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ORIGINAL

HEART RATE VARIABILITY AND EXERCISE, IS THERE A PHYSIOLOGICAL BASIS?

VARIABILIDAD DE LA FRECUENCIA CARDIACA Y EJERCICIO. ¿FUNDAMENTACIÓN FISIOLÓGICA?

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ABSTRACT

This work has two objectives: 1) to give a pedagogical view about the complexity of the mathematical treatment of heart rate variability and 2) to analyze whether the mathematical treatment of the RR signal (distance between two R waves shown in an electrocardiogram) has a physiological basis.

We reviewed the physiological mechanisms that explain one of the basic phenomena for the analysis of heart rate variability: respiratory sinus arrhythmia.

The elementary mathematical bases as well as the mathematical methods of assessing the variability are analyzed. Finally, we offer a critical review of the physiological significance of the frequency bands obtained by the various methodologies of the RR signal processing.

It is not clear whether the mathematical methods of RR signal processing can be an assessment tool for vegetative function. Therefore, this variable must be interpreted with caution, especially in the context of physical exercise and training.

KEY WORDS: ECG, Heart Rate, Physical Training, Physical Activity.

RESUMEN

Este trabajo pretende dos objetivos: 1º) dar una visión pedagógica de la complejidad relativa al tratamiento matemático de la variabilidad de la frecuencia cardiaca y 2º) analizar si el tratamiento matemático de la señal RR (distancia entre dos ondas R del electrocardiograma) tiene una base fisiológica.

Se revisan los mecanismos fisiológicos que explican uno de los fenómenos de base para el análisis de la variabilidad: la arritmia sinusal respiratoria. Se analizan las bases matemáticas, así como los métodos matemáticos de valoración, de la variabilidad. Finalmente, se realiza una revisión del significado fisiológico de las bandas de frecuencia obtenidas mediante las diversas metodologías del tratamiento de la señal RR.

No está claro si los métodos matemáticos de tratamiento de la señal RR pueden ser una herramienta de valoración de la función vegetativa. Por ello, debemos tener precaución al interpretar esta variable, sobre todo en el contexto del ejercicio físico y entrenamiento.

PALABRAS CLAVE: ECG, Frecuencia Cardiaca, Entrenamiento Físico, Actividad Física.

INTRODUCTION

Since the first article on heart rate variability (HRV) was published (Malmo et al., 1948), interest in this methodology has seen an exponential increase in terms of the number of articles published (Figure 1). Likewise, in the Pubmed database the first term is HRV among more than 20 terms. Technological advances allow complex mathematical calculations to be made in a few minutes and the teamwork of mathematicians, physicists and physiologists are the reasons for this increase in the publication of articles.

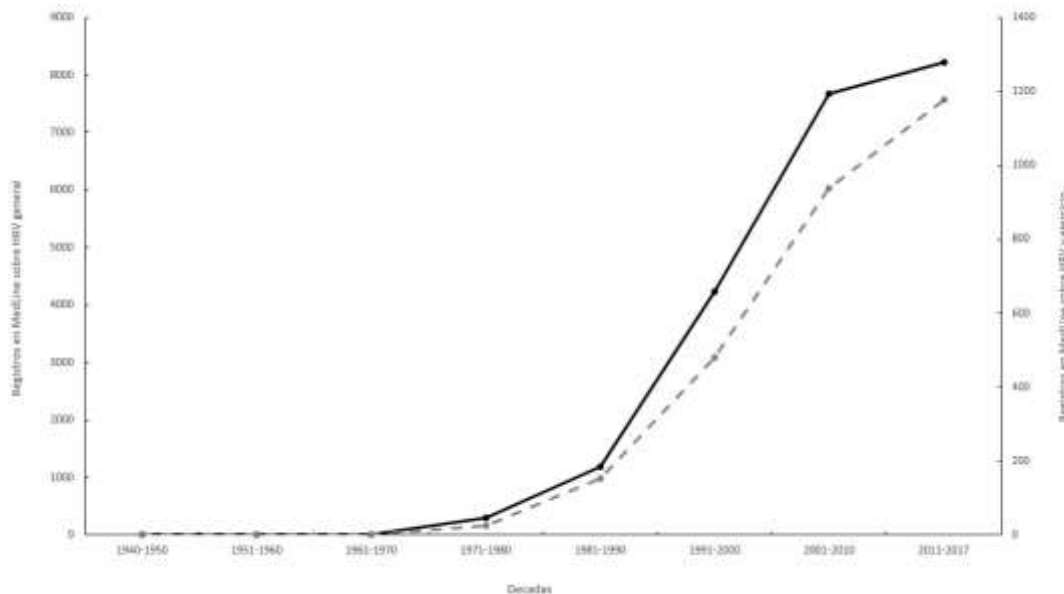


Figure 1. Number of articles published on HRV in general (continuous line) and in relation to exercise (discontinuous line) after searching the PubMed database (own elaboration).

