The effect of persistent U-shaped patterns in RR night-time series on the heart rate variability complexity in healthy humans

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Abstract

Objective: U-shaped patterns, characteristic periods of time observed in tachograms, are a specific subgroup among very low frequency components characterized by relatively short periods of smooth accelerations followed by decelerations of heart rhythm. In this study, we characterize this phenomenon and its effect on heart rate variability (HRV) parameters.

Approach: We calculated linear (the mean and standard deviation of RR intervals, RMSSD, pNN50 and the power of the frequency components) and nonlinear (V0, V1 and V2 Porta's symbolic analysis, Shannon and Sample entropy, Guzik's and Porta's asymmetry indexes, the exponents \( \alpha_1 \) and \( \alpha_2 \) of detrended fluctuation analysis and the Hurst surface \( h(q,s) \) of multiscale multifractal analysis (MMA)) HRV parameters for 65 RR interval night-time series (39 females, 37.5(11.3) years old and 26 males, 41.7(16.5) years old; all without organic heart diseases). All parameters were calculated for original data and for the three kinds of test data in which the following parts of the time series were replaced by 1/f noise: (A) the U-shape patterns annotated in a given data set, (B) randomly chosen windows of similar size as the U-shaped patterns, (C) acceleration-deceleration events shorter than U-shaped patterns.

Main results: We found that the U-shaped patterns, as the most persistent structures in RR night-time intervals series, affect the long-range correlation properties (measured by \( \alpha_2 \)). We also found that the U-shaped patterns importantly strictly affect the shape of \( h(q,s) \) surface at different scales \( s \). Removing the U-shaped patterns results in the shape of the \( h(q,s) \) surface losing the properties characteristic for healthy heart rhythm. The largest quantitative effect of U-shaped patterns was obtained for the power of the VLF component. The mean percentage difference of the VLF component between the original data and the A to C type test data were 19.4%, −4.3% and 5.3%, respectively.

Significance: Although percentage contribution of U-shaped patterns is small compared to the whole night-time series (on the average 3.1%(1.7%) with a standard deviation of 1.7%), these patterns have a considerable impact on the HRV parameters describing the VLF, persistency, nonlinear correlations and multifractal properties.

1. Introduction

The complexity of the RR interval time series, which consists of the time intervals between consecutive R peaks annotated in an electrocardiogram (ECG), is a product of a nonlinear combination of many physiological processes (Huikuri et al 2003, Voss et al 2009). The word 'complexity' means, in this context, a specific set of properties expressed in the form of short-time and long-range correlations, self-similarity, a characteristic power spectrum, persistency and/or multifractality (Ivanov et al 2001).
Figure 1. Examples of U-shaped patterns observed in a RR time interval series at night obtained from a healthy subject. The arrows in the tachogram from the whole night (a) indicate selected, representative U-shaped patterns in the time series. These examples are depicted in figures (b) and (c), respectively. In addition, in figure 1(d) we show an example of a short acceleration-deceleration event which was not classified as U-shaped due to a too-short duration and symmetric acceleration and deceleration slopes.

The main physiological foundation of these properties, neural autonomic control, varies under many oscillatory mechanisms at different scales (Hagerman et al. 1996). Many models of heart rate variability (HRV) reconstruct these properties, with various performance quality, using random (stochastic) processes such as: 1/f noise (Peng et al. 1995), bimodal cascade (Lin and Hughson 2001), inverse Fourier transform with shuffled phases of a predefined spectrum (Mcsharry et al. 2002, Mcsharry and Clifford 2005), or random variables based on exponential and power law distributions (Kantelhardt et al. 2003).

Although a major part of heart rate variability appears to be 1/f noise, a detailed observation of real data, especially during the night, reveals periods of persistency which cannot be obtained using stochastic models. These periods of the time, observed in tachograms, have a characteristic shape similar to the 'U' letter with very smooth and asymmetric slopes. Examples of such U-shaped patterns are presented in figure 1(b) and (c). An example of a pattern which was not classified as U-shaped, due to a too-short duration, symmetric acceleration and a too-small relative amplitude, called later in this paper as short acceleration-deceleration event (the criteria of U-shaped patterns classification are described in chapter III A. U-shaped pattern detection), is presented in figure 1(d).

Initially, the first effects of the U-shaped patterns were obtained in the heart rate variability (HRV) model described in Soliński et al. (2016). The model was an extension of an earlier model created by Kantelhardt et al and based on a random process associated with sleep architecture (2003). The parameters of the model allow us to determine the mean value of RR time intervals, the power of the cardiorespiratory interactions or the level of the correlations of RR time intervals in a particular sleep phase. An additional model extension, introduced in Soliński et al (2016), was the incorporation of synthetic U-shaped patterns simulated using two parabolic functions joined at the local minimum and modulated by normal distributed random variables. Analysis of the simulated data showed that the addition of the synthetic U-shaped patterns changes the multifractal properties of the data, making it resemble more the properties of real heart rate variability recordings of healthy individuals.

