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Fractal fluctuations in human respiration

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[1]*Department of Pharmacology and Toxicology, Michigan State University, East Lansing, Michigan 48824; and* [2]*Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas 75390*

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Fadel, Paul J., Susan M. Barman, Shaun W. Phillips, and Gerard L. Gebber. Fractal fluctuations in human respiration. *J Appl Physiol* 97: 2056–2064, 2004. First published July 30, 2004; doi: 10.1152/japplphysiol.00657.2004.—The present study was designed to characterize respiratory fluctuations in awake, healthy adult humans under resting conditions. For this purpose, we recorded respiratory movements with a strain-gauge pneumograph in 20 subjects. We then used Allan factor, Fano factor, and dispersional analysis to test whether the fluctuations in the number of breaths, respiratory period, and breath amplitude were fractal (i.e., time-scale-invariant) or random in occurrence. Specifically, we measured the slopes of the power laws in the Allan factor, Fano factor, and dispersional analysis curves for original time series and compared these with the slopes of the curves for surrogates (randomized data sets). In addition, the Hurst exponent was calculated from the slope of the power law in the Allan factor curve to determine whether the long-range correlations among the fluctuations in breath number were positively or negatively correlated. The results can be summarized as follows. Fluctuations in all three parameters were fractal in nine subjects. There were four subjects in whom only the fluctuations in number of breaths and breath amplitude were fractal, three subjects in whom only the fluctuations in number of breaths were fractal, and two subjects in whom only fluctuations in breath number and respiratory period were fractal. Time-scale-invariant behavior was absent in the two remaining subjects. The results indicate that, in most cases, apparently random fluctuations in respiratory pattern are, in fact, correlated over more than one time scale. Moreover, the data suggest that fractal fluctuations in breath number, respiratory period, and breath amplitude are controlled by separate processes.

Allan and Fano factors; breath amplitude and frequency; dispersional analysis; Hurst exponent

RESPIRATION IN AWAKE, HEALTHY adult humans is characterized by considerable variability in the frequency, duration, and amplitude of breaths (5, 8, 18, 24, 31). The aim of the present study was to define the basis for the variability of these respiratory parameters. Two possibilities were considered.

First, except for some short-range correlations (4, 10), the fluctuations in respiration might be random, i.e., uncorrelated (6, 16, 32). That is, although influenced by events (breaths) in the recent past, the present value of the measured parameter would not be related to events in the distant past.

The second possibility is that long-range correlations also exist among the fluctuations in one or more of the respiratory parameters. If so, it would be important to define the duration of the memory in the system. Here, the term "memory" is used in the context of the time frame over which a series of events are correlated. If the memory extends across more than one time scale, the fluctuations would be best modeled as arising from a fractal (time-scale-invariant) process in which the present value of the measured property is related to events in the distant past (2, 12, 23, 34). The term "time scale" refers to the temporal resolution used to measure the parameters of interest. In this paper, each time scale is represented by a decade of window sizes (in seconds) plotted on a log scale. The results of the present study demonstrate time-scale-invariant behavior in the system responsible for breathing in awake humans under resting conditions.

METHODS

All recordings were performed at the University of Texas Southwestern Medical Center (Dallas, TX). The Institutional Review Board approved the protocols, and each of the 20 subjects (14 men and 6 women) provided informed, written consent to participate in the study. The subjects were free of any known cardiovascular or respiratory diseases and were instructed to refrain from smoking cigarettes and drinking alcohol or caffeine-containing beverages for ≥12 h before the recording session. Their ages ranged from 22 to 58 yr. Mean blood pressure measured with an automated sphygmomanometer (Welch Allen) averaged 91 ± 2 mmHg in the 20 subjects, and mean heart rate derived from lead II of ECG was 1.1 ± 0.1 beats/s.

Recordings

Recording sessions lasted 75–208 min, with the subject in a supine position, relaxed and breathing spontaneously in a quiet room. We also studied two subjects in whom breathing was paced by a metronome at a frequency close to their normal respiratory rate. Respiratory movements were recorded with a strain-gauge pneumograph placed in a stable position over the upper abdomen. Upward deflections in the records denote inspiratory movements and downward deflections denote expirations. This methodology is routinely used in human studies to monitor respiratory variability because it avoids having the subject breathe through a mouthpiece, which is known to alter both the duration and depth of breathing (18, 25).

Data Analysis

Data originally saved by use of a recording adaptor (model 4000 PCM, Vetter, Rebersberg, PA) and a videocassette recorder (model SLV-750 HF, Sony) were played back and acquired with software and an analog-to-digital converter board (Axon Instruments, Union City, CA) by using a sampling rate of 200 Hz. The analyses were performed using software developed by Gebber et al. (15) and Lewis et al. (22) at Michigan State University.

Parameters. After the peak and trough of each respiratory movement were detected, the following measurements were made: *1*) the interval between the peaks of successive breaths (referred to as respiratory period or peak-to-peak breath interval) and *2*) the trough-to-peak breath amplitude (normalized on a scale of 0–1.0). Fluctuations in the former parameter reflect the variability of respiratory rate, whereas fluctuations in the latter reflect the variability of the depth of

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breathing. From these cycle-by-cycle measurements, time series and frequency distributions were constructed. For a respiratory period of 4 s, the error of measurement is 1% with a bin resolution of 40 ms and 1.5% with a resolution of 60 ms. Values in the text are means ± SE.

Fractal analysis of respiratory fluctuations. Two methods were used to determine whether fluctuations in the number of breaths occurring in time windows of specified length were fractal or random. The primary method involved calculation of the Allan factor, A(T), for window sizes of different lengths. Thurner et al. (30) and Turcott and Teich (33) define A(T) as the ratio of the event-number Allan variance to twice the mean number of events (i.e., respiratory cycles) in a window size of specified length (T):

$$\mathrm{A}(T) = \frac{\langle [N_{i+1}(T) - N_i(T)]^2 \rangle}{2\langle N_i(T) \rangle}$$

where $N_i(T)$ is the number of events in the ith window of length T. Note that the Allan variance is expressed in terms of the variability of the difference in the number of events in successive windows. This measure was first introduced in connection with the stability of atomic-based clocks (1).

