



Heart Rate Variability: Influence of Pre-processing Methods in Identifying Single-Night Sleep-Deprived Subjects

Jose Gallardo¹ · Giannina Bellone² · Santiago Plano² · Daniel Vigo³ · Marcelo Risk⁴

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Abstract

Purpose Autonomic nervous system (ANS) activity can be non-invasively estimated from the heart rate variability (HRV) signal obtained from the electrocardiogram (ECG). The aim of this work is to find useful parameters that allow to establish the presence of a single night sleep deprivation in healthy subjects.

Methods The study included two experimental groups of subjects: Non-sleep-deprived (sleep ≥ 4 h, $N = 13$) and sleep-deprived (sleep < 4 h, $N = 10$). The RR series extracted from 5 min resting ECG signals were pre-processed using four different algorithms to detect and edit artifacts. The RR series were analyzed in terms of time-domain, frequency-domain and using the Poincaré plot, in order to determine differences in HRV indexes across domains and subject groups. Statistical analyses were performed with the Friedman and Mann–Whitney tests, along, with correlation analysis.

Results Pre-processing methods showed a moderate level of agreement. In subjects with 4 h of single-night sleep deprivation, results differed according to the selected method.

Conclusion SD21 index derived from the Poincaré plot was the only HRV index showing differences between sleep-deprived and non-deprived subjects.

Keywords Heart rate variability · Single night sleep · RR series · Poincaré plot

✉ Jose Gallardo
jmg@df.uba.ar

Giannina Bellone
gbellone@uca.edu.ar

Santiago Plano
santiagoplano@uca.edu.ar

Daniel Vigo
danielvigo@uca.edu.ar

Marcelo Risk
marcelo.risk@hospitalitaliano.org.ar

(UCA) and National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina

³ Chronophysiology Lab., Institute for Biomedical Research (BIOMED), Catholic University of Argentina (UCA) and National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina

⁴ National Technological University (UTN, FRBA), Translational Medicine and Biomedical Engineering Institute (IMTIB) and National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina

¹ National Technological University (UTN, FRBA) and National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina

² Department of Science and Technology, Laboratory of Chronobiology, National University of Quilmes and Chronophysiology Lab., Institute for Biomedical Research (BIOMED), Catholic University of Argentina

1 Introduction

Previous research has established that daily sleep duration has continuously decreased over the last decades [1]. Sleep deprivation affects attention, working memory, long-term memory, decision-making; it also triggers anxiety and it is an important factor contributing to accidents, including road accidents [2, 3].

Most studies evaluate the impact of long periods of sleep deprivation on physical, cognitive and autonomic function, but few evaluate the effects of a single period of total or partial restriction of night-time sleep [4, 5]. Studies involving vehicle drivers show a slight increase in road traffic accidents after a moderate reduction of 4 h in the previous night sleep [6]. Therefore, identifying sleep deprivation may be useful for reducing accident frequency rates.

In recent years, there has been a growing interest in physiological measurements for drowsiness detection. Physiological measurements (electroencephalography, EEG), eyelid movement (electrooculography), muscle tone (electromyogram), and electrical activity of the heart (electrocardiography, ECG) have been reported to detect early-stage sleepiness. The ECG signal is unique to each person and depends on several factors such as age, anthropometry, anatomy, and sex, all of which makes it a suitable biometric verification for human identification [7]. Although the heart rate variability (HRV) signal is obtained from the ECG, HRV indexes may be too weak to identify a person; however, they are useful for discriminating conditions in which autonomic system activity changes as part of reactive or predictive homeostasis mechanisms [8].

Recent evidence suggests that sleep deprivation is associated with decreases in HRV, which proves HRV analysis a promising method for driver sleepiness detection [9–11], although no studies have investigated the detection of single-night sleep deprivation so far.

Heart rate variability (HRV) refers to the beat-to-beat changes in heart rate and is analyzed using the series of RR-intervals (RR)—i.e. the time between successive QRS complexes—derived from the ECG signal. These signals may present distortions or deformations resulting from technical (electrode disconnection, line noise, etc.) or biological (ectopic beats, etc.) factors. For these reasons, it is necessary to correct the RR series estimates through effective pre-processing algorithms before performing HRV analysis. Currently, there is no consensus among researchers or clear recommendations in the literature on the most appropriate methods for detecting and correcting doubtful heartbeats previous to HRV analysis [12]. Therefore, it is desirable to determine whether the use of

different pre-processing strategies for the RR series used in HRV multi-domain analyses can have an impact on the HRV indexes obtained and the detection of single-night sleep-deprived subjects.

