectra are identical [Theiler et al., 1992].

It has been shown recently that the EEG is generated, at least in part, by low dimensional chaotic sources [Babloyantz and Destexhe, 1986; Krystal et al., 1996; Theiler and Rapp, 1996; Micheloyannis et al., 1998; Fell et al., 2000]. It is possible, therefore, that the choice of a linear method to analyze the effect of cell phone fields on brain electrical activity caused some positive studies to appear negative.

Because the EEG is partly nonlinear (generated by a system governed by nonlinear differential equations), it is reasonable to consider the possibility that the effects of fields on the EEG might also be partly nonlinear. If so, methods more sensitive than spectral analysis could be useful for detecting changes due to the cell phone radiation.

Many techniques are available for analyzing time series data from nonlinear systems. Recurrence quantification analysis (RQA) seemed particularly attractive because it can be used to quantify activity according to objective rules, irrespective of the number or dynamical nature of the individual sources, or of how their outputs might combine to produce the measured signal [Webber, 1991; Zbilut and Webber, 1992; Webber and Zbilut, 1994]. On the basis of a complexity conjecture (explained below), we modeled the effect of the field from a cell telephone on the EEG of rabbits and used RQA in a novel methodological procedure to test the hypothesis that the field altered the EEG in individual animals.

METHODS

Exposure System

EMF exposure of rabbits to the signal from a cellular telephone was produced using a standard commercial telephone (Nokia 5120) operating on a digital network (TDMA technology) in the 824–849 MHz band. The nominal maximum radiated power was 600 mW; the actual radiated power, which was determined by the distance between the telephone and the base station antenna, was not measured. The presence or absence of the signal, however, was observed directly using a field detection meter (CellSensor, Tech International, Hallandale Beach, FL). After a call connection was established, the transmission path of the signal was alternated between two antennas, using a computer controlled radiofrequency switch (SPUT, Model SW203; M/A-com, Lowell, MA). One antenna was placed horizontally along the rabbit's midline, 1 cm above its head ("head antenna"); the other antenna ("distant antenna") was 3 m distant (Fig. 1). The switching occurred instantaneously (<1 μs). Antennas were external magnetic mount models for Nokia 5120 (pricesnap.com, Nicksville, NY), with the ceramic magnet removed.

The rabbit was restrained in an acrylic box during the experiment. This box was 20 cm high, 18 cm × 48 cm at the base, tapering to 18 cm × 41 cm at the top, made of 1.3 cm Plexiglas, fastened with acrylic cement (Weld-On, IPS Corp., Gardinia, CA). The only metal parts were two hinge pins, 2.5 cm long, of stainless steel. Animals lay directly on the plastic. To minimize environmental influences and standardize the sensory environment experienced by the rabbit, the box was mounted inside a wooden box. It eliminated the entry of light and minimized the entry of sound and odor, while providing ventilation and the passages of measurement