The Allan factor curve is constructed by plotting A(T) as a function of the window size on a log-log scale. For a data block of length $T_{\max}$, the window size, T, is progressively increased from a minimum of a single bin (40 or 60 ms) to a maximum of $T_{\max}/6$ so that ≥ 6 nonoverlapping windows are used for each measure of A(T). For a random process in which fluctuations in the number of events are uncorrelated, A(T) = 1 for all window sizes (29, 33). For a periodic process, the variance decreases and A(T) approaches zero as the window size is increased (29, 33). For a fractal process, A(T) increases as a power of the window size and may reach values ≥1.0 (29, 33). This reflects the greater variance in number of events with increasing window size. The increase in variance relative to the mean occurs because long window lengths are more apt to reveal rarer clusters of events (e.g., periods of relatively rapid or slowed breathing). The power law relationship between A(T) and window size appears as a straight line with a positive slope, α, on the log-log scale. The α, which is also known as the scaling exponent, is the power to which fluctuations in number of events measured on one time scale are proportional (i.e., statistically self-similar) to those measured on other time scales. The correlation coefficient (r) is used to test for linearity on the log-log scale, and linear regression is used to calculate α.

The Allan factor curve for the original time series is routinely compared with those of 10 surrogate data sets in which the intervals between successive breaths have been shuffled. Specifically, we assigned random numbers to the peak-to-peak breath intervals in the original time series and then sorted the random numbers by size (7, 11, 22). This creates a randomized data set for which the mean, variance, and frequency distribution are identical to those of the original time series of peak-to-peak breath intervals, but with no correlations among events (7, 22, 29, 33). If shuffling of the data eliminates the power law in the Allan factor curve, it can be concluded that fluctuations in the number of breaths were fractal.

Alpha, which is bounded in a range of 0–3 (30, 33), is used to calculate the Hurst exponent (H, range 0–1). As described by Eke et al. (9) and Thurner et al. (30), H is calculated with the following formula when $0 < \alpha < 1$

$$\mathrm{H} = \frac{\alpha + 1}{2}$$

and with the following formula when $1 < \alpha < 3$

$$\mathrm{H} = \frac{\alpha - 1}{2}$$

As explained by Feder (12) and Bassingthwaighte and Raymond (3), H = 0.5 for a time series in which events are uncorrelated, whereas H ≠ 0.5 implies that the time series is fractal providing that the power law in the Allan factor curve extends over more than one time scale (decade on log scale). When H > 0.5, events are positively correlated [persistence; values larger (smaller) than the mean tend to be followed by values also larger (smaller) than the mean]. When H < 0.5, events are negatively correlated (antipersistence; values larger than the mean tend to be followed by values smaller than the mean and vice versa).

The second method used to test whether fluctuations in the number of breaths were fractal was Fano factor analysis. Teich (28) and Turcott and Teich (33) define the Fano factor, F(T), as the ratio of the variance of the number of events, var[$N_i(T)$], to the mean number of events, mean[$N_i(T)$], in a window size of specified length T:

$$\mathrm{F}(T) = \frac{\mathrm{var}[N_i(T)]}{\mathrm{mean}[N_i(T)]}$$

Note that the Fano variance is expressed in terms of the variability of the number of events in individual windows rather than in terms of the difference in the number of events in successive windows as is the case with Allan factor analysis. The Fano factor curve is constructed similarly to the Allan factor curve, and surrogate data sets are also used to test whether the power law in the Fano factor curve for the original time series reflects fractal fluctuations in the number of events. An advantage offered by Fano factor analysis is that the window size at which the power law begins is usually much smaller than for Allan factor analysis (11, 29, 30, 33). Thus Fano factor analysis may reveal a power law relationship extending over more than one time scale (indicative of fractal behavior) when the data block is too short to show this with Allan factor analysis. However, mathematical constraints prevent F(T) from increasing faster than $\sim T^1$, thereby limiting the range of the slope (α) of the power law in the Fano factor curve to 0–1.0 (29). Thus the slope of the Fano factor curve should not be used to estimate H because this might lead to erroneous conclusions as to whether the long-range correlations among events were persistent or antipersistent.

Dispersional analysis was used to test directly whether fluctuations in respiratory period and breath amplitude were fractal. The algorithm as originally described by Bassingthwaighte and Raymond (3) involves calculation of the standard deviation (SD) of the mean values of the measured parameter for groups of data points of a specified number (m). Specifically, the mean value for each group of m data points is obtained, and the SD of these values is calculated for the total number of groups. The process is repeated each time m is increased progressively from a minimum of one data point to a maximum of one-quarter of the total number of data points. In the present study, dispersional analysis was performed on first differences derived from the original time series. As described in our earlier studies (7, 11), a new time series of the absolute differences between successive respiratory periods or breath amplitudes is constructed and the SD of the mean first differences is calculated for all groups of size m. This modification of the basic method removes slow trends (i.e., nonstationarities) in the data such as progressive increases or decreases in the value of the measured parameter (17). Allan factor analysis, which is also based on first differences, similarly removes slow trends in the data (30, 33).

SD is plotted against m on a log-log scale, yielding a straight line with a negative slope. For a random process with no correlations among events, the slope of the dispersional analysis plot is −0.5 (3). For a fractal process, the slope is different from −0.5 over a range of m extending more than one decade (3). The decision on whether fluctuations are fractal is made by comparing the slope of the dispersional analysis plot for the original time series with those of the plots for 10 surrogates derived by shuffling the peak-to-peak breath intervals or breath amplitudes.

Although H can be calculated as the difference between the negative slope of the dispersional analysis curve and 1.0 (p. 67–70 in Ref. 2), Eke et al. (9) showed that the estimate provided may misidentify long-range correlations as persistent when, in fact, they are antipersistent. For this reason, values of H in this study are derived only from α in the Allan factor curve and, thus, refer solely to fluctuations in number of breaths.

