Method for detection of changes in the EEG induced by the presence of sensory stimuli

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A B S T R A C T

The onset and offset of sensory stimuli evoke transient changes in the electroencephalogram (EEG) that can be detected by linear and/or nonlinear analysis. However, there is presently no systematic procedure to quantify the brain-electrical-activity correlate of the presence of a stimulus (as opposed to its onset evoked potential). We describe a method for detecting a stimulus-related change in brain electrical activity that persists while the stimulus is present (presence effect). The method, which is based on phase-space embedding of the EEG time series followed by quantitative analysis of the recurrence plot of the embedded signal, was used to demonstrate the occurrence of a presence effect in separate groups of human subjects exposed to sound, a magnetic field, and light. Any form of law-governed dynamical activity induced in the EEG can be detected, particularly activity that is nonlinearly related to the stimulus. Salient mathematical features of the method were reproduced in a model EEG system containing known nonlinear determinism.

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1. Introduction

The onset and/or offset of sensory stimuli evoke transient changes in the baseline electroencephalogram (EEG) that can be detected by linear or nonlinear methods, depending on the type of law that governs the stimulus–response relationship (Sanei and Chambers, 2007). When stimuli are maintained beyond the latency of the onset evoked potential, cognitive processing of the afferent signal continues, as evidenced by the subject's ability to continue to perceive the stimulus. However, there is presently no reliable method for measuring the brain-electrical-activity correlate of the presence of a stimulus (presence effect), as opposed to its onset evoked potential.

A presence effect could be linear (consistent magnitude and time dependence of the response following repetitive applications of the stimulus) or nonlinear (inconsistent responses). Phase-space embedding of a time series followed by quantitative analysis of the system's recurrence plot permits detection of both linear and nonlinear evoked potentials (Carrubba et al., 2006). Our purpose was to extend this approach to the detection of a presence effect. We describe the method and illustrate its use for detecting the pres-

ence of auditory, magnetic-field, and visual stimuli in a subject's environment. To help explain some of the properties of the method, we applied it to a mathematical model created by adding nonlinear waveforms to baseline EEGs.

2. Methods

2.1. Subjects

Fifteen clinically normal subjects were enrolled in the study after being informed of the goals, methods, and general design of the investigation; written informed consent was obtained from each subject prior to participation in the study. The subjects were randomly assigned to receive one of three stimuli (five subjects per group). The Institutional Review Board at the LSU Health Sciences Center approved all experimental procedures.

2.2. Stimuli

The sound stimulus was a binaural 424-Hz tone; the sound pressure at the location of the subject was 65 dB. Light was obtained from a red-light-emitting diode that produced 50 cd; the source was 30 cm from the eye and the light could be seen by the subjects while their eyes were closed. Uniaxial magnetic fields, 2 gauss (200 μT), 60 Hz were applied by means of coaxial coils; details regarding the field exposure system are given elsewhere (Carrubba

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et al., 2006). The field strengths were below the level that results in conscious perception, and were comparable to those in the general and workplace environments. All stimuli were applied for 2 s, with an inter-stimulus period of 5 s.

2.3. EEG measurements

EEGs were recorded from O_1, O_2, C_3, C_4, P_3, and P_4 (International 10–20 system) referenced to linked ears, using gold-plated electrodes attached to the scalp with conductive paste; electrode impedances were less than $10 k\Omega$. The signals were amplified (Nihon Kohden, Irvine, CA), analog-filtered to pass 0.5–35 Hz, sampled at 300 Hz using a 12-bit analog-to-digital converter (National Instruments, Austin, TX), and analyzed offline.

Each EEG signal, $V(t)$, was divided into consecutive 7-s intervals (trials), with stimulus onset at $t = 0$, field offset at $t = 2$ s, and the inter-stimulus period at $2 s < t \leq 7$ s. Trials containing artifacts as assessed by visual inspection (Klem, 2003) were discarded (<5% of the trials), and the artifact-free trials were digitally filtered between 0.5 and 35 Hz.

