SUPPLEMENTARY MATERIALS

Methods

Detrended Fluctuation Analysis (DFA)

The DFA method quantifies the detrended fluctuation function of heart rate at different time scales n.[1] For each chosen time scale n, the DFA method involves the following steps: i) integrating the time series; ii) dividing the integrated time series into non-overlapped bins of equal size n (the chosen time scale); iii) in each bin, fitting the integrated time series with a second order polynomial function, which defines 'local' trends assumed to be the result of external influences (second order polynomial functions were used to better remove trends in original data); iv) detrending the integrated time series by subtracting the local trend; and v) calculating the root mean square of the residuals in all bins to obtain the value of fluctuations at the time scale n. The above procedure is repeated for different time scales n to obtain the detrended fluctuation function F(n).

Effect of sampling on the detrended fluctuation analysis

Unlike other studies that used continuous beat-to-beat intervals to quantify the scale-invariant patterns in cardiac dynamics, we used heart rate data that were collected every 4 minutes based on 10-second sampling in this study. To assess possible effect of this 'sampling' procedure on the DFA results, we simulated the sampling characteristics of the current study from 10-day recordings of beat-to-beat intervals collected in five healthy human subjects that were analyzed in a previous published paper.[2] The five young subjects (4 males; 1 female) had a mean age of 25.8 years (range 20 to 33 years). Subjects had no medical disorders, as assessed by history, physical examination,

overnight polysomnography, psychological examination, a 12 lead ECG, and routine blood and urine chemistry. Data were collected during a 10-day forced desynchrony protocol, where subjects' sleep-wake behavior cycles were adjusted to 28 hours after two days of baseline. Subjects had no external time cue and stayed in a room with a constant dim light (<10 lux). The human study conformed to the Declaration of Helsinki. Beat-to-beat intervals were divided into non-overlapping 4 min windows, and in each window, average heart rate was obtained from the first 10 seconds. We applied DFA to the original beat-to-beat interval data and to the re-sampled heart rate signals. The scaling exponent of the re-sampled human heart rate data (α= 0.84±0.03; mean ± SEM) was systematically smaller than that of original human heartbeat intervals (0.99±0.02) by 0.15.

Although the amount of data available in each bin (i.e., 10 sec in each 4 minutes) can affect the scaling exponent, a separate concern is that the scaling exponent may depend on the window size (or the number of beats), which could be important because the baseline heart rate of rats is different from humans. Thus, we performed additional simulations and found that the bin size did not affect the scaling exponent so that it is not necessary to compensate for the different mean heart rates between humans and rats by using different bin sizes (e.g., 4 min for rats and 20 min for humans to achieve the same number of beats). In this additional analysis we: (1) obtained the average heart rate in non-overlapping windows of continuous beat-to-beat recordings of humans, with different window size ranging from 10 seconds to 4 minutes for different realizations, and (2) applied the DFA to the generated heart rate signals. The scaling exponent of these heart rate data was not significantly affected by window size, or number of beats (10-sec window α=0.98±0.03, mean ± SEM; 4-min window 1.03±0.05; repeated measures analysis of variance, $p>0.5$). We note that although the bin size has no influence on the

mean value of the scaling exponent, it does affect the time scale resolution and the minimum time scale of fractal behavior that can be tested. For instance, a larger bin size can lead to a smaller range of time scales and fewer data points in the detrended fluctuation function, which can statistically introduce larger variations in the results.

References

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