As cardiac activity is a time-function, it can be treated using different calculation methodologies. This periodicity can be explained from a physiological point of view. Thus, the study of the HRV has had several objectives. In general, the interest of the researchers has been to study the vegetative balance from physiological (C. Silva, Pereira, Cardoso, Moore, & Nakamura, 2014; V., C. Silva, Pereira, Cardoso, Moore, & Nakamura, 2014). P. Silva, Oliveira, Silveira, Mello, & Deslandes, 2015) and pathological perspectives.

From a physiological point of view, the interest in the study of HRV has been to use it as a control of fatigue or overtraining due to the modification of the vegetative balance in order to characterize cardiac recovery process (Mourot et al., 2004) and training bradycardia (Borresen & Lambert, 2008; GR Sandercock, Bromley, & Brodie, 2005).

However, this "alliance" of such disparate sciences (mathematics and biology) has not been as positive as it might seem a priori. When an attempt has been made to match the different mathematical index with the vegetative activity on the heart, the prevailing confusion is considerable. It is assumed that the different indexes provided by mathematics correspond to the different vegetative activity (sympathetic and/or parasympathetic). This is naturally a gross error, as a relationship between the different indices proposed and the vegetative activity of the two components of the vegetative nervous system has not been firmly demonstrated (Casadei, Cochrane, Johnson, Conway, & Sleight, 1995).

Therefore, the aim of this review is to attempt to assess the physiological significance of a widely used measurement "tool" (Figure 1) of heart vegetative activity. Given the complexity of the different mathematical methods to assess HRV, this review is mainly focused on the physiological part. However, although the mathematical training to understand the different methods is limited, an attempt will be made to explain them as pedagogically as possible.

MATERIAL AND METHODS

In order to meet the objectives, a bibliographic review has been carried out in which all those scientific articles on the heart rate variability during exercise were included. The bibliographic search was carried out in the Web of Science and PubMed databases, including a range of years from 1940 to 2017. The terms used were "heart rate variability", "HRV", "LF/HF" and "autonomic control of heart rate", in combination with "exercise" and "training".

Five hundred and eighty-six results were found. Of this total, those written in languages other than Spanish, English or German were discarded. Then, by reading the abstract, we selected those papers that dealt with physiological aspects of heart rate variability. Of the 136 selected after the first two steps, all articles that were presentations in congresses or when it was not possible to find complete text were also discarded. This selection process gave a result of 43 research articles, which have been used for the present review.

PHYSIOLOGICAL FUNDAMENTALS OF HEART RATE VARIABILITY

Like many organs, the heart has a double innervation of the vegetative nervous system (SNV). Figure 2 shows this innervation schematically. In addition to the reflex mechanisms that can be established, mainly the baroreflex, the higher nervous centers can influence the heart rate.

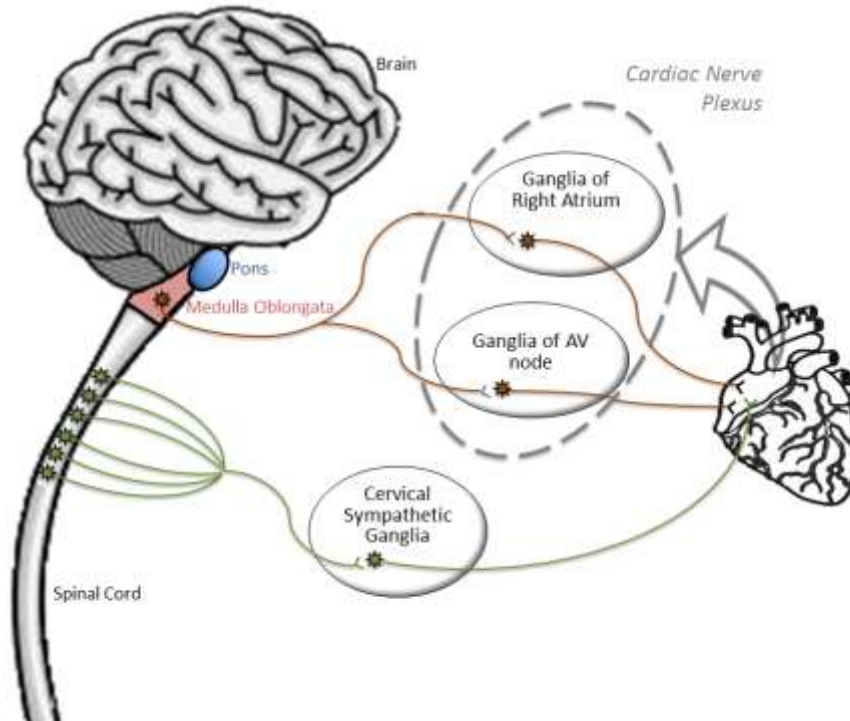


Figure 2. Schematic representation of the vegetative innervation of the heart (own elaboration).

There are three zones of the central nervous system related to vegetative activity on the heart.