2 Materials and Methods

2.1 Subjects and Design

Twenty-three subjects aging from 21 to 25 years old, voluntarily participated in the experiment. The subjects were healthy and free from any medication. Every subject provided written consent before starting the experiment and all subjects were free to terminate the experiment at any time. The subjects were divided in two groups: non-deprived (sleep > 4 h) ($N_{\text{total}} = 13$, $N_{\text{women}} = 5$) and with a single-night-deprived (sleep ≤ 4 h) ($N_{\text{total}} = 10$, $N_{\text{women}} = 7$). This study went through ethics approval from the Research Committee at National University of Quilmes, Buenos Aires, Argentina (04/07/2016/No. 3).

2.2 Analysis of HRV

The ECG signal from each subject was obtained in resting position during 5 min by a V1 Holter with a sampling frequency of 225 Hz. The ECG signal was pre-processed using a 50 Hz notch filter and the trends were eliminated by polynomials of low order. The filtered ECG signal was re-sampled at 1 KHz to achieve a high-quality R-peak detection system and reliable HRV analysis [12–15]. The modified Pan-Tompkins [16] algorithm was used to detect the R peaks, and the DC component and the linear trend were eliminated to calculate the series of time intervals [13, 14].

Artifacts and ectopic beats of the RR series were identified using two methods:

1. (SD) The SD method [11, 17, 18], considering normal an adjacent RR presenting up to four standard deviations ($4*SD$) around the mean of all RR of the epoch (5 min).
2. (IRF) Impulse rejection filter [19–21], a nonlinear filter that is considered more appropriate for artifact removal in biomedical signals because it only alters the signal in segments where an artifact is detected.

Two techniques were applied for the correction of doubtful points:

1. (DEL) Deletion exclusion of the detected artifact [9, 11, 12, 18, 22].
2. (RMV) Replacement of each anomalous value by the median value of the previous five values and the following five [17, 23].

With these methods, four algorithms were performed for RR series pre-processing: SDDEL (SD and DEL), SDRMV (SD and RMV), IRFDEL (IRF and DEL) and IRFRMV (IRF and RMV).

The analysis of HRV was conducted in the time domain through statistic calculations including mean of RR intervals (RRM); standard deviation of RR intervals (SDNN); root mean square of the differences between consecutive RR intervals (RMSSD); and percentage value of frequency of successive differences of RR intervals that spanned more than 50 ms (pNN50). In the frequency domain analysis, the Lomb periodogram was used to estimate the power spectral density (PSD) for non-equispaced RR series; this method has been recommended due to its advantages when dealing with noising signals and because, unlike FFT method, it does not require re-sampling of the RR series [24, 25]. The indexes resulting from the PSD analysis can be presented in different frequency bands: low frequency (LF) (0.04–0.15 Hz), high frequency (HF) (0.15–0.4 Hz), normalized parameters (LFn.u.), (HFn.u.) and LF/HF ratio [14].

The Poincaré domain geometric indexes describe the correlation between consecutive RR intervals. The SD1 index reflects the short-term variability of heartbeats, the SD2 index reflects the long-term variability, and the SD2/SD1 (SD21) ratio is a measure of the relation between the long- and short-term variability similar to the LF/HF ratio by its analogy and properties [26–29].

The algorithms for signal processing and calculation of the several HRV indexes were made with GNU Octave software.

2.3 Statistical Analysis

The data were analyzed using algorithms developed with the R free software. Differences in the same HRV index after using different doubtful beat detection and correction algorithms were analyzed through the Friedman test followed the Wilcoxon signed rank test with the Bonferroni (B) correction for the evaluation of pairwise comparisons. The differences in HRV indexes between the two groups of subjects were evaluated through the Mann–Whitney test followed by the Benjamini–Hochberg (BH) correction. Data were expressed as median and interquartile range. Correlations across the HRV measures were evaluated using the Spearman correlation test. Statistical significance was accepted at $p < 0.05$.

3 Results

The average percentage of detected doubtful beats was 0.30% for SD and 0.61% for IRF. IRF detected twice as many doubtful beats as SD.