RESULTS

Spontaneous Breathing Patterns

Figure 1 illustrates the variability in respiratory period and in breath amplitude observed in a spontaneously breathing 41-yr-old man. The raw record of respiratory movements (90 s in length) in Fig. 1*A* shows a period of reasonably constant peak-to-peak breath intervals and breath amplitudes followed by a relatively long peak-to-peak breath interval (12.6 s), and then considerable variability of the two measured parameters. Cycle-by-cycle measurements of the peak-to-peak breath interval and normalized breath amplitude for the complete time series (8,940 s in length) are shown in Fig. 1, *B* and *C*, respectively. The variability depicted in these time series is similar to that observed in all of our subjects as well as that reported in previous studies of healthy humans (5, 8, 18, 31). The corresponding frequency distributions of 1,932 peak-to-peak breath intervals and 1,933 breath amplitudes recorded from this subject are shown in Fig. 3, *A* and *B*, respectively. The mean peak-to-peak breath interval was 4.62 s (13.0 breaths/min), and the maximum peak-to-peak breath interval was close to 15 s. As was most often the case, such frequency distributions were gammalike in shape (22, 26), with a longer tail extending to the right than to the left of the mode. The coefficient of variation (CV) of the distribution of peak-to-peak breath intervals was 0.24 and that of the distribution of breath amplitudes was 0.29. The distribution of peak-to-peak breath intervals was positively skewed (0.43), whereas the distribution of breath amplitudes was negatively skewed in this case (−0.12).

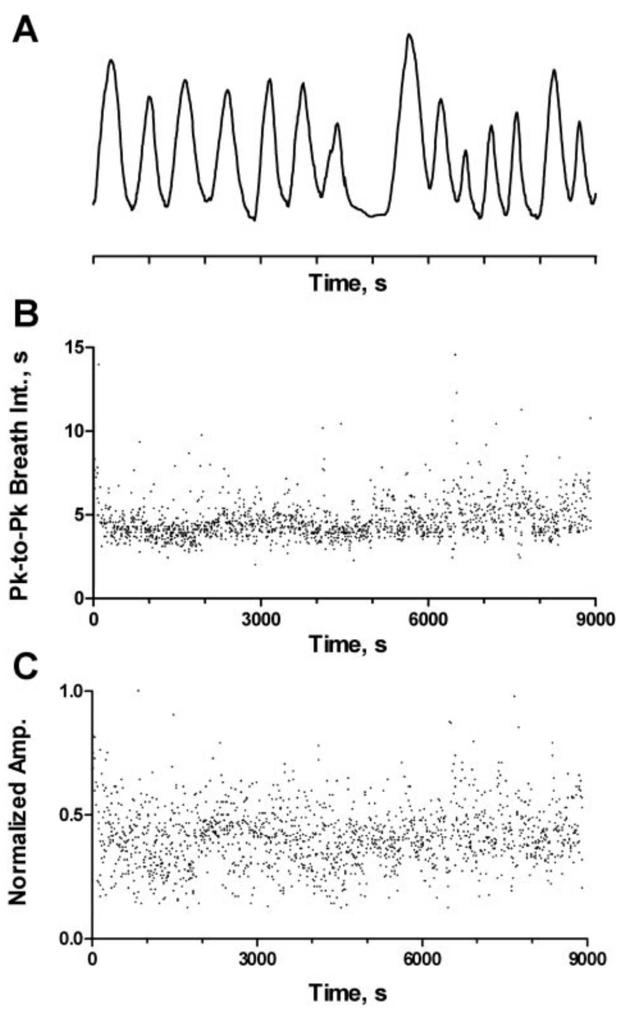

Fig. 1. Breathing pattern in an awake human. *A*: respiratory movements recorded with a strain-gauge pneumograph. Inspiration is upward deflection. Time base is 10 s/division. *B*: time series of peak-to-peak breath intervals. *C*: time series of breath amplitudes normalized on a scale of 0 to 1.0.

Table 1. *Fractal respiratory patterns*

Group	*1*	*2*	*3*	*4*	*5*
Men	8	3	0	1	2
Women	1	1	3	1	0
Fractal fluctuations, no. of breaths	Yes	Yes	Yes	Yes	No
Fractal fluctuations, respiratory period	Yes	No	No	Yes	No
Fractal fluctuations, breath amplitude	Yes	Yes	No	No	No
Persistent (H > 0.5)	6	3	3	2	
Antipersistent (H < 0.5)	3	1	0	0	

Subjects are divided into 5 groups depending on whether the fluctuations in each of 3 parameters of spontaneous breathing were fractal. Persistence and antipersistence signify whether the fractal fluctuations in number of breaths were positively or negatively correlated, respectively.

Data length averaged 7,262 ± 441 s in the 20 spontaneously breathing subjects. The data blocks contained an average of 1,850 ± 130 peak-to-peak breath intervals. The mean peak-to-peak breath interval was 3.99 ± 0.14 s, and the maximum peak-to-peak breath interval averaged 16.4 ± 1.3 s. The mean CV of the distributions of peak-to-peak breath intervals was 0.29 ± 0.02 and that of the distributions of breath amplitudes was 0.40 ± 0.04. All but one of the distributions of peak-to-peak breath intervals were positively skewed with a mean value of 0.31 ± 0.04. The value was −0.24 for the one negatively skewed distribution. Eleven of the 20 distributions of breath amplitudes were positively skewed with a mean value of 0.27 ± 0.09. The mean was −0.21 ± 0.06 for the nine negatively skewed distributions of breath amplitudes.

Fractal Analysis

In nine spontaneously breathing subjects (*group 1* in Table 1), fluctuations in the number of breaths, respiratory period, and breath amplitude were fractal with long-range correlations among events. The results from a 22-yr-old man are presented in Fig. 2. The distribution of 1,884 peak-to-peak breath intervals from a time series whose length was 8,580 s is shown in Fig. 2*A*. The CV of the distribution was 0.50 and skewness was 0.55 reflecting the long tail to the right of the modal interval. The mean peak-to-peak breath interval was 4.55 s (13.2 breaths/min).

