Nonlinear Features of Neonatal Heart Rate Dynamics

Barbora Czippelova[1], Lenka Chladekova[1], Zuzana Turianikova[1], Ingrid Tonhajzerova[1], Kamil Javorka[1], Zuzana Uhrikova[2], Mirko Zibolen[2] , Michal Javorka[1]

[1]Department of Physiology, Comenius University, Jessenius Faculty of Medicine, Martin, Slovak Republic
[2]Clinic of Neonatology, Comenius University, Jessenius Faculty of Medicine, University Hospital, Martin, Slovak Republic

Abstract

The aim of this study was to investigate the short-term heart rate variability (HRV) as an index of the cardiac autonomic control development in healthy full-term neonates using various new complexity and irreversibility measures.

HRV in 20 healthy full-term neonates was compared to HRV recorded in healthy young adults. Besides traditional time and frequency domain measures, we assessed HRV complexity measures including normalized complexity index (NCI), normalized unpredictability index (NUPI), pattern classification (0V%, 1V%, 2LV%, 2UV%) and multiscale irreversibility indices (P%, G%, E).

HRV magnitude was significantly decreased in the neonatal group compared to the adults. HRV complexity measures, i.e. indices NCI, NUPI and pattern indices 1V%, 2LV%, were also significantly reduced. Pattern classification parameter 0V% and Porta's irreversibility index P% showed significant increase in newborns compared to adults suggesting the shift in the sympathovagal balance of neonates towards sympathetic predominance. Moreover, surrogate data analysis of irreversibility indices revealed asymmetrical nature of the HRV series present already in the neonatal age suggesting the nonlinear nature of HRV dynamic even very shortly after birth.

1. Introduction

Cardiovascular system represents a very precisely and promptly controlled physiological system of the human body. The instantaneous "beat-to-beat" modulation is provided mainly by the autonomic nervous system (ANS). Autonomic cardiovascular control is then reflected in the spontaneous fluctuations of the cardiac cycle duration – heart rate variability (HRV) and its analysis can provide valuable information about the cardiac autonomic regulation [1].

HRV is traditionally performed by the linear analysis in the time and frequency domains evaluating primarily the magnitude of the oscillations [2]. Given the nonlinear nature of the physiological systems, the nonlinear analysis can be more suitable, precise and sensitive as it reflects the complex dynamics of the heart rate modulation. The nonlinear methods are independent from the traditionally used linear measures and focus on the qualitative characteristics of the oscillations, including complexity, asymmetry, unpredictability or irregularity. [3].

The cardiovascular control of the newborns has its specific features and limits, as the feedback and feedforward mechanisms enabling optimal control of the heart are yet not fully developed [4].

In this study we focused on the novel measures of HRV in a group of healthy full-term newborns in comparison to the adults. The aim of the study was to describe the differences in heart rate dynamics using traditional linear analysis and a set of nonlinear measures quantifying different aspects of HRV – complexity, pattern occurrence and temporal asymmetry. We proposed that the ability of novel measures to detect the difference between developing (newborn) and adult heart rate control will indicate the suitability of the given measures to be used as a marker of autonomic control maturation / immaturity.

2. Methods

20 healthy full-term eutrophic infants (gestational age 39 ± 1 weeks, 11 female, 9 male, birth weight: 3326 ± 300 g) underwent the recording of spontaneous heart rate oscillations. All infants were spontaneously delivered. HRV indices of the newborns were compared to indices

of 28 young adults (21 female, 7 male) aged 20.4 ± 0.2 years. The adult subjects were examined in supine position.

To avoid movement artefacts, we analysed the segments lasting 1000 heart beats where the stationarity (mean and variance do not change over time) of the time series was acceptable for the subsequent offline analysis.

The study was approved by the Ethics Committee of Jessenius Faculty of Medicine, Comenius University. All parents of the infants and adult participants gave their written informed consent prior to the examination.

3. Data analysis

HRV was analysed by standard linear measures represented by time and frequency domain parameters [2] and nonlinear measures represented by symbolic dynamics [5] and multiscale time asymmetry indices [1]. We also investigated the presence of the time irreversibility in the recordings of both groups using the surrogate data method.

3.1. Linear analysis

Time domain analysis

We computed the three most commonly used measures:
- mean RR – mean RR interval duration
- SDRR – the standard deviation of RR intervals reflecting the overall HRV magnitude
- rMSSD – the root-mean-square of successive beat-to-beat differences reflecting the average magnitude of the changes between two consecutive beats that is usually regarded as a marker of vagal heart rate control

Frequency domain analysis

We computed spectral powers in two frequency bands associated with different physiological rhythms:
- Low frequency band (LF: 0.04 – 0.15 Hz, in both groups) reflecting the baroreflex mediated heart rate oscillations;
- High frequency band (HF: 0.15 – 0.4 Hz in adult group, 0.15–1.4 Hz in newborn group) determined by the respiratory sinus arrhythmia which is regarded as a marker of the cardiac vagal control. [4].