- 1) The neurons of the lateral intermediate horn have some spontaneous activity (Billman, 2015).
- 2) The medulla oblongata, responsible for the control of respiration, blood pressure and heart rate (Schramm, 2006).
- 3) The hypothalamus exerts control over the cardiovascular system (Cherniack, Adams, Prabhakar, Haxhiu, & Mitra, 1989) and the cerebral cortex can bring to bear effects on the heart rate (Jindal, Gupta, & Das, 2013; P. Korner, 1971; P. I. Korner, 1971).

All these structures are related vertically and horizontally. Vegetative tonic activity probably originates in multiple locations of the nervous system (longitudinal direction), although it is currently thought that there could be central "pacemakers" that are difficult to locate and are incorrectly referred as the singular central command (Cherniack et al., 1989; Verberne & Owens, 1998). The discharge of these pacemakers is influenced by the activity of the baroreceptors, respiratory mechanisms and local conditions in the CNS.

For the purpose of this review article, vegetative activity of the heart focuses on the heart rate (HR). This is the result of the electrical activity of pacemaker cells

located in the sinoatrial and atrioventricular nodes. This electrical activity is modulated by the nerve endings that reach the two nodes. Therefore, the action of the vegetative system on the HR is performed on both nodes.

The pioneering work of Rosenbluth and Simeone (Turner, 1991) gives an idea of the complexity of the vegetative function of the heart. These authors studied cardiac response on isolated stimulation (sympathetic or parasympathetic) and on the combined action of both. The effects of parasympathetic stimulation are most evident when the sympathetic terminations are stimulated. The mechanism that partly explains this interaction is the tendency of acetylcholine or nucleotides to decrease the amount of noradrenaline released by sympathetic terminations or to interact in the membrane of pacemaker cells (Rosenbluth & Simeone, 1934). At rest, there is a vagal predominance since the decrease in activity with atropine triggers tachycardia, while the decrease in sympathetic activity causes a smaller decrease in heart rate (Boron & Boulpaep, 2012).

On the other hand, the origin of the HRV study was to determine the physiological mechanisms that could explain respiratory sinus arrhythmia (ASR). This represents the variations in heart rhythm due to the effect of respiration and has been studied since the 19th century (Das, 1989). It was observed that the heart rate fluctuates with respiratory movements (Coleridge & Coleridge, 1986; Ludwig, 1847). In other words, the cardiovascular system functions in "synchrony" with the respiratory system. HR increases with inhalation and decreases during exhalation. Nevertheless, the exact relationship between heart rate and the phases of the respiratory cycle depends on respiratory rate and tidal volume (Katona & Jih, 1975) (Jewett, 1964). Six theories have been proposed to explain the development of respiratory sinus arrhythmia (Kunze, 1972):

- 1) respiratory reflexes: Vagal feedback originating in the pulmonary stretching receptors is determinant for neural activation and mediation of ASR at rest. Other respiratory reflex mechanisms, originating in the respiratory musculature, may contribute to cardio-respiratory coordination,
- 2) central mechanism. In mammals, two main mechanisms that generate ASR are accepted: direct cardiac modulation of preganglionic vagal neurons by central respiratory impulses and inhibition of cardiac vagal efferent activity during pulmonary inspiration,
- 3) reflex originating in receptors of the right atrium,
- 4) local mechanism involving the sinus node,
- 5) reflexes originating in the baroreceptors and chemoreceptors. The efferent fibers of vagal origin are most potently excited during exhalation by stimulation of chemoreceptors and arterial baroreceptors.

6) oscillations of PpCO₂ and arterial pH parameters.

All of the above mechanisms are responsible for the ASR. However, the characteristics of respiration affect heart rate control. The amplitude of the ASR is higher at 5-6 breath/min and decreases progressively as the respiratory rate increases. Initial work showed that cervical vagotonia abolished ASR, indirect evidence of its nervous origin and against the hypothesis that it was vegetative modifications of the heart caused by lung expansion. It seems that sympathetic innervation is not essential in the development of arrhythmia, although its contribution is not excluded (Coleridge & Coleridge, 1986; Katona & Jih, 1975). Subsequently, through mathematical analysis of HRV, it is thought that ASR could play an active physiological role. The synchronization of alveolar ventilation and the HR in each respiratory cycle could in some way lead to energy savings by "suppressing" unnecessary beats during exhalation and "avoiding" inefficient ventilation (Katona & Jih, 1975).

METHODS OF ANALYSIS OF HEART RATE VARIABILITY

The time between two R waves, even at rest, is not always the same. Thus, the variability of the heart rate consists of the "variation" experienced by the time duration of two or more heartbeats. The problem arises when one tries to analyze mathematically how the interval between two R waves varies over a certain period.

Elementary Mathematics and HRV

Figure 3 shows complete data of a 120 min task carried out in our laboratory (Laboratory of Exercise Physiology, Technical University of Madrid) with ECG (Jaeger Oxycon Pro, Erich Jaeger, Viasys Healthcare, Germany). In order to better illustrate the RR intervals, figure 4 shows partial data of a 1.5 minutes period.

