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Different approaches of symbolic dynamics to quantify heart rate complexity

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Abstract— **The analysis of symbolic dynamics applied to physiological time series is able to retrieve information about dynamical properties of the underlying system that cannot be gained with standard methods like e.g. spectral analysis. Different approaches for the transformation of the original time series to the symbolic time series have been proposed. Yet the differences between the approaches are unknown. In this study three different transformation methods are investigated: (1) symbolization according to the deviation from the average time series, (2) symbolization according to several equidistant levels between the minimum and maximum of the time series, (3) binary symbolization of the first derivative of the time series. Each method was applied to the cardiac interbeat interval series RR_i and its difference ΔRR_I of 17 healthy subjects obtained during head-up tilt testing. The symbolic dynamics of each method is analyzed by means of the occurrence of short sequences ('words') of length 3. The occurrence of words is grouped according to words without variations of the symbols (0V%), words with one variation (1V%), two like variations (2LV%) and two unlike variations (2UV%). Linear regression analysis showed that for method 1 0V%, 1V%, 2LV% and 2UV% changed with increasing tilt angle. For method 2 0V%, 2LV% and 2UV% changed with increasing tilt angle and method 3 showed changes for 0V% and 1V%. In conclusion, all methods are capable of reflecting changes of the cardiac autonomic nervous system during head-up tilt. All methods show that even the analysis of very short symbolic sequences is capable of tracking changes of the cardiac autonomic regulation during head-up tilt testing.**

I. Introduction

Physiological time series such as the series of successive cardiac interbeat intervals, i.e. heart beat periods, contain rich information. Different linear and nonlinear approaches have been used to characterize dynamical features. E.g. spectral analysis has been used to quantify the amount of sinus-like oscillations, thus disregarding statistical moments of order higher than two. Low (0.04-0.15 Hz) and high frequency (0.15-0.4 Hz) oscillations have then been linked to the modulations of both branches of the autonomic nervous system (ANS) [1-3]. Dynamical aspects of physiological time series may be analyzed by means of symbolic dynamics. Different approaches have been developed and applied to physiological time series. One approach to symbolize the times series is based on the amount of deviation from the average heart rate (or, equivalently, average interbeat interval) [4,5]. The complexity of the resulting symbolic patterns has been quantified using Shannon or Renyi entropy [5]. Furthermore, the amount of occurrence (or non-occurrence, i.e. 'forbidden words') of symbolic patterns complements information retrieved from spectral analysis in patients threatened by sudden cardiac death [6]. This symbolization approach has also been extended to quantify time-delayed couplings between e.g. heart rate and blood pressure modulations [7] or to quantify cardiorespiratory interaction [8]. Another approach spans the interval between the minimum and the maximum of the time series over a fixed amount of symbols [9]. This interval is divided into several equidistant steps. The resulting symbolic patterns were classified according to the amount of variations in the patterns. The amount of occurrence of patterns with 0, 1 or 2 variations also complements the information from spectral analysis of a cardiac interbeat interval series [10,11]. The analysis of symbolic patterns during graded head-up tilt showed that the occurrence of specific symbolic patterns is linked to sympathetic and parasympathetic modulations of the ANS [11]. A third approach uses only two symbols and is used in two different ways. One method symbolizes the succession of acceleration and deceleration of the instantaneous heart rate [12,13] Using this method it has been shown that the interbeat interval series from healthy subjects contains a large amount of regular binary patterns, i.e. patterns with a low number of changes between 0s and 1s [14]. Furthermore, these patterns are also capable of reflecting changes of the cardiac autonomic regulation during head-up tilt [15,16]. The occurrence of regular binary patterns is linked to sympathetic modulations whereas the occurrence of irregular binary patterns is linked to parasympathetic modulations. The other method distinguishes between small and large differences between successive interbeat intervals using two symbols [5]. It has been shown that this approach is able to detect differences in heart rate dynamics before the onset of ventricular tachycardia [17] or during different stages of general anesthesia [18]. Both methods retain relevant dynamical properties although a considerable amount of information is disregarded. Each approach to symbolize the interbeat interval series retrieves specific information that cannot be gained with standard methods like e.g. spectral analysis. However, it is unclear if the approaches deliver different

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information. In this study we compare three different symbolic dynamics approaches in their ability to track the changes in cardiac sympathetic and vagal modulations during graded head-up tilt.

II. METHODS

A. Construction of symbolic sequences

In the following three different approaches to transform a time series into a symbolic series are presented. The approaches are presented for the general case of a time series x_i.

