Are Spectral Estimates of Heart Rate Variability Dependent on Heart Rate? A Formula to Correct When Needed

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Abstract

Heart rate variability (HRV) investigated by spectral analysis is widely accepted as a tool for the investigation of the autonomic influence on heart activity.
The possibility that HRV indexes should be corrected per the heart rate, before using them is currently overlooked. RR interval derived from EKG recording in 15 healthy subjects, during quiet supine mute resting has been analysed over consecutive 256-beat long windows by autoregressive spectral analysis. The formula ln(Power Spectral Density) / ln(RR interval) was then applied when a dependence of power values from RR interval was found, Spectral total power, VLF, LF, and HF power were significantly related to RR interval.
After the application of the correction formula no significant correlation was found.
In conclusion, some spectral indexes (associated with parasympathetic drive to the sinus node and with sympatho/vagal balance) are dependent of heart rate and need a correction before analysis and interpretation. A simple effective formula to make spectral indexes independent by heart rate is proposed which is effective.

1. Introduction

Heart rate variability investigated by spectral analysis is widely accepted as a tool for the investigation of the autonomic influence on heart activity: spectral indexes are currently considered as independent markers either of sympathetic or vagal modulation of sinus node [1].
Actually, the influence of heart rate per se upon HRV is frequently ignored, among the possible confounders (age, sex, others), although its variation, even when not evoked by autonomic drive to the heart, do induce significant HRV changes. Physiological, pathophysiological or external stimuli, other than autonomic outflow, acting on absolute heart rate level may vary HRV: body temperature, endocrine factors, drug administration (e.g. during fever, anemia, hyperthyroidism, etc.). Moreover, one would differentiate the "true autonomic" contribution to HRV, without either the enhancing or the blunting effect due to bradycardia or tachycardia, even in physiological conditions. For all these reasons, need for a correction of the influence of heart rate upon the other HRV indexes requires a (small but significant) theoretical effort, similar to the many attempts made to free the electrocardiographic marker of ventricular repolarization (QT interval) by the effect of heart rate, from the first attempt of Bazett to the more recent ones [2]. To test this hypothesis, a correction factor was applied to spectral findings from HRV analysis in healthy controls studied either during a one-hour study protocol in steady-state controlled conditions, or during free-living 24-hour ECG recordings. The effectiveness in discarding HR influence on HRV was then tested by statistical approach.

2. Methods

RR interval derived from EKG recording in 15 healthy subjects (24 ± 3 years, 13 males), during a 50-minute long quiet supine mute resting has been analysed over consecutive 256-beat long windows by autoregressive spectral analysis (Levinson-Durbin algorithm, model order 12), as described elsewhere [3]. Furthermore, ten 24-hour recordings of ECG by a bipolar lead FM Holter recorder system (Remco Italia, Cardioline, Milan) were collected in healthy volunteers during free-living conditions. The following conventional indexes were computed: RR interval, total power, very low (VLF, 0,003-0.03 Hz) power and frequency, absolute and normalized values of low (LF, 0,03-0.15 Hz) and high frequency (HF, 0,15-0.50 Hz) components, as their central frequency, LF/HF ratio.

Due to the non normal distribution of the data, as observed by Kolmogorov-Smirnov test, logarithmic transformation has been performed before their analysis.

Variance analysis was used to assess the interdependence between RR interval and the other indexes; the correlation among the variables has been assessed by Pearson coefficient computation and 2-tailed significance.

The formula

$$Ln(Power)\,|_{corr} = \frac{Ln(Power)}{Ln(RR)}$$

was applied when a dependence of power values from RR interval was found, and then the former step of analysis has been repeated; the correction by the natural logarithm of RR has been introduced, having singled out a statistically significance of a logarithmic relation between RR and power values. A p value of 0.05 has been accepted as statistically significant. Statistical analysis has been performed by SPSS (software package for Windows, 1995).