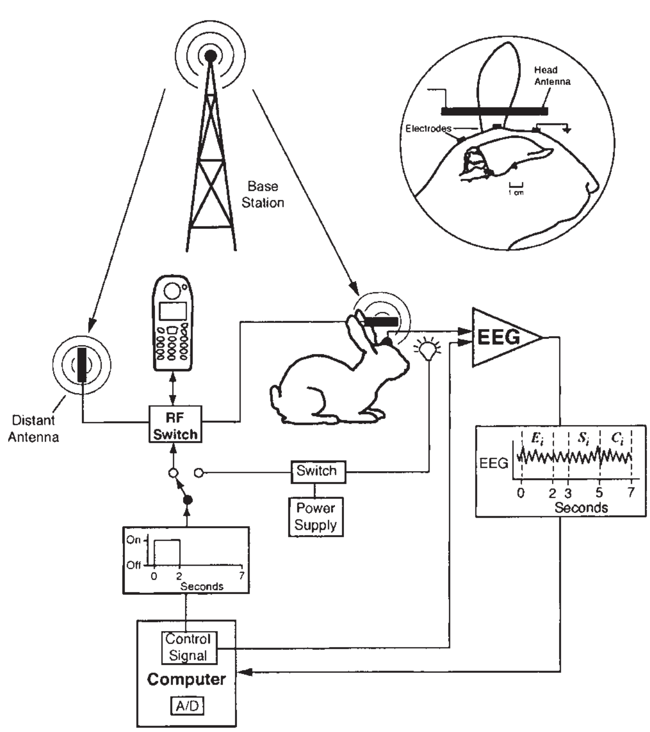

Fig. 1. Schematic representation of the experimental system. The detail shows the location of the electroencephalogram (EEG) electrodes relative to the head antenna.

and control signals. The box was constructed of 1.3 cm painted plywood, made without metal fasteners, 56 cm × 91 cm × 44 cm high. Its interior was lined with 1.3 cm thick styrofoam to lessen noise transmission.

The cell phone field at the head electrode was a subliminal stimulus to the rabbits, as judged by the complete absence of a behavioral response when the field was presented; its presentation was not accompanied by any sensory cues to the rabbit (the telephone was 2.5 m from the rabbit and 0.5 m from the distant antenna). A weak red light from a light emitting diode was used as a positive control; the diode was mounted inside the light tight box, 10 cm from the rabbit, and produced approximately 50 lumens at the corneal surface of the eye. The rise time of the currents in the diode circuit was less than 1 μs.

Animals

Five female (nos. 1–5) and five male (nos. 6–10) New Zealand rabbits were used in the study. All animal procedures were approved by the Institutional Animal Care and Use Committee. The EEG was recorded over the occipital region, which was under the easily palpable suture of the parietal and interparietal cranial bones. The indifferent and ground electrodes were respectively 2.5 cm and 5 cm rostral. The electrodes (0.5 cm in diameter) were attached to the shaved scalp using conducting paste (EC2, Grass, Quincy, MA); the impedance (1–3 kΩ) was measured before and after each experiment (EZM 5, Grass, MA). At the conclusion of the experiments, the rabbits were sacrificed by intravenous injection of pentobarbital.

Procedure

The EEG was measured continuously after the rabbit was placed in the wooden box, using an amplifier (Model 4400, Nihon Kohden, Irvine, CA) capable of resolving source voltages of 0.1 μV. Electrodes, 0.6 cm diameter, Model (F-E6GH-48, Grass Instrument Co., Quincy, MA) were connected to gold-plated silver leads, 1.2 m (48 in) long.The signal was filtered to pass 0.3–35 Hz, amplified, digitized at 512 Hz (12 bit), and stored on a hard drive.

Independent experiments were performed on each rabbit to allow a determination of each animal's ability to detect the field. Presentation of the telephone signal commenced 5 min after the rabbit was placed in the light tight box. A trial consisted in the application of the field to the rabbit for 2 s (*E* epoch), followed by a field free period of 5 s produced by switching the transmission path of the signal to the distant antenna (Fig. 1). A minimum of 60 trials were run, and then the call was terminated. Occasionally, a call ended prematurely because the handshake between the telephone and the network was lost. In these cases, the data were discarded and the experiment was repeated. In separate sessions, the experiments were repeated using light as the stimulus.

The voltage from the last 2 s of each trial was used as the control (*C* epoch) for the corresponding *E* epoch. The voltage from the 2 s proceeding the *C* epoch was defined as the sham (*S* epoch); it was used as a control for our statistical procedure. Some experiments were performed with the head antenna repositioned parallel to one side of the rabbit, 1 cm from the thoracic region. As an additional control, after the rabbits were killed, the cell phone field was applied using the head antenna, and voltage measurements were made from the scalp electrodes to evaluate the possibility of passive electrical interactions with the electrodes.