U-shaped patterns have not been widely described before. Yazdani et al showed that the number of U-shaped patterns varies from night to night in individual patients (2018) and revealed only a moderate correlation between U-shaped patterns and movements during the sleep (2019). Moreover, our preliminary observations using polysomnography (PSG) recordings showed that they are not associated with one sleep stage. However, the scope of this study was not to describe the physiological mechanisms and possible origins of U-shaped patterns.

The aim of this paper was to observe as many as possible effects of the U-shaped patterns on HRV properties obtained from healthy subjects and set the directions for the analysis of the other groups of
patients (e.g. with sleep disturbances) for future studies. We also wanted to compare this effect to the influence of short acceleration-deceleration events which occur much more frequently in RR time interval series. Therefore, we wanted to describe these effects in an as thorough as possible, detailed way using a variety of HRV parameters (in the time and frequency domain, linear and nonlinear methods).

2. Data

Heart rate variability data were extracted from two anonymous 24 h Holter ECG databases of the Institute of Cardiology (Warsaw, Poland) and the Medical University of Gdańsk (Gdańsk, Poland). Sixty-five RR interval time series, obtained from 39 females, 37.5 (11.3) years old and 26 males, 41.7 (16.5) years old, without organic heart disease, were analyzed. All signals were checked for artifacts by qualified cardiologists. Several recordings contained sporadic abnormally long RR intervals (>4 s) which were removed from the time series. The sampling frequency of the data was 128 Hz.

U-shaped patterns were detected for 63 RR time interval series. In two cases there were no such patterns and these recordings were excluded from the comparative analysis.

3. Methods

3.1. U-shaped patterns definition and detection

The first step to discriminating the U-shaped patterns was to observe all acceleration-deceleration events that occurred in the RR intervals time series and find some specific features of this phenomenon. In general, we observed two groups of acceleration-deceleration events: those that we consider to be the U-shaped patterns and shorter events usually with a smaller amplitude (comp. figure 1). The differences of the properties of the two groups led us to specify what is a U-shaped pattern.

We defined it as an acceleration-deceleration event, where the acceleration takes a longer time than the deceleration following it (the shape of the patterns is similar to a mirror image of the letter ‘U’ written using an italic font). The duration of these patterns is within 20–40 s. For the night-time periods, we assumed that the amplitude of a U-shaped pattern should be smaller than 85% of the mean RR interval. This last criterion is not met for the U-shaped patterns found during the day because the mean value of the RR intervals was smaller than the mean at night and some U-shaped patterns could not be discerned from normal, local variations of the RR intervals. Moreover, detection of the U-shaped patterns during the day was more difficult than during the night due to interruptions by the daily physical activity and by other external factors. Considering these difficulties, we decided to limit the analysis of the RR interval time series to night-time periods only.

We used a simple threshold method for determining candidates for U-shaped patterns. We detected all local minima of RR intervals less than 85% of mean RR interval calculated for whole night-time signals. Next, we found the onsets and offsets for each candidate as the RR interval indexes where the differences between the value of the local minimum of the candidate and the particular interval exceeded the threshold $2\sigma$, where $\sigma$ was the standard deviation calculated within the range of ±100 intervals from the local minimum. All candidates which lasted less than 20 s were excluded. Finally, we manually checked every RR interval time series in short, contiguous windows (500 intervals) and classified most of the minima preselected automatically as U-shaped patterns.

3.2. U-shaped patterns features

Simple properties of the U-shaped patterns were determined: the number of U-shaped patterns in the RR time series, their contribution to the whole series (in percent; calculated as a percentage of the number of RR time intervals which create U-shaped patterns compared to all intervals in the recording), the mean length of the patterns in the number of RR intervals and in seconds and also their relative amplitude (with respect to the nighttime mean RR interval).

3.3. Short acceleration-deceleration events

Short acceleration-deceleration events were detected using a self-adapted, iterative algorithm based on the similarity analysis of the candidates for these events with predefined pattern. The algorithm follows three steps:

1. Determining the initial pattern of short acceleration-deceleration event: the first step was to determine the pattern of short acceleration-deceleration event by averaging (with 95% confidential intervals, 95%CI) all RR time interval periods which met the following criteria: (a) monotonic decreasing of at least four RR time intervals (minimum length of the left slope), (b) local minimum of the candidate less than 85%
of mean RR interval calculated in 100-intervals length window (from both sides of the candidate), (c) the amplitude of left and right slopes larger than 15% of mean RR intervals calculated in the 100-intervals length window. The index of the beginning of the candidate was the first interval of monotonic decreasing of RR intervals; the last index of the candidate was the last interval of monotonic increasing of RR intervals after achieving the local minimum. An additional action was to exclude all events which were previously classified as U-shaped patterns in point 3.1. All of the candidates that met these criteria were used for calculating the pattern of the short acceleration-deceleration event. The length of the pattern was 21 RR time intervals with the local minimum in the middle.