3. Short-term recordings

Results of spectral analysis of interval variability in these series are presented in the Table below:

Descriptive Statistics

	N	Minimum	Maximum	Mean		Std.
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
RRMED	15	690.20	1036.70	865.4667	22.6028	87.5401
PTOT	15	316.70	2626.90	1425.04	192.4848	745.4904
VLF	15	0	798	189.39	63.15	244.59
LF	15	162.00	1602.80	809.9533	120.6405	467.2385
HF	15	138.50	1496.90	596.0933	100.4290	388.9597
LF_HF	15	.42	4.74	1.8027	.2880	1.1152
FR_VLF	15	.00	.03	1.1E-02	2.8E-03	1.1E-02
FR_LF	15	.08	.12	9.7E-02	2.9E-03	1.1E-02
FR_HF	15	.22	.32	.2631	7.3E-03	2.8E-02
LNPTOT	15	5.76	7.87	7.1046	.1605	.6215
LN_VLF	15	.00	6.68	3.2157	.7330	2.8390
LN_LF	15	5.09	7.38	6.4970	.1826	.7072
LN_HF	15	4.94	7.31	6.2149	.1585	.6139
Valid N (listwise)	15					

Table 1. Spectral findings.

The logarithmic transformed spectral power indices, after the application of the correction formula are presented in Table 2.

Descriptive Statistics

	N	Minimum	Maximum	Mean		Std.
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
C_LNPTOT	15	.87	1.16	1.0506	2.2E-02	8.4E-02
C_LNVLF	15	.00	.98	.4727	.1074	.4159
C_LNLF	15	.77	1.08	.9607	2.5E-02	9.8E-02
C_LNHF	15	.74	1.06	.9191	2.2E-02	8.4E-02
Valid N (listwise)	15					

Table 2. Corrected power spectral values.

Before the application of the formula a significant linear correlation with Ln(RR) has been found for most spectral indices, as shown in Table 3. The correction was effective in cancelling the influence of RR interval:

	Before Correction	After Correction
Ln(TotP)	R=0.592* p=0.02	R=0.482 p=0.07
Ln(VLF)	R=0.542* p=0.037	R=0.476 p=0.073
Ln(LF)	R=0.537* p=0.039	R=0.400 p=0.14
Ln(HF)	R=0.508 p=0.053	R=0.218 p=0.435
LN(LF/HF)	R=0.298 p=0.281	R=0.248 p=0.306

Table 3. Correlation coefficients and two-tailed significance before and after the correction

4. Long-term recordings

As concerns 24-hour long recordings in free-living healthy volunteers, the results of the application of the correction formula are shown in table below:

	Before Correction	After Correction
Ln(VLF)	R=0.154 p=0.690	R=0.216 p=0.435
LN(LF)	R=0.432 p=0.125	R=0.337 p=0.295
HF	R=0.361 p=0.063	R=0.388 p=0.125
TotP	R=0.387* p=0.043	R=0.448 p=0.098
LF/HF	R=0.412 p=0.079	R=0.278 p=0.329

Table 4. Correlation coefficients and two-tailed significance before and after the correction by ln(RRmed), for 24-hour spectral findings.