Figure 1 shows the differences in the detected and corrected doubtful beats across the different algorithms. Significant differences were observed between IRFDEL and IRFRMV ($p < 0.05$) in the pNN50 index (Fig. 1a), between SDDEL and IRFDEL ($p < 0.01$), SDRMV and IRFDEL ($p < 0.01$), IRFDEL and IRFRMV ($p < 0.01$) in the SDNN index (Fig. 1b), and between SDDEL and IRFDEL ($p < 0.01$) in the LF index (Fig. 1c). No significant differences were observed across algorithms in the RRM, RMSSD, LFn.u., HF, HFn.u., LF/HF, SD1, SD2 and SD21 indexes.

Tables 1, 2, 3 and 4 show HRV differences between deprived and non-deprived subjects for each pre-processing

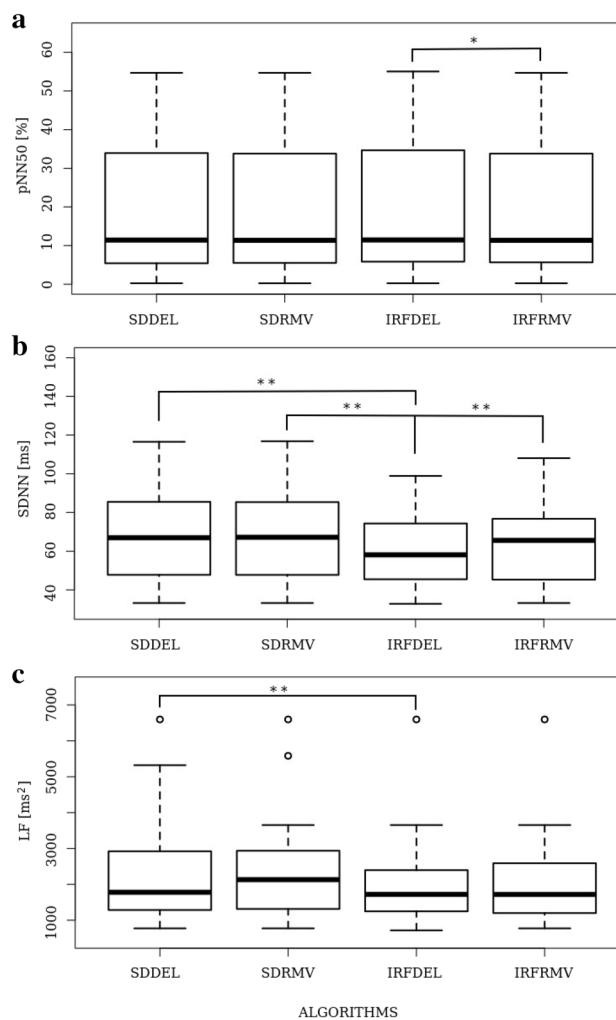


Fig. 1 Differences in the detected and corrected doubtful beats across algorithms using Friedman test followed by Wilcoxon signed rank test for pairwise comparisons and corrected by Bonferroni method. **a** Significant differences between IRFDEL and IRFRMV in the pNN50 index. **b** Significant differences between SDDEL and IRFDEL, SDRMV and IRFDEL, IRFDEL and IRFRMV in the SDNN index. **c** Significant differences between SDDEL and IRFDEL in the LF index. * $p < 0.05$, ** $p < 0.01$

Table 1 Results of Mann–Whitney test [30]

Indexes	Non-deprived	Deprived	<i>p</i>
RRM [ms]	850.16 [780.98 1000.64]	785.76 [668.97 916.45]	0.26
pNN50 [%]	26.10 [4.81 42.19]	8.83 [1.63 38.93]	0.37
SDNN [ms]	67.49 [45.91 88.69]	63.19 [39.44 98.68]	0.69
RMSSD [ms]	43.81 [25.05 84.58]	36.77 [21.21 70.23]	0.34
LF [ms ²]	1778.54 [1250.32 3566.90]	1928.82 [866.76 3335.66]	0.93
LFn.u.	63.43 [47.93 70.90]	70.26 [48.80 80.98]	0.26
HF [ms ²]	786.78 [399.44 2762.63]	831.20 [282.63 2168.02]	0.41
HFn.u.	32.72 [23.46 42.68]	25.62 [15.81 42.16]	0.21
LF/HF	1.94 [1.02 3.02]	2.76 [1.27 5.25]	0.28
SD1 [ms]	31.03 [17.73 59.90]	26.04 [15.02 49.73]	0.34
SD2 [ms]	85.57 [56.43 111.72]	79.23 [52.95 130.69]	0.83
SD21	2.56 [2.00 3.22]	3.45 [2.63 3.57]	0.10

