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Physica A 319 (2003) 447–457
PHYSICA A
www.elsevier.com/locate/physa

Breathing during REM and non-REM sleep: correlated versus uncorrelated behaviour

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Received 29 August 2002

Abstract

Healthy sleep can be characterized by several stages: deep sleep, light sleep, and REM sleep. Here we show that these sleep stages lead to different autonomic regulation of breathing. Using the detrended fluctuation analysis up to the fourth order we find that breath-to-breath intervals and breath volumes separated by several breaths are long-range correlated during the REM stages and during wake states. In contrast, in the non-REM stages (deep sleep and light sleep), long-range correlations are absent. This behaviour is very similar to the correlation behaviour of the heart rate during the night and may be related to the phase synchronization between heartbeat and breathing found recently. We speculate that the differences are caused by different cortically influenced control of the autonomic nervous system.

PACS: 05.45.Tp; 87.19.Nn; 87.19.Uv; 05.40.−a

Keywords: Breathing; Sleep stages; Autonomic regulation; Scaling analysis; Long-range correlations; Detrended fluctuation analysis

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0378-4371/03/$ - see front matter
PII: S0378-4371(02)01502-9

1. Introduction

In recent years it has been recognized that in many natural sequences the elements are not positioned randomly, but exhibit long-range correlations [1,2]. Prominent examples include non-coding DNA sequences [3–7], weather and climate records [8–11], neuron spikes [12,13], human gait [14], as well as heart rate sequences [15–20]. The common feature of all these diverse systems is that the long-range correlations decay by a power law, where a characteristic correlation scale is absent. These findings are useful, e.g. in DNA for distinguishing between coding and non-coding sequences [2], and in atmospheric science for testing state-of-the-art climate models [11], and in physiology to characterize different sleep and wake states as well as diseases [16–18].

Although the rapid and irregular breathing pattern in rapid eye movement (REM) sleep is well known [21,22], a detailed analysis of breath-to-breath variability and ventilation during sleep has not been presented so far. The correlation properties of human breath-to-breath intervals recorded during wake have been investigated by studies of the auto-correlation function on short time scales [23], and very recently long-range correlations have been found in day-time records [24]. Here we concentrate on the breathing correlations in the different sleep stages, where external stimuli (which might give rise to additional trends that are difficult to deal with) are absent. In addition to the correlation properties of the breath-to-breath intervals we also study the properties of breath volume series.

It is well known that healthy sleep consists of cycles of roughly 1–2 h duration. Each cycle is characterized by a sequence of sleep stages starting usually with light sleep and followed by deep sleep (slow-wave sleep) and REM sleep. While the specific functions of the different sleep stages are not well understood, it is believed that the deep sleep stage is essential for physical recreation, while the REM stage is important for mental recreation. During the recording time there are also initial and intermediate segments where the subjects do not sleep (wake states).

Here, we investigate the breathing rhythm within the different sleep stages and during wake. We find the intriguing result that during non-REM sleep, which covers about 80 per cent of the total sleep period, the breath-to-breath intervals show almost no correlations. Pronounced long-range correlations occur solely during REM sleep. The correlations are even stronger than those found during wakefulness. It is interesting to note that the scaling behaviour of the breathing rhythm during the different sleep stages is very similar to the scaling behaviour of the heart rate [18]. Differences do occur only during wake, where the breathing is less correlated than the heart rate. This might be due to a randomizing effect of consciousness on breathing which can be affected by will, while the heart rate cannot be affected by will in general. This underlines the importance of a study during sleep where external stimuli are absent or at least significantly reduced.

2. Correlation analysis

In our analysis, we consider 29 breathing records from different healthy individuals (22 male; 7 female; age 26 ± 3 years; subjects gave informed consent, and the study