(2) Updating of the pattern: the second step was to match the pattern with the new sets of candidates selected using only criterion (a). The candidates were compared with the pattern and its upper and lower 95%CI using the cross-correlation function (thus, three correlation coefficients were calculated for each candidate). All candidates for which the largest correlation coefficient was larger than 0.85 and the minimum value of the candidate was less than 85% of the mean of RR intervals calculated in a 100-intervals length window were selected for calculating the new pattern of the short acceleration-deceleration event.

(3) Obtaining the final set of events: step (2) was repeated 10 times until a constant number of the candidates that meet the criteria of the similarity were achieved. All candidates which were used for calculating the 10th level pattern were taken to be a short acceleration-deceleration event. The last step was a visual inspection of all recordings and in short, contiguous windows (500 intervals) the final annotation of the events was determined.

3.4. Test data
To determine the effect of the U-shaped patterns on heart rate variability, for each RR time interval series three kinds of test data were formed: (A) the annotated U-shaped patterns were replaced by 1/f noise; (B) randomly chosen windows were replaced by 1/f noise; (C) short acceleration-deceleration events were replaced by 1/f noise.

We used three different methods to create the test data. For the first, we created a sequence of intervals using a random permutation. As the second, we used 1/f noise to substitute for each U-shape RR interval sequence. Finally, we used random variables from a uniform distribution to substitute for each sequence of RR intervals forming a U-shaped pattern. We did not observe significant differences of the results obtained using these test signals. We selected the 1/f noise as a ‘filler’ because it was found to be a good approximation of the scaling properties of heart rate variability observed for healthy subjects (Ivanov et al 2001). The mean and standard deviation of RR intervals used as the inputs for generating the noise periods were calculated in 100-length RR intervals windows. However, adding 1/f noise (and any other noise) alone is not completely neutral and also affects HRV parameter values. The study of this effect was the main motivation for considering group B surrogate data in the analysis.

For a given RR interval series analyzed, the number and lengths of the random windows used in the test data sets were the same as those for the annotated U-shaped patterns. Thus, the number of intervals in the signals compared was the same. The rationale for this approach was to compare the effect on the properties of the time series due to the removal of the U-shape patterns with the effect of removing random windows from the signal without the loss of the number intervals.

The number of shorter acceleration-deceleration events is different than U-shaped patterns, so the sharing of added noise is slightly different and here the disproportion with cases A and B could not be avoided. However, this is not a significant weakness of the analysis, because its purpose was to check how the HRV parameters will change when we remove one type of event (or random windows) and replace it with noise, while the remaining types of events occur in the signal.

3.5. HRV parameters
HRV parameters were calculated for the original and the test data. The null hypothesis is that the mean values of the HRV parameters between these datasets are equal. The alternative hypothesis is that there are significant differences of the HRV parameters between the original and the test data.

The complexity of RR time interval series was evaluated using nonlinear methods such as: Shannon entropy (1948), sample entropy (Richman and Moorman 2000), detrended fluctuation analysis (DFA) (Peng et al 1995) and multiscale multifractal analysis (MMA) (Gieraltowski et al 2012).

DFA describes scale-invariant (fractal) correlations embedded in a non-stationary time series. The mathematical tool used in this method is the fluctuation function F(n) which calculates the amount of fluctuations in a locally detrended time series at different scales (estimated separately in windows of length n). Typically, the value of the F(n) function increases with the length of the window. This relationship, in double log scale, can be characterized by a scaling exponent α which is a measure of information about the autocorrelation in the time series, where α < 0.5 indicates an anti-correlated (or anti-persistent) time series;
The case of $\alpha = 1$ indicates 1/f noise and $\alpha = 3/2$ Brownian noise. A constant value of the exponent $\alpha$ within a range of scales indicates fractality of the analyzed signal. In this study, the scaling exponent $\alpha$ was calculated for different time scales to distinguish the short- and long-range correlations. The scaling exponent $\alpha_1$ for short scales was calculated by a least squares fit of $\log F(n)$ vs $\log n$ for $4 \leq n \leq 16$, while the exponent for the long-range scales was calculated for $16 \leq n \leq 64$. An extension of the DFA method, taking into account multifractal properties in many time scales simultaneously, is MMA. The result of the method, the local Hurst exponent $h(q,s)$, is a two-dimensional surface which, similarly to DFA, is a measure of long-range correlations in the time series but it depends both on the scale $s$ and the magnitude of the fluctuations (through the parameter $q$). This makes MMA a sophisticated method for analyzing multifractal properties of time series. The range of scales obtained by this method for heart rate variability corresponds mostly to the very low frequency band. Implementation of DFA and MMA are available for general use in the PhysioToolkit on the Physionet (Goldberger et al 2006).