EEG Analysis

The complexity conjecture (Fig. 2) formed the basis of our analytical method. The baseline EEG was regarded as a combination of contributions from different brain regions. The conjecture that the cell phone field caused a change in the EEG by altering one or more of its components was tested by comparing quantifiers measured in the presence and the absence of the field. Our method differed from those used by others [Reiser et al., 1995; Mann and Roschke, 1996; Röschke and Mann, 1997; Vorobyov et al., 1997; Eulitz et al.,

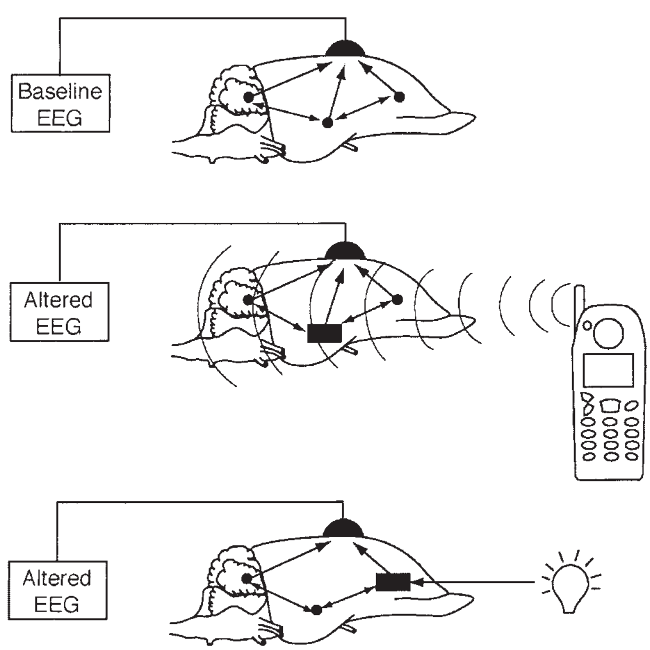

Fig. 2. The complexity conjecture. The baseline EEG is a complex combination of signals from many regions of the brain. The combined signal, as characterized by recurrence quantification analysis, is altered as a consequence of field transduction.

1998; Freude et al., 1998; Wagner et al., 1998; Borbély et al., 1999; Krause et al., 2000; Wagner et al., 2000], principally in that our method was designed to capture any structure that might exist in the EEG, not simply linear structure.

Trials containing movement artifacts were removed from the recorded voltage. The artifacts were identified by visual inspection of the analog record of the signal, where they appeared as brief (usually 1–2 s) discontinuous change. The artifact free trials were sent through a series of filters (described below) designed to attenuate specific frequencies; the aim was to maximize the possibility of observing an effect of the cell phone field by removing frequencies that did not contribute to the discrimination between the exposed and control epochs. The frequency filtered trials constituted a scalar time series, S_t, consisting of voltages at discrete times t=1,2,3…N. S_t was embedded in a five dimensional state space using a time delay of one [Elbert et al., 1994], and portions of the attractor not within a fixed distance of its center of mass were removed. Our purpose was to increase the sensitivity of the analysis by removing portions of the attractor that were not responsive to the presence of the field. The removal of some system states interrupted the trajectory in phase space and was equivalent in the time domain to removing the voltage at specific time points (five time points removed for each five dimensional state vector that was removed). The resulting trajectory described the evolution of the dynamical system's state vector $\mathbf{X}_t$ for all remaining time points.

A local recurrence plot was obtained for each *E*, *C*, and *S* epoch in each trial, as follows [Eckmann et al., 1987]. A point was plotted in two-dimensional space at the location addressed by (i,j) whenever $\mathbf{X}_j$ was near $\mathbf{X}_i$. Two states were defined as near only if both were contained within a hypersphere having a radius less than 15% of the minimum radius such that all points were near. The recurrence plot was quantified using percent recurrence (%R) and percent determinism (%D), defined, respectively, as the number of recurrent points divided by the possible number of recurrent points and the number of recurrent points located on lines parallel to the main diagonal of the diagram divided by the number of recurrent points [Webber, 1991; Zbilut and Webber, 1992; Webber and Zbilut, 1994]. %R is a measure of the extent to which the signal is correlated with itself in phase space. %D characterizes the tendency of the system to revisit the same area of the attractor and is, therefore, a measure of the amount of rule-obeying structure in the signal. Calculation of %R and %D was carried out using software provided by Webber [Webber, 2001], with the radius and line parameters set at 15 and 2, respectively. The software has been used successfully in other studies [Riley et al., 1999; Gonzalez et al., 2000; Guiliani et al., 2000; Ikegawa et al., 2000; Censi et al., 2002; Marino et al., 2002].

