Sleep-Wake Differences in Scaling Behavior of the Human Heartbeat

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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 cases we find a greater degree of anticorrelation in the heartbeat fluctuations during sleep. The sleep-wake difference in the scaling exponents for all 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 heart beat.

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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 – even at rest [3]. The complex behavior of the heart beat manifests itself also through the nonstationarity and nonlinearity of interbeat interval sequences [Fig. 1] [4–6]. In recent years the study of the statistical properties of these interbeat interval sequences has attracted the attention of researchers from different fields [7–13].

Analysis of heart beat fluctuations focused initially on short time oscillations associated with breathing, blood pressure and neuroautonomic control [14,15]. Studies of longer heart beat records, however, revealed 1/f-like behavior [16,17]. Recent analysis of very long time series (up to 24h: $n \approx 10^5$ beats) show that under healthy conditions, interbeat interval increments exhibit power-law anticorrelations [18]. These scaling features change with disease and advanced age [19]. The emergence of scale-invariant properties in the seemingly "noisy" heart beat fluctuations is believed to be a result of highly complex, nonlinear mechanisms of physiologic control that generate fluctuations on a wide range of time scales [20].

It is known that sleep and wake phases in the circadian rhythms are associated with periodic changes in key physiological processes [2,3,21]. Here, we ask the question if there are characteristic differences in the scaling behavior between sleep and wake cardiac dynamics [22]. We hypothesize that sleep and wake changes in the cardiac control may occur on all time scales and thus could lead to systematic changes in the scaling properties of the heart beat dynamics. Elucidating the nature of these sleep-wake rhythms could lead to better understanding of the neuroautonomic mechanisms of cardiac regulation.

We analyze a database containing 24-hour of interbeat interval records from 18 healthy subjects and 12 patients with congestive heart failure [23]. We analyze the nocturnal and diurnal fraction of the record of each subject which correspond to the 6 hours ($n \approx 22,000$ beats) from midnight to 6am and noon to 6pm.

We apply the detrended fluctuation analysis (DFA) method [24] to quantify long-range correlations embedded in nonstationary heart beat time series. This method avoids spurious detection of correlations that are an artifact of nonstationarity. Briefly, we first integrate the interbeat interval time series and then divide it into boxes of equal length, n. In each box we fit the data with a least-squares line which represents the trend in that box. Next, we detrend the integrated time series by subtracting the local trend in each box. The root-mean-square fluctuation $F(n)$ of this integrated and detrended time series is calculated for different time scales (box sizes) n. The power law relation between the average fluctuation $F(n)$ as a function of the number of beats n in a box indicates the presence of scaling. Under such conditions, the fluctuations can be characterized by a scaling exponent α, defined as $F(n) \sim n^{\alpha}$.

We find that at large time scales ($n > 60$) the data during wake hours display long-range correlations over two decades with an average exponent $\alpha_W \approx 1.05$ for the healthy group and $\alpha_W \approx 1.2$ for the heart failure patients. For the sleep data we find a consistent crossover at scale $n \approx 60$ beats followed by scaling regime over two decades characterized by a smaller exponent: $\alpha_S \approx 0.85$ for the healthy 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 sleep heart beat dynamics is characterized by a smaller exponent [Table I and Fig. 3].

To clarify these results we perform our 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 on Fig. 2a. Both surrogate sets display uncorrelated random walk fluctuations with a scaling exponent of 1.5 (Brownian noise) [Fig. 2d]. A scaling exponent higher then 1.5 would indicate persistent correlated behavior, while exponents with values smaller then 1.5 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 anticorrelations (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 heart beat 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 a 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.