HRV indexes calculated after pre-processing by SDDEL algorithm. Values for each group expressed in median and [1st; 3rd] quartile. No significant differences were found between non-deprived and deprived subjects

Table 2 Results of Mann–Whitney test

Indexes	Non-deprived	Deprived	<i>p</i>
RRM [ms]	850.16 [780.98 1000.64]	785.82 [668.97 916.45]	0.26
pNN50 [%]	25.93 [5.30 42.26]	8.93 [1.62 38.93]	0.38
SDNN [ms]	69.05 [45.88 88.69]	63.08 [39.30 98.68]	0.60
RMSSD [ms]	43.66 [24.92 84.50]	36.70 [21.19 70.23]	0.28
LF [ms ²]	2233.35 [124.31 3540.69]	1924.37 [866.76 3335.66]	0.69
LFn.u.	61.42 [47.69 67.97]	70.20 [48.69 80.96]	0.22
HF [ms ²]	1312.60 [399.44 2762.63]	814.59 [287.33 2197.76]	0.28
HFn.u.	35.36 [24.10 44.51]	25.71 [15.81 42.23]	0.13
LF/HF	1.74 [1.01 2.70]	2.75 [1.28 5.25]	0.15
SD1 [ms]	30.92 [17.65 59.85]	25.99 [14.10 49.73]	0.28
SD2 [ms]	89.64 [56.49 111.72]	79.18 [52.73 130.69]	0.78
SD21	2.56 [1.96 3.13]	3.33 [2.63 3.57]	0.07

HRV indexes calculated after pre-processing by SDRMV algorithm. Values for each group expressed in median and [1st; 3rd] quartile. No significant differences were found between non-deprived and deprived subjects

algorithm. No significant differences in HRV indexes were observed between groups after using the SDDEL or SDRMV algorithms. The SD21 index showed differences after using the IRFDEL algorithm (Table 3, $p = 0.04$) and after using the IRFRMV algorithm (Table 4, $p = 0.02$).

This can be seen in the Poincaré graphs of Fig. 2, which show a smaller lobe in a sleep-deprived subject (SD1= 17.95 ms, SD2= 54.22 ms, SD21= 3.03) than in a non-deprived one (SD1= 30.83 ms, SD2= 74.95 ms, SD21= 2.44).

Table 5 presents the correlations between the SD21 index and time (SDNN, RMSSD) and frequency domain

(LF, HF, LF/HF) indexes corresponding to the 23 subjects and pre-processed by IRFRMV. Interestingly, the correlation between LF/HF and SD2/SD1 (SD21) suggests similar behavior for both indexes.

4 Discussion

The main results of this study show that the average percentage of detected doubtful beats was 0.30% for SD and 0.61% for IRF. Overall, IRF detected twice as many doubtful beats as SD. These results, obtained using a threshold of $\pm 4*SD$, are in agreement with those obtained by [11] also using $\pm 4*SD$ with subjects in motion. In turn, a possible explanation for the differences observed between IRF and SD is that the IRF algorithm detects artifacts in segments, according to [19, 20].

The results of the HRV processing algorithms showed no significant differences for most of the indexes, although the agreement across methods was lower for the time and frequency domains. The differences in SDNN may be given by both the detection and the editing methods; this result may be explained by the fact that the SDNN index is more susceptible to abnormal heartbeat detection methods [13] and that DEL is a simple editing method for removing doubtful heartbeats with no subsequent interpolation of the deleted beats. Although in some cases interpolation methods such as RMV (interpolation of degree zero) are superior to DEL [22, 31], the pNN50 differences may be given by the edition methods, which is also in line with the findings of [12, 31]. LF index differences in the frequency domain were also observed, which may be explained by the different number of doubtful heartbeats detected by each method which in turn generate series with different lengths. Of note, the