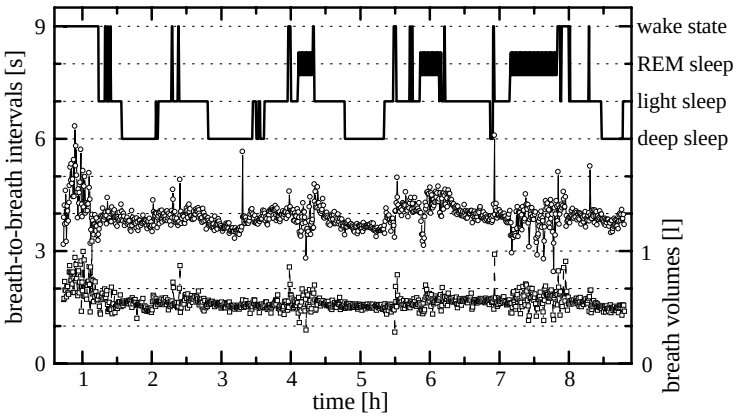

Fig. 1. Representative one-night record for a healthy subject. The breath-to-breath intervals represent averages of the τ_i over 30 s (center curve and left axis). The same averaging procedure has been used for the breath volumes V_i (bottom curve and right axis). The sleep stages have been determined by visual evaluation of electrophysiological recordings of brain activity [32] and are shown in the top part of the figure.

was approved by the local ethical committee). Ventilation was continuously measured during a full night polysomnography in a sleep laboratory using a pneumotachograph attached to a full-face mask with leak control (for details, see Ref. [25]).

Fig. 1 shows the breath-to-breath intervals τ_i and their variations in the sleep stages for one representative subject. The breath volumes V_i are also shown. The largest fluctuations occur usually at the transitions between sleep states and wake states, often associated with body movements. To eliminate these large fluctuations representing local trends, we analyse the sleep stages separately and skip 45 s at the beginning and the end of each stage. We also skip all those sleep stages where the volumes of inspiration and expiration differ by more than 0.1 l for more than 30 per cent of the breaths and those where more than 1 percent of the breath-to-breath intervals are unrealistically large (longer than 15 s) or unrealistically small (shorter than 1.5 s). In addition, the unrealistic intervals are eliminated in all approved stages. By this procedure, the number of records with sufficiently long episodes of light sleep, deep sleep, REM sleep, and wake is reduced to 28, 24, 21, and 14, respectively.

Quantitatively, correlations between breath-to-breath intervals τ_i separated by s breaths are defined by the (auto)correlation function

$$C(s) \equiv \langle \Delta\tau_i \Delta\tau_{i+s} \rangle = \frac{1}{L-s} \sum_{i=1}^{L-s} \Delta\tau_i \Delta\tau_{i+s} \,, \tag{1}$$

where L is the number of breaths in the considered record, $\Delta\tau_i \equiv \tau_i - \langle\tau\rangle$, and $\langle\tau\rangle$ is the average breath-to-breath interval. If the $\Delta\tau_i$ are uncorrelated, $C(s)$ is zero for s positive. If correlations exist up to a certain number of beats $s_\times$, the correlation function will be positive up to $s_\times$ and vanish above $s_\times$. For the relevant case of long-range correlations, $C(s)$ decays as a power law

$$C(s) \sim s^{-\gamma}, \quad 0 < \gamma < 1 \,. \tag{2}$$

A direct calculation of $C(s)$ is hindered by the level of noise present in the finite records, and by possible nonstationarities in the data.

Here, we apply the detrended fluctuation analysis (DFA) method [6,16,18]. In recent years this method has become a widely used technique for the detection of long-range correlations in noisy, nonstationary time series [26–29]. It has successfully been applied to diverse fields such as DNA sequences [6], heart rate dynamics [16–18], neuron spiking [12,13], human gait [14], long-time weather records [8–10], cloud structure, geology, ethnology, economics time series, and solid state physics. One reason we employ the DFA method is to avoid spurious detection of correlations that are artefacts of nonstationarities in the time series. An alternative method is the wavelet technique. Other techniques for the detection of correlations like the autocorrelation function, Eq. (1), and the power spectrum are not suited for nonstationary time series.