σ-Method

The time series x_i is transformed into the symbol sequence $S_{\sigma;i}$ (i = 1,…,N) using the alphabet A = {0,1,2,3} as follows [5]:

$$S_{\sigma,i} = \begin{cases} 0 & : \quad \mu < x_i \leq (1+a)\cdot\mu \\ 1 & : \quad (1+a)\cdot\mu < x_i < \infty \\ 2 & : \quad (1-a)\cdot\mu < x_i \leq \mu \\ 3 & : \quad 0 < x_i \leq (1-a)\cdot\mu \end{cases} \tag{1}$$

This transformation transforms the time series according to the deviation from the average of x_i. The transformation uses three different quantization levels: μ denotes the average x_i, (1+a)μ and (1-a)μ are thresholds above respectively below the average according to the parameter a. In this study a is set to 0.05, i.e. the upper and lower threshold are 5% above respectively below the average. This choice has proven to yield reliable results if applied to the cardiac interbeat interval time series [5].

Max-min-Method

To obtain a symbolic time series $S_{max-min;i}$ that comprises the full range of dynamics of the time series x_i the difference between the minimum and the maximum of x_i is divided into a ξ quantization bins of size l = (max(x_i)-min(x_i))/ξ. Hence, this transformation has the alphabet A={0,1,…,ξ-1} [11]. The transformation is as follows:

$$S_{max-min,i} = \begin{cases} 0 & : \quad \min(x_i) \leq x_i < 1\cdot l \\ 1 & : \quad 1\cdot l \leq x_i < 2\cdot l \\ & \vdots \\ \xi-1 & : \quad (\xi-1)\cdot l \leq x_i \leq \max(x_i) \end{cases} \tag{2}$$

The number of quantization levels is set to ξ=6 and the sequence length is set to k = 3. This is a good compromise for short time series [11]. This defi nition is also applied to the interbeat interval series RR_i, i=1,…,N (absolute values) and to the differences between successive interbeat intervals $\Delta RR_i=RR_i- RR_{i-1}$, i=2,…,N.

Binary Δ-coding-Method

In difference to the two former methods this transformation makes use of differences between successive elements of the time series x_i instead of taking the absolute values of the time series. A binary series $S_{bin\Delta,i}$ (i=1,…,N-1) was created using the differences $\Delta x_i=x_i- x_{i-1}$, (i=2,…,N) using a binary alphabet A={0,1} [12]:

$$S_{bin\Delta,i} = \begin{cases} 0 & : \quad \Delta x_{i+1} \geq 0 \\ 1 & : \quad \Delta x_{i+1} < 0 \end{cases} \tag{3}$$

$\Delta RR_i=RR_i-RR_{i-1}$, i=2,…,N is used as the time series Δx_i. Hence, in this definition the 'decelerations' of the interbeat intervals are symbolized by 0s, 'accelerations' by 1s. A variation of this method is used for binary coding if the symbolization is to reflect small and large differences between successive interbeat intervals [5]:

$$S_{bin\Delta,\tau,i} = \begin{cases} 0 & : \quad |\Delta x_{i+1}| < \tau \\ 1 & : \quad |\Delta x_{i+1}| \geq \tau \end{cases} \tag{4}$$

Like in other studies τ=10 ms is used as threshold between small and large differences between successive interbeat intervals [17,18]. Note that the absolute values of Δx_{i+1} are used in this definition.

B. Analysis of symbolic dynamics

The dynamics of the symbolic series S_i is analyzed using symbolic sequences of length k (also referred to as 'words'). I.e. symbolic sequences are constructed using delayed coordinates as $w_i=(S_i,S_{i+1},…,S_{i+k-1})$, i=1,…,N-k+1. In this study symbolic sequences of length k = 3 are analyzed. The sequences of length k categorized according to their amount of variations between successive symbols as follows [11]:

- No variation between successive symbols (0V sequences)

- One variation between successive symbols (1V sequences)

- Two like variations between successive symbols (2LV sequences). I.e. two successive increases or decreases (e.g. '321' or '123').

- Two unlike variations between successive symbols (2UV sequences). I.e. one decrease followed by an increase or vice versa.