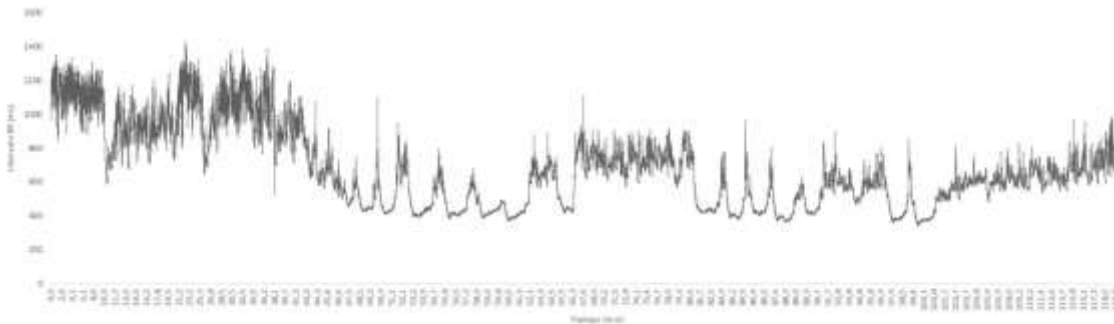


Figure 3. Data from a 120-minute heart rate register

Two observations can be made: 1) the RR intervals "vary" over time; and 2) the RR/time function can resemble a sine function.

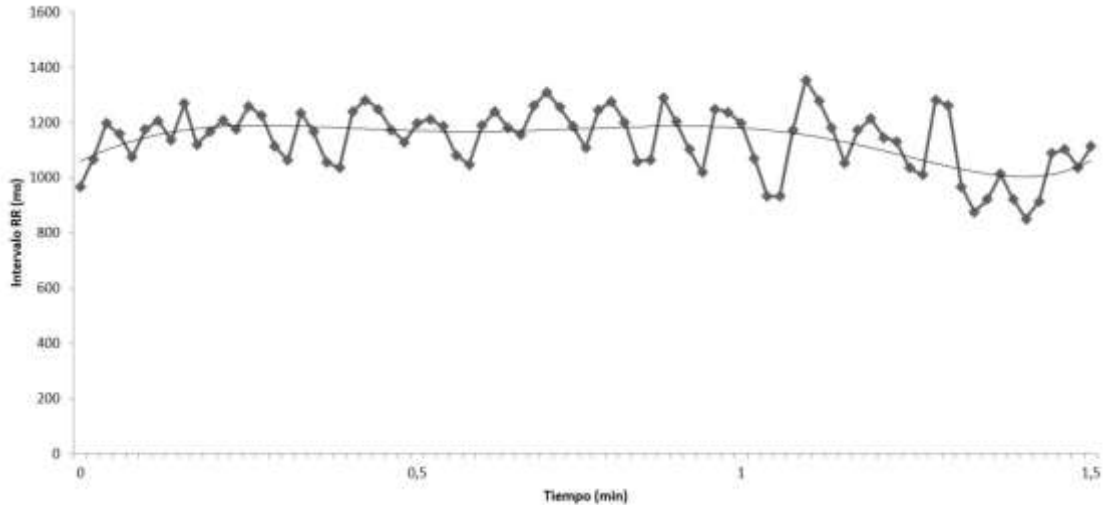


Figure 4. Data from a 1.5-minute heart rate recording (own elaboration).

From the 1.5-minute log, data is obtained only for the 30 seconds from minute 1 to 1.5 (Figure 5). In this instance, the RR intervals are even more like a sine function (better polynomial setting with excel program). This function ($RR = f(t)$) sine can also be set to a cosine function.

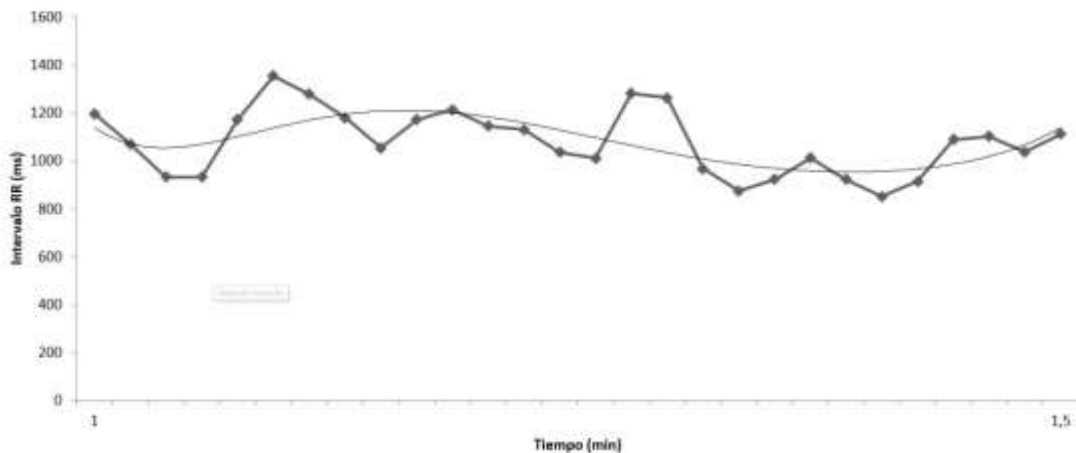


Figure 5. Data from a heart rate record for 30 seconds (from minute 1 to minute 1.5) (own elaboration).