The DFA procedure consists of four steps. First we determine the "profile" $Y(i) \equiv \sum_{k=1}^{i} \tau_k - \langle\tau\rangle$, $i = 1,\ldots,L$, of the data series τ_k of length L. Second we divide the profile $Y(i)$ into $L_s \equiv \mathrm{int}(L/s)$ nonoverlapping segments of equal length s. Since the length L of the series is often not a multiple of the considered time scale s, a short part at the end of the profile may remain. In order not to disregard this part of the series, the same procedure is repeated starting from the opposite end. Thereby, $2L_s$ segments are obtained altogether. Thirdly, we calculate the local trend for each of the $2L_s$ segments by a least-square fit of the data. Then we determine the variance

$$F_s^2(v) \equiv \frac{1}{s}\sum_{i=1}^{s}[Y((v-1)s+i) - p_v(i)]^2 \tag{3}$$

for each segment v, $v = 1,\ldots,2L_s$. Here, $p_v(i)$ is the fitting polynomial in segment v. Linear, quadratic, cubic, or higher order polynomials can be used in the fitting procedure (conventionally called DFA1, DFA2, DFA3, etc.) [18].

In the fourth step we average over all segments and take the square root to obtain the fluctuation function

$$F(s) \equiv \left[\frac{1}{2L_s}\sum_{v=1}^{2L_s} F_s^2(v)\right]^{1/2} . \tag{4}$$

We are interested in how $F(s)$ depends on the time scale s. Hence, we have to repeat steps 2–4 for several time scales s. It is apparent that $F(s)$ will increase with increasing s. If data τ_i are long-range power-law correlated according to Eq. (2), $F(s)$ increases, for large values of s, as a power law,

$$F(s) \sim s^{\alpha}, \quad \alpha = 1 - \gamma/2 . \tag{5}$$

We plot $F(s)$ as a function of s on double logarithmic scales and calculate α by a linear fit. For uncorrelated data, the profile $Y(i)$ corresponds to the displacement of a random walker from his starting point, $F(s)$ corresponds to the root-mean-square displacement R of the walk, and $\alpha = 0.5$ corresponds to Fick's diffusion law: $R(t) \sim t^{1/2}$. For short-range correlated data, a crossover to $\alpha = 0.5$ occurs above the correlation time $s_\times$. If the time series is stationary, we can apply standard spectral analysis techniques and calculate the power spectrum $S(f)$ as a function of the frequency f. Then, the

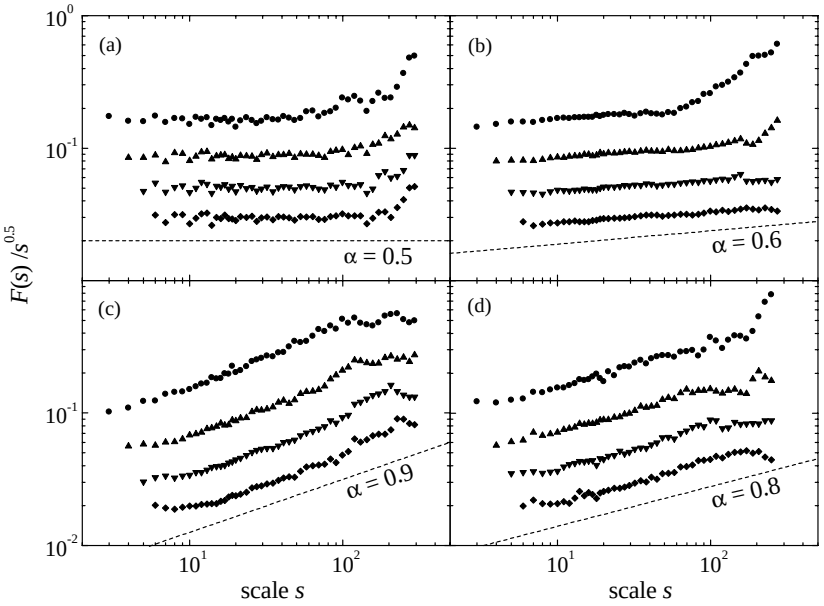

Fig. 2. DFA for the breath-to-breath interval data of the representative subject shown in Fig. 1. The scaled fluctuation functions $F(s)/s^{1/2}$ obtained from DFA1 (●), DFA2 (▲), DFA3 (▼), DFA4 (◆) are plotted as a function of scale s for the three sleep stages: (a) deep sleep; (b) light sleep; (c) REM sleep; and (d) wake states during night. Nearly uncorrelated behaviour ($\alpha \approx 0.5$) is observed during deep and light sleep, while long-range correlations ($\alpha > 0.5$) occur during REM sleep and wake states. For comparison, dashed straight lines representing the indicated scaling exponent α are also shown.

exponent β in the scaling law $S(f) \sim f^{-\beta}$ is related to the mean fluctuation function exponent α by $\beta = 2\alpha - 1$.

