

Sleep-wake differences in scaling behavior of the human heartbeat: Analysis of terrestrial and long-term space flight data

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Abstract. – We compare scaling properties of the cardiac dynamics during sleep and wake periods for healthy individuals, cosmonauts during orbital flight, and subjects with severe heart disease. For all three groups, we find a greater degree of anticorrelation in the heartbeat fluctuations during sleep compared to wake periods. The sleep-wake difference in the scaling exponents for the three groups is comparable to the difference between healthy and diseased individuals. The observed scaling differences are not accounted for simply by different levels of activity, but appear related to intrinsic changes in the neuroautonomic control of the heartbeat.

The normal electrical activity of the heart is usually described as a “regular sinus rhythm” [1, 2]. However, cardiac interbeat intervals fluctuate in an irregular manner in healthy subjects (fig. 1)—even at rest or during sleep [3]. The complex behavior of the heartbeat manifests itself through the nonstationarity and nonlinearity of interbeat interval sequences [4]. In recent years, the intriguing statistical properties of interbeat interval sequences have attracted the attention of researchers from different fields [5-11].

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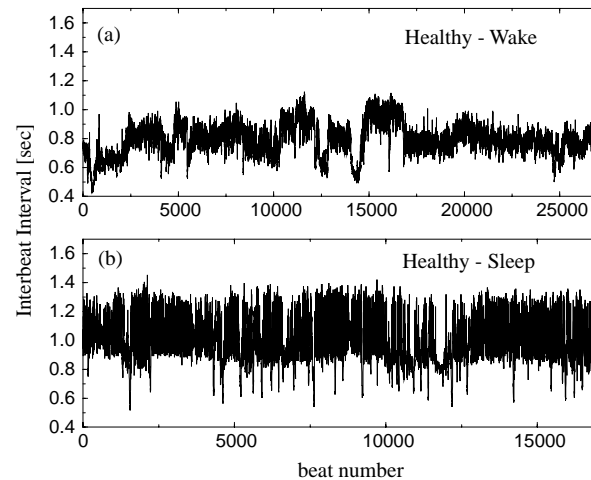


Fig. 1. – Consecutive heartbeat intervals are plotted *vs.* beat number for 6 hours recorded from the same healthy subject during: (a) wake period: 12 pm to 6 pm and (b) sleep period: 12 am to 6 am. (Note that there are fewer interbeat intervals during sleep due to the larger average of the interbeat intervals, *i.e.* slower heart rate.)

Analysis of heartbeat fluctuations focused initially on short time oscillations associated with breathing, blood pressure and neuroautonomic control [12, 13]. Studies of longer heartbeat records, however, revealed $1/f$ -like behavior [14, 15]. Recent analysis of very long time series (up to 24 h: $n \approx 10^5$ beats) shows that under healthy conditions, interbeat interval increments exhibit power law anticorrelations [16], follow a universal scaling form in their distributions [17], and are characterized by a broad multifractal spectrum [18]. These scaling features change with disease and advanced age [19]. The emergence of scale-invariant properties in the seemingly “noisy” heartbeat fluctuations is believed to be a result of highly complex, nonlinear mechanisms of physiologic control [20].

It is known that circadian rhythms are associated with periodic changes in key physiological processes [2, 4, 21, 22]. Here, we ask the question if there are characteristic differences in the scaling behavior between sleep and wake cardiac dynamics⁽¹⁾. We hypothesize that sleep and wake changes in cardiac control may occur on all time scales and thus could lead to systematic changes in the scaling properties of the heartbeat dynamics. Elucidating the nature of these sleep-wake rhythms could lead to a better understanding of the neuroautonomic mechanisms of cardiac regulation.

We analyze 30 datasets—each with 24 h of interbeat intervals—from 18 healthy subjects and 12 patients with congestive heart failure [23]. We analyze the nocturnal and diurnal fractions of the dataset of each subject which correspond to the 6 h ($n \approx 22000$ beats) from midnight to 6 am and noon to 6 pm.

We apply the detrended fluctuation analysis (DFA) method [24] to quantify long-range correlations embedded in nonstationary heartbeat time series. This method avoids spurious detection of correlations that are artifacts of nonstationarity. Briefly, we first integrate the

⁽¹⁾ Typically the differences in the cardiac dynamics during sleep and wake phases are reflected in the average (higher in sleep) and standard deviation (lower in sleep) of the interbeat intervals [21]. Such differences can be systematically observed in plots of the interbeat intervals recorded from subjects during sleep and wake periods (fig. 1).