2.4. Modeling

To mimic nonlinear determinism occurring in the EEG in response to a sensory stimulus, 1-s segments of a 10-Hz sine wave or of a solution of the nonlinear system of Lorenz equations (Abarbanel, 1996; Lorenz, 1963) (parameters chosen so that a system was in the chaotic domain) were added to baseline EEG trials; the amplitude of the added signal was adjusted to 40% (rms) of that of the EEG epoch to which it was added. The resulting composite signals were analyzed using linear and nonlinear methods to assess their relative ability to detect the added determinism.
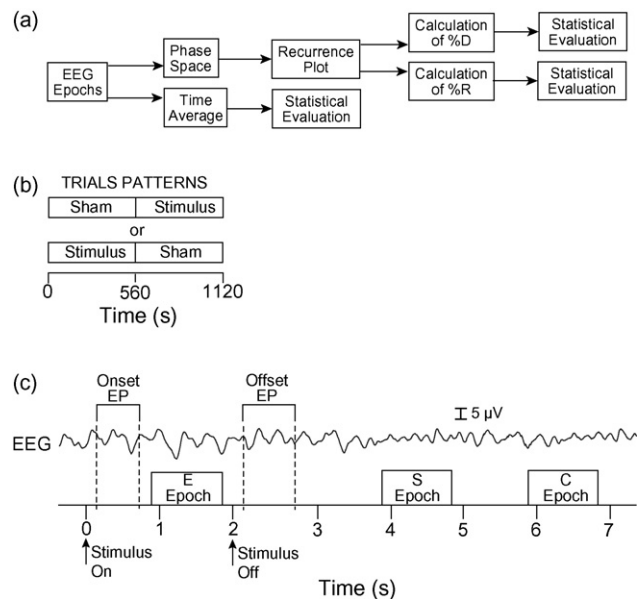
2.5. Nonlinear analysis

To identify deterministic changes in the EEG caused by sensory stimuli, $V(t)$ was embedded in phase space (Takens, 1981), and the resulting trajectory was displayed as a recurrence plot (Eckmann et al., 1987) and quantified using percent recurrence (%R) (the ratio of the number of recurrent points to the total number of points in the recurrence matrix) and percent determinism (%D) (the fraction of the points in the recurrence plot that formed diagonal lines of a predetermined minimum length) (Webber and Zbilut, 1994; Zbilut and Webber, 2006). A recurrence plot was constructed for each epoch of interest, leading to values for %R and %D. Based on our previous studies (Carrubba et al., 2006; Carrubba et al., 2007) we used a five-dimensional phase space, a time delay of 5 points, a radius of 15%, the Euclidean norm for calculating distances, and defined a line as ≥2 points along a diagonal (Fig. 1a). The calculations were carried out using freeware (Webber, 2007), and independently verified using a custom code (Matlab, Mathworks, Natick, MA).

2.6. Experimental design and statistics

Each subject underwent two blocks of trials (80 trials/block), with the stimulus applied in either the first or second block (determined randomly from subject to subject) (Fig. 1b). In the block where the stimulus was not applied, the data was analyzed as a negative control (sham exposure).

The portion of the signal containing the onset evoked potential was excluded. For example (Fig. 1c), the latency of the onset potential evoked by the auditory stimulus was 0.1–0.7 s, depending on the subject (Carrubba et al., 2006); we analyzed 0.7–1.7 s (E epoch) for evidence of a presence effect due to sound. The sham (S) and control (C) epochs corresponding to an E epoch were located in the

Fig. 1. Detection of changes in the EEG induced by the presence of a stimulus. (a) Procedure for nonlinear and linear analyses. (b) Organization of trials (subjects randomly assigned to receive one of the patterns). (c) EEG trial showing the locations of the epochs used to study the presence of a stimulus. EP, evoked potential; E, exposed; S, sham-exposed; C, control.

same trial 3 and 5 s later, respectively. The values of the recurrence variables %D and %R computed for the E and C epochs were compared to detect the presence of the stimulus; the values for the S and C epochs were compared to assess whether the presence effect was reversible (ended after cessation of the stimulus). Both E versus C and S versus C comparisons were also made for the sham trials to show that the analytical procedures did not produce false-positive results.