The Fano and Allan factor curves derived from the original time series are shown in Fig. 2, *C* and *D* (black traces), respectively. At window sizes <1 s, the values of F(T) and A(T) were close to 1.0. This standard feature of the curves is consistent with a Bernoulli process with a low probability of success (28). That is, for window sizes much smaller than the shortest peak-to-peak breath interval, either zero or one event

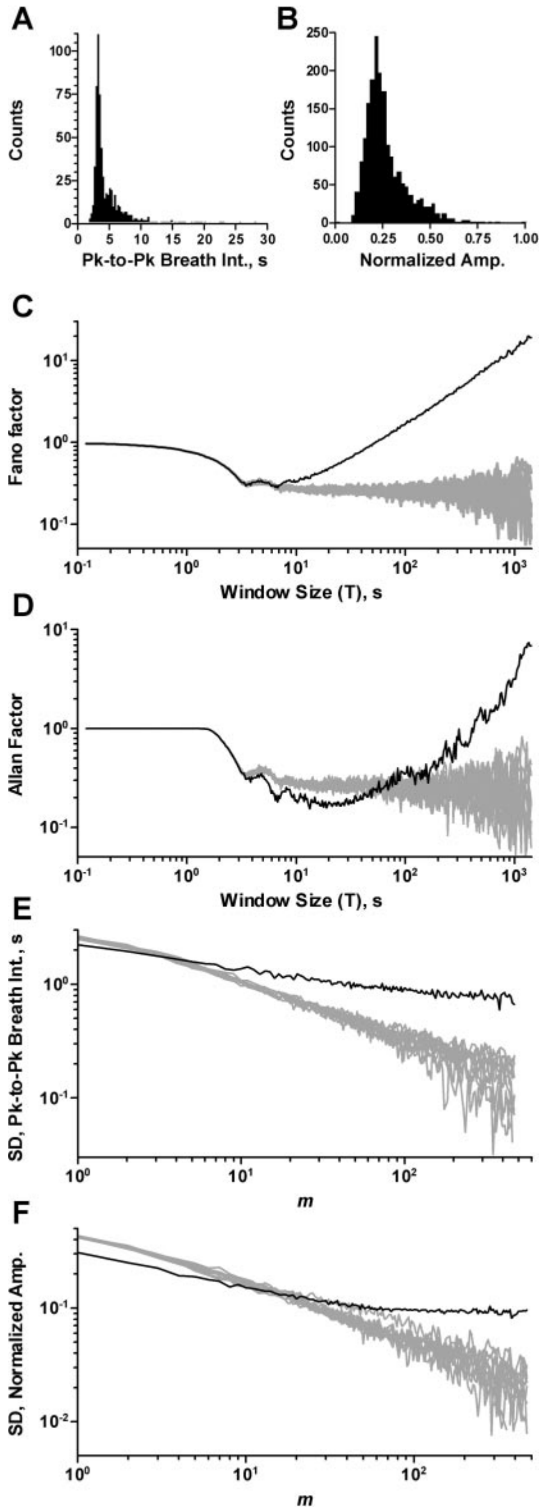

Fig. 2. Fractal analysis of breathing pattern in a subject in whom fluctuations in number of breaths, respiratory period, and breath amplitude were fractal. *A*: distribution of 1,884 peak-to-peak breath intervals (Pk-to-Pk Breath Int.). *B*: distribution of 1,885 normalized breath amplitudes (Amp.). There is at least 1 count at a normalized amplitude of 1.0 in this and all subsequent amplitude distributions. *C*: Fano factor curves for original time series (black trace) and 10 surrogates (gray traces). *D*: Allan factor curves for original time series (black trace) and 10 surrogates (gray traces). *E*: dispersional analysis of original time series of peak-to-peak breath intervals (black trace) and 10 surrogates (gray traces). SD, standard deviation. *F*: Dispersional analysis of original time series of breath amplitudes and 10 surrogates.

is counted, with the former outcome more likely to occur. F(T) and A(T) then dipped to $<$1.0 before a power law appeared beginning at a window size of ~10 s in the Fano factor curve and ~100 s in the Allan factor curve. The dips can be attributed to the strong periodic component of the respiratory signal that leads to a decrease in the variance with increasing window size (30, 33). The power laws in these curves extended over more than one time scale (up to the maximum allowable window size of 1,430 s, one-sixth of the data block length). The slopes (α) of the power laws in the Fano and Allan factor curves were 0.84 and 1.35, respectively. H derived from α of the power law in the Allan factor curve was 0.18, thereby indicating that the long-range correlations among the fluctuations in number of breaths were antipersistent. That the power laws indeed reflected long-range correlations among events is indicated by the fact that the curves derived from the original time series fell outside of the range of the curves for 10 surrogates (gray region) at window sizes between 10 and 1,430 s (Fano factor) and 100 and 1,430 s (Allan factor). Note that after the initial dip in the Fano and Allan factors below 1.0, the slopes of the curves for the surrogates were essentially flat.

Dispersional analysis demonstrated that fluctuations in respiratory period and breath amplitude were fractal in the same subject. The frequency distribution of 1,885 breath amplitudes is shown in Fig. 2*B*. The CV of the distribution was 0.43, and skewness was 0.36. The slope of the dispersional analysis plot derived from the original time series of peak-to-peak breath intervals (dark trace) was -0.18 for $m \geq 5$ (Fig. 2*E*), whereas the slope of the plot for the time series of breath amplitudes was -0.10 for $m \geq 23$ (Fig. 2*F*). These slopes fell outside of the range of those (near -0.5) of the plots for 10 surrogates (gray regions).

For the nine spontaneously breathing subjects in whom fluctuations in breath number, respiratory period, and breath amplitude were fractal, H values derived from the slope of the power law in the Allan factor curve were antipersistent in three cases (H = 0.11 ± 0.04) and persistent in six cases (H = 0.81 ± 0.07).