3. Results for the breath-to-breath intervals

We begin by applying the DFA to the breath-to-breath interval data of Fig. 1. The results for DFA1–DFA4 and the three different sleep stages as well as wake states are shown in Fig. 2. The scaled fluctuation functions $F(s)/s^{1/2}$ in the double-logarithmic representation have a slope that is reduced by 0.5 compared to $F(s)$. This type of plot allows to recognize long-range correlations easily, since the curves are approximately horizontal for uncorrelated data and have a positive slope only for long-range correlated data.

The analysis reveals that the correlations in the different states are significantly different. (i) In non-REM sleep (deep sleep and light sleep) the fluctuation exponent α is close to $\frac{1}{2}$, indicating the *loss* of correlations. (ii) In REM sleep and during the wake states we observe a positive slope indicating the presence of long-range correlations. For the wake states we find a scaling exponent $\alpha \approx 0.8$, which is approximately in

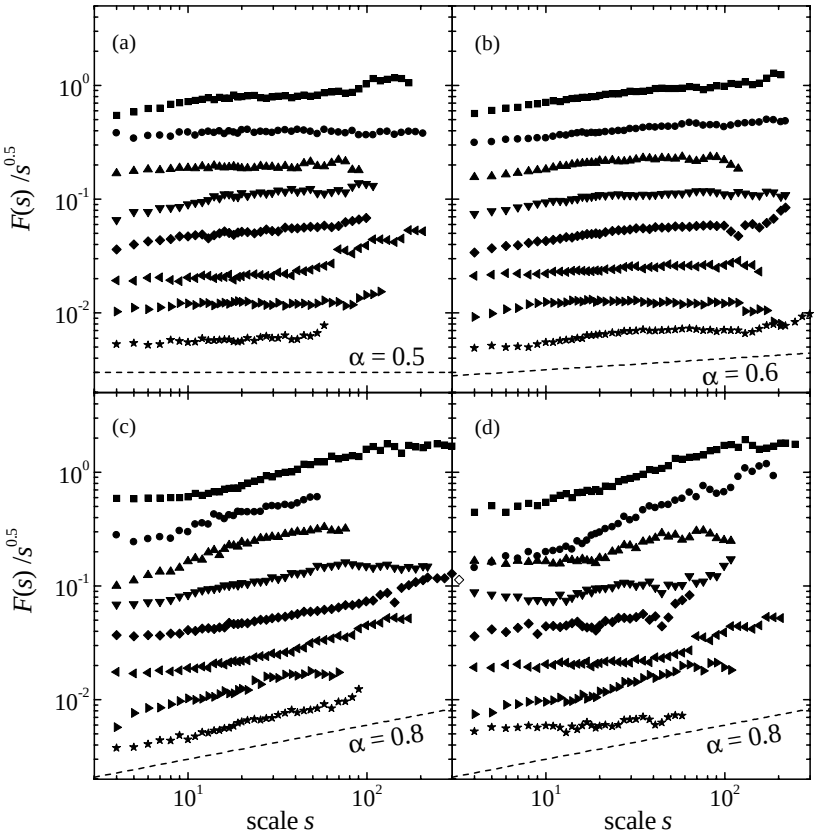

Fig. 3. DFA2 of breath-to-breath intervals of eight other records (different symbols). The scaled fluctuation functions $F(s)/s^{1/2}$ are plotted as a function of scale s for the three sleep stages, (a) deep sleep; (b) light sleep; (c) REM sleep, and for (d) wake states during night. They show the same characteristic features as described in Fig. 2.

agreement with the results found very recently during wakefulness [24]. Fig. 2 shows that the results are not affected by trends: Trends lead to the crossovers to higher slopes at large scales in the DFA1 curves for deep and light sleep, but they are eliminated in the higher order DFA results.

Fig. 3 shows the fluctuation functions for eight other records. The characteristic features (long-range correlations for REM sleep and wake states, loss of correlations for deep and light sleep) are the same as in Fig. 2. Note that the slopes of the curves scatter quite strongly for the wake states, but run more parallel for the sleep stages. This underlines our suggestion that records during wake can be affected by will and external influences, while records obtained during sleep show the intrinsic regulation behaviour of the breathing control considerably more homogeneously.