3.2. Nonlinear analysis

The nonlinear analysis of the HRV series was performed by two different groups of methods.

Symbolic dynamics

The concept of symbolic dynamics is based on a simple description of the system dynamics with a limited amount of symbols. In HRV analysis, consecutive R-R intervals are encoded, according to given transformation rule, into a few symbols of a certain alphabet (according to the procedure described by Porta et al. [5], to 6 different symbols {0 – 5}). As a transform rule, nonuniform equiprobable quantization keeping constant the number of samples associated with each quantization level was applied [6]. The resulting symbolic time series were analysed by three different approaches:

- Normalized complexity index (NCI) is a measure of the amount of information carried by the L-th sample when the previous L-1 samples are known (L stands for a length of a pattern). NCI is a measure of the complexity of pattern distribution. It ranges from zero (maximum regularity of the time series) to one (maximum complexity of the time series).

- Normalized unpredictability index (NUPI) measures the unpredictability of the L-th sample when the previous L-1 samples are known. NUPI decreases to zero in the case of fully predictable signals. The larger the NUPI, the more unpredictable the time series is.

- Pattern classification is a process of grouping all the patterns (symbolic sequences) with $L = 3$ into 4 families according to the number and type of variations from one symbol to the next one. The patterns were grouped into: 1) patterns with no variation (0V, all three symbols are equal); 2) patterns with one variation (1V, two consecutive symbols are equal and the remaining one is different); 3) patterns with two like variations (2LV, three symbols form an ascending or descending ramp), 4) patterns with two unlike variations (2UV, three symbols form a peak or a valley). The rates of occurrence of these patterns are indicated as 0V%, 1V%, 2LV% and 2UV%. These indices are proposed to follow the changes of the sympathovagal balance – an increase of 0V% was associated with an increase of sympathetic activity, while a decrease in 2LV% accompanied the vagal withdrawal in adults [7].

Time irreversibility analysis

A signal is said to be time irreversible if its statistical properties change after its time reversal, i.e. it is characterized by a temporal asymmetry. It is specific for nonequilibrium systems [8] and its extensive presence in cardiovascular signals results from the complexity of the highly adaptable cardiovascular control system.

Three indices were used to measure time irreversibility of heart rate oscillations: Porta's index P%, Guzik's index G% and Ehler's index E. These indices are based on the quantification of the number, direction and magnitude of two consecutive RR intervals length changes according to different formulas defined elsewhere [1,8,9]. P% and G% range from 0 to 100% and time irreversibility is characterized by values of these indices significantly larger or smaller than 50%. E does not have a predefined range, but a significant distance from 0 indicates time irreversibility.

Surrogate data method was used to confirm the presence of time irreversibility in the HRV time series and its dependence on system nonlinearity. Iteratively amplitude adjusted Fourier transform surrogates (IAAFT) were generated according to the procedure described by

Schreiber and Schmitz [10]. One hundred realisations of surrogate data were constructed from each original time series to test if P% and G% are significantly different from 50% and E is significantly different from 0. Irreversibility indices were calculated for all original and surrogate data. An irreversibility index of an original time series falling within the 2.5th and 97.5th percentile of the index' surrogate data distribution was considered to be consistent with the null hypothesis. Otherwise, the null hypothesis of the presence of a reversible linear process was rejected and the original series was considered to be time irreversible.

In order to gain more information from irreversibility analysis, we investigated time irreversibility on 4 time scales (τ). The coarse-graining procedure [11] was employed for the multiscale approach – the data inside non-overlapping windows of τ points are averaged.

The differences in the calculated parameters between adults and neonates were analysed using the nonparametric Mann-Whitney test. A p values < 0.05 (# in the figures) were considered to be statistically significant.

4. Results

4.1. Linear analysis

Both time domain and frequency domain measures showed a decrease in the HRV magnitude in newborns compared to adults. The linear analysis showed significant between-groups differences in all time domain parameters: meanNN ($p < 0.0005$), SDNN ($p < 0.005$), rMSSD ($p < 0.0005$) and also in the spectral powers in both frequency bands: LF ($p < 0.0005$), HF ($p < 0.0005$).

4.2. Nonlinear analysis

Symbolic dynamics

Significantly lower values of complexity – NCI ($p < 0.005$) and unpredictability – NUPI ($p < 0.0005$) indices in the neonatal compared to the adult group were found (Fig.1a). The analysis of the patterns occurrence rates showed significantly higher values of 0V% ($p < 0.00005$) and reduced values of 1V% ($p < 0.00005$) and 2LV% ($p < 0.0005$) in neonates compared to the adults (Fig.1b).

Time irreversibility analysis

The higher values of P%(τ) were observed in neonates compared to adults for time scales 1 ($p < 0.02$) and 4 ($p < 0.05$). No between-group differences in G%(τ) and E(τ) indices were found for any analysed scale (Fig. 2).