In four spontaneously breathing subjects (*group 2* in Table 1), fluctuations in the number of breaths and breath amplitude were fractal, but fluctuations in respiratory period were not. The results from a 41-yr-old man are presented in Fig. 3. The distributions of the 1,932 peak-to-peak breath intervals (Fig. 3*A*) and 1,933 breath amplitudes (Fig. 3*B*) were described earlier with reference to Fig. 1. The slopes of the power laws (extending over more than one time scale) in the Fano factor (Fig. 3*C*) and Allan factor (Fig. 3*D*) curves for the original time series were 0.54 and 0.41, respectively. H = 0.71 calculated from the slope of the power law in the Allan factor curve indicated the presence of long-range persistent correlations for window sizes between 41 and 1,490 s. As was typically the case, the slopes of the Allan and Fano factor curves for the surrogates were essentially flat in this range. The slope of the dispersional analysis plot for peak-to-peak breath interval fell within the range of those of the plots for 10 surrogates at $m \geq 5$ (Fig. 3*E*). Thus fluctuations in peak-to-peak breath interval were considered random. In contrast, the slope (-0.29) of the dispersional analysis curve for breath amplitude ($m > 11$) fell outside the range of those of the surrogates (Fig. 3*F*). Thus fluctuations in breath amplitude were considered fractal.

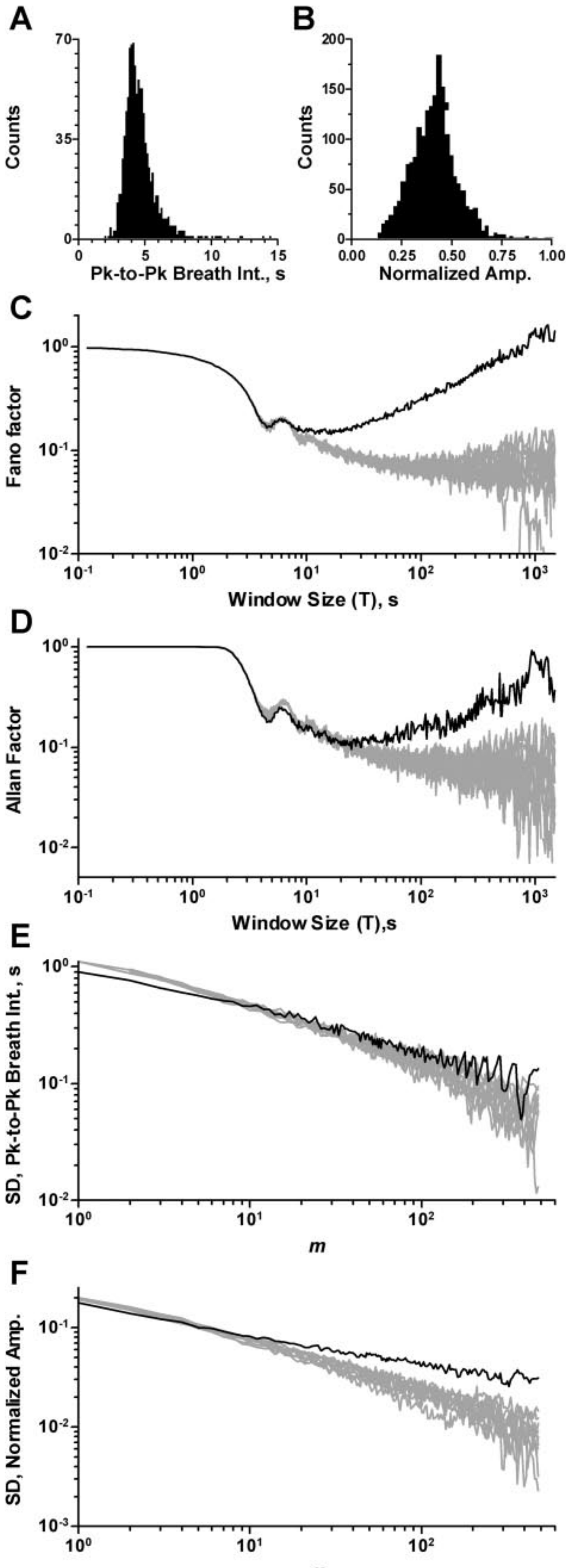

Fig. 3. Fractal analysis of breathing pattern in a subject in whom fluctuations in breath number and breath amplitude but not respiratory period were fractal. Sequence and format of *A–F* are the same as in Fig. 2. Analysis was based on 1,933 breaths.

For the four spontaneously breathing subjects in whom fluctuations in breath number and breath amplitude (but not respiratory period) were fractal, H values derived from the slope of the power law in the Allan factor curve were persistent in three cases (H = 0.75 ± 0.12) and antipersistent in one case (H = 0.24).

In three spontaneously breathing women (*group 3* in Table 1), fluctuations in the number of breaths were fractal, but fluctuations in respiratory period and breath amplitude were not. The results from a 46-yr-old subject appear in Fig. 4. The distribution of 1,470 peak-to-peak breath intervals (Fig. 4*A*) had a CV of 0.46 and was positively skewed (0.36). The mean peak-to-peak breath interval was 3.87 s (15.5 breaths/min). The distribution of 1,471 breath amplitudes (Fig. 4*B*) had a CV of 0.61 and was essentially normal (skewness, 0.01). The time series were 5,700 s long. The slopes of the power laws in the Fano factor (Fig. 4*C*) and Allan factor (Fig. 4*D*) curves for the original time series were 0.40 and 0.44, respectively. A persistent H = 0.72 was calculated from the slope of the power law in the Allan factor curve, which was measured over a range of window sizes between 60 and 600 s. Although this range encompassed only one decade on a log scale, the fluctuations in number of breaths were considered fractal because the power law of the Fano factor curve extended over more than one time scale. Note also that the slopes of the curves for the surrogates were flat. In contrast, the slopes of the dispersional analysis plots for peak-to-peak breath interval (−0.41 in Fig. 4*E*) and breath amplitude (−0.53 in Fig. 4*F*) fell within the range of the slopes for 10 surrogates. Thus the fluctuations in peak-to-peak breath interval and breath amplitude were considered random.

H (0.78 ± 0.06) derived from the slope of the power law in the Allan factor curves was persistent in the three subjects in whom fluctuations in breath number, but not respiratory period or breath amplitude, were fractal.