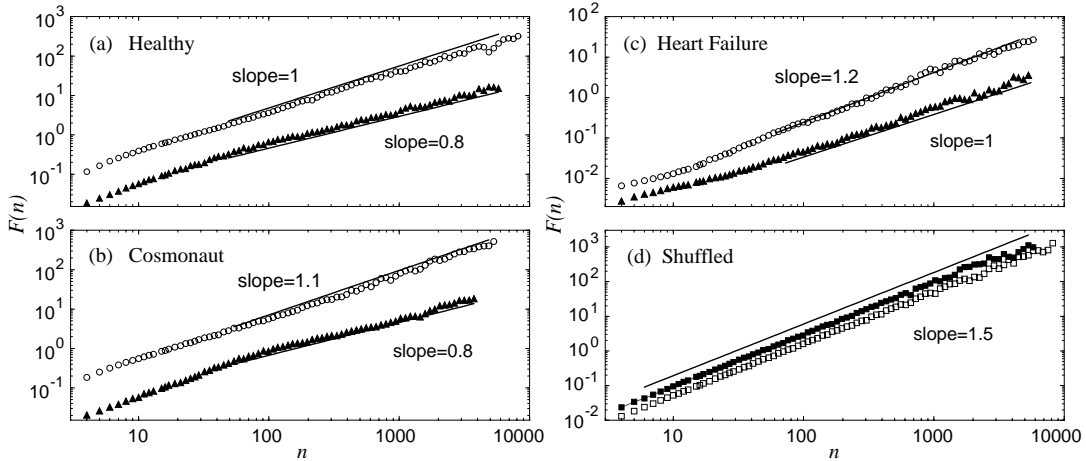


Fig. 2. – Plots of $\log F(n)$ vs. $\log n$ for 6 hour long wake records (open circles) and sleep records (filled triangles) of (a) one typical healthy subject; (b) one cosmonaut (during orbital flight); and (c) one patient with congestive heart failure. Note the systematic lower exponent for the sleep phase (filled triangles), indicating stronger anticorrelations. (For some individuals we observe weak crossovers in the scaling of the fluctuation function $F(n)$ in the range $100 < n < 2000$. However, there is no typical characteristic time scale n at which these crossovers occur and a crossover at given time scale n , for the wake data, does not appear to be associated with a crossover for the night data from the same individual. Such weak crossover events might be subject-specific and could be related to the particular record of an individual, *i.e.* a repeat recording from the same subject might not show such a crossover.) (d) As a control, we reshuffle and integrate the interbeat increments from the wake and sleep data of the healthy subject presented in (a). We find a Brownian noise scaling over all time scales for both wake and sleep phases with an exponent $\alpha = 1.5$, as one expects for random-walk-like fluctuations.

interbeat-interval time series. We then divide the time series into boxes of length n and perform, in each box, a least-squares linear fit to the integrated signal. The linear fit represents the local trend in each box. Next, we calculate in each box the root-mean-square deviations $F(n)$ of the integrated signal from the local trend. We repeat this procedure for different box sizes (time scales) n . A power law relation between the average fluctuation $F(n)$ and the number of beats n in a box indicates the presence of scaling; the correlations in the heartbeat fluctuations can be characterized by the scaling exponent α , defined as $F(n) \sim n^\alpha$.

We find that at scales above ≈ 1 min ($n > 60$) the data during wake hours display long-range correlations over two decades with average exponents $\alpha_W \approx 1.05$ for the healthy group and $\alpha_W \approx 1.2$ for the heart failure patients. For the sleep data we find a systematic crossover at scale $n \approx 60$ beats followed by a scaling regime extending over two decades characterized by a smaller exponent: $\alpha_S \approx 0.85$ for the healthy group and $\alpha_S \approx 0.95$ for the heart failure group (fig. 2a, c). Although the values of the sleep and wake exponents vary from subject to subject, we find that for all individuals studied, the heartbeat dynamics during sleep are characterized by a smaller exponent (table I and fig. 3).