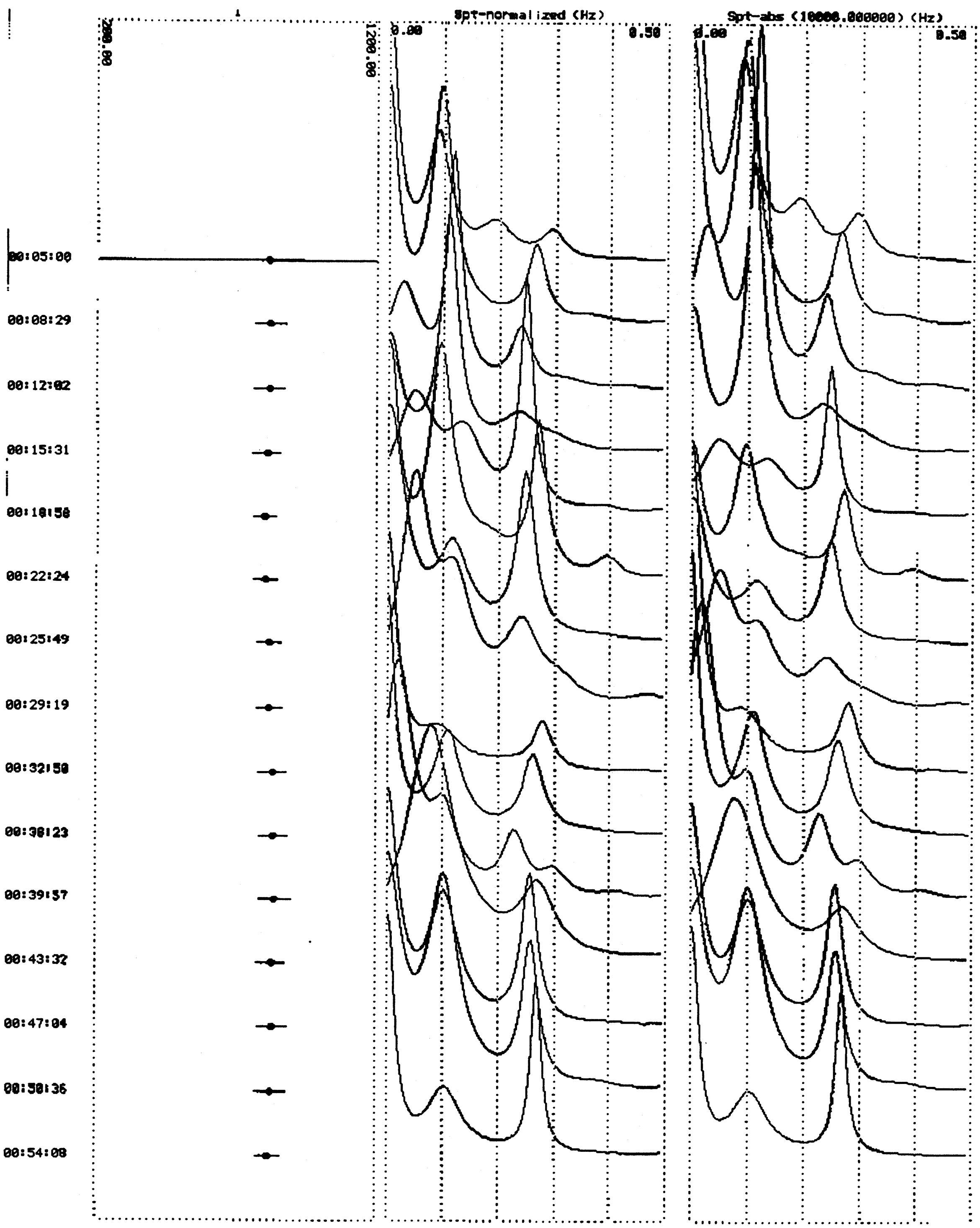

Figure 1: Spectral analysis of RR interval in a protocol subject. Left panel (top to bottom): average± SD value of RR interval referring to 256 beat consecutive RR sequences and corresponding spectra (center: normalized up to the maximum spectral height, right: up to 10000 msec2/Hz - spectral amplitude).

5. Discussion

A mathematical reappraisal has been invoked for the use of HRV findings to criticize some theoretical constraints in the use of spectral indexes [4].

Recently, some authors pointed out the need to consider the influence of fundamental physiological variables on heart rate variability (e.g. respiration) [5], before analysis interpretation in clinical research.

Heart rate "per se" is a powerful independent confounding factor in determing heart rate variability: some spectral indexes (associated with parasympathetic drive to the sinus node and with sympatho/vagal balance) are dependent of heart rate and need to be corrected before analysis and interpretation. A simple effective formula to make spectral indexes independent by heart rate is proposed resulting effective, namely in steady state conditions.

References

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