In two spontaneously breathing subjects (*group 4* in Table 1), fluctuations in breath number and respiratory period were fractal, but fluctuations in breath amplitude were not. The results from a 31-yr-old man are presented in Fig. 5. The distribution of 1,501 peak-to-peak breath intervals (Fig. 5*A*) had a CV of 0.15 and was negatively skewed (−0.24). The mean peak-to-peak breath interval was 3.99 s (15.0 breaths/min). The distribution of 1,502 breath amplitudes (Fig. 5*B*) had a CV of 0.51 and was positively skewed (0.98). The time series were 6,000 s long. In this case, the power law in the Allan factor curve (Fig. 5*D*) extended over less than one decade of window sizes. This likely was the consequence of the large window size (~150 s) at which the power law began and the fact that the time series was below average in length, thereby limiting the maximum allowable window size to 1,000 s. Nonetheless, we consider the fluctuations in number of breaths to be fractal on the basis of the power law in the Fano factor curve (Fig. 5*C*), which extended over more than one time scale. The slope of the power law in the Allan factor curve for window sizes between 150 and 1,000 s was 0.94, yielding a persistent H = 0.97. The H value (0.6) obtained from the second subject in this group also was persistent. Dispersional analysis showed that fluctuations in the peak-to-peak breath interval were fractal because the slope of the plot (−0.24) for $m \geq 8$ fell outside of the range of the slopes for the surrogates (Fig. 5*E*). However, this was not the case for the dispersional analysis plot for breath amplitude, which had a slope of −0.52

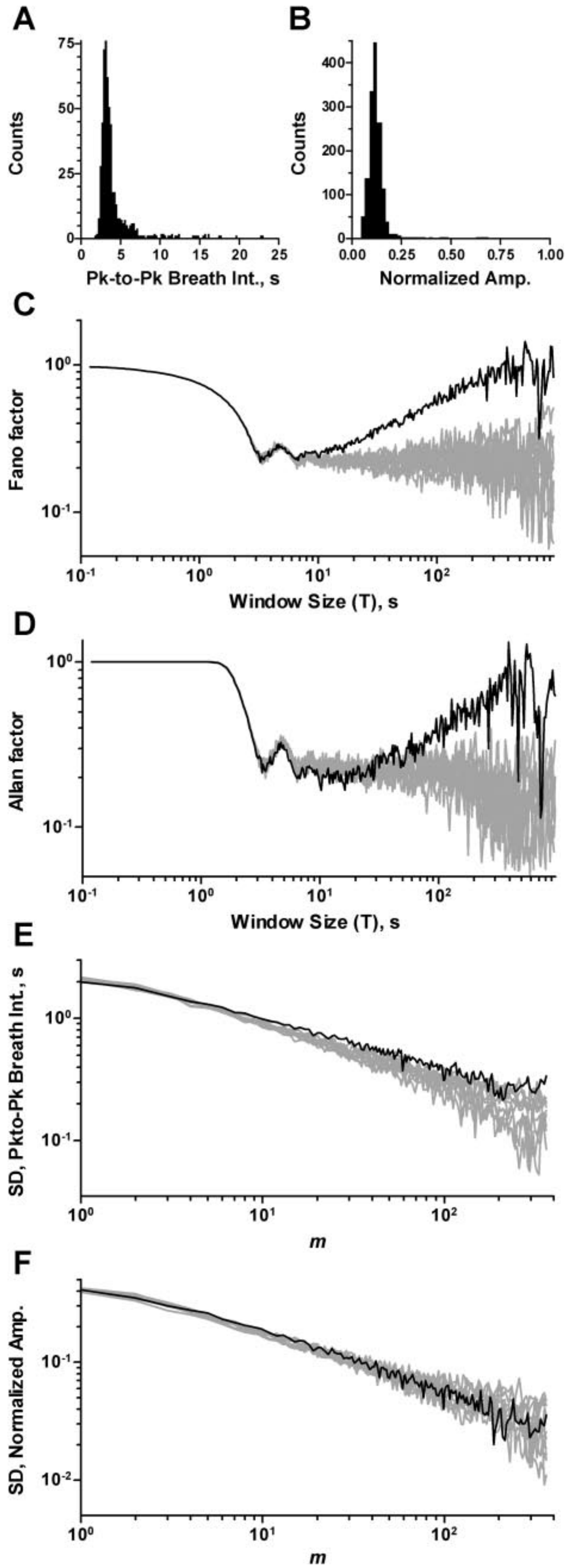

Fig. 4. Fractal analysis of breathing pattern in a subject in whom fluctuations in breath number were fractal but fluctuations in respiratory period and breath amplitude were not. Sequence and format of *A–F* are the same as in Fig. 2. Analysis was based on 1,471 breaths.