Value of P% and G% significantly different from 50% and E significantly different from 0 indicates the presence of time irreversible dynamics in the HRV series. The presence of significant time irreversibility was identified by the IAAFT surrogate method and demonstrated in a significant percentage of recordings in both investigated groups. For the original HRV series (i.e. for scale 1) the heart rate oscillations were irreversible in about 46%, 75% and 75% of the adult subjects (evaluated by P%, G% and E, respectively) and reached the values 65%, 70% and 75% (for P%, G% and E, respectively) in the neonatal group. No significant between-group differences (chi-square test) in the irreversible heart rate time series percentage were found across all assessed indices and time scales (Fig. 3).

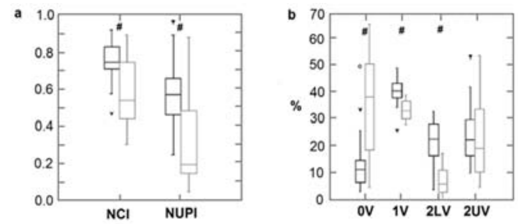

Figure 1. Box-and-whisker plots representing (a) complexity (NCI) and unpredictability index (NUPI) and (b) pattern classification indices 0V%, 1V%, 2LV%, 2UV% in the neonates (grey) and adults (black)

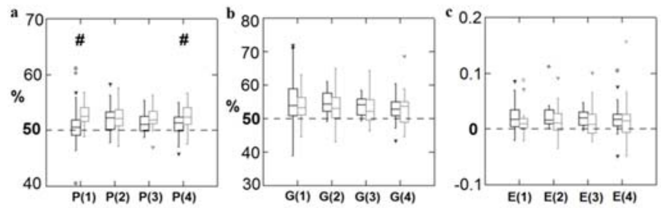

Figure 2. Box-and-whisker plots representing irreversibility indices P% (a), G% (b) and E (c) derived from the HRV time series for multiple time scales (τ = 1, 2, 3, 4) in the neonates (grey) and adults (black)

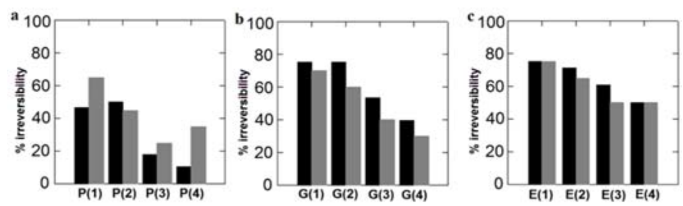

Figure 3. Bar graphs representing the percentage of the irreversible dynamics detected in the HRV time series by P% (a), G% (b) and E (c) on multiple time scales (τ = 1 – 4); in the neonates (grey) and adults (black)

5. Discussion

Linear analysis of HRV is focused on the overall and beat-to-beat heart rate oscillations magnitude. The progressive increase of time and frequency domain measures after birth reflects the autonomic maturation, as has been previously described [3,4]. As expected, we observed reduced magnitude in all investigated time and frequency domain measures in newborns compared to adults.

Nonlinear methods provide different, more suitable view on HRV as the cardiovascular system is regulated by complex nonlinear regulatory mechanisms.

Our study revealed lower values of complexity (NCI) and unpredictability (NUPI) indices in the neonates compared to the adults. These results indicate relatively less complex heart rate dynamics in newborns compared to adults as a new feature of developing control system. The analysis of specific patterns occurrence in neonates showed significantly higher occurrence of 0V patterns and lower 2LV% indicating a shift in the cardiac control towards sympathetic dominance in newborns (increase in 0V% and decrease in 2LV% are associated with the shift of the cardiac neural regulation towards sympathetic dominance [12]).

Our results of irreversibility analysis indicate higher irreversibility of neonatal heart rate compared to adults on scale 1 (P%). This finding also supports the concept of a relative sympathetic dominance in newborns as higher values of P% were found during orthostatic maneuver and head-up tilt [1, 13].

One of the most important findings of this study is the detection of temporal asymmetries within heart rate dynamics even shortly after birth. We observed the nonlinearity resulting in time irreversibility in the majority of neonatal heart rate recordings and the occurrence rate of this type of dynamics was comparable to adults. These results support the concept of nonlinearity as a universal property of the biological control system even in the early stage of the system maturation.

6. Conclusion

We detected the presence of nonlinear behaviour of HRV dynamic even in the neonatal age and the ability of novel nonlinear measures to detect the changed heart rate regulation dynamics in a developing organism. These findings support the application of nonlinear methods to HRV analysis.

Acknowledgements

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Address for correspondence.

Dr Barbora Czippelova
Department of Physiology, Jessenius Faculty of Medicine, Comenius University
Malá Hora 4
036 01 Martin, Slovakia
Czippelova@jfmed.uniba.sk