Linear methods in the time and frequency domain were also used as a complementary analysis of the effect of U-shaped patterns. The calculated time domain linear parameters were: the mean RR interval, standard deviation of normal heart beats (SDNN), pNN50 and RMSSD. Frequency domain analysis was performed by calculating the power spectrum of the RR time series using the fast Fourier transform in three frequency bands: the very low frequency (0–0.04 Hz), the low frequency (0.04–0.15 Hz) and the high frequency (0.15–0.4 Hz) bands in the form of direct (HF, LF and VLF) and relative parameters (LF/HF, LFnu/LF, LF/HF, where $X_{\text{nu}} = X_F/(L + H)$ and $X = L$ or $H$).

Symbolic analysis used here was based on the method by Porta et al (2001). The output of this method are two parameters: $V_0$ related to a low variability of RR intervals and the opposite case: the $V_2$ parameter depending on a high variability. These parameters are also estimators of the time series persistency—the larger $V_0$ (and smaller $V_2$), the higher (lower) level of the signal persistency. According to the original article, the two parameters may be associated with the activity of the sympathetic and parasympathetic branches of the autonomic nervous system (Porta et al 2001). Considering the asymmetry of the U-shaped patterns (the acceleration takes a longer time than the deceleration following it), we used irreversibility analysis as well. Irreversibility analysis is dedicated to detecting a class of nonlinear dynamics as a result of the presence of asymmetric patterns. We used (1) Porta’s index (2006) which is the percentage of the negative differences between consecutive RR intervals ($\Delta RR < 0$) with respect to the total number of $\Delta RR$ differences, and (2) Guzik’s index (2006) calculated as the dispersion of $\Delta RR$ from diagonal in a Poincaré plot.

### 3.6. Statistical analysis

The results of computation of the HRV parameters are presented as $X(Y)$, where $X$ means arithmetic mean and $Y$ means the standard deviation (STD). To compare HRV parameters, the mean percentage differences and 95% confidence intervals between original and processed data were calculated. To determine the significance of these differences, a paired $t$ Student test or paired Wilcoxon rank sum test was used, depending on the normality of the results and equality of the variances.

Correlation between the age and the U-shaped pattern features was evaluated using the Pearson coefficient. The differences of these features for female and male subjects were evaluated using unpaired $t$ Student test or Mann–Whitney test. For all calculations, we used MATLAB 2019a and R Studio (v. 1.2.1335) with R version: 3.6.0.

### 4. Results

The total number of the U-shaped patterns detected during the night-time RR time series equaled 1374 (which was 85% of all detected U-shaped patterns including the ones occurring during the day). The mean number of these events at night per recording was 21(11) (3.8(4.4) during the day) and the percentage contribution equaled only 3.1(1.7)%). The mean length of the U-shaped patterns was 37.4(5.5) intervals or 29.8(4.1) in seconds. The mean relative amplitude of these patterns was 26.5(7.0)%. Short acceleration-deceleration events were much more frequent than the U-shaped patterns. There were 3476 events detected at nights with the mean number 53(43) per recording (mean percentage contribution equaled 3.6(2.4)%). The correlation coefficient between the number of U-shaped patterns and number of shorter events calculated for each subject equaled 0.23. Figure 2 shows the averaged U-shaped pattern and averaged short acceleration-deceleration event calculated from all detected events.

There were no significant differences of the properties of the U-shaped patterns between the female ($n = 39$) and the male ($n = 26$) subjects. Correlation analysis between the properties of the U-shaped patterns and age showed that the only parameters with a significant, non-zero correlation coefficient were the number of U-shaped patterns per subject ($r = −0.39$, figure 3(a)) and the percent share of these patterns
Figure 2. Averaged (a) U-shaped patterns (solid red line) with 95% CI (dotted red lines) and (b) the short acceleration-deceleration event. All detected U-shaped patterns \((n = 1374)\) and short acceleration-deceleration events \((n = 3476)\) are marked by grey markers.

Figure 3. Correlation plot between the number of U-shaped patterns (a) and short acceleration-deceleration events (b) with age.

Figure 4. Probability density and mean values of the occurrence of the U-shaped patterns (a) short acceleration-deceleration events (b) in the last 5 h of sleep. The probability of the occurrence of the U-shaped patterns was the largest in the last hours of sleep, while the probability calculated for short acceleration-deceleration events are approximately constant in all hours of sleep.

We observed no significant correlation between the number of short acceleration-deceleration events and the age \((r = -0.19, p = 0.12, \text{figure 3(b)})\).

The probability density of the occurrence of the U-shaped patterns increases with sleep duration and is the largest in the last hour of sleep (figure 4(a)). By contrast, the probability density of the occurrence short acceleration-deceleration events is similar in each hour (figure 4(b)).