We have obtained similar findings for all 29 subjects. The results are summarized in Fig. 4(a)–(d) where the histograms for the exponents α in the three sleep stages and

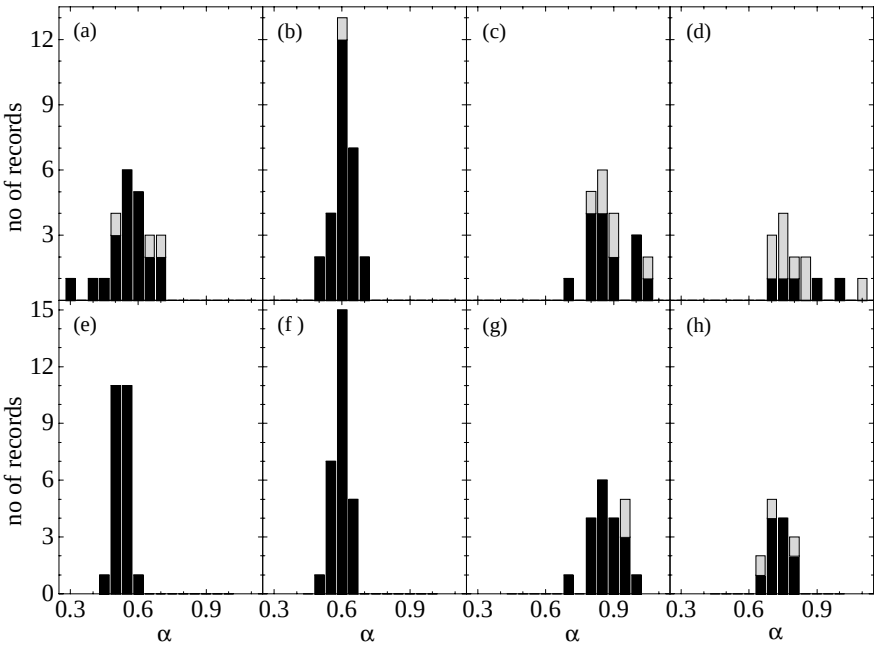

Fig. 4. (a)–(d) Histograms of the fluctuation exponents α obtained from linear fits to log–log plots of $F(s)$ for the breath-to-breath interval data versus s in the regime $7 < s < L/4$ for (a) deep sleep, (b) light sleep, (c) REM sleep, and (d) wake states, where L represents the duration of the longest stage for each record and type of sleep. The fitting range has been chosen to be below the scales where the statistical errors become too large due to the finite duration of the states. The black bars indicate results with good fits ($\chi^2 < 0.004$ per data point) and the grey bars indicate fits where stronger deviations from straight line scaling occur ($\chi^2 \geqslant 0.004$ per data point). (e)–(h) The corresponding results for control data sets. The artificial series consist of correlated random numbers with $\alpha = 0.55$, 0.6, 0.9 and 0.8 for (e) deep sleep, (f) light sleep, (g) REM sleep, and (h) wake states, respectively. The durations of the control series are identical to those of the data.

during wake are shown. For deep and light sleep, the histograms are centred around $\alpha \approx 0.55$ and 0.6, respectively, and show a large overlap. Both histograms are well separated from the histograms of REM sleep and wake states that are centred around $\alpha \approx 0.9$ and 0.8, respectively.

These results for the breath-to-breath interval records are very similar to those that we obtained for heartbeat interval time series in a previous study [18]: During deep and light sleep the heartbeats are close to uncorrelated, while there are long-range correlations during REM sleep ($\alpha \approx 0.85$) and wake states ($\alpha \approx 0.95$). Thus, the present study of the breath-to-breath intervals supports the idea of different autonomic regulation during REM and non-REM sleep.