As a control, we also perform an identical analysis on two surrogate data sets obtained by reshuffling and integrating the increments in the interbeat intervals of the sleep and wake records from the same healthy subject presented in fig. 2a. Both surrogate sets display uncorrelated random-walk fluctuations with a scaling exponent of 1.5 (Brownian noise) (fig. 2d). The value 1.5 arises from the fact that we analyze the integral of the signal, leading to an increase by 1 of the usual random-walk exponent of $1/2$. A scaling exponent larger than $3/2$

TABLE I. – Comparison of the statistics for the scaling exponents from the three groups in our database. Here, N is the number of datasets in each group, α is the corresponding group average value and σ is the standard deviation of the exponent values for each group. The differences between the average sleep and wake phase exponents for all three groups are statistically significant ($p < 10^{-5}$ by the Student's *t*-test).

Group	N	α	σ
Healthy wake	18	1.05	0.07
Healthy sleep	18	0.85	0.10
Cosmonaut wake	17	1.04	0.12
Cosmonaut sleep	17	0.82	0.07
Heart failure wake	12	1.20	0.09
Heart failure sleep	12	0.95	0.15

would indicate persistent correlated behavior, while exponents with values smaller than $3/2$ characterize anticorrelations (a perfectly anticorrelated signal would have an exponent close to zero). Our results therefore suggest that the interbeat fluctuations during sleep and wake phases are long-range anticorrelated but with a significantly greater degree of anticorrelation (smaller exponent) during sleep.

An important question is whether the observed scaling differences between sleep and wake cardiac dynamics arise trivially from changes in the environmental conditions (different daily activities are reflected in the strong nonstationarity of the heartbeat time series). Environmental “noise”, however, can be treated as a “trend” and distinguished from the more subtle fluctuations that may reveal intrinsic correlation properties of the dynamics. Alternatively, the interbeat fluctuations may arise from nonlinear dynamical control of the neuroautonomic system rather than being an epiphenomenon of environmental stimuli, in which case only the fluctuations arising from the intrinsic dynamics of the neuroautonomic system should show long-range scaling behavior.

A possible explanation of the results from our analysis is that the observed sleep-wake scaling differences are due to intrinsic changes in the cardiac control mechanisms for the following reasons: i) The DFA method removes the “noise” due to activity by detrending the nonstationarities in the interbeat interval signal related to polynomial trends and analyzing the fluctuations along the trends. ii) Responses to external stimuli should give rise to a different type of fluctuations having characteristic time scales, *i.e.* frequencies related to the stimuli. However, fluctuations in both diurnal and nocturnal cardiac dynamics exhibit scale-free behavior. iii) The weaker anticorrelated behavior observed for all wake phase records cannot be simply explained as a superposition of stronger anticorrelated sleep dynamics and random noise of day activity. Such noise would dominate at large scales and should lead to a crossover with an exponent of 1.5. However, such crossover behavior is not observed in any of the wake phase datasets (fig. 2). Rather, the wake dynamics are typically characterized by a stable scaling regime up to $n = 5 \times 10^3$ beats.

To test the robustness of our results, we analyze 17 datasets from 6 cosmonauts during long-term orbital flight on the Mir space station [25]. Each dataset contains continuous periods of 6 h data under both sleep and wake conditions. We find that for all cosmonauts the heartbeat fluctuations exhibit an anticorrelated behavior with average scaling exponents consistent with those found for the healthy terrestrial group: $\alpha_W \approx 1.04$ for the wake phase and $\alpha_S \approx 0.82$ for the sleep phase (table I). This sleep-wake scaling difference is observed not only for the group averaged exponents but for each individual cosmonaut dataset (fig. 2b and fig. 3). Moreover,

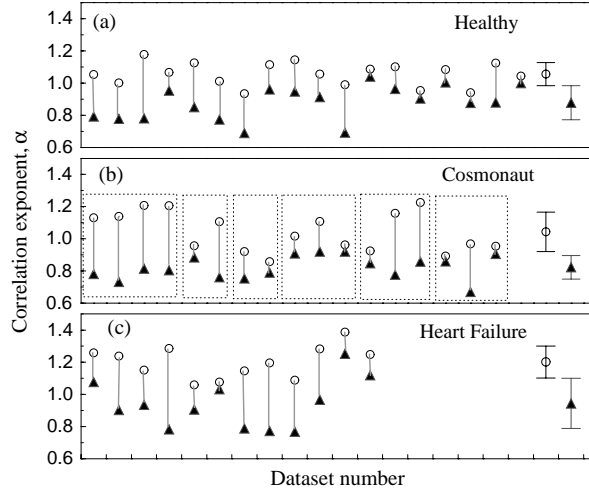


Fig. 3. – Values for the sleep (filled triangles) and wake activity (open circles) exponents for all individual records of (a) the healthy, (b) the cosmonaut, and (c) the heart failure groups. For the healthy and heart failure groups each dataset corresponds to a different individual. Data from the 6 cosmonauts are grouped in 6 blocks, where each block contains data from the same individual, recorded on different days during orbital flight and ordered from early to late flight, ranging from the 3rd to the 158th day in orbit. For all individuals in all groups, the day exponent exhibits systematically a higher value than the sleep exponent. The sleep and wake group averages and standard deviations are presented on the right of each panel.