The percentage differences of HRV parameters between the original data versus the RR interval time series with U-shaped patterns replaced by 1/f noise (test data A), the case of randomly chosen windows replaced by 1/f noise (test data B) and short acceleration-deceleration events replaced by 1/f noise (test data C) are presented in table 1. The largest difference between original data and one of the test data, in the time domain, was observed for pNN50 in case A (8.2%).

The changes in the frequency domain were either relatively small \((LF_\text{nu}, HF_\text{nu}, LF/HF)\) between the study conditions A and B, however, for case C LF/HF decreased by 10.8% (due to a decrease LF by 6.0% and an
Table 1. Mean values, standard deviations and percentage differences (with standard deviations and 95% CI) calculated for the HRV parameters obtained for the original data and the three test data sets: (a) U-shaped patterns, (b) random windows and (c) short acceleration-deceleration events were replaced by 1/f noise between original data and these conditions. All values of HRV parameters shown in table 1 were calculated using complete night-time RR time series.

|               | N = 63 | Case A: U-shaped pattern removal | %Diff (95%CI) | Case B: Random removal of windows | %Diff (95%CI) | Case C: Short acceleration-deceleration event removal | %Diff (95%CI) |
|---------------|--------|----------------------------------|---------------|----------------------------------|---------------|-----------------------------------------------------|---------------|
| Shannon entropy | 2.70(0.12) | 2.72(0.12) | -0.66* (-0.85– -0.48) | 2.69(0.13) | 0.29* (-0.18–0.76) | 2.70(0.12) | -0.12* (-0.22– -0.02) |
| Sample entropy | 1.15(0.26) | 1.21(0.28) | -5.1* (-7.2– -3.0) | 1.15(0.26) | -0.03 (-1.19–1.14) | 1.18(0.27) | -2.3* (-3.3– -1.3) |
| \(\alpha_1\) (DFA) | 1.12(0.20) | 1.09(0.18) | 3.2* (2.6–3.8) | 1.12(0.19) | -0.11 (-0.44–0.22) | 1.08(0.18) | 3.7* (3.1–4.3) |
| \(\alpha_2\) (DFA) | 1.02(0.11) | 0.87(0.10) | 14.4* (12.6–16.2) | 1.00(0.10) | 1.19* (0.83–1.54) | 1.01(0.11) | 0.61* (0.07–1.16) |
| Mean h(qs) | 0.86(0.06) | 0.83(0.07) | 3.8* (3.0–4.6) | 0.88(0.07) | -2.2 (-4.7–-0.3) | 0.86(0.06) | -0.11 (-0.63–0.41) |
| Mean RR | 985(116) | 990(117) | -0.51* (-0.60– -0.43) | 985(115) | 0.022* (0.006–0.038) | 987(117) | -0.25* (-0.29– -0.21) |
| STD | 109.8(43.7) | 104.5(43.3) | 5.1* (4.3–6.0) | 111.0(43.7) | -1.38 (-3.07–0.30) | 107.7(43.3) | 2.0* (1.7–2.4)* |
| RMSSD | 62.7(45.1) | 64.2(45.0) | -3.3* (-4.2– -2.5) | 63.1(44.4) | -1.25* (-1.94–-0.57) | 62.9(44.5) | -1.25 (-2.15– -0.35) |
| pNN50 | 24.6(17.0) | 25.8(17.3) | -8.2* (-10.2– -6.2) | 24.9(16.8) | -2.8* (-3.8– -1.8) | 25.4(17.0) | -5.5* (-7.5– -3.6) |
| LF | 61.7(14.8) | 61.4(13.7) | -0.03 (-0.74–0.68) | 62.0(14.0) | -0.87* (-1.44–-0.30) | 59.3(13.8) | 3.7* (3.0–4.4) |
| HF | 38.3(14.8) | 38.6(13.7) | -2.48 (-4.02– -0.94) | 38.0(14.0) | -0.20* (-1.15–-0.76) | 40.7(13.8) | -9.0* (-11.6– -6.3) |
| LF/HF | 2.11(1.50) | 1.98(1.25) | 1.95 (-0.02–1.94) | 2.07(1.35) | -0.87 (-2.30– -0.87) | 1.79(1.11) | 10.8* (8.4–13.1) |
| LF | 1950(1854) | 2080(1950) | -6.7* (-8.0– -5.4) | 2033(1910) | -4.7* (-6.5– -2.9) | 1807(1757) | 6.0* (4.2–7.7) |
| HF | 1761(3336) | 1833(3370) | -9.5* (-11.9– -7.0) | 1763(3263) | -4.1* (-6.5– -1.7) | 1786(3358) | -6.3* (-9.3– -3.3) |
| VLF | 8483(7273) | 6982(6377) | -19.4* (-21.6–-22.1) | 8663(7440) | -4.3* (-10.7–-2.2) | 8086(7101) | 5.3* (4.5–6.1) |
| V1 | 0.71(0.14) | 0.68(0.15) | 3.8* (1.4–6.1) | 0.72(0.14) | -1.56 (-3.48–0.35) | 0.69(0.14) | 1.89* (0.25–4.04) |
| V2 | 0.23(0.10) | 0.24(0.10) | -4.7 (-8.7– -0.7) | 0.23(0.10) | 0.47 (-2.0–2.9) | 0.24(0.10) | -6.7* (-13.3– -0.01) |
| Porta's index | 50.5(2.0) | 50.4(1.9) | 0.25* (0.18–0.33) | 50.5(1.9) | 0.04 (-0.01–0.08) | 50.3(1.8) | 0.48 (0.37–0.60) |
| Guzik's index | 54.7(3.7) | 54.2(3.4) | 0.59* (0.34–0.85) | 54.0(4.0) | 0.99* (0.24–1.73) | 53.4(3.0) | 2.0* (1.5–2.6) |