The changes in heartbeat and breathing intervals during the different sleep stages are very similar. This suggests that there is either significant coupling between the autonomic regulation of heartbeat and breathing or that the changes in both systems are generated by the same source. While the existence of a weak coupling has been

suggested in studies of synchronization of heart rate and breathing [30,31] we have speculated that the long-range correlations during REM sleep (the dreaming phase) might be induced by cortically influenced control of the autonomic nervous system [18]. The two explanations do not contradict each other and may both contain part of the real picture, although the correlation behaviour during the wake states seems to support the second explanation. The scaling exponent of the breath-to-breath interval series during wake ($\alpha \approx 0.8$) is significantly smaller than the corresponding scaling exponent for the heartbeat ($\alpha \approx 0.95$). Thus, the coupling of breathing and heartbeat is probably reduced at least during wake. On the other hand, the difference could be explained in the second picture: breathing becomes more random during wake (smaller exponent) because it can be affected by the will while the heartbeat cannot be affected by the will.

In order to test further the significance of the DFA results, we have generated artificial control sequences for each of the 29 records. In the procedure, the lengths of the sleep stages were chosen identical to those of the real records, but the breath-to-breath intervals were replaced by correlated random numbers. The histograms of the exponents α obtained from the fluctuation functions for the control sequences are shown in Fig. 4(e)–(h). The exponents have been determined in exactly the same way as for the real records. It can be seen that the broadness of the histograms is partly due to the short duration of the records (which is the same for real and control series) and partly due to some intrinsic scatter of the real data, especially during deep sleep and wake.

4. Results for the breath volume series

Next we have analysed by DFA the breath volume data of Fig. 1. Fig. 5 shows the results of DFA1–DFA4 for the three different sleep stages as well as wake states. Again we find nearly uncorrelated behaviour during non-REM sleep and long-range correlations during REM sleep and during the wake states.

Fig. 6 shows the histogram of effective scaling exponents for the breath volume data. These histograms are astonishingly similar to those for the breath-to-breath interval data in Fig. 4, although some of the fits are worse here. The only significant difference is the further reduced scaling exponent α during wake. Thus, the results from the breath volumes support our conclusion drawn from the breath-to-breath interval series, that when the brain is more active, in the "dream"-REM stage, the breathing control shows a long-time memory. The long-range correlations during wake are weaker, probably because the breathing rhythm during wake is affected by will and thus becomes more random. In deep sleep the memory of the breath-to-breath intervals and the breath volumes vanishes after a small number of breaths or is completely absent. In light sleep finally, the breathing seems to become uncorrelated as well, but possible weak correlations remain in some subjects. These findings are similar to our findings for the heartbeat correlation behaviour during sleep. The characteristic differences of heartbeat and breathing regulation during the different sleep stages can lead to a better understanding of autonomic regulation and cortically influenced control of it.