All comparisons were based on a minimum of 50 trials, 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). It can be shown that the probability of observing ≥2 significant differences by chance at $p < 0.05$ in 6 tests (6 electrodes) is 0.024. Consequently, if ≥2 tests involving either %R or %D were pair-wise significant, we planned to conclude that the presence of the field had altered the brain electrical activity of the subject. We evaluated the reliability of this statistical design by analyzing the data from the sham trials to empirically determine the likelihood of a false-positive decision regarding detection.

All of the comparisons described above were repeated using $V(t)$ to determine whether the effect of the field could be detected directly from the EEG using linear analysis. In each of the trials, $V(t)$ was averaged over the E epochs ($V_{RMS} = [\sum_{i=1}^{300} V_i^2 / 300]^{1/2}$), and compared with the corresponding values from the C epochs to test for the presence of linear effects. We planned to regard a change in brain electrical activity as nonlinearly related to the stimulus if the change was detected in %D or %R but not in $V(t)$.

3. Results

3.1. Presence effect

Changes in brain electrical activity due to the presence of a sound stimulus were detected in all five subjects using nonlinear analysis, and in one subject using linear analysis (Figs. 2 and 3; Table 1). The onset and offset auditory evoked potentials triggered by the sound stimulus occurred at 0.1–0.7 s and 2.1–2.7 s, respectively (Carrubba
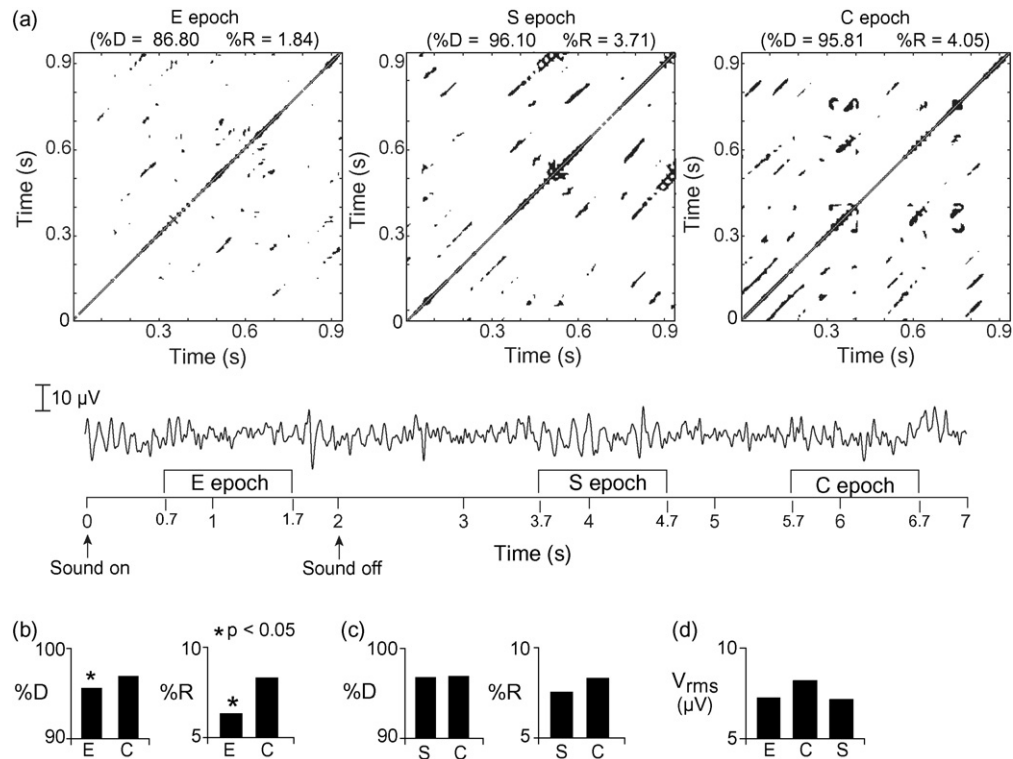
Fig. 2. Recurrence analysis of the effect of sound on the EEG from O_1 in subject S1. (a) Recurrence plots for exposed (E), sham-exposed (S), and control (C) epochs in one trial. (b), (c) Recurrence variables in exposed and sham-exposed trials, respectively. (d) Time averages of the EEG (V_{rms}). $N \geq 50$ trials for all comparisons. The SE not resolved at the scale shown.