*p < 0.05, ** -11.2 (-16.4– -6.0) after removing outliers (case A); *** -5.6 (-9.8– -1.6) after removing outliers (case C).
Figure 5. Examples of h(q,s) surfaces obtained from MMA using the original data (a) and signals under the following conditions: (b) the U-shaped patterns were replaced by 1/f noise, (c) n random windows were replaced by 1/f noise, where n is the number of the annotated U-shaped patterns (n = 38 in this example); the length of the windows correspond to the lengths of the U-shaped patterns in the particular signal, (d) RR time interval series were shuffled except for the U-shaped patterns, (e) all RR time intervals were shuffled, (f) short acceleration-deceleration events were replaced by 1/f noise. A characteristic ‘ridge’ along the range of q parameter between 0 and 2 and whole range of scales s was marked in (a) by red ellipse.

increase of HF by 6.3%). There was a much larger difference for the VLF parameter for case A versus B and C: 19.4% in case A vs 4.3% in case B and 5.3% in case C.

Large differences were observed also in case A and case C for symbolic analysis, especially for the parameter V2. However, there were two outlier values found for this parameter. After removing them from the results, the percentage difference decreased from −36.3% (95%CI: −80.5%−7.5%) to −11.2% (95%CI: −16.4%−6.0%) in case A and from 11.3% (95%CI: −20.3−2.3) to −5.6(95%CI: −9.6−1.6) in case C.

Irreversibility analysis (Porta’s and Guzik’s indexes) showed similar results considering U-shaped pattern removal (test data A), random removal of windows (test data B) or removal short acceleration-deceleration events. The percentage differences of Porta’s and Guzik’s indexes between the original data and test data A,B and C were not larger than 2%.

Test data A (substitution of the U-shaped patterns by 1/f noise), in comparison to the other test data, caused a larger change of sample entropy (−5.1% vs. -0.03% in test data B and −2.3% in test data C) than obtained for Shannon entropy (−0.66% vs. −0.29% for test data B and −0.12% for test data C). The mean percentage change of the DFA α-exponents were also higher for test data A vs. B vs. C (3.2% vs. −0.11% vs. 3.7% for $\alpha_1$ and 14.4% vs. 1.19% vs. 0.61% for $\alpha_2$ DFA).

Examples of the shapes of the Hurst surfaces calculated for a single RR interval time series under different conditions are shown in figure 5. The shape depicted for the original data (part a) has a characteristic ‘ridge’ along the range of q parameter between 0 and 2 and for all scales s (although the ‘ridge’ changes direction for lower scales). Such a ridge is observed usually for healthy subjects (this ‘ridge’ is marked in figure 5(a) by a red ellipse) (Gieraltowski et al 2012, Kokosińska et al 2018). Figure 5(b) depicts the shape of the Hurst surface obtained from the same RR time series, but with the U-shaped patterns replaced by 1/f noise. The characteristic ‘ridge’ has disappeared and the whole surface is flatter. In contrast, the shape of the surfaces in figure 5(c) obtained for the RR time series with randomly situated windows replaced by 1/f noise is similar to the original surface. The surfaces shown in figures 5(d) and (e) were calculated from still other test data—in both the samples of the original time series were randomly shuffled, but in figure 5(d), the U-shaped patterns were retained at their locations. In both cases (figures 5(d) and (e)) the mean h(q,s) exponent was smaller than for the original time series. In the case presented in figure 5(e), the h(q,s) surface is flat for whole range of parameters q and s. Note, however, that this is in contrast to the surface in figure 5(d) where the shape of the surface is similar to the one obtained from the original data, apart from the area of very small scales s and the smallest negative values of the q parameter. The h(q,s) surface in figure 5(f) was calculated after replacing short acceleration-deceleration by 1/f noise and as in figure 5(c) it is similar to the original surface (figure 5(a)).
5. Discussion

The largest impact of the U-shaped patterns on the HRV parameters was for the VLF component. Removing these patterns from RR time series (test data A, see section 3) caused a reduction of the VLF component on average by 19.4%.