This categorization can only be applied to the symbolic series $S_{\sigma;i}$ and $S_{max-min;I}$ because the binary symbolic series $S_{bin\Delta,i}$ and $S_{bin\Delta,\tau,i}$ cannot differentiate between 'two like variations' and 'two unlike variations' (see below). For $S_{\sigma;i}$ this categorization of the 4^3=64 different sequences results in four 0V sequences, 24 1V sequences, 8 2LV sequences and 28 2UV sequences. The percent occurrence of these patterns were designated 0V%, 1V%, 2LV% and 2UV%. For example, 0V% was calculated as (No. of occurrence of 0V sequences)=(N-2)*100 and likewise for the other categories. For $S_{max-min;I}$ the categorization of the 6^3=216 different sequences results in six 0V sequences, 60 1V sequences, 40 2LV sequences and 110 2UV sequences. The percent occurrences of these patterns were designated 0V%, 1V%, 2LV% and 2UV%.

$S_{\sigma;i}$ and $S_{max-min;I}$ can be created using the interbeat interval series RR_i, i=1,…,N (absolute values) and the differences between successive interbeat intervals $\Delta RR_i=RR_i- RR_{i-1}$, i=2,…,N. Hence, an appropriate subscript is added to the mentioned quantities to distinguish them with respect to the original series (e.g. $0V\%_a$: 0V% for absolute values RR_i; $0V\%_d$: 0V% for differences ΔRR_i).

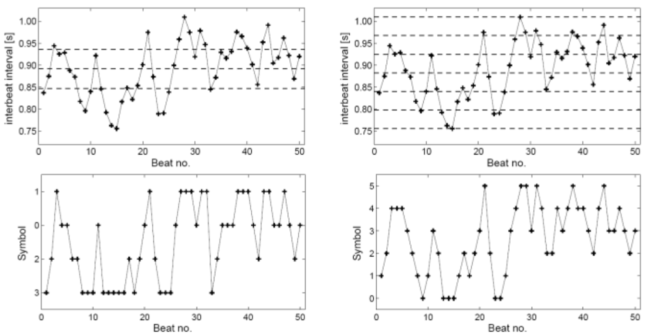

Figure 1. Examples of σ-method and Max-min-method. Top left: Transformation based on average interbeat interval (middle dashed line), average+5% (upper dashed line) and average-5% (lower dashed line). Top right: Transformation based on maximum and minimum interbeat interval and six quantization levels (see dashed lines). Lower diagrams show resulting symbolic series.

The binary sequences $S_{bin\Delta,i}$ and $S_{bin\Delta,\tau,i}$ can be categorized in a similar fashion. Again, binary sequences of length k=3 are analyzed. The classification of the 2^3=8 different sequences is analogously to the above mentioned categorization. E.g. the sequence '000' has no variation whereas e.g. '001' has one variation and '010' has two variations (0→1 and 1→0). Using this scheme the maximum amount of variations for binary patterns of length k is k-1. Hence, k = 3 results in a categorization of binary sequences in analogy to the other two symbolizations approaches: no variation: 0V (two binary sequences), one variation: 1V (four binary sequences), two variations: 2V (two binary sequences). The rate occurrences of these patterns were designated 0V%, 1V% and 2V%.

C. *Experimental Protocol*

17 healthy subjects (non-smoker, median age: 28 years, age range 21±54 years, 7 women) were enrolled in the study at the University of Milan [11]. The subjects did not take any medication, nor did they consume any caffeine- or alcohol-containing beverages in 24h before the recording. While the subjects were on the tilt table, they were supported by two belts at the level of the thigh and the waist. Both feet touched the footrest of the tilt table. The subjects breathed spontaneously but were not allowed to talk during the protocol. The study complies to the principles of the Declaration of Helsinki and has been approved by the review board of the L. Sacco Hospital, University of Milan.

ECG (lead II) was recorded during the procedure at a sampling rate of 1000 Hz. After 7 min at rest, the subject were subjected to 10 min of tilt with table angles randomly chosen within the set {15°,30°,45°,60°,75°,and 90°}. Each tilt session was preceded by a rest period and followed by 3 min of recovery. All subjects were able to complete the overall sequence of tilt table inclinations without a sign of presyncope.

D. *Data extraction*

After the QRS complex was detected on the ECG and the apex of the R wave was located using parabolic interpolation, the heart period was automatically calculated on a beat-to-beat basis as the time between two consecutive R peaks (RR interval). All QRS determinations were carefully checked to avoid erroneous detections or missed beats. The length N of the series RR_i ranged from 220 to 260 beats and was kept constant while the experimental condition was varied in the same subject.

