Symbolic Analysis of Short-Term Heart Period Variability during Graded Head-up Tilt

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Abstract

Recently very simple parameters derived from symbolic analysis were proposed as a tool to non-invasively assess cardiac autonomic modulation from short (less than 300 samples) heart period variability series. They have been found capable to respond to physiological stimuli and pharmacological interventions inducing changes of the autonomic tone. However, it is not known if the same indexes are capable to follow the gradual shift of the sympatho-vagal balance.

In this study we utilize a graded head-up tilt protocol to produce a gradual increase of the sympathetic modulation and we demonstrate that one of these indexes derived from symbolic dynamics and applied to short heart period variability series is capable to follow the gradual changes of the sympatho-vagal balance, thus suggesting that it might be a valid alternative to more standard linear indexes based on spectral analysis.

1. Introduction

Symbolic analysis is an emerging approach in signal processing. It proposes to convert a time series into a sequence of symbols, to group them into "words" and to study the dynamics of the "words" instead of that of the original samples. Depending on the significance of the code the new series may enhance specific information that is masked by noise in the original series. Although in the past symbolic analysis methods were applied to heart rate variability series [1,2], only recently a method based on symbolic dynamics [3] has provided indexes that have been reliably linked to cardiac autonomic modulation [4]. However, to be reliably used in clinical settings these indexes should be able to follow the gradual change of the autonomic modulation. Graded tilt provides a unique possibility to provoke a gradual change of the autonomic activities: indeed, the variation of the venous return and the associated tachycardic response are strictly related to the inclination of the tilt table [5].

The aim of this study is to validate the recently proposed approach based on symbolic dynamics [3,4] in connection with a graded head-up tilt protocol to assess the capability of the method to follow a gradual sympathetic activation.

2. Symbolic analysis

The approach, set in [3], is based on: i) the transformation of short heart period variability series (~300 cardiac beats) into a sequence of integers (i.e. the symbols); ii) on the construction of patterns (i.e. the "words"); iii) on the reduction of the number of patterns by grouping them into a small number of families; iv) on the evaluation of the rates of occurrence of these families. Sects.2.1, 2.2, 2.3. 2.4 will describe the points i), ii), iii) and iv) respectively.

2.1. Coarse graining

Given the series $x=\{x(i), i=1,\dots,N\}$, where i is the progressive sample counter and N is the series length, x is transformed into a sequence of symbols using a coarse graining approach based on a uniform quantization procedure [3]. Briefly, the full range of the series is spread over ξ symbols with a resolution of $(x_{max}-x_{min})/\xi$, where x_{max} and x_{min} are the maximum and the minimum of the series. After quantization x becomes a sequence $x_\xi=\{x_\xi(i), i=1,\dots,N\}$ of integer values ranging from 0 to ξ-1.

2.2. Pattern construction

The series x_ξ is transformed into a sequence of patterns $x_{\xi,L}=\{x_{\xi,L}(i), i=L,\dots,N\}$ with $x_{\xi,L}(i)=(x_\xi(i),x_\xi(i-1),\dots, x_\xi(i-L+1))$ using the technique of the delayed coordinates. The number of possible $x_{\xi,L}(i)$ is ξ^L. As ξ^L grows very rapidly with L and ξ, both parameters have to be small, thus limiting the length of the pattern, L, and the resolution of the coarse graining procedure, ξ. For applications over short data sequences (about 300 samples) the best compromise is ξ=6 and L=3 [3].

2.3. Redundancy reduction

With ξ=6 and L=3 the number of possible patterns are 216. Although this number is not high, following the changes of the rate of appearance of all these patterns may be difficult. Therefore, a procedure of redundancy reduction is applied and all the patterns are grouped without any loss into four families according to the number and types of variations from one symbol to the next one [3]. The pattern families are: i) pattern with no variation (0V, all the symbols are equal, e.g. (4,4,4) or (0,0,0)); ii) patterns with one variation (1V, two consecutive symbols are equal and the remaining one is different, e.g. (1,3,3) or (5,2,2)); iii) patterns with two like variations (2LV, the three symbols form an ascending or descending ramp, e.g. (2,3,5) or (4,3,0)); iv) patterns with two unlike variations (2UV, the three symbols form a peak or a valley, e.g. (2,4,3) or (5,2,4)).