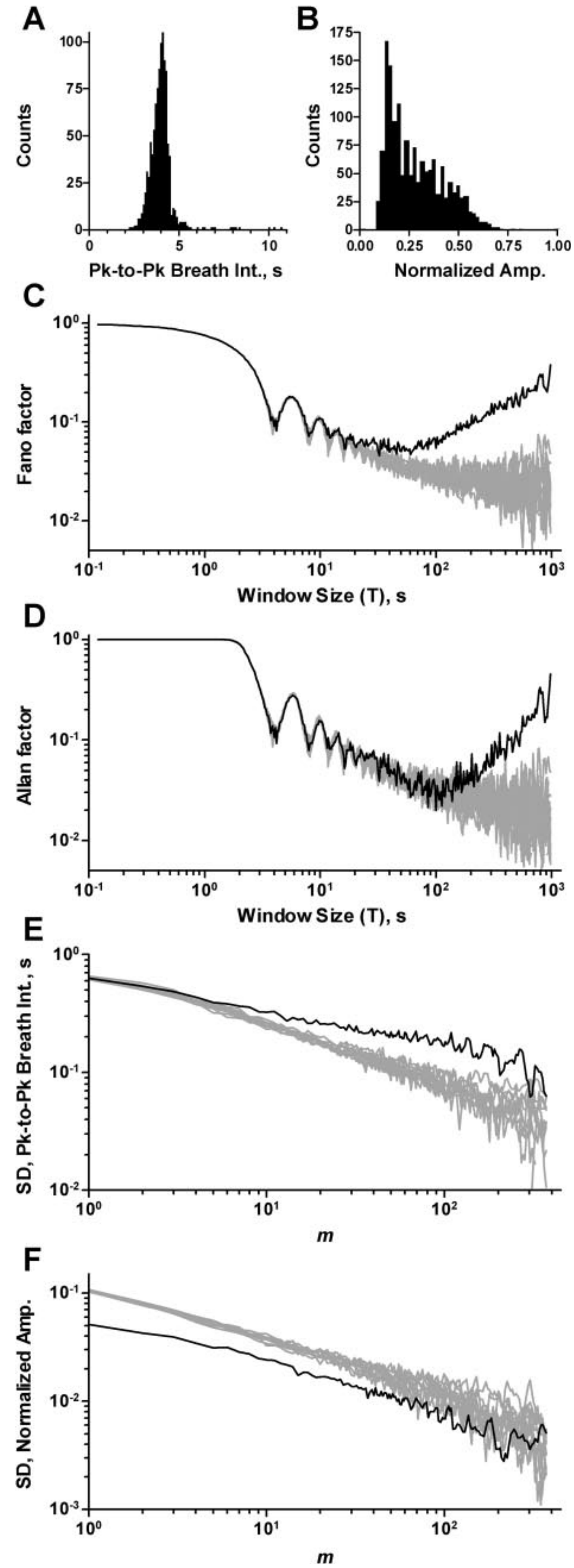

Fig. 5. Fractal analysis of breathing pattern in a subject in whom fluctuations in breath number and respiratory period, but not breath amplitude, were fractal. Sequence and format of *A–F* are the same as in Fig. 2. Analysis was based on 1,502 breaths.

for $m \geq 5$. Offsetting of the *y*-intercept of the plot for the original time series from the *y*-intercepts of the plots for the surrogates caused the former curve to fall outside of the gray region for $m \leq 60$, even though their slopes were essentially the same. Offsetting of the *y*-intercepts occurred in some cases because the surrogates were constructed by shuffling the peak-to-peak breath intervals or breath amplitudes rather than their first differences.

There were two men in whom fluctuations in all three parameters of spontaneous breathing (breath number, respiratory period, and breath amplitude) were not fractal (*group 5* in Table 1). This was also the case in two subjects in whom breathing was paced by a metronome at a frequency (14 min^{-1}) close to their normal respiratory rate. The results from one of these subjects are illustrated in Fig. 6. The time series were 3,000 s in length and contained 698 peak-to-peak breath intervals (Fig. 6*A*) and 699 breath amplitudes (Fig. 6*B*). As expected, the variability of peak-to-peak breath interval was markedly reduced during paced breathing. In this case, the distribution of peak-to-peak breath intervals had a CV of 0.06 and was positively skewed (0.11). The distribution of breath amplitudes had a CV of 0.16 and was negatively skewed (−0.86). Note that the Fano factor (Fig. 6*C*) and Allan factor (Fig. 6*D*) curves for the original time series did not show a power law and fell within the range of the curves for the surrogates. Also, the slopes of the dispersional analysis plots for peak-to-peak breath interval (Fig. 6*E*) and breath amplitude (Fig. 6*F*) fell within the range of the slopes of the plots for the surrogates despite offsetting of the *y*-intercepts. Thus the residual fluctuations in number of breaths, peak-to-peak breath interval, and breath amplitude during paced breathing were random rather than fractal in nature.

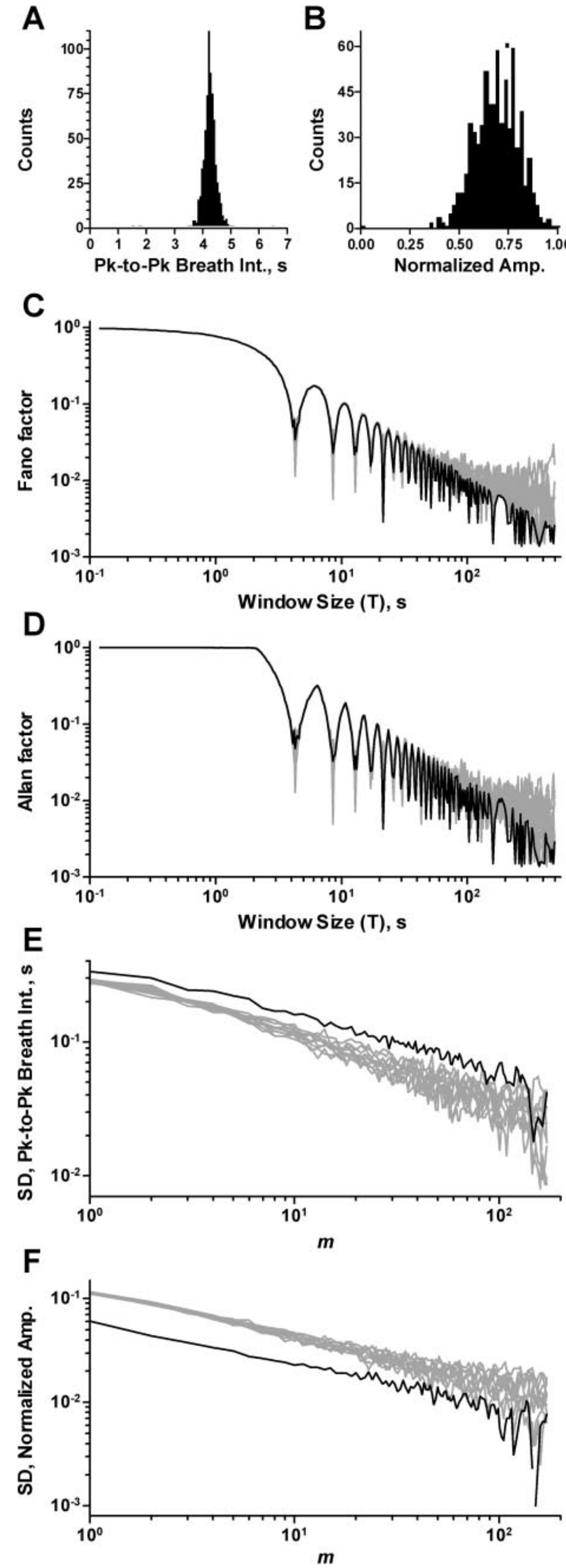

Fig. 6. Fractal analysis of paced breathing (14/min) in 1 subject. Fluctuations in breath number, respiratory period, and breath amplitude occurred randomly. Sequence and format of *A–F* are the same as in Fig. 2. Analysis was based on 699 paced breaths.