Statistics

In preliminary studies involving only rabbit no. 1, we followed an iterative procedure to maximize the probability (*P*) of detecting a difference between the *E* and *C* epochs, using %R. Various portions of the epochs were considered ("windows"), in combination with various combinations of frequency and phase space filters, using the Wilcoxon signed-rank test to evaluate *E* versus *C* and *S* versus *C*. The window and filter parameters that yielded the lowest *P*'s for *E* versus *C* when $P > 0.05$ for *S* versus *C* were then applied prospectively to evaluate the effect of the cell phone field on %R and %D in the remaining nine rabbits.

In each statistical test, the first five trials were discarded, and the next 50 artifact free trials were used in the analysis. The data is presented in terms of the mean ± SD of the quantifiers, and the mean ± 95% confidence limits of the Wilcoxon signed rank test metric $\left[\sum_{i=1}^{50} 2(E_i - C_i)^2/(\bar{E} + \bar{C})\right]^{\frac{1}{2}}$, where E_i and C_i are respectively the quantifier values in the exposed and control epochs, and $\bar{E}$ and $\bar{C}$ are the corresponding epoch means. The RQA quantifiers were regarded as independent planned comparisons, and were each evaluated for statistical significance at $P < 0.05$.

RESULTS

Using rabbit no. 1, we systematically compared portions of the signal in the *E* and *C* epochs (using the Wilcoxon signed-rank test) after the signal had been filtered in the frequency domain and in phase space. All reasonable combinations of epoch segment length and location, frequency filtering, and filtering in phase space were considered. We found that %R and %D differed significantly between the *E* and *C* epochs when the frequency filter was set to remove 3, 4, and 8–12 Hz, the EEG window was 300 ms, centered at 250 ms from the beginning of the epoch, and only 85% of the attractor volume was included in the calculation of the recurrence plot. When the conditions thus obtained were applied to rabbit no. 1, the average (± SD) result for %D was 18.3 ± 4.6% for the *E* segments (centered at 250 ms, width of 300 ms), compared with 19.9 ± 3.4% for the controls (5.25 s, 300 ms) ($P < 0.05$); the %D in the sham segments (20.1 ± 3.6%, 3.25 s, 300 ms) did not differ from the controls.

When the portion of the *E* epoch between 0.1–0.4 s was compared with the similar portion of the *C* epoch (5.1–5.4 s) in the remaining nine rabbits using the frequency and phase space filters identified from the signal of rabbit no. 1, we found that the cell phone field affected the EEG in every rabbit except rabbit no. 9 (Fig. 3). The direction of the effect was always to reduce the amount of determinism in the EEG. There were no cases of a false positive result when the *S* (3.1–3.4 s) and *C* epoch segments were compared using the same filter settings employed for *E* vs. *C*. Each of the experiments was replicated and the results were essentially the same as those found initially, including the failure to find an effect in rabbit no. 9 and the absence of false positive results when *S* and *C* segments were compared.

When light was applied as the stimulus, a robust, consistent increase in %D was found in every experiment, using a window of 250 ms centered at 175 ms (Fig. 4); the frequency and phase space filters were unnecessary. Again, there were no false positive results.

When the head antenna was relocated to the thoracic region, no effect of the field on brain activity was observed (Fig. 5). In this position, the antenna was horizontal, centered along the cranial–caudal and dorsal–ventral axes approximately 10 cm cranial to the hip joint. After the rabbits were killed and the absence of cardiac activity was verified, the experiments were repeated using the head antenna to evaluate the possibility that the results (Fig. 3) were due to an interaction of the cell phone field with the scalp electrodes. The baseline %D and %R measured under this condition essentially reflected the determinism of the output of the EEG amplifier in the absence of an input, which was near zero; no change was seen when the cell phone field was presented (Fig. 6).