the scaling differences are persistent in time, since records of the same cosmonaut taken on different days (ranging from the 3rd to the 158th day in orbit), exhibit a higher degree of anticorrelation in sleep.

We find that even under the extreme conditions of zero gravity and high stress activity, the sleep and wake scaling exponents for the the cosmonauts are statistically consistent ($p = 0.7$ by Student’s t -test) with those of the terrestrial healthy group⁽²⁾. Thus, the larger values for the wake phase scaling exponents cannot be a trivial artifact of activity. Furthermore, the larger value of the average wake exponent for the heart failure group compared to the other two groups (table I) cannot be attributed to external stimuli either, since patients with severe cardiac disease are strongly restricted in their physical activity. Instead, our results suggest that the observed scaling characteristics in the heartbeat fluctuations during sleep and wake phases are related to intrinsic mechanisms of neuroautonomic control.

The mechanism underlying heartbeat fluctuations may be related to countervailing neuroautonomic inputs. Parasympathetic stimulation decreases the heart rate, while sympathetic stimulation has the opposite effect. The nonlinear interaction between the two branches of the nervous system is the postulated mechanism for the type of complex heart rate variability recorded in healthy subjects [2,4]. The fact that during sleep the scaling exponents differ more from the value $\alpha = 1.5$ (indicating “stronger” anticorrelations) may be interpreted as a result of stronger neuroautonomic control. Conversely, values of the scaling exponents closer to 1.5 (indicating “weaker” anticorrelations) for both sleep and wake activity for the heart failure group are consistent with previously reported pathologic changes in cardiac dynamics [16].

⁽²⁾ Those findings are not inconsistent with the presence of other manifestations of altered autonomic control during long-term spaceflight (T. Brown *et al.*, preprint).

However, the average sleep-wake exponent difference remains the same (≈ 0.2) for all three groups. The observed sleep-wake changes in the scaling characteristics may indicate different regimes of intrinsic neuroautonomic regulation of the cardiac dynamics, which may “switch” on and off associated with circadian rhythms.

Surprisingly, we note that for the regime of large time scales ($n > 60$) the average sleep-wake scaling difference is comparable to the scaling difference between health and disease; cf. table I and footnote ⁽³⁾. We also note that the scaling exponents for the heart failure group during sleep are close to the exponents observed for the healthy group (table I). Since heart failure occurs when the cardiac output is not adequate to meet the metabolic demands of the body, one would anticipate that the manifestations of heart failure would be most severe during physical stress when metabolic demands are greatest, and least severe when metabolic demands are minimal, *i.e.*, during rest or sleep. The scaling results we obtain are consistent with these physiological considerations: the heart failure subjects should be closer to normal during minimal activity. Of related interest, recent studies indicate that sudden death in individuals with underlying heart disease is most likely to occur in the hours just after awakening [26]. Our findings raise the intriguing possibility that the transition between the sleep and wake phases is a period of potentially increased neuroautonomic instability because it requires a transition from strongly to weakly anticorrelated regulation of the heart.

Finally, the finding of stronger heartbeat anticorrelations during sleep is of interest from a physiological viewpoint, since it may motivate new modeling approaches [27, 28] and supports a reassessment of the sleep phase as a surprisingly active dynamical state. Perhaps the restorative function of sleep may relate to an increased reflexive-type responsiveness of neuroautonomic control, not just at one characteristic frequency, but over a broad range of time scales.

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⁽³⁾ At small time scales ($n < 60$), we do not observe systematic sleep-wake differences. The scaling exponents obtained from 24 h records of healthy and heart failure subjects in the asymptotic region of large time scales are in agreement with the results for the healthy and heart failure groups during the wake phase only. Since the weaker anticorrelations associated with the wake phase are characterized by a larger exponent while the stronger anticorrelated behavior during sleep has a smaller exponent, at large scales the superposition of the two phases (in 24 h records) will exhibit behavior dominated by the larger exponent of the wake phase.

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