et al., 2006). We therefore examined the EEG signals at 0.7–1.7 s to detect the putative presence effect. The recurrence plots for the E, S, and C epochs yielded %D and %R values in the ranges 85–97% and 2–8%, respectively, and an EEG of 5–10 μV (rms), depending on the trial; the results of a trial from the O_1 derivation in subject

Fig. 3. Recurrence analysis of the effect of sound on the EEG in subject S1. A nonlinear effect was not found using the signals from O_2 and P_4.

S1 (Fig. 2a) were typical. When the means of the E and C epochs from all O_1 trials were compared, a significant decrease ($p < 0.05$) was found in both %D and %R (Fig. 2b); the S versus C comparisons were not significantly different, indicating that the deterministic effect of the presence of the field on brain activity ended less than 2 s after field offset (Fig. 2c). The sound-induced change in brain activity was seen in three additional derivations in subject S1 using recurrence analysis (Fig. 3). The presence effect was not detected by linear analysis of $V(t)$ from O_1 (Fig. 2d) or from any other electrode derivations (data not shown). Overall, a presence effect due to sound was found in all the subjects by means of recurrence analysis, and in one subject using linear analysis (Table 1).

A presence effect due to the magnetic-field stimulus was detected in all subjects and found to be nonlinearly related to the field (Table 2). The EEG was analyzed as previously except that the presence effect was sought at 0.5–1.5 s post-onset because the onset magnetosensory evoked potential occurred at 0.1–0.5 s (Carrubba et al., 2007). The effect sought was found in all subjects using %D, but in none of the subjects using linear analysis (Table 2); as with the sound stimulus, the magnitude of %D was reduced during the presence of the field.

A presence effect due to light was detected in four of five subjects using recurrence analysis, and in one subject using time averaging (Table 3). The visual evoked potential occurred with latencies <0.7 s (Marino et al., 2004). Consequently the EEG signals between 0.7 and 1.7 s were analyzed for an effect associated with the presence of the light. Four subjects exhibited an effect in either %D or %R that was mostly manifested as an increase in the recurrence quantifier (Table 3).

During the recurrence analysis of the sham trials we performed 15 subjects × 6 derivations × 2 quantifiers = 180 tests; there were 3 pair-wise significant tests due to chance but no instances of a false-positive decision regarding detection of a presence effect. In
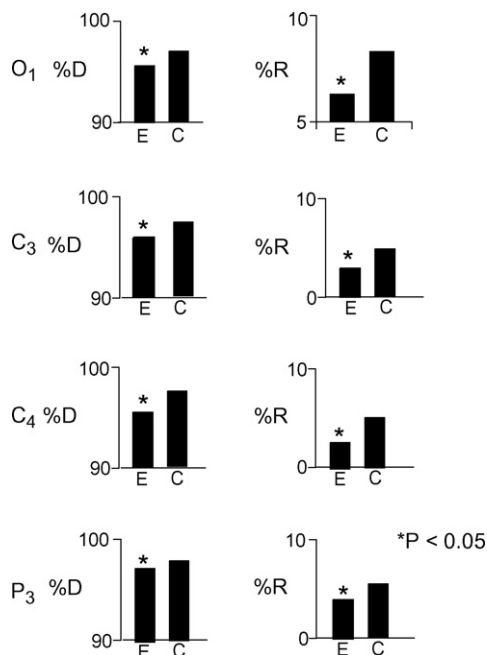
Table 1
Detection of the presence of the sound stimulus