In short, there is no single adjustment function. Therefore, one should "search" for the functions that best fit, usually a combination of both (sines and cosines). Finally, it is crucial to point out the difficulties that can be encountered when analyzing a certain RR function. If during recording (figure 5), some data was lost, signal reconstruction becomes more difficult. The frequency with which data must be obtained in order to guarantee reconstruction of the signal is called the Nyquist frequency and must be at least twice the highest frequency represented by the signal.

The next step in the HRV analysis is to know the values corresponding to the frequencies. This is achieved thanks to Fourier's theorem, which states that any function can be broken down into the mathematical product of two or more functions ($f(x) = \sin x$ and $f(x) = \cos x$) that represent all data. The product of the functions that determine the RR function is power (PSD = ms^2), which is fundamental in understanding the information provided by the HRV analysis! The amplitudes of the different sine and cosine functions are known as Fourier coefficients. The calculation of Fourier coefficients is very laborious, but the capacity of computers has allowed the development of different tools such as the Integral Fourier Transform, Fast Fourier Transform or the Discrete Fourier Transform. The advantage of these procedures is that the form of the function can be reconstructed from the frequency coefficients.

HRV Mathematical Valuation Methods

The different mathematical procedures are based on considering whether the function $RR = f(t)$ follows a linear or random behavior. However, since the RR signal is normally recorded for a finite duration (in the example of Figure, 3 it is 120 minutes), there is no relationship between the signal obtained and the mathematical result of its processing (Fast Fourier Transform or Discrete Fourier Transform). Thus, mathematicians look for a solution consisting of forming a new succession of values, but of finite duration. This procedure is called "windowing" because it allows the sequence $RR = f(t)$ to be observed partially. However, the disadvantage of the method is that there is no "suitable window" in general but it depends on each individual series! Table 1 shows the main methods applied to the valuation of the HRV.

Most HRV studies are based on signal processing from linear methodologies (stationary signals), such as time-domain-based methods (statistical methods and geometric methods) and frequency-domain methodologies (Fourier transforms). Whether the body is at rest or subjected to exercise stress, the temporal behavior of the HRV does not adjust to a stationary signal. Therefore, mathematical treatment with non-linear methodologies is necessary (Table 1).

Table 1. Summary of the main mathematical methods of spectral analysis of the RR intervals

<p>Linear methods</p> <ol style="list-style-type: none"> 1. In the domain of time <ol style="list-style-type: none"> a. Statistics b. Geometrical 2. In the frequency domain: Fast Fourier Transform (FFT) and Auto Regressive Model (AR)
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3. In the time-scale domain: transformed Wavelets.

Non-linear methods

1. Correlation function

2. Return maps

3. Reconstruction of the phase space

- Poincaré diagram: SD1 (Transverse axis): Represents the standard deviation of the instantaneous variation RR intervals. It is seen as the smallest diameter of the ellipse. It indicates the functional randomness of the system and measures the parasympathetic influence on the system.
- SD2 (Longitudinal axis or line of identity): Represents the standard deviation of the continuous variation of the RR intervals. It is seen as the largest diameter of the ellipse. It indicates the global dispersion of the values of the series.
- SD1n: Obtained by dividing the value of SD1 by the mean of the RR intervals and multiplying the result by 1000. Represents a measurement of vagal activity.

Other methods: bio-spectrum and chaos diagnosis

The most intuitive and simple thing in any RR data series is to calculate statistical data, such as mean and standard deviation. The data for Figures 3, 4 and 5 indicate considerable variation in RR values: 679 ± 273 (Figure 3), 1140 ± 112 (Figure 4) and 1089 ± 137 (Figure 5). As experts in this field point out, the signal is not stationary because both the mean and the deviation are not constant. The Task Force (Taylor et al., 2014) has made a series of recommendations to evaluate HRV at rest in long series (24 hours)! (Table 2)

Tabla 2. Statistical and geometric Methods for HRV assessment

Statistical Methods	
Variable	Definition
SDNN (ms)	Standard deviation of RR intervals
SDANN (ms)	Standard deviation of the average values RR intervals 5 minutes registered

RMSSD (ms)	Square root of the mean of the sum of the squares of the differences between the values of each RR and the adjacent one
SDNN index (ms)	Mean of the standard deviations of the RR intervals for all recorded 5-minute segments
SDSD (ms)	Standard deviation of differences between adjacent RR values
NN50 count	Number of pairs of adjacent RR intervals greater than 50 ms in the whole record performed. Three possible variations can be made: 1) count all the RR pairs, 2) count only the pairs in which the first of these is longer and 3) count only the pairs in which the second of these is longer.
pNN50	Number of pairs of adjacent RR intervals greater than 50 ms record set performed divided by total number of RR intervals
Geometric Methods	
Triangular index	Integral density distribution (number of all RR intervals) divided by maximum density distribution
Triangular interpolation of the RR interval histogram	Baseline width of the distribution measured as the base of a triangle approximating the distribution of the RR intervals (the smallest difference squared is used to find the triangle)
Correlations between statistical and geometric methods	
<ul style="list-style-type: none"> - SDNN, triangular HRV index, TNN with total Power - RMSSD, SDSD, NN50 and pNN50, differential index with HF - SDANN correlates with ULF 	