Our analysis suggests that the observed sleep-wake scaling differences are due to intrinsic changes in the cardiac dynamics. Such an interpretation is supported by several considerations. (i) The DFA method removes the "noise" due to activity by detrending the nonstationarities in the interbeat interval signal 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 wakephase datasets [Fig. 2]. Rather, the wake dynamics is typically characterized by a stable scaling regime up to $n = 10^4$ 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 6h data under both sleep and wake conditions (day-night distinction is not possible during orbital flight). We find that for all cosmonauts the heart beat fluctuations also 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, the scaling differences are persistent in time, since records of the same cosmonaut taken on different days in orbit (ranging from the 3rd to the 158th day), exhibit a higher degree of anticorrelations at sleep.

We find that even under 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 the Student's t-test) with those of the terrestrial healthy group. 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 heart beat fluctuations during sleep and wake phase are related to the 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 [2,3]. The smaller values of the scaling exponent (stonger anticorrelations) during sleep observed for all three groups may be interpreted as a result of stronger neuroautonomic control. Conversely, the larger values of the scaling exponents (weaker anticorrelations) for both sleep and wake activity for the heart failure group are consistent with a previously reported pathologic breakdown of scaling [18]. We note, however, that the average sleep-wake scaling difference remains the same (≈ 0.2) for all three groups. Surprisingly, we also note that for the studied regime of large time scales the average sleep-wake scaling difference is comparable to the scaling difference between health and disease; cf. Table I and [26].

The finding of stronger anticorrelations in the heart beat during sleep is of interest from a physiological viewpoint since it motivates new modeling approaches and supports a picture where the sleep phase emerges as a surprisingly active dynamical state. Perhaps the restorative function of sleep may relate to an increased reflexive responsiveness not only at one scale but over a broad range of time scales.

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[22] Typically the differences in the cardiac dynamics during sleep and wake phase are reflected in the average (higher at sleep) and standard deviation (lower at 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 [Fig. 1].
[23] *Heart Failure Database* (Beth Israel Deaconess Medical Center, Boston, MA). The database now includes 18 healthy subjects (13 female and 5 male, with ages between 20 and 50, average 34.3 years), and 12 congestive heart failure subjects (3 female and 9 male, with ages between 22 and 71, average 60.8 year) in sinus rhythm.
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[26] At small time scales ($n < 60$) we do not observe systematic sleep-wake differences.

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 exponent 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

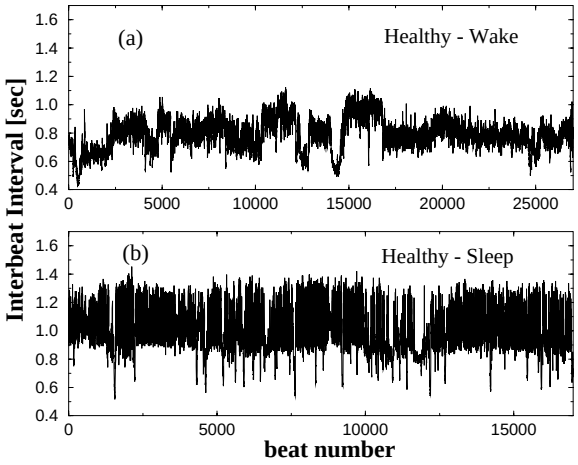

FIG. 1. Consecutive heartbeat intervals are plotted vs beat number for 6 hours recorded from the same healthy subject during: (a) wake activity: 12pm to 6pm and (b) sleep: 12am to 6am.