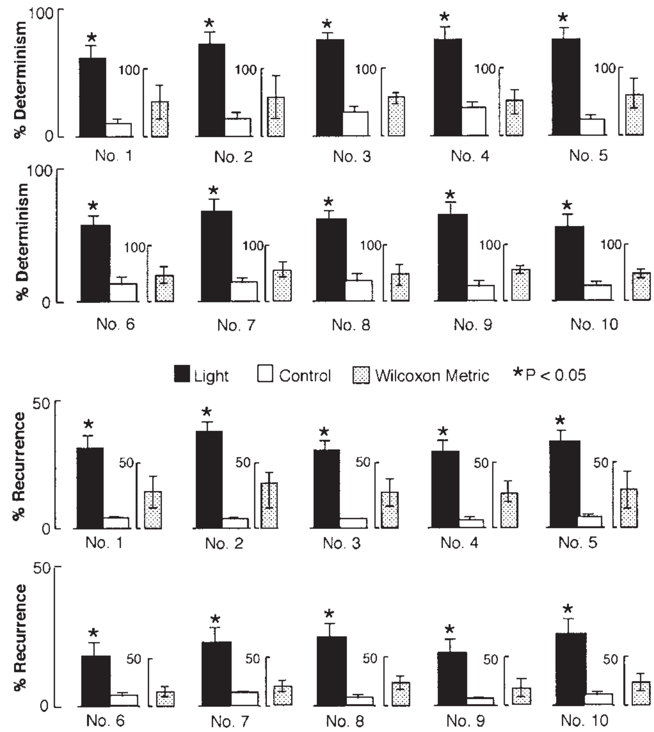

Fig. 4. Effect of light on the EEG in ten rabbits, as assessed using the nonlinear quantifiers %D and %R. The average values (±SD) of the quantifiers are shown. The average and 95% confidence limits of the test metrics are shown for each rabbit in the third bar.

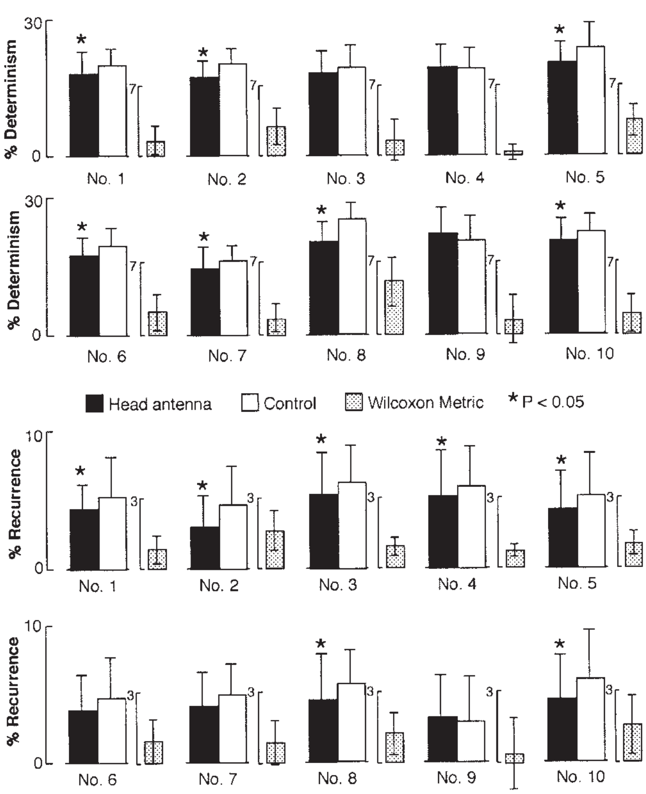

Fig. 3. Effect of cell phone field on the EEG in ten rabbits, as assessed using the nonlinear quantifiers % determinism (%D) and % recurrence (%R). The average values (±SD) of the quantifiers are shown. The average and 95% confidence limits of the test metrics are shown for each rabbit in the third bar.