2.4. Definition of indexes

We evaluate the rates of occurrence of these families indicated as 0V%, 1V%, 2LV% and 2UV% in the following. These indexes can be obtained simply by counting the number of times that a pattern $x_{\xi=6,L=3}(i)$ belonging to a specific family is found in $x_{\xi=6,L=3}$ divided by ξ^L=216 (multiplied by 100).

3. Experimental protocol and data analysis

In 12 healthy young humans (age from 24 to 54, median=26; 4 female and 8 male) ECG (lead II) and respiration via thoracic belt were recorded at rest (R) and during head-up tilt (T). The signals were sampled at 1000 Hz. After 10 minutes at R, the subjects underwent a session (lasting 10 minutes) of T with table angles randomly chosen in the set {15,30,45,60,75,90} (T15, T30, T45, T60, T75, T90). Each T session was always preceded by an R session. The heart period was derived as the temporal distance between successive QRS complexes (RR interval). Sequences of about 250 cardiac beats were analyzed. As no significant difference was observed during the repeated R sessions, we selected the R session before T15 as reference for linear regression analysis. At R and during T15, T30, T45, T60, T75, T90 mean RR was 991±131 (mean±sd), 936±145, 848±96, 793±97, 757±97, 731±87, 737±97 ms respectively (Fig.1), thus confirming the gradual shift of the sympatho-vagal balance towards sympathetic activation with a saturation of the RR response at T75. Correlation between tilt angles and all the parameters was evaluated using linear regression analysis. Linear regression analysis was carried out both globally (i.e. pooling

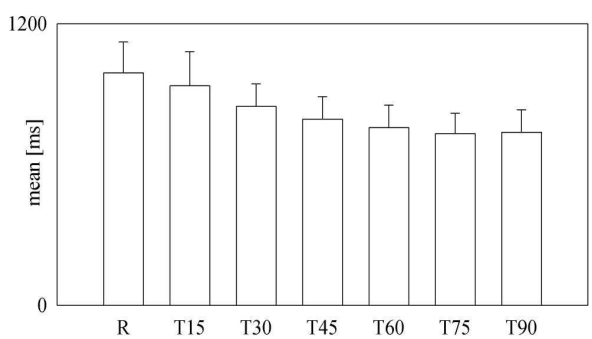

Figure 1. Bar-graph representing mean RR during the gradual head-up tilt protocol.

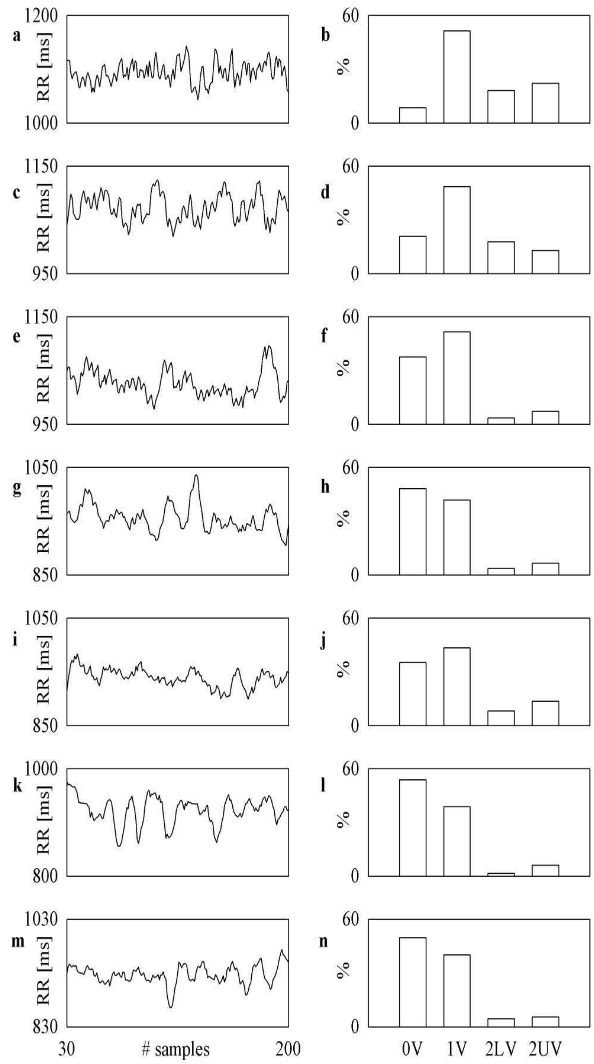

Figure 2. RR series derived from the same subject at R and during T15, T30, T45, T60, T75, T90 (a,c,e,g,i,k,m) and distribution of considered pattern families (b,d,f,h,j,l,n). Only 170 heart periods are shown to facilitate the visualization of the temporal features, while the analyses were always carried out on about 250 samples.