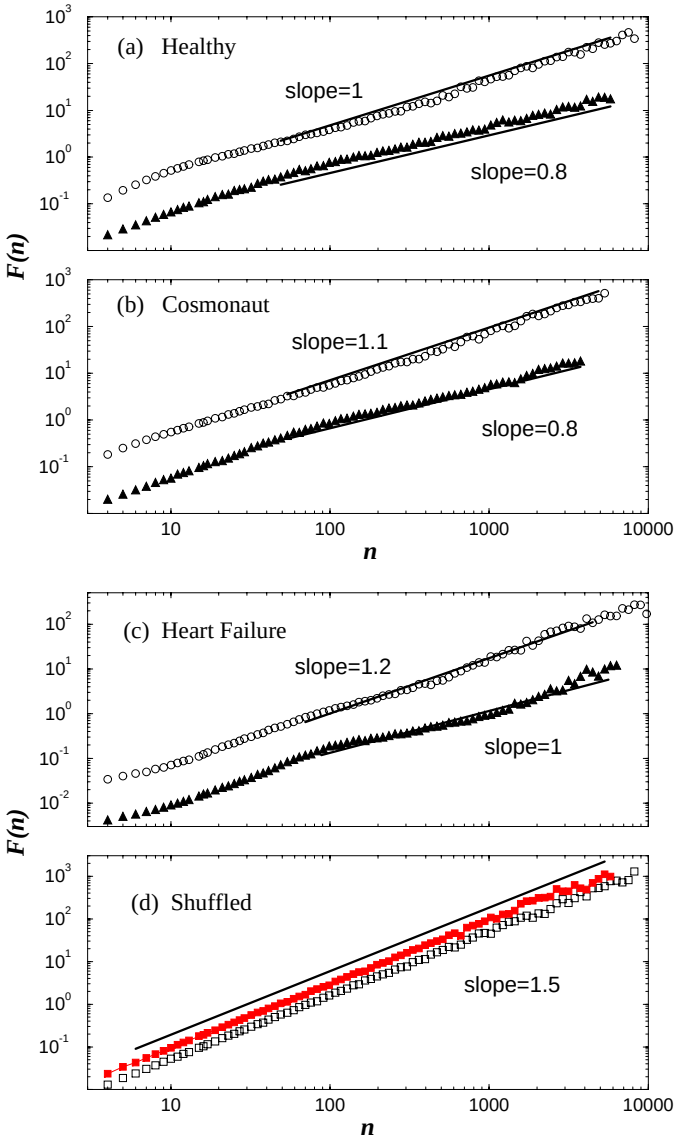

FIG. 2. Plots of $\log F(n)$ vs. $\log n$ for 6h wake (open circles) and sleep records (filled triangles) of (a) one typical healthy subject; (b) one cosmonaut (during orbital flight); and (c) one patient with congestive heart failure. Note the systematic lower exponent for the sleep phase (filled triangles), indicating stronger anticorrelations. (d) As a test we reshuffle and integrate the interbeat increments from the day and sleep records 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.

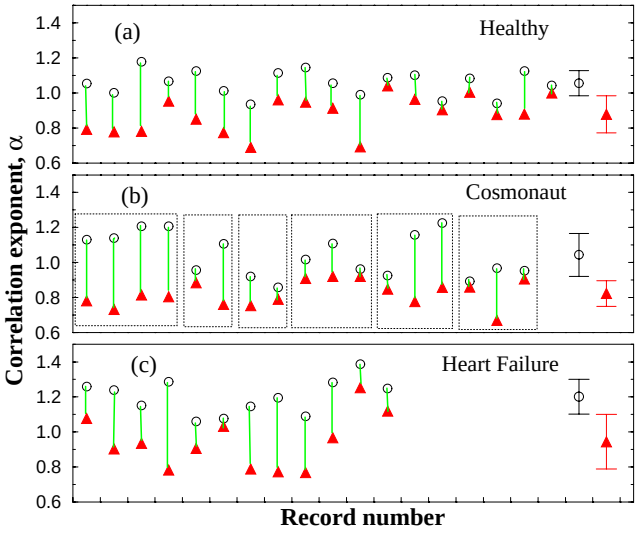

FIG. 3. Values for the sleep (filled triangles) and wake activity (open circles) exponents for all individual records of (a) the healthy, (b) the cosmonaut, and (c) the heart failure groups. For the healthy and heart failure groups each record corresponds to a different individual. Data from the 6 cosmonauts 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 night group averages and standard deviations are presented on the right of each panel.