It is not completely clear which factors affect the VLF component of the RR time intervals. Standard explanation of VLF fluctuations of RR time intervals associates them with thermoregulation and/or humoral regulation (Togo et al 2005, Tripathi 2011). This frequency band was found to be a predictor of congestive heart failure (Hadase et al 2004) and infectious complications in the immediate post-stroke period (Brämer et al 2019). In these both studies, the VLF component, calculated from night-time recordings, decreased in the observed group in comparison to the control group, however there were no investigation on which specific features of RR time interval series changed. Khatri and Freis (1967) followed by Togo et al (2005) study suggest that in healthy humans, sympathetic nervous system activity might occasionally be activated in deep sleep and cause nonstationary periodic patterns in VLF. Changes of VLF were also correlated with physical activity in stroke patients (Usui and Nishida 2015a) and mental tasks (2015b).

We found that the reduction of VLF depends on the number of the U-shaped patterns (figure 6). The Pearson correlation coefficient obtained for the correlation of the number of the U-shaped patterns and the percentage difference of VLF calculated between the original and test data type A (the U-shaped patterns replaced by 1/f noise, see section 3) equals 0.67. Strong correlation coefficients are also observed for $\alpha_1$, $\alpha_2$ and mean $h(q,s)$ exponents (0.56, 0.73 and 0.50, respectively). This shows that DFA and MMA are very sensitive to the occurrence of these events.

Such a high correlation between the number of U-shaped patterns and VLF is not so unexpected when we consider the fact that the U-shaped patterns is a fluctuation with a period of approximately 60 s (if we assume that one U-shaped pattern is equivalent to a half period of a sinusoidal function). This period corresponds to a frequency of 0.0167 Hz which is within the VLF frequency band. Based on the Wiener–Khinchin theorem (Wiener 1930, Khinchin 1938), the changes in the power spectrum due to the removal of the U-shaped patterns should be directly associated with the changes in the autocorrelation of the signal. In contrast, we found lower values of Pearson correlation coefficients calculated in an analogously analysis for the shorter acceleration-deceleration events: 0.26 for VLF, $p = 0.04$; $-0.18$ for mean $h(q,s)$, $p = 0.15$; $0.41$ for $\alpha_1$, $p < 0.001$ and $-0.26$ for $\alpha_2$, $p = 0.04$. These results suggest that the number of short acceleration-deceleration events does not determine directly their effect on the long-term HRV parameters.

The largest effect of the U-shaped patterns on the linear parameters in the time domain was observed for pNN50. This is a predictable result, because within the U-shaped patterns consecutive RR intervals do not differ by much (certainly less than 50 ms). Thus, when we replace them by 1/f noise (so with a signal with a much larger variability between consecutive samples), the mean value of pNN50 increases. Some studies consider also thresholds different than 50 milliseconds for this parameter, which is generally called pNNx (Mietus et al 2002). We calculated additionally the mean percentage differences between original data and the case A (U-shaped patterns replaced by 1/f noise) for pNNx, where $x$ was within the 10–100 milliseconds range. We found that mean percentage differences between the datasets considered vary from $-1.1\%$ for 10 ms to $-36.8\%$ for 100 ms. Thus, the larger the $x$ threshold, the larger the difference of pNNx we should expect between the original data and case A. Some studies indicate that pNNx for $x < 50$ ms have a larger discrimination potential between healthy subject and patients with chronic heart failure (CHF) (Mietus et al...
independent of the age. In turn, we observe a similar effect of the short acceleration-deceleration events (in persistency, affect long-range correlation properties (measured by baroreceptors activity (Cohen and Taylor 1983, Franco et al 2003). The adaptive value of sighs seems to be in preventing atelectasis. They can be followed by central apnea events or can occur as isolated events (Nguyen et al 2012). Sighs are associated with cardiac response and decreasing-increasing patterns of heart rate (Perez-Padilla et al 1983, Eiselt et al 1992, Franco et al 2003). Perez-Padilla et al (1983) showed that in a group of 12 healthy adult volunteers (mean age 28.5), the mean number of sighs during sleep per subject was 10.33(7.85). In our study, the mean number of U-shaped patterns was 21(10), and even more in a subgroup of younger subjects. However, both U-shaped patterns and sighs are characterized by great intrasubject variability (1–25 sighs vs. 0–46 U-shaped patterns). Comparison of RR time intervals series with respiratory signals during sleep is necessary for the latter analysis. This will, however, require the analysis of polysomnographic data which was not done in the present text.

The U-shaped patterns appear to be different from the asymmetry phenomenon observed by Porta et al (2006) and their effect on the indexes of asymmetry is comparable with replacing the random windows by 1/f noise (test set B, see table 1). The RR time intervals that create the U-shaped patterns are always the shortest intervals in the whole signal while the asymmetry phenomenon described in the Porta et al study concerns a wide range of RR intervals values and much shorter patterns of acceleration-deceleration events which are distributed relatively evenly during the whole night-time RR time interval series. Such a description fits better to the short acceleration-deceleration events, observed in our study. Note that the U-shaped patterns are relatively rare events of asymmetry.