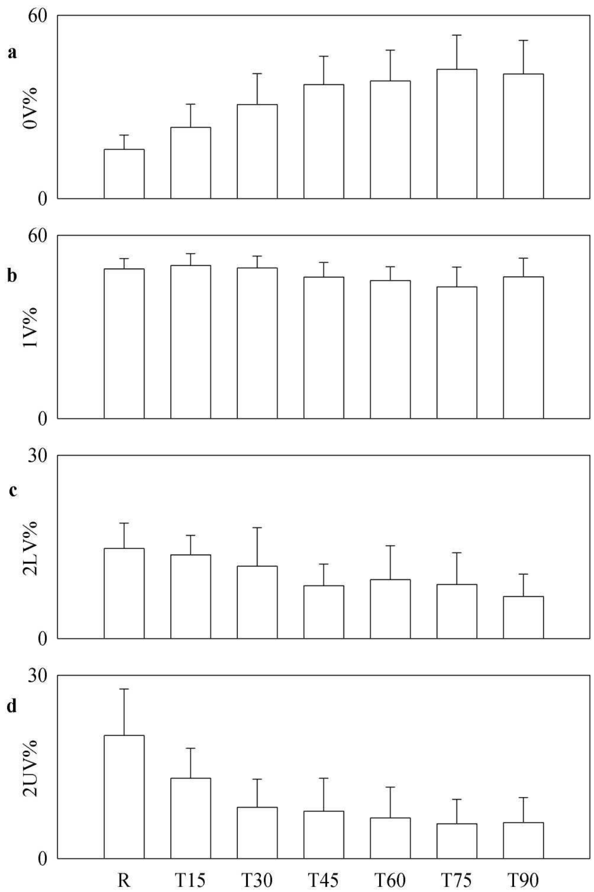

Figure 3. Bar-graphs representing 0V% (+sd), 1V%, 2LV% and 2UV% respectively (a,b,c,d).

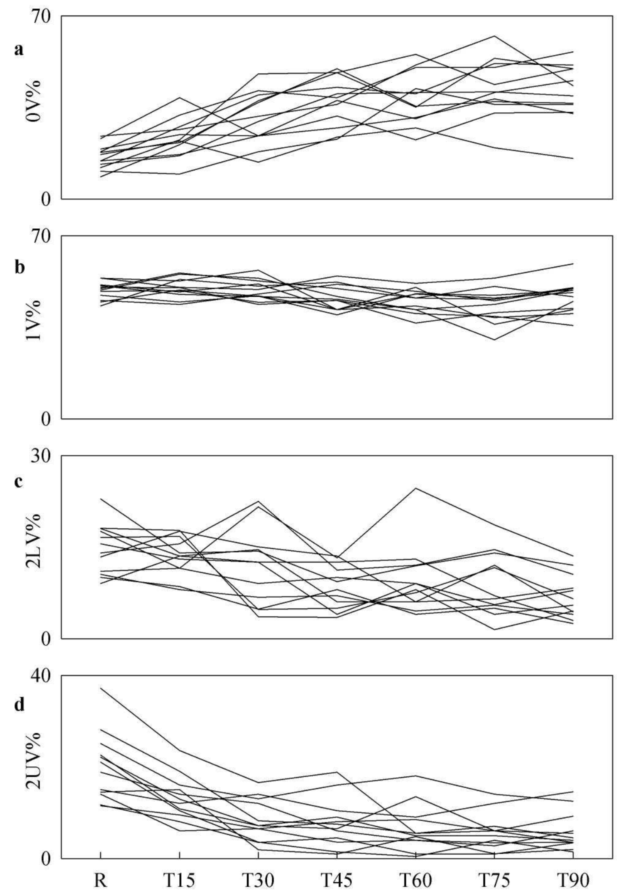

Figure 4. Individual trends of 0V%, 1V%, 2LV% and 2UV% respectively (a,b,c,d).

together all data) and individually (i.e. considering only one subject at time).

4. Statistical analysis

F test, or χ^2 test when applicable, was utilized to check whether the R sessions were indistinguishable. Correlation between tilt angles and all the parameters was evaluated using Pearson product moment correlation analysis. A $p<0.05$ was considered significant.