Table 3 Results of Mann–Whitney test

Indexes	Non-deprived	Deprived	<i>p</i>
RRM [ms]	850.16 [780.98 1000.64]	782.81 [668.97 916.45]	0.21
pNN50 [%]	25.31 [5.41 40.43]	8.95 [2.10 39.26]	0.38
SDNN [ms]	63.45 [41.88 84.82]	55.26 [38.14 97.89]	0.93
RMSSD [ms]	43.81 [24.65 62.02]	31.28 [21.16 59.41]	0.28
LF [ms ²]	1413.81 [1067.34 3115.89]	1746.49 [866.76 3335.66]	0.93
LFn.u.	61.93 [55.62 78.03]	72.80 [56.39 80.90]	0.22
HF [ms ²]	786.78 [356.68 2103.25]	522.44 [275.23 2165.41]	0.38
HFn.u.	32.61 [21.04 44.38]	23.59 [15.81 42.15]	0.17
LF/HF	1.88 [1.25 3.71]	3.11 [1.34 5.25]	0.15
SD1 [ms]	31.03 [17.45 43.92]	22.147 [14.98 42.08]	0.28
SD2 [ms]	79.23 [56.56 102.49]	74.92 [51.86 130.69]	0.98
SD21	2.56 [2.04 3.22]	3.45 [2.70 3.70]	0.04*

HRV indexes calculated after pre-processing by IRFDEL algorithm. Values for each group expressed in median and [1st; 3rd] quartile. SD21 index in the deprived group shows a significantly higher value, **p* = 0.04

Table 4 Results of Mann–Whitney test

Indexes	Non-deprived	Deprived	<i>p</i>
RRM [ms]	850.16 [780.98 1000.64]	783.91 [668.97 916.45]	0.23
pNN50 [%]	25.59 [5.30 38.91]	8.80 [1.39 38.93]	0.41
SDNN [ms]	67.27 [44.17 86.72]	55.38 [39.32 98.68]	0.74
RMSSD [ms]	43.66 [25.52 62.02]	30.63 [21.12 59.41]	0.19
LF [ms ²]	1778.54 [1015.26 3401.60]	1690.07 [866.76 3335.66]	0.93
LFn.u.	61.42 [50.96 69.48]	73.43 [56.34 83.03]	0.14
HF [ms ²]	833.19 [399.44 2132.40]	420.31 [272.67 2188.04]	0.21
HFn.u.	35.36 [23.73 45.03]	33.46 [14.63 42.22]	0.09
LF/HF	1.74 [1.14 2.93]	3.16 [1.33 5.53]	0.08
SD1 [ms]	30.93 [18.08 43.92]	21.69 [14.95 42.08]	0.98
SD2 [ms]	85.34 [54.13 102.49]	74.14 [52.75 130.69]	0.98
SD21	2.56 [2.00 3.03]	3.45 [2.70 3.85]	0.02*

HRV indexes calculated after pre-processing by IRFRMV algorithm. Values for each group expressed in median and [1st; 3rd] quartile. SD21 index in the deprived group shows a significantly higher value, **p* = 0.02

SDDEL RR series is longer than the IRFDEL RR series, and these differences can affect the LF index [31].

According to [11], even measurable differences provide no evidence as to which method is best for a particular application. On the other hand, [22] suggests that the lack of statistical significance does not constitute reliable evidence of the lack of differences across the calculated HRV indexes. As shown by our results, this may imply that the choice of the outlier detection and editing methods can impact on the evaluation of single-night sleep deprivation despite the small differences observed in HRV indexes after applying these methods.

Only the SD21 index-after using the IRFDEL and IRFRMV algorithms- presented statistically significant differences between deprived and non-deprived subjects, with

a better discrimination value in the latter case. Although the DEL removal procedure is simple and may perform well in some situations, interpolation may yield better results by decreasing the error attributable to ectopic beats depending on the HRV parameters under consideration [15, 22]. On the one hand, despite different study situations, our conclusions are comparable to those of [11] and [18]; on the other hand, it seems plausible that the quality of HRV analysis results may be improved through careful detection of doubtful beats and appropriate choice of editing methods [12].