Increasing heart rate due to leg movements seems also to not be linked to the U-shaped patterns in RR time series. Winkelman (1999) showed the patterns of acceleration-deceleration of heart rate in response of periodic leg movement during sleep, but the time of these events are shorter (about eight cardiac cycles) then the average time of U-shaped patterns. They are similar to the short acceleration-deceleration events.

In a previous study, we found that the U-shaped patterns and ageing are responsible for the modulation of the different scales of autocorrelation and so of the fractal properties (Soliński et al 2019). We divided the night-time RR time interval series used in this study, into two groups (32 subjects in one group and 33 subjects in the second group) according to the number of U-shaped patterns. The cutoff level for the number of U-shaped patterns separating the two groups was 20 patterns per recording. We calculated the percentage differences for the HRV parameters values between these groups. We found that the percentage differences between the two groups for the mean RR intervals, the standard deviation, RMSSD, pNN50, the power of HF, LF and VLF, the symbolic parameters V0, V2, Shannon entropy, Sample entropy and the DFA α2 exponent were significant. Next, we repeated the same comparison analysis but with regard to age. We divided the night-time RR time interval series used in this study, into two groups. In the first group there were the subjects under 39 years (32 subjects) and in the second group the older ones (33 subjects). The results showed statistically significant percentage differences for most linear HRV parameters such as: the SDNN, RMSSD, pNN50, LFnu, HFnu, LF/HF, LF, HF, VLF but only one nonlinear parameter: α1. While a significant decrease of short-range correlation (measured by α1) with age can be explained by a reduction of baroreceptors activity (Cohen and Taylor 2002), the occurrence of the U-shaped patterns, each a short period of persistency, affect long-range correlation properties (measured by α2). This effect is found to be independent of the age. In turn, we observe a similar effect of the short acceleration-deceleration events (in comparison to U-shaped patterns) on α1 exponent, but a very small effect on α2 exponent.

In the DFA method, the mean variation (or fluctuation function to be precise) of the detrended signal is calculated in windows of different lengths (i.e. for different scales). For short scales (approximately shorter than the length of U-shaped pattern), the U-shaped patterns are removed during the DFA procedure and do not affect the scaling exponent. For large scales, these patterns increase the variance of the signal. Because the fluctuation function depends on the square of the increments of the RR intervals, the U-shaped patterns, as outliers, have much more influence on its value than the rest of the signal. This effect is enhanced by the fact that the larger the scale, the more U-shaped patterns occur within the given window.

In turn, the changes in the correlation at different scales are also visible in the modulation of the shape of the Hurst surface h(q,s) obtained from MMA. Removing the U-shaped patterns from the RR time interval series resulted in a flattened shape of h(q,s) surface, especially affecting the characteristic ‘ridge’ typical for heart rate variability in healthy individuals. This result is not so unexpected although the U-shaped patterns...
are on average only 3.1% of the whole night-time signal. These patterns have the most laminar (large persistency) in comparison to the rest of the RR interval time series. However, short acceleration-deceleration events do not change the shape of the Hurst surface; they are fluctuations from the border of the VLF and LF bands and are taken into account by MMA. These observations should be also be taken into account in the interpretation of the results obtained, in general, by other nonlinear and multifractal analyses.

6. Conclusions

The U-shaped pattern in heart rate variability is a phenomenon observed both in male and female healthy subjects from all age groups. There is a moderate correlation between the age of the subject and the number of these events ($r = -0.39$). The U-shaped patterns have a considerable impact on the HRV parameters characterizing the very low frequency power spectrum, persistency, nonlinear correlations (for long-range time scales) and multifractality properties, although the sum of the lengths of the patterns in a given RR interval time series is relatively small compared to the whole night-time time series (3.1(1.7)%). They are the most laminar and persistent structures in the night-time signals. In turn, short acceleration-deceleration events, occurring approximately 2.5 times more often, have less impact on the nonlinear properties of HRV. They are also less correlated with the age and are equally distributed during the whole sleep period, in contrast to U-shaped patterns (figure 4). These observations suggest that U-shaped patterns and short acceleration-deceleration events may have a different physiological background.

The effect of the U-shaped patterns on HRV properties appears to be much stronger than expected from their total length compared to the length of the signal (usually only 3–4 %). This fact should be taken account in the future analysis of phenomena in heart rate variability, especially in the case of its clinical significance.

A limitation of this study was to focus only on RR time interval series. We proposed some potential physiological events which may be associated with U-shaped patterns during sleep; they can be analyzed using polysomnography recordings in future studies. It will be particularly interesting to investigate the relationship between the changes in the nonlinear properties of HRV signal during particular sleep stages (as observed by Kantelhardt et al (2002)) and the occurrence of U-shaped patterns and their coincidence with respiratory events.

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