5. Results

Fig.2 shows the RR series derived from the same subject at R (a) and during T15 (c), T30 (e), T45 (g), T60 (i), T75 (k), T90 (m). As expected mean RR decreases while increasing tilt angles (from top to bottom panels). As to the RR variability, the fast oscillations decrease (from top to bottom panels), while slow oscillations become more important (Fig.2i and 2m render this tendency less clear). Fig.2 shows the results of the symbolic analysis (Fig.2b,d,f,h,j,l,n) carried out on the series depicted in Fig.2a,c,e,g,i,k,m. The parameters 0V% tends to increase (from top to bottom panels). Again Fig.2i and 2m tend to blur this tendency. The parameter 1V% is not dramatically modified and 2LV% and 2UV% tend to decrease for small tilt angles (below 30 degrees) and, then, to stabilize over larger inclinations.

As summarized in Fig.3, at R and during T15, T30, T45, T60, T75, T90 0V% was 16.07±4.73, 23.33±7.57, 30.76±10.19, 37.27±9.37, 38.50±10.10, 42.29±11.19, 40.76±11.02; 1V% was 49.00±3.38, 50.11±3.85, 49.31±3.91, 46.31±4.77, 45.19±4.5, 43.09±6.5, 46.44±6.08; 2LV% was 14.75±4.14, 13.67±3.24, 11.86±6.28, 8.64±3.58, 9.66±5.55, 8.85±5.19, 6.91±3.62; 2UV% was 20.17±7.57, 13.16±4.88, 8.38±4.6, 7.77±5.38, 6.63±5.05, 5.71±3.97, 5.88±4.13. Figure 3 clearly indicates that no important difference was observable between T75 and T90.

The individual trends of 0V%, 1V%, 2LV% and 2UV% are depicted in Fig.4a,b,c,d. Figure 4a confirms the tendency of 0V% to increase even on an individual basis and the saturation of the values at T75. No trend is visible in case of 1V% (Fig.4b), while in case of 2LV% and 2UV% a trend is more easily detectable when small tilt angles are considered (i.e. below 45 degrees,

Fig.4c,d).

As T75 and T90 appeared to be indistinguishable, T90 was excluded from linear regression analysis. Global linear regression detected a significant association between tilt angles and all parameters. The association was positive with 0V% and negative with 1V%, 2LV% and 2UV%. Individual regression analysis detected a significant correlation between tilt angles and the parameters 0V%, 1V%, 2LV% and 2UV% in 75, 33, 42, and 50 percent of the subjects respectively, thus indicating that 0V% is the most sensible to the progressive increase of the sympathetic modulation induced by graded tilt.

6. Discussion

We confirm that the sympathetic activation produced by head-up tilt test increases 0V% and decreases 2LV% and 2UV% [3], thus giving further support to the relationship between these indexes and sympatho-vagal balance [4]. As a novelty this study demonstrates that one of these indexes (i.e. 0V%) is capable to follow the gradual variation of the sympathetic modulation induced by graded head-up tilt test both globally and individually. Indeed, we found a significant association between 0V% and tilt angles (over the range from 0 to 75 degrees) when pooling together all the data and this association was confirmed even on an individual basis over 75% of the considered subjects. Even 1V%, 2LV% and 2UV% show a global linear association with tilt angles but it is weaker when evaluated on an individual basis.

This result is important because it demonstrates that a non linear index (i.e. 0V%) based on symbolic dynamics might be a valid alternative in assessing sympatho-vagal balance to linear indexes based on the evaluation of absolute or normalized powers in low frequency (LF) and high frequency (HF) bands [6,7]. With respect to spectral indexes 0V% has several advantages: i) it is less complex and its calculation does not require any mathematical expertise; ii) it is non linear, thus being more suitable in experimental conditions eliciting non linear components (e.g. during controlled respiration at slow breathing rates [8]); iii) it does not require the definition of the frequency bands whose inferior and superior limits are set by convention [9].

7. Conclusions

This study proves the ability of one non linear index based on symbolic dynamics (i.e. 0V%) to evaluate cardiac sympathetic modulation from short-term heart period variability data in young healthy subjects. Further studies are necessary to evaluate its performances compared to those of more standard linear indexes based on spectral analysis and to verify its applicability in healthy older or pathological populations.

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