Few studies have investigated the impact of single-night sleep deprivation through HRV. In this work, the IRFDEL and IRFRMV algorithms revealed an increase in the SD2/SD1 ratio in sleep-deprived subjects. In addition, the correlations found suggest that SD2/SD1 could be regarded as

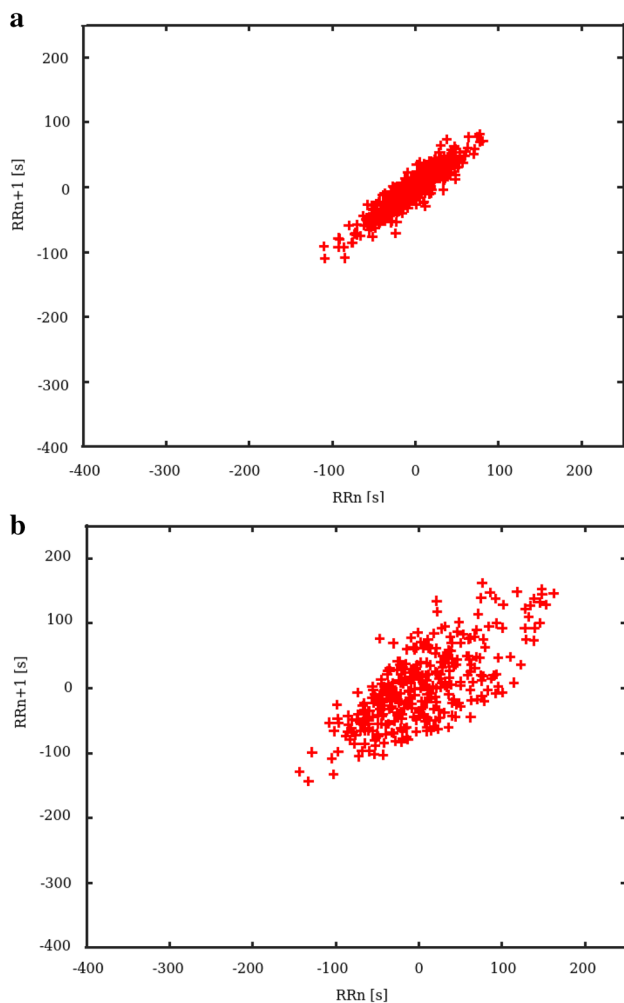


Fig. 2 Poincaré graph showing a smaller lobe in **a** a sleep-deprived subject (SD1= 17.95ms, SD2= 54.22ms, SD21= 3.03) than in **b** a non-deprived one (SD1= 30.83ms, SD2= 74.95ms, SD21= 2.44)

Table 5 Correlation between the SD21 index and time (SDNN, RMSSD) and frequency domain (LF, HF, LF/HF) indexes corresponding to the 23 subjects

Indexes	SD21
SDNN	0.47*
RMSSD	0.77**
LF	0.30
HF	- 0.65**
LF/HF	0.64**

The RR series were pre-processed using the IRFRMV algorithm. * $p < 0.05$, ** $p < 0.01$

an alternative for LF/HF [27–29]. We interpret the SD2/SD1 ratio as a measure of the long/short-term HRV ratio by its analogy with LF/HF. In both relationships, the numerators correspond to a parameter depending on long-term (low frequency) variability-which recognizes parasympathetic and sympathetic influences-, while the denominators depend on

short-term variability-which recognizes solely parasympathetic influences. Thus, higher SD2/SD1 values may express an increase in sympathetic predominance [27–29, 32], and the increase observed in the SD2/SD1 ratio can be interpreted as the sympathetic activation of a subject trying to stay awake in the context of sleep demand [10].

The limitations of this work include, on the one hand, sample size, which should be increased in future studies; on the other hand, even if the threshold values used in outlier detection methods were obtained from the literature, different thresholds should be tested in future assays and more editing methods should be analyzed.

5 Conclusions

In conclusion, even if HRV pre-processing methods showed a moderate level of agreement, they influenced the final discrimination between sleep-deprived and non-deprived subjects. In addition, this study reinforces the notion that the Poincaré plot SD21 index is more sensitive for determining sympathetic predominance than the traditionally used LF/HF. Further research should be carried out to confirm these results and test other methods for detecting and editing artifacts.

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Compliance with Ethical Standards

Conflict of interest The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval This study went through ethics approval from the Research Committee at National University of Quilmes, Buenos Aires, Argentina (04/07/2016/No. 3).

Consent for Publication The Author warrants and represents that the Contribution does not infringe upon any copyright or other rights, and that it does not contain infringing or other unlawful matter, that he/she was the sole and exclusive owner of the rights herein conveyed to the Publisher.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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