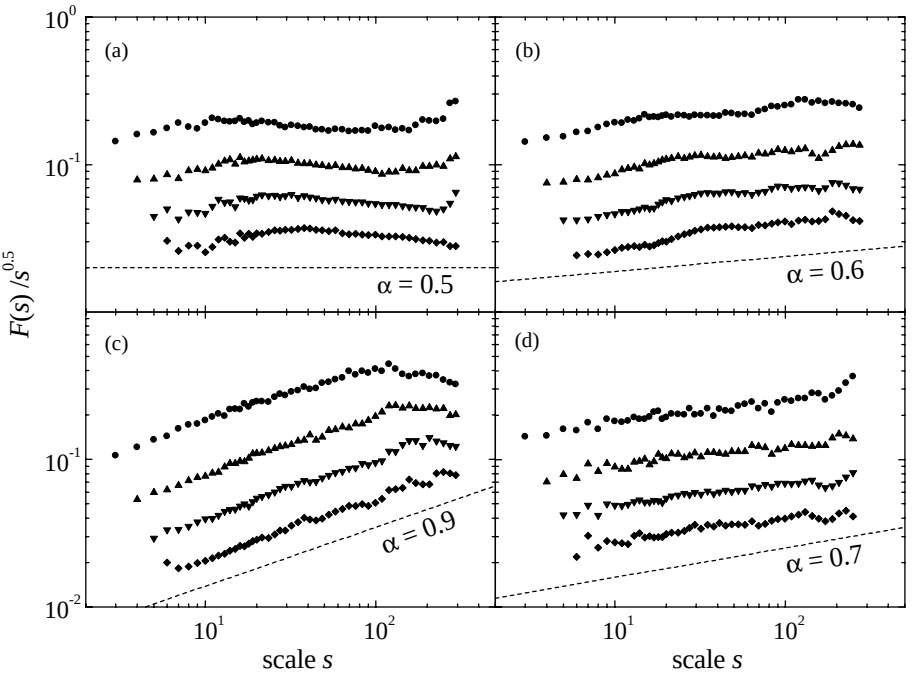

Fig. 5. DFA for the breath volume data of the representative subject shown in Fig. 1. The scaled fluctuation functions $F(s)/s^{1/2}$ obtained from DFA1 (●), DFA2 (▲), DFA3 (▼), DFA4 (♦) are plotted as a function of scale s for the three sleep stages: (a) deep sleep; (b) light sleep; (c) REM sleep; and (d) wake states during night. The scaling behaviour is very similar to that for the breath-to-breath intervals. Nearly uncorrelated behaviour ($\alpha \approx 0.5$) is observed during deep sleep and also during light sleep, while long-range correlations ($\alpha > 0.5$) occur during REM sleep and wake states. For comparison, dashed straight lines representing the indicated scaling exponent α are also shown.

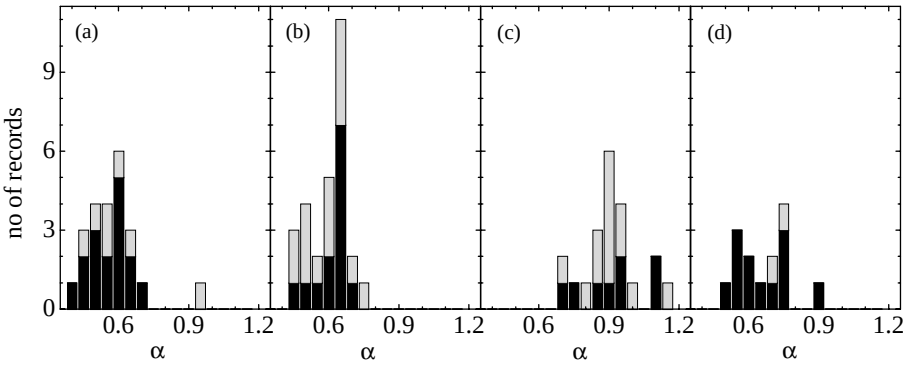

Fig. 6. Histograms of the fluctuation exponents α obtained from linear fits to log–log plots of $F(s)$ for the breath volume data. The fitting procedure is the same as for Fig. 4.

Acknowledgements

We would like to thank the German Academic Exchange Service (DAAD), the German Science Foundation (DFG), and the Minerva Foundation for financial support. The healthy volunteers were recorded as part of a study on the regulation of breathing during sleep funded by an unrestricted grant from UCB pharma, Kerpen-Sindorf, Germany.