Subject number	Age/Gender	%D	%R	V_{rms}
S1	30/M	O1, C3, C4, P3	O1, C3, C4, P3	ND
S2	45/M	O1, O2, C3, C4, P3, P4	O2, C3, C4, P3, P4	ND
S3	32/F	O1, O2, C4, P4	ND	ND
S4	29/F	ND	C3, C4, P4	ND
S5	28/F	O1, C3, C4, P3	O1, P4	O1, C3, C4, P3

Sound onset and offset were at $t = 0$ and $t = 2$ s, respectively. Using nonlinear (%D, %R) and linear (V_{rms}) analysis, brain electrical activity at 0.7–1.7 s was compared with that at the inter-stimulus epoch 3.7–4.7 s for each of the six derivations from each subject. The derivations for which the comparisons differed significantly ($p < 0.05$) are listed; in each case the magnitude of the recurrence variable was less during the presence of the stimulus. The presence effect was not detected by linear analysis (V_{rms}) except in S5 (in μV, E-C epochs, 3.9–4.7 (O_1), 7.4–8.6 (C_3), 7.0–7.8 (C_4), 6.3–7.1 (P_3)). ND, not detected.

Table 2
Detection of the presence of the field stimulus

Subject number	Age/Gender	%D	%R	V_{rms}
S6	18/F	O1, C3, C4, P3, P4	ND	ND
S7	30/M	O1, O2, C3, C4, P3, P4	O1, P3, P4	ND
S8	50/F	O1, O2, C3, C4, P3, P4	ND	ND
S9	49/F	O1, O2, C3, C4, P3, P4	O1, O2, P3, P4	ND
S10	46/F	O1, C3, C4, P3	ND	ND

Field onset and offset were at $t = 0$ and $t = 2$ s, respectively. Using nonlinear (%D, %R) and linear (V_{rms}) analysis, brain electrical activity at 0.5–1.5 s was compared with that at the inter-stimulus epoch 3.5–4.5 s for each of the six derivations from each subject. The derivations for which the comparisons differed significantly ($p < 0.05$) are listed; in each case the magnitude of the recurrence variable was less during the presence of the stimulus. ND, not detected.

the linear analysis 15 subjects × 6 derivations = 90 tests yielded 2 pair-wise false-positive comparisons but no cases of false-positive detection.

3.2. Modeling

The stimulus-induced changes in the EEG were mimicked by the addition of a known nonlinear deterministic signal to baseline EEG, and several salient characteristics of the presence effect were demonstrated (Figs. 4 and 5, Table 4). In our model of brain electrical activity (Fig. 4a), the baseline EEG contains law-governed electrical activity originating in the brain as a consequence of its autonomous activity and its numerous inputs and outputs. The baseline activity is law-governed but typically aperiodic and nonstationary ("dynamical noise"), indicating that the governing laws change with time. Application of a stimulus causes an additional signal and associated dynamical noise. To mimic this process (Fig. 4b), 1-s segments of a solution to the Lorenz equation were added at 0.5–1.5 s to baseline EEG trials; the amplitude of the added signal was 0.4 (rms) of that of the epoch to which it was added (Fig. 5a). When the Lorenz and control epochs were compared, the added determinism was detected as a decrease in %D,