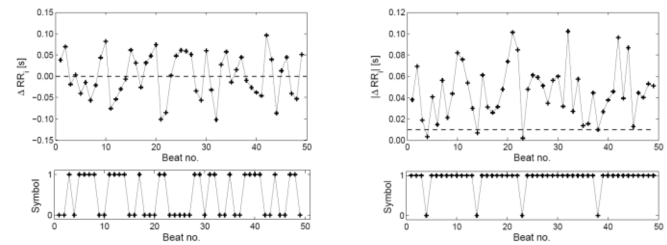

Figure 2. Examples of Binary Δ-coding-method. Left column: transformation based on acceleration ($\Delta RR_i<0$, 1s) and deceleration ($\Delta RR_i>0$, 0s) of successive interbeat intervals. Right column: transformation based on small (0s) and large differences (1s) between successive interbeat intervals (dashed line: threshold). The lower diagrams show the resulting binary series.

E. *Statistical Analysis*

Linear regression analysis between all the parameters and tilt angles was carried out using Spearman rank-order correlation. Global linear regression (GLR) was calculated using pooled data from all subjects. For individual linear regression (ILR) analysis, only one subject was considered at a time. ILR analysis was carried out only if global linear regression analysis was significant; in this case, we calculated the percentage of subjects with a significant ILR analysis (ILR%). $P < 0.05$ was considered significant.

III. RESULTS

An example illustrating the different approaches to symbolic dynamics is shown in Figs. 1 (σ- and Max-min-method) and 2 (Binary Δ-coding-methods). A qualitative comparison between the two symbolic series in Fig. 1 shows that both methods resemble dynamical aspects of the original time series. It is evident that the more quantization levels used for the transformation the more detailed the dynamical aspects. The binary representation (Fig. 2) delivers different information because it is not based on the absolute values of the interbeat interval series but on the series of differences between successive interbeat intervals. The series $S_{bin\Delta,i}$ represents each change of the sign of ΔRR, i.e. the changes between acceleration and deceleration of the heart rate. It is evident that the series $S_{bin\Delta,10,i}$ shows a more regular binary series, i.e. longer successions of successive 0s and 1s, because it distinguishes between small and large variations of $|\Delta RR_i|$ and this example mostly contains large variations.

During the head-up tilt test the average interbeat interval RR_i progressively decreases with increasing tilt angle, i.e. the heart rate increases. The results of the corresponding linear regression analysis are summarized in Table 1. The results of the global linear regression analysis correspond to the aforementioned results - the parameters of the binary coding yield the highest rates of individual linear regression (0V%: 94%, 1V%: 88%).

TABLE I. RESULTS OF GLOBAL (GLR) AND INDIVIDUAL LINEAR REGRESSION (ILR) ANALYSIS OF SYMBOLIC INDEXES VS. TILT ANGLES.

Method	RR_i			ΔRR_i		
	Index	GLR	ILR%	Index	GLR	ILR%
σ-method	$0V\%_a$	Yes	76%	$0V\%_d$	Yes	82%
	$1V\%_a$	Yes	35%	$1V\%_d$	Yes	76%
	$2LV\%_a$	Yes	59%	$2LV\%_d$	No	-
	$2UV\%_a$	Yes	65%	$2UV\%_d$	No	-
Max-min-method	$0V\%_a$	Yes	76%	$0V\%_d$	Yes	47%
	$1V\%_a$	No	-	$1V\%_d$	No	-
	$2LV\%_a$	Yes	41%	$2LV\%_d$	Yes	47%
	$2UV\%_a$	Yes	65%	$2UV\%_d$	Yes	47%
Binary Δ-coding ($S_{bin\Delta,i}$)				0V%	Yes	82%
				1V%	Yes	76%
				2V%	No	-
Binary Δ-coding ($S_{bin\Delta,10,i}$)				0V%	Yes	94%
				1V%	Yes	88%
				2V%	No	-

IV. DISCUSSION

A major finding of this study is that the three presented transformations from interbeat interval series to symbolic series are capable of reflecting changes of cardiac autonomic regulation during head-up tilt. This finding is regardless of whether absolute values RR_i or differences ΔRR_i were used to generate the symbolic series. Hence, symbolic indexes were linearly correlated with tilt angle.

It has to be noted that the graded head-up tilt test is an experimental maneuver that activates sympathetic modulations and withdraws parasympathetic modulations [20, 21]. This is reflected by the decrease of the average interbeat interval with increasing tilt angle. Using RR_i for the construction of the symbolic series $0V\%_a$ increased with increasing tilt angle for both, the σ-method and the max-min-method. Hence, they reflect the increase of sympathetic modulations. On the other hand $2LV\%_a$ and $2UV\%_a$ decreased with increasing tilt angle and, hence, they reflect the decrease of parasympathetic modulations [11]. Using ΔRR_i for the construction of the symbolic series leads to similar interpretations with respect to the max-min-method. For the σ-method applied to ΔRR_i the physiological interpretation of the indices is slightly different. $0V\%_d$ reflects sympathetic modulations because it is linearly correlated to the tilt angle. Parasympathetic modulations are reflected by $1V\%_d$ because this index is negatively correlated to the tilt angle.