The RR signal is interpreted as a non-autonomous rhythm resulting from the coupling of an autonomous internal rhythm originating in the heart muscle itself and regulated by the vegetative system and one or more external disturbances. These are periodic, as in other biological systems (circadian rhythms, breathing, etc.) and cause different types of phenomena (coupling of the system and the disturbance, quasi-periodicity, chaos, etc.). One of the problems with analyzing biological signals is the "noise". These are certain patterns associated with complex behaviors that are detected by analyzing frequency spectra. An example is when the power is proportional to the inverse of the frequency, $1/f$, which is relatively common in biology.

The frequency bands

The frequency bands have been related to the components of vegetative function and other physiological functions (see relationship between mathematical indices of the HRV assessment and vegetative balance). Regardless of the method used

in the frequency or time-scale domains, the following frequency bands (ms²) are usually described:

- 1) ULF (ultra low frequency), which describes the power in a range lower than 0.003 Hz. Cycle length >5 hours.
- 2) VLF (very low frequency), which describes the power in a range lower than 0.4 Hz. Cycle length > 25 s.
- 3) LF (low frequency), which describes the power in a frequency range of 0.04-0.15 Hz. Cycle length > 6 s.
- 4) HF (high frequency), which describes the power in the frequency range of 0.15-0.4 Hz. Cycle length 2.5 to 6.0 s.
- 5) VHF (very high frequency), which describes the power in the range 0.40-1.00 Hz.
- 6) TP (total potency) describing the RR intervals during the period. Approximate frequency range < 0.4 Hz (0.00066-0.34 Hz).

Likewise, it is common to normalize and determine the relative values with respect to the total power of each of the bands: normalized LF and HF (relative value of each power component with respect to the total power minus the VLF component) and the relationships $LF_{normalized}/(TP-VLF)100$, $HF_{normalized}/(TP-VLF)100$ and LF/HF. Normalized units tend to minimize the effects of changes in total power corresponding to the values of the LH and HF components. However, the standard units should always be quoted together with the absolute values of LH and HF in order for the power distribution in all spectral components (Hz) to be fully described.

RELATIONSHIP BETWEEN HRV ASSESSMENT METHODS AND VEGETATIVE FUNCTION

Methodological problems regarding the interpretation of the HRV signal

For the valuation of the HRV at rest, there is an agreement on the minimum methodological conditions that must be met when making a short (3 to 5 minutes) or long (24 hours) recording, the latter carried out using Holter.

1. Experimental models for the study of the HRV/physiological functions relationship. Preparations of perfused isolated hearts have been widely used to study changes in heart function without the influence of external factors, such as the action of the central nervous system, circulating hormones or nervous reflexes. In animals and humans it is possible to

proceed to the contribution of diverse pharmacological agents that simulate external factors allowing the researcher to control, manipulate and evaluate the effects on cardiac activity.

2. Experimental control of the animal or human being. At rest, the spectral response of the HRV is limited to 0.5 Hz and can be decomposed for analysis. The person should preferably be lying supine and, failing that, seated and in as much rest as possible. It is not recommended to take measurements with the subject standing up. This is due to hemodynamic adjustments that occur with changes in position. Recommendations are different if the objective of the study is to analyze the changes in the frequency spectrum due to posture changes.
3. Breathing control: effects of breathing on HRV. The influence of respiration on HRV is considerable, as previously noted by several authors (Cardiology, 1996; Francois Cottin, Durbin, & Papelier, 2004). Differences have been found in the power of the heart rate spectrum when breathing at different frequencies (0.15, 0.20, 0.30, 0.40 and 0.50 Hz). As the respiratory rate increases, the HF component of the spectrum decreases and the LF/HF ratio increases. Exhalation causes an increase in HRV and a greater vagal manifestation. It is therefore recommended that the respiratory rate ranges from 0.15 to 0.25 Hz or from 12 to 14 resp/min.
4. Measurement protocol. Correct evaluation of the RR signal requires a series of not less than 10 times the wavelength of LF (6 to 25 seconds), with the objective of a stable signal. Thus, although it is established as a standard measurement of short duration for up to 5 min (1025 points), the recording should have duration of no less than 2 min in order to ensure stationary series that adequately describe each frequency spectrum. Therefore, the recordings presented in Figures 4 and 5 are incorrect, but are used to simplify the presentation of HRV analysis. On the other hand, using statistical methods during exercise or post-exercise invalidates the results.
5. Other factors: age, sex, environmental conditions (temperature, humidity, altitude), blood volume, level of physical condition and heredity. It seems demonstrated that a predominance of the sympathetic nervous system is observed in neonates, but it is questionable whether this mechanism is maintained throughout age. In general, with age parasympathetic activity decreases, decreasing the variability of RR intervals (F Cottin, Papelier, & Escourrou, 1999; C.-D. Kuo et al., 1999; Tanaka et al., 2000). On the other hand, a vagal predominance has been suggested in males with respect to females in the same age group (T. B. Kuo et al., 1999), while Umetani et al. did not observe differences in HRV in females of 30 years with respect to males of the same age (Evans et al., 2001). Higher HF and lower LF values (Umetani, Singer, McCraty, & Atkinson, 1998) reveal bradycardia. Likewise, cardiorespiratory condition is associated with the genetic load that can affect