Table 3
Detection of the presence of the light stimulus

Subject number	Age/Gender	%D	%R	V_{rms}
S11	51/F	↓C3, ↑P4	ND	ND
S12	29/M	ND	ND	ND
S13	50/M	ND	↑O1, ↑C4	↓C4, ↓P4
S14	46/F	↑O1, ↑O2, ↑P3, ↑P4	ND	ND
S15	31/F	↑O1, ↑C4	ND	ND

Light onset and offset were at $t = 0$ and $t = 2$ s, respectively. Using nonlinear (%D, %R) and linear (V_{rms}) analysis, brain electrical activity at 0.7–1.7 s was compared with that at the inter-stimulus epoch 3.7–4.7 s for each of the six derivations from each subject. The derivations for which the comparisons differed significantly ($p < 0.05$) are listed. ↑, (↓), magnitude of the variable was greater (less) during the presence of the stimulus. The presence effect was not detected by linear analysis (V_{rms}) except in S5 (in μV, E-C epochs, 7.3–8.0 (C_4), 10.6–12.2 (P_4)). ND, not detected.
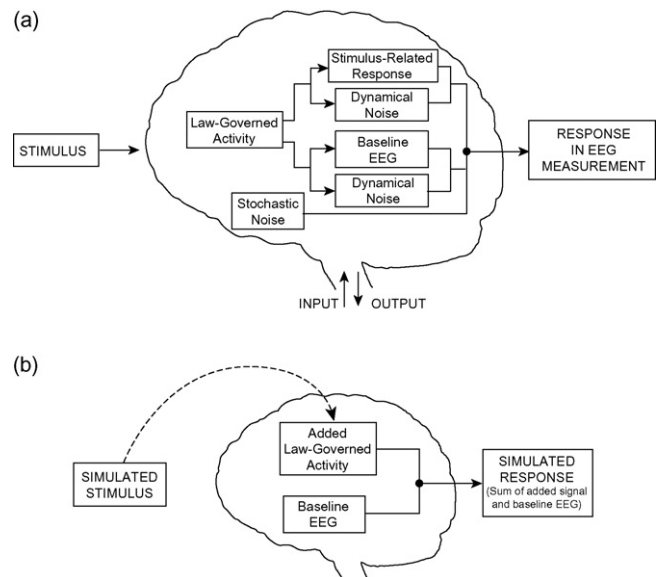

Fig. 4. Models of brain electrical activity. (a) A typical EEG measurement contains contributions from multiple sources, only one of which is governed by the stimulus. (b) Basis of a mathematical model to mimic a stimulus–response relationship detected in an EEG measurement.

but was not detected using linear analysis (Fig. 5b). The entire procedure was repeated a total of six times using both Lorenz segments and a 10-Hz sine wave (amplitude ratio of 0.4). The sine also mimicked nonlinear determinism because the phase of the signal at $t = 0.05$ s varied randomly from trial to trial. Overall, we found that nonlinear determinism could be consistently detected by nonlinear analysis, but not by time averaging (Table 4); whether the added signal resulted in an increase or decrease in

Table 4
Detection of the presence of nonlinear determinism added at 0.5–1.5 s to baseline EEG

Replicate	Lorenz			Random-phase sine		
	%D	%R	V_{rms}	%D	%R	V_{rms}
1	↓Sig	ND	ND	ND	↓Sig	ND
2	↓Sig	↓Sig	ND	ND	↓Sig	ND
3	ND	ND	ND	ND	ND	ND
4	↑Sig	ND	ND	ND	↓Sig	ND
5	↓Sig	ND	ND	ND	↓Sig	ND
6	↑Sig	↓Sig	↑Sig	↑Sig	↓Sig	ND