DISCUSSION

Whereas respiration is generally treated as a rhythmic process, the variability in cycle-by-cycle measurements of respiratory period and breath amplitude is, in fact, considerable in awake, healthy adult humans. This is indicated by the gammalike shape of the frequency distributions of these parameters, with CVs averaging 0.29 for peak-to-peak breath interval and 0.40 for breath amplitude. The basis for the fluctuations in these parameters was the issue dealt with in the present study.

Peng et al. (24) used detrended fluctuation analysis to demonstrate the fractal nature of interbreath interval fluctuations in healthy adult subjects. We have confirmed this finding using a different method of fractal analysis, and, in addition, demonstrated fractal fluctuations of two other respiratory parameters. Fractal analysis revealed long-range correlations among the fluctuations in the number of breaths and breath amplitude, as well as peak-to-peak breath interval. Such long-range correlations were reflected by the power law relationships in the Fano factor and Allan factor curves as well as the dispersional analysis plots. That the power law relationships indeed monitored the presence of fractal (i.e., time-scale-invariant) behavior was shown to be the case by comparing the curves for the original time series with those of surrogate data blocks. Time-scale-invariant fluctuations in respiration reflect a form of memory in that the present value of the measured parameter is related to those in the distant past. As such, and in contrast to a random process with no correlations among events, recognition of the fact that one is dealing with a fractal process should be of value in roughly predicting future behavior of the respiratory system.

To our knowledge, the present study is the first to determine whether the fluctuations in one or more of three simultaneously measured respiratory parameters were fractal in the same subject. Previous to this report, Frey et al. (14) demonstrated that the probability density distribution of interbreath intervals in sleeping infants followed a power law. In another study using Fano factor analysis, Larsen et al. (21) concluded that the fluctuations in interbreath interval in sleeping infants were statistically self-similar (i.e., fractal). However, neither of these studies dealt with fluctuations in breath amplitude. This was also the case in the study of Szeto et al. (27), which demonstrated that the probability density distribution of interbreath intervals in fetal lambs followed a power law. Whereas Hoop et al. (19) used rescaled range analysis to demonstrate fractal fluctuations in breath volume in adult rats, their study did not deal with fluctuations in the breath number and respiratory period.

Our data suggest that the processes responsible for the fractal fluctuations in number of breaths, respiratory period, and breath amplitude can function independently of each other. Whereas there was a fractal component of the fluctuations in all three of these parameters in 9 of 20 spontaneously breathing subjects, there were four subjects in whom only the fluctuations in number of breaths and breath amplitude were fractal, three subjects in whom only the fluctuations in number of breaths were fractal, and two subjects in whom fluctuations in number of breaths and respiratory period but not breath amplitude were fractal. None of the parameters exhibited time-scale-invariant behavior in the two remaining spontaneously breathing subjects. Not surprisingly, there were no fractal fluctuations during breathing paced by a metronome, which essentially eliminated the variability in respiratory period. Barring major differences in the sensitivities of the methods used to test for time-scale-invariant behavior or differential degrees of randomness for the three measured parameters, these results point to the existence of potentially independent fractal mechanisms controlling the number of breaths, respiratory period, and breath amplitude. These processes may function at different levels of the central networks controlling respiration. For example, fractal fluctuations in number of breaths and respiratory period presumably would involve the rhythm generator in some way, whereas the fluctuations in breath amplitude might occur in a pattern generator made up of follower circuits (13).

The data are suggestive of two types of encoding of time-scale-invariant fluctuations in breathing frequency. We refer to the first as a fractal form of rate coding (20). A fractal rate code is suggested by seven cases in which time-scale-invariant fluctuations in the number of breaths occurred in the absence of fractal ordering of the peak-to-peak breath intervals. In such cases, the Fano and Allan factor curves contained a power law extending over more than one time scale, but the dispersional analysis plot for peak-to-peak breath intervals had a slope in the range of those of the plots for the surrogate data sets. For these cases, it is assumed that random shuffling of the peak-to-peak breath intervals to construct the surrogates indirectly destroyed fractal ordering of the number of breaths occurring over time, thereby eliminating the power laws in the Fano factor and Allan factor curves.

There were 11 subjects in whom the slope of the dispersional analysis plot for peak-to-peak breath interval fell outside of the range of the slopes of the plots for the surrogates. This always occurred in combination with the appearance of a power law in the corresponding Fano factor and Allan factor curves. Such cases point to fractal ordering of the peak-to-peak breath intervals, and we consider this to be a form of temporal coding (20). The physiological implications of rate vs. temporal coding of time-scale-invariant fluctuations in respiratory frequency remain to be determined.

For reasons given in METHODS, we derived values of H only from the slope (α) of the Allan factor curve. In the 18 subjects in whom fluctuations in the number of breaths were fractal, the long-range correlations were persistent in 14 subjects and antipersistent in 4 subjects. Thus the data could be either positively or negatively correlated. H measures the smoothness of a fractal time series with antipersistent values (negatively correlated data) reflecting a high degree of roughness and persistent values (positively correlated data) reflecting relative smoothness in the time series (2, 12, 23). The functional implications attached to positive vs. negative long-range correlations among the number of breaths remain to be investigated.

The mechanisms responsible for the fractal fluctuations in the number of breaths, respiratory period, and breath amplitude remain to be determined. One or more of the following factors might be involved in producing fractal fluctuations in each of these parameters. First, fractal fluctuations might reflect the inherent properties of the respiratory oscillator. Second, peripheral feedback from the lungs and/or thoracic mechanoreceptors might lead to fractal fluctuations in respiratory pattern. Third, suprapontine inputs to the respiratory network might be a source of the observed fractal fluctuations. Fourth, a feedback loop involving fractal fluctuations in blood-gas concentrations might be involved. Fifth, inputs to the respiratory network from the external world might be ordered as a fractal rather than random sequence of events. Sixth, fractal fluctuations in respiratory pattern might arise from changes in the level of wakefulness and attention. Finally, it also remains to be determined whether the long-range correlations observed in the present study reflect deterministic chaos within the respiratory system.

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