Two indexes of the binary analysis were also able to reflect the changes of both branches of the ANS during graded head-up tilt. For both binary series, $S_{bin\Delta,i}$ and $S_{bin\Delta,\tau,i}$, 0V% increases with increasing tilt angle and, hence, reflects the increase of sympathetic modulations. 1V% decreases with increasing tilt angle and reflects the decrease of parasympathetic modulations. With respect to $S_{bin\Delta,i}$ both, 0V% and 1V% account for more than 80% of all binary sequences. This result suggests that large parts of the dynamical properties are hidden in the sequence of acceleration and deceleration of the instantaneous heart rate.

It seems to be obvious by the definitions that $0V\%_a$ of both, the σ-method and the max-min-method applied to RR_i, reflect sympathetic modulations whereas $2LV\%_a$ and $2UV\%_a$ of both methods reflect parasympathetic modulations: sympathetic modulations are slower than parasympathetic modulations and, hence, they are captured be $0V\%_a$. In turn, faster modulations are captured by $2LV\%_a$ and $2UV\%_a$. This observation is supported by simulations of the autonomic regulation [22]. The physiological interpretation of the indexes $0V\%_d$ and $1V\%_d$ obtained by the σ-method applied to ΔRR_i is less evident. The threshold parameter *a* (cf. equation 1) was the same regardless of whether the method was applied to RR_i or ΔRR_i. If applied to ΔRR_i symbolic sequences containing mostly zero or one variation are constructed (approx. 80% of the sequences are classified by the indexes $0V\%_d$ or $1V\%_d$) whereas two like variations hardly occur within symbolic sequences ($2LV\%_d$ is close to zero). Similar to the σ-method applied to RR_i, symbolic sequences with zero variation reflect sympathetic modulations. It has to be noted that the threshold parameter *a* could be adapted for the application to ΔRR_i. However, it remains to be explored whether a different threshold results in symbolic indexes that unambiguously reflect both branches of the autonomic nervous system.

It remains to be explored whether the relationship between symbolic indexes and modulations of the ANS could be related to some intrinsic characteristics of symbolic analysis, such as the interpretation of nonlinear components, to the elimination of conventional definition of frequency bands, or to the specific pattern decomposition scheme exploited by this analysis or strategies to group patterns into a small number of classes.

REFERENCES

[1] M. Malik et al., Circulation 93, (1996) 1043-1065
[2] G.G. Berntson et al., Psychophysiology 34, (1997) 623-648
[3] S. Akselrod et al., Science 213, (1981) 220-222
[4] J. Kurths et al., Chaos 5, (1996) 88-94
[5] N. Wessel et al., Int J Bifurcat Chaos 17, (2007) 3325-3371
[6] A. Voss et al., Cardiovasc Res 31, (1996) 419-433
[7] A. Suhrbier et al., Chaos 20, (2010) 045124
[8] M.M. Kabir et al., Ann Biomed Eng 39, (2011) 2604-2614
[9] A. Porta et al., IEEE Trans Biomed Eng 48, (2001) 1282-1291
[10] S. Guzzetti et al., Circulation 112, (2005) 465-470
[11] A. Porta et al., Am J Physiol Heart Circ Physiol 293, (2007) H702-H708
[12] D. Cysarz et al., Am J Physiol Heart Circ Physiol 278, (2000) H2163-H2172
[13] J.W. Kantelhardt et al., Phys Rev E 65, (2002) 051908
[14] D. Cysarz et al., Am J Physiol Regul Integr Comp Physiol 292, (2007) R368-R372
[15] C. Cammarota and E. Rogora, Phys Rev E 74, (2006) 042903
[16] D. Cysarz et al., Comp Biol Med 42, (2012) 313-318
[17] U. Meyerfeldt et al., Int J Cardio 84, (2002) 141-152
[18] R. Huhle et al., Physiol Meas 33, (2012) 207-217
[19] C. Bandt, and B. Pompe, Phys Rev Lett 88, (2002) 174102
[20] W.H. Cooke et al., J Physiol 517, (1999) 617-628
[21] R. Furlan et al., Circulation 101, (2000) 886-892
[22] E. Tobaldini et al., IEEE Eng Med Biol Mag 28, (2009) 79-85.