DISCUSSION

Because the brain is a dynamical organ, the earliest signs of impairment of its activity would be expected to be reflected in its functional properties, an outstanding example of which is the EEG. In nine of ten independent experiments, the EEG recorded during exposure to the cell phone field was found to differ significantly from the EEG recorded during field-free intervals (*E* versus *C*). No significant differences were found when two field-free intervals were compared (*S* versus *C*). It can therefore be concluded that the consistent pattern of differences between the *E* and

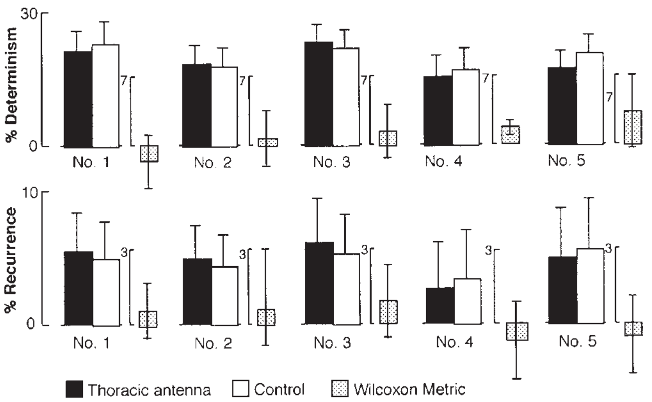

Fig. 5. Effect of relocating the head antenna to the thoracic region, 1 cm from the rabbit, as assessed using the nonlinear quantifiers %D and %R. The average values (±SD) of the quantifiers are shown. The average and 95% confidence limits of the test metrics are shown for each rabbit in the third bar.

C epochs was caused by the field from the cell telephone, and was not somehow a consequence of our statistical method.

Several cogent considerations indicated that the effect on the EEG (Fig. 3) was a true physiological response, not a physical effect due to an interaction of the field with the electrodes. First, when the experimental conditions were duplicated after the rabbits had been killed, there was essentially no determinism in the voltage measured from the scalp (as expected), and no change in the determinism when the cell phone field was applied (Fig. 6). Any artifactual signal would have been detected under the conditions of the measurement. Second, the changes detected in the EEG were localized

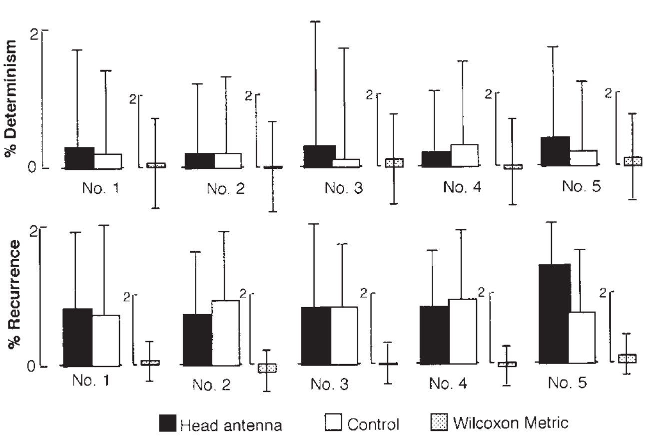

Fig. 6. Results of control experiments performed on dead rabbits, as assessed using the nonlinear quantifiers %D and %R. The average values (±SD) of the quantifiers are shown. The average and 95% confidence limits of the test metrics are shown for each rabbit in the third bar.

to a 300 ms window in the 2 s exposure epoch. Differences were not observed when the window was located elsewhere. Further, the effects occurred only after a time delay following presentation of the cell phone field. Both properties of the observations were far better explained under the assumption that they were true physiological responses, because pure physical effects would likely have occurred immediately upon presentation of the field and lasted throughout its presentation. Third, the cell phone signal was designed by the manufacturer to function within the constraints of a particular digital system and was, therefore, nearly completely deterministic (%R = %D = 100). Any putative electrode artifact would therefore have increased the determinism in the measured signal; thus, our observations that the RQA quantifiers decreased can better be attributed to a biological response to the field that manifested itself as a decrease in the determinism of brain electrical activity. We conclude that the field consistently affected brain electrical activity in the rabbits. It seems likely that a similar effect occurs when comparable cell telephones are used by human subjects because the exposure conditions used in the study mimicked reasonably well those conditions associated with the normal use of a cell telephone.