Either Lorenz or random-phase sine waves (10 Hz) were added at 0.5–1.5 s and the determinism in the combined signal was compared with that in the control epochs (5.5–6.5 s) using recurrence and linear analysis. The signal-to-noise ratio (added-signal/baseline-EEG) was 0.4. In each replicate, $N = 50$ trials for each of the two added signal. Sig, instances where the added determinism was detected ($p < 0.05$). ↑, (↓), magnitude of the variable was greater (less) during the presence of the stimulus. Six independent replicates. ND, not detected.
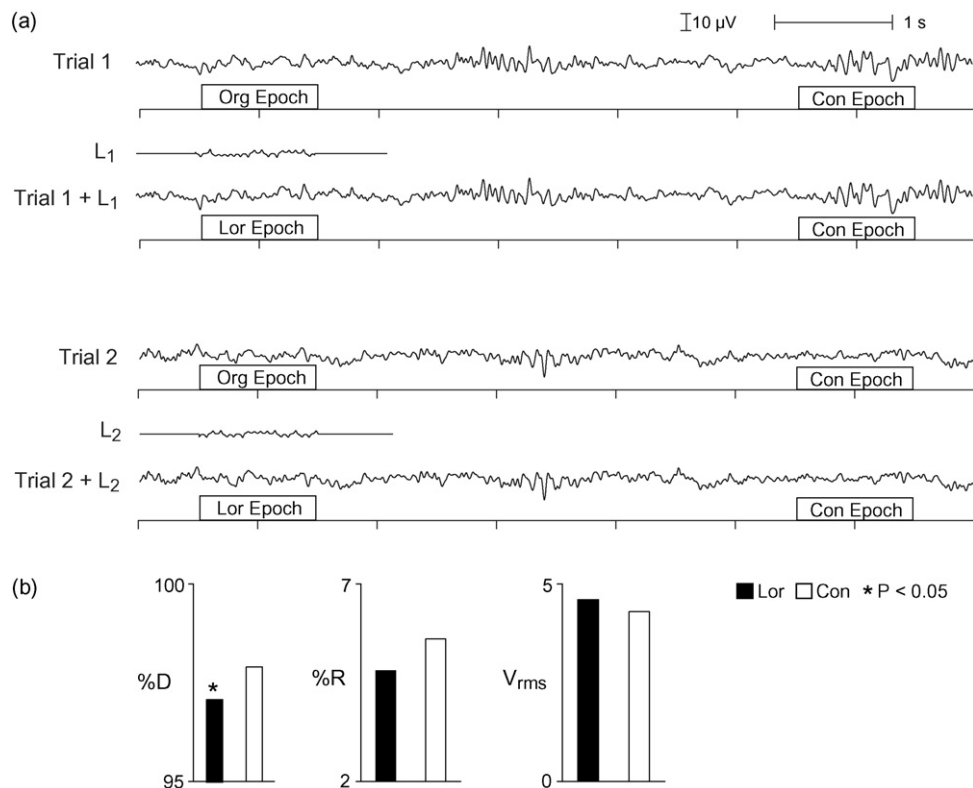
Fig. 5. Detection of the presence of a nonlinear signal added to baseline EEG. (a) One-second segments of a solution to the Lorenz equation were added to baseline EEG trials (signal/noise of 0.4). The upper curve in each set is the baseline EEG. The middle curve is the Lorenz segment. The lower curve is the sum of the two signals. The result from two representative trials are shown. (b) Overall results obtained using recurrence and linear analysis ($N = 50$ trials). The Lorenz model parameters (σ, r, and b, respectively) were 10, 28, and 2.67 (Abarbanel, 1996); the signals were obtained by choosing different initial conditions. The SE are not resolved at the scale shown. (Data from the first replicate.) Lor, Lorenz; Org, Original; Con, Control.

the nonlinear quantifier depended on the properties of the added signal.