the RR signal (Achten & Jeukendrup, 2003; Singh, Larson, O'Donnell, & Levy, 2001; Singh et al., 2002; Singh et al., 1999).

6. Individual reproducibility of the HRV signal. (1999) (39) found correlation coefficients (r^2) between 0.86-0.90 for temporal analyses and 0.67-0.96 for spectral analyses on two occasions spaced one week apart. For spectral analyses separated by two months the correlation coefficients ranged from 0.76-0.80 (40).

Relationship between frequency bands and physiology

Few studies have attempted to simultaneously "measure" vegetative activity and HRV (Hughson, Sutton, Fitzgerald, & Jones, 1977; Pagani et al., 1986; Tsuji et al., 1996). Thus, protocols that attempt to explain the results of HRV without having measured vegetative activity are questionable. The objectives of the study of the relationship between HRV and exercise have been:

1. Study of resting HRV (training effect) and possible modifications during a training period, which could indicate a correct or incorrect (over-training) process of adaptation by the body. The modification of the Poincare diagram has been proposed because of a cardiac fatigue process.
2. Study of the exercise HRV to try to explain cardio-respiratory adjustments to exercise of different characteristics: incremental, stable, intermittent, dynamic versus static, etc.

Table 3 shows the data of some authors who have investigated HRV. In general, it has been established that:

- HF frequency spectrum is related to vagal activity and breathing pattern. In addition, it has been related to sympathetic modulation of peripheral vascular resistances.
- Initially, the LF frequency spectrum was related to sympathetic activity, as changes in the power of this spectrum were produced by the renin-angiotensin-aldosterone system and other factors at the local level. These physiological phenomena were evidenced by changes in blood volume due to changes in posture. Subsequently, the LF spectrum has been linked to both sympathetic and parasympathetic activity. In addition, a relationship between thermoregulation and amplitude of the LF power has been established.
- In addition to the LF spectrum, the VLF spectrum has also been related to: renin-angiotensin-aldosterone system, thermoregulation, blood volume, vasomotor tone and both sympathetic and parasympathetic activity.

- ULF spectrum has been related to some circadian rhythms such as temperature.
- LF/HF relationship has been related to vegetative balance, parasympathetic activity, thermoregulation and changes in blood volume due to posture. It has been estimated that the quotient should be between 1.5 and 2.0 or its percentage equivalent (15-200%) during a five-minute supine recording. Values above this range would indicate a greater sympathetic predominance and values below would reflect a greater parasympathetic predominance. At rest and in a healthy subject, a high value of this index is an indicator of risk, suggesting that a significant decrease in HF could indicate a vagal alteration.

Table 3. Studies that have addressed the relationship between frequency bands resulting from HRV analysis and physiological mechanisms.

Autor	Bandas de frecuencia descritas	Relación fisiológica establecida
Sayers (1973)	- Low frequency (<0,05 Hz) - Medium frequency (0,06 a 0,10 Hz) - High frequency (>0,15 Hz)	- Thermoregulation - Baroreflex control - Breathing pattern
Chess y col. (1975)	- High frequency	- Parasympathetic activity
Akselrod y col. (1985)	- High frequency (> 0,15 Hz) - Low and medium frequency (0,05 a 0,10)	- Parasympathetic activity - Sympathetic activity and renin-angiotensin system
Huang y col. (1997)	- High frequency (HF: 0,15 a 0,5 Hz), - Medium frequency (MF: 0,08 a 0,15 Hz) - Low frequency (LF: 0,02 a 0,08 Hz).	
Hedellin y col. (2001)	- ultra-low frequency - Low frequency	- Parasympathetic activity - Sympathetic modulation of peripheral vascular resistances.
Serrador y col. (1999)	- ultra-low frequency	- Circadian heart rate rhythm and hypothalamic control
Bonaduce y col. (1998)	- Increased spectral activity and VLF	- Renin-angiotensin system (angiotensin converting enzyme inhibition); changes in blood volume and baroreflex
Spinelli y col. (1999)	- Increased spectral activity - Very low frequency	- changes in blood volume and baroreflex - Sistema parasimpático
Taylor y col. (1998)	- Potencia espectral - VLF	- Parasympathetic system - Parasympathetic-sympathetic system
Bianchi y col. (1991)	- VLF	- Circadian rhythms (sleep/wakefulness)