The cell phone stimulus resulted in increased randomness, which was opposite to the direction of change caused by light (Figs. 3 and 4). One possible explanation is that the field was not detected by a specialized sensor as, for example, rhodopsin in the detection of EMFs at light frequencies (Fig. 4). EMF frequencies in the 800 MHz band did not exist during evolution at levels remotely comparable to those in the modern environment, and consequently a specific mechanism to detect 800 MHz fields probably did not develop via natural selection. This may mean that the body's ability to detect cell phone fields was a consequence of a vulnerability of one or more of the mechanisms evolutionarily chosen to detect other external or internal stimuli, or a vulnerability of one or more mechanisms evolutionarily chosen to process transduced signals. Looked at in this way, cell phone fields can be said to "interfere" with normal brain function.

We assumed that the filter settings and window values for revealing a deterministic effect on brain function were identical for all animals. There is no good reason why this should be the case, and it could be argued that the assumption is more suited to a linear model than to one based on the complexity conjecture. Our assumption might explain why an effect of the field was found in only nine of the ten independent experiments. It is possible that the brain activity of the nonresponding animal was sufficiently different from that of the others as to require individualized filter

TABLE 1. Comparison of Low-Frequency Spectral Power in Rabbit no. 9 With That of the Other Male Rabbits

	Spectral power (v^2)		
Rabbit no.	<3 Hz	<4 Hz	<5 Hz
9	14.1	17.0	19.5
6	8.2	10.7	13.0
7	6.7	9.2	11.5
8	7.3	9.6	11.7
10	9.3	11.7	13.7

settings and window values. This is supported by our finding that the power spectrum of the nonresponding rabbit was concentrated in the low frequency region (Table 1). Tailoring the filters and window values to the baseline power spectrum of rabbit no. 9 might have revealed an effect of the field on the brain. (A suitable control for such an analysis would consist in the *S* versus *C* comparison.)

The United States Federal Communications Commission (FCC) adopted the specific absorption rate (SAR) as a pertinent unit of measurement for assessing the safety of cellular telephones (47CFR§2.1093). Importantly, although only telephones operating below the FCC limit are lawful, the agency does not explicitly maintain that such telephones are ‘‘safe,’’ a term that presently is undefined. The FCC’s choices of the SAR and a particular ‘‘permissible’’ numerical limit (1.6 W/kg) were based on the opinions of expert committees [National Council on Radiation Protection and Measurements, 1986; American National Standards Institute, 1992]. The experts found no convincing evidence of biological effects due to cell phone fields and recommended that the regulations be based on concepts of thermal physiology developed in the middle of the last century [Pattishall, 1957; Schwan and Piersol, 1957]. It remains an open question whether an EMF that alters brain activity in the manner reported here is ‘‘safe.’’

The effect of the field was critically dependent on the type of tissue that absorbed the cell phone energy, as determined by the different results found when the head antenna was relocated to the thoracic region (Figs. 3 and 5). Under the present SAR regulation, if a gram of fat and a gram of hypothalamus absorb the same amount of energy in the same amount of time, they have the same SAR, irrespective of any physiological consequences. Our finding that the physiological consequences following the absorption of cell phone energy depended on whether or not it was absorbed by the brain raises the question whether the FCC ought to use the SAR for gauging risk.

In summary, the results showed that radiation from a standard cellular telephone affected the brain electrical activity of rabbits exposed to the radiation under conditions that simulated normal human use of the telephone. The effect was not seen when the possible contribution of the brain to the SAR was minimized.

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