4. Discussion

Our goal was to develop a method for detecting a response in the EEG that persisted beyond the latency of the onset evoked potential when the stimulus was maintained. Traditional methods such as time-averaging and spectral analysis can detect a linear stimulus–response relationship but they provide only a linear approximation when the relationship is nonlinear. We based our method on the use of recurrence analysis because it captures both linear and nonlinear deterministic activity, and therefore is sensitive to any type of law-like activity in the EEG governed by a stimulus. Using the method, we detected a presence effect due to sound, magnetic fields, and light (Tables 1–3), with no cases of false-positive detection in sham trials. There were also two cases where the relation between stimulus presentation and a change in brain electrical activity was detected by linear analysis. Thus the method is suitable for detecting a brain electrical correlate of the presence of a stimulus in the subject's environment regardless of whether the effect is linear or nonlinear.

Efficient detection of a stimulus-governed presence contribution to the EEG (Fig. 4a) depended on a choice of embedding conditions and recurrence parameters that optimized the differences in %R and %D in the presence and absence of the stimuli. There is no general procedure for reliably identifying the optimal conditions and parameters, and they must therefore be chosen empirically. Those used here were originally chosen to maxi-

mize detection of magnetosensory evoked potentials (Carrubba et al., 2006), and we made no attempt to maximize sensitivity for detecting the presence effect due to sound or light because our main purpose was to describe the general method, not optimize it for each stimulus. We expect that other choices of embedding conditions and/or recurrence-parameter values would yield even stronger evidence of a presence effect due to sound, light, and other stimuli. We also did not attempt to analyze spatio-temporal relationships; such investigations might provide useful information concerning the presence effect.

A drawback with the use of %R and %D for analyzing brain electrical activity is that, unlike time averaging or spectral analysis, the variables have no clear relation to physiological or even physical quantities. As examples, the time-averaged EEG is a direct surrogate for changes in brain electrical behavior, and Fourier components often correspond directly to physiological oscillators, such as alpha waves. In contrast to these linear statistics, %R and %D are abstract quantities with no presently discernable link to conventional biological parameters.

A property of %D and %R that at first seems counter-intuitive is that they have no unique interpretation in terms of increases or decreases in law-governed activity, at least when they are used to compare two signals, because an effect can be manifested as an increase or decrease in either variable (Tables 1–4). Consequently, at this stage of our understanding of the method, it is a suitable basis for assessing whether a specific experimental intervention resulted in changes in the EEG, but the method does not directly quantify stimulus-induced determinism in the sense that a linear addition of determinism always results in an increase in %R or %D (Table 4). Even so, reliable knowledge that an effect occurred is crucial in

many contexts because it entails the inference that a biological phenomenon of interest had occurred. In the cases considered here, the inferred process was signal transduction. While such a conclusion is not surprising with regard to light or sound, it is a novel finding with regard to magnetic fields.

The recurrence plot can be quantitated using *%R*, *%D*, or other variables (Zbilut and Webber, 2006), and a question arises concerning the relation of the variables. Percent recurrence is mathematically identical with the correlation sum, which was developed as a key mathematical definition in computing the dimension of an attractor in phase space (Kantz and Schreiber, 1997). Unlike the correlation dimension which is invariant, the correlation sum depends on the choice of the radius parameter; when the choice is made, *%R* is defined. In the corresponding recurrence plot, many points typically fall along diagonal lines of varying lengths (quantified by *%D*). One possibility is that *%D* contains dynamical information not captured by *%R* (Webber and Zbilut, 1994). However, it is presently unclear whether *%D* (or changes in *%D*) is reliably interpretable in terms of the dynamical activity of the system in a manner that differs from the interpretation of *%R* (or changes in *%R*). We employed *%D* and *%R* as independent variables precisely because the difference in their dynamical significance, if any, is unknown. Use of two quantifiers afforded a second chance at detecting the effects of an intervention if it should happen that a true effect was not recognized using a single quantifier due to stochastic fluctuations (type 2 statistical error).

In conclusion, the method presented here is appropriate for inferring the existence of a stimulus-induced presence effect in the EEG, but general principles have not yet been elaborated that would permit changes in *%R* or *%D* to be uniquely or reasonably associated with an increase or decrease in deterministic behavior, or within a particular physiological parameter.

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