References

[1] A. Bunde, J. Kropp, H.-J. Schellnhuber (Eds.), The science of disaster: climate disruptions, market crashes, and heart attacks, Springer, Berlin, 2002.
[2] S.V. Buldyrev, A.L. Goldberger, S. Havlin, C.-K. Peng, H.E. Stanley, in: A. Bunde, S. Havlin (Eds.), Fractals in Science, Springer, Berlin, 1994.
[3] C.-K. Peng, S.V. Buldyrev, A.L. Goldberger, S. Havlin, F. Sciortino, M. Simons, H.E. Stanley, Nature 356 (1992) 168.
[4] R.F. Voss, Phys. Rev. Lett. 68 (1992) 3805.
[5] S.V. Buldyrev, A.L. Goldberger, S. Havlin, C.-K. Peng, M. Simons, F. Sciortino, H.E. Stanley, Phys. Rev. Lett. 71 (1993) 1776.
[6] C.-K. Peng, S.V. Buldyrev, S. Havlin, M. Simons, H.E. Stanley, A.L. Goldberger, Phys. Rev. E 49 (1994) 1685.
[7] A. Arneodo, E. Bacry, P.V. Graves, J.F. Muzy, Phys. Rev. Lett. 74 (1995) 3293.
[8] E. Koscielny-Bunde, A. Bunde, S. Havlin, Y. Goldreich, Physica A 231 (1996) 393.
[9] E. Koscielny-Bunde, A. Bunde, S. Havlin, H.E. Roman, Y. Goldreich, H.-J. Schellnhuber, Phys. Rev. Lett. 81 (1998) 729.
[10] P. Talkner, R.O. Weber, Phys. Rev. E 62 (2000) 150.
[11] R.B. Govindan, D. Vyushin, A. Bunde, S. Brenner, S. Havlin, H.-J. Schellnhuber, Phys. Rev. Lett. 89 (2002) 028 501.
[12] S. Blesic, S. Milosevic, D. Stratimirovic, M. Ljubisavljevic, Physica A 268 (1999) 275.
[13] S. Bahar, J.W. Kantelhardt, A. Neiman, H.H.A. Rego, D.F. Russell, L. Wilkens, A. Bunde, F. Moss, Europhys. Lett. 56 (2001) 454.
[14] J.M. Hausdorff, S.L. Mitchell, R. Firtion, C.-K. Peng, M.E. Cudkowicz, J.Y. Wei, A.L. Goldberger, J. Appl. Physiol. 82 (1997) 262.
[15] C.-K. Peng, J. Mietus, J.M. Hausdorff, S. Havlin, H.E. Stanley, A.L. Goldberger, Phys. Rev. Lett. 70 (1993) 1343.
[16] C.-K. Peng, S. Havlin, H.E. Stanley, A.L. Goldberger, Chaos 5 (1995) 82.
[17] P.Ch. Ivanov, A. Bunde, L.A.N. Amaral, S. Havlin, J. Fritsch-Yelle, R.M. Baevsky, H.E. Stanley, A.L. Goldberger, Europhys. Lett. 48 (1999) 594.
[18] A. Bunde, S. Havlin, J.W. Kantelhardt, T. Penzel, J.-H. Peter, K. Voigt, Phys. Rev. Lett. 85 (2000) 3736.
[19] Y. Ashkenazy, P.Ch. Ivanov, S. Havlin, C.-K. Peng, A.L. Goldberger, H.E. Stanley, Phys. Rev. Lett. 86 (2001) 1900.
[20] J.W. Kantelhardt, Y. Ashkenazy, P.Ch. Ivanov, A. Bunde, S. Havlin, T. Penzel, J.-H. Peter, H.E. Stanley, Phys. Rev. E 65 (2002) 051 908.
[21] E. Aserinsky, N. Kleitman, Science 118 (1953) 273.
[22] D.W. Hudgel, R.J. Martin, B. Johnson, P. Hill, J. Appl. Physiol. Respirat. Environ. Exercise Physiol. 56 (1984) 133.
[23] T. Brack, A. Jubran, M.J. Tobin, Am. J. Respir. Crit. Care Med. 157 (1998) 1756.
[24] C.-K. Peng, J.E. Mietus, Y. Liu, Ch. Lee, J.M. Hausdorff, H.E. Stanley, A.L. Goldberger, L.A. Lipsitz, Ann. Biomed. Eng. 30 (2002) 683.

[25] S. Rostig, A. Jerrentrup, T. Penzel, W. Cassel, J.-H. Peter, C.F. Vogelmeier, H.F. Becker, 2002, preprint.
[26] M.S. Taqqu, V. Teverovsky, W. Willinger, Fractals 3 (1995) 785.
[27] J.W. Kantelhardt, E. Koscielny-Bunde, H.H.A. Rego, S. Havlin, A. Bunde, Physica A 295 (2001) 441.
[28] K. Hu, P.Ch. Ivanov, Z. Chen, P. Carpena, H.E. Stanley, Phys. Rev. E 64 (2001) 011 114.
[29] Z. Chen, P.Ch. Ivanov, K. Hu, H.E. Stanley, Phys. Rev. E 65 (2002) 041 107.
[30] C. Schäfer, M.G. Rosenblum, J. Kurths, H.-H. Abel, Nature 392 (1998) 239.
[31] C. Schäfer, M.G. Rosenblum, H.-H. Abel, J. Kurths, Phys. Rev. E 60 (1999) 857.
[32] A. Rechtschaffen, A. Kales, A Manual of Standardized Terminology, Techniques, and Scoring System for Sleep Stages of Human Subjects, US Government Printing Office, Washington, 1968.