Houle y Billman (1999)	- LF	- Parasympathetic-sympathetic system
Arai y col. (1989)	- LF	- Baroreflex, thermoregulation and cardiovascular adjustment to different situations
Tulppo y col. (2003)	- Changes LF/HF	- Vegetative balance
Iellamo y col. (2002)	- Changes LF/HF	- Vegetative balance
(Pomerantz y col., 1985); (Hayano y col., 1996)	- HF	- Breathing pattern, vagal tone
Hedelin y col. (2000)	- HF	- Vegetative balance sobre corazón and peripheral vascular resistances
Pichot y col., 2000); Pagani y col. (1986).	- LF/HF	- Vegetative balance
Jensen-Urstad (1997)	- LF/HF	- Sympathetic activity
Mateo y col. (2001)	- VLF	- Sympathetic activity and ischemia

The information above shows that the relationship between HRV parameters and physiological mechanisms is unclear. It seems to be accepted that HF reflects vagal activity, while the LF component is more controversial. It is unknown whether it is the result of sympathetic activity alone or of the two SNV divisions. Therefore, the LF/HF ratio does not demonstrate a specific vegetative activity as opposed to what some researchers point out (Piccirillo et al., 2009). Finally, the physiological role of the other two components of the spectrum (ULF and VLF), which sometimes make up more than 90% of the total power of the spectrum, is unknown. It is therefore problematic to explain the HRV mechanism in relation to the two conditions mentioned above: rest and exercise.

1. Study of the HRV at rest. At rest, highly trained endurance athletes should show a high value in the HF spectrum, a not very pronounced decrease in the LH component and the LF/HF ratio. This behavior should be indicative of predominance of the parasympathetic SNV justifying bradycardia. However, the spectrum power values indicated have not been firmly demonstrated (Pagani et al., 1986; GRH Sandercock & Brodie, 2006). Among other reasons is the "physiological" interpretation of the signal and probably due to individual differences (GR Sandercock et al., 2005). Furthermore, the influence of intrinsic and extrinsic "modulators" of vegetative activity is not taken into account:

- a) Intrinsic modulation. As Rosenbluth pointed out almost a century ago (Goldberger, Challapalli, Tung, Parker, & Kadish, 2001), the interrelationship between the two SNV divisions is very remarkable. Thus, in any situation, both divisions (sympathetic and/or parasympathetic) act constantly. The parasympathetic nerve endings at the sinus node level are rich in acetylcholinesterase causing the effect of any "vagal pulse" to be relatively brief because acetylcholine is hydrolyzed. However, at rest, the influence of the vagus probably prevails by a reduction of noradrenaline released by the sympathetic terminations and a decrease in cholinergic activity to the adrenergic stimulus.
 - b) Extrinsic modulation. The upper nerve centers and reflex mechanisms intervene in cardio-respiratory control. It seems that these mechanisms could function in an oscillatory form in short or long periods generating neuronal discharge rhythms, which further complicates the inferences that can be extracted from the HRV analysis.
2. Study of the HRV during exercise. The relationship between HRV analysis methods and physiological mechanisms during exercise generates more confusion. For example, as FC increases, the HF band should lose magnitude in total power. However, some authors have shown an HF increase in the maximum effort limits attributed to the exaggerated increase in respiratory activity that would exert a "mechanical" effect on the heart (Rosenbluth & Simeone, 1934). Therefore, HF should decrease and increase the proportion of total spectral power of the LF component, with the consequent increase in the LF/HF ratio. This has not been conclusively demonstrated (Sarmiento Montesdeoca et al., 2009).

The "physiological" difficulty of HRV interpretation suggests that more concrete parameters of the frequency spectra are proposed. The mechanism of biological variables is subject to chaos theory (Lombardi, 2000; GRH Sandercock & Brodie, 2006). For this reason, methods adapted to this type of mechanisms have been used. The use of inappropriate methods, such as statistics, to assess HRV during exercise is a considerable error (Hagerman, Berglund, Lorin, Nowak, & Sylvén, 1996). Despite the efforts of the researchers, the results are inconclusive and it is not possible to establish a relationship between the different frequency bands and to provide a single coherent physiological explanation (Casadei et al., 1995).

In summary, it is still too early to establish that the different mathematical methods of RR signal processing can be a tool for assessing and diagnosing vegetative function in the clinical setting (Casadei et al., 1995). The complexity of HRV analyses is due to the following reasons: 1) the anatomical-functional complexity of the vegetative activity of the heart, preferably on the sinus and atrioventricular nodes, 2) the activity of the central mechanisms and reflexes that can regulate the vegetative

activity on the heart, 3) the effects that acetylcholine and catecholamines can have on the level of the sinus and atrioventricular node and 4) because the treatment of signals requires a mastery of the different analysis techniques, which can be mediated by a good relationship between mathematics and physiology. Nevertheless, if we are still far from assuming the study of HRV in the clinical setting, the problem increases when different methodologies are applied to cardiac response and